CHAPTER 1

MOLYBDENUM-CATALYZED ASYMMETRIC ALLYLIC ALKYLATIONS

CHRISTINA MOBERG

KTH School of Chemical Science and Engineering, Organic Chemistry, SE 100 44 Stockholm, Sweden

CONTENTS

PAGE

ACKNOWLEDGEMENTS . . . 2
INTRODUCTION . . . 2
MECHANISM AND STEREOCHEMISTRY . . . 4
Catalytic Cycle . . . 4
Stereochemistry . . . 6
Enantiodifferentiation . . . 11
Memory Effects . . . 14
Kinetic Resolution . . . 16
SITE SELECTIVITY . . . 18
SCOPE AND LIMITATIONS . . . 19
The Allylic Substrate . . . 19
The Leaving Group . . . 21
Functional-Group Compatibility . . . 22
The Nucleophile . . . 22
Chiral Ligands . . . 23
APPLICATIONS TO SYNTHESIS . . . 25
α-Amino Acids . . . 25
α-Hydroxy Acids . . . 26
(3*S*,4*S*)-3-(3-Fluorophenyl)-4-(hydroxymethyl)cyclopentanone . . . 26
Tipranavir . . . 27
(*R*)-Baclofen . . . 28
(−)-Physostigmine . . . 29
(−)-Δ^9-*trans*-Tetrahydrocannabinol . . . 29
COMPARISON WITH OTHER METHODS . . . 29
Metal-Catalyzed Allylations . . . 29
Organocatalytic Allylations . . . 35
EXPERIMENTAL CONDITIONS . . . 36
EXPERIMENTAL PROCEDURES . . . 37

kimo@kth.se

Organic Reactions, Vol. 84, Edited by Scott E. Denmark et al.

Tricarbonyltris(propionitrile)molybdenum(0) 37
Tricarbonyl(cycloheptatriene)molybdenum(0) 37
Dimethyl 2-[(*S*)-1-Phenyl-2-propenyl]propanedioate [Allylation of a Malonate] 38
Dimethyl 2-[(*S*)-1-Phenyl-2-propenyl]propanedioate [Microwave-Assisted Allylation of a Malonate] 38
Dimethyl 2-[(*R*)-1-Methyl-2-propenyl]propanedioate [Allylation of a Malonate with an Alkyl-Substituted Allylic Carbonate] 39
Dimethyl 2-[3-(*S*,*E*)-4-Methylhexa-1,4-diene]propanedioate [Allylation of a Malonate with a Dienylic Carbonate] 40
(*R*)-3-Allyl-1-methyl-3-(3-(trimethylsilyl)prop-2-ynyl)indolin-2-one [Allylation of an Alkyloxindole] 41
(*R*)-5-Methyl-5-[(*S*)-(1-phenyl)-2-propenyl]-2-phenyloxazol-4(5*H*)-one [Allylation of an Oxazolidine-4-one] 42
TABULAR SURVEY 42
Chart 1. Ligands Used in Tables 44
Table 1. Allylation of Malonates 46
Table 2. Allylation of Cyano Esters 61
Table 3. Allylation of α-Imino Esters and α-Imino Lactones 62
Table 4. Allylation of Oxalactims 63
Table 5. Allylation of Oxindoles 64
REFERENCES 71

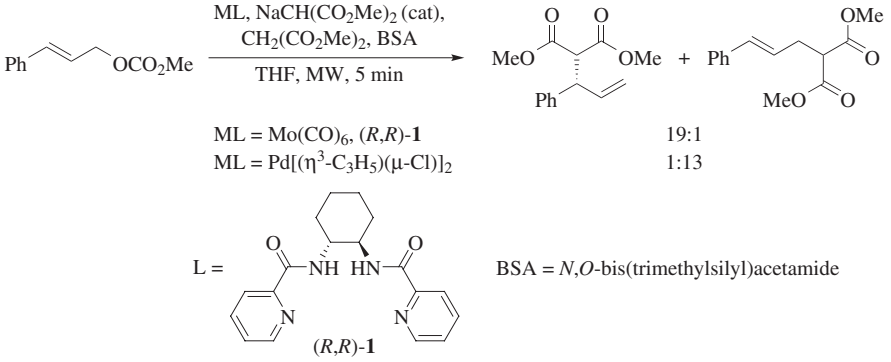
ACKNOWLEDGEMENTS

I wish to thank Professor Guy C. Lloyd Jones and Professor Barry M. Trost for valuable comments on the manuscript. I also want to thank Professor Scott E. Denmark for valuable suggestions and for guiding me through the last stages of the chapter, and Dr. Linda S. Press for professional help throughout the preparation of the manuscript.

INTRODUCTION

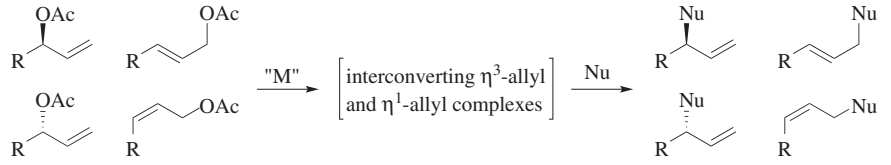
Metal-catalyzed asymmetric allylic alkylations constitute synthetically versatile reactions whereby carbon–carbon and carbon–heteroatom bonds are formed, often with high chemo-, site-, and stereoselectivities. A variety of transition-metal complexes containing Pd, Mo, W, Ir, Ru, Rh, Fe, Cu, Ni, and Pt[1-3] catalyze the process by activating otherwise slow-reacting allylic groups. The substrates most commonly used are derivatives of allylic alcohols such as allylic acetates or other carboxylic esters, allylic carbonates, or phosphates. Stabilized or non-stabilized carbanions as well as nitrogen, oxygen, and sulfur nucleophiles can be used to displace the electrophile. The reactions usually occur under milder conditions than ordinary S_N2 or S_N2' reactions of halides or sulfonates. Catalysts containing palladium have been explored most extensively and applied in asymmetric synthesis.[4,5] The first molybdenum-catalyzed reactions were introduced by Trost and Lautens.[5a] Molybdenum,[6] as well as iridium[7] catalysts exhibiting high site- and stereoselectivity are known and serve as useful complements to the palladium catalysts since

they typically form products with different connectivity. For example, whereas the molybdenum-catalyzed microwave-mediated reaction of 3-phenyl-2-propenyl methyl carbonate with sodium dimethyl malonate in the presence of ligand **1** provides the branched and linear products in a 19:1 ratio, the analogous palladium-catalyzed reaction gives the same isomers in a ratio of 1:13 (Scheme 1).[8]



Scheme 1

All asymmetric allylic alkylations (Pd, Mo, W, Ir, Ru, Rh, Fe, Cu, Ni, Pt) proceed via η^3- and/or η^1-allylmetal intermediates. The site- and stereoselectivities of the reactions are governed by several equilibria. Depending on the nature of the initially formed allyl complex and the extent of equilibration of the allyl intermediates, the original constitution and configuration of the substrate may be retained, inverted, or lost (Scheme 2). Loss of substrate constitution and configuration may lead to high selectivity even from mixtures of substrates differing in absolute configuration, configuration of the olefinic bond, and the site of the substituent, since the isomerization may lead to a single allyl intermediate. Under appropriate conditions, such selectivity is observed in reactions using catalysts based on palladium as well as molybdenum and iridium. The actual result of the catalytic reactions is a function of several factors, including the metal, the ligand, the nucleophile, and the substituents on the allyl system. For this reason the different types of catalysts can be highly complementary.



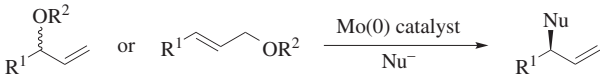
Scheme 2

Previous reviews covering molybdenum-catalyzed asymmetric allylic alkylations (AAA) are available.[9] Surveys of Mo-catalyzed AAA are also included in more general reviews that cover other metal-containing catalysts[1–3,6,10,11] or several types of

processes.[12] Allylations catalyzed by Mo(0) complexes containing chiral ligands are described and listed in the Tables. Reactions proceeding via Mo(II)[13,14] and Mo(IV)[15] complexes are also known, but have different characteristics and proceed by a different mechanism. No examples of asymmetric induction in the Mo(II)/Mo(IV) processes are known, and therefore these reactions are not included here.

MECHANISM AND STEREOCHEMISTRY

The mechanism of molybdenum-catalyzed nucleophilic substitutions of allylic acetates or carbonates has been studied in detail, in particular by Lloyd-Jones. The reactions proceed via oxidative addition of the substrate to a ligated Mo(0) species to form an asymmetric η^3-allylmolybdenum(II) complex, followed by coordination of the nucleophile to the metal, and final reductive elimination to form the product. The η^3-allyl complexes that are intermediates are rapidly equilibrating, which leads to the formation of a single major complex and thereby to high site- and stereoselectivity in the catalytic reactions (Scheme 3). Equilibration of intermediate η^3-allyl complexes is usually rapid in comparison to nucleophilic attack, and therefore close to equal mixtures of enantiomers and constitutional isomers are obtained from enantioenriched or racemic branched substrates as well as from linear substrates. However, under conditions where equilibration is slow compared to nucleophilic attack, lower enantioselectivity is observed in reactions using branched racemic substrates.

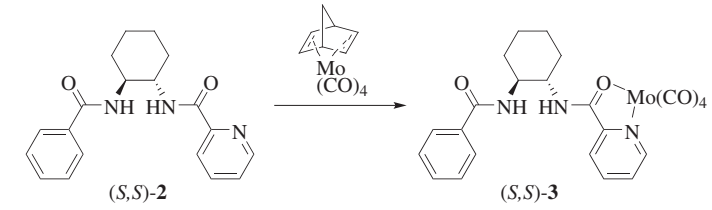


R^2 = CO_2Me, CO_2Et, CO_2t-Bu, COMe, P(O)$(OEt)_2$

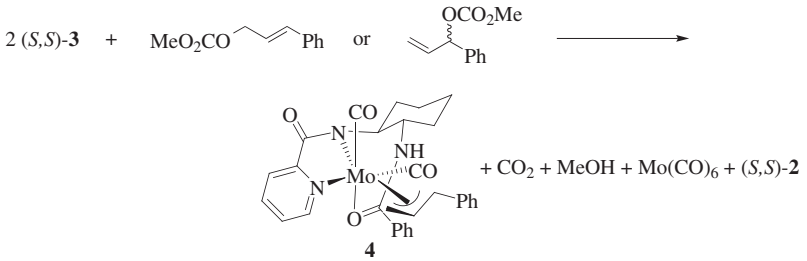
Scheme 3

Catalytic Cycle

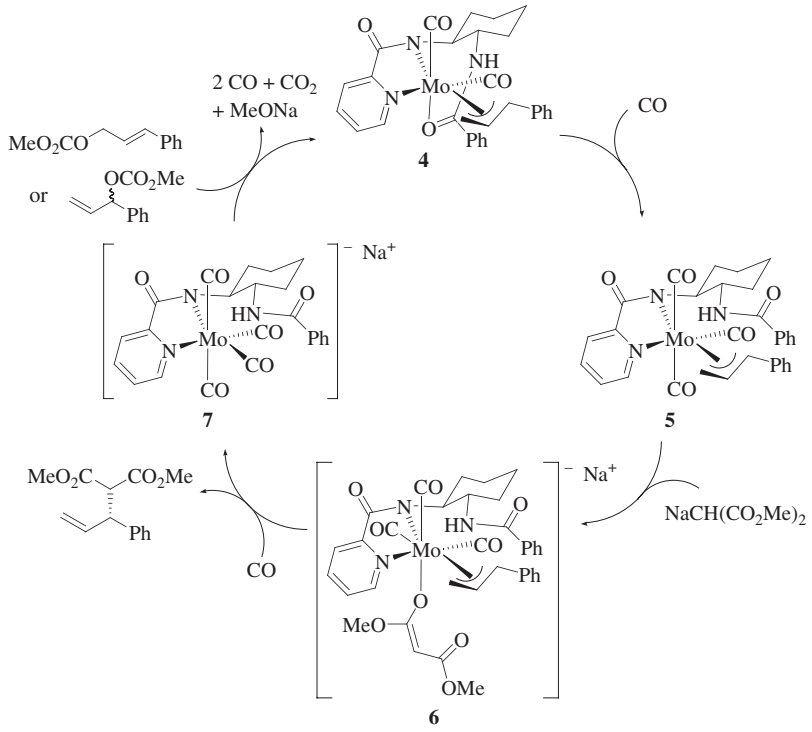
Detailed mechanistic studies have been performed using the monopyridine ligand (*S,S*)-**2**.[16] The generation of the catalytic intermediate is shown in Eqs. 1 and 2, and the catalytic cycle proposed for the reaction, which is in accordance with NMR spectroscopic and single-crystal X-ray structural data as well as with results from deuterium-labeling studies (see Enantiodifferentiation section), is shown in Scheme 4.[16,17] Ligand **2** combines with $Mo(CO)_4$(norbornadiene) to yield the neutral Mo(0) complex **3** (Eq. 1). Complex **3** then reacts with the substrate (linear or branched) to generate complex **4**, an 18-electron η^3-allylmolybdenum(II) complex with close to octahedral geometry, as determined by X-ray crystallography (Eq. 2).[18] The stoichiometry for the generation of complex **4** involves formation of one equivalent each of complex **4**, CO_2, MeOH, $Mo(CO)_6$, and free ligand from two equivalents of complex **3** and one equivalent of the allylic carbonate.



(Eq. 1)



(Eq. 2)



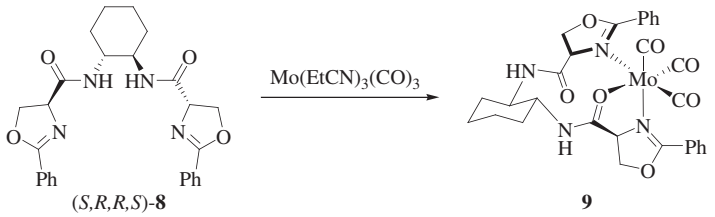
Scheme 4

The ligand (*S*,*S*)-**2** coordinates to the metal in a tridentate, *fac*-binding mode through the pyridine nitrogen, a deprotonated amide nitrogen, and the benzamide

oxygen. The allyl group is slightly non-symmetrically bound ((1*R*,2*R*) configuration, close to η^3 coordination), is *syn* orientated with respect to two CO ligands, and is situated *trans* to the picolinamide nitrogen and *cis* to the benzamide oxygen.[17] The solid-state structure is consistent with that found in solution (see Enantiodifferentiation section).[19] The computed structure is also in good agreement with the observed structure.[20]

In the next step, the weakly bound amide carbonyl oxygen in structure **4** is replaced by a CO ligand (with formation of complex **5**), followed by coordination of malonate, likely through oxygen as shown in the suggested structure **6** (Scheme 4). Final reductive elimination yields the product and complex **7**, which together with complex **4** is the major ligand-containing species observed in solution. No reaction occurs when sodium malonate is added to isolated complex **4** in the absence of CO, since CO is needed for the formation of complex **5**, which reacts with malonate.[18] When $Mo(CO)_6$ is added to the mixture, it serves as the source of CO and the allylation reaction occurs.

