CHAPTER 1

RING-EXPANDING CARBONYLATION OF EPOXIDES

JOHN W. KRAMER, JOHN M. ROWLEY, AND GEOFFREY W. COATES

Department of Chemistry and Chemical Biology, Baker Laboratory, Cornell University, Ithaca, NY 14853-1301

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coates@cornell.edu

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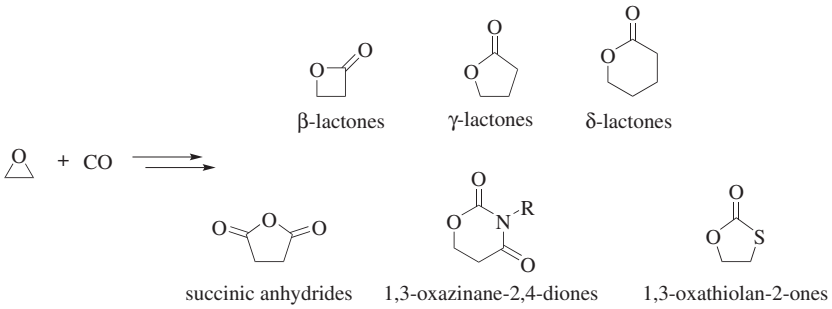
INTRODUCTION

Epoxide carbonylation represents a powerful synthetic method for the production of ring-expanded heterocycles in an atom-economical manner. Reactions involving the incorporation of carbon monoxide, particularly in the formation of new carbonyl-containing compounds, are among the most important industrial and synthetic transformations.[1−4] The carbonylation of epoxides has received much interest in recent years and has been reviewed.[5−10]

Epoxides are particularly attractive substrates, as there are many commercially available epoxides and a variety of practical methods for their synthesis.[11] Furthermore, a number of excellent methods for producing enantiopure epoxides exist,[12−16] and this enantiopurity is retained in the carbonylation products.

This chapter focuses on the ring-expanding carbonylation of epoxides, defined as reactions in which both an epoxide and CO are incorporated into a larger heterocyclic ring. The ring-expanding carbonylation of epoxides has received the most attention for its application to the synthesis of strained β-lactones.[17−41] However, a number of five- and six-membered heterocycles are also accessible through epoxide carbonylation, including γ-lactones,[28,42−45] δ-lactones,[24,40,46−53] succinic anhydrides,[21,54] 1,3-oxazinane-2,4-diones,[22,25] and 1,3-oxathiolan-2-ones[55,56] (Scheme 1). In this chapter, each of these product classes will be discussed separately, focusing primarily on the scope and limitations of the carbonylations, but also on the reaction mechanism and non-carbonylative routes to similar products.



Scheme 1

Although these reactions are thermodynamically favored, they are kinetically inaccessible, requiring the addition of catalytic or stoichiometric amounts of reagents to sequester and insert CO into the epoxide ring. Thus, the development of transition-metal catalysts for epoxide carbonylation has enabled much of the research in this field and has led to the discovery of new epoxide carbonylation reactions.

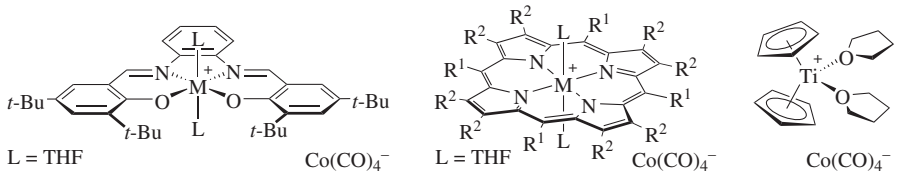
Epoxide carbonylation has also been employed for the production of ring-opened β-hydroxy esters,[57−59] amides,[60] and aldehydes,[61] as well as the direct copolymerization of epoxides and CO to produce poly(β-hydroxyalkanoates);[31,62,63] these topics are outside the scope of this chapter, but have been previously reviewed.[5,6,8] Likewise, other heterocycles including aziridines,[64,65] azetidines,[66] β-lactones,[54] oxetanes,[54,67] tetrahydrofuran,[68] and oxazolines[69,70] have been carbonylated. These reactions were recently reviewed[5,7−10] and are not discussed within this chapter.

EPOXIDE CARBONYLATION TO β-LACTONES

β-Lactones have found numerous applications both as synthetic intermediates[71,72] and as monomers for the ring-opening polymerization to produce poly(β-hydroxyalkanoates),[73] a class of biodegradable and biocompatible polyesters.[74,75] Furthermore, these strained heterocycles are common in a number of biologically active natural products,[76] in which the β-lactone moiety is necessary for bioactivity. One of these important natural product classes includes tetrahydrolipstatin and valilactone which, along with other related natural products, have shown potent activity as lipase inhibitors.[77]

Despite the well-established significance of β-lactones in synthetic chemistry, only a few methods for their synthesis have been developed.[72,76,78,79] Traditional methods are still used, but recently the ring-expanding carbonylation of epoxides to β-lactones has received a good deal of attention.[5] Within epoxide carbonylation, two distinct classes of reactions exist, which are treated separately in this section. The first utilizes bimetallic catalysts comprised of a Lewis acid and a metal carbonyl anion, typically $[Co(CO)_4]^-$. These catalyst systems can either be formed in situ[31−33,36,37] or prepared as discrete complexes.[21,26−30,34,35] In particular, the well-defined, bimetallic complexes shown in Fig. 1 are highly active and selective catalysts for the carbonylation of a broad range of epoxides to β-lactones. However, these catalysts are ineffective for carbonylation of alkenyl epoxides.

The second class of epoxide carbonylations, which are specific for alkenyl-substituted epoxides, relies on neutral metal complexes of palladium and iron and operates through a different mechanism than the Lewis acid derived catalysts. Thus



salphAl; M = Al
salphCr; M = Cr

TPPAl; M = Al, R^1 = 4-ClC_6H_4, R^2 = H
TPPCr; M = Cr, R^1 = Ph, R^2 = H
OEPCr; M = Cr, R^1 = H, R^2 = Et

Cp_2Ti

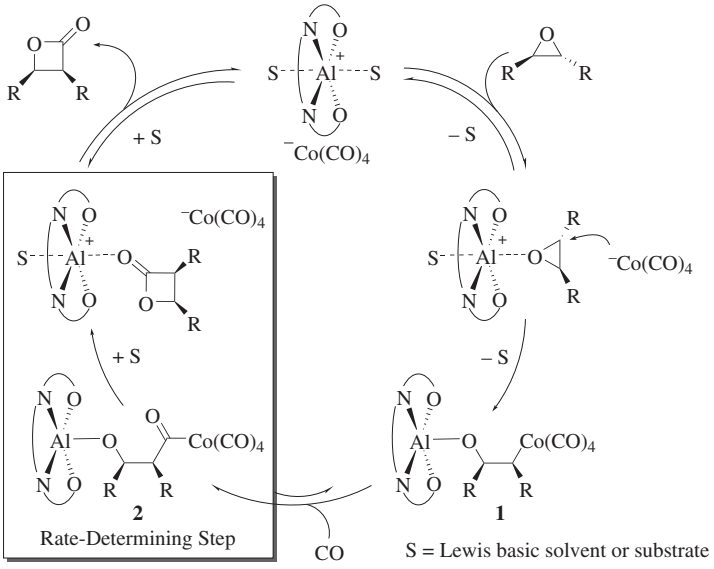
Figure 1. Well-defined, [Lewis acid]$^+$[$Co(CO)_4$]$^-$ Catalysts that are highly active for epoxide carbonylation to form β-lactones.

two complementary sets of substrates and metal reagents are available for epoxide carbonylation to β-lactones.

MECHANISM AND STEREOCHEMISTRY

[Lewis Acid]$^+$[Co(CO)$_4$]$^-$ Catalysts

The mechanism of epoxide ring-expanding carbonylation to β-lactones has been the subject of a number of studies employing a variety of methods and catalytic systems.[21,25,32,33,80] Though each [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalyst system has its nuances, the general mechanism remains the same (Scheme 2). First, the Lewis acid coordinates an epoxide, activating it for ring-opening nucleophilic attack by [Co(CO)$_4$]$^-$ at the less hindered carbon of the epoxide. This attack occurs in an S_N2 fashion, with complete inversion of the stereocenter. The resulting cobalt alkyl species **1** undergoes migratory insertion into a bound CO, followed by coordination of another CO to the cobalt to give intermediate **2**. Nucleophilic attack of the metal alkoxide onto the cobalt acyl group of intermediate **2** closes the β-lactone ring and releases catalyst to complete the cycle.



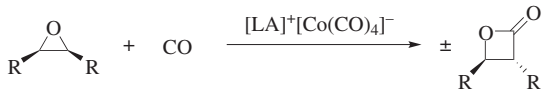
Scheme 2

Detailed experimental investigations have been carried out on three specific catalysts, which all feature a cationic aluminum atom as the Lewis acid.[21,25,33] In the presence of an epoxide and CO, these catalysts react rapidly to form intermediate **2**, the resting state of the catalytic cycle. Ring closing of intermediate **2** is the rate-determining step for production of the β-lactone (Scheme 2). Formation of this resting state complex and its subsequent reactivity are crucial in determining both catalyst

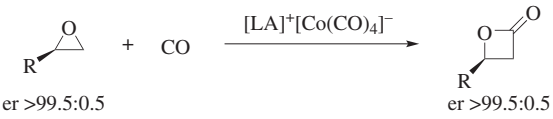
activity[21,25] and product selectivity.[21,22] The Lewis acidity of the catalyst component determines the relative lability of the metal alkoxide bond, and thereby the ease of ring closing; thus, selection of the Lewis acid component is crucial for efficient catalysis. In addition, the Lewis acidity may be modulated by solvent coordination that weakens the metal alkoxide bond and stabilizes the Lewis acidic cation, thus accelerating the rate of ring closing. The importance of solvent coordination has been demonstrated by kinetic experiments which show that for salphAl and TPPAl (Fig. 1), the reaction displays a first-order dependence on the concentration of a donor solvent such as THF: rate = k[epoxide]^0[CO]^0[catalyst]^1[THF]^1. The practical implication of these studies is that using THF as the reaction solvent greatly accelerates the carbonylation of epoxides to β-lactones using salphAl[25] and TPPAl.[21,81]

The general mechanism in Scheme 2 is believed to hold for all [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts; however, some catalysts display slightly different reactivity. In particular, the rate of carbonylation with salphCr slows in THF solvent. In this case, THF may be too strongly donating, coordinating to the chromium center in competition with the epoxide.[19]

The S_N2-type ring opening of an epoxide by [Co(CO)$_4$]$^-$ results in complete inversion of the stereocenter adjacent to the inserted carbonyl. Thus, *trans*-disubstituted epoxides are carbonylated to form *cis*-lactones (Scheme 2), and *cis*-disubstituted epoxides are carbonylated to form *trans*-lactones (Scheme 3).[26,28–30,34,36] Ring opening of monosubstituted epoxides occurs with excellent site selectivity, with attack occurring at the unsubstituted carbon. Because the more hindered stereocenter retains its configuration, monosubstituted epoxides are carbonylated to the corresponding β-lactones with excellent conservation of enantiomeric purity (Scheme 4).[18,34,35]



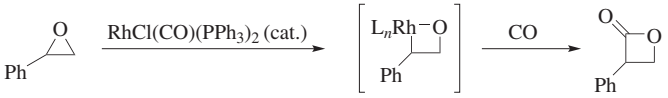
Scheme 3



Scheme 4

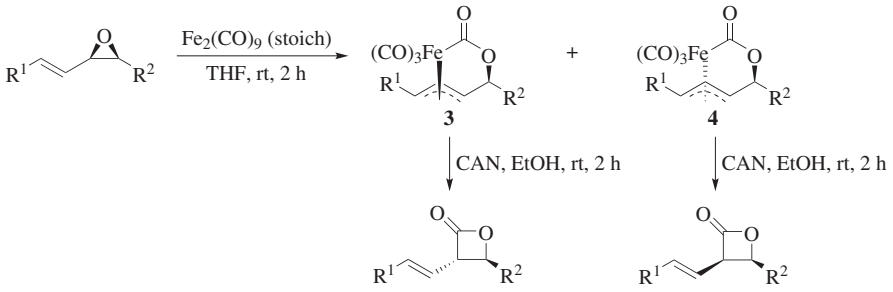
Rhodium, Iron, and Palladium Catalysts

A few examples of ring-expanding carbonylation of epoxides to β-lactones are mediated by rhodium,[41] iron,[39,40,51] and palladium.[38] These reactions likely proceed by an alternative mechanism, as only epoxides with adjacent alkenyl or aryl groups are reactive. In the case of rhodium-catalyzed carbonylation, styrene oxide is the only substrate that forms significant amounts of the β-lactone, and CO is inserted adjacent to the aromatic ring (Scheme 5). Possible pathways have been proposed, but the mechanism of this catalytic transformation remains unknown.[41]



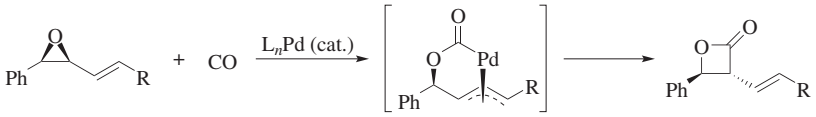
Scheme 5

The mechanism of the stoichiometric, iron-mediated carbonylation of alkenyl epoxides has been established for the formation of δ-lactones,[40,51] and an analogous mechanism is presumed for β-lactones. First, $Fe(CO)_4$, which is formed in situ from either $Fe(CO)_5$ or $Fe_2(CO)_9$, reacts with an alkenyl epoxide to form an isolable π-allyltricarbonyliron lactone complex as a 4:1 mixture of *exo*-isomer **3** and *endo*-isomer **4** (Scheme 6).[39] In both isomers the iron has site selectively inserted into the carbon–oxygen bond of the epoxide adjacent to the alkene, thus forming an allyl complex. Separation of the *exo*-isomer **3** followed by oxidation gives the β-lactone in moderate yield as a single *trans*-diastereomer (Scheme 6), which represents a net inversion of configuration from the *cis*-epoxide. Oxidation of the *endo* π-allyltricarbonyliron complex **4** affords the *cis*-lactone.[39,40,51]



Scheme 6

The palladium-catalyzed ring-expanding carbonylation of epoxides is proposed to occur via a mechanism similar to that of reactions that employ a stoichiometric amount of iron. Epoxides bearing both aryl and alkenyl substituents are opened with inversion of configuration at the carbon adjacent to the alkene, thus forming an allyl–Pd complex that undergoes insertion of CO. The intermediate metallolactone is not isolated and undergoes reductive elimination to form the β-lactone and regenerate the catalyst (Scheme 7). However, it remains unexplained why only phenyl-substituted epoxides are effective substrates for β-lactone formation, and why palladium and rhodium exhibit different site selectivities.[38]

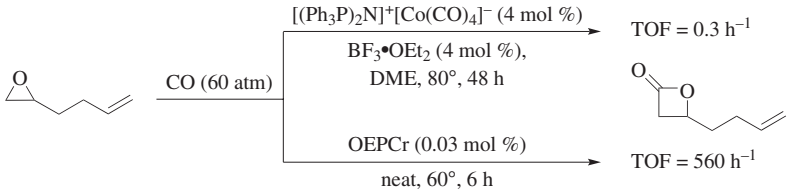


Scheme 7

SCOPE AND LIMITATIONS

[Lewis Acid]$^+$[Co(CO)$_4$]$^-$ Catalysis

Catalysts. Active catalysts for the carbonylation of epoxides to β-lactones contain both a Lewis acidic component and a nucleophilic metal carbonyl. To date, all of these catalyst systems have utilized [Co(CO)$_4$]$^-$ as the metal carbonyl either as a discrete complex or generated in situ.[5] On the other hand, a diverse family of Lewis acids have been employed that have shown similar scope but significantly different reaction rates. These Lewis acids can be either neutral or cationic. In general, in situ generated catalysts using Lewis acids, such as BF_3•OEt_2,[36] $B(C_6F_5)_3$,[36] or $AlMe_3$[32,33] in combination with cobalt tetracarbonyl salts, show relatively low activity (Scheme 8). The activity of these catalyst systems is in contrast to the well-defined [Lewis acid]$^+$[Co(CO)$_4$]$^-$ complexes, which display high turnover numbers (TON) and turnover frequencies (TOF).[21,26–30,35] As previously shown in Fig. 1, these well-defined catalysts consist of aluminum[21,27,30,35] or chromium[26,28,29] cations ligated by salen-type[26,27,30,35] or porphyrin[21,28,29] ligands, with one example of a titanocene cation.[34] In each case, the counter anion is [Co(CO)$_4$]$^-$. Among these well-defined catalysts, the porphyrin-based catalysts[21,28] are generally the most active for epoxide carbonylation (Scheme 8). The trade-off for well-defined catalysts is that although they exhibit higher activity and selectivity, they typically require a few steps to synthesize.

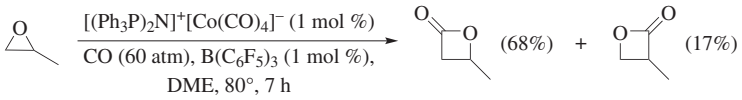


Scheme 8

A Lewis acid is necessary to activate the epoxide for carbonylation.[35] In the cases when [Co(CO)$_4$]$^-$ salts with non-Lewis acidic cations, such as PPh_4^+, $(n\text{-}Bu)_4N^+$, or the coordinatively saturated Cp_2Co^+, are used, no carbonylation activity is observed. Simple metal carbonyl catalysts such as $Co_2(CO)_8$ produce small amounts of β-lactone;[36] however, this activity is proposed to result from the dissociation of $Co_2(CO)_8$ in the presence of a Lewis base to form $[L_2Co(CO)_3]^+[Co(CO)_4]^-$.[82] This hypothesis is further supported by the observation that $Co_2(CO)_8$ catalyzed epoxide carbonylations are more efficient in Lewis basic solvents such as THF than in the non-coordinating solvent benzene.[36]

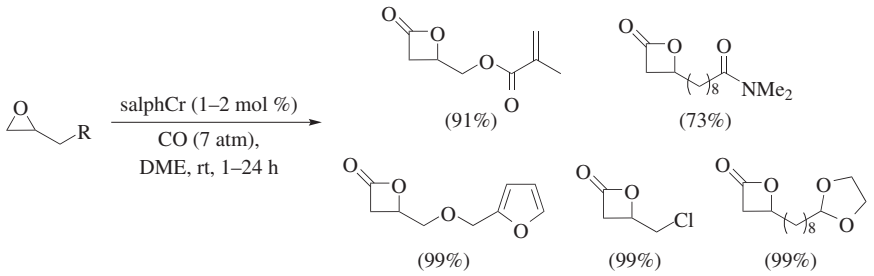
Although a Lewis acid is required for activity, the use of strong Lewis acids can reduce site selectivity in β-lactone formation. In one particular reaction,[36] use of the highly Lewis acidic $B(C_6F_5)_3$ in place of BF_3•OEt_2 for the carbonylation of propylene oxide gives a 4:1 mixture of the expected β-substituted lactone and the constitutionally isomeric α-substituted lactone (Scheme 9). Although trace amounts

of α-substituted lactones are produced using the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, this generally accounts for <1% of the total conversion.



Scheme 9

Functional Group Tolerance. The carbonylation of epoxides catalyzed by [Lewis acid]$^+$[Co(CO)$_4$]$^-$ complexes has a very broad functional group tolerance, and in general all of the different catalysts are tolerant of the same types of functional groups. Catalysts that are formed in situ with either boron- or aluminum-based Lewis acids and cobaltate sources have demonstrated success for many alkyl-, alkenyl-, and ether-substituted epoxides.[32,33,36] The well-defined [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, which display higher activities under milder conditions than their in situ generated analogs, have been successful for the carbonylation of a broader range of epoxides that includes esters, amides, aromatics, nitriles, halides, acetals, and unprotected alcohols (Scheme 10).[17−21,23,26,28,29,34,35]

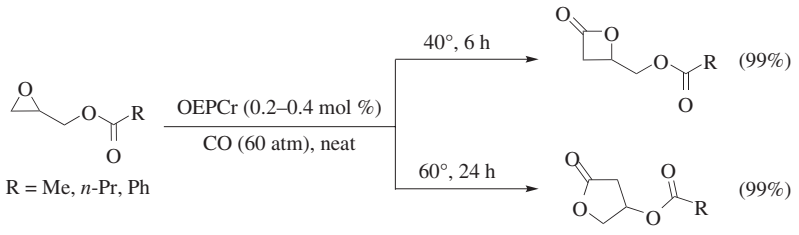


Scheme 10

Some functional groups are not tolerated by Lewis acid derived catalysts. One such functionality is the vinyl group, which in certain cases causes the catalysts to be inactive. Substrates containing alkenes separated from the epoxide by at least one carbon are active, but the attempted carbonylation of 3,4-epoxy-1-butene results in a number of unidentified products.[83] Amines are also not tolerated, as it is thought that such strong Lewis bases likely bind irreversibly to the Lewis acid, precluding epoxide coordination. Although they have not been examined, it is presumed that epoxides tethered with other strong Lewis bases such as phosphines would likely exhibit a similar lack of reactivity.

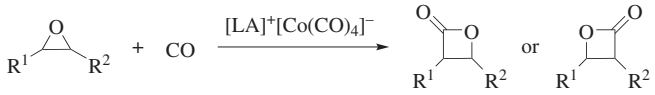
Glycidol and other epoxides with β-hydroxy groups are carbonylated exclusively to γ-lactones instead of β-lactones (see the γ-lactone section). Glycidyl esters require particularly mild reaction conditions to produce β-lactones. At room temperature or 40°, the β-lactone is produced efficiently and in good yield (Scheme 11).[18,26,28] However, at reaction temperatures of 60° or higher, the β-lactone that is produced is not

stable in the presence of the Lewis acid and undergoes a catalytic rearrangement to the ring-expanded γ-lactone (Scheme 11).[28] This rearrangement is discussed further in the γ-lactone section of this chapter.



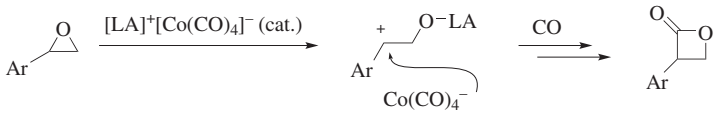
Scheme 11

Epoxide Substitution. The number and configuration of epoxide substituents are important factors for both conversion and product distribution. Because the ring opening can occur at either of the two epoxide carbon–oxygen bonds, two constitutionally isomeric products are always possible (Scheme 12). The ability to control the epoxide ring opening is thus important for obtaining the desired β-lactone product. Because nearly all of the known bioactive β-lactones are single constitutional isomers of *trans*-1,2-disubstituted β-lactones,[77] site control in epoxide carbonylation is of particular importance.



Scheme 12

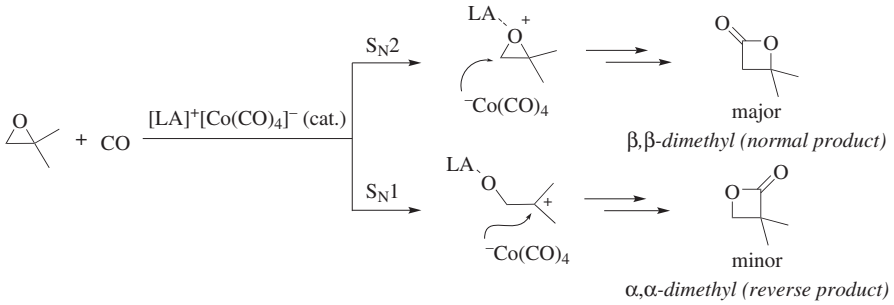
Monosubstituted epoxides are carbonylated with >100:1 selectivity for CO insertion at the less-substituted carbon. An exception to this trend are aryl-substituted epoxides such as styrene oxide, which insert CO into the more substituted C–O bond to produce α-substituted β-lactones. It is believed that this opposite site selectivity results from an S_N1-like mechanism in which epoxide ring opening occurs to form a stable benzylic carbocation that is then trapped by $[Co(CO)_4]^-$ (Scheme 13).[21]



Scheme 13

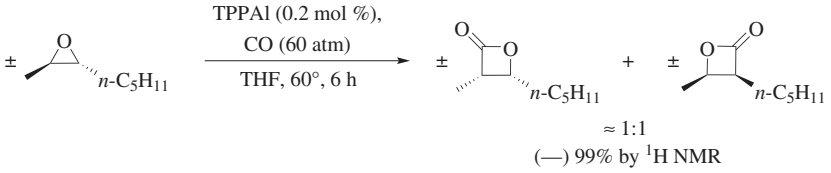
The carbonylation of 1,1-disubstitued epoxides is complicated by the production of constitutional isomers. Although the unsubstituted site is more sterically accessible to an S_N2-type ring opening, the disubstituted carbon is able to effectively sustain

a partial positive charge upon activation by the Lewis acid (Scheme 14). Thus, ring opening occurs at both sites and a mixture of constitutionally isomeric β-lactones is formed. To date, attempts to produce either α,α- or β,β-dimethyl β-propiolactone cleanly from 2-methyl-1,2-epoxypropane have proven unsuccessful. Attempts to carbonylate trisubstituted and tetrasubstituted epoxides using Lewis acid based catalysts have resulted in mixtures of unidentified products, possibly resulting from an analogous S_N1-type ring opening at the geminally disubstituted carbon.



Scheme 14

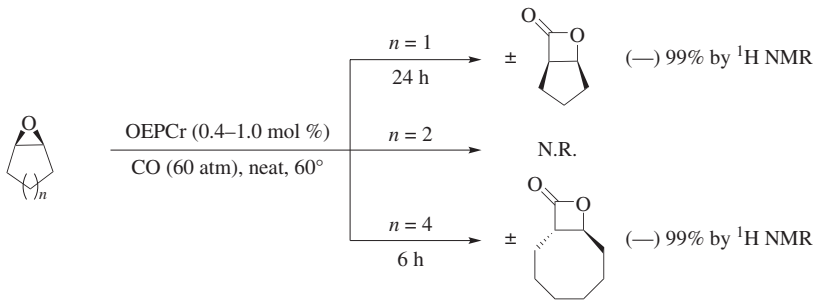
Lewis acid derived catalysts are effective for the carbonylation of 1,2-disubstituted epoxides. The reaction occurs with inversion of configuration at the carbon adjacent to the inserted CO. *cis*-1,2-Disubstituted epoxides are typically carbonylated faster than their *trans*-analogs, a result of a faster ring closing due to less steric repulsion while forming the *trans*-β-lactone ring. 1,2-Disubstituted epoxides are not carbonylated with site selectivity. Thus, in the carbonylation of unsymmetrically substituted epoxides, the two isomers are formed in an approximately 1:1 ratio as shown by the carbonylation of *trans*-2,3-epoxyoctane (Scheme 15).[21]



Scheme 15

Alicyclic epoxides present a special case of 1,2-disubstituted epoxides. For epoxides fused to rings with at least eight atoms, the carbonylation proceeds in the usual manner, in that *cis*-epoxides are converted into *trans*-lactones.[26,28,29] Epoxides fused to smaller rings, however, do not produce the expected β-lactones. Cyclohexene oxide does not produce any carbonylated product; the expected *trans*-[4.2.0] bicyclic β-lactone is not stable because of high ring strain.[28] The carbonylation of cyclopentene oxide with OEPCr does produce a β-lactone, though

it is not the expected *trans*-product. Instead, only the more stable *cis*-β-lactone is observed, and it is proposed that the mechanism involves a carbocation intermediate (Scheme 16).[28]



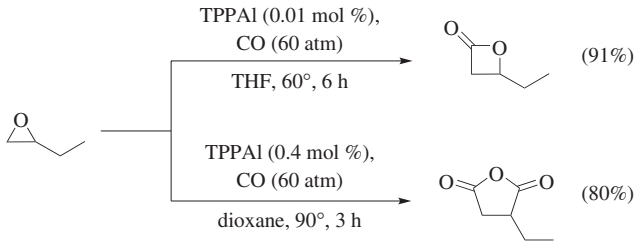
Scheme 16

Reaction Conditions *Reaction Solvent.* In all of the epoxide carbonylation systems, the solvent is a significant factor for both reaction rate and product ratios. Some of the carbonylation systems have been studied in great detail, and the mechanistic role of solvent is well-understood;[21,25] in other systems the solvent effects are simply empirical. Several catalysts have been demonstrated to work efficiently in the absence of solvent,[28,29,35] which permits relatively simple isolation of the neat β-lactones from catalyst residue. Solvent-free reactions are, however, more prone to produce poly(β-lactone)s, common side products observed at high temperatures when reactions are run to complete conversion. The use of solvent generally eliminates this oligomerization.[21]

Solvents significantly affect the rate of reaction. This effect has been most thoroughly studied with the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts. For most of these catalysts, ethers are optimal solvents, with more strongly donating ethers generally increasing the rate of carbonylation.[25] For example, the carbonylation of 1,2-epoxybutane to β-valerolactone is nearly twice as fast in THF as the analogous reaction in any other ethereal solvent. This effect has been attributed to donicity rather than polarity, as the hindered solvents 2-methyl-THF and 2,5-dimethyl-THF[84] do not facilitate the carbonylation as well as THF,[25] despite their similar polarities. This solvent trend is reversed for one catalyst, salphCr, as THF actually diminishes the carbonylation rate significantly.[19] For this particular catalyst, more weakly donating ethers such as DME, dioxane, or 2,5-dimethyl-THF are optimal solvents. The rate of carbonylation of 1,2-disubstituted epoxides by any of the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts is also retarded by the use of donating solvents such as THF. In both of these cases, it is believed that THF binding to the Lewis acid inhibits epoxide coordination and activation, thus reducing the rate of carbonylation.