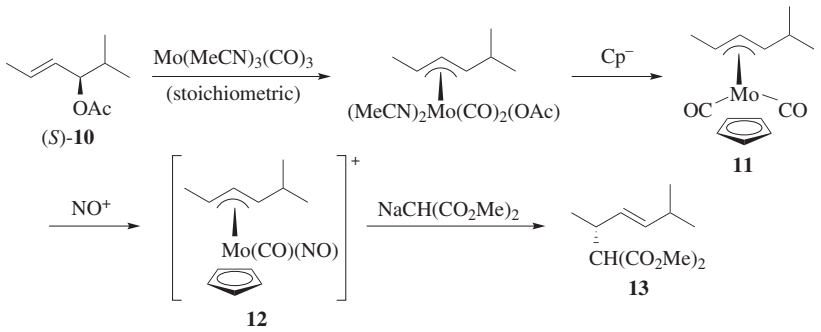
A Mo(0) complex of tetradentate bisoxazoline ligand (*S,R,R,S*)-**8** is obtained from reaction of the ligand with $Mo(EtCN)_3(CO)_3$ and its structure (complex **9**) has been determined by single-crystal X-ray analysis (Eq. 3).[21] The ligand binds to the metal via the two dihydrooxazole nitrogen atoms and one of the amide carbonyl groups. The remaining coordination sites are occupied by CO ligands. It is probable that an analogous complex, with both nitrogen atoms in the pyridine rings taking part in coordination to Mo, is initially formed in the catalytic cycle involving the bispyridinylamide ligand **1**.



(Eq. 3)

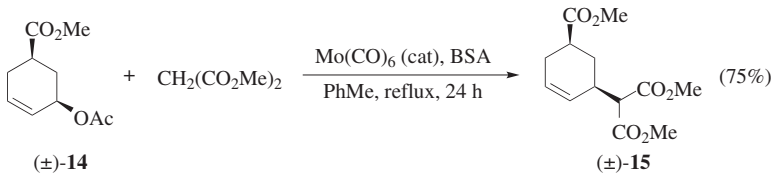
Stereochemistry

Oxidative addition of allylic acetates to Mo(0) species can proceed through either a retentive or an invertive mechanism. Addition of non-racemic acetate (*S*)-**10** to a stoichiometric amount of $Mo(MeCN)_3(CO)_3$ yields, after ligand exchange, η^5-cyclopentadienyl complex **11** with retention of configuration (Scheme 5), as established by X-ray crystallography.[22] (The same stereochemical course is observed upon oxidative addition of a cyclic allylic acetate to $Mo(MeCN)_3(CO)_3$).[23] Reaction of the cationic complex **12**–obtained by displacement of one carbonyl group of complex **11** by NO^+–with the sodium salt of dimethyl malonate at the more sterically accessible site affords the product (**13**) with inversion of configuration.[22] Net inversion of configuration is thus observed for the stoichiometric reactions.



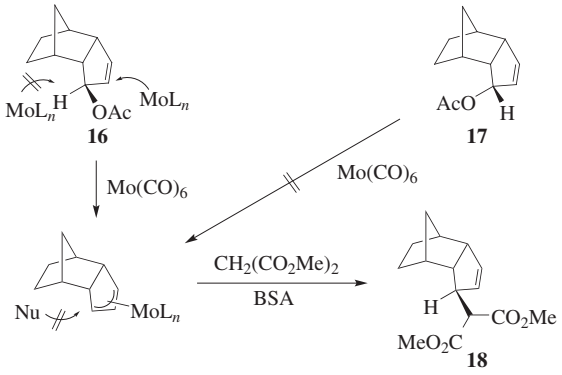
Scheme 5

In contrast, the major products obtained from chiral substrates (racemic or enantiomerically enriched) under catalytic conditions are those formed by overall retention of configuration, as shown by the reaction of racemic acetate **14** to yield malonate **15** (Eq. 4).[24,25]



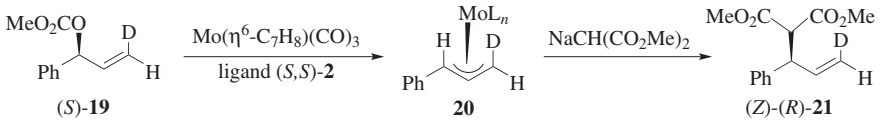
(Eq. 4)

The stereochemical course observed in Eq. 4 may be the result of either double inversion or double retention of configuration. Diastereomeric acetates **16** and **17**, which are inert toward attack from the *endo* face, serve as probes to elucidate the stereochemical course of each step in the catalytic process.[26] Whereas allylic acetate **16** reacts readily with $Mo(CO)_6$ followed by dimethyl malonate to provide product **18**, epimer **17** is inert, suggesting a mechanism in which both steps proceed by retention of configuration (Scheme 6).

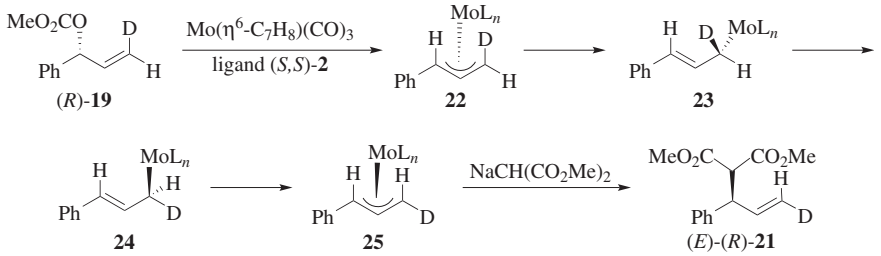


Scheme 6

Conclusive evidence for a retention-retention pathway was obtained using ligand (*S,S*)-**2** and Mo(η^6-C_7H_8)$(CO)_3$ in reactions of deuterium-labeled allylic carbonates (*S*)- and (*R*)-**19** with $NaCH(CO_2Me)_2$ as the nucleophile.[27] Substrate (*S*)-**19** affords malonate (*Z*)-(*R*)-**21** as the final product (Scheme 7), whereas (*R*)-**19**, which is the mismatched substrate, gives a product with the same absolute configuration but with inversion of configuration of the olefinic bond, malonate (*E*)-(*R*)-**21** (Scheme 8). The crystal structure of the protio allyl complex containing ligand (*S*,*S*)-**2**, complex **4** (see Catalytic Cycle section), corresponds to η^3-allyl complex **20**. This complex reacts with malonate to give the same product as substrate (*S*)-**19**, i.e., malonate (*Z*)-(*R*)-**21**. This result shows that substrate (*S*)-**19** affords an η^3-allyl complex with retention of configuration (**20**) and that the final product is obtained with retention of both absolute and geometrical configuration (Scheme 7). In contrast, allylic carbonate (*R*)-**19** forms an intermediate allyl complex that undergoes η^3–η^1–η^3 equilibration (intermediate **22** -> **23** -> **24** -> **25**, Scheme 8).[28,29] These results demonstrate that the reactions of the deuterated compounds are stereospecific. Both isomers of the substrate react with retention of configuration at the allylic carbon center, the apparent inversion of one isomer being the result of equilibration of the allyl complex. Overall, the two reactions are stereoconvergent at the allylic center.

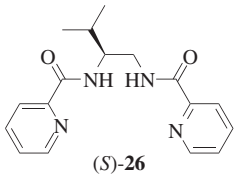


Scheme 7



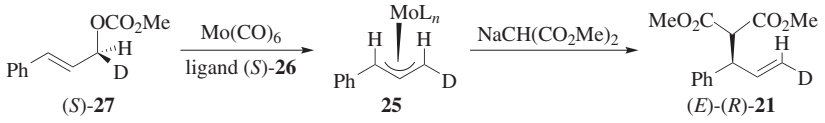
Scheme 8

Reactions of allylic carbonates (*S*)- and (*R*)-**19** in the presence of ligand (*S*)-**26** lead to the same products as those obtained using ligand (*S*,*S*)-**2**.[28] In the presence of the enantiopure ligand, the two enantiomers of carbonate **19** react at different rates: the fast-reacting isomer, (*S*)-**19**, is matched with ligand (*S*)-**26** and its enantiomer is mismatched. A small portion of slow-reacting enantiomer (*R*)-**19** (about 2.5% of the total amount of product) reacts with net inversion, possibly as a result of Mo–Mo transfer with inversion.



(*S*)-**26**

Linear substrates with a deuterium in the 1-position also react by a retention-retention pathway. Thus, linear, enantiomerically enriched deuterium-labeled carbonate (*S*)-**27** combines with $Mo(CO)_6$ and ligand (*S*)-**26** to form the η^3-allyl complex **25**, wherein the metal enters from the same side as the leaving group (Scheme 9).[27] Reaction of complex **25** with sodium dimethyl malonate yields product (*E*)-(*R*)-**21** with retention of configuration at the stereogenic center and at the newly formed double bond.

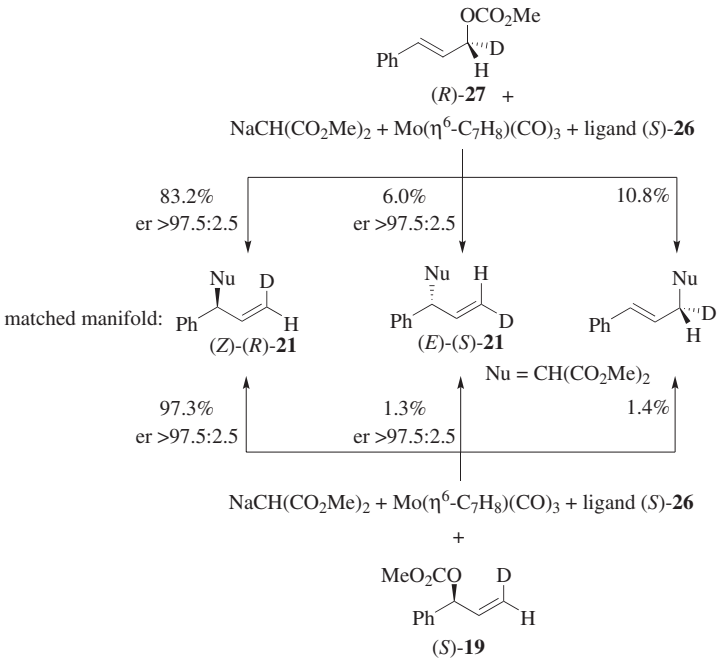


(*S*)-**27** **25** (*E*)-(*R*)-**21**

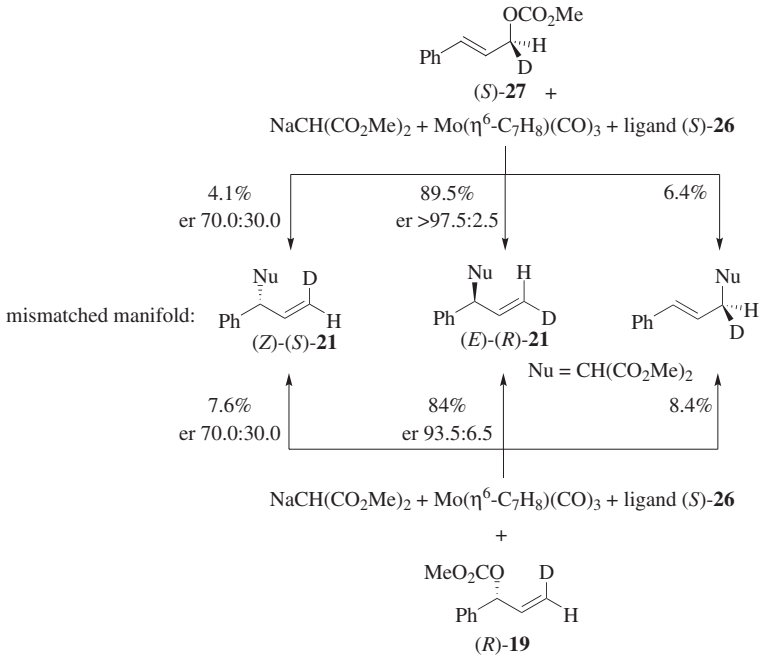
Scheme 9

The enantiomeric substrate, (*R*)-**27**, affords a branched product with the same absolute configuration as that obtained from allylic carbonate (*S*)-**27**, but with a (*Z*) configuration of the double bond. The minor, linear, constitutional isomer obtained from substrate (*R*)-**27** has the (*R*) configuration, whereas that formed from substrate (*S*)-**27** has the opposite absolute configuration; i.e., in both cases net retention of configuration is observed.[28] The reactions are summarized in Schemes 10 and 11, which show the matched and mismatched manifolds, respectively.[28] The matched and mismatched substrates provide branched products with the same absolute configuration, but the enantiomeric purity of that from the former is higher.

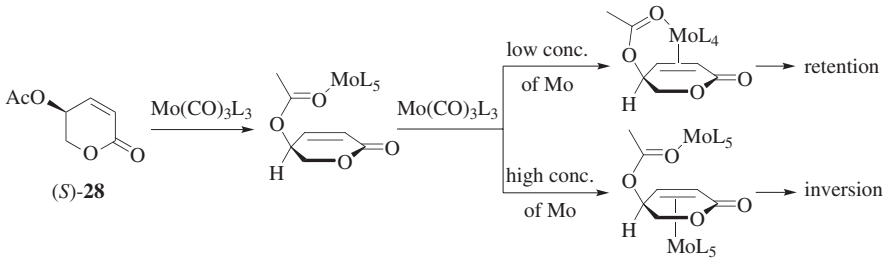
A rationale for the divergent stereochemical course of stoichiometric (net inversion) and catalytic (net retention) processes is provided on the basis of results from the oxidative addition of dihydropyranone (*S*)-**28** to $Mo(DMF)_3(CO)_3$, $Mo(toluene)_3(CO)_3$, and $Mo(CO)_6$.[30] Retention of configuration is favored at low effective concentration of the molybdenum complex (dilute solution, $\leq$1 equivalent of Mo(0)) and with easily displaced ligands, whereas inversion is observed at higher concentrations of Mo(0) (concentrated solution, $>$1 equivalent of Mo(0)). This suggests that transition structures leading to products from retention and inversion of configuration involve one and two Mo centers, respectively (Scheme 12). In contrast, initial coordination to the olefinic bond is observed with palladium catalysts under catalytic conditions, leading to oxidative addition with inversion of configuration.[31]



Scheme 10



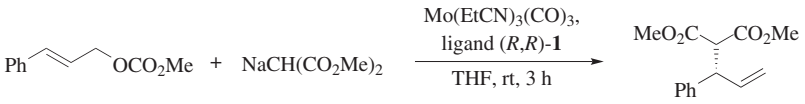
Scheme 11



Scheme 12

Enantiodifferentiation

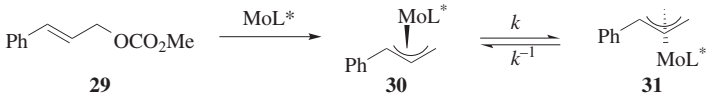
The first enantioselective molybdenum-catalyzed reactions were discovered by Trost and coworkers.[32] A range of chiral ligands can be used to control the stereochemical course of the reactions of achiral or racemic substrates in molybdenum-catalyzed reactions. The most commonly used ligand is the readily accessible bis(pyridinylamide) **1** (Eq. 5),[32] although somewhat better results are achieved with derivatives carrying π-donating substituents on one[33] or both[34] pyridine rings (see Chart 1 and the Tabular Survey).