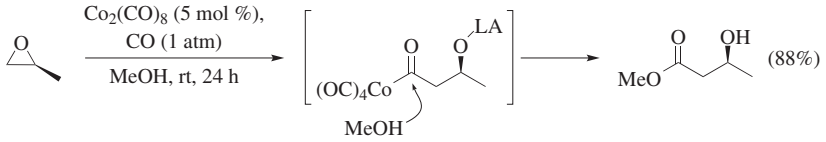
Solvent also affects the rate of formation of side products. Succinic anhydrides can be formed with most [Lewis Acid]$^+$[Co(CO)$_4$]$^-$ catalysts as a result of subsequent carbonylation of the β-lactone product (see below). The formation of anhydride

is negligible with donor solvents such as THF, but in less polar solvents such as dioxane, the β-lactone product is rapidly converted into an anhydride. For example, using TPPAl and the proper reaction solvent, either β-lactone or succinic anhydride can be formed with >100:1 selectivity (Scheme 17).[21]



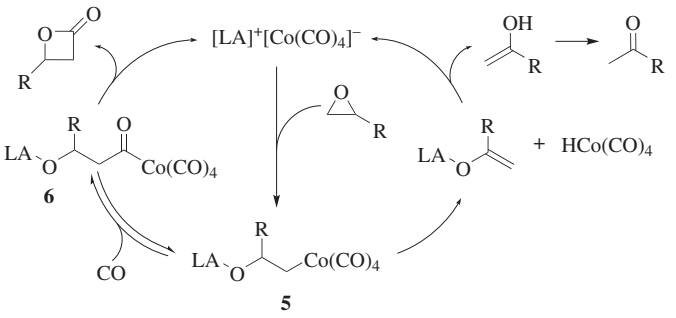
Scheme 17

Some solvents are not practical for epoxide carbonylation using Lewis acid derived catalysts. Noncoordinating and nonpolar solvents such as hexanes do not lead to β-lactone formation. The poor activity in hexanes has, however, been exploited for the development of a carbonylative multicomponent coupling reaction involving epoxides that is discussed later in this chapter.[22] Alcohol solvents are also not practical as the alcohol can react with the ring-opened cobalt acyl to form a β-hydroxy ester (Scheme 18).[57] Other solvents, including CH_2Cl_2 and MeCN, inhibit carbonylation and are thought to react with either the cobaltate anion or the Lewis acid.



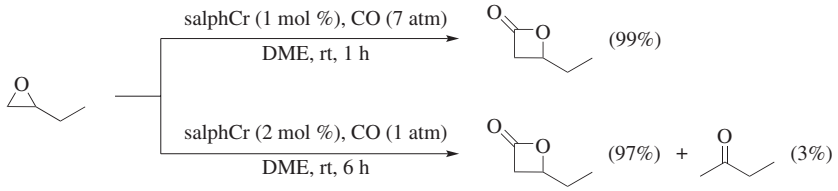
Scheme 18

CO Pressure. Lewis acid derived epoxide carbonylation catalysts generally require at least 14 atm of CO for efficient carbonylation, and most examples use 50–60 atm. Although the reaction is zero-order in CO, at lower CO pressures it is proposed that diffusion of CO into solution may become rate limiting. Furthermore, low concentrations of CO in solution coupled with higher temperatures result in the non-carbonylative rearrangement of epoxides to ketones (Scheme 19). It is believed that ketones are produced through a β-hydride elimination from intermediate **5** followed by protonation of the metal alkoxide to form an enol; tautomerization forms the ketone and the catalyst is regenerated.[26,35] Because intermediate **5** is in equilibrium with the CO-inserted species **6** and higher pressures of CO shift the equilibrium towards intermediate **6**,[85] CO pressures greater than 14 atm are often used to produce β-lactones cleanly without ketone contamination.



Scheme 19

Epoxide carbonylation can be performed under pressures of CO as low as 1 atm. However, to avoid rearrangement to ketones, a sufficient concentration of CO must be maintained in solution. This is accomplished by running the reactions at lower temperatures and with solvent, thus decreasing the rate of CO consumption. High selectivity at low CO pressure was first demonstrated with SalphCr.[26] At 7 atm of CO, several functionally diverse epoxides are carbonylated to β-lactones with complete conversion and 99% selectivity (1 mol % of salphCr, TOF = 33–100 h^{-1}) (Scheme 20). When the pressure is dropped further to 1 atm, the carbonylation takes 6 hours to complete (2 mol % of salphCr, TOF = 8 h^{-1}) and small quantities of a ketone (generally <5%) are produced.[26] Under these reaction conditions, carbonylation of epoxides can be performed in standard glassware, in contrast to the stainless steel reactors required for carbonylation reactions performed at high pressure.



Scheme 20

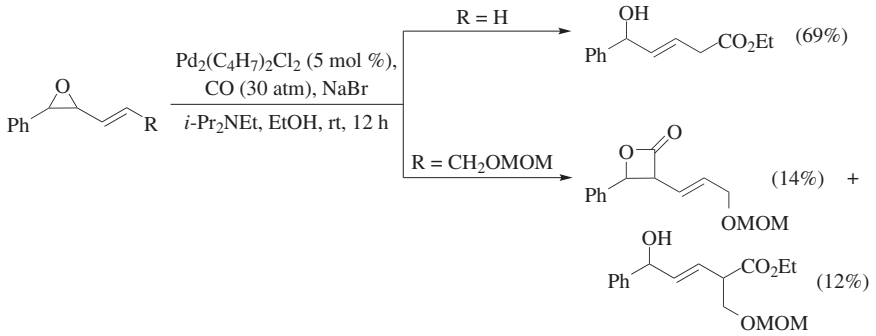
Catalytic Reactions Using Rh and Pd, and Stoichiometric Reactions Using Fe Complexes

Relatively simple, commercially available transition-metal complexes of rhodium, palladium, and iron have demonstrated activity for the carbonylation of aryl and vinyl epoxides to form β-lactones. For example, the carbonylation of vinyl epoxides to β-lactones proceeds using catalytic amounts of $Pd_2(C_4H_7)_2Cl_2$[38] or stoichiometric amounts of $Fe(CO)_5$[40,51] and $Fe_2(CO)_9$.[39] These metal complexes are only viable with vinyl epoxides because, as has been discussed previously, the mechanism of carbonylation requires alkene coordination followed by ring opening to produce a π-allyl complex. Furthermore, yields of β-lactone are generally low due to formation

of side products including ring-expanded δ-lactones,[40,51] β- and δ-hydroxy esters,[38] and 1,3-dienes which result from decarboxylation of the β-lactone product.[38] The carbonylation of styrene oxide and propylene oxide to the respective β-lactones has been reported using $RhCl(CO)(PPh_3)_2$.[41]

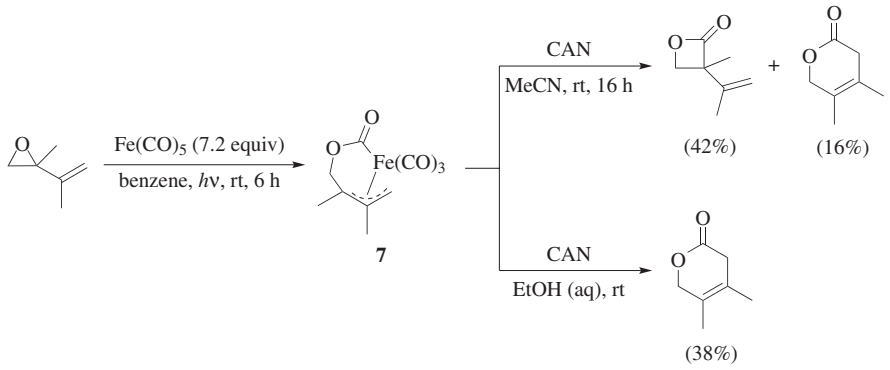
Functional Group and Substitution Tolerance. Few studies have examined the functional group tolerance of vinyl epoxide carbonylations. Iron-mediated carbonylations have been performed primarily with alkyl-substituted vinyl epoxides,[40,51] with one isolated reaction of a hydroxyl-substituted epoxide, albeit in low yield.[39] To test whether the hydroxyl group was the cause of the low yield, the alcohol was protected as an acetate and the yield improved nearly two-fold. Palladium-catalyzed carbonylations of vinyl epoxides have an equally narrow functionality tolerance, as only alkyl- and ether-substituted epoxides are viable substrates.[38]

The carbonylation of vinyl epoxides by iron or palladium is compatible with highly substituted epoxides and, unlike the case of Lewis acid catalyzed carbonylation, vinyl epoxide carbonylation is perfectly site selective for CO insertion at the allylic carbon. Therefore, mono-, di-, and trisubstituted epoxides are all suitable substrates and produce a single β-lactone product. Iron-mediated carbonylations are equally compatible with terminal and internal alkenes.[40] The substitution on the alkene is important for Pd-catalyzed carbonylations, in that terminal vinyl epoxides react with the solvent to produce δ-hydroxy esters, whereas epoxides with internal alkenes produce some β-lactone (Scheme 21).[38]



Scheme 21

Reaction Conditions. The choice of reaction solvent has a dramatic effect on the product distribution. For example, the $Fe(CO)_5$ mediated carbonylation of vinyl epoxides can form both β- and δ-lactones from the same intermediate. The tricarbonyliron lactone intermediate complex **7** is oxidized with ceric ammonium nitrate (CAN) to induce lactonization (Scheme 22). When this oxidation is performed in acetonitrile, the β-lactone is formed as the major product. However, when the reaction solvent is aqueous ethanol, no β-lactone is formed and the δ-lactone is the only product observed.[40]



Scheme 22

The CO pressure required for the carbonylation of vinyl epoxides varies greatly depending on the particular catalyst system. The stoichiometric carbonylation of vinyl epoxides mediated by iron carbonyl compounds, either $Fe_2(CO)_9$ or $Fe(CO)_5$, does not require CO.[39,40] In these reactions, the CO that is incorporated into the β-lactone comes from the iron reagent. On the other hand, palladium-catalyzed carbonylations of vinyl epoxides do require CO. Thirty atm of CO is the optimal pressure when $Pd_2(C_4H_7)_2Cl_2$ is used as a catalyst, although even under these conditions, 1,3-dienes are the major products formed due to decarboxylation.[38]

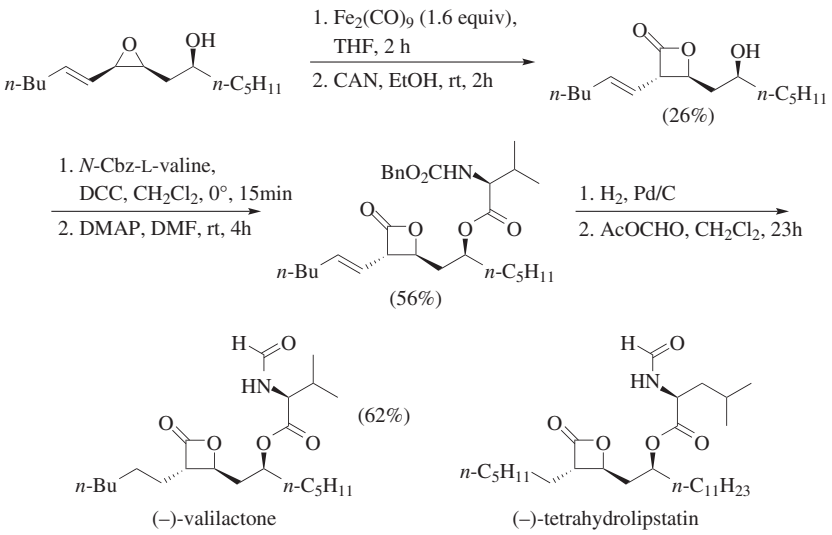
APPLICATIONS TO SYNTHESIS

(−)-Valilactone

Valilactone is a β-lactone-containing natural product belonging to the family of biologically active natural products that includes tetrahydrolipstatin (THL) (Scheme 23).[86] Both compounds are potent lipase inhibitors. In fact, THL is the active compound in the pharmaceutical Xenical, which is marketed for the treatment of obesity.[87] Because both of these natural products contain a β-lactone, they are attractive targets for demonstrating the effectiveness of epoxide carbonylation as a route to produce β-lactones. (−)-Valilactone has been synthesized using epoxide carbonylation to install the β-lactone functionality. Although the 26% yield for the carbonylation step is disappointing, (−)-valilactone is prepared in 9% overall yield from the vinyl epoxide through two further straightforward steps (Scheme 23).[39] This method would likely be useful for the synthesis of other members of this natural product family, including THL.

COMPARISON WITH OTHER METHODS

Although the first synthesis of β-lactones was reported in 1881,[88,89] for many years there were relatively few methods for the synthesis of these strained heterocycles.[72] Recently, however, renewed interest in synthetic methods for β-lactones has stemmed

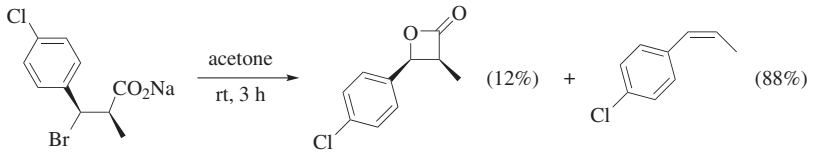


Scheme 23

from the fact that this moiety is present in a number of biologically active natural products.[76] Moreover, the ring-opening polymerization of β-lactones produces biodegradable polyesters with potentially important biomedical applications.[75] Other than epoxide carbonylation, the two most common methods for the synthesis of β-lactones are the ring closing of carboxylic acid derivatives and the [2+2] cycloaddition of ketenes and carbonyl compounds.[72]

Ring Closing of β-Halo Carboxylic Acids

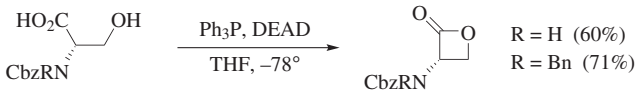
Base-catalyzed ring closing of β-halo carboxylic acids produce β-lactones with inversion of configuration at the carbon bearing the halogen.[90] This was the first known method for β-lactone preparation,[88] and it is generally performed in aqueous media, though examples in organic solvents exist. Although some substrates are efficient ring-closing precursors, this method is limited by the deleterious elimination of HX and CO_2 to form alkenes (Scheme 24).[91] Because more efficient ring-closing methods have been developed, and particularly ring closing of β-hydroxy carboxylic acids, lactonization from β-halo carboxylic acids is rarely used.



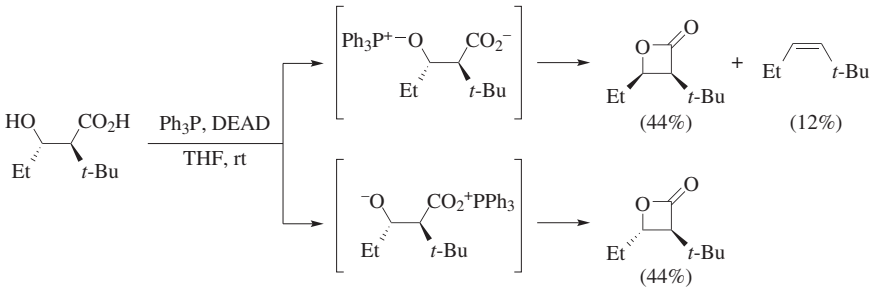
Scheme 24

Ring Closing of β-Hydroxy Carboxylic Acids

The synthesis of β-lactones by ring closing of hydroxy acids requires activation of either the hydroxy functionality or the carboxylic acid. By the use of standard Mitsunobu conditions,[92] the hydroxy group can be activated by Ph_3P for attack by the carboxylate, producing β-lactones with inversion of configuration at the hydroxyl-substituted carbon (Scheme 25).[93,94] Unfortunately, 2,3-disubstituted hydroxy acids are not suitable for Mitsunobu cyclization because they are prone to undergo elimination to form alkenes (Scheme 26),[95] as is the case with β-halo carboxylic acids. Furthermore, for certain substrates, Mitsunobu activation of the hydroxyl group is competitive with activation of the carboxylic acid by Ph_3P. Because carboxylic acid activation results in a β-lactone with retention of configuration, whereas hydroxyl activation results in inversion, this mixture of intermediates produces both diastereomers of the β-lactone product (Scheme 26).[96]

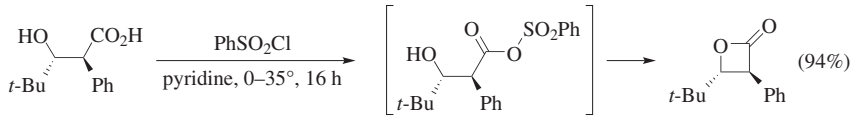


Scheme 25



Scheme 26

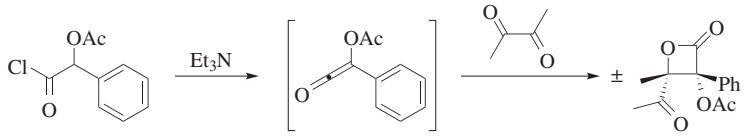
To avoid these problems, selective activation of the carboxylic acid portion of the hydroxy acid is commonly employed, most often using an arenesulfonyl chloride.[97] The latter produces β-lactones in good yields with retention of configuration at the hydroxyl-bearing carbon (Scheme 27).[98] Furthermore, this ring-closing method is compatible with diversely substituted hydroxy acids.



Scheme 27

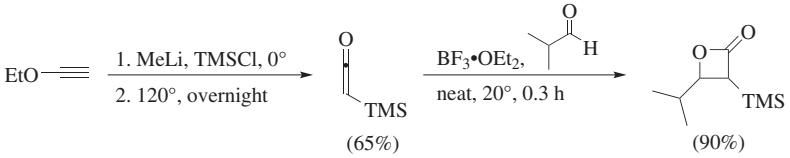
[2+2] Cycloaddition of Ketenes and Carbonyl Compounds

Ketenes have been shown to react with a wide range of carbonyl compounds, which makes this cycloaddition a versatile synthetic method.[99,100] One of the most challenging aspects of the [2+2] cycloaddition method for the synthesis of β-lactones is the generation of ketenes. Only a few ketenes are stable, and most are known to dimerize and react readily with water;[101] therefore, most ketenes are generated in situ (Scheme 28).[102−104] Ketenes are most commonly generated through the dehydrohalogenation of acid chlorides,[105,106] though other methods have also been successful.[107,108]



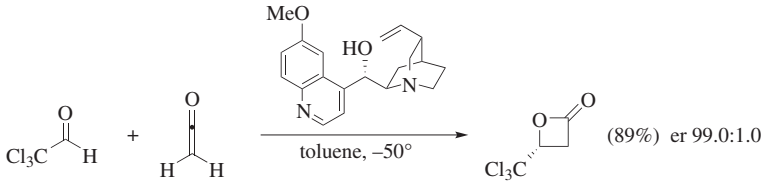
Scheme 28

Although many [2+2] cycloaddition reactions occur spontaneously due to the high reactivity of ketenes, some require a catalyst to efficiently produce β-lactones. Relatively stable ketenes, such as trimethylsilyl-substituted ketenes, often undergo Lewis acid catalyzed cycloaddition with aldehydes (Scheme 29),[109] as the Lewis acid effectively activates the aldehyde toward attack.[110] Alternatively, Lewis bases have been used to activate the ketene for attack of the aldehyde; tertiary amines are common catalysts for this purpose.[111]

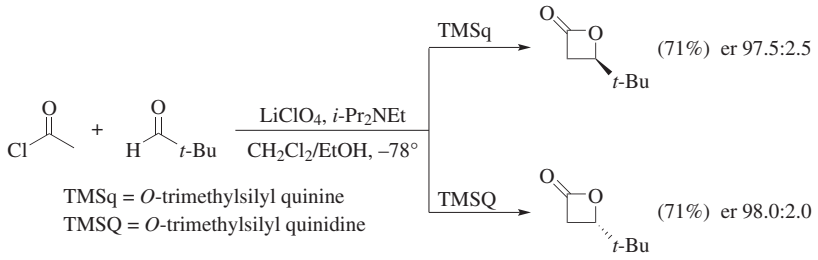


Scheme 29

A large body of work describes the enantioselective synthesis of β-lactones by [2+2] cycloaddition.[102,111−118] Both chiral Lewis acids and Lewis bases have been shown to successfully catalyze the enantioselective addition, and each has its advantages and disadvantages. The reaction of ketene with chloral is catalyzed by the *cinchona* alkaloid quinidine, a naturally occurring chiral Lewis base (Scheme 30).[112] Unfortunately, this method is successful only for the highly activated aldehyde chloral, but this innovation inspired further exploration into asymmetric β-lactone synthesis through Lewis base catalyzed [2+2] cycloaddition.[111,113,114] An example is a tandem *cinchona* alkaloid–Lewis acid catalyzed reaction that is both highly enantioselective and active for non-activated aldehydes (Scheme 31).[102] Enantiomeric ratios range from 92.0:8.0 to 99.5:0.5, and both enantiomers of the β-lactones can be obtained through the proper choice of the *cinchona* alkaloid catalyst.

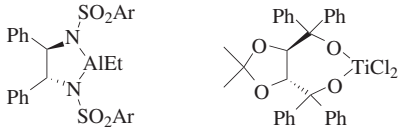


Scheme 30



Scheme 31

Chiral Lewis acids have been explored for enantioselective [2+2] cycloaddition of non-activated aldehydes, but they have not shown the high selectivities associated with the base-catalyzed reactions discussed above. Examples include bis(sulfonamide) aluminum catalysts **8** (Fig. 2)[115,116] and TADDOL titanium complexes **9** (Fig. 2),[117] but the enantiomeric purity of the β-lactone products is only moderate. Lewis acid catalyzed reactions do not, however, suffer from reduced activity when non-activated aldehydes are used, so more diverse β-lactones can be prepared.[81,118]



8 **9**

Ar = 3,5-$(CF_3)_2C_6H_3$

Figure 2. Chiral Lewis acids employed in the enantioselective [2+2] cycloaddition of ketenes and aldehydes.

EPOXIDE CARBONYLATION TO γ-LACTONES

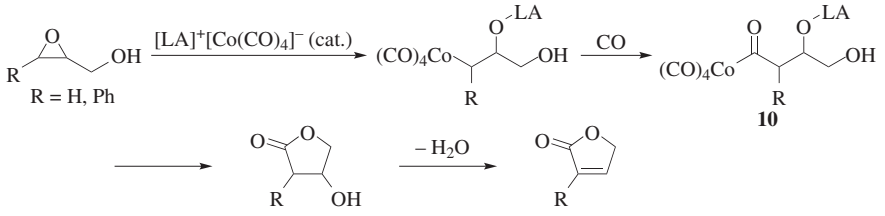
The γ-lactone core commonly appears in natural products,[119] many of which exhibit bioactivity attributed to this functionality.[120] Butenolides, a class of unsaturated γ-lactones, have been the focus of much research, and their synthesis

and reactivity have been reviewed.[121−123] γ-Lactones are arguably the most easily synthesized type of lactones due to their low ring strain. As such, there are a multitude of possible synthetic methods,[124,125] and even within epoxide carbonylation, a number of diverse routes to γ-lactones are known.[28,42−45]

MECHANISM AND STEREOCHEMISTRY

Carbonylation of Glycidols

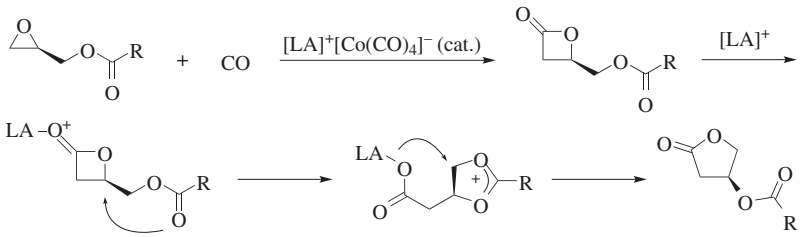
The mechanism of glycidol carbonylation has not been studied in detail, as the active catalytic species are not well-defined for most systems.[42,43] One common feature is that all catalysts contain a cobalt carbonyl compound. Most systems are believed to react via similar pathways, and a general mechanism is presented which illustrates the important steps in the reaction (Scheme 32). First, the epoxide ring is opened by cobalt at either the less-substituted (R = H) or benzylic carbon (R = Ph). Insertion of CO forms intermediate **10**, and then nucleophilic attack of an alcohol or alkoxide on this acyl ligand forms the lactone. Selectivity for γ-lactone is dictated by the presence of a nucleophilic oxygen in the γ-position. Closing from this alcohol to form a five-membered ring is highly favored over closing from the epoxide oxygen to form a strained β-lactone. Post-carbonylation dehydration of the product yields α,β-unsaturated-γ-lactones (Scheme 32).[42,43] In one system, further carbonylation of the γ-lactone is possible; however, the mechanism of this transformation is unclear.[43]



Scheme 32

Carbonylation of Glycidyl Esters

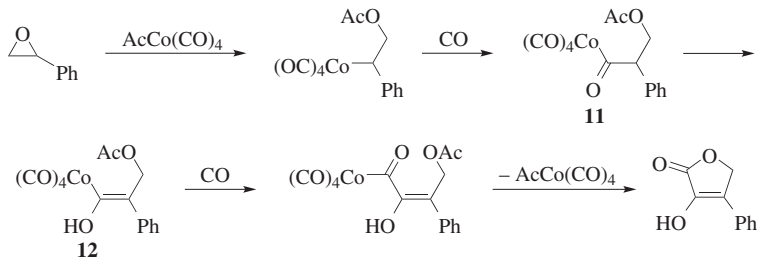
If the alcohol of glycidol is protected, then epoxide carbonylation proceeds with [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts to form the expected β-lactones (Scheme 33). However, in the specific case of glycidyl esters, the product β-lactone can undergo an in situ Lewis acid catalyzed rearrangement to a γ-lactone (Scheme 33). The proposed mechanism involves coordination of the β-lactone to the Lewis acid catalyst, activating it for ring-opening attack by the ester carbonyl, which proceeds with inversion of configuration to form an intermediate 1,3-dioxolanyl cation. Ring closing of the carboxylate reforms the ester and the expanded lactone.[28]



Scheme 33

Double Carbonylation of Styrene Oxides

In epoxide carbonylation reactions, aryl epoxides typically ring open such that the cobalt is bound to the benzylic carbon. Double carbonylation of styrene oxides is unique in that two molecules of CO are inserted adjacent to one another in the ring. Although migratory insertion of CO into a cobalt alkyl bond is facile, a second insertion of CO into cobalt acyl **11** is not observed.[126] However, the aryl group helps to stabilize tautomerization to enol **12**, which is more electron-donating and thus allows insertion of CO.[127] Once the second CO is inserted, ring closing can occur, forming a γ-lactone (Scheme 34).[44]

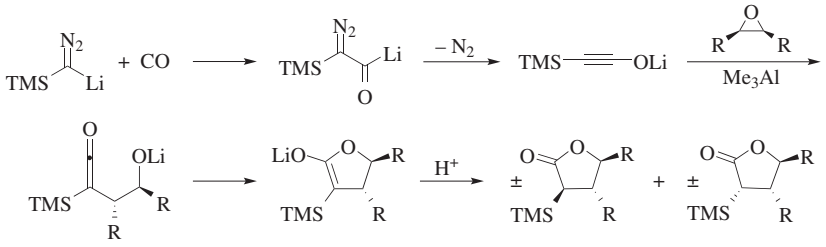


Scheme 34

Carbonylation of Epoxides with Ynolates

Unlike most epoxide carbonylations, this method does not employ a catalytic amount of cobalt to sequester CO. Instead, CO is trapped by a stoichiometric amount of an organolithium compound and is converted into a reactive ynolate, which then undergoes a ring-expanding reaction with an epoxide. A relatively straightforward mechanism has been proposed (Scheme 35). First, trimethylsilyldiazomethane is deprotonated with BuLi and is exposed to CO, forming a highly reactive acyllithium reagent that rapidly loses nitrogen to form a silylethynolate. In the presence of a

Lewis acid, this ynolate ring opens an epoxide, unmasking a ketene, which readily closes to a five-membered ring. Protic workup provides the γ-lactone product.[45]



Scheme 35

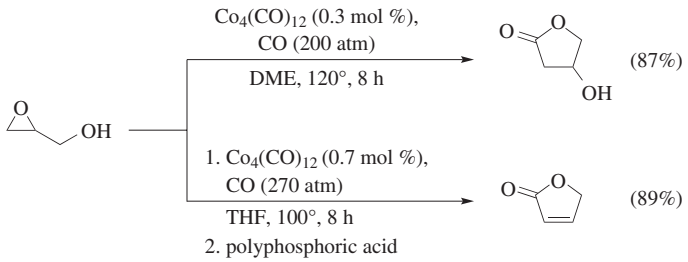
Nucleophilic attack of the epoxide always occurs at the carbon of the ynolate and opens the epoxide with inversion of configuration at this site. Thus, *cis*-epoxides are carbonylated to *trans*-lactones (Scheme 35) and *trans*-epoxides to *cis*-lactones. This reaction is highly site selective and stereospecific with regard to ring opening of the epoxide; however, the orientation of the silyl group is less controlled and is determined by the protonation step (Scheme 35). One diastereomer typically predominates, and its yield can be increased through the use of a bulky proton source, but the configuration at this center has not been definitively established.[45]

SCOPE AND LIMITATIONS

Although a number of routes to γ-lactones via ring-expanding carbonylation of epoxides exist, the scope of these methods has remained largely unexplored. For each method just a handful of examples are known. Extending these reactions to more general syntheses of γ-lactones remains to be explored.