(70%) er 99.5:0.5
branched/linear = 49:1

(Eq. 5)

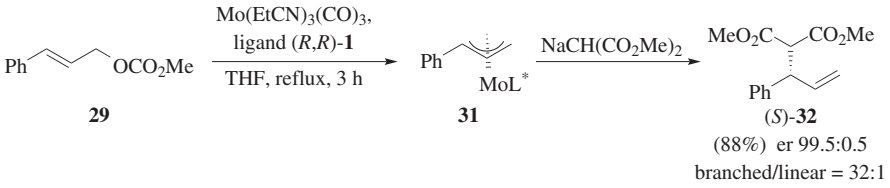
In reactions with linear, achiral substrates such as allylic carbonate **29**, the catalyst may recognize one of the enantiotopic faces leading to selective formation of one of the diastereomeric η^3-allyl complexes **30** or **31** (Scheme 13). Alternatively, the two complexes may be in dynamic equilibrium, with one of them being preferentially attacked by the nucleophile. Both situations may lead to efficient enantiodiscrimination.



29 **30** **31**

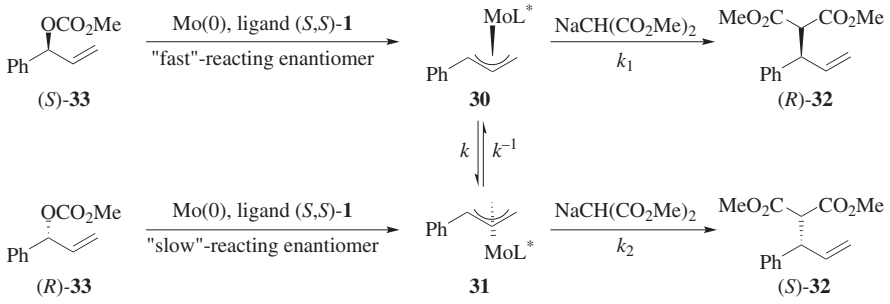
Scheme 13

In the presence of a catalyst prepared from $Mo(EtCN)_3(CO)_3$ and ligand (*R*,*R*)-**1**, (*E*)-3-phenyl-2-propenyl methyl carbonate (**29**) reacts with sodium dimethyl malonate to give malonate (*S*)-**32** as the major product (Scheme 14).[32] Knowing that the reaction proceeds via a retention-retention pathway, the major product must therefore be formed via complex **31**.



Scheme 14

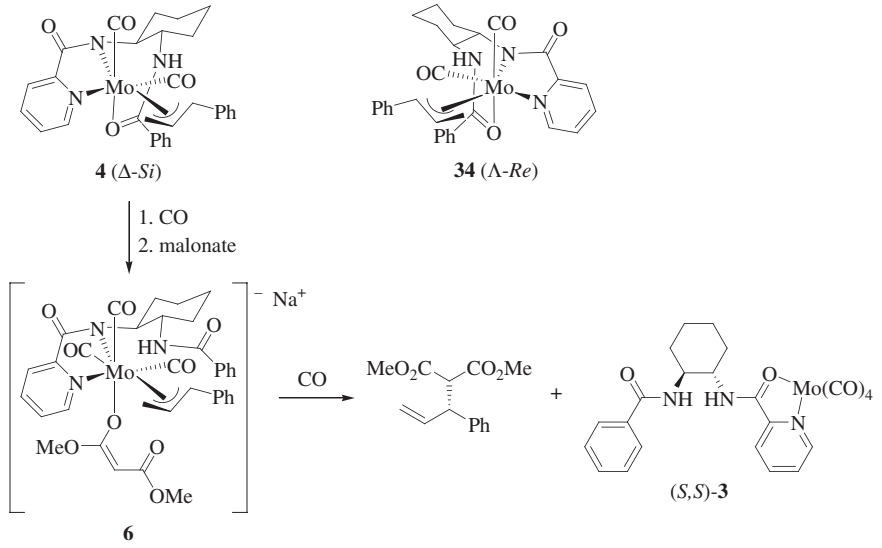
Oxidative addition of allylic carbonates (*S*)-and (*R*)-**33** to the Mo•(*S*,*S*)-**1** catalyst leads to complexes **30** and **31**, respectively (Scheme 15; in the published[35] scheme an inversion-inversion mechanism was depicted). The absolute configuration of the product is determined by whether complex **30** or **31** reacts with the nucleophile. In contrast to the situation with linear substrates, reaction of the branched substrates in racemic form would, in the absence of isomerization of intermediate allyl complexes, inevitably lead to the formation of racemates. If, in contrast, equilibration of the diastereomeric η^3-allyl complexes is fast compared to nucleophilic attack, a dynamic kinetic asymmetric transformation (DYKAT)[36] results, which may lead to formation of a single enantiomer.[35] Branched substrates frequently react with somewhat lower enantioselectivity than the corresponding linear substrates, demonstrating that equilibration under certain conditions is not sufficiently rapid, resulting in a memory effect (see Memory Effects section). The isomerization process interconverting complexes **30** and **31** proceeds mainly via η^1-allylmolybdenum intermediates, although an analysis of the results from deuterium-labeling studies (Schemes 10 and 11) suggests that Mo–Mo transfer with accompanying inversion of configuration may account for the small portion of the net inversion observed[28] (compare Scheme 12).



Scheme 15

Several stereoisomers of the octahedral Mo(II) complex from oxidative addition of the allylic substrate to the Mo(0) precursor are possible. Pyridinylamide **2**, with only one pyridine ring, coordinates facially via the pyridine nitrogen atom, one deprotonated amide nitrogen atom, and one carbonyl oxygen atom (see Catalytic Cycle section), resulting in either of two diastereomeric complexes (with opposite

configurations at Mo). In each structure, three diastereotopic coordination sites remain for the allylic group (opposite to pyridine, to nitrogen, and to oxygen), which can bind via either of its two faces, thus giving rise to twelve possible stereoisomers. In addition, the allylic group can rotate around the Mo–allyl axis. A single major compound is observed in solution. This major allyl complex is in dynamic equilibrium with a diastereomeric complex with molybdenum bound to the same face of the allylic group, present in about 1% abundance. By multinuclear solution NMR studies of the major complex, its structure is identified as having either Δ-*Si* (**4**) or Λ-*Re* (**34**) configuration (Scheme 16);[17] the former structure corresponds to that found in the solid state.[18]



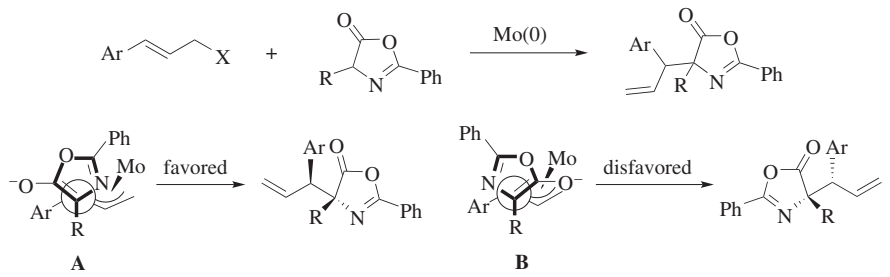
Scheme 16

Although one face of the allylic group in **4** clearly is open for approach by the nucleophile, attack by malonate from that direction leads to the product of opposite configuration to that observed.[16] The product obtained in the catalytic reaction may therefore be the result of nucleophilic attack on a minor, not observed, complex or of pre-coordination of the nucleophile to the metal followed by reductive elimination, and thus attack occurs at the allylic group from the side of the metal. ^{1}H NMR spectroscopic studies of the η^3-allyl complexes and products obtained using deuterated substrates (*S*)-**19** and (*R*)-**19** reveal that the latter situation is what actually occurs (Scheme 16, compare Schemes 7 and 8). The retention-retention pathway can thus be rationalized by the mechanism that proceeds via CO coordination to form a tris(CO) intermediate followed by complexation of the nucleophile to form a seven-coordinate intermediate, which undergoes reductive elimination to yield the final product (see Scheme 4).

According to DFT calculations, complex **4** is the most stable of the possible isomers for electronic as well as steric reasons; bonding and back-bonding interactions

between molybdenum and the η^3-allyl ligand are maximized and steric interactions are minimized.[20]

Rationales for the stereochemical course observed in reactions with other nucleophiles have been provided on the basis of stereochemical course of the catalytic process with malonate. In reactions of prochiral α-imino lactone enolates and cinnamyl derivatives (Scheme 17), the facial selectivity with respect to the allylic unit is the same as with malonate. This conclusion is deduced from the absolute and relative configurations of the amino acid obtained by hydrolysis of one of the products (with Ar = 2-bromophenyl, R = methyl), as determined by single-crystal X-ray analysis. Structures **A** and **B**, which represent different face selectivities with respect to the enolate, have been suggested as models for the transition structure. The observed product is that originating from structure **A**, where the enolate reacts from its *Re* face. MM2 calculations suggest this diastereomer to be more stable than that originating from structure **B**.[37] Analogous models are suggested to explain the diastereoselectivity in reactions with prochiral oxalactims[38] and 3-aryloxindoles.[39]

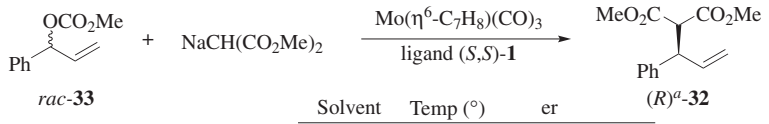


Scheme 17

Memory Effects

With some ligands, slightly different enantio- and site selectivities are observed in products obtained from linear and branched substrates; the slower-reacting, mismatched enantiomer of the branched precursor may result in a product with lower enantiomeric purity. For example, in the presence of ligand (*S,S*)-**1** and Mo(η^6-C_7H_8)$(CO)_3$, carbonate (*R*)-**33** is the mismatched, slower-reacting substrate.[35] Transformation of substrate (*R*)-**33** to the major product enantiomer, (*R*)-**32**, requires isomerization of the intermediate allyl complex (see Scheme 15). Incomplete isomerization leads to the formation of a higher proportion of the minor enantiomer, (*S*)-**32**, from (*R*)-**33** than from (*S*)-**33**, resulting in a memory effect. (A memory effect can be defined as a situation in which isomeric substrates, e.g., enantiomers, lead to different products or product ratios, when the basic mechanism predicts that they should not.[40]) The extent of this memory effect is dependent on the solvent because the relative rates of the two processes vary with different solvents (Scheme 18).[35] In the presence of ligand (*S,S*)-**1**, carbonate (*S*)-**33** thus reacts faster, with higher enantioselectivity, and with higher branched to linear ratio with dimethyl malonate than its enantiomer.[35] For this reason, the product obtained during the first half of the

reaction of racemic carbonate **33** has high enantiomeric purity, which deteriorates as the reaction proceeds (from er 99.0:1.0 to er 93.5:6.5 at 48° in THF) at the same time as the branched to linear ratio decreases from 35:1 to 25:1. The k_{rel} for the two enantiomers is 9 (see Kinetic Resolution section, Scheme 21). Under the same conditions, the enantiomeric ratio of the product obtained from linear substrate **29** is constant over time (98.5:1.5 er).[35]



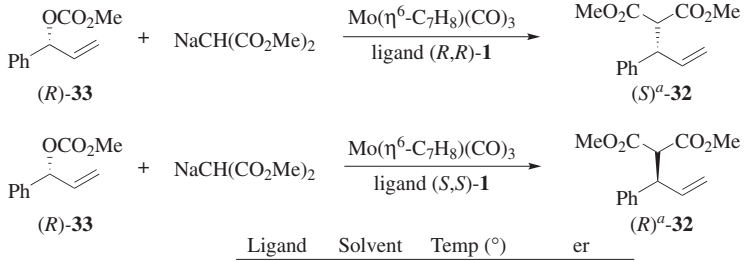
rac-**33** (*R*)[a]-**32**

Solvent	Temp (°)	er
THF	48	93.5:6.5
MeCN	48	91.5:8.5
PhMe	60	98.0:2.0

[a] Erroneously reported with the opposite absolute configuration in ref. 35.

Scheme 18

Reaction of allylic carbonate (*R*)-**33** in the presence of the matched ligand (*R*,*R*)-**1** affords malonate (*S*)-**32** with er 99.5:0.5 and er 99.0:1.0 in THF and MeCN, respectively (Scheme 19).[35] In the presence of mismatched ligand (*S*,*S*)-**1**, carbonate (*R*)-**33** provides a product with opposite configuration with er 85.0:15.0 and er 72.0:28.0 in THF and MeCN, respectively (Scheme 19).[35] For the mismatched case in THF, the enantioselectivity is improved to er 95.5:4.5 by slow addition of the nucleophile, consistent with the assumption that slow equilibration of the diastereomeric η^3-allyl complexes is the reason for the memory effect (compare Scheme 15). A more reactive nucleophile, dimethyl methylmalonate,[25] accordingly results in a more pronounced memory effect.



(*R*)-**33** (*S*)[a]-**32**

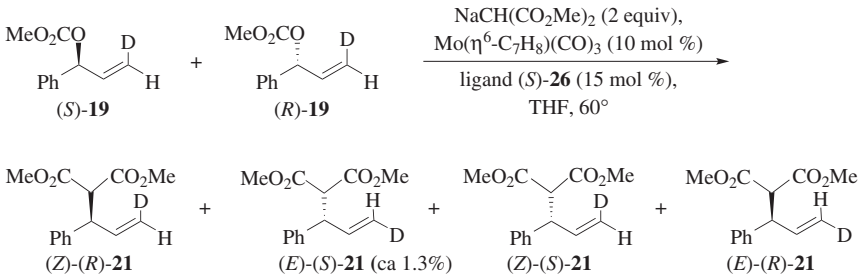
(*R*)-**33** (*R*)[a]-**32**

Ligand	Solvent	Temp (°)	er
(*R*,*R*)-**1**	THF	48	99.5:0.5
(*S*,*S*)-**1**	THF	48	85.0:15.0
(*R*,*R*)-**1**	PhMe	60	99.75:0.25
(*S*,*S*)-**1**	PhMe	60	95.0:5.0
(*R*,*R*)-**1**	MeCN	48	99.0:1.0
(*S*,*S*)-**1**	MeCN	48	72.0:28.0

[a] Erroneously reported with the opposite absolute configuration in ref. 35.

Scheme 19

Reaction of allylic carbonate *rac*-**19** with sodium dimethyl malonate in the presence of $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ and ligand (*S*)-**26** permits the fate of the two individual enantiomers to be determined over time.[28] Substrate (*S*)-**19**, which is the matched enantiomer with regard to ligand (*S*)-**26**, affords product (*Z*)-(*R*)-**21** with high selectivity, along with trace amounts of (*E*)-(*S*)-**21**, which has inverted double bond geometry (Scheme 20). In the initial phase of the reaction (at <30% conversion) the mismatched substrate, (*R*)-**19**, affords predominantly the opposite enantiomer, (*Z*)-(*S*)-**21**, but because of the different rates of reaction of the two enantiomers, (*Z*)-(*R*)-**21** is the major product, although with low er. After about 30% conversion, the memory effect disappears and generation of malonate (*Z*)-(*S*)-**21** thus ceases. For this reason the er of malonate (*Z*)-(*R*)-**21** increases, from 78.5:21.5 after 46% conversion to 98.0:2.0 at 46–100% conversion; at full conversion the overall er is 90.0:10.0. The origin of the attenuation of the memory effect as the reaction proceeds is in this case not due to a decrease in concentration of the nucleophile, since an excess of malonate was used. Instead it may be related to depletion of carbon monoxide and/or $Mo(CO)_6$ due to the high reaction temperature (60°); carbon monoxide is essential for catalytic turnover and a lower concentration results in lower rate of nucleophilic attack, which leads to more efficient equilibration of the diastereomeric η^3-allyl complexes (see Scheme 15).



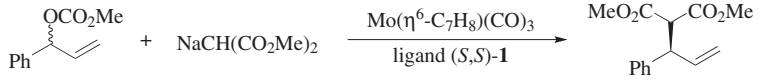
at 60% conversion: (*Z*)-(*R*)-**21** major, er 78.5:21.5
at 100% conversion: (*Z*)-(*R*)-**21** major, er 90.0:10.0

Scheme 20

Kinetic Resolution

In the presence of a chiral, nonracemic ligand and a molybdenum source, reaction of a racemic, branched carbonate leads to two diastereomeric allylmolybdenum complexes (via retentive oxidative addition). Because of rapid equilibration of the diastereomeric η^3-allylmolybdenum complexes, the same major enantiomer of the product is obtained from either enantiomer of the substrate. The rates by which the two enantiomers of the carbonate react with the chiral molybdenum complex may be different, the fast-reacting enantiomer leading to the matched complex and the slow-reacting isomer leading to the mismatched complex. The result is a kinetic resolution, which may afford both enantioenriched starting material and product.

A large difference in relative rates of reaction of the two enantiomers does not necessarily lead to large memory effects, as this effect is a result of the equilibrium being slow compared to nucleophilic attack. For carbonate *rac*-**33**, k_{rel} values in the range 8–13 are observed in reactions with sodium dimethyl malonate in different solvents catalyzed by $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ and ligand (*S*,*S*)-**1** (Scheme 21).[35]



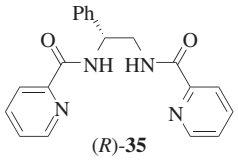
rac-**33**

Solvent	Temp (°)	k_{rel}[a]
THF	48	9
MeCN	48	8
PhMe	60	13
i-PrOAc	48	8
tetrahydropyran	48	8
$ClCH_2CH_2Cl$	75	10

[a] Determined from $k_{rel} = \ln[(1 - c)(1 - ee)]/\ln[(1 - c)(1 + ee)]$ at 50% conversion.

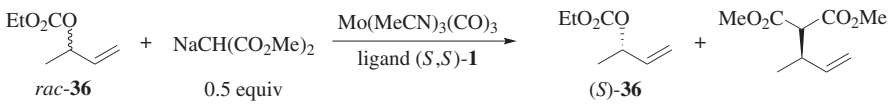
Scheme 21

The relative rates of the reactions of the carbonate enantiomers are dependent on the ligand. Thus, lower selectivity factors are observed in reactions with ligands (*S*)-**26** and its (*R*)-phenyl analogue (*R*)-**35** ($k_{rel} = 2$ in favor of the (*S*)-substrate and $k_{rel} = 3$ in favor of the (*R*)-substrate, respectively, in THF)[28] than in reactions with ligand (*S*,*S*)-**1**.



(*R*)-**35**

Kinetic resolution of carbonate *rac*-**36** takes place in the allylation of sodium dimethyl malonate in the presence of $Mo(MeCN)_3(CO)_3$ and ligand (*S*,*S*)-**1**. Use of substoichiometric amounts of malonate affords carbonate (*S*)-**36** in up to er 82.0:18.0 at 47% conversion (Eq. 6).[41] The process thus constitutes a method for the preparation of enantioenriched allylic carbonate (*S*)-**36** and, after hydrolysis, the corresponding alcohol.



rac-**36** 0.5 equiv (*S*)-**36** er 82.0:18.0 at 47% conv.

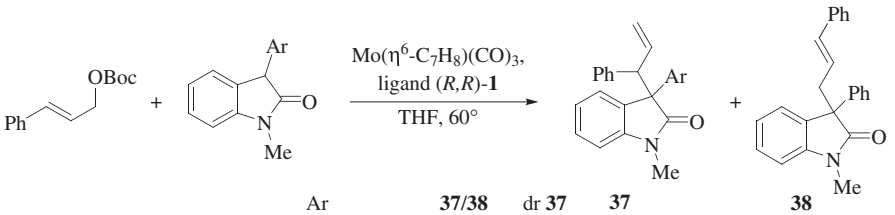
(Eq. 6)

SITE SELECTIVITY

The site selectivity is a function of the ligand, the allylic substrate, and the nucleophile. In early studies complexes with achiral ligands exhibited rather poor site selectivity. The site selectivity has been suggested to be governed by the charge, the more positive carbon atom in the allylmetal fragment being preferentially attacked by the nucleophile.[42] Consideration of frontier-orbital overlap leads to the same conclusion.[42]

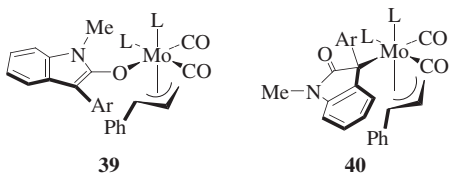
The site selectivity is not a consequence of reaction via an η^1-allylmolybdenum species bound through the C(3)-allylic carbon since that mechanism would not explain the observed memory effect, as branched and linear carbonates would lead to the same η^1-allyl intermediate.[16] Therefore, η^3-allyl complexes are more likely intermediates.

Enolates can bind to Mo(II) via carbon[43] as well as oxygen[44] and the mode of binding as well as the rate of interconversion of the two types of complexes has been suggested to influence the constitution of the product.[39] A relationship between the electronic properties of the *para*-substituent of 3-aryloxindoles and the branched/linear selectivity is observed: increasing the electron-withdrawing character of the substituent leads to both lower branched to linear (products **37**/**38**) selectivity and diastereoselectivity (Scheme 22).[39] In contrast to expectations, oxindoles with sterically demanding aryl groups, such as 3-(2-tolyl) and 3-(1-naphthyl), have a strong preference for the formation of branched products, whereas those containing smaller aryl groups, such as 2-thienyl and *N*-methyl-3-indolyl, afford exclusively linear products.[39] This outcome is rationalized by suggesting that larger aryl groups should favor the sterically less-congested oxygen-bound enolate structure **39** over carbon-bound structure **40**. In addition, lower steric strain in the oxygen-bound enolate allows bond formation to the substituted allylic terminus to occur.



Ar	**37**/**38**	dr **37**
Ph	18:1	8:1
4-$MeOC_6H_4$	18:1	8:1
4-ClC_6H_4	13:1	5.5:1
4-NCC_6H_4	7:1	4.5:1

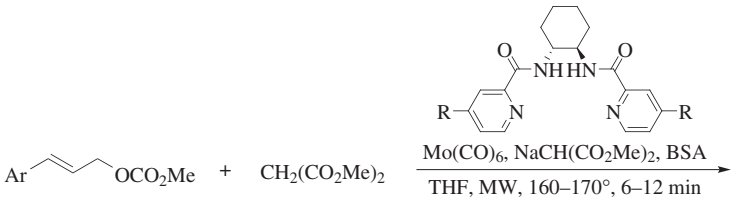
Scheme 22

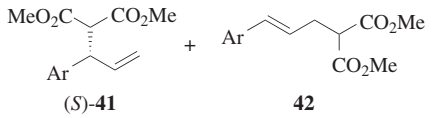


39 **40**

A reaction mechanism involving divergent modes of reaction for oxygen-bound (**39**) and carbon-bound (**40**) enolate complexes has been suggested to rationalize the different site selectivities observed with different nucleophiles.[45]

The site selectivity is also influenced by the substituents on the electrophile and on the ligand. In reactions with 4-substituted (*E*)-cinnamyl methyl carbonates with sodium dimethyl malonate in the presence of ligand (*R,R*)-**1** (R = H), or derivatives of ligand (*R,R*)-**1**, and $Mo(CO)_6$ under microwave conditions, lower branched/linear site selectivity (products **41/42**) is observed for substrates with electron-withdrawing substituents (Scheme 23).[34] π-Donating substituents in the ligand lead to increased site selectivity (Scheme 23).[34]





(*S*)-**41** **42**

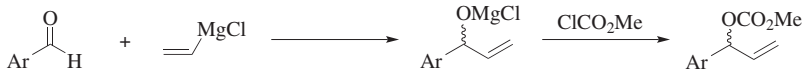
Ar	R	**41/42**
Ph	H	19:1
Ph	Cl	74:1
Ph	1-pyrrolidinyl	88:1
4-$MeOC_6H_4$	H	51:1
4-$MeOC_6H_4$	Cl	57:1
4-ClC_6H_4	H	32:1
4-ClC_6H_4	Cl	47:1
4-$CF_3C_6H_4$	H	11:1
4-$CF_3C_6H_4$	Cl	22:1

Scheme 23

SCOPE AND LIMITATIONS

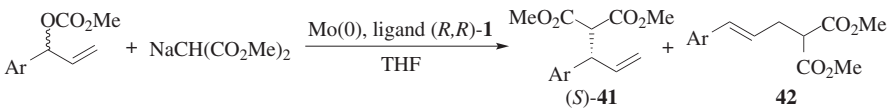
The Allylic Substrate

Because allylic carbonates are more reactive substrates than allylic acetates, the comparison of allylic moieties will be done for their carbonates. *rac*-1-Aryl-2-propenyl methyl carbonates are conveniently prepared by the addition of vinylmagnesium chloride to the appropriate aryl aldehyde and subsequent treatment with methyl chloroformate (Scheme 24).[46] Cinnamyl derivatives are less readily available, and although enantioselectivities due to memory effects may be somewhat lower starting from the branched substrates, the latter are usually the substrates of choice because of their availibility. Isomerization of branched to linear substrates is, however, possible using both palladium(0)[47] and palladium(II)[48] catalysts.



Scheme 24

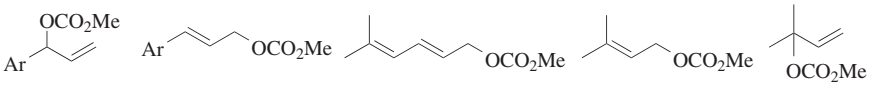
Allylic substrates with aryl (carbonates **43** and **44**) and alkenyl substituents (e.g., carbonate **45**[49]) undergo reaction, although the latter type of substrate requires higher reaction temperatures. Both electron-rich (e.g., methyl 1-(2-thienyl)-2-propenyl carbonate[32] and methyl 3-(4-methoxyphenyl)-2-propenyl carbonate[34]) and electron-deficient (e.g., methyl 1-(2-pyridinyl)-2-propenyl carbonate[32] and methyl 3-(4-(trifluoromethyl)phenyl)-2-propenyl carbonate[34]) aromatic compounds, as well as moderately hindered (methyl 1-(1-naphthyl)-2-propenyl carbonate) aromatic substrates provide high yields of products, with the branched to linear ratio as well as the enantiomeric purity of the branched product depending on the nature of the substrate and the catalyst (Scheme 25). Substrates with alkyl substituents, such as carbonates **46** and **47**, react sluggishly and therefore require prolonged reaction times, and substrates **48**–**51** fail to react.[50] Allyl sulfones have been used but only in combination with achiral catalysts; the sulfone group proves to be a better leaving group than an aliphatic chloride substituent.[51]



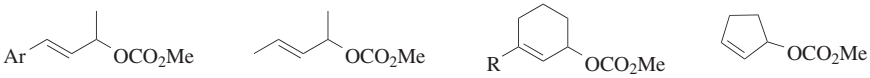
(*S*)-**41** **42**

Ar	Conditions	Yield (%) **41** + **42**	**41**/**42**	er	Refs.
2-thienyl	$Mo(EtCN)_3(CO)_3$, reflux, 2–3 h	78	19:1	94.0:6.0	32
2-pyridinyl	$Mo(EtCN)_3(CO)_3$, reflux, 2–3 h	69	8:1	98.0:2.0	32
Ph	$Mo(EtCN)_3(CO)_3$, reflux, 2–3 h	70	13:1	96.0:4.0	32
Ph	$Mo(CO)_6$, MW, 165°, 6 min	76	13:1	98.0:2.0	34
4-ClC_6H_4	$Mo(CO)_6$, MW, 165°, 6 min	78	26:1	98.0:2.0	34
4-$CF_3C_6H_4$	$Mo(CO)_6$, MW, 165°, 6 min	48	10:1	99.0:1.0	34
1-naphthyl	$Mo(EtCN)_3(CO)_3$, reflux, 2–3 h	82	99:1	93.5:6.5	32

Scheme 25

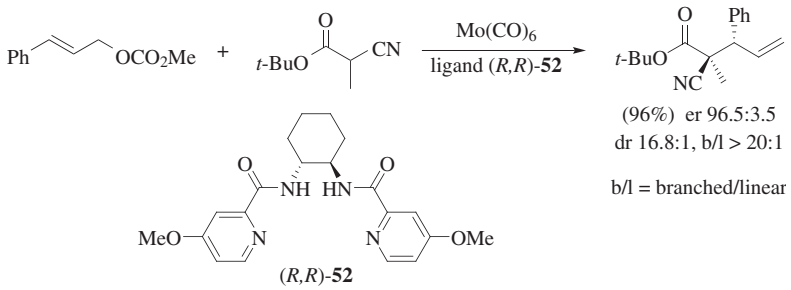


43 **44** **45** **46** **47**



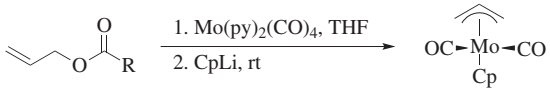
48 **49** **50** **51**

Quaternary centers on the nucleophile can be created with good stereocontrol.[37−39,52] Cyano-esters, for example, react with allylic carbonates in the presence of $Mo(CO)_6$ and ligand **52** (Eq. 7).[52]



(Eq. 7)

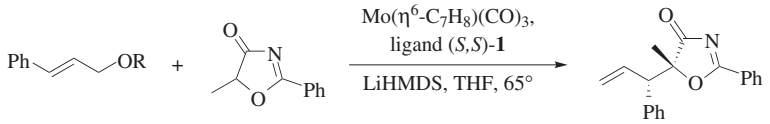
The Leaving Group. The rate of oxidative addition of the allylic substrate to Mo(0) is dependent on the donor ability of the leaving group. This observation is in line with the proposed mechanism, which involves initial coordination of Mo to the carbonyl oxygen. An optimum among acyl groups in terms of reaction time and yield is reached with the unsubstituted benzoate (Scheme 26).[53] A further increase in donor capacity of the leaving group leads to further increase in reaction rate, but yields decrease.