Carbonylation of Glycidols

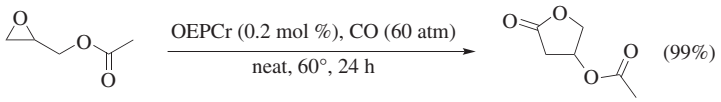
The parent glycidol is readily carbonylated to afford good yields of 3-hydroxy-γ-lactone using cobalt carbonyl catalysts, with or without a well-defined Lewis acid (Scheme 36).[5,42] Substituted glycidols also give the desired products, although the yields are generally lower and often poor in the case of aryl-substituted epoxides.[43] Although only alkyl and aryl substituents have been reported, it is expected this reaction may also be tolerant of a range of functional groups similar to that seen for epoxide carbonylation to β-lactones. Further research is required to examine the broader applicability of this method to the synthesis of substituted 3-hydroxy-γ-lactones. Alternative products may also be formed by in situ dehydration of the hydroxy lactone to give the α,β-unsaturated-γ-lactone (Scheme 36).[42]



Scheme 36

Carbonylation of Glycidyl Esters

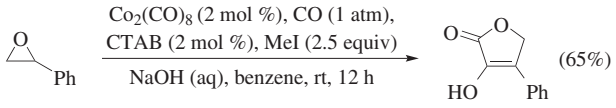
Glycidyl esters are a distinctive class of protected glycidols that form β-lactones upon carbonylation but, due to a pendant ester group, readily rearrange to form γ-lactones. The Lewis acid promoted rearrangement of glycidyl esters is observed with all $[\text{Lewis acid}]^+[Co(CO)_4]^-$ catalysts at elevated temperatures. Functional group tolerance is essentially the same as for carbonylation to β-lactone (see above), but a β-alkanoate substituent is required. The reaction is both stereospecific and nearly quantitative. Lower reaction temperature (40°) results in formation of β-lactone without rearrangement (Scheme 11), but higher temperatures and longer times cause complete rearrangement to the γ-lactone product (Scheme 37).[28]



Scheme 37

Double Carbonylation of Styrene Oxides

Only two examples of this transformation are known; thus, the scope of the reaction has not been explored. The primary substrate requirement is that epoxides must be able to form the relatively stable enolate intermediate **12** (Scheme 34) that is required for the insertion of a second molecule of CO.[127] Styrene oxide gives a moderate yield of γ-lactone (Scheme 38), but only a 34% yield is obtained with β-methylstyrene oxide.[44]

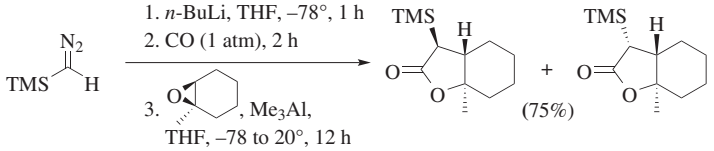


Scheme 38

Carbonylation of Epoxides with Ynolates

This reaction is a unique method for the incorporation of CO into an epoxide, as CO is sequestered by an organolithium reagent rather than a transition metal. This

method has the advantage of being able to produce fused ring systems in a stereo- and regiospecific manner. Thus far, the substrate scope only includes di- and trisubstituted epoxides with alkyl and alkenyl substituents which form the product in good yield, but as a mixture of two diastereomers that were not separated (Scheme 39).[45] To increase the general utility of this reaction, further studies are required to extend this method to monosubstituted and more functionally diverse substrates.[45] Although the reaction has only been demonstrated to form 2-trimethylsilyl γ-lactones, the silyl group can be used as a reactive functional group for further synthetic transformations.[128–131]

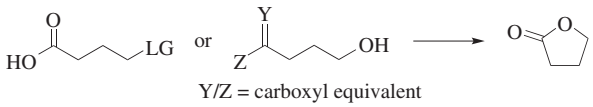


Scheme 39

COMPARISON WITH OTHER METHODS

Unlike for strained β-lactones, there are a multitude of methods for the synthesis of γ-lactones, and this topic has recently been reviewed.[124] A comprehensive discussion of the many other methods is beyond the scope of this work; thus, only very general methods and those that form the same products as ring-expanding epoxide carbonylation are covered.

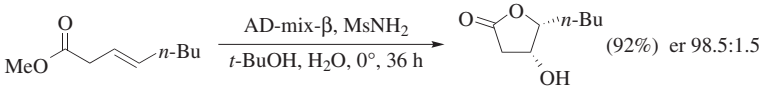
The simplest method of forming a γ-lactone is the intramolecular condensation of a γ-hydroxy acid. This type of reaction is not limited to hydroxy acids, and may be extended to a very general ring closing involving any molecule containing an acid and a leaving group in the γ-position, or containing a γ-alcohol and a carboxyl equivalent (Scheme 40). There are numerous examples,[124] and some common variations of these ring closings include Mitsunobu lactonization,[92] halo lactonization,[132] as well as addition of activating agents such as trifluoroacetic acid[133] or *N*,*N*′-dicyclohexylcarbodiimide[134] to γ-hydroxy acids. Alternative syntheses include the ring-expanding Baeyer-Villiger oxidation of cyclobutanes,[135] reduction of succinic anhydrides,[136] and oxidative coupling with furans.[137,138]



Scheme 40

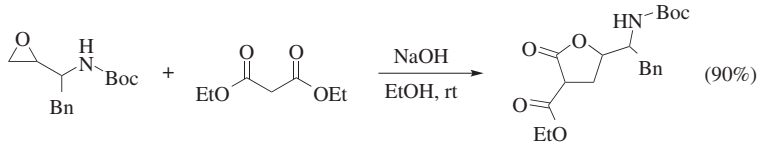
Of particular relevance to glycidol carbonylation is the synthesis of 3-hydroxy γ-lactones via asymmetric dihydroxylation[139] of a β,γ-unsaturated ester, followed by spontaneous lactonization (Scheme 41).[140] This versatile method produces γ-lactones

with good yields and enantioselectivities, and the starting material is readily available through a modified Knoevenagel condensation.[141]



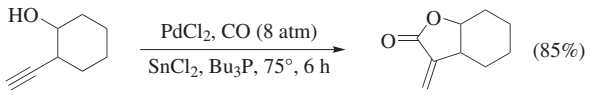
Scheme 41

γ-Lactones can also be made through non-carbonylative ring expansion of epoxides by incorporating C_2 fragments in a method comparable to epoxide coupling with ynolates. For example, the sodium salt of diethyl malonate opens an epoxide to give an intermediate that then closes to form a γ-lactone (Scheme 42).[142]



Scheme 42

Palladium-catalyzed carbonylations of alkenols[143] and alkynols[144] also produce γ-lactones (Scheme 43). Although this method provides an alternative carbonylation route, yields are variable depending on the substrate substitution pattern. Ring-expanding carbonylation of oxetanes, the four-membered analogs of epoxides, with a $[\text{Lewis acid}]^+[Co(CO)_4]^-$ catalyst yields nearly quantitative conversion to γ-lactones.[54,67] However, the utility of this route is diminished as methods for the synthesis of substituted oxetanes are limited.



Scheme 43

Ring-expanding carbonylation of epoxides is a viable method for the synthesis of γ-lactones, and it has the advantage of employing readily accessible starting materials that can be made with high enantiomeric purity. However, this method has not yet demonstrated applicability to a broad range of substrates or to the synthesis of larger, more structurally and functionally complex molecules, for which numerous other synthetic pathways exist. Because of the mechanism of lactone formation, the scope is limited to a handful of specific product substitution patterns (2-silyl, 3-hydroxy, 3-alkanoxy, 2-hydroxy, 3-aryl, and α,β-unsaturated γ-lactones). For these particular product classes, epoxide carbonylation is an efficient and effective synthetic method and more research in this area is warranted.

EPOXIDE CARBONYLATION TO δ-LACTONES

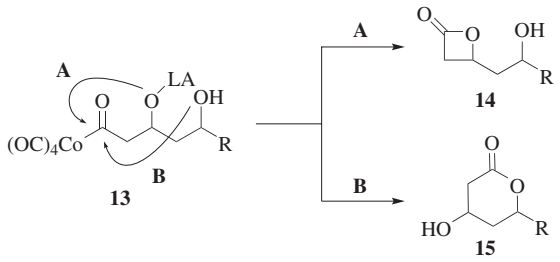
The δ-lactone functionality is also ubiquitous in synthetic chemistry as both a vital intermediate as well as an important synthetic target.[145] The two classes of δ-lactones that are accessible through epoxide carbonylation include 3-hydroxy δ-lactones and α,β-unsaturated δ-lactones. These products are particularly important because of their dense functionality as well as their prevalence in biologically relevant natural products. 3-Hydroxy δ-lactones are most prominent in the class of HMG-CoA reductase inhibitors known as statins, which are among the most potent cholesterol-lowering drugs available.[146,147] The α,β-unsaturated δ-lactone motif, on the other hand, is one of the most commonly occurring lactone frameworks in natural products.[119] These lactone scaffolds occur in bioactive natural products including antiproliferative agents, immunosuppressants, and enzyme inhibitors.[148] Epoxide carbonylation offers a versatile route to a diverse set of important δ-lactones that are difficult to access through other straightforward means.

MECHANISM AND STEREOCHEMISTRY

The mechanism for the carbonylation of epoxides to δ-lactones varies according to the particular epoxide substrate and catalyst system. All of these carbonylation reactions can be divided into two main categories, consisting of reactions employing homoglycidol substrates and carbonylations of vinyl and alkynyl epoxides. Because the catalyst systems and mechanisms for these two substrate classes are significantly different, each is discussed in turn, and vinyl and alkynyl epoxides are treated separately due to their mechanistic differences.

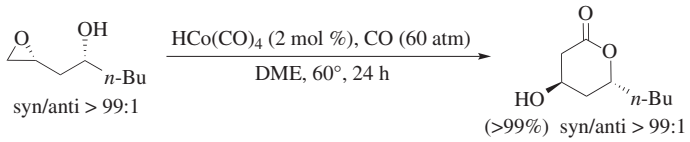
Carbonylation of Homoglycidols

Homoglycidols are effectively carbonylated to form 3-hydroxy δ-lactones using $[Co(CO)_4]^-$ based catalysts.[24] The key to efficient catalysis is the selectivity for the formation of δ-lactone over β-lactone, as both potential products are formed from a common intermediate (Scheme 44). The initial step of the reaction involves coordination of the epoxide by the Lewis acid followed by ring opening by $[Co(CO)_4]^-$. Insertion of CO into the cobalt alkyl forms cobalt acyl intermediate **13**, which can ring close to form the two different lactone products. As seen in β-lactone synthesis, pathway **A** produces the hydroxy-substituted β-lactones **14**. However, in pathway **B** the cobalt acyl is attacked by the alcohol substituent to form the 6-membered δ-lactones **15**. Hydroxy-substituted β-lactones are also known to undergo rearrangement to δ-lactones;[149] however, under conditions optimized for δ-lactone synthesis, this pathway has been discounted because β-lactones cannot be observed by infrared spectroscopy during the reaction, and independently synthesized β-lactones do not produce δ-lactones when subjected to these reaction conditions.[24] The choice of catalyst has a significant impact on product ratios, as is discussed in the Scope and Limitations section, and judicious selection of catalyst and reaction conditions provides complete and selective conversion to δ-lactones.



Scheme 44

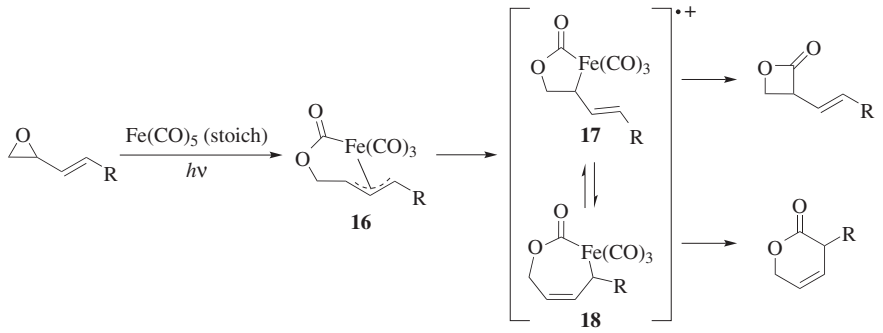
The configuration of the δ-lactone products is predictable based on that of the homoglycidol substrates. Although a stereoselective method for the carbonylation of racemic homoglycidols is not known, when enantiopure substrates are employed, δ-lactones are produced with complete retention of configuration at the hydroxyl-bearing carbons (Scheme 45).[24]



Scheme 45

Carbonylation of Vinyl Epoxides

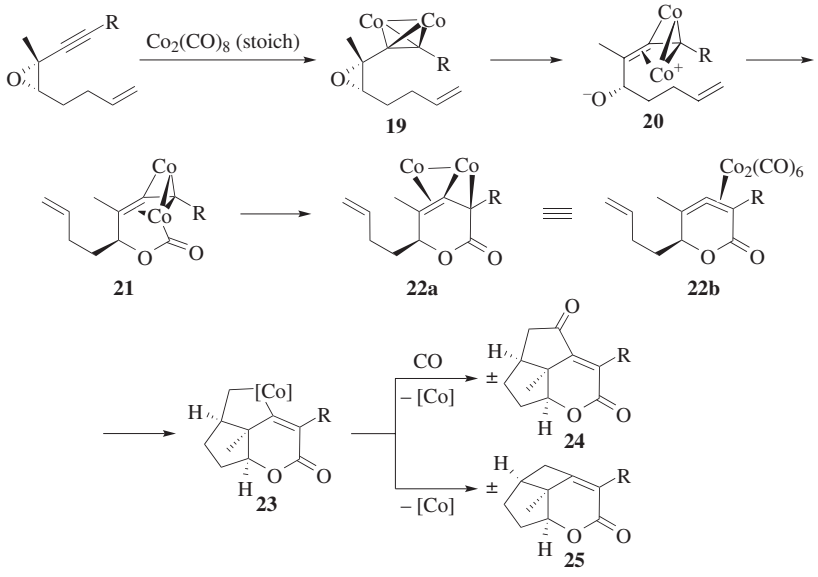
The carbonylation of vinyl epoxides to δ-lactones takes place through a different mechanism than that of homoglycidol carbonylation (Scheme 46). The metal carbonyl reagent typically used for this substrate class is $Fe(CO)_5$, which coordinates to the vinyl group upon loss of CO. Oxidative addition and insertion of CO forms the π-allyltricarbonyliron acyl intermediate **16**, which is isolable and has been characterized.[40] Reductive elimination of intermediate **16** is initiated by either oxidation with reagents such as cerium ammonium nitrate,[40] or by thermolysis under an argon atmosphere[51] or high pressures of CO.[52] As with homoglycidol carbonylation, the carbonylation of vinyl epoxides to δ-lactones is complicated by the formation of β-lactones. An equilibrating mixture of radical cation intermediates **17** and **18** is proposed to form after oxidation, followed by reductive elimination to form vinyl-substituted β-lactones and β,γ-unsaturated δ-lactones, respectively (Scheme 46).[40] Product ratios are determined by reaction conditions and the epoxide substrates used.



Scheme 46

Carbonylation of Alkynyl Epoxides

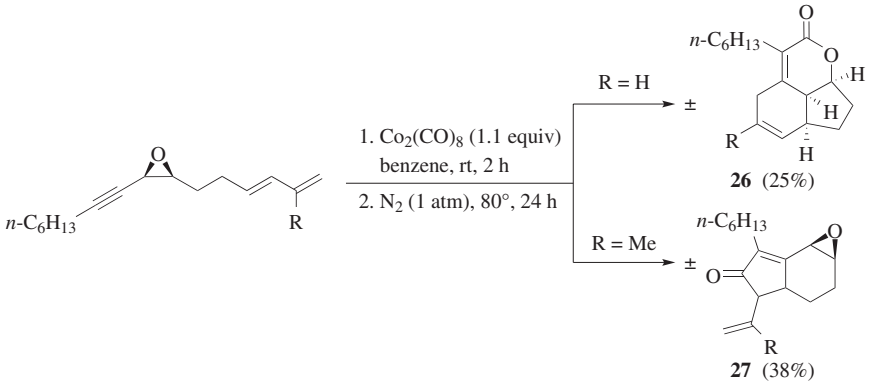
The mechanism of the carbonylation of alkynyl epoxides is comparable to that of the Pauson–Khand reaction[150] with $Co_2(CO)_8$ as the catalyst (Scheme 47; CO ligands are omitted from [Co] in the scheme). The reaction is formally a [5 + 1]/[2 + 2 + 1] cycloaddition in which, depending on the reaction conditions, one or two molecules of CO are incorporated to produce a tricyclic product. The initial step involves coordination of both cobalt centers to the alkyne with concomitant loss of two CO molecules to produce complex **19**[47] (Scheme 47), which has been observed in the Pauson–Khand reaction.[151] The epoxide is then ring opened by nucleophilic attack of the $Co_2(CO)_6$ fragment to give the zwitterion **20**. The alkoxide of intermediate **20** can attack one of the bound CO molecules to give intermediate **21**, which undergoes a reductive elimination to produce the core δ-lactone structure in complex **22a**. This allene-containing δ-lactone



Scheme 47

(as depicted in structure **22b**) is well-suited for cyclization with the tethered alkene to produce the tricyclic metallocyclopentane **23**. This metallocycle is the common intermediate for two different products, depending on the reaction conditions. When the cyclization is run under relatively high pressures of CO (3.5 atm), product **24** is formed via CO insertion followed by reductive elimination. However, under 1 atm CO or N_2, significant quantities of cyclobutane product **25** are formed from the direct reductive elimination of the metallocyclopentane. The relative configuration of the epoxide is very important for successful reaction. The alkyne and alkene substituents of the epoxides must be in a *cis* orientation; the *trans*-epoxides do not produce any cyclic products and only epoxide starting material is recovered (see footnote a in Table 3B).[46]

An alternative reaction pathway that is operative for dienynes involves a [5+1]/[4+2] cyclization to form δ-lactone **26** or a competing [2+2+1] cyclization to form the traditional Pauson–Khand ketone product **27**. Subtle changes in alkene substitution can result in exclusive formation of product **26** or product **27**, or mixtures of the two (Scheme 48).[46]

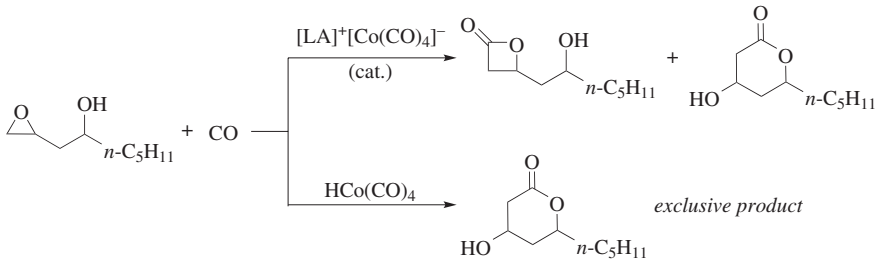


Scheme 48

SCOPE AND LIMITATIONS

Carbonylation of Homoglycidols

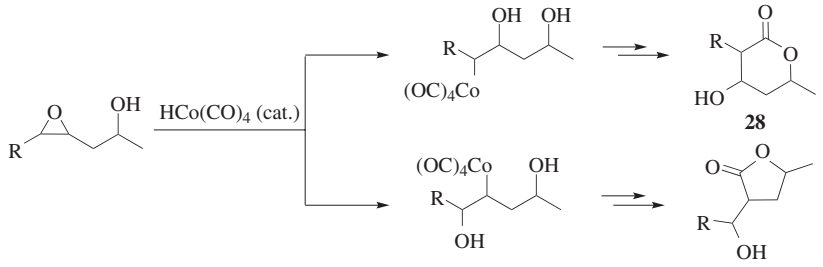
The choice of catalyst is vital for the efficient carbonylation of homoglycidols to δ-lactones. Although a number of Lewis acid based catalysts successfully produce 3-hydroxy δ-lactones, these reactions are always complicated by β-lactone formation. The δ- to β-lactone ratios range from about 4:1 to 1:4, but neither product is cleanly produced in any of these examples. The only catalyst that has been demonstrated to cleanly convert homoglycidols to 3-hydroxy δ-lactones is $HCo(CO)_4$ (Scheme 49).[24] This catalyst is ineffective for the carbonylation of epoxides to β-lactones,[59] and it is speculated that a β-hydroxy cobalt acyl species is formed but does not ring close. Such a species is analogous to structure **13** (Scheme 44, LA = H) such that only pathway B is kinetically accessible, resulting in a δ-lactone as the exclusive product (Scheme 49).



Scheme 49

When $HCo(CO)_4$ is employed under the optimized reaction conditions, a functionally diverse set of 3-hydroxy δ-lactones can be prepared (see Table 3A). A number of sterically diverse alkyl-substituted homoglycidols are efficient substrates. Despite $HCo(CO)_4$ being a common catalyst for olefin hydroformylation,[152] homoglycidols with pendant olefins are selectively carbonylated at the epoxide without reaction of the olefin. Ethers and halogenated side chains are also compatible.

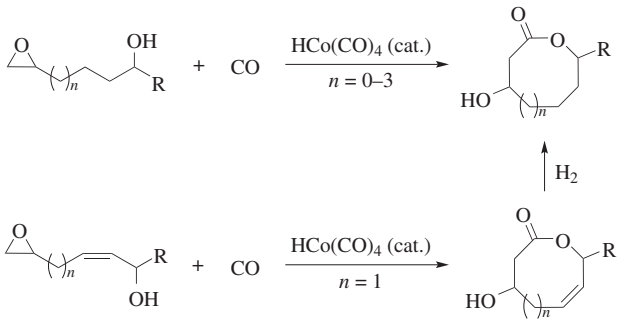
One limitation to this procedure is that it is only selective with monosubstituted homoglycidols. Epoxide ring opening by $[Co(CO)_4]^-$ is highly dependent on epoxide substitution.[25] Therefore, ring opening of monosubstituted epoxides occurs exclusively at the unsubstituted position to produce an intermediate that is well-suited for ring closing to form δ-lactones. Although ring opening of 1,1-disubstituted epoxides has not been attempted, 1,2-disubstituted epoxides ring open at both positions without site selectivity, producing two different intermediates that ring close to produce both δ- and γ-lactones (Scheme 50). Therefore, δ-lactones with substituents at the 2-position (product **28**, R ≠ H) are not selectively produced through homoglycidol carbonylation.



Scheme 50

An extension of alcohol-substituted epoxide carbonylation that has not yet been attempted is the synthesis of larger lactone rings (Scheme 51). Although ring closing to form lactones with ring sizes of seven, eight, nine, and ten has been shown to be several orders of magnitude slower than the analogous four-, five-, and six-membered ring closing,[153] one strategy that improves ring closing is the incorporation of *cis* double bonds into the tether.[154,155] Because alkenes are tolerated under epoxide

carbonylation conditions,[24] this strategy may also be applicable to the carbonylation of hydroxy-substituted epoxides (Scheme 51). Thus, extending the range of lactones accessible through epoxide carbonylation could have applications in the synthesis of macrolactone-containing natural products.[156]

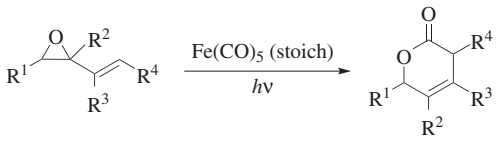


Scheme 51

Carbonylation of Vinyl Epoxides

The carbonylation of vinyl epoxides is generally catalyzed by iron carbonyl species. Both $Fe_2(CO)_9$[50] and $Fe(CO)_5$[52] have been used. Iron pentacarbonyl requires irradiation to form the reactive $Fe(CO)_4$ species, and the same catalytic species can be formed through the thermolysis of $Fe_2(CO)_9$.[157] Other transition metal catalysts containing palladium, rhodium, and cobalt have been used with varying degrees of success.[52,53]

Highly substituted vinyl epoxides are viable substrates for the iron-mediated carbonylation to form δ-lactones. 1,1-Disubstituted, 1,2-disubstituted, and trisubstituted epoxides all are reactive, and although the ratios of δ- to β-lactones are variable, overall yields are not diminished with highly substituted epoxides. Furthermore, substituted alkenes (both 1,1- and 1,2-disubstituted) are effective substrates. The high tolerance for substituted epoxides allows access to substitution at every carbon of the δ-lactone product (Scheme 52). Unfortunately, the functional group tolerance has not been well studied, as alkyl groups are the only substituents that have been reported for this carbonylation.

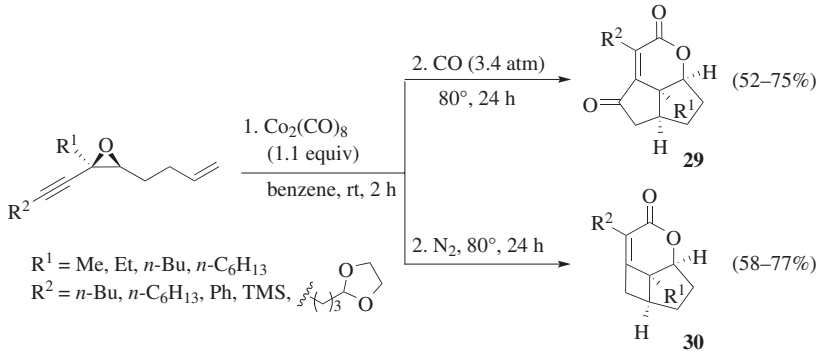


Scheme 52

Carbonylation of Alkynyl Epoxides

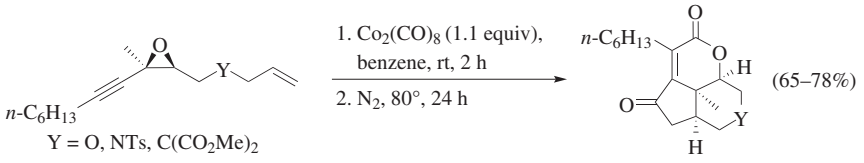
As mentioned above, the cobalt-mediated carbonylation of alkynyl epoxides has the potential to form two different tricyclic δ-lactone products via [5+1]/[2+2+1]

and [5+1]/[2+2] cycloadditions. The product ratios are highly dependent on both the reaction conditions and the epoxide substrates. When the reaction is run under a pressure of CO, the [5+1]/[2+2+1] mechanism generally dominates to form product **29** exclusively (Scheme 53, see footnote a in Table 3B).[46] However, under a nitrogen atmosphere, the intermediate cobalt metallocycle **23** (Scheme 47) undergoes a reductive elimination without CO insertion to form product **30** predominantly.[46] Reductive elimination prior to CO insertion is not observed with some substrates: disubstituted epoxides and epoxides with an ether linkage in the alkene side chain do not form cyclobutane-containing products, even when the reaction is performed without CO. In these cases, two molecules of CO are provided by $Co_2(CO)_8$ to give the [5+1]/[2+2+1] products. Similar reactivity with heteroatom-containing substrates has been documented for the Pauson–Khand reaction.[151,158]

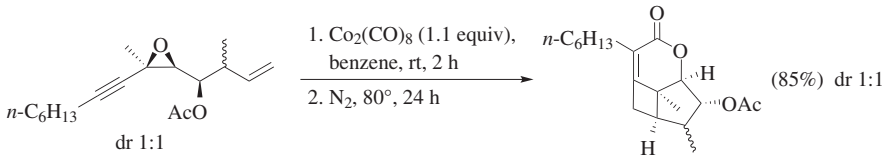


Scheme 53

The cyclocarbonylation of alkynyl epoxides is tolerant of a number of functional groups and substitution patterns. Trimethylsilyl- and 1,3-dioxolane-substituted alkynes afford tricyclic products that are well-suited for further functionalization (Scheme 53).[46] Alkenes with propylene tether lengths result in 6-membered rings fused to the δ-lactones, and the inclusion of heteroatoms such as an oxygen or tosylamide in the tether facilitates the cycloaddition (Scheme 54, see footnote a in Table 3B).[46] Functional groups on the alkene tether are well-tolerated, as epoxides with methyl, methoxy, and acetoxy substitution form δ-lactone products under standard conditions (Scheme 55, see footnote a in Table 3B).[46] Finally, further substitution on the fused ring can be achieved with a 1,2-disubstituted alkene and an α,α-dimethyl alkene, though harsher conditions are required for reaction of these substrates.[46]



Scheme 54

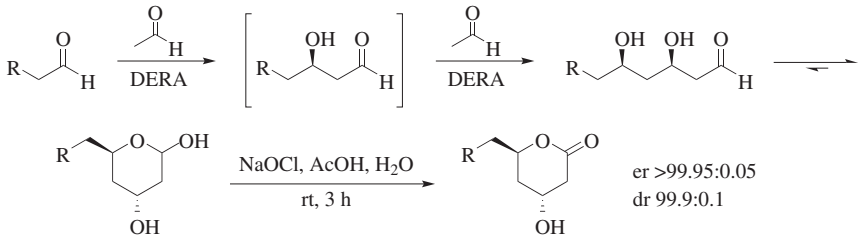


Scheme 55

COMPARISON WITH OTHER METHODS

δ-Lactones are commonly prepared through the acid-induced ring closing of δ-hydroxy acids and esters.[124] Although this ring closing is relatively efficient, it is not as facile as the analogous procedure for producing γ-lactones and can sometimes be complicated by polymer formation.[124] There are, however, many methods for producing δ-lactones, and this section focuses on alternative syntheses specific to 3-hydroxy δ-lactones and α,β-unsaturated δ-lactones, which are the primary products from epoxide carbonylation.