R	Time (h)	Yield (%)
CF_3	25	70
Me	10	75
4-FC_6H_4	8	82
4-ClC_6H_4	7	88
Ph	6.5	94
4-$MeOC_6H_4$	5.5	80
4-$Me_2NC_6H_4$	4	47

Scheme 26

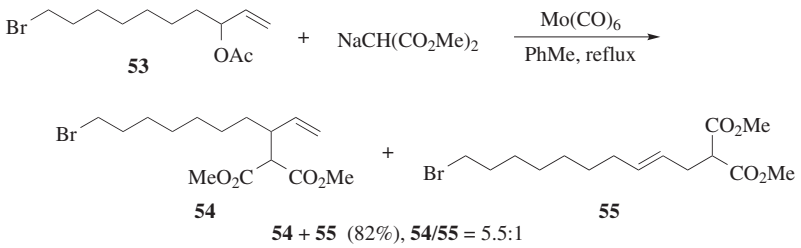
In reactions with oxalactims (oxazolidine-4-ones), the carbonate serves as a better leaving group than the phosphate, as demonstrated by the higher branched to linear ratio, diastereomeric ratio, and enantiomeric purity of the product (Scheme 27).[38]



R	er	dr	b/l
MeO_2C	>99.5:0.5	11.5:1	99:1
$(EtO)_2PO$	98.0:2.0	8.1:1	7:1

Scheme 27

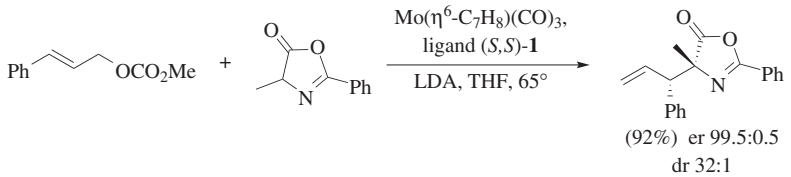
Functional-Group Compatibility. Molybdenum-catalyzed allylic alkylations are compatible with the presence of ketone, enone, ester, sulfone, acetal, olefin, alkyl halide, silyl,[54] allyl ether, silyl ether, and enol ether functional groups.[25,51] In the presence of $Mo(CO)_6$ displacement of only acetate by malonate takes place in bromo-substituted allylic acetate **53** in refluxing toluene to yield compounds **54** and **55** in a ratio of 5.5:1 (Eq. 8), whereas in the absence of the molybdenum complex displacement of bromide occurs instead.[25] In contrast to the situation with palladium catalysts, silicon substituents in allylic or vinylic position are not protodesilylated.[25] (*E*) Double bonds are preferentially formed over (*Z*) double bonds from substrates with both (*E*) and (*Z*) configurations.[25]



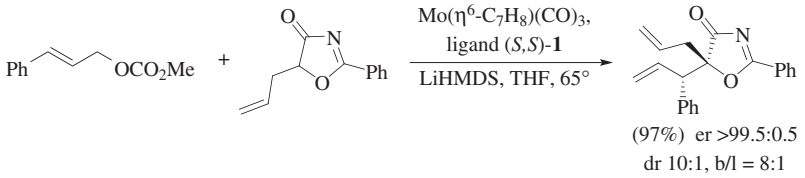
(Eq. 8)

The Nucleophile

Molybdenum-catalyzed allylic substitutions are currently limited to the use of stabilized carbon nucleophiles. Most reactions to date have been performed using dialkyl malonates as the nucleophiles. The more hindered diethyl methylmalonate reacts readily, but a further increase in steric bulk to diethyl allylmalonate slows the reaction.[32] β-Diketones and β-keto esters are usually not sufficiently reactive to serve as the nucleophiles, but the sodium salt of 2-carbomethoxycyclopentanone is allylated by 2-[(trimethylsilyl)methyl]allyl acetate under ligand-free conditions ($Mo(CO)_6$, toluene, reflux).[55] In contrast, the anions of 4-alkyl-2-phenyloxazol-5(4*H*)-ones (α-imino lactones, Eq. 9),[37] 5-alkyl-2-phenyloxazol-4(5*H*)-ones (oxalactimes, Eq. 10)[38] and oxindoles (Eq. 11)[39,45,56,57] are competent as nucleophiles and represent the first examples of control of configuration at the nucleophile. 3-Aryloxindoles with sterically demanding aryl groups, such as 2-naphthyl and 2,4-diphenyl-5-oxazolyl, are readily allylated with high preference for bond formation at the internal allylic position. From these reactions, highly functionalized chiral oxindoles bearing a quaternary stereocenter and an adjacent tertiary stereocenter are obtained.

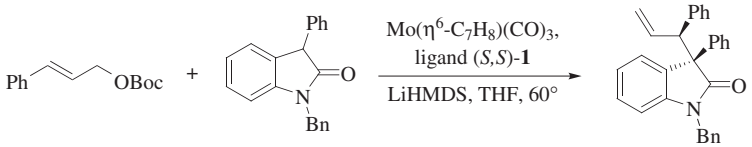


(Eq. 9)



(97%) er >99.5:0.5
dr 10:1, b/l = 8:1

(Eq. 10)



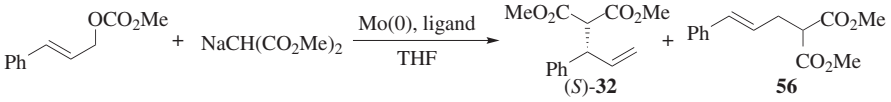
(85%) er 95.0:5.0
dr 9:1, b/l = 17:1

(Eq. 11)

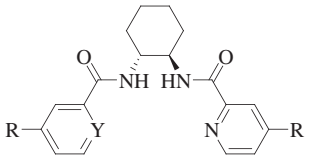
Chiral Ligands

Molybdenum(0) complexes such as $Mo(EtCN)_3(CO)_3$, $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (C_7H_8 = cycloheptatriene), or $Mo(CO)_6$ can be used as catalyst precursors together with chiral ligands. Enantiomerically enriched *trans*-1,2-bis[(2-pyridinylcarbonyl)amino]cyclohexane (**1**) and derivatives of this ligand[58] impart high enantio- and site selectivity (branched product **32** versus linear product **56**) in molybdenum-catalyzed asymmetric allylic alkylations (Scheme 28).[32] The parent ligand **1**, is conveniently prepared in one step,[59] even on large scale,[60] and is also commercially available in both enantiomeric forms. Ligands wherein one 2-pyridinyl ring is replaced by either a 3-pyridinyl or a phenyl group (ligand **2**) afford comparable or even higher asymmetric induction compared to ligand **1**, although the catalytic activity is reduced, whereas replacement of both pyridinyl groups by phenyl groups results in a poor ligand.[19] Increased steric bulk leads to reduced reactivity, as demonstrated by ligands containing one or two 2-quinolyl groups instead of 2-pyridinyl groups; use of the former results in only traces of product.[19] The presence of π-donating substituents in the 4-position of one or both of the pyridinyl rings (ligand **52**) increases the enantio- and site selectivities (Scheme 28).[33,34,45]

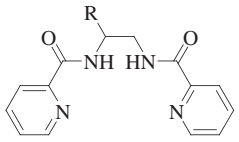
Methylation of one of the ligand amide groups results in reduced activity, and methylation of both groups affords an unreactive ligand.[28] Replacement of an amido group with an ester group produces ligands with very low (**58**)[28] or no (**59**)[61] activity, and ligands with two ester groups are inactive.[19] C_1-Symmetric pyridinylamides, prepared from readily available amino alcohols (obtained by reduction of naturally occurring amino acids) are viable alternatives to C_2-symmetric ligand **1**.[19,28] The enantioselectivities obtained with the C_1-symmetric ligands vary with the nature of the substituent on the diamine and decrease in the order *i*-Pr (ligand **26**) > Ph (ligand **35**) > CH_2Ph > *t*-Bu.[28] Thus, two rigid amide groups, one stereocenter, and one pyridine ring are essential in the ligand for the asymmetric allylic alkylation reaction to proceed selectively.



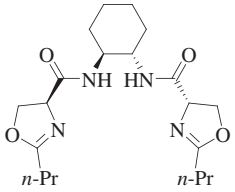
Ligand	Mo catalyst	Conditions	Yield (%) 32 + 56	32/56	er	Config.	Refs.
(*R*,*R*)-**1**	$Mo(EtCN)_3(CO)_3$	65°, 3 h	88	32:1	99.5:0.5	(*S*)	32
(*R*,*R*)-**52**	$Mo(CO)_6$	MW, 4 min	88	41:1	>99.5:0.5	(*S*)	33
(*S*,*S*)-**2**	$Mo(EtCN)_3(CO)_3$	—	90	60:1	99.5:0.5	(*R*)	19
(*S*)-**26**	$Mo(EtCN)_3(CO)_3$	60°, 12 h	68	32:1	99.0:1.0	(*R*)	33a
(*R*)-**35**	$Mo(EtCN)_3(CO)_3$	60°, 4 h	63	8:1	96.0:4.0	(*S*)	33a
(*S*,*S*,*S*,*S*)-**57**	$Mo(EtCN)_3(CO)_3$	70°, 1 d	83	6:1	99.0:1.0	(*R*)	21



(*R*,*R*)-**1**, Y = N, R = H
(*R*,*R*)-**52**, Y = N, R = OMe
(*S*,*S*)-**2**, Y = CH, R = H

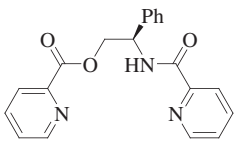


(*S*)-**26**, R = *i*-Pr
(*R*)-**35**, R = Ph

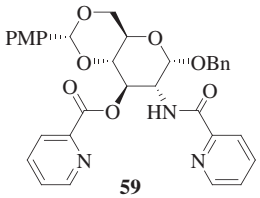


(*S*,*S*,*S*,*S*)-**57**

Scheme 28

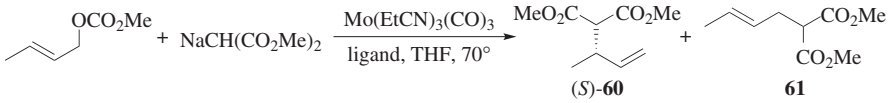


58



59

Ligands such as **8** (see Eq. 3) and **57**, containing dihydrooxazole rings in place of pyridinyl rings, provide products with high site- (branched product **60** versus linear product **61**) and enantioselectivities (Scheme 29).[21,62] The presence of four stereocenters presents the opportunity for the preparation of diastereomeric ligands.



Ligand	Time (d)	Yield (%) 60 + 61	60/61	er	Config.
(*S*,*R*,*R*,*S*)-**8**	3	76	7:1	92.5:7.5	(*S*)
(*S*,*S*,*S*,*S*)-**57**	1	81	9:1	98.5:1.5	(*R*)

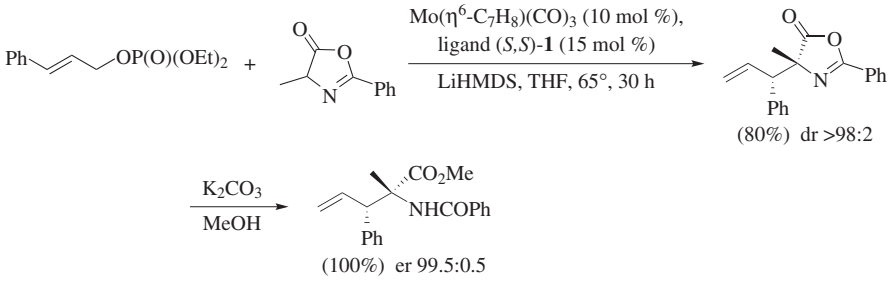
Scheme 29

APPLICATIONS TO SYNTHESIS

Appropriately substituted allylic derivatives serve as starting materials for the preparation of various biologically active compounds using molybdenum-catalyzed asymmetric allylic alkylation as a key step.

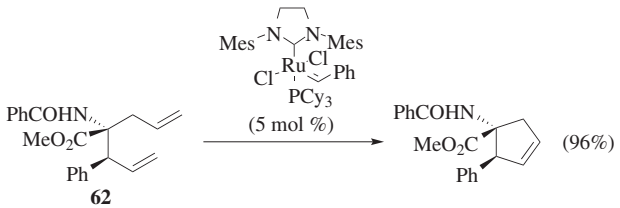
α-Amino Acids

Unnatural α-substituted α-amino acids are obtained with high enantiomeric excess by reactions of allylic carbonates or phosphates with 4-alkyl-2-phenyloxazol-5(4*H*)-ones (α-imino lactones).[37] The use of lithium hexamethyldisilazane as the base affords, in most cases, only the branched isomer, whereas some linear product is obtained when sodium or potassium hexamethyldisilazane is used. Hydrolysis without isolation of the initially formed product provides high isolated yields (76–92%) of the branched isomers (Scheme 30).[37] Lower catalyst loading (examined with cinnamyl methyl carbonate and 4-benzyl-2-phenyloxazol-5(4*H*)-one) gives the product with equally high diastereoselectivity although with somewhat lower enantioselectivity and increasing amounts of the linear isomer. The reaction is an example of control of stereochemistry at the nucleophile as well as the electrophile.