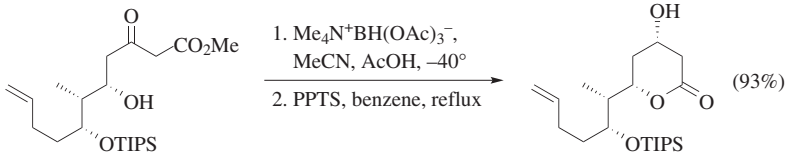
Substituted 3-hydroxy δ-lactones constitute the biologically relevant portion of HMG-CoA reductase inhibitors, commonly known as statin drugs.[159] Because of their importance in pharmaceutical development, a large body of work has focused on their efficient synthesis. Biocatalytic routes have shown a good deal of promise, as δ-lactones can be prepared with excellent enantioselectivity from prochiral starting materials.[160] The most established of these methods involves the DERA-catalyzed (DERA = 2-deoxyribose-5-phosphate aldolase) tandem aldol reaction to form an enantiopure lactol that can be oxidized to the lactone (Scheme 56).[159,161] This is an excellent method for the few specific substrates that are important pharmaceutical intermediates, but poor substrate generality and the necessity for enzyme optimization limit the broad applicability of this reaction for the synthesis of diversely substituted δ-lactones.



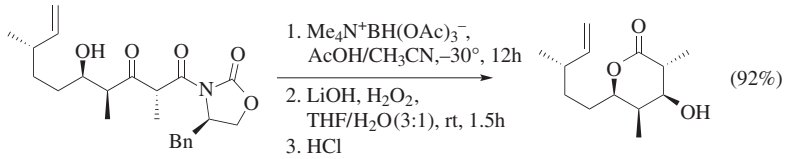
Scheme 56

In the chemical synthesis of 3-hydroxy δ-lactones, a common step prior to ring closing is the reduction of a β-keto ester, which can be performed stereoselectively using a directing group. As shown in Scheme 57, a hydroxy group with defined configuration can be used for that purpose.[162] Another strategy employs a chiral auxiliary to direct consecutive aldol additions. Then, directed reduction of the β-keto amide

followed by acid-promoted ring closing forms the diastereomerically pure 3-hydroxy δ-lactone (Scheme 58).[163]

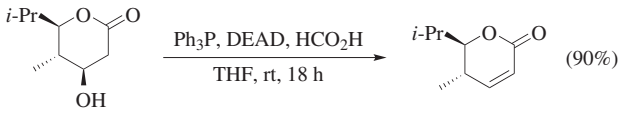


Scheme 57

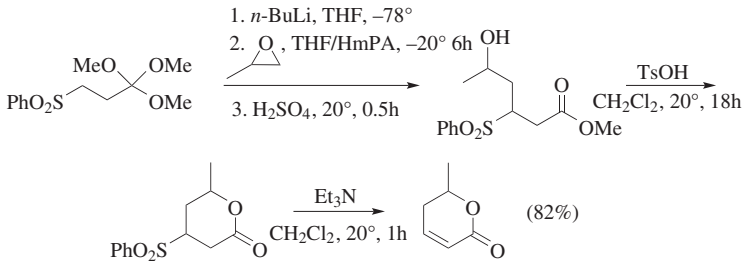


Scheme 58

Unsaturated δ-lactones are commonly produced by the elimination of a suitable leaving group in the 3-position of the lactone. For example, 3-hydroxy δ-lactones, which can be prepared by homoglycidol carbonylation as well as the methods discussed above, can be dehydrated to form α,β-unsaturated δ-lactones under typical Mitsunobu conditions (Scheme 59).[164] Another method employs epoxide ring opening by trimethyl 3-(phenylsulfonyl)orthopropanoate, a practical homoenolate equivalent, which forms an intermediate that undergoes lactonization upon acidic workup (Scheme 60).[165,166] Elimination of the sulfonyl group under basic conditions produces the corresponding α,β-unsaturated δ-lactones in good yields when monosubstituted epoxides are used.



Scheme 59



Scheme 60

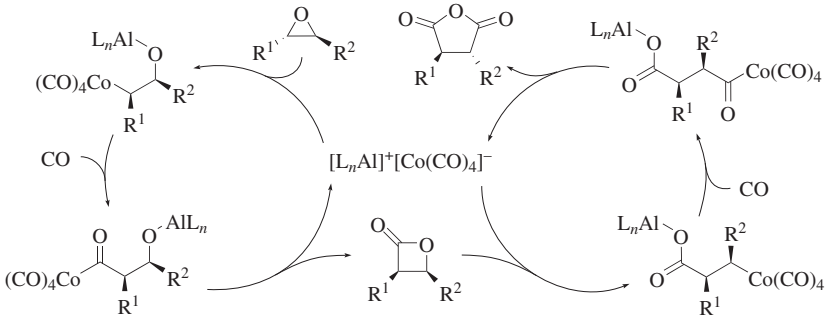
These elimination methods are useful for the preparation of α,β-unsaturated lactones, but lactones with unsaturation elsewhere are not accessible. One the other hand, the carbonylation of vinyl epoxides has the potential advantage of producing both α,β- and β,γ-unsaturated δ-lactones (Table 3B).

EPOXIDE CARBONYLATION TO SUCCINIC ANHYDRIDES

Succinic anhydrides may be formed by the catalytic insertion of two molecules of CO, one into each carbon–oxygen bond of the epoxide. β-Lactones formed from the single carbonylation of epoxides may undergo a second ring-expanding carbonylation to afford the five-membered succinic anhydrides. Under favorable reaction conditions this double carbonylation may be performed in one pot. The product succinic anhydrides are useful as synthetic intermediates[167−169] and as monomers for polymerization.[170,171]

MECHANISM AND STEREOCHEMISTRY

The mechanism of epoxide double carbonylation has been the subject of a detailed study.[21] In every case, the reaction first effects carbonylation of the epoxide to a β-lactone, followed by a second catalytic carbonylation to yield the anhydride (Scheme 61). Both epoxide and lactone carbonylation cycles proceed through the same elementary steps: (1) coordination to the Lewis acidic cation, which activates the substrate for ring-opening S_N2-type attack by $[Co(CO)_4]^-$; (2) migratory insertion of CO; and (3) nucleophilic attack of the alkoxide or carboxylate on the cobalt acyl, resulting in ring closing and formation of the product. Ring closing is the rate determining step for the first cycle and ring opening is the rate determining step for the second.[21]

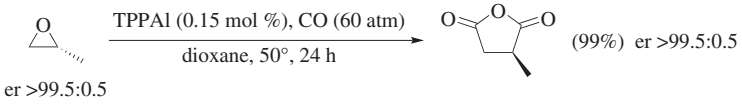


Scheme 61

An interesting and practical consequence of the different rate-determining steps in each of these parallel cycles is that the first carbonylation of the epoxide to the β-lactone proceeds to completion before any of the β-lactone intermediate is consumed to form the anhydride in the second carbonylation step. Furthermore, the donicity and polarity of the reaction solvent drastically affect the rate of each carbonylation, such

that the choice of solvent determines whether single or double carbonylation will occur (Scheme 17). Kinetic studies indicate that epoxide carbonylation is accelerated by coordinating solvents such as THF, whereas lactone carbonylation is inhibited by THF and accelerated by nonpolar solvents such as toluene. Thus, to obtain good activity for both of these catalytic cycles, the reaction is performed in 1,4-dioxane, which has the appropriate combination of moderate donating ability and low polarity.[21]

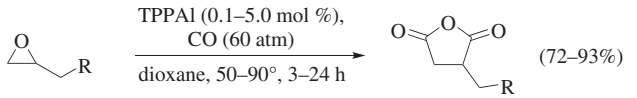
A significant outcome of the S_N2-type mechanism as opposed to an oxidative addition/reductive elimination mechanism is that the stereocenter adjacent to each inserted carbonyl is inverted with each ring-opening step, resulting in a net double inversion. Thus, *cis*-epoxides are carbonylated to *cis*-anhydrides via *trans*-lactones, and *trans*-epoxides are carbonylated to *trans*-anhydrides via *cis*-lactones (Scheme 61). Because each carbonylation occurs with complete inversion of configuration, anhydrides with high diastereomeric and enantiomeric purity are produced. For example, (*R*)-propylene oxide is converted into (*S*)-methylsuccinic anhydride with excellent preservation of enantiopurity (Scheme 62).[21] Given the many excellent methods for the highly stereoselective synthesis of epoxides,[12−16] this method can be used to produce diastereomerically and enantiomerically pure anhydrides. One limitation is that under typical reaction conditions, the catalyst epimerizes the product after it is formed. However, epimerization can easily be avoided by carrying out the carbonylation at lower temperatures (Scheme 62).[21,54]



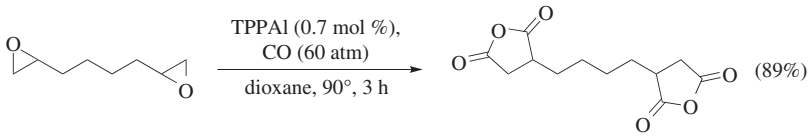
Scheme 62

SCOPE AND LIMITATIONS

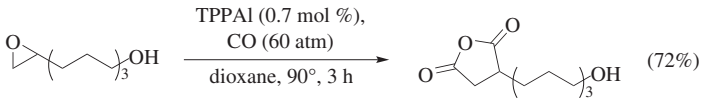
Epoxide double carbonylation is effective for the majority of substrates that can be carbonylated to β-lactones, and it is compatible with a range of functional groups including alkanes, alkenes, aromatics, ethers, esters, ketones, acetals, alcohols, nitriles, and amides (Scheme 63), as well as substrates with multiple epoxides (Scheme 64).[21] Tolerance of the alcohol functional group is particularly interesting, as epoxides are known to react with alcohols under carbonylation conditions, resulting in ring-opening alkoxycarbonylation. Furthermore, alcohols may react with the product anhydride; however, the use of solvent reduces intermolecular reactions, and steric or geometric constraints may prevent intramolecular reactions (Scheme 65).[21]



Scheme 63



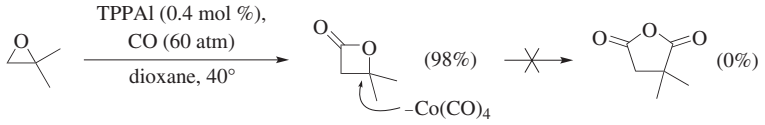
Scheme 64



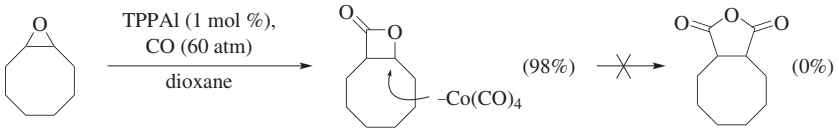
Scheme 65

Epoxides containing strongly Lewis basic groups such as primary amines are typically unreactive for anhydride formation, presumably due to competitive coordination of these groups to the Lewis acidic catalyst. Anhydrides are generally not formed in good yield from glycidyl esters, as the β-lactone intermediates preferentially rearrange to form γ-lactones (see above), and epoxides with multiple sites for nucleophilic attack, such as epichlorohydrin and 1,2-epoxy-3-butene, do not form anhydrides cleanly.[21]

Anhydrides are readily obtained from both monosubstituted and vicinally disubstituted epoxides. Products with *trans*-substituents generally require lower catalyst loading and are formed with higher selectivity than the corresponding *cis*-substituted products, which have more steric hindrance. Geminally disubstituted epoxides are unreactive. For example, 1,2-epoxy-2-methylpropane is carbonylated to the β-lactone, but further carbonylation would require an S_N2 attack on the tertiary center of the lactone, which is not observed (Scheme 66).[21] Disubstituted epoxides as part of fused rings have, thus far, also been unreactive for anhydride formation (Scheme 67).[83]



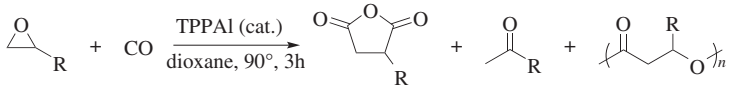
Scheme 66



Scheme 67

The selectivity for anhydride formation is typically very high, but it can be significantly affected by reaction conditions. The most common side products are ketones

(Scheme 68), which result from the catalytic isomerization of the epoxides under low CO pressures and high temperatures (see above). Thus, to avoid ketone formation at the higher temperatures (90°) used for accelerating the reaction, high CO pressure (14–60 atm) must be used. However, it is possible to maintain good selectivity and moderate activity at lower CO pressure (4–7 atm) if the reaction mixture is not heated until after the starting epoxide has been converted into the β-lactone. Polyesters are the other potential side products (Scheme 68), which are formed by the ring-opening polymerization of β-lactone intermediates. However, substrate concentrations of 1.0–2.0 M are typically dilute enough to avoid this polymerization and maintain high selectivity (>98%) for the anhydrides.[21]

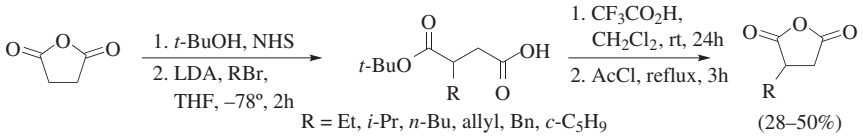


Scheme 68

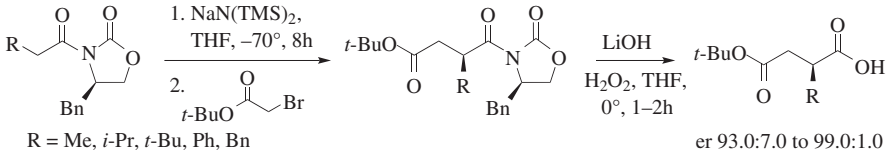
Ring-expanding carbonylation of epoxides to succinic anhydrides is only possible in the presence of a catalyst, and the majority of catalysts that are efficient for carbonylation of epoxides to β-lactones will also carbonylate β-lactones to succinic anhydrides. However, higher temperatures and longer reaction times, as well as the appropriate solvent, are typically required for efficient conversion. The double carbonylation can be run in a number of solvents, but it is uniquely rapid in 1,4-dioxane, which facilitates both the first and second carbonylation steps. The most active catalysts for carbonylation to anhydrides are based on the [Lewis acid]$^+$[Co(CO)$_4$]$^-$ motif, and contain porphyrin metal cations. Catalysts with chromium porphyrin cations tend to produce more poly(lactone) side products. Thus the preferred catalysts, which demonstrate the highest activity and selectivity, are based on porphyrin aluminum cations, such as the commercially available TPPAl (Fig. 1). As with all [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, TPPAl is air-sensitive, and must be handled under nitrogen. Thus, solvents and substrates are typically dried and degassed prior to carbonylation.[21]

COMPARISON WITH OTHER METHODS

Substituted succinic anhydrides have previously been synthesized by a number of methods.[172] Ring-closing condensation of 1,4-diacids or their derivatives is a straightforward transformation, and there are many reagents known to facilitate anhydride formation.[173] There are many methods for the synthesis of succinate esters, which can be cyclized to the corresponding anhydride (Scheme 69).[172,174] The most widely used approach to enantiomerically enriched succinates employs chiral enolates (Scheme 70).[175–177] Although this method is more versatile for the synthesis of highly substituted anhydrides, the diastereoselectivity of vicinally substituted succinates synthesized via chiral enolates[178] is lower than in succinates made by epoxide carbonylation.

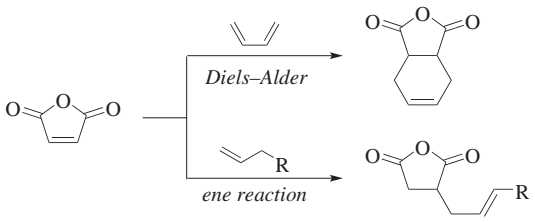


Scheme 69



Scheme 70

Derivatization of maleic anhydride via the Diels–Alder or ene reactions is another common method for the synthesis of succinic anhydrides (Scheme 71). Maleic anhydride is an excellent dienophile,[179] readily forming fused rings which are inaccessible via epoxide carbonylation. The ene reaction, a mono-alkene variation of the Diels–Alder reaction,[180–182] is used industrially for the synthesis of alkenyl succinic anhydrides. Substrates other than epoxides, such as alkenes,[183,184] alkynes,[185] and alkenoic acids,[186] can also be carbonylated to succinic anhydrides; however, these carbonylations are less synthetically useful due to low yields, formation of significant amounts of side products, or lack of demonstrated substrate generality.



Scheme 71

In general, the advantage of the epoxide double carbonylation is its efficiency as a catalytic method for the synthesis of anhydrides in a single step from readily available epoxides and catalysts. The products can be mono- or disubstituted and contain a range of functional groups, and high levels of stereochemical purity are retained through the carbonylation. The reaction is limited by the requirements for high-pressure and air-free reaction conditions and by the scope of substrates containing strong electrophiles and nucleophiles or steric and conformational restrictions.

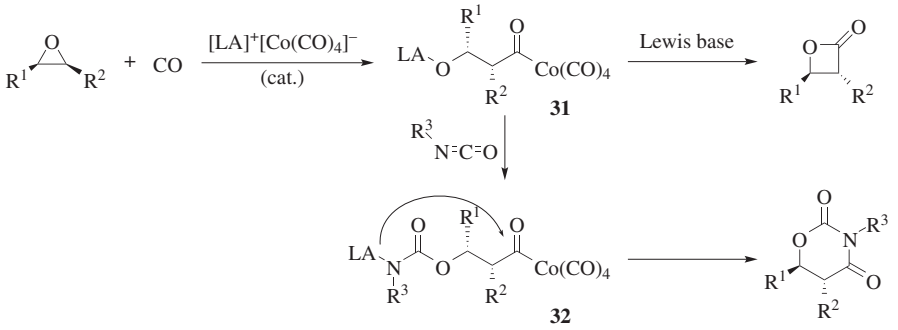
EPOXIDE CARBONYLATION TO 1,3-OXAZINANE-2,4-DIONES

The carbonylation of epoxides has been expanded to include multicomponent coupling reactions. The addition of isocyanate to an epoxide carbonylation reaction

results in formation of a 1,3-oxazinane-2,4-dione.[22] This class of heterocycles has received interest as synthetic intermediates[187−190] and has been investigated as potential therapeutic agents.[191−194]

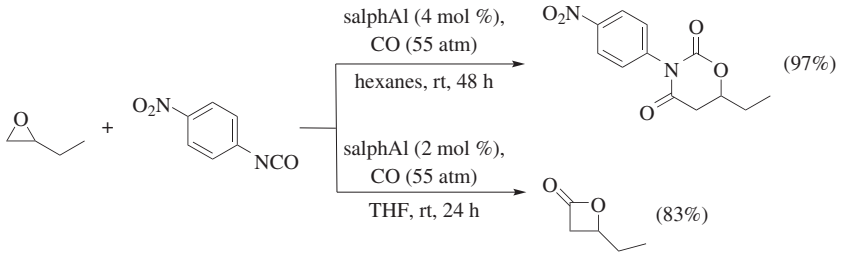
MECHANISM AND STEREOCHEMISTRY

The discovery of epoxide carbonylation to oxazinanediones resulted from mechanistic studies of epoxide carbonylation to β-lactones.[22,25] The initial steps of β-lactone and oxazinanedione formation are identical (Scheme 2 and Scheme 72). The mechanisms diverge when the catalytic resting state **31** is intercepted by an isocyanate, resulting in the formation of an aluminum carbamate **32**. Nucleophilic attack on the cobalt acyl by this carbamate closes the ring, regenerates catalyst, and forms the product oxazinanedione. Conditions that slow the formation of a β-lactone will increase the relative lifetime of the catalyst resting state, thus improving the probability that it will react with an isocyanate to form the oxazinanedione.[22,25]



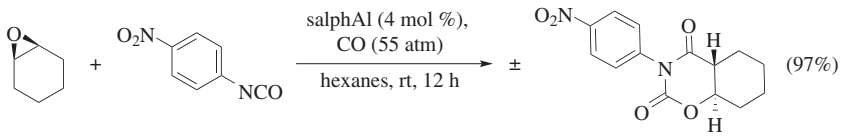
Scheme 72

As with other epoxide carbonylations employing [Lewis acid]$^+$[Co(CO)$_4$]$^-$ catalysts, the solvent dramatically influences product selectivity (Scheme 73).[22] Coordinating Lewis basic solvents such as THF accelerate the formation of β-lactones, whereas nonpolar and noncoordinating solvents such as hexanes slow the ring-closing step, increasing the lifetime of the catalyst resting state **31**. Thus hexane, which is a poor solvent for β-lactone formation, facilitates the reaction of the ring-opened epoxide with an isocyanate prior to ring closing, improving the selectivity for oxazinanedione.[22]

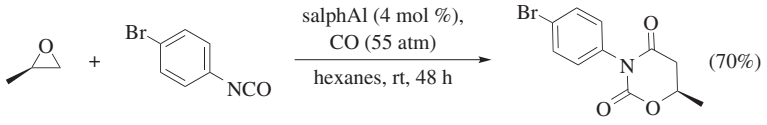


Scheme 73

As in most other epoxide carbonylations, initial nucleophilic attack by $[Co(CO)_4]^-$ occurs with excellent site selectivity at the least-substituted carbon of the epoxide. This attack results in inversion of the stereocenter, while the configuration of the other stereocenter is retained. For example, cyclohexene oxide is carbonylated to the *trans*-oxazinanedione (Scheme 74),[22] whereas (*R*)-propylene oxide gives the (*R*)-oxazinanedione (Scheme 75).[22]



Scheme 74

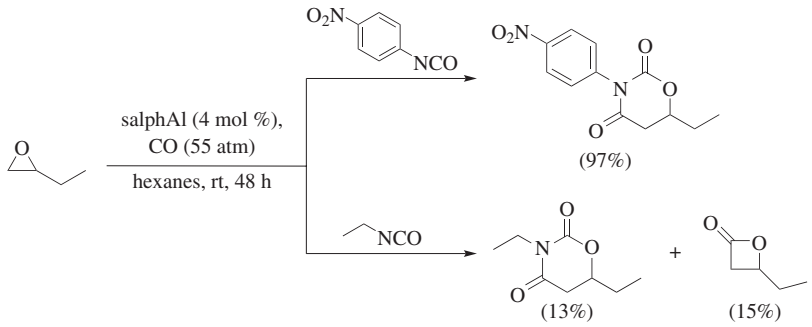


Scheme 75

SCOPE AND LIMITATIONS

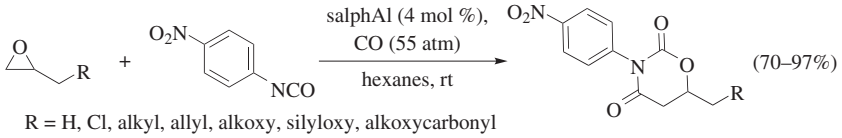
The multicomponent coupling of epoxides, isocyanates, and CO is typically run in hexanes at room temperature and 50 atm of CO with 1.0 equivalent of an isocyanate and 0.04 equivalent of salphAl. The primary concern in optimizing reaction conditions is improving the selectivity for oxazinanediones over β-lactones. For this reason, salphAl is the preferred catalyst because it is one of the slowest well-defined catalysts for β-lactone ring closing. The addition of an excess of isocyanate decreases selectivity for oxazinanedione, as it can accelerate the ring closing to β-lactone. Higher temperature and lower catalyst loading also result in decreased selectivity. Finally, the high pressure of CO is used to avoid the catalytic isomerization of epoxide to ketone that has been observed in other carbonylation systems at low CO pressures (Scheme 19).[22]

Selectivity for oxazinanedione also depends critically on the electrophilicity of the isocyanate. Electron-rich alkyl isocyanates react slowly with the aluminum alkoxide **31**, which permits the competitive, intramolecular ring closing to form β-lactones. More electron-deficient aryl isocyanates react faster with alkoxide **31**, diverting the ring-opened epoxide intermediate away from β-lactone formation and improving selectivity for the oxazinanedione. Thus, whereas most isocyanates react to form some oxazinanedione, the multicomponent coupling is most efficient using highly electrophilic aryl isocyanates with electron-withdrawing substituents (Scheme 76).[22]



Scheme 76

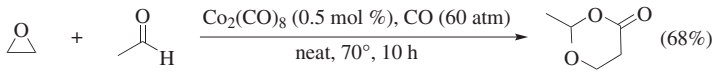
The epoxide component may include a much broader scope of starting materials than the isocyanate, and a number of pendant functional groups are tolerated (Scheme 77). Depending on the specific substrate, selectivity for oxazinanedione versus β-lactone varies, but is generally >10:1, and when using 4-nitrophenyl isocyanate, oxazinanedione is generally the only product observed. Epoxides with bulky substituents, such as 1,2-epoxy-3,3-dimethylbutane, give low conversion and poor selectivity for oxazinanedione and styrene oxide is inactive.[22] However, most of the epoxides that are active for carbonylation with Lewis acid cobaltate catalysts (see β-lactone section) are also expected to be active for the formation of oxazinanediones.



Scheme 77

Bicyclic and *cis*-disubstituted epoxides readily undergo carbonylation and trapping with isocyanates to afford the corresponding *trans*-oxazinanediones (Scheme 74). However, *trans*-disubstituted epoxides exhibit much lower activity, which may be due to the increased steric hindrance in forming the *cis*-product. Cyclohexene oxide does not carbonylate to form a β-lactone, due to the ring strain of *trans*-[4.2.0] bicyclic rings (Scheme 16), but it readily forms the much less strained *trans*-oxazinanedione (Scheme 74).[22]

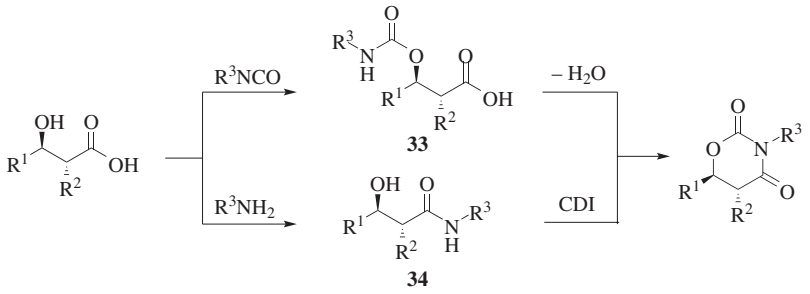
Although isocyanates are the only reagents that have been successfully employed, it is possible that other amphoteric electrophiles may be used to intercept the ring-opened intermediate **31** (Scheme 72) in epoxide carbonylation. These other electrophiles would result in new multicomponent coupling products via epoxide carbonylation. For example, a report in the patent literature describes the coupling of epoxide, CO, and aldehyde using a cobalt carbonyl catalyst (Scheme 78).[195]



Scheme 78

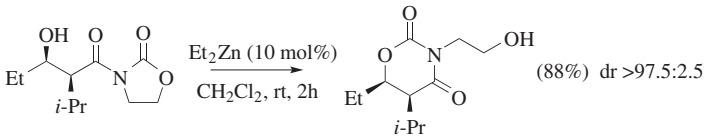
COMPARISON WITH OTHER METHODS

Oxazinanediones have been synthesized by a few methods, most often via a β-hydroxy acid derivative, commonly by reaction with a cyanate or an isocyanate to form intermediate **33** followed by cyclization (Scheme 79, top).[190,196–199] Formation of β-hydroxy amide **34**, followed by ring closing using a carbonyl equivalent such as carbonyl diimidazole (CDI) or diphosgene, also gives good yields of the products (Scheme 79, bottom).[191,200,201] Although these methods require two steps and necessarily generate byproducts, they have the advantage of being applicable to a broader range of substrates than epoxide carbonylation.



Scheme 79

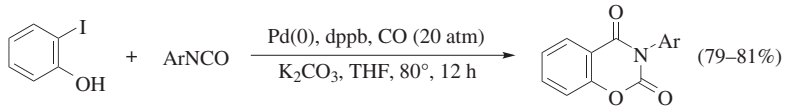
The rearrangement of β-hydroxy-*N*-acyl-2-oxazolidinones is another route to oxazinanediones (Scheme 80).[202] This method is stereoselective and can produce highly stereo-enriched products. Additionally, the aldol reaction is a convenient method to access a large number of possible starting materials. This rearrangement is specific for the formation of *N*-(β-hydroxyalkyl)-substituted oxazinanediones, a class of products that is inaccessible via epoxide carbonylation.



Scheme 80

Carbonylation of iodophenols in the presence of isocyanates is a complementary method for oxazinanedione synthesis in that it forms benzo-fused products which are inaccessible via epoxide carbonylation (Scheme 81).[203] This method proceeds in

good yields and is one of the few transition-metal-catalyzed multicomponent coupling reactions that involve incorporation of CO.[22] Benzo-1,3-oxazinane-2,4-diones have received attention as biologically active compounds.[191–194]



Scheme 81

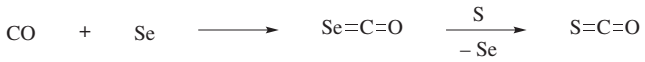
The main advantages of epoxide carbonylation as a route to oxazinanediones are the availability of epoxides, the conservation of stereochemical purity, and its efficiency as a one-pot, atom-economical, multicomponent coupling reaction.

EPOXIDE CARBONYLATION TO 1,3-OXATHIOLAN-2-ONES

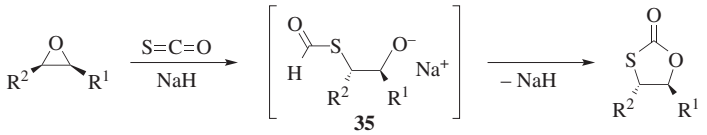
In most ring-expanding carbonylations of epoxides, CO is activated and introduced to the ring via coordination to a transition metal. In the case of epoxide carbonylation to 1,3-oxathiolan-2-ones, insertion of CO is mediated by sulfur, which is also incorporated into the expanded heterocycle.[55,56] Oxathiolanones have demonstrated some utility as synthetic intermediates.[204,205]

MECHANISM AND STEREOCHEMISTRY

The ring-expanding conversion of epoxides into oxathiolanones occurs by first reacting CO with elemental sulfur to generate carbonyl sulfide, which subsequently reacts with an epoxide to form the product. The mechanism of this transformation has not been fully elucidated, but a reaction pathway has been proposed.[55] Carbonyl sulfide is formed catalytically in the presence of base, and this reaction is facilitated by selenium (Scheme 82).[206] The authors propose that nucleophilic ring opening of the epoxide by thioformate results in inversion of the stereocenter bearing the inserted sulfur. Ring closing of the proposed alkoxide intermediate **35** forms the oxathiolane and regenerates the catalyst (Scheme 83).[55] A more plausible mechanism to this and related transformations involves the catalytic action of trace amounts of NaOH in the NaH.

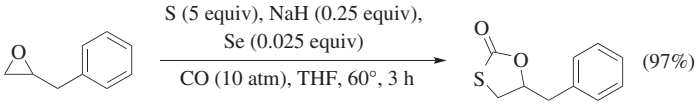


Scheme 82



Scheme 83

Ring-opening inversion of the epoxide converts *cis*-epoxides into *trans*-oxathiolanones (Scheme 83), and *trans*-epoxides into *cis*-oxathiolanones. Nucleophilic attack occurs at the least hindered carbon of the epoxide, resulting in good site selectivity for product 1,3-oxathiolan-2-ones in which the 5-position is the most heavily substituted (Scheme 84).[55]

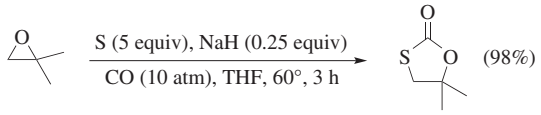


Scheme 84

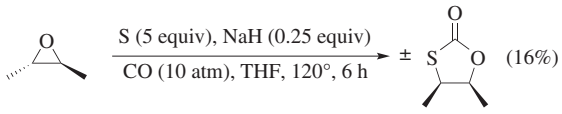
SCOPE AND LIMITATIONS

The carbonylation of epoxides in the presence of sulfur is catalyzed by a number of metal hydrides, as well as amines, such as 1,8-diazabicyclo[5.4.0]undec-7-ene. However, the choice of base is crucial for activity, and NaH gives the highest yields of oxathiolanones (the likely role of NaOH in these reactions, see above). Optimal conditions for this reaction include 5 equivalents of sulfur, 10 atm of CO, and a temperature of 60°. Decreasing the reaction temperature or equivalents of reagents results in lower yields. Using THF as the solvent provides the highest yield, whereas no product is formed in toluene or hexane. Though the cause remains unclear, addition of selenium sometimes catalyzes the reaction, increasing yields for substrates with aryl and benzyl groups but decreasing yields for all other substrates.[55]

Thus far, with the exception of phenyl glycidyl ether, only hydrocarbon-substituted epoxides have demonstrated reasonable activity for this carbonylation; other functional groups remain either unexamined or result in poor yields. The epoxide substitution pattern dramatically affects the yield. Monosubstituted and geminally disubstituted epoxides give high yields of products (Scheme 85),[55] but vicinally disubstituted epoxides are carbonylated in reduced yield. In particular, trisubstituted and *trans*-disubstituted epoxides give very poor yields (Scheme 86).[55]



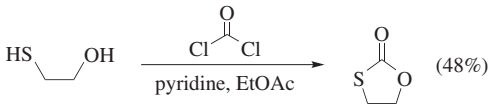
Scheme 85



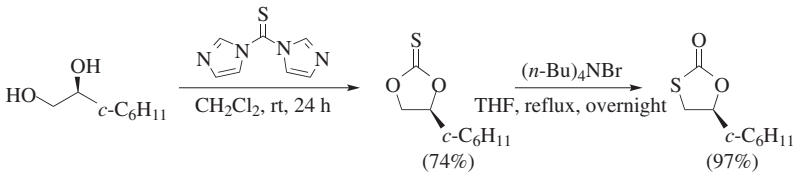
Scheme 86

COMPARISON WITH OTHER METHODS

A straightforward method for the formation of oxathiolanones is the condensation of a β-hydroxythiol with a carbonyl equivalent such as phosgene;[205] however, this pathway is undesirable because it requires the synthesis and handling of malodorous thiols as well as hazardous phosgene (Scheme 87). Other less hazardous carbonyl equivalents, such as ethylene carbonate[207] or ethyl chloroformate,[208,209] have been used in a few examples. A more practical method may be the condensation of a diol with a thiocarbonyl equivalent such as thiophosgene[210] or thiocarbonyldiimidazole,[204,211] followed by a catalyzed rearrangement (Scheme 88).[211] Diols are an attractive starting material, as they are less noxious and excellent methods for their stereoselective synthesis are available.[139]

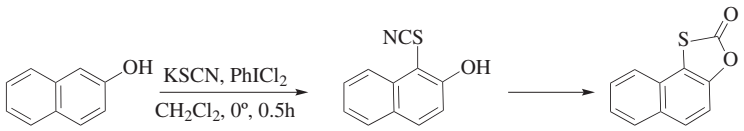


Scheme 87



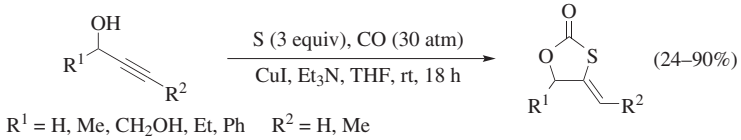
Scheme 88

Benzo-fused oxathiolanones, which cannot be synthesized directly from epoxides, can be formed by the methods discussed above, as well as by a few reactions that are specific to aromatic substrates.[212,213] For example, benzo-oxathiolanones can be synthesized from phenols and potassium thiocyanate (Scheme 89).[214]



Scheme 89

A major advantage of the epoxide carbonylation method is that elemental sulfur is easy to handle and carbonyl sulfide is formed in situ. In a similar reaction, alkynols can be used in place of epoxides to yield analogous products (Scheme 90).[215,216]



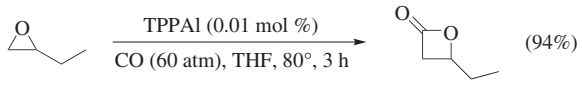
Scheme 90

EXPERIMENTAL CONDITIONS

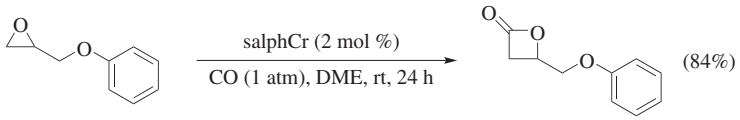
As discussed throughout this chapter, the optimal conditions for epoxide carbonylation reactions are quite diverse. However, one consistent feature to all reactions is that the various catalysts are sensitive to water and O_2. To avoid catalyst decomposition and the occurrence of side reactions, carbonylations are performed in dry reactors using solvents and reagents that have been thoroughly dried and degassed. This restriction likely necessitates the use of a drybox for preparing the reactions, though standard Schlenk techniques can be employed as well.

The reagents required for the carbonylation of epoxides can be hazardous if handled improperly. Epoxides, and particularly the low boiling ones, are highly toxic and as such should only be used in fume hood. Carbon monoxide is a highly toxic gas that is both invisible and odorless. All manipulations involving CO must be performed in a well-ventilated fume hood equipped with a working CO detector. Finally, there is an inherent risk involving any reaction run under elevated pressures. The proper equipment should always be employed (see manufacturer's specifications for pressure ratings), and reactors under pressure should be equipped with a pressure-release device and shielded at all times.

EXPERIMENTAL PROCEDURES

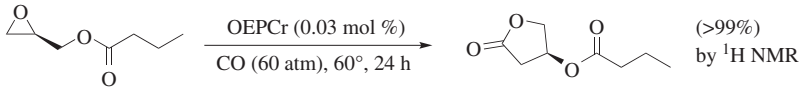


β-Valerolactone [Epoxide Carbonylation to a β-Lactone at High CO Pressure].[81] In a nitrogen-filled drybox, a 300 mL stainless steel Parr reactor was charged with TPPAl (38 mg, 35 μmol), 1,2-epoxybutane (30-mL, 0.35 mol), and THF (30 mL). The reactor was removed from the drybox and pressured with CO (60 atm), followed by rapid stirring and slow heating to 80°. After 3 h, the reactor was cooled on dry ice and carefully vented. The reaction mixture was rinsed out of the reactor and solvent was removed by rotary evaporation. Vacuum distillation gave the product as a clear colorless oil (33 g, 94%): IR 1825 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.44 (dddd, ^3J = 4.3, 5.8, 5.9, 7.0 Hz, 1H), 3.47 (dd, ^3J = 5.8 Hz, ^2J = 16.3 Hz, 1H), 3.03 (dd, ^3J = 4.3 Hz, ^2J = 16.3 Hz, 1H), 1.81 (m, 2H), 0.99 (t, ^3J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.53, 72.38, 42.39, 27.75, 8.93.

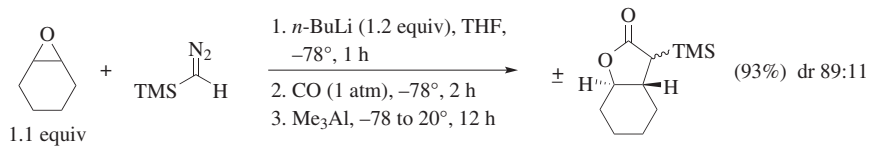


4-Phenoxymethyl-2-propiolactone [Epoxide Carbonylation to a β-Lactone at Low CO Pressure].[18] In a drybox, salphCr (182 mg, 0.200 mmol) was weighed into a 500-mL, oven-dried, three-neck round-bottomed flask with a magnetic stir bar. A dry, 50-mL addition funnel was attached, along with a stopper and a rubber

septum. DME (9.0 mL) was drawn into a Gastight syringe while phenyl glycidyl ether (1.50 g, 10.0 mmol) was drawn into a separate syringe with 1.0 mL DME. The flask was removed to a fume hood where the flask was sparged with CO for 10 min before a double balloon of CO was attached to the flask using a needle to puncture the septum. The flask was then placed into an ice bath, the DME was added to the catalyst, and the mixture was stirred for 10 min. The epoxide solution was added dropwise at 0° via the addition funnel over the course of 30 min while stirring. After epoxide addition was complete, the ice bath was removed and the flask was allowed to warm to rt and the mixture was stirred for 24 h. The flask was vented in a fume hood and the reaction mixture was concentrated under vacuum to an oil. The crude oil was purified by chromatography through silica gel with CH_2Cl_2, and then was recrystallized from CH_2Cl_2/hexanes to afford 4-phenoxymethyl-2-propiolactone (1.5 g, 84%): mp 75–77°; IR (neat, NaCl) 1818 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.31 (t, $^3J = 7.9$ Hz, 2H), 7.00 (t, $^3J = 7.3$ Hz, 1H), 6.92 (d, $^3J = 8.2$ Hz, 2H), 4.83 (dddd, $^3J = 3.0, 4.4, 5.1, 9.5$ Hz, 1H), 4.32 (dd, $^2J = 11.1$ Hz, $^3J = 3.0$ Hz, 1H), 4.19 (dd, $^2J = 11.1$ Hz, $^3J = 4.2$ Hz, 1H), 3.55 (d, $^3J = 5.1$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 158.1, 129.8, 121.8, 114.8, 68.5, 67.3, 40.0; HRMS (EI) *m/z*: calcd for $C_{10}H_{10}O_3$, 178.0630; found, 178.0630.

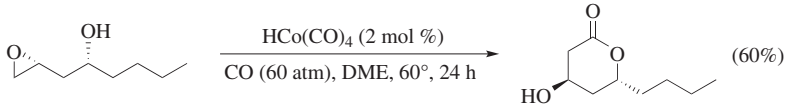


(*S*)-β-Butyroxy-γ-butyrolactone [Epoxide Carbonylation to a γ-Lactone].[28] In a nitrogen-filled drybox at rt, a 4-mL glass vial equipped with a stir bar was charged with OEPCr (9.0 mg, 12 μmol) and (*R*)-glycidyl butyrate (515 mg, 3.57 mmol). The vial was transferred to a stainless steel high-pressure reactor. The reactor was pressured with CO (60 atm) and heated to 60° with stirring. The temperature was held constant for 6 h, at which point the reactor was placed in dry ice for 15 min. After careful venting of excess CO, the glass vial was removed and the mixture was analyzed by ^1H NMR (>99% product). Separation of product from catalyst was accomplished by filtering through a short column of silica gel with $CHCl_3$: IR (neat, KCl) 1789 (C=O), 1738 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.40 (dd, $^3J = 5, 7$ Hz, 1H), 4.48 (dd, $^3J = 5$ Hz, $^2J = 11$ Hz, 1H), 4.31 (d, $^2J = 11$ Hz, 1H), 2.84 (dd, $^3J = 7$ Hz, $^2J = 18$ Hz, 1H), 2.55 (d, $^2J = 18$ Hz, 1H), 2.28 (t, $^3J = 7$ Hz, 2H), 1.61 (sext, $^3J = 7$ Hz, 2H), 0.91 (t, $^3J = 7$ Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 174.9, 173.2, 73.4, 69.8, 36.0, 34.8, 18.4, 13.8; HRMS (EI) *m/z*: calcd for $[C_8H_{12}O_4 + H]^+$, 173.0814; found, 173.0812.



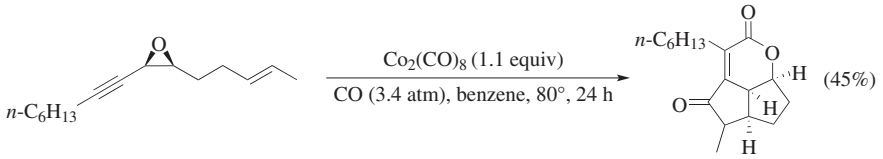
3-(Trimethylsilyl)hexahydrobenzofuran-2(3*H*)-one [Epoxide Carbonylation to a γ-Lactone Using an Ynolate].[45] A 30-mL, round-bottomed flask equipped with a magnetic stir bar, three-way stopcock, and a nitrogen line was flame

dried under a stream of nitrogen. In the reaction flask were placed anhydrous THF (10 mL) and a 2 M hexane solution of trimethylsilyldiazomethane (1 mL, 2 mmol), and the solution was cooled to −78°. A 1.5 M hexane solution of BuLi (1.6 mL, 2.4 mmol) was added dropwise to the solution, which was stirred for 1 h. The three-way stopcock was then connected to a vacuum line and to a balloon of CO through a glass column packed with soda lime and anhydrous calcium sulfate. After two cycles of evacuation and refilling with CO, the reaction mixture was stirred under an atmosphere of CO for 2 h at −78°. A hexane solution of Me_3Al (1.1 mL) was added to the solution of ynolate, which was then warmed to 0° and stirred for 1 h. The solution was cooled to −78° for addition of cyclohexene oxide (215 mg, 2.2 mmol), then gradually warmed to 20° and stirred for 12 h. The resulting mixture was quenched with saturated aqueous NH_4Cl (2.0 mL) at −78°. The solution was filtered through Celite 545, and the residue was washed with Et_2O (2 × 20 mL). The filtrate was washed with saturated aqueous NH_4Cl (20 mL), and the aqueous layer was extracted with Et_2O (2 × 20 mL). The combined ether solutions were dried over anhydrous K_2CO_3, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/EtOAc, 15:1, R_f = 0.09, 0.06) to give a mixture of diastereomers (89:11) as a white solid (93%), mp 39–42°. The isomers were separated by HPLC. Major isomer (R_f = 0.09): IR (KBr) 1759 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.65 (td, ^3J = 10.8, 3.5 Hz, 1H), 2.25–1.20 (m, 10H), 0.15 (s, 9H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 178.65, 85.52, 46.88, 36.71, 30.05, 29.24, 25.59, 24.10, −2.33. Minor isomer (R_f = 0.06): IR (KBr) 1744 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) δ 3.82 (td, ^3J = 10.5, 3.8 Hz, 1H), 2.40–2.15 (m, 3H), 2.00–1.20 (m, 7H), 0.22 (s, 9H); ^{13}C NMR ($CDCl_3$, 67.5 MHz) δ 178.71, 83.25, 47.73, 38.49, 30.84, 28.45, 25.73, 23.99, −0.63. Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.33; H, 9.71.

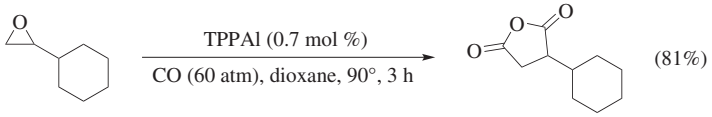


(4*R*,6*R*)-6-Butyl-4-hydroxytetrahydro-2-pyranone [Epoxide Carbonylation to a δ-Lactone].[24] In a drybox, $Ph_3SiCo(CO)_4$[69] (52 mg, 0.12 mmol) and 4-toluenesulfonic acid (21 mg, 0.12 mmol) were weighed into separate flame-dried vials. DME (6.0 mL) was divided evenly into the vials to completely dissolve the catalyst components, then the two solutions were combined to form a colorless solution of $HCo(CO)_4$ (6 mL, 0.02 M in DME). In a drybox an 8-mL vial was charged with (2*R*,4*R*)-4-hydroxy-1,2-epoxyoctane (140 mg, 1.0 mmol) and a magnetic stir bar. A portion of the freshly prepared $HCo(CO)_4$ solution (1.0 mL, 0.02 M in DME) was transferred to the vial via syringe. The vial was transferred to a stainless-steel reactor and pressured with CO (60 atm) and heated at 60° with stirring. After 24 h, the reactor was cooled in dry ice for 10 min then vented in a well-ventilated fume hood. The mixture was concentrated to an oil under vacuum, and the crude product was passed through silica gel, first using hexanes/EtOAc

(70:30) to remove catalyst residue, then with EtOAc/hexanes (70:30) to elute (4*R*,6*R*)-6-butyl-4-hydroxy-δ-lactone (103 mg, 60%): $[\alpha]^{23}_{D}$ + 32.6 (*c* 1.0, $CHCl_3$); IR (neat, NaCl) 3423 (OH), 1719 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.67 (dddd, ^3J = 3.1, 5.1, 7.5, 11.1 Hz, 1H), 4.37–4.30 (m, 1H), 2.97 (d, ^3J = 3.3 Hz, 1H), 2.68 (dd, ^3J = 4.8 Hz, ^2J = 17.7 Hz, 1H), 2.58 (ddd, ^4J = 1.6 Hz, ^3J = 3.6 Hz, ^2J = 17.7 Hz, 1H), 1.95 (dddd, ^4J = 1.6 Hz, ^3J = 4.8 Hz, 3.3 Hz, ^2J = 14.4 Hz, 1H), 1.76–1.24 (m, 7H), 0.89 (t, ^3J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.45, 76.34, 62.65, 38.74, 35.94, 35.33, 27.11, 22.61, 14.09; HRMS (EI) *m*/*z*: calcd for $C_9H_{16}O_3$, 172.1100; found, 172.1102.

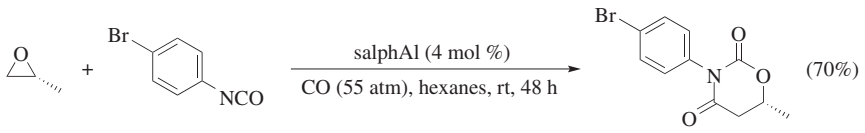


***rel*-(5a*S*, 7a*R*, 7b*R*)-3-Hexyl-5-methyl-2,4,5,5a,6,7,7a,7b-octahydropentaleno[1,6,*bc*]pyran-2,4-dione [Epoxide Carbonylation to a Fused δ-Lactone].[46]** To a benzene solution (5 mL) of the epoxy enyne (100 mg, 0.45 mmol; see footnote a in Table 3B) was added $Co_2(CO)_8$ (170 mg, 0.50 mmol) under nitrogen, and the mixture was stirred for 2 h at rt. The solution was transferred to a high-pressure reactor and heated to 80° under CO (3.4 atm) for 24 h. The solution was filtered through a short silica pad; the filtrate was concentrated and purified using preparative TLC (silica gel, Et_2O/hexane, 1:1) to afford the title product (56 mg, 45%): IR (neat) 1722, 1710 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 5.08 (q, ^3J = 8.0 Hz, 1H), 3.36 (t, ^3J = 6.8 Hz, 1H), 2.91–2.81 (m, 1H), 2.64–2.57 (m, 1H), 2.97–2.03 (m, 1H), 2.35–2.20 (m, 2H), 2.02–1.85 (m, 2H), 1.49–1.12 (m, 8H), 1.14 (d, ^3J = 7.6 Hz, 3H), 1.18–0.98 (m, 1H), 0.83 (t, ^3J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 209.0, 163.7, 141.8, 136.0, 81.3, 50.8, 43.1, 40.4, 31.4, 30.6, 29.6, 29.3, 29.2, 25.8, 22.5, 17.3, 14.0; HRMS *m*/*z*: calcd for $C_{17}H_{24}O_3$, 276.1725; found, 276.1722.

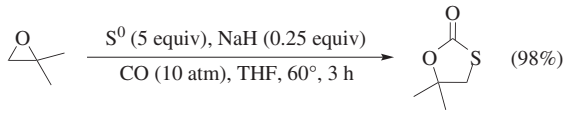


3-Cyclohexyl-3,4-dihydrofuran-2,5-dione [Epoxide Carbonylation to a Succinic Anhydride].[21] A 100-mL, stainless-steel Parr reactor was dried overnight at 120° under vacuum. In a nitrogen drybox, the reactor was charged with TPPAl (262 mg, 0.240 mmol) and 1,4-dioxane (20 mL), then closed and removed from the drybox. The reactor was pressured with CO (14 atm), and the contents were stirred for 10 min to dissolve CO into solution, then the reactor was vented down to 1.5 atm without stirring. 2-Cyclohexyloxirane (4.88 mL, 36.0 mmol) was injected via syringe into the CO-filled reactor at rt, and the reactor was immediately pressured to 60 atm

of CO, followed by rapid stirring and heating to 90°. After 3 h, the reactor was placed on dry ice, cooled to below 0°, and slowly vented. Volatiles were removed under vacuum, and the resulting oil was vacuum distilled to afford a clear oil that solidified on standing. Recrystallization from Et_2O/hexanes yielded the crystalline product (5.32 g, 81%): mp 36°; IR (melt, NaCl) 1861 (C=O), 1785 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.00 (m, 2H), 2.74 (m, 1H), 1.90 (m, 1H), 1.78 (m, 3H), 1.69 (m, 1H), 1.58 (m, 1H) 1.36–0.95 (m, 5H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.14, 170.70, 46.50, 39.12, 31.36, 30.34, 28.47, 26.07, 25.88; HRMS (EI) *m/z*: calcd for $C_{10}H_{14}O_3$, 182.0943; found, 182.0945.



(*R*)-3-(4-Bromophenyl)-6-methyl-1,3-oxazinane-2,4-dione [Epoxide Carbonylation to a 1,3-Oxazinane-2,4-dione].[22] A 60-mL, stainless steel, high-pressure Parr reactor was dried at 120° under vacuum for 16 h, refilled with N_2, and brought into a nitrogen drybox. In the drybox, salphAl (43.7 mg, 0.050 mmol) was weighed into an oven-dried glass insert, and a stir bar was added. Dry hexanes (5.0 mL), (*R*)-propylene oxide (88.0 μL, 1.26 mmol), and 4-bromophenyl isocyanate (248 mg, 1.5 mmol) were added. The reactor was sealed, removed from the drybox, and pressured with CO (55 atm). After stirring the mixture at rt for 48 h, the reactor was vented slowly. Volatiles were removed by rotary evaporation, and the resulting solid was washed through silica gel with EtOAc to remove catalyst residue. The filtrate was concentrated under reduced pressure, then redissolved in CH_2Cl_2, and layered with hexanes to afford the crystalline product (0.250 g, 70%): ^1H NMR ($CDCl_3$, 300 MHz) δ 7.59 (pseudo-d, 2H), 7.07 (pseudo-d, 2H), 4.81 (m, 1H), 2.94 (dd, ^2J = 17.1 Hz, ^3J = 6.3 Hz, 1H), 2.81 (dd, ^2J = 17.1 Hz, ^3J = 11.1 Hz, 1H), 1.56 (d, ^3J = 6.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.9, 151.2, 133.7, 132.8, 130.2, 123.3, 71.3, 38.6, 20.4; HRMS (EI) *m/z*: calcd for $C_{11}H_{10}NO_3{}^{79}Br$, 282.9831; found, 282.9834; calcd for $C_{11}H_{10}NO_3{}^{81}Br$, 284.9824; found, 284.9825.



5,5-Dimethyl-1,3-oxathiolan-2-one [Epoxide Carbonylation to a 1,3-Oxathiolan-2-one].[55] In a 50-mL stainless steel autoclave were placed powdered sulfur (0.321 g, 10 mmol), THF (2 mL), isobutylene oxide (144 mg, 2 mmol), and NaH (24 mg in mineral oil, 0.5 mmol). The apparatus was flushed several times with CO and then was charged with 10 atm of CO. The mixture was heated with stirring at 60° for 3 h. The reaction was quenched with water and the resulting mixture was extracted with diisopropyl ether (15 × 3 mL). The combined organic

layers were dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography on silica gel (hexane/EtOAc, 3:1) gave the title product as a yellow oil (282 mg, 98%): IR (neat) 2981, 2937, 1732 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.38 (s, 2H), 1.58 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.66, 85.38, 42.43, 26.45; MS *m/z*: M^+ 132. Anal. Calcd for $C_5H_8O_2S$: C, 45.43; H, 6.10; S, 24.26. Found: C, 45.27; H, 6.21; S, 24.35.

TABULAR SURVEY

To remain consistent with the organization of this chapter, the following tabular survey of ring expanding carbonylation reactions is organized according to the heterocyclic products formed. However, several of the tables are further divided by substrates or reaction conditions in the cases where significantly dissimilar conditions are utilized to produce the same class of products. Within each table the entries are organized by increasing carbon count for the epoxide substrate, but the following groups are not included in the carbon count: typical protecting groups, simple alkyl ethers, the OR group of esters, the NR_2 group of amides, and carbon-bound silyl groups. In situations where many procedures have been employed to produce the same products, the catalyst (including catalyst loading) is highlighted to emphasize the different selectivity and activity obtained using each procedure. The tabular survey includes reactions reported up through 2008. References appearing after 2008 are listed at the end of the bibliography, organized by table.