Scheme 30

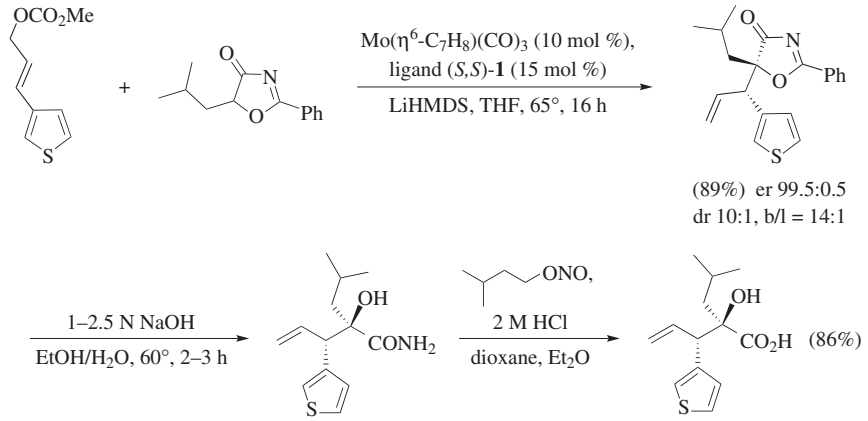
Further synthetic manipulations of these products can lead to other amino acids. A product with two terminal olefinic bonds, amino acid **62**, undergoes ring-closing metathesis to give a cyclic amino acid derivative (Eq. 12).[37]



(Eq. 12)

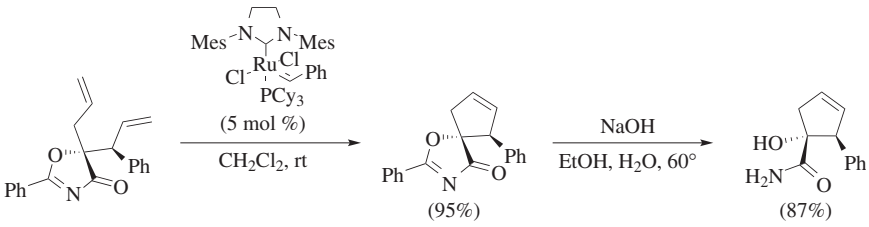
α-Hydroxy Acids

α-Hydroxy acids are obtained with high stereocontrol with respect to both the nucleophile and the electrophile by the analogous reaction with 5-alkyl-2-phenyloxazol-4(5*H*)-ones (oxalactims) (Scheme 31).[38] The site selectivity (5.5:1 to 49:1 in favor of the branched isomer) is dependent on the nature of both the 2- and 5- substituents and decreases somewhat with increasing size of the C-5 alkyl group.



Scheme 31

An oxalactim with a 2-propenyl group at C-5 results in an allylated compound containing two terminal olefinic bonds. Subjection of these compounds to ring-closing metathesis affords products that can be converted into cyclic hydroxy carboxamides by hydrolysis (Scheme 32).[38]

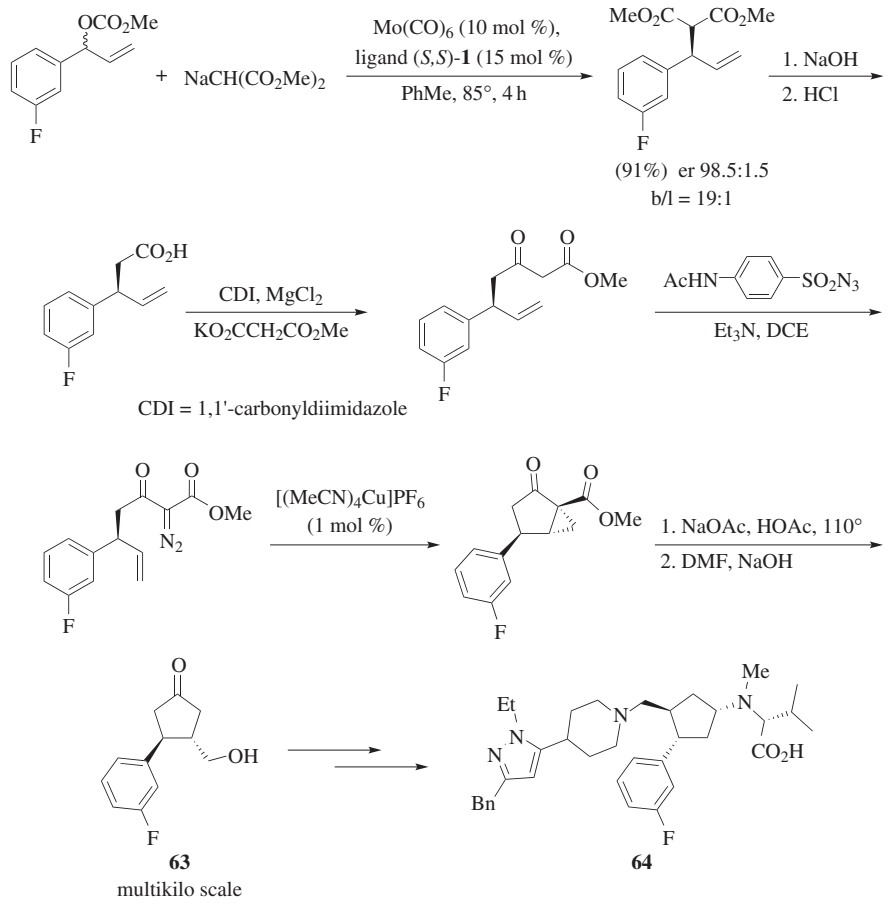


Scheme 32

(3*S*,4*S*)-3-(3-Fluorophenyl)-4-(hydroxymethyl)cyclopentanone

(3*S*,4*S*)-3-(3-Fluorophenyl)-4-(hydroxymethyl)cyclopentanone (**63**), a key intermediate in the synthesis of the anti-HIV drug candidate **64**,[63] is prepared employing molybdenum-catalyzed allylation for the installation of the first stereocenter (Scheme 33).[64] Alkylation of *rac*-1-(3-fluorophenyl)-2-propenyl methyl carbonate with sodium dimethyl malonate, using a catalyst obtained by heating $Mo(CO)_6$

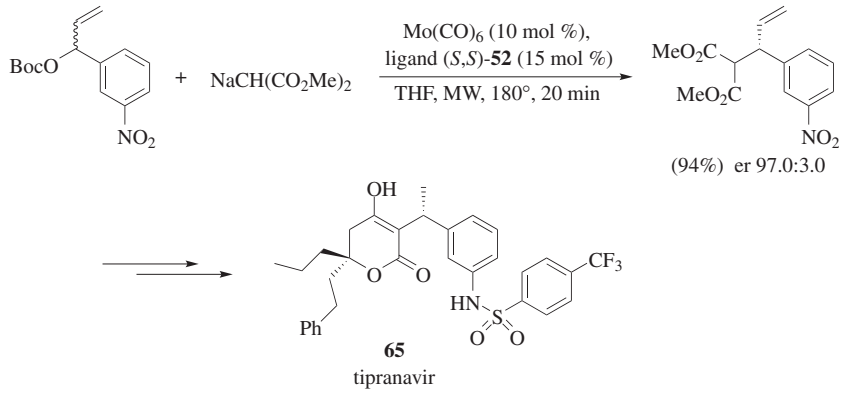
(10 mol %) and ligand (*S*,*S*)-**1** (15 mol %) at 85–88° for 4 hours, affords the desired dimethyl 2-[(1*R*)-1-(3-fluorophenyl)-2-propenyl]propanedioate in 91% yield and er 98.5:1.5, and with a branched/linear ratio of 19:1 after 15 hours at 85° in toluene.



Scheme 33

Tipranavir

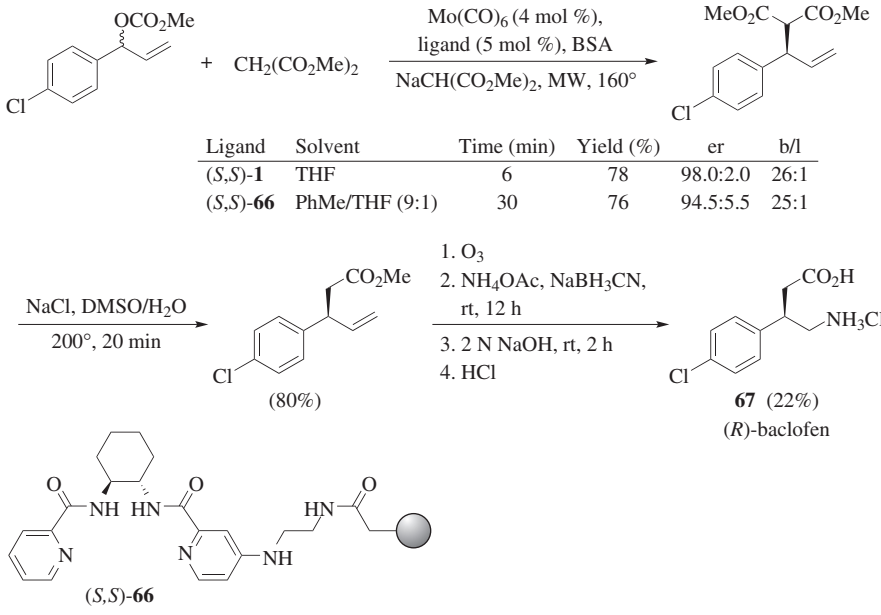
A convergent synthesis of tipranavir (**65**), a nonpeptidic HIV-protease inhibitor, uses molybdenum-catalyzed substitution of *rac*-1-(3-nitrophenyl)-2-propenyl *tert*-butyl carbonate with sodium dimethyl malonate to prepare a key intermediate (Scheme 34).[65] The desired branched isomer is obtained in excellent yield (94%) and enantioselectivity (er 98.0:2.0) using a catalyst prepared from $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ and ligand (*S*,*S*)-**1** at 67°. Under microwave irradiation, the reaction (catalyzed by $Mo(CO)_6$ and ligand (*S*,*S*)-**52**) is complete within 20 minutes, as compared to 24 hours at 67°, and the product is obtained with only a slight loss in enantioselectivity (er 97.0:3.0) (Scheme 34).[65]



Scheme 34

(*R*)-Baclofen

(*R*)-Baclofen (**67**) is an analogue of γ-aminobutyric acid (GABA), an important neurotransmitter in the central nervous system. Baclofen activates $GABA_B$ receptors and is used for the treatment of spastic movement.[66] The therapeutically active (*R*)-enantiomer is prepared using allylation of dimethyl malonate in the presence of $Mo(CO)_6$ and either ligand (*S,S*)-**1** or its immobilized analogue (*S,S*)-**66** under microwave conditions for the introduction of the stereogenic center (Scheme 35).[67]

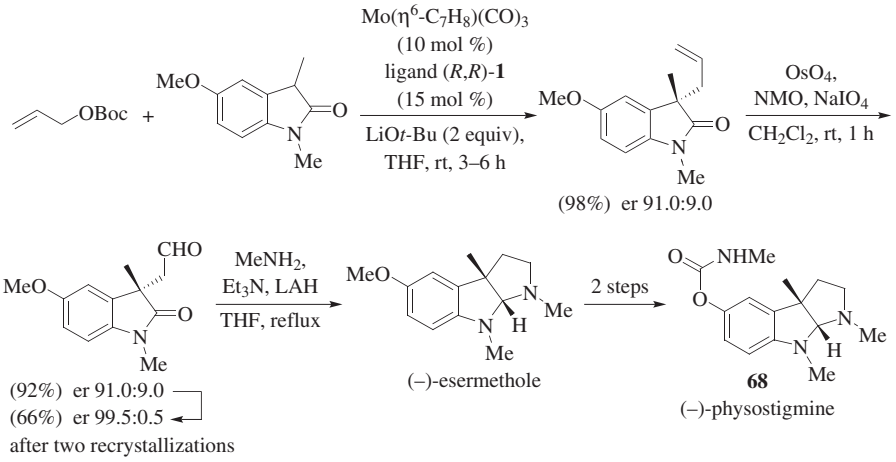


Ligand	Solvent	Time (min)	Yield (%)	er	b/l
(*S,S*)-**1**	THF	6	78	98.0:2.0	26:1
(*S,S*)-**66**	PhMe/THF (9:1)	30	76	94.5:5.5	25:1

Scheme 35

(−)-Physostigmine

In contrast to the palladium-catalyzed process, molybdenum-catalyzed asymmetric allylic alkylations of 3-aryl-[39] and 3-alkyloxindoles[56] proceed with high enantioselectivity to yield 3,3-disubstituted oxindoles, which are versatile building blocks for alkaloid synthesis.[68] The utility of the reaction is demonstrated by a formal total synthesis of (−)-physostigmine (**68**), a powerful inhibitor of acetyl cholinesterase (Scheme 36).[56]



Scheme 36

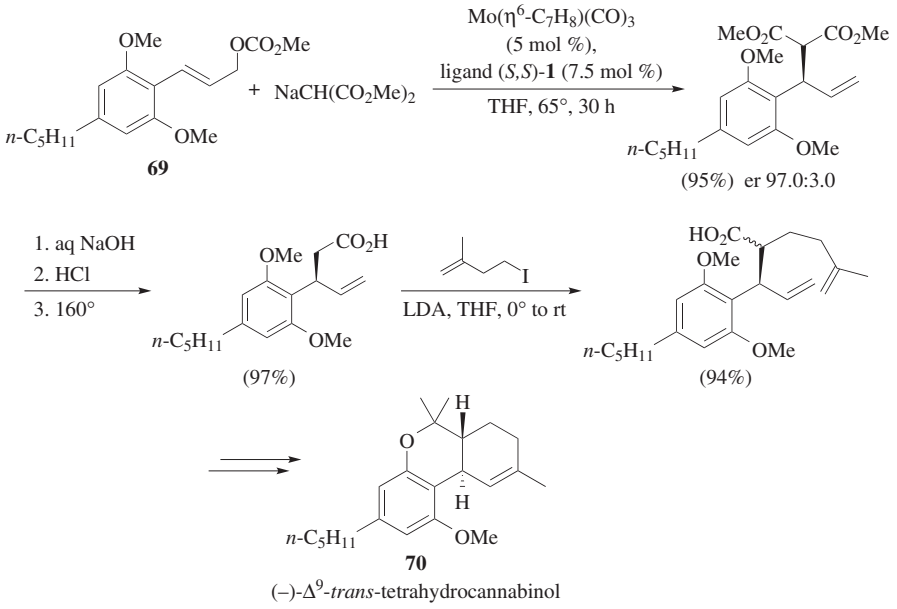
(−)-Δ^9-*trans*-Tetrahydrocannabinol

Molybdenum-catalyzed asymmetric allylic alkylation is employed as a key step in the synthesis of (−)-Δ^9-*trans*-tetrahydrocannabinol (**70**) (Scheme 37), the primary psychoactive component in marijuana.[48] Carbonate **69**, which is sensitive to both acid and base, is prepared at −78° and used after washing with cold water. Due to severe steric hindrance in the substrate, the reaction is slow, but affords the branched product exclusively in high yield and with high enantioselectivity (er 97.0:3.0). After an additional six steps, the final product is obtained in 30% overall yield.

COMPARISON WITH OTHER METHODS

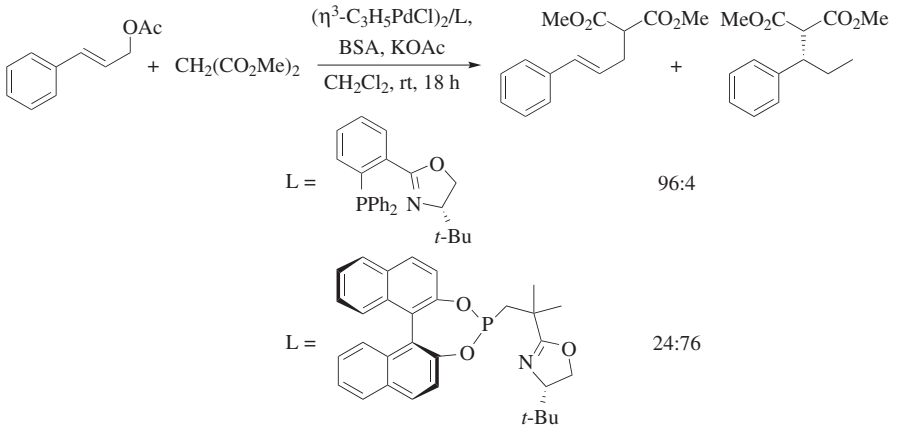
Metal-Catalyzed Allylations

Palladium complexes have been most extensively studied and employed in synthetic applications of asymmetric allylic alkylations.[4,69,70] High enantioselectivity can be achieved with different types of allylic substrates. A large variety of chiral ligands that induce high enantioselectivity are known, most of them bidentate with P–P, P–N, or N–N donor atoms, although recently also several monodentate ligands have been successfully employed.[71] As a general rule, palladium-catalyzed substitutions



Scheme 37

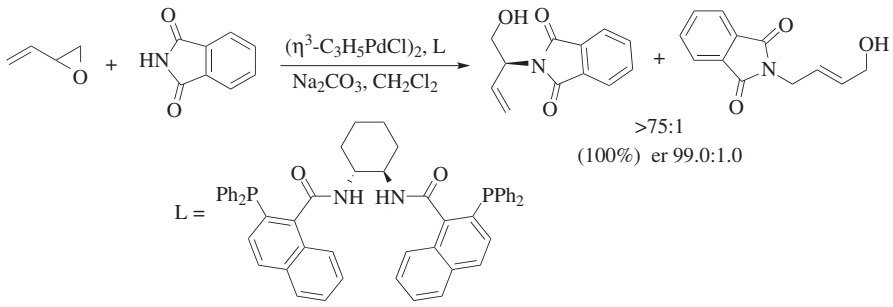
result in formation of linear, achiral products from monosubstituted allylic substrates, although electron-deficient ligands may lead to branched isomers (Scheme 38[72]).[10,73]



Scheme 38

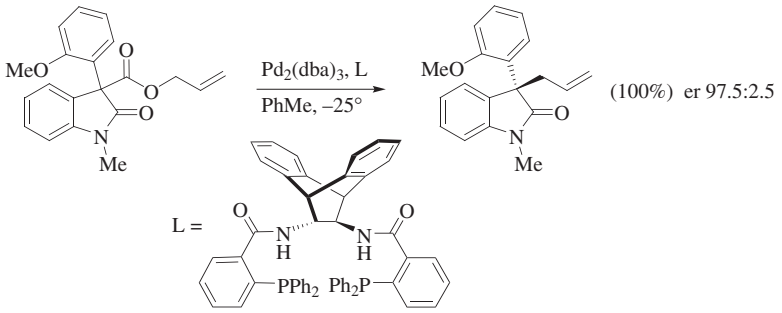
The mechanism of palladium-catalyzed allylations is well known.[31] Oxidative addition of the allylic substrate to the Pd(0) complex occurs with inversion of configuration and the allylic ligand is attacked by stabilized nucleophiles *trans* to palladium

without pre-coordination to the metal, again resulting in inversion of configuration. Although oxidative addition and nucleophilic attack occur with opposite stereochemical course using molybdenum and palladium catalysts, both processes thus proceed with net overall retention of configuration. Memory effects are common and may be powerful in the palladium-catalyzed allylations, in particular in the mismatched manifold.[74,75] Palladium catalysts are generally more reactive in allylic alkylations than catalysts containing molybdenum.[76] In addition to the type of substrates that undergo molybdenum-catalyzed allylations, allylic epoxides react in the presence of Pd(0) catalysts (Eq. 13).[77] Stabilized carbon nucleophiles, including enolates,[78–80] can be used as well as oxygen, nitrogen, and sulfur nucleophiles. The compatibility with functional groups is similar to that observed in molybdenum-catalyzed reactions, although silyl functional groups are cleaved under palladium catalysis and not molybdenum catalysis.



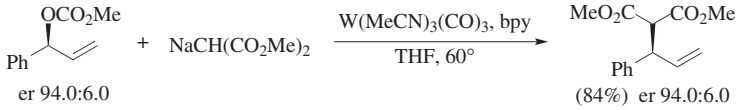
(Eq. 13)

In cases where the same product is obtained from palladium- and molybdenum-catalyzed processes, the enantioselectivities may differ. As noted earlier (Scheme 36), allylations of 3-alkyloxindoles proceed with excellent enantio- and site selectivity using a catalyst prepared from Mo(0) and ligand **1**, whereas modest enantioselectivity is observed using palladium catalysts.[56] However, highly selective decarboxylative allylations of aryl- and alkyloxindoles takes place in the presence of palladium catalysts (Eq. 14).[81]



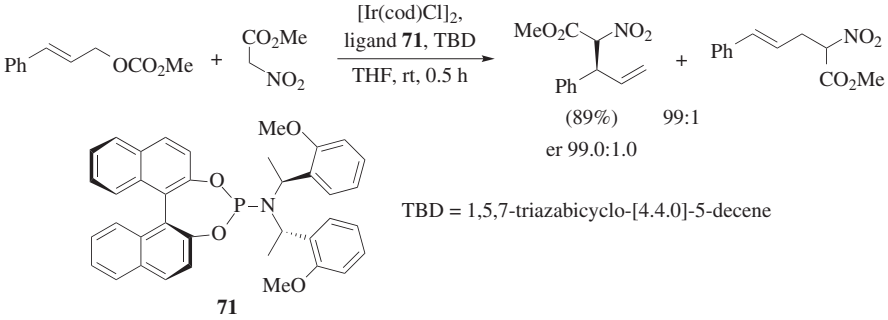
(Eq. 14)

Iridium-, ruthenium-, and tungsten-catalyzed allylic alkylations using monosubstituted allylic substrates result mainly in chiral, branched products, and thus display the same constitutional selectivity as the molybdenum-catalyzed reactions. Tungsten complexes with phosphinooxazoline ligands can be used for enantioselective substitutions using linear substrates,[82] although the enantioselectivity is lower than with molybdenum. Ligand **1** together with tungsten affords a lower yield of product than molybdenum, and the reactions are slower.[32] Reactions catalyzed by tungsten are stereospecific (Eq. 15),[83] and therefore no enantioselectivity is observed in reactions with branched racemic substrates.

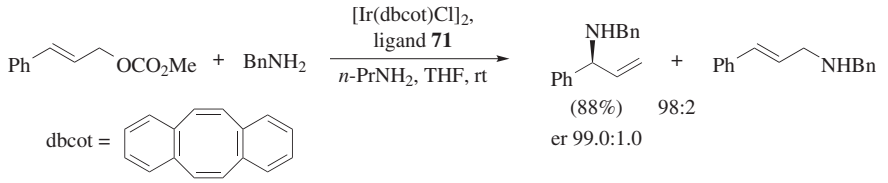


(Eq. 15)

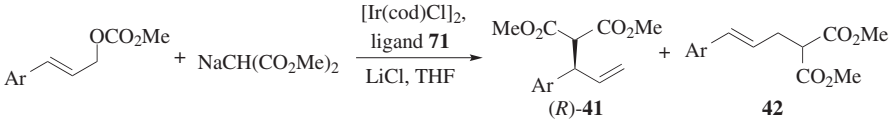
The iridium-catalyzed process[7] proceeds by an inversion-inversion mechanism.[84] A wider range of nucleophiles can be employed with iridium than with molybdenum. In addition to stabilized carbon nucleophiles (including ketone enolates[85]), both nitrogen and oxygen nucleophiles such as amines (including sulfonylamines as well as diacyl derivatives of amines), phenolates, alkoxides, and hydroxylamine derivatives can be allylated.[86] In contrast to molybdenum catalysts, iridium complexes also catalyze the allylation of nitro compounds using phosphoramidite ligands such as **71** (Eq. 16).[87] Distinct memory effects are observed in some iridium-catalyzed reactions. Thus, linear substrates with (*Z*) configuration give linear (*Z*) products. The memory effect is, however, a function of the ligand, and iridium catalysts that provide products with excellent site- and enantioselectivities are known.[70] For example, a catalyst prepared from $[Ir(dibenzocyclooctatetraene)Cl]_2$ is stable in air and affords allylation products with high enantio- and site-selectivities (Eq. 17).[88] With malonate as the nucleophile, enantioselectivities similar to those obtained with molybdenum catalysts containing, for example, ligand **1** are observed in the presence of $[Ir(cod)Cl]_2$ with phosphoramidite ligands, but the branched to linear ratios are higher with the iridium catalyst (Scheme 39).[89]



(Eq. 16)



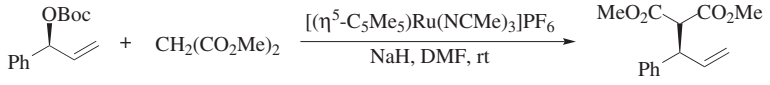
(Eq. 17)



Ar	Temp°	Yield (%)	**41/42**	er
Ph	rt	82	99:1	99.0:1.0
4-ClC_6H_4	35	90	>99:1	98.5:1.5
4-$MeOC_6H_4$	35	99	>99:1	98.5:1.5

Scheme 39

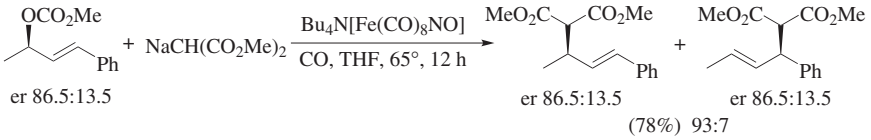
Ruthenium(II)(Cp*) catalysts afford branched products from allylic alkylations, but few examples of enantioselective reactions are known.[90,91] In contrast to molybdenum and tungsten catalysts, the ruthenium complexes exhibit high reactivity with heteroatom (N, O, S) nucleophiles.[92] As in reactions with palladium, molybdenum, and tungsten catalysts, the site selectivity is not dependent on the nature of the starting substrate, although under certain conditions strong memory effects, with retained configuration of branched substrates, are observed (Eq. 18).[93] In contrast to reactions involving molybdenum catalysts, the diastereomeric ruthenium complexes formed from racemic or enantiomerically enriched substrates in the presence of chiral ligands do not equilibrate. As a consequence, products with the same enantiomeric purity as the substrates are obtained.[93] For ruthenium catalysts the site selectivity favoring branched products has been proposed to be governed by frontier orbital overlap on the basis of X-ray and computational studies.[94]



(Eq. 18)

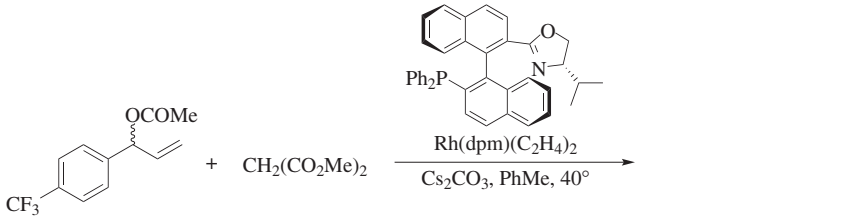
Rhodium and iron allyl complexes isomerize slowly. Thus, the configuration is retained in branched substrates using iron (Eq. 19)[95] and rhodium.[96] Similarly, linear substrates afford predominantly linear products. Iron catalysts are attractive due to their low price and low toxicity, but can give rise to substantial memory effects, the extent of which is a function of ligand structure.[97] For rhodium catalysts the site selectivity is determined by the position of the leaving group,[98] but under certain

conditions S_N2' displacement occurs.[99] However, by selecting conditions such that nucleophilic addition becomes slow compared to isomerization of the intermediate allyl complexes, high enantioselectivity may be achieved in rhodium-catalyzed reactions (Eq. 20).[100] Rhodium complexes catalyze aminations and etherifications,[96] as well as allylations of nonstabilized nucleophiles.[99,101]



er 86.5:13.5 er 86.5:13.5 (78%) 93:7 er 86.5:13.5

(Eq. 19)



dpm = dipivaloylmethanato er 98.5:1.5 (97%) 99:1

(Eq. 20)

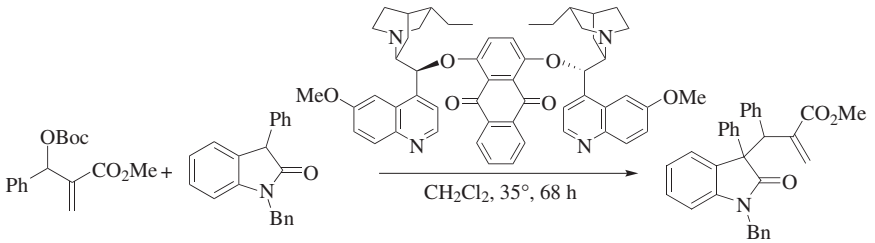
Nickel catalysts can be used for reactions with both stabilized (including amines)[102] and non-stabilized nucleophiles.[103] Allylations of nonstabilized nucleophiles,[104] such as diethylzinc[105,106] and magnesium reagents,[107] occur with high enantioselectivity using copper catalysts.[108] The reactions usually occur via S_N2'-type mechanisms and are therefore site selective. Allylic acetates, carbonates, phosphates, halides, and ethers also react under copper catalysis.[109,110]

When enantiomerically enriched branched products are desired, the most viable alternatives to molybdenum catalysts are those based on iridium, particularly iridium complexes containing phosphoramidite ligands.[111] Since molybdenum compounds are inexpensive and Mo(0) in the form of the stable $Mo(CO)_6$ can be employed together with stable ligands for in situ preparation of catalysts, molybdenum-catalyzed allylations are preferable for certain stabilized carbon nucleophiles (see Tables). An important advantage with iridium catalysts is, however, that a wider range of nucleophiles can be used.