The following abbreviations (excluding those listed in "*The Journal of Organic Chemistry* Standard Abbreviations and Acronyms") are used within the Tabular Survey:

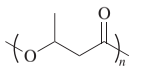
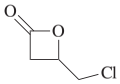
CDI	1,1′-carbonyldiimidazole
CF_3TPPAl	[(tetrakis(4-trifluoromethylphenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
Cp_2Ti	$[Cp_2Ti(THF)_2]^+[Co(CO)_4]^-$
CTAB	cetyltrimethylammonium bromide
1,2-DFB	1,2-difluorobenzene
2,5-DMTHF	2,5-dimethyltetrahydrofuran (*cis*/*trans* mixture)
FTPPAl	[(tetrakis(4-fluorophenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
HTPPAl	[(tetrakis(phenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
MeTPPAl	[(tetrakis(4-methylphenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
OEP	octaethylporphyrin
OEPCr	$[(OEP)Cr(THF)_2]^+[Co(CO)_4]^-$
PPN	bis(triphenylphosphine)iminium
salph	*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-phenylenediamine
salphAl	$[(salph)Al(THF)_2]^+[Co(CO)_4]^-$
salphCr	$[(salph)Cr(THF)_2]^+[Co(CO)_4]^-$
TDA-1	tris(poly-oxaheptyl)amine
TMTU	*N*,*N*′-tetramethylthiourea
TPP	tetraphenylporphyrin
TPPAl	[(tetrakis(4-chlorophenyl)porphyrin)Al$(THF)_2]^+[Co(CO)_4]^-$
TPPCr	$[(TPP)Cr(THF)_2]^+[Co(CO)_4]^-$

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_2				
	$[PPN]^+[Co(CO)_4]^-$ (2 mol %), $BF_3{\bullet}OEt_2$ (2 mol %)	CO (60 atm), DME, 80°, 24 h	 (—), 44	36
C_3				
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96) +  **II** (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 63	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	$Co(acac)_3$ (0.6 mol %), $AlEt_3$ (0.6 mol %)	CO (90 atm), 105°, 48 h	**I** (25)	33
	$[PPN]^+[Co(CO)_4]^-$ (0.6 mol %), $BF_3{\bullet}OEt_2$ (0.6 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (79)	32
	$[PPN]^+[Co(CO)_4]^-$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (60)	32
	$NaCo(CO)_4$ (1.2 mol %)	CO (60 atm), diglyme, 75°, 20 h	**I** (10)	32
	$NaCo(CO)_4$ (1.2 mol %), Et_2AlCl (1.2 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (64)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (92)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 95°, 1.5 h	**I** (92)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 105°, 0.5 h	**I** (91)	33
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (1.2 mol %)	CO (60 atm), diglyme, 75°, 5 h	**I** (96)	32
	$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 75°, 4 h	**I** (92)	32

$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 75°, 5 h	**I** (93)		33
$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 95°, 2 h	**I** (92)		32
$Co_2(CO)_8$ (0.6 mol %), $AlMe_3$ (2.5 mol %)	CO (60 atm), diglyme, 95°, 4 h	**I** (92)		32
$Co_2(CO)_8$ (0.3 mol %), $AlMe_3$ (1.3 mol %)	CO (60 atm), diglyme, 75°, 10 h	**I** (92)		33
$Co_2(CO)_8$ (0.2 mol %), $AlMe_3$ (0.6 mol %)	CO (60 atm), diglyme, 95°, 7 h	**I** (94)		33
$Co_2(CO)_8$ (0.08 mol %), $AlMe_3$ (0.3 mol %)	CO (60 atm), diglyme, 95°, 16 h	**I** (72)		32, 33
salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	**I** (95)		35
$NaCo(CO)_4$ (2 mol %)	CO (70 atm), triglyme, 80°, 16 h	**I** (6)		35
Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (95)		34
$RhClCO(PPh_3)_2$ (1 mol %)	CO (30 atm), MeOH, 20°, 170 h	**I** (5)		41
$RhClCO(PPh_3)_2$ (0.5 mol %)	CO (30 atm), MeOH, 110°, 14 h	**I** (4)		41
$[PPN]^+[Co(CO)_4]^-$ (1 mol %), $BF_3{\bullet}OEt_2$ (1 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (64)		36
$[PPN]^+[Co(CO)_4]^-$ (1 mol %), $BF_3{\bullet}OEt_2$ (1 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (77)		36
$[PPN]^+[Co(CO)_4]^-$ (1 mol %), $B(C_6F_5)_3$ (1 mol %)	CO (60 atm), DME, 80°, 7 h	**I** (68)	+  (17)	36
$Co_2(CO)_8$ (5 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (7)		36
$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), $BF_3{\bullet}OEt_2$ (x mol %)	CO (60 atm), DME, 80°, 24 h	**I**	x: 1 (13); 2 (11)	36

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_3 	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), THF, 80°, 24 h	 **I** (35)	36
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), dioxane, 80°, 24 h	**I** (11)	36
	$Co_2(CO)_8$ (0.5 mol %), PPNCl (1 mol %), BF_3•OEt_2 (1 mol %)	CO (60 atm), benzene, 80°, 24 h	**I** (<5)	36
	$Co_2(CO)_8$ (1 mol %), PPNCl (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (76)	36
	$Co_2(CO)_8$ (1 mol %), CTAB (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), THF, 80°, 24 h	**I** (23) +  (15)	36
 er 99.5:0.5	salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	 **I** (95) er 99.5:0.5	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (95) er 99.5:0.5	34
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	 **I** (98)	26
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (31) +  (4)	26
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 9.5 h	**I** (73)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 5 h	**I** (60)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (83)	36

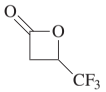
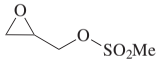
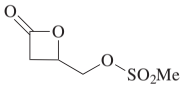
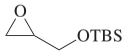
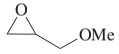
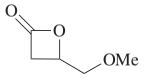
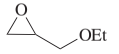
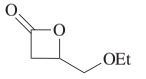
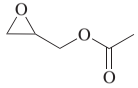
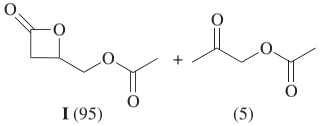
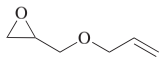
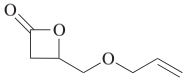
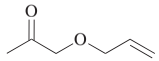
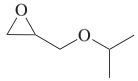
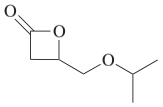
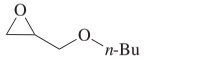
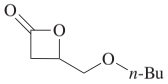
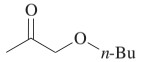
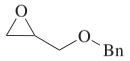
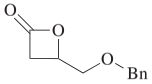
	salphCr (2 mol %)	CO (7 atm), DME, rt	 Time (h): 8 (26); 48 (87)	19 23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (37)	23
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96) + **II** (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (98)	26
	OEPCr (0.06 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (30)	29
	OEPCr (0.13 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
	TPPAl (0.1 mol %)	CO (60 atm), THF, 50°, 2 h	 (99)	83
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (95) (5)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 82	18
	OEPCr (0.3 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (99)	28

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_3				
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (91), 75	18
			+  **II** (9)	
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	18
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (93) + **II** (7)	18
	OEPCr (0.4 mol %)	CO (60 atm), toluene, 60°, 6 h	**I** (88)	28
	[PPN]$^+$[Co(CO)$_4$]$^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	 (—), 86	36
	salphCr (2 mol %)	CO (7 atm), DME, 80°, 0.01 h	 **I** (99), 98	81
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (99), 88	26
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (89) +  (11)	26
	OEPCr (0.04 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 99	18
	OEPCr (0.1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28

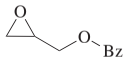
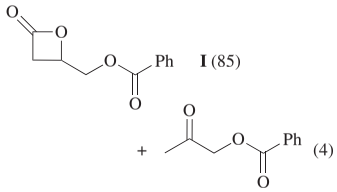
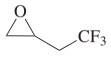
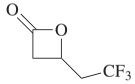
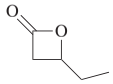
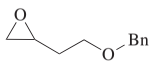
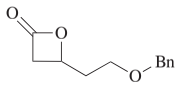
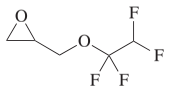
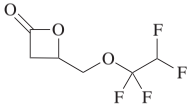
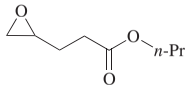
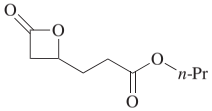
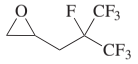
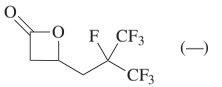
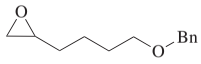
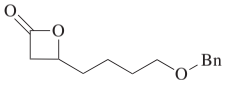
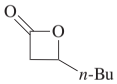
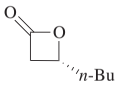
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (85) + (4)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (98)	26
	OEPCr (0.4 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (97)	28
C_4				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99)	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (97) +  (3)	26
	TPPAl (0.01 mol %)	CO (60 atm), THF, 80°, 2 h	**I** (99)	21
	salphCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (98)	26
	salphAl (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (46)	26
	TPPCr (1 mol %)	CO (7 atm), DME, rt, 1 h	**I** (66)	26
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (60)	29
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 2.5 h	**I** (99)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (99)	34
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1.5 h	 (99)	23

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

	Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_5		salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 79	19
		OEPCr (0.07 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
C_6					
		salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	 (—)	19
		salphCr (2 mol %)	CO (7 atm), DME, rt, 20 h	 (99)	23
		salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 93	18
		OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
		TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
		$[PPN]^+[Co(CO)_4]^-$ (2 mol %), $BF_3{\bullet}OEt_2$ (2 mol %)	CO (60 atm), DME, 80°, 24 h	**I** (—), 66	36
	 er 99.5:0.5	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 (99), 92 er 99.5:0.5	18

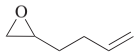
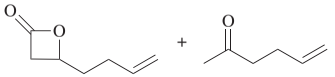
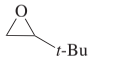
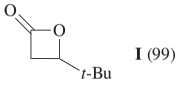
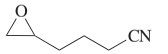
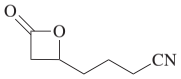
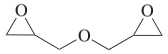
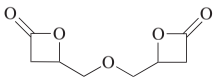
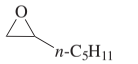
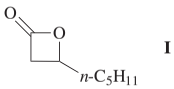
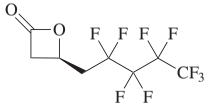
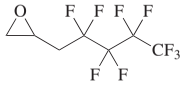
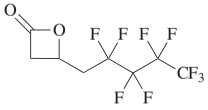
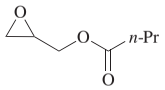
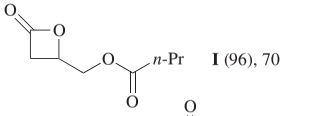
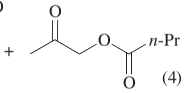
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (95) + (5)	26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 94	18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 4 h	**I** (90)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $BF_3{\bullet}OEt_2$ (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (—), 63	36
	OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (99)	28
	TPPCr (0.1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	TPPAl (0.2 mol %)	CO (60 atm), THF, 60°, 6 h	 (—)	21
	salphCr (2 mol %)	CO (7 atm), DME, rt, 3 h	 (—)	23
C_7				
	OEPCr (0.02 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (99)	28
	TPPCr (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.3 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (40)	29

TABLE 1A. β–LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_7				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h		19
er 99.5:0.5			**I** (99), 88, er 99.5:0.5	
	salphCr (2 mol %)	CO (55 atm), DME, rt, 6 h	 **I** (99)	19
	salphCr (2 mol %)	CO (30 atm), DME, rt, 6 h	**I** (99)	19
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 85	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	**I** (44)	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (36)	19
	salphCr (1 mol %)	CO (7 atm), toluene, rt, 3 h	**I** (18)	19
	salphCr (1 mol %)	CO (7 atm), 1,2-DFB, rt, 3 h	**I** (46)	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 3 h	**I** (9)	19
	salphCr (1 mol %)	CO (7 atm), 2,5-DMTHF, rt, 3 h	**I** (47)	19
	salphCr (1 mol %)	CO (7 atm), dioxane, rt, 3 h	**I** (43)	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96), 70	18
			+  (4)	
	OEPCr (0.2 mol %)	CO (60 atm), neat, 40°, 6 h	**I** (99)	28

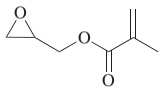
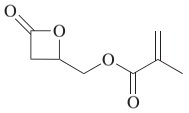
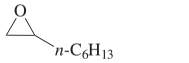
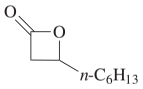
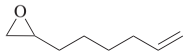
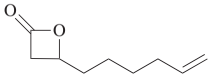
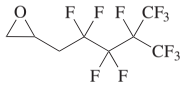
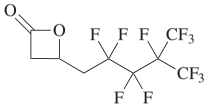
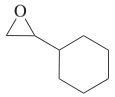
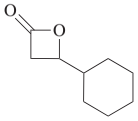
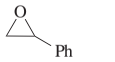
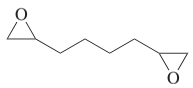
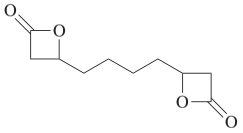
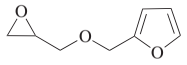
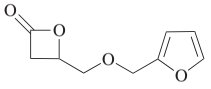
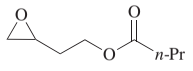
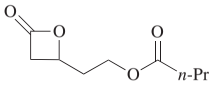
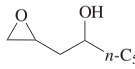
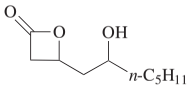
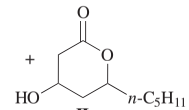
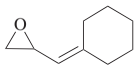
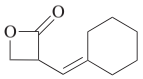
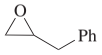
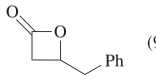
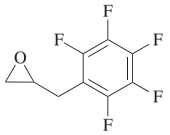
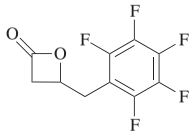
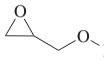
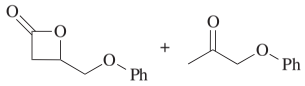
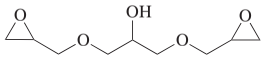
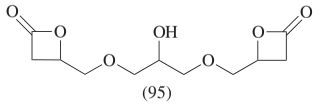
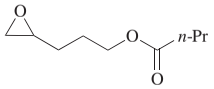
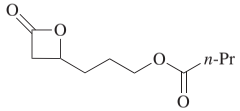
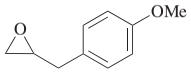
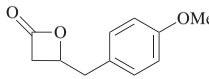
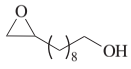
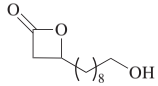
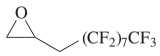
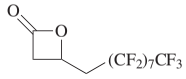
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1 h		(91)	23
C_8					
	[PPN]$^+$[Co(CO)$_4$]$^-$ (2 mol %), BF_3•OEt_2 (2 mol %)	CO (60 atm), DME, 80°, 24 h		(—), 77	36
	TPPAl (0.1 mol %)	CO (60 atm), THF, 60°, 6 h		**I** (—)	21
	[PPN]$^+$[Co(CO)$_4$]$^-$ (4 mol %), BF_3•OEt_2 (4 mol %)	CO (60 atm), DME, 80°, 48 h	**I** (—), 87		36
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h		(99), 91	19
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h		(99), 92	18
	TPPAl (0.5 mol %)	CO (60 atm), THF, 50°, 50 h		**I** (—)	21
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (25 atm), MeOH, 110°, 20 h	**I** (—), 67		41
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (95 atm), MeOH, 110°, 20 h	**I** (3)		41
	$RhClCO(PPh_3)_2$ (2 mol %)	CO (95 atm), MeOH, 110°, 2 h	**I** (3)		41

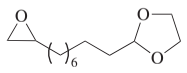
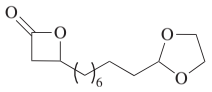
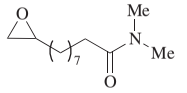
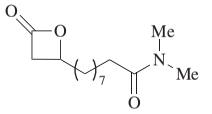
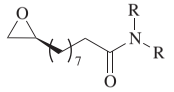
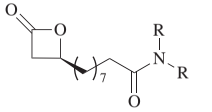
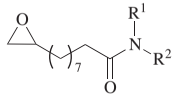
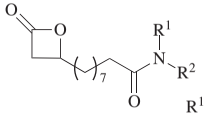
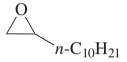
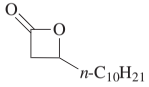
TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_8				
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	 **I** (99), 86	18
	salphCr (2 mol %)	CO (7 atm), DME, rt, 2 h	**I** (99)	23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 23 h	 **I** (99)	23
	OEPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h	 (99)	28
C_9				
	Catalyst (2 mol %)	CO (55 atm), DME, 60°, 24 h	 **I**  **II** **I + II** (—)	24
			Catalyst — **I/II** $HCo(CO)_4$ — 1:99 Cp_2Ti — 17:83 salphAl — 27:73 $Co_2(CO)_8$ — 33:67 HTPPAl — 42:58 TPPCr — 67:33 salphCr — 84:16	
	—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –78°	 (—)[a]	40

	TPPAl (0.1 mol %)	CO (60 atm), THF, 60°, 18 h		(99)	81
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h		(99), 82	19
	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (96), 86 + (4)		18
	salphCr (1 mol %)	CO (7 atm), DME, rt, 6 h	**I** (99), 96		18
	TPPAl (0.03 mol %)	CO (60 atm), THF, 75°, 15 h	 (95)		81
	OEPCr (0.03 mol %)	CO (60 atm), neat, 60°, 6 h		(99)	28
	salphCr (2 mol %)	CO (7 atm), DME, rt, 1.5 h		(99)	23
	TPPAl (0.5 mol %)	CO (60 atm), THF, 90°, 3 h		(—)	83
	salphCr (2 mol %)	CO (7 atm), DME, rt, 6 h		(99), 71	19

C_{11}

TABLE 1A. β-LACTONES FROM MONOSUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_{11} 	salphCr (2 mol %)	CO (7 atm), DME, rt, 2.5 h	 (99)	23
	salphCr (2 mol %)	CO (7 atm), DME, rt, 3 h	 **I** (73)	23
	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	salphCr (2 mol %)	CO (60 atm), DME, 60°, 6 h	 R: Me (99), *i*-Pr (99)	24
	salphCr (2 mol %)	CO (7 atm), DME, rt, 24 h	 R^1 R^2: H *c*-C_6H_{11} (71); *i*-Pr *i*-Pr (85)	23
C_{12} 	salphCr (2 mol %)	CO (1 atm), DME, rt, 6 h	 **I** (99), 93	18, 26
	salphCr (1 mol %)	CO (7 atm), DME, rt, 2 h	**I** (98)	26
	OEPCr (0.01 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	28
	TPPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (10)	29

[a] The β-lactone product was not stable enough to be characterized, so it was reduced to the diol with $LiAlH_4$ for characterization.

TABLE 1B. β-LACTONES FROM DISUBSTITUTED EPOXIDES

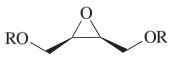
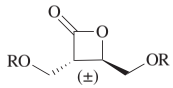
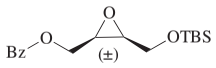
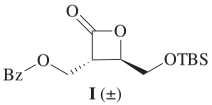
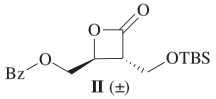
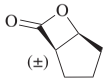
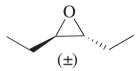
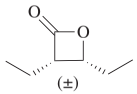
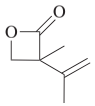
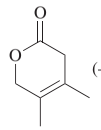
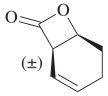
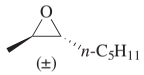
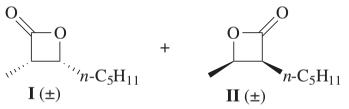
Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4				
	salphCr (2 mol %)	CO (7 atm), DME, rt, 8 h	 **I** (98)	26
	OEPCr (0.2 mol %)	CO (60 atm), toluene, 60°, 6 h	**I** (88)	28
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 20 h	**I** (99)	30
	TPPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)	29
	salphAl (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (56)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 10 h	**I** (99)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $B(C_6F_5)_3$ (4 mol %)	CO (60 atm), DME, 110°, 48 h	**I** (—), 20	36
	salphAl (1 mol %)	CO (60 atm), neat, 75°, 7.5 h	 **I** (40)	30
	TPPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (56)	29
	salphAl (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (20)	29
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 60°, 10 h	**I** (75)	34
	$[PPN]^+[Co(CO)_4]^-$ (4 mol %), $B(C_6F_5)_3$ (4 mol %)	CO (60 atm), DME, 110°, 48 h	**I** (24)	36
	salphAl (1 mol %)	CO (60 atm), neat, 50°, 1 h	 **I** (83) +  **II** (7)	35
	Cp_2Ti (5 mol %)	CO (60 atm), DME, 50°, 3 h	**I** (72) + **II** (18)	34
	TPPAl (1 mol %)	CO (60 atm), THF, 2 h		20
			R Temp (°) TBS 60 (95), 63	20
			Bn 60 (95)	81
			Bz 30 (90), 48	20

TABLE 1B. β-LACTONES FROM DISUBSTITUTED EPOXIDES (*Continued*)

	Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4		TPPAl (2 mol %)	CO (50 atm), THF, 40°, 24 h	 **I** (±) +  **II** (±) **I** + **II** (95), **I/II** = 1:1	81
C_5		OEPCr (1 mol %)	CO (60 atm), neat, 60°, 24 h	 (99)	28
C_6		TPPAl (1 mol %)	CO (60 atm), THF, 50°, 24 h	 (—)	21
		—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, rt, 16 h	 (—), 42 +  (—), 16	40
		—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, EtOH, –5°	 (—), 28	40
C_8		TPPAl (0.5 mol %)	CO (60 atm), THF, 50°, 24 h	 **I** (±) + **II** (±) **I** + **II** (99), **I/II** = 50:50	83

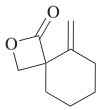
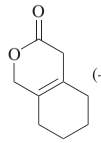
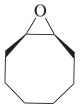
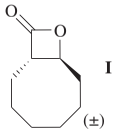
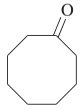
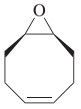
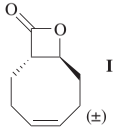
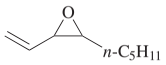
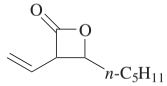
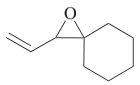
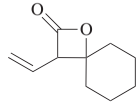
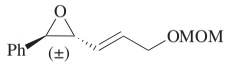
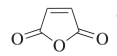
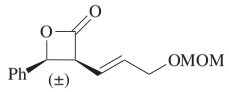
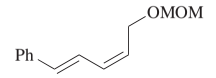
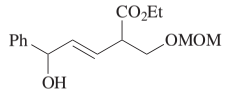
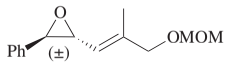
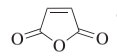
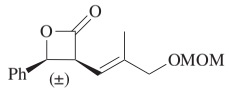
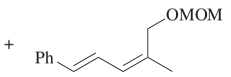
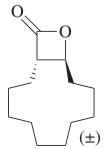
	—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –5°, 16 h		(—), 15	+ 	(—), 55	40
	salphCr (1 mol %)	CO (7 atm), DME, 60°, 24 h	 (±)	**I** (94)	+ 	(3)	26
	OEPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)				28
	TPPCr (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)				29
	salphAl (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (10)				29
	salphCr (2 mol %)	CO (7 atm), DME, rt, 24 h	 (±)	**I** (20)			23
	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)				28
	TPPCr (0.6 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (99)				29
	salphAl (0.4 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (20)				29
C_9							
 (±) cis/trans	—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –30°	 (±) cis/trans	(—), 68			40

TABLE 1B. β-LACTONES FROM DISUBSTITUTED EPOXIDES (*Continued*)

Epoxide	Catalyst	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_9 	—	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –5°	 (—), 52	40
C_{11} 	$Pd_2(C_4H_7)_2Cl_2$ (5 mol %),  (10 mol %)	CO (30 atm), NaBr, $(i\text{-Pr})_2NEt$, EtOH, rt, 12 h	 (—), 14 +  (—), 44 +  (—), 12	38
C_{12} 	$Pd_2(C_4H_7)_2Cl_2$ (5 mol %),  (10 mol %)	CO (30 atm), NaBr, $(i\text{-Pr})_2NEt$, EtOH, rt, 12 h	 (—), 9 +  (—), 55	38
 66% *cis*	OEPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (66) 99% *trans*	28
	TPPCr (0.2 mol %)	CO (60 atm), neat, 60°, 6 h	**I** (66) 97% *trans*	29

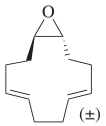
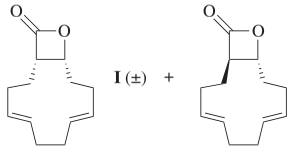
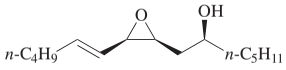
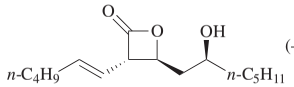
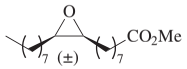
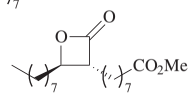
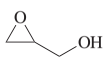
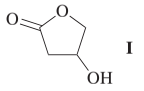
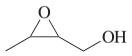
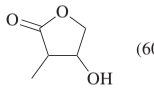
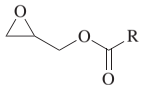
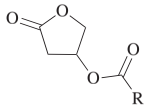
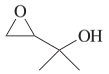
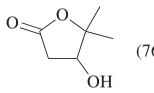
	96% *trans*	OEPCr (1 mol %)	CO (60 atm), neat, 60°, 6 h	 **I** (±) + **II** (±)	28
				I + **II** (57), **I/II** = 93:7	
	87% *trans*	TPPCr (0.5 mol %)	CO (60 atm), neat, 60°, 6 h	**I** + **II** (35), **I/II** = 66:34	29
C_{15}					
	—		1. $Fe_2(CO)_9$, THF, 2h 2. CAN, EtOH, 2h	 (—), 26	39
C_{18}					
		TPPAl (0.5 mol %)	CO (60 atm), THF, 60°, 6 h	 **I** (±) +  **II** (±)	81
				I + **II** (99), 83, **I/II** = 50:50	

TABLE 2A. γ-LACTONES FROM EPOXIDES

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3			
	CO (270 atm), $Co_4(CO)_{12}$, THF, 100°, 8 h	 **I** +  **II** **I** + **II** (93), **I/II** = 80:20	42
	CO (60 atm), $[PPN]^+[Co(CO)_4]^-$, BF_3•OEt_2, DME, 80°, 24 h	**I** (—)	5
	CO (200 atm), H_2 (4 atm), $Co_2(CO)_8$, THF, 100°, 2 h	**I** + **II** (89), **I/II** = 93:7	42
	CO (200 atm), H_2 (4 atm), $Co_2(CO)_8$, THF, 100°, 4 h	**I** + **II** (97), **I/II** = 70:30	42
	CO (200 atm), $Co_2(CO)_8$, THF, 100°, 2 h	**I** + **II** (86), **I/II** = 94:6	42
	CO (200 atm), $Co_4(CO)_{12}$, DME, 120°, 8 h	**I** (87)	42
	1. CO (270 atm), $Co_4(CO)_{12}$, THF, 100°, 8 h 2. Polyphosphoric acid	**II** (89)	42
	CO (200 atm), $Ni(acac)_2$, THF, 100°, 8 h	**I** + **II** (80), **I/II** = 60:40	42
C_4			
	CO (240 atm), $Co_4(CO)_{12}$, THF, 120°, 8 h	 (60)	42
C_{4-7}			
	CO (60 atm), OEPCr, neat, 60°, 24 h	 R: Me (99); *n*-Pr (99); Ph (99)	28
C_5			
	CO (240 atm), $Co_4(CO)_{12}$, THF, 120°, 8 h	 (76)	42

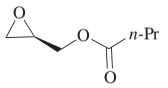
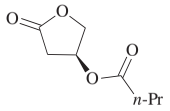
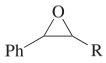
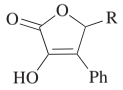
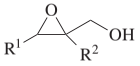
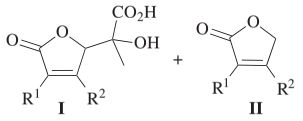
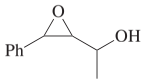
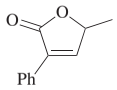
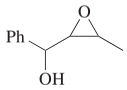
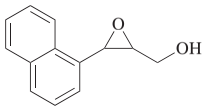
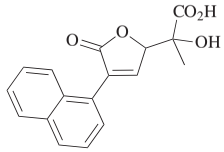
C_7  er 99.5:0.5	CO (60 atm), OEPCr, neat, 60°, 24 h		(99) er 99.5:0.5	28
C_{8-9} 	CO (1 atm), $Co_2(CO)_8$, CTAB, MeI, NaOH (aq), benzene, rt, 12 h		R: H (65); Me (34)	44
C_{9-10} 	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h	 **I** + **II**	R^1 / R^2: Ph/H (42) (10); Ph/Me (33) (36); 4-MeC_6H_4/H (50) (0)	43
C_{10} 	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h	 (—) +  (—)		43
C_{13} 	CO (1 atm), $Co_2(CO)_8$, TDA-1, MeI, NaOH (aq), toluene, rt, 12 h		(46)	43

TABLE 2B. γ-LACTONES FROM EPOXIDES VIA A SILYL YNOLATE

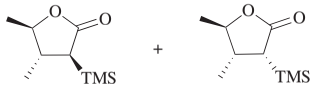
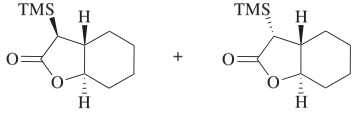
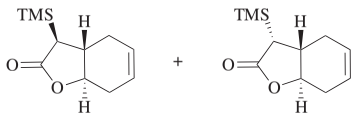
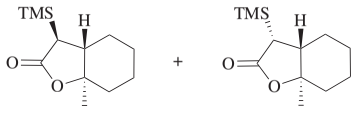
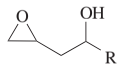
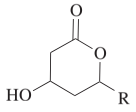
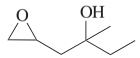
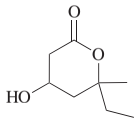
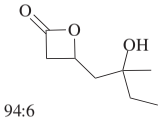
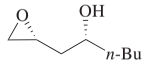
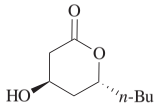
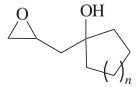
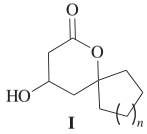
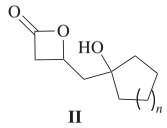
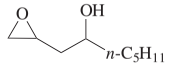
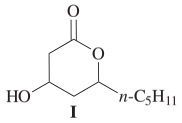
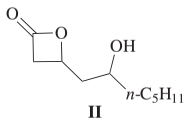
Epoxide	Reagent	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4				
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 **I** (±) + **II** (±)	**I** + **II** (72)	45
 (±)		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 **I** (±) + **II** (±)	**I** + **II** (71)	45
C_6				
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 **I** (±) + **II** (±)	**I** + **II** (93)	45
		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 **I** (±) + **II** (±)	**I** + **II** (72)	45
C_7				
 (±)		1. *n*-BuLi, THF, –78°, 1 h 2. CO (1 atm), 2 h 3. Me_3Al, THF, –78 to 20°, 12 h	 **I** (±) + **II** (±)	**I** + **II** (75)	45

TABLE 3A. δ-LACTONES FROM HOMOGLYCIDOLS

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
$C_{5–10}$ 	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 R = Me (73); $ClCH_2$ (81); $TBSOCH_2$ (52); CH_2=$CHCH_2$ (76); *n*-Bu (60); Ph (81)	24
C_7 	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 **I** (58) +  **II** (—) **I/II** = 94:6	24
C_8  er >99.5:0.5	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 (—) er >99.5:0.5	24
$C_{8–15}$ 	CO (55 atm), $HCo(CO)_4$, DME, 60°, 24 h	 **I** +  **II**	24

n	**I**	**II**	**I/II**
1	(67)	(—)	96:4
8	(75)	(—)	96:4

TABLE 3A. δ-LACTONES FROM HOMOGLYCIDOLS (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	CO (55 atm), catalyst, DME, 60°, 24 h	 **I** +  **II**	24

Catalyst	**I + II**	**I/II**
$HCo(CO)_4$	(—)	99:1
Cp_2Ti	(—)	83:17
salphAl	(—)	73:27
$Co_2(CO)_8$	(—)	67:33
HTPPAl	(—)	58:42
TPPCr	(—)	33:67
salphCr	(—)	16:84

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES

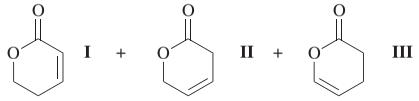
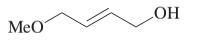
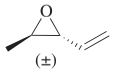
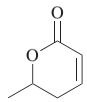
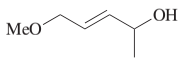
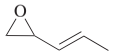
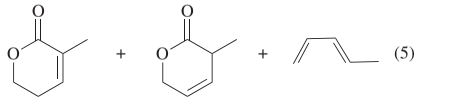
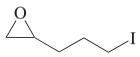
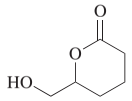
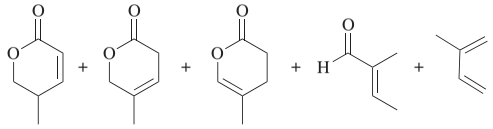
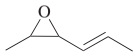
Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4			
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	 **I** + **II** + **III** **I** + **II** + **III** (80), **I/II/III** = 58:32:10	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** + **II** (40), **I/II** = 23:77 +  (45)	52
C_5			
 (±)	1. $Fe_2(CO)_9$, THF 2. CO (60 atm), benzene, 195°, 4 h	 **I** (23)	50
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	**I** (65) +  (5)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** (15) +  (50)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	 (5) **I** **II** **I** + **II** (67), **I/II** = 7:93	52
	1. $Na^+[CpMo(CO)_3]^-$, THF 2. PPh_3, MeCN 3. $SnCl_4$ (5 eq), CH_2Cl_2, 0°, 0.5 h 4. $NaBH_4$, MeOH 5. Pyridine *N*-oxide, CH_2Cl_2, rt, 4 h	 (18)	49

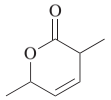
TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_5			
		 **I** **II** **III** **IV** **V**	
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), benzene, 16 h	**I** (37) + **II** (48) + **III** (15)	52
	1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h 2. CO (300 atm), MeOH, 16 h	**I** (17) + **II** (66)	52
	CO (150 atm), $(CODRhCl)_2$, CCl_4, 70°, 50 h	**I** (75)	53
	CO (200 atm), Na_2PdCl_4, THF, 75°, 17 h	**II** (6) + **IV** (57)	52
	CO (200 atm), Na_2PdCl_4, LiBr, THF, 75°, 17 h	**II** (86) + **IV** (1) + **V** (1)	52
	CO (200 atm), $Pd(acac)_2$, THF, 75°, 17 h	**II** (1) + **IV** (71)	52
	CO (200 atm), $Pd(acac)_2$, PPh_3, THF, 75°, 17 h	**II** (40) + **IV** (1)	52
	CO (200 atm), $Co_2(CO)_8$, benzene, 85°, 20 h	**II** (37) + **IV** (13) + **V** (19)	52

C_6



1. $Fe_2(CO)_9$, ultrasound, 1 h
2. CO (300 atm), 90°, 24 h

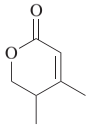
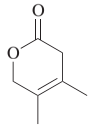
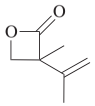


I (49) dr 1:1 — 50

1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h
2. CO (300 atm), benzene, 16 h

I (75) — 52

1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h
2. CO (300 atm), solvent, 16 h

 **I** +  **II** +  **III** — 52

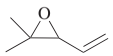
Solvent	**I**	**II**	**III**
benzene	(45)	(45)	(—)
MeOH	(24)	(56)	(—)

1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h
2. CAN, rt, solvent, 16 h

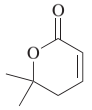
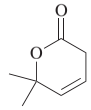
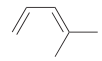
II + **III**

Solvent	**II**	**III**
EtOH/H_2O	(38)	(0)
MeCN	(16)	(42)

— 40

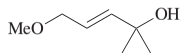


1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h
2. CO (300 atm), benzene, 16 h

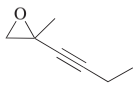
 **I** +  **II** +  (10) — 52

I + **II** (75), **I**/**II** = 66:33

1. $Fe(CO)_5$, *hv*, benzene, 20°, 2 h
2. CO (300 atm), MeOH, 16 h

I + **II** (65), **I**/**II** = 20:80 +  (20) — 52

C_7



1. CO (1 atm), $Pd(PPh_3)_4$, MeOH, rt, 18 h
2. Me_2CuLi, Et_2O, –78 to –40°

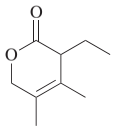
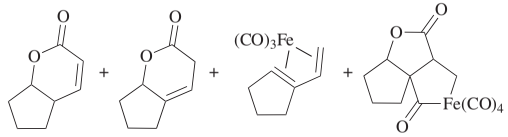
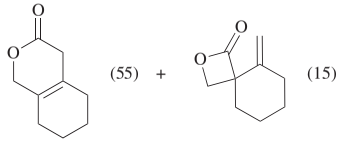
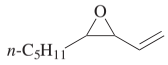
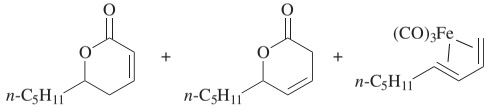
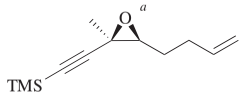
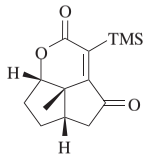
 (41) — 48

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. Benzene, 70°, 12 h	 **I** (50) + **II** (9) + **III** (7) + **IV** (5)	51
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. THF, 70°, 2.5 h	**I** (40) + **II** (16) + **III** (30)	51
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, rt, 16 h	**I** + **II** (80)	40
C_8			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN, –5°, 16 h	 (55) + (15)	40
C_9			
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. THF, 70°, 3 h	 (8) (6) (40)	51
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 **I** (65)	46, 47

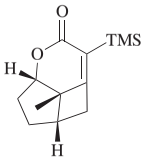
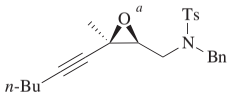
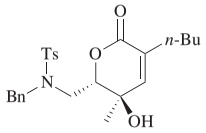
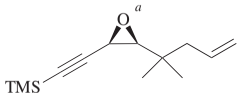
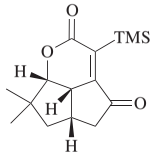
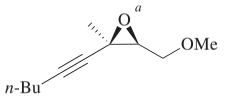
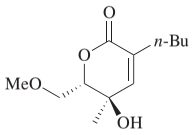
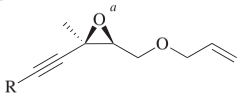
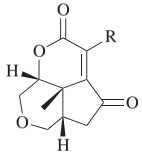
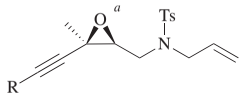
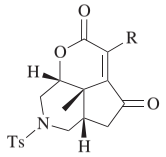
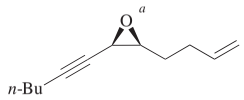
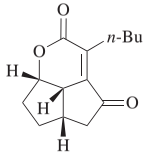
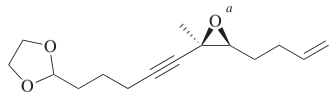
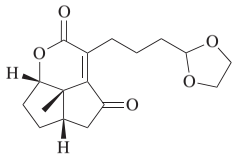
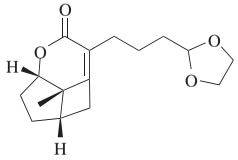
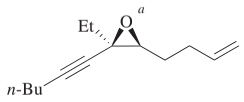
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	**I** (2) + 	(75)	46, 47
C_{10}				
	1. $Co_2(CO)_8$ 2. H_2O/THF, rt, 8 h 3. CO (1 atm), 75°, 6 h		**I** (25)	46, 47
	1. $Co_2(CO)_8$ 2. Pyridine *N*-oxide, 80°, 8 h 3. CO (1 atm), 75°, 6 h	**I** (35)		46, 47
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h		(73)	46
	1. $Co_2(CO)_8$ 2. H_2O/THF, rt, 8 h 3. CO (1 atm), 75°, 6 h		(28)	46, 47
C_{10-12}				
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h		R *n*-Bu (75) *n*-C_6H_{13} (78)	46, 47

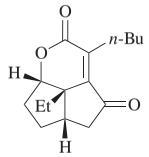
TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10-12} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (1 atm), benzene, 80°, 24 h	 R: *n*-Bu (66); *n*-C_6H_{13} (68)	46, 47
C_{12} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 *x*: 0 (82); 3.4 (7)	46
C_{13} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 (66)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (52)	46

C_{14}



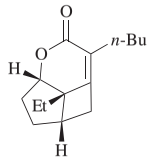
1. $Co_2(CO)_8$, benzene, rt, 2 h
2. CO (3.4 atm), benzene, 80°, 24 h



(71)

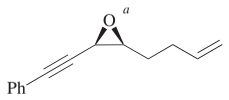
46

1. $Co_2(CO)_8$, benzene, rt, 2 h
2. Benzene, 80°, 24 h

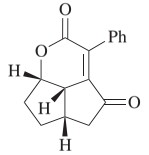


(68)

46



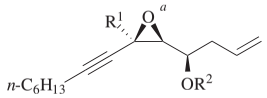
1. $Co_2(CO)_8$, benzene, rt, 2 h
2. Benzene, 80°, 24 h



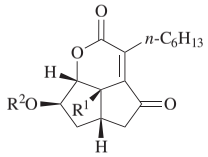
(82)

46

$C_{14–15}$



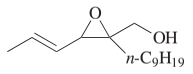
1. $Co_2(CO)_8$, benzene, rt, 2 h
2. CO (*x* atm), benzene, 80°, 24 h



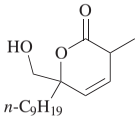
R^1	R^2	*x*	
H	Ac	0	(83)
Me	Me	1	(74)
Me	Ac	1	(77)

46, 47

C_{15}



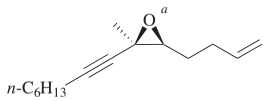
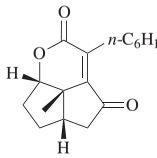
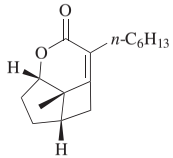
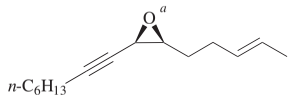
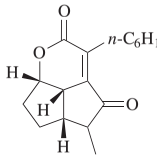
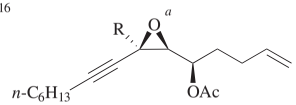
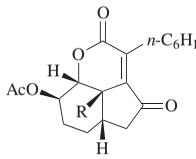
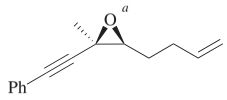
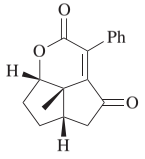
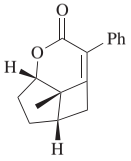
1. $Fe_2(CO)_9$, THF
2. CO (300 atm), 90°, 24 h



(53)

50

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 +  **I** **II** *x* **I** **II** 0 (3) (72) 1 (34) (39) 3.4 (77) (0)	46
	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (45)	46
C_{15-16} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 R H (70) Me (65)	46
C_{15} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (*x* atm), benzene, 80°, 24 h	 +  **I** **II** *x* **I** **II** 0 (3) (75) 1 (38) (32) 3.4 (74) (0)	46

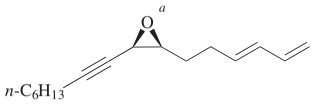
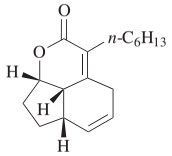
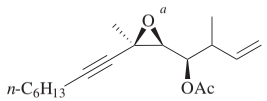
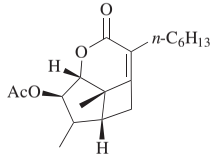
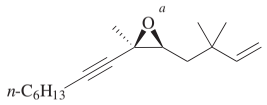
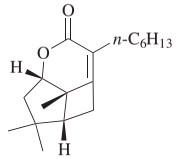
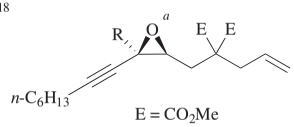
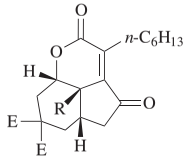
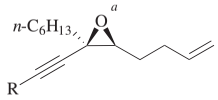
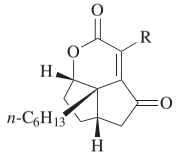
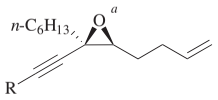
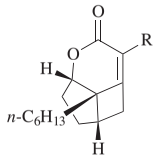
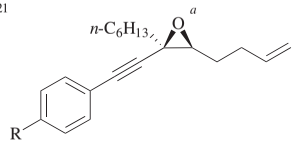
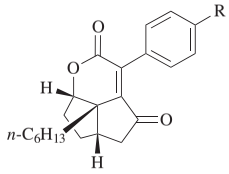
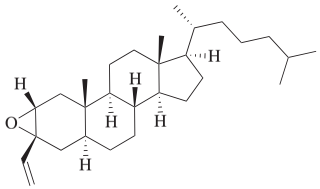
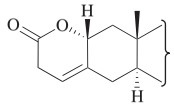
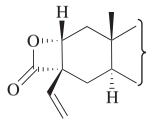
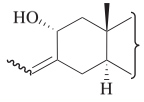
C_{16}		1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (25)	46
		1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (85)	46, 47
C_{17}		1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 (89)	46, 47
C_{17-18}		1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (x atm), benzene, 80°, 24 h	 R x H 0 (71) Me 1 (71)	46, 47
C_{20}		1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 R n-C_6H_{13} (59) Ph (58)	46

TABLE 3B. δ-LACTONES FROM VINYL AND ALKYNYL EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{20} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. Benzene, 80°, 24 h	 R: *n*-C_6H_{13} (63); Ph (61)	46
C_{20-21} 	1. $Co_2(CO)_8$, benzene, rt, 2 h 2. CO (3.4 atm), benzene, 80°, 24 h	 R: F (59); MeO (63)	46
C_{29} 	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. CAN, MeCN/benzene (1:1), rt, 16 h	 **I** (26) +  (6)	40
	1. $Fe(CO)_5$, *hv*, benzene, rt, 6 h 2. THF, 70°, 2.5 h	**I** (31) +  (36)	51

[a] The epoxide configuration as shown is opposite that depicted in the original disclosure, which used racemic epoxides. Based on the current mechanistic understanding, the enantiomer of epoxide shown should produce the enantiomer of product shown.

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES

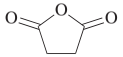
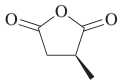
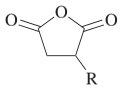
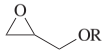
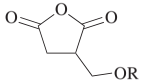
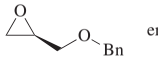
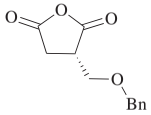
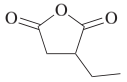
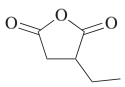
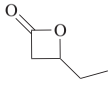
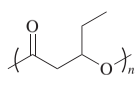
	Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_2		CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (98), 93	21
C_3	 er >99.5:0.5	CO (60 atm), TPPAl, dioxane	 Temp (°) Time (h) er 90 3 (97) 98.5:1.5 50 24 (99) >99.5:0.5	21
$C_{3–9}$		CO (60 atm), TPPAl, dioxane, 90°, 3 h	 R Me (99), 89 *n*-Bu (97), 88 $NC(CH_2)_3$ (99), 77 $CH_2{=}CH(CH_2)_4$ (99), 85 *c*-C_6H_{11} (97), 81 Bn (99), 78	21
C_3		CO (60 atm), TPPAl, dioxane, 90°, 3 h	 R TBS (98), 83 *n*-Bu (99), 80 Bn (96), 87	21
	 er >99.5:0.5	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 (96), 87 er >99.5:0.5	21
C_4		CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (99), 80	21

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_4			
	CO (60 atm), catalyst, solvent, 60°, 6 h	 +  +  **I** **II** **III**	21

Catalyst	Solvent	**I**	**II**	**III**
salphAl	none	(0)	(99)	(0)
salphAl	toluene	(0)	(58)	(0)
OEPCr	none	(7)	(0)	(93)
OEPCr	toluene	(33)	(0)	(67)
TPPAl	none	(22)	(0)	(78)
TPPAl	toluene	(99)	(0)	(0)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
	CO (60 atm), catalyst, dioxane, 90°, 2 h	**I + II + III**	21

Catalyst	**I**	**II**	**III**
Cp_2Ti	(0)	(6)	(0)
salphAl	(2)	(85)	(0)
salphCr	(32)	(64)	(0)
TPPCr	(47)	(38)	(12)
OEPCr	(76)	(4)	(19)
OEPAl	(68)	(31)	(0)
HTPPAl	(80)	(19)	(0)
MeTPPAl	(79)	(19)	(0)
FTPPAl	(84)	(14)	(0)
TPPAl	(83)	(16)	(0)
CF_3TPPAl	(81)	(16)	(0)

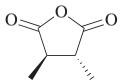
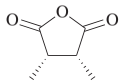
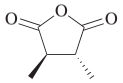
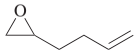
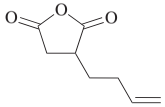
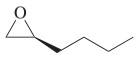
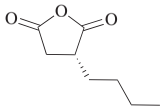
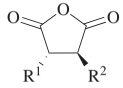
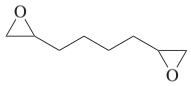
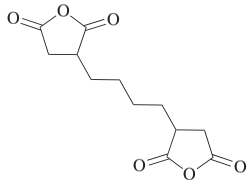
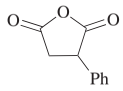
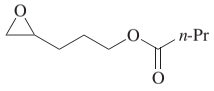
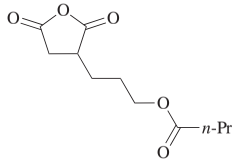
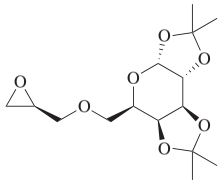
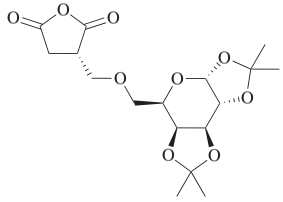
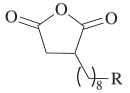
		CO (60 atm), TPPAl, solvent, 90°, 2 h	**I** + **II** + **III**	Solvent	**I**	**II**	**III**	21
				hexane	(16)	(9)	(66)	
				toluene	(45)	(37)	(4)	
				Et_2O	(38)	(42)	(11)	
				DME	(43)	(55)	(0)	
				dioxane	(80)	(19)	(0)	
				THF	(18)	(82)	(0)	
				EtOAc	(42)	(51)	(6)	
				acetone	(17)	(52)	(30)	
				1,2-difluorobenzene	(12)	(83)	(0)	
				MeCN	(0)	(93)	(4)	
		CO (60 atm), TPPAl, dioxane, 50°, 24 h	 **I** +  **II**					21
			I + **II** (95), **I**/**II** = 1:20					
		CO (60 atm), TPPAl, dioxane, 50°, 24 h	 **I** (99)					21
		CO (60 atm), salphAl, neat, 50°, 24 h	**I** (—)					54
C_6								
		CO (60 atm), TPPAl, dioxane, 50°, 3 h	 (90), 82					21
	 er >99.5:0.5	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 (99) er >99.5:0.5					21

TABLE 4. SUCCINIC ANHYDRIDES FROM EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and Conversion(s) (%), % Yield	Refs.
C_{6-8}			
	CO (60 atm), TPPAl, dioxane, 50°, 24 h	 R^1 R^2: Et Et (99); Me n-C_5H_{11} (99)	21
C_8			
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (98), 89	21
	CO (60 atm), TPPAl, dioxane, 50°, 12 h	 (93), 72	21
C_9			
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (99), 89	21
	CO (60 atm), TPPAl, dioxane, 90°, 3 h	 (95)	81

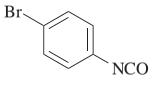
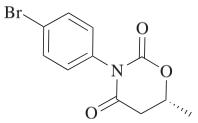
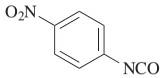
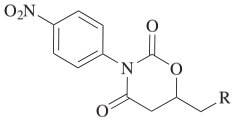
C_{11-12}

CO (60 atm), TPPAl, dioxane, 90°

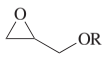
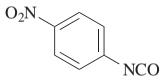
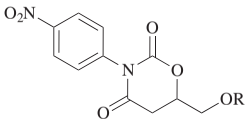
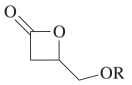


R	Time (h)		
Me_2NCO	24	(98), 79	21
$HOCH_2$	3	(93), 72	
Et	3	(99), 93	

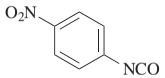
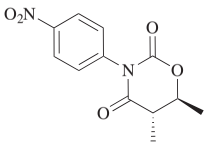
TABLE 5. 1,3-OXAZINANE-2,4-DIONES FROM EPOXIDES AND ISOCYANATES

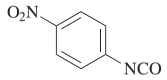
Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_3 		CO (55 atm), salphAl, hexanes, rt, 48 h	 (97), 70[a]	22
C_{3-6} 		CO (55 atm), salphAl, hexanes, rt, 12 h		22

R	
H	(97)
Cl	(70)
Me	(97)
n-Pr	(97)
CH_2=$CHCH_2$	(97)

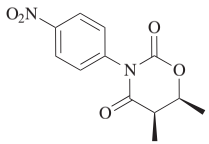
C_3 		CO (55 atm), salphAl, hexanes, rt, 12 h	 **I** +  **II**	22

R	**I**	**II**
TBS	(97)	(3)
CH_2=$CHCH_2$	(94)	(6)
n-Bu	(97)	(2)
Bn	(80)	(8)

C_4 		CO (55 atm), salphAl, hexanes, rt, 12 h	 (89) +  (11)	22



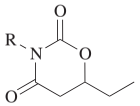
CO (55 atm), salphAl, hexanes, rt, 24 h

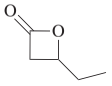


(19) 22

RNCO

CO (55 atm), salphAl, hexanes, rt, 48 h

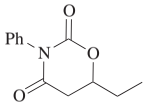


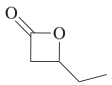
I +  **II** 22

R	**I**	**II**
Et	(13)	(15)
Bn	(39)	(19)

PhNCO

CO (55 atm), salphAl, hexanes, rt, 48 h



I (97), 71[a] +  **II** (0) 22

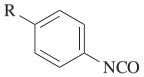
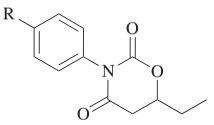
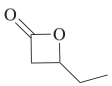
PhNCO

CO (55 atm), salphAl, solvent, rt, 24 h

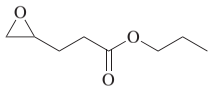
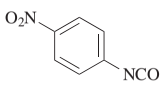
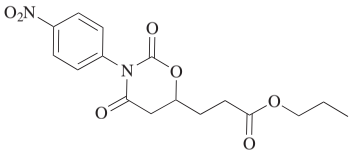
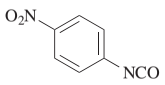
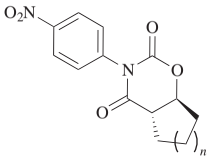
Solvent[b]	**I**	**II**
hexanes	(40)	(8)
pentane	(24)	(5)
toluene	(10)	(20)
Et_2O	(17)	(36)
1,2-difluorobenzene	(14)	(36)
t-BuOMe	(13)	(34)
tetrahyropyran	(4)	(74)
MeCN	(3)	(77)
dioxane	(0)	(97)
DME	(0)	(91)
THF	(0)	(83)

22

TABLE 5. 1,3-OXAZINANE-2,4-DIONES FROM EPOXIDES AND ISOCYANATES (*Continued*)

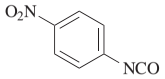
Epoxide	Isocyanate	Conditions	Product(s) and Conversion(s) (%)	Refs.
C_4 		CO (*x* atm), salphAl, solvent, rt	 **I** +  **II**	

R	*x*	Solvent	Time (h)	**I**	**II**	Refs.
F	55	hexanes	48	(97)	(0)	22
F	20	DME	5	(7)	(93)	25
Br	55	hexanes	48	(97)	(0)	22
MeO	55	hexanes	48	(60)	(20)	22
Me	55	hexanes	48	(42)	(14)	22
Me	20	DME	5	(17)	(83)	25

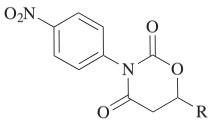
C_5 		CO (55 atm), salphAl, hexanes, rt, 12 h	 (97)	22
C_{5-6} 		CO (55 atm), salphAl, hexanes, rt, 12 h		22

n	
1	(97)
2	(97)

C_{6-8}



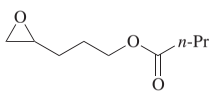
CO (55 atm), salphAl, hexanes, rt, 12 h

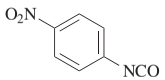


I +  **II** 22

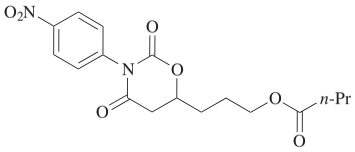
R	**I**	**II**
t-Bu	(10)	(9)
c-C_6H_{11}	(94)	(3)

C_9





CO (55 atm), salphAl, hexanes, rt, 12 h

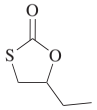
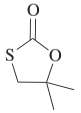
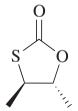
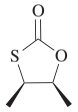
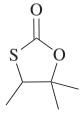
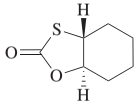


(97) 22

[a] The value is the yield of isolated product (%).

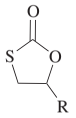
[b] The epoxide concentration was 0.5 M in the solvent.

TABLE 6. 1,3-OXATHIOLAN-2-ONES FROM EPOXIDES

Epoxide	Conditions	Product(s) and GC Yield(s) (%)	Refs.
C_4			
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 60°, 3 h	 (87)	56
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 60°, 3 h	 (98)	56
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h	 *x*: 0 (87); 0.025 (31)	55
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h	 *x*: 0 (16); 0.025 (7)	55
C_5			
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 150°, 8 h	 *x*: 0 (4); 0.025 (4)	56 55
C_6			
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 60°, 3 h	 *x*: 0 (61); 0.025 (16)	55

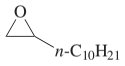
C_{8-9}

S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 60°, 3 h

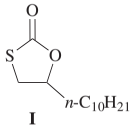


R	*x*		
Ph	0	(39)	56
Ph	0.025	(79)	56
4-BrC_6H_4	0	4	55
4-BrC_6H_4	0.025	(22)	55
4-MeC_6H_4	0	(53)	55
4-MeC_6H_4	0.025	(50)	55
Bn	0	(53)	56
Bn	0.025	(97)	56
$PhOCH_2$	0	(24)	56
$PhOCH_2$	0.025	(66)	56

C_{12}



S (5 eq), CO (*x* atm), NaH (1 eq), THF, 3 h



I

x	Temp (°)		
10	60	(95), 92[a]	55
10	50	(72)	
10	40	(29)	
5	60	(37)	
1	60	(0)	

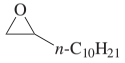
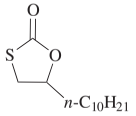
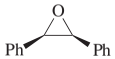
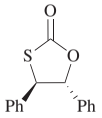
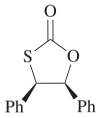
S (*x* eq), CO (10 atm), NaH (1 eq), THF, 60°, 3 h **I**

x		
1	(28)	55
2	(67)	
3	(76)	
4	(85)	
5	(96)	

S (5 eq), CO (10 atm), NaH (1 eq), solvent, 60°, 3 h **I**

Solvent		
dioxane	(22)	55
DMSO	(56)	
DMF	(82)	
MeCN	(60)	
toluene	(0)	
hexane	(0)	

TABLE 6. 1,3-OXATHIOLAN-2-ONES FROM EPOXIDES (*Continued*)

Epoxide	Conditions	Product(s) and GC Yield(s) (%)	Refs.
C_{12}			
	S (5 eq), CO (10 atm), base (0.25 eq), THF, 60°, 3 h		Base **I** LiH (0) KH (28) KH (82)[b] NaH (95) $NaBH_4$ (7) CaH_2 (61) DBU (56) DBN (23) NMP (0) Et_3N (0) pyridine (0) NaOH (0)	55
C_{14}			
	S (5 eq), CO (10 atm), NaH (0.25 eq), Se (*x* eq), THF, 120°, 6 h		*x* 0 (35) 0.025 (10)	55
	S (5 eq), CO (10 atm), NaH (0.25 eq), THF, 120°, 6 h		(0)	55

[a] The value is the yield of isolated product (%).

[b] Dibenzo-18-crown-6 (25 mol %) was added to the reaction mixture.

REFERENCES

1 Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987.
2 Heck, R. F. In *Organic Synthesis via Metal Carbonyls*; Wender, I., Pino, P., Eds.; Interscience: New York, 1968.
3 Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation: Direct Synthesis of Carbonyl Compounds*; Plenum Press: New York, 1991.
4 Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Sausalito, CA, 1994.
5 Church, T. L.; Getzler, Y.; Byrne, C. M.; Coates, G. W. *Chem. Commun.* **2007**, 657.
6 Nakano, K.; Nozaki, K. *Top. Organomet. Chem.* **2006**, *18*, 223.
7 Vasapollo, G.; Mele, G. *Curr. Org. Chem.* **2006**, *10*, 1397.
8 Liu, J.; Chen, J. *Huaxue Jinzhan* **2004**, *16*, 989.
9 Vasapollo, G.; Mele, G. *Targets in Heterocycl. Systems* **2002**, *6*, 197.
10 Khumtaveeporn, K.; Alper, H. *Acc. Chem. Res.* **1995**, *28*, 414.
11 *Aziridines and Epoxides in Organic Synthesis*; Yudin, A. K., Ed.; Wiley-VCH: Weinheim, 2006.
12 Xia, Q.-H.; Ge, H.-Q.; Ye, C.-P.; Liu, Z.-M.; Su, K.-X. *Chem. Rev.* **2005**, *105*, 1603.
13 Shi, Y. *Acc. Chem. Res.* **2004**, *37*, 488.
14 Schaus, S. E.; Brandes, B. D.; Larrow, J. F.; Tokunaga, M.; Hansen, K. B.; Gould, A. E.; Furrow, M. E.; Jacobsen, E. N. *J. Am. Chem. Soc.* **2002**, *124*, 1307.
15 Tokunga, M.; Larrow, J. F.; Kakiuchi, F.; Jacobsen, E. N. *Science* **1997**, *277*, 936.
16 Katsuki, T.; Martin, V. S. *Org. React.* **1995**, *48*, 1.
17 Dekker, F. J.; Balamurugan, R.; Wetzel, S.; Koch, M. A.; Kramer, J. W.; Coates, G. W.; Odermatt, A.; Waldmann, H. Manuscript in preparation.
18 Kramer, J. W.; Treitler, D. S.; Coates, G. W. *Org. Synth.* **2009**, *86*, 287.
19 Kramer, J. W.; Coates, G. W. *Tetrahedron* **2008**, *64*, 6973.
20 Liang, Y.; Hnatiuk, N. E.; Rowley, J. M.; Whiting, B. T.; Coates, G. W.; Rablen, P. R.; Morton, M.; Howell, A. R. *J. Org. Chem.* **2011**, *76*, 9962.
21 Rowley, J. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 4948.
22 Church, T. L.; Byrne, C. M.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 8156.
23 Coates, G. W.; Kramer, J. W. Intl. Patent WO **2007**/106329 (*2007*).
24 Kramer, J. W.; Joh, D. Y.; Coates, G. W. *Org. Lett.* **2007**, *9*, 5581.
25 Church, T. L.; Getzler, Y. D. Y. L.; Coates, G. W. *J. Am. Chem. Soc.* **2006**, *128*, 10125.
26 Kramer, J. W.; Lobkovsky, E. B.; Coates, G. W. *Org. Lett.* **2006**, *8*, 3709.
27 Getzler, Y. D. Y. L.; Schmidt, J. A. R.; Coates, G. W. *J. Chem. Educ.* **2005**, *82*, 621.
28 Schmidt, J. A. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2005**, *127*, 11426.
29 Schmidt, J. A. R.; Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Org. Lett.* **2004**, *6*, 373.
30 Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *Pure Appl. Chem.* **2004**, *76*, 557.
31 Allmendinger, M.; Zintl, M.; Eberhardt, R.; Luinstra, G. A.; Molnar, F.; Rieger, B. *J. Organomet. Chem.* **2004**, *689*, 971.
32 Molnar, F.; Luinstra, G. A.; Allmendinger, M.; Rieger, B. *Chem.—Eur. J.* **2003**, *9*, 1273.
33 Allmendinger, M.; Eberhardt, R.; Luinstra, G. A.; Molnar, F.; Rieger, B. Z. *Anorg. Allg. Chem.* **2003**, *629*, 1347.
34 Mahadevan, V.; Getzler, Y. D. Y. L.; Coates, G. W. *Angew. Chem., Int. Ed.* **2002**, *41*, 2781.
35 Getzler, Y. D. Y. L.; Mahadevan, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 1174.
36 Lee, J. T.; Thomas, P. J.; Alper, H. *J. Org. Chem.* **2001**, *66*, 5424.
37 Drent, E.; Kragtwijk, E. European Patent 577206 (1994).
38 Shimizu, I.; Maruyama, T.; Makuta, T.; Yamamoto, A. *Tetrahedron Lett.* **1993**, *34*, 2135.
39 Bates, R. W.; Fernandez-Moro, R.; Ley, S. V. *Tetrahedron* **1991**, *47*, 9929.
40 Annis, G. D.; Ley, S. V.; Self, C. R.; Sivaramakrishnan, R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 270.
41 Kamiya, Y.; Kawato, K.; Ohta, H. *Chem. Lett.* **1980**, 1549.
42 Brima, T. S. U.S. Patent 4968817 (1990).
43 Alper, H.; Eisenstat, A.; Satyanarayana, N. *J. Am. Chem. Soc.* **1990**, *112*, 7060.
44 Alper, H.; Arzoumanian, H.; Petrignani, J. F.; Saldana-Maldonado, M. *J. Chem. Soc., Chem. Commun.* **1985**, 340.
45 Kai, H.; Iwamoto, K.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **1996**, *118*, 7634.
46 Odedra, A.; Lush, S.-F.; Liu, R.-S. *J. Org. Chem.* **2007**, *72*, 567.

[47] Odedra, A.; Wu, C.-J.; Madhushaw, R. J.; Wang, S.-L.; Liu, R.-S. *J. Am. Chem. Soc.* **2003**, *125*, 9610.
[48] Knight, J. G.; Ainge, S. W.; Baxter, C. A.; Eastman, T. P.; Harwood, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3188.
[49] Marson, C. M.; Randall, L.; Winter, M. J. *Tetrahedron Lett.* **1994**, *35*, 6717.
[50] Horton, A. M.; Ley, S. V. *J. Organomet. Chem.* **1985**, *285*, C17.
[51] Annis, G. D.; Ley, S. V.; Self, C. R.; Sivaramakrishnan, R.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1355.
[52] Aumann, R.; Ring, H.; Kruger, C.; Goddard, R. *Chem. Ber.* **1979**, *112*, 3644.
[53] Aumann, V. R.; Ring, H. *Angew. Chem.* **1977**, *89*, 47.
[54] Getzler, Y. D. Y. L.; Kundnani, V.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2004**, *126*, 6842.
[55] Nishiyama, Y.; Katahira, C.; Sonoda, N. *Tetrahedron* **2006**, *62*, 5803.
[56] Nishiyama, Y.; Katahira, C.; Sonoda, N. *Tetrahedron Lett.* **2004**, *45*, 8539.
[57] Denmark, S. E.; Ahmad, M. *J. Org. Chem.* **2007**, *72*, 9630.
[58] Hinterding, K.; Jacobsen, E. N. *J. Org. Chem.* **1999**, *64*, 2164.
[59] Heck, R. F. *J. Am. Chem. Soc.* **1963**, *85*, 1460.
[60] Goodman, S. N.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2002**, *41*, 4703.
[61] Nakano, K.; Katayama, M.; Ishihara, S.; Hiyama, T.; Nozaki, K. *Synlett* **2004**, 1367.
[62] Lee, J. T.; Alper, H. *Macromolecules* **2004**, *37*, 2417.
[63] Allmendinger, M.; Eberhardt, R.; Luinstra, G.; Rieger, B. *J. Am. Chem. Soc.* **2002**, *124*, 5646.
[64] Davoli, P.; Moretti, I.; Prati, F.; Alper, H. *J. Org. Chem.* **1999**, *64*, 518.
[65] Piotti, M. E.; Alper, H. *J. Am. Chem. Soc.* **1996**, *118*, 111.
[66] Roberto, D.; Alper, H. *J. Am. Chem. Soc.* **1989**, *111*, 7539.
[67] Wang, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20.
[68] Jenner, G.; Kheradmand, H.; Kiennemann, A. *J. Organomet. Chem.* **1984**, *277*, 427.
[69] Byrne, C. M.; Church, T. L.; Kramer, J. W.; Coates, G. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 3979.
[70] Xu, H. Y.; Jia, L. *Org. Lett.* **2003**, *5*, 1575.
[71] Wang, Y.; Tennyson, R. L.; Romo, D. *Heterocycles* **2004**, *64*, 605.
[72] Pommier, A.; Pons, J.-M. *Synthesis* **1993**, 441.
[73] Rieth, L. R.; Moore, D. R.; Lobkovsky, E. B.; Coates, G. W. *J. Am. Chem. Soc.* **2002**, *124*, 15239.
[74] Lenz, R. W.; Marchessault, R. H. *Biomacromolecules* **2005**, *6*, 1.
[75] Müller, H.-M.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 477.
[76] Pommier, A.; Pons, J.-M. *Synthesis* **1995**, 729.
[77] Wu, Y.; Sun, Y.-P. *J. Org. Chem.* **2006**, *71*, 5748.
[78] Schneider, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 744.
[79] Yang, H. W.; Romo, D. *Tetrahedron* **1999**, *55*, 6403.
[80] Stirling, A.; Iannuzzi, M.; Parrinello, M.; Molnar, F.; Bernhart, V.; Luinstra, G. A. *Organometallics* **2005**, *24*, 2533.
[81] Rowley, J. M. Ph. D. Dissertation, Cornell University, 2008.
[82] Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987; pp 266–267.
[83] Coates, et al., Cornell University, Ithaca, NY, unpublished results.
[84] Wax, M. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 7028.
[85] Roe, D. C. *Organometallics* **1987**, *6*, 942.
[86] Wedler, C.; Costisella, B.; Schick, H. *J. Org. Chem.* **1999**, *64*, 5301.
[87] Sjostrom, L.; Rissanen, A.; Anderson, T.; Boldrin, M.; Golay, A.; Koppeschaar, H. P. F.; Krempf, M. *The Lancet* **1998**, *352*, 167.
[88] Einhorn, A. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2208.
[89] Zaugg, H. E. *Org. React.* **1954**, *8*, 305.
[90] Bartlett, P. D.; Rylander, P. N. *J. Am. Chem. Soc.* **1951**, *73*, 4275.
[91] Noyce, D. S.; Banitt, E. H. *J. Am. Chem. Soc.* **1966**, *31*, 4043.
[92] Hughes, D. L. *Org. React.* **1992**, *42*, 335.
[93] Arnold, L. D.; Drover, J. C. G.; Vederas, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4649.
[94] Arnold, L. D.; Kalantar, T. H.; Vederas, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 7105.
[95] Pansare, S. V.; Vederas, J. C. *J. Org. Chem.* **1989**, *54*, 2311.
[96] Mulzer, J.; Bruentrup, G.; Chucholowski, A. *Angew. Chem.* **1979**, *91*, 654.
[97] Adam, W.; Baeza, J.; Liu, J.-C. *J. Am. Chem. Soc.* **1972**, *94*, 2000.
[98] Black, T. H.; Hall, J. A.; Sheu, R. G. *J. Org. Chem.* **1988**, *53*, 2371.
[99] Staudinger, H.; Bereza, S. *Liebigs Ann. Chem.* **1911**, *380*, 243.
[100] Orr, R. K.; Calter, M. A. *Tetrahedron* **2003**, *59*, 3545.

[101] Tidwell, T. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 5778.
[102] Zhu, C.; Shen, X.; Nelson, S. G. *J. Am. Chem. Soc.* **2004**, *126*, 5352.
[103] Masters, A. P.; Sorensen, T. S. *Tetrahedron Lett.* **1989**, *30*, 5869.
[104] Dominguez, D.; Cava, M. P. *Tetrahedron Lett.* **1982**, *23*, 5513.
[105] Taggi, A. E.; Hafez, A. M.; Wack, H.; Young, B.; Ferraris, D.; Lectka, T. *J. Am. Chem. Soc.* **2002**, *124*, 6626.
[106] Lynch, J. E.; Riseman, S. M.; Laswell, W. L.; Tschaen, D. M.; Volante, R. P.; Smith, G. B.; Shinkai, I. *J. Org. Chem.* **1989**, *54*, 3792.
[107] Brady, W. T.; Smith, L. *J. Org. Chem.* **1971**, *36*, 1637.
[108] Kagan, H. B.; Jacques, J. *Bull. Soc. Chim. Fr.* **1958**, 1600.
[109] Brady, W. T.; Saidi, K. *J. Org. Chem.* **1979**, *44*, 733.
[110] Pons, J.-M.; Oblin, M.; Pommier, A.; Rajzmann, M.; Liotard, D. *J. Am. Chem. Soc.* **1997**, *119*, 3333.
[111] Cortez, G. C.; Tennyson, R. L.; Romo, D. *J. Am. Chem. Soc.* **2001**, *123*, 7945.
[112] Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166.
[113] France, S.; Guerin, D. J.; Miller, S. J.; Lectka, T. *Chem. Rev.* **2003**, *103*, 2985.
[114] Cortez, G. C.; Oh, S. H.; Romo, D. *Synthesis* **2001**, 1731.
[115] Dymock, B. W.; Kocienski, P. J.; Pons, J.-M. *Synthesis* **1998**, 1655.
[116] Dymock, B. W.; Kocienski, P. J.; Pons, J.-M. *Chem. Commun.* **1996**, 1053.
[117] Yang, H. W.; Romo, D. *Tetrahedron Lett.* **1998**, *39*, 2877.
[118] Tamai, Y.; Yoshiwara, H.; Someya, M.; Fukumoto, J.; Miyano, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2281.
[119] Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; Waldmann, H. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 17272.
[120] Chen, M. J.; Lo, C. Y.; Chin, C. C.; Liu, R. S. *J. Org. Chem.* **2000**, *65*, 6362.
[121] Brückner, R. *Curr. Org. Chem.* **2001**, *5*, 679.
[122] Knight, D. W. *Contemp. Org. Synth.* **1994**, *1*, 287.
[123] Rao, Y. S. *Chem. Rev.* **1976**, *76*, 625.
[124] Gil, S.; Parra, M.; Rodriguez, P.; Segura, J. *Mini-Rev. Org. Chem.* **2009**, *6*, 345.
[125] Laduwahetty, T. *Contemp. Org. Synth.* **1995**, *2*, 133.
[126] des Abbayes, H.; Salaün, J.-Y. *Dalton Trans.* **2003**, 1041.
[127] Cassar, L. *Ann. N. Y. Acad. Sci.* **1980**, *333*, 208.
[128] Tan, Z.; Negishi, E. *Org. Lett.* **2006**, *8*, 2783.
[129] Larson, G. L.; Deperez, R. M. B. *J. Org. Chem.* **1985**, *50*, 5257.
[130] Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer: Berlin, 1983.
[131] Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981.
[132] Chamberlin, A. R.; Dezube, M.; Dussault, P.; McMills, M. C. *J. Am. Chem. Soc.* **1983**, *105*, 5819.
[133] D'Aniello, F.; Mann, A.; Mattii, D.; Taddei, M. *J. Org. Chem.* **1994**, *59*, 3762.
[134] Nicolaou, K. C.; Pfefferkorn, J. A.; Kim, S.; Wei, H. X. *J. Am. Chem. Soc.* **1999**, *121*, 4724.
[135] Belluš, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797.
[136] Bailey, D. M.; Johnson, R. E. *J. Org. Chem.* **1970**, *35*, 3574.
[137] Ma, S. M.; Lu, L. H.; Lu, P. *J. Org. Chem.* **2005**, *70*, 1063.
[138] Bur, S. K.; Martin, S. F. *Tetrahedron* **2001**, *57*, 3221.
[139] Kolb, H. C.; Vannieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
[140] Harcken, C.; Brückner, R. *Angew. Chem., Int. Ed.* **1997**, *36*, 2750.
[141] Ragoussis, N.; Ragoussis, V. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3529.
[142] Chun, J.; Yin, Y. I.; Yang, G. L.; Tarassishin, L.; Li, Y. M. *J. Org. Chem.* **2004**, *69*, 7344.
[143] Alper, H.; Leonard, D. *Tetrahedron Lett.* **1985**, *26*, 5639.
[144] Murray, T. F.; Samsel, E. G.; Varma, V.; Norton, J. R. *J. Am. Chem. Soc.* **1981**, *103*, 7520.
[145] Oguma, T. *J. Chromatogr. B: Biomed. Sci. Appl.* **2001**, *764*, 46.
[146] de Lorenzo, F.; Feher, M.; Martin, J.; Collot-Teixeira, S.; Dotsenko, O.; McGregor, J. L. *Curr. Med. Chem.* **2006**, *13*, 3385.
[147] Tolbert, J. A. *Nat. Rev. Drug Discovery* **2003**, *2*, 517.
[148] Leßmann, T.; Leuenberger, M. G.; Menninger, S.; Lopez-Canet, M.; Müller, O.; Hümmer, S.; Bormann, J.; Korn, K.; Fava, E.; Zerial, M.; Mayer, T. U.; Waldmann, H. *Chem. Biol.* **2007**, *14*, 443.
[149] Fournier, L.; Gaudel-Siri, A.; Kocienski, P. J.; Pons, J.-M. *Synlett* **2003**, 107.
[150] Ojima, I.; Tzamarioudaki, M.; Li, Z.; Donovan, R. J. *Chem. Rev.* **1996**, *96*, 635.
[151] Krafft, M. E.; Scott, I. L.; Romero, R. H.; Feibelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199.
[152] Heck, R. F.; Breslow, D. S. *J. Am. Chem. Soc.* **1961**, *83*, 4023.
[153] Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591.

154 Buszek, K. R.; Sato, N.; Jeong, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5511.
155 Nicolaou, K. C.; McGarry, D. G.; Somers, P. K.; Kim, B. H.; Ogilvie, W. W.; Yiannikouros, G.; Prasad, C. V. C.; Veale, C. A.; Hark, R. R. *J. Am. Chem. Soc.* **1990**, *112*, 6263.
156 Dai, W.-M.; Guan, Y.; Jin, J. *Curr. Med. Chem.* **2005**, *12*, 1947.
157 Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. In *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Sausalito, CA, 1987; pp 750–751.
158 Krafft, M. E.; Scott, I. L.; Romero, R. H. *Tetrahedron Lett.* **1992**, *33*, 3829.
159 Greenberg, W. A.; Varvak, A.; Hanson, S. R.; Wong, K.; Huang, H.; Chen, P.; Burk, M. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5788.
160 Thayer, A. M. *Chem. Eng. News* **2006**, *84* (33), 26.
161 Gijsen, H. J.; Wong, C.-H. *J. Am. Chem. Soc.* **1995**, *117*, 7585.
162 Evans, D. A.; Black, W. C. *J. Am. Chem. Soc.* **1993**, *115*, 4497–4513.
163 Mulzer, J.; Pichlmair, S.; Green, M. P.; Marques, M. M. B.; Martin, H. *J. Proc. Natl. Acad. Sci. USA* **2004**, *101*, 11980–11985.
164 Csaky, A. G.; Mba, M.; Plumet, J. *Synlett* **2003**, 2092.
165 Carretero, J. C.; Ghosez, L. *Tetrahedron Lett.* **1988**, *29*, 2059.
166 De Lombaert, S.; Nemery, I.; Roekens, B.; Carretero, J. C.; Kimmel, T.; Ghosez, L. *Tetrahedron Lett.* **1986**, *27*, 5099.
167 Bercot, E. A.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 247.
168 Chen, Y. G.; McDaid, P.; Deng, L. *Chem. Rev.* **2003**, *103*, 2965.
169 Stoncius, A.; Nahrwold, M.; Sewald, N. *Synthesis* **2005**, 1829.
170 Jeske, R. C.; DiCiccio, A. M.; Coates, G. W. *J. Am. Chem. Soc.* **2007**, *129*, 11330.
171 Ranucci, E.; Liu, Y.; Lindblad, M. S.; Albertsson, A. C. *Macromol. Rapid Commun.* **2000**, *21*, 680.
172 Arason, K. M.; Bergmeier, S. C. *Org. Prep. Proced. Int.* **2002**, *34*, 337.
173 Sustmann, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, **1991**; Vol. *6*, pp 309–316.
174 Bergmeier, S. C.; Ismail, K. A. *Synthesis* **2000**, 1369.
175 Evans, D. A.; Wu, L. D.; Wiener, J. J. M.; Johnson, J. S.; Ripin, D. H. B.; Tedrow, J. S. *J. Org. Chem.* **1999**, *64*, 6411.
176 Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 77.
177 Fadel, A.; Salaün, J. *Tetrahedron Lett.* **1988**, *29*, 6257.
178 Beckett, R. P.; Crimmin, M. J.; Davis, M. H.; Spavold, Z. *Synlett* **1993**, 137.
179 Kloetzel, M. C. *Org. React.* **1948**, *4*, 1.
180 Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021.
181 Benn, F. R.; Dwyer, J.; Chappell, I. *J. Chem. Soc., Perkin Trans. 2* **1977**, 533.
182 Rondestvedt, C. S.; Filbey, A. H. *J. Org. Chem.* **1954**, *19*, 548.
183 Heck, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 2712.
184 Stille, J. K.; Divakaruni, R. *J. Org. Chem.* **1979**, *44*, 3474.
185 Chiusoli, G. P.; Costa, M.; Cucchia, L.; Gabriele, B.; Salerno, G.; Veltri, L. *J. Mol. Catal. A: Chem.* **2003**, *204*, 133.
186 Osakada, K.; Doh, M. K.; Ozawa, F.; Yamamoto, A. *Organometallics* **1990**, *9*, 2197.
187 Feuillet, F. J. P.; Cheeseman, M.; Mahon, M. F.; Bull, S. D. *Org. Biomol. Chem.* **2005**, *3*, 2976.
188 Kamino, T.; Murata, Y.; Kawai, N.; Hosokawa, S.; Kobayashi, S. *Tetrahedron Lett.* **2001**, *42*, 5249.
189 Kende, A. S.; Kawamura, K.; Devita, R. J. *J. Am. Chem. Soc.* **1990**, *112*, 4070.
190 Katagiri, N.; Hirose, M.; Sato, M.; Kaneko, C. *Chem. Pharm. Bull.* **1989**, *37*, 933.
191 Kurz, T. *Tetrahedron* **2005**, *61*, 3091.
192 Chollet, A. M.; Le Diguarher, T.; Kucharczyk, N.; Loynel, A.; Bertrand, M.; Tucker, G.; Guilbaud, N.; Burbridge, M.; Pastoureau, P.; Fradin, A.; Sabatini, M.; Fauchere, J. L.; Casara, P. *Bioorg. Med. Chem.* **2002**, *10*, 531.
193 Heinisch, L.; Wittmann, S.; Stoiber, T.; Berg, A.; Ankel-Fuchs, D.; Mollmann, U. *J. Med. Chem.* **2002**, *45*, 3032.
194 Mu, F. R.; Lee, D. J.; Pryor, D. E.; Hamel, E.; Cushman, M. *J. Med. Chem.* **2002**, *45*, 4774.
195 Yamashita, M.; Nishida, H. Japanese Patent 09087275 (1997).
196 Shibuya, I.; Goto, M.; Shimizu, M.; Yanagisawa, M.; Gama, Y. *Heterocycles* **1999**, *51*, 2667.
197 Boontheung, P.; Perlmutter, P. *Tetrahedron Lett.* **1998**, *39*, 2629.
198 Lapkin, I. I.; Semenov, V. I.; Saitkulova, F. G. *Zh. Org. Khim.* **1982**, *18*, 2468.
199 Testa, E.; Fontanella, L.; Cristiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1928.
200 Kolasa, T.; Miller, M. J. *Tetrahedron* **1989**, *45*, 3071.
201 Shapiro, S. L.; Rose, I. M.; Freedman, L. *J. Am. Chem. Soc.* **1957**, *79*, 2811.
202 Feuillet, F. J. P.; Niyadurupola, D. G.; Green, R.; Cheeseman, M.; Bull, S. D. *Synlett* **2005**, 1090.

[203] Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 9194.
[204] Roush, W. R.; Gustin, D. *Tetrahedron Lett.* **1994**, *35*, 4931.
[205] Reynolds, D. D. *J. Am. Chem. Soc.* **1957**, *79*, 4951.
[206] Sonoda, N.; Mizuno, T.; Murakami, S.; Kondo, K.; Ogawa, A.; Ryu, I.; Kambe, N. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 452.
[207] Hata, S.; Goto, H.; Tanaka, S.; Oku, A. *J. Appl. Polym. Sci.* **2003**, *90*, 2959.
[208] Reynolds, D. D.; Johnson, D. L.; Fields, D. L. *J. Org. Chem.* **1961**, *26*, 5119.
[209] Reynolds, D. D.; Johnson, D. L.; Fields, D. L. *J. Org. Chem.* **1961**, *26*, 5122.
[210] Ko, S. Y. *J. Org. Chem.* **1995**, *60*, 6250.
[211] Hauptman, E.; Fagan, P. J.; Marshall, W. *Organometallics* **1999**, *18*, 2061.
[212] Traxler, J. T. *J. Org. Chem.* **1979**, *44*, 4971.
[213] Shimizu, M.; Kikumoto, H.; Konakahara, T.; Gama, Y.; Shibuya, I. *Heterocycles* **1999**, *51*, 3005.
[214] Prakash, O.; Kaur, H.; Pundeer, R.; Dhillon, R. S.; Singh, S. P. *Synth. Commun.* **2003**, *33*, 4037.
[215] Dorofeev, A.; Mal'kina, A. G.; Trofimov, B. A. *Chem. of Heterocycl. Comp.* **2001**, *37*, 903.
[216] Mizuno, T.; Nakamura, F.; Ishino, Y.; Nishiguchi, I.; Hirashima, T.; Ogawa, A.; Kambe, N.; Sonoda, N. *Synthesis* **1989**, 770.

TABLE 1A

Kramer, J. W.; Treitler, D. S.; Coates, G. W. *Org. Synth.* **2009**, *86*, 287.
Woelfle, H.; Kopacka, H.; Wurst, K.; Preishuber-Pfluegl, P.; Bildstein, B. *J. Organomet. Chem.* **2009**, *694*, 2493.
Dunn, E. W.; Coates, G. W. *J. Am. Chem. Soc.* **2010**, *132*, 11412.

TABLE 1B

Ganji, P.; Doyle, D. J.; Ibrahim, H. *Org. Lett.* **2011**, *13*, 3142.
Liang, Y.; Hnatiuk, N.; Rowley, J. M.; Whiting, B. T.; Coates, G. W.; Rablen, P. R.; Morton, M.; Howell, A. R. *J. Org. Chem.* **2011**, *76*, 9962.
Chen, Q.; Mulzer, M.; Shi, P.; Beuning, P. J.; Coates, G. W.; O'Doherty, G. A. *Org. Lett.* **2011**, *13*, 6592.
Ganji, P.; Ibrahim, H. *Chem. Commun.* **2012**, *48*, 10138.
Mulzer, M.; Whiting, B. T.; Coates, G. W. *J. Am. Chem. Soc.* **2013**, *135*, 10930.
Mulzer, M.; Ellis, W. C.; Lobkovsky, E. B.; Coates, G. W. *Chem. Sci.* **2014**, *5*, 1928.