Exceptions to the general guidelines outlined here exist as the stereochemical course is a function not only of the metal but also of other parameters, in particular the ligand structure.

Organocatalytic Allylations

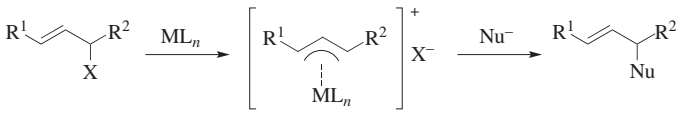
Metal-free allylations of 3-aryloxindoles using chiral, nonracemic Morita-Baylis-Hillman adducts furnish products such as oxindole **72** in up to er 98.0:2.0 and dr 87:13 (Eq. 21).[112] The enantioselectivity is comparable to that of the molybdenum-catalyzed process (compare Table 5), but higher than that reported for palladium-catalyzed allylations of aryloxindoles.[113]



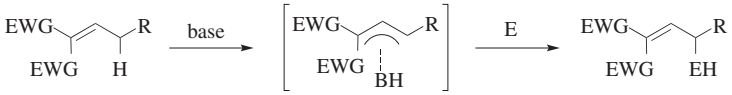
72 (82%)
er 98.0:2.0, dr 87:13

(Eq. 21)

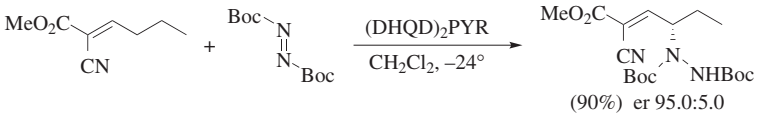
In the allylations described thus far an electrophilic allylic group reacts with a nucleophile through the intermediacy of a π-allylmetal complex (Scheme 40). Allylic derivatives can also be obtained by using reagents with reversed polarities (Scheme 41). The nucleophile is generated by abstraction of an allylic proton from an olefin; electron-withdrawing substituents are required in order to stabilize the allylic anion (Eqs. 22[114] and 23).[115] The reactions are catalyzed by chiral bases, typically cinchona alkaloid derivatives.



Scheme 40

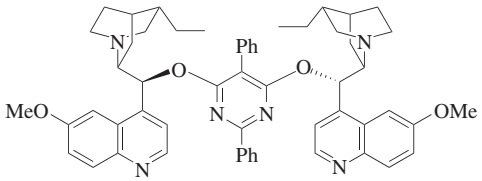


Scheme 41

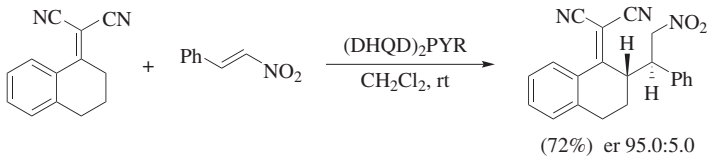


(90%) er 95.0:5.0

(DHQD)$_2$PYR =



(Eq. 22)



(72%) er 95.0:5.0 (Eq. 23)

EXPERIMENTAL CONDITIONS

The complex $Mo(EtCN)_3(CO)_3$ is most commonly used as the molybdenum source. It is prepared from the crystalline, stable, and commercially available $Mo(CO)_6$ by heating in propionitrile at reflux.[116] *The procedure is hazardous, particularly on a large scale, because propionitrile is toxic and decomposes upon heating and because carbon monoxide evolves*. Comparable results from the catalytic reactions are obtained with $Mo(\eta^6\text{-}C_7H_8)(CO)_3$.[117] Both complexes are air-sensitive and require cautious handling, although the latter complex is somewhat easier to prepare and is more air-stable.[118] Both are commercially available.

The molybdenum complex is usually treated with the ligand for about an hour at 60–70° prior to the addition of the allylic substrate and the nucleophile.[21,32] The catalytic reactions are generally run at 60–80°, although occasionally room temperature or even lower temperatures are sufficient. At higher temperatures, higher yields are obtained and sometimes only a moderate decrease in enantioselectivity and lower site selectivity are observed.[32] THF and toluene are the most frequently used solvents. Carbonates are more reactive than acetates[21] and are the preferred allylic substrates; allylic phosphates have been used as substrates only in a few cases.[37,38] Catalyst loadings are generally quite high: typically 15 mol % of ligand and 10 mol % of molybdenum complex are used.

The results are essentially independent of the order of addition of the reagents: (1) concurrent addition of the substrate and deprotonated dimethyl malonate to the catalyst solution (prepared at 70° during 1 hour), (2) catalyst pretreatment with dimethyl malonate, and (3) catalyst pretreatment with substrate before addition of malonate give essentially the same results[21] when oxazoline ligands such as **8** are used.

The less reactive $Mo(CO)_6$ can be used as the molybdenum source, although higher reaction temperatures or initial activation are required. Heating a 0.175 M toluene solution of $Mo(CO)_6$ with 1.5 equivalents of ligand **1** at 85–90° for 4 hours (or a THF solution at 65° for 2–3 hours) results in complete formation of a complex.[119] It is important that sufficient time is allowed for the formation of the catalyst as $Mo(CO)_6$ is able to catalyze the reaction, although at a lower rate, leading to decreased site- and enantioselectivities. Under these conditions the enantioselectivity is higher when toluene is used as the solvent; other solvents (DMF, DME, or DCE) are less effective. Results obtained under these conditions are identical to those obtained starting from $Mo(EtCN)_3(CO)_3$ or $Mo(\eta^6\text{-}C_7H_8)(CO)_3$.

Under conditions of microwave irradiation the reactions occur smoothly starting from $Mo(CO)_6$.[8] The asymmetric allylic alkylation reactions normally need to be

performed under inert conditions, but microwave-mediated reactions can be run in air. Reactions are typically complete within 4–5 minutes and no activation of the catalyst is required prior to the catalytic reaction. In addition, lower amounts of catalyst (5 mol % ligand and 4 mol % molybdenum complex) are used for reactions run under microwave conditions.

EXPERIMENTAL PROCEDURES

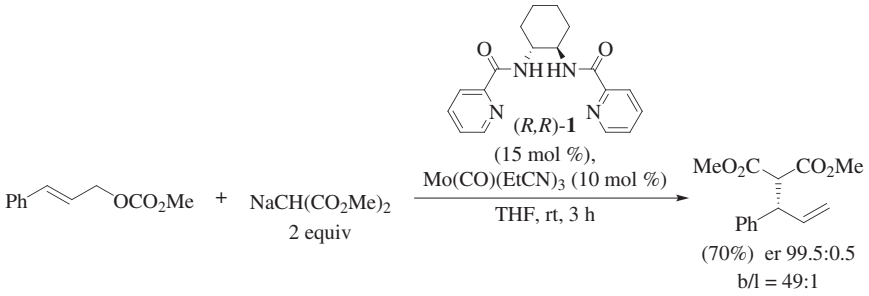
$$Mo(CO)_6 + 3\,EtCN \xrightarrow[1\ d]{\text{reflux}} Mo(EtCN)_3(CO)_3 + 3\,CO \quad (64\%)$$

Tricarbonyltris(propionitrile)molybdenum(0).[116] *Nitriles are very toxic and the synthesis should be carried out in a well-ventilated hood. CO, which is highly toxic, is released during the reaction*. A mixture of $Mo(CO)_6$ (6.0 g, 22.7 mmol) and propionitrile (60 mL) was placed into a flask equipped with a magnetic stirrer and a reflux condenser with an efficient exit for evolved CO. Heating to reflux under nitrogen gradually dissolved the hexacarbonyl complex and induced stepwise replacement of three CO ligands. After one day about one-half of the solvent was removed and Et_2O (30 mL) was added. Filtration afforded 5.0 g (64% yield) of $Mo(CO)_3(EtCN)_3$ as light tan fine needles. Reduction of the filtrate volume to 5 mL gave a second crop (2.09 g, total yield 91%). The complex is air-sensitive and becomes dark brown within an hour. IR 1919, 1800 cm^{-1}.

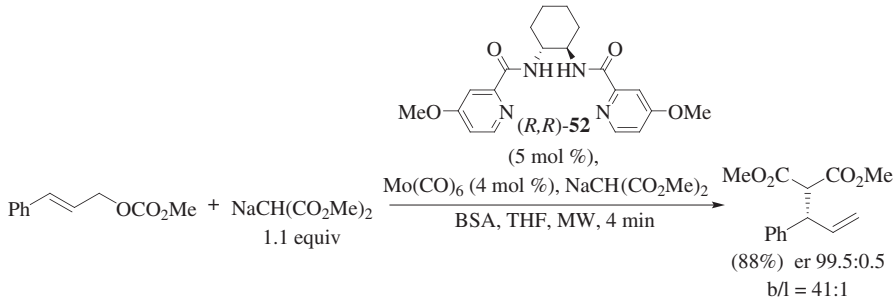
$$Mo(CO)_6 + \text{(1.2 equiv)} \xrightarrow[n\text{-octane}]{\text{reflux}} Mo(\eta^6\text{-}C_7H_8)(CO)_3 + 3\,CO \quad (58\%)$$

Tricarbonyl(cycloheptatriene)molybdenum(0).[117] A mixture of cycloheptatriene (11 g, 119 mmol, slight excess, used without purification) and $Mo(CO)_6$ (26 g, 98.5 mmol) in *n*-octane (25 mL) was heated to reflux for 8 h. During the reaction, unreacted $Mo(CO)_6$ sublimed into the condenser and needed to be scraped back into the reaction flask. After being cooled, the brown precipitate was collected by filtration and was washed with *n*-pentane (20 mL) to remove any unreacted cycloheptatriene. Evaporation of the filtrate afforded some unreacted $Mo(CO)_6$, which together with that collected in the condenser amounted to 3 g. The brown residue was extracted overnight in a Soxhlet apparatus with *n*-pentane. Red hexagonal prisms precipitated to afford 14 g (58% yield based on consumed $Mo(CO)_6$) of the desired product. The crystals were collected by filtration and were air-dried; they were pure enough for most purposes but could be recrystallized from *n*-hexane using an acetone–dry ice cooling bath. IR 1985, 1919, 1889 cm^{-1}.

The product decomposes at 95° and sublimes rapidly at 85° under vacuum. It is very soluble in alcohol, acetone, benzene, $CHCl_3$, and CH_2Cl_2, moderately soluble in Et_2O, and only sparingly soluble in *n*-hexane. It decomposes in CCl_4. The solutions are sensitive to air and light, and the solid is best stored in the dark.

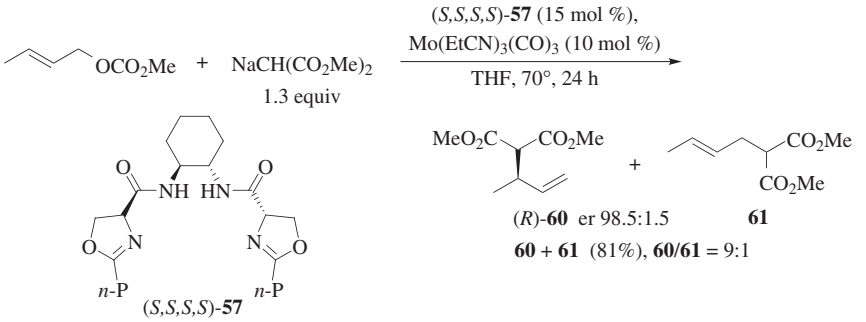


Dimethyl 2-[(*S*)-1-Phenyl-2-propenyl]propanedioate [Allylation of a Malonate].[32] A solution of $Mo(EtCN)_3(CO)_3$ (10 mol %) and chiral ligand (*R,R*)-**1** (15 mol %) in THF (1 mL) was stirred at 60° for 1 h. A solution of sodium dimethyl malonate in THF (1 mL), prepared from dimethyl malonate (578 mg, 4.37 mmol) and NaH (160 mg of 60% dispersion, 4.00 mmol in THF (10 mL), and (*E*)-3-phenyl-2-propenyl methyl carbonate (0.2 mmol) were successively added at rt. After stirring at rt for 3 h, water (2 mL) was added to quench the reaction. The mixture was extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with brine (10 mL) and dried ($MgSO_4$). The solvents were evaporated and the residue was purified by chromatography on silica gel (petroleum ether/EtOAc) to afford the product (35 mg, 70% purified yield, 90% yield by GLC) as a 49:1 mixture of branched (er 99.5:0.5) and linear isomers. Branched isomer: HPLC (Daicel Chiralcel OD, heptane/PrOH, 99.5:0.5, 0.5 mL/min, 220 nm) t_R (minor, *R*) 26.89 min, t_R (major, *S*) 29.11 min; R_f 0.32 (hexane/EtOAc, 6:1); $[\alpha]_D^{20}$ – 34.2 (*c* 2.02, $CHCl_3$); IR (neat) 3031, 2954, 1737, 1435, 1263, 1197, 1163, 1027, 993, 926, 765, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.19 (m, 5H), 6.05–5.93 (m, 1H), 5.15–5.07 (m, 2H), 4.14–4.08 (m, 1H), 3.87 (d, J = 11.0 Hz, 1H), 3.74 (s, 3H), 3.49 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.3, 167.9, 140.0, 137.8, 128.7, 127.9, 127.2, 116.7, 57.2, 52.5, 52.3, 49.6.



Dimethyl 2-[(*S*)-1-Phenyl-2-propenyl]propanedioate [Microwave-Assisted Allylation of a Malonate].[33] Sodium dimethyl malonate [prepared by adding dimethyl malonate (66 μL, 0.58 mmol) to a suspension of 60% NaH (2 mg,

0.050 mmol) in THF (1 mL)] was added to the ligand (*R*,*R*)-**52** (0.025 mmol) and $Mo(CO)_6$ (5 mg, 0.02 mmol) in a heavy-walled pyrex tube, followed by (*E*)-3-phenyl-2-propenyl methyl carbonate (102 mg, 0.53 mmol) in THF (0.5 mL) and BSA (156 μL, 0.63 mmol). The tube was sealed and the sample was irradiated using a single-mode cavity microwave reactor with a power of 200 W for 4 min. Directly after heating, the dark-colored reaction mixture was cooled in a water bath at rt and diluted with Et_2O to a volume of 10 mL, whereupon a precipitate appeared. The yellow-orange mixture was filtered, the filtrate was concentrated, and the crude product was purified by silica gel column chromatography (EtOAc/hexanes) to afford 116 mg of product (88% purified yield; >95% yield by GLC) in a 41:1 branched to linear ratio, and with er >99.5:0.5 of the major isomer. The ^1H and ^{13}C NMR spectra were identical to those of the compound prepared under thermal conditions (see above).[32]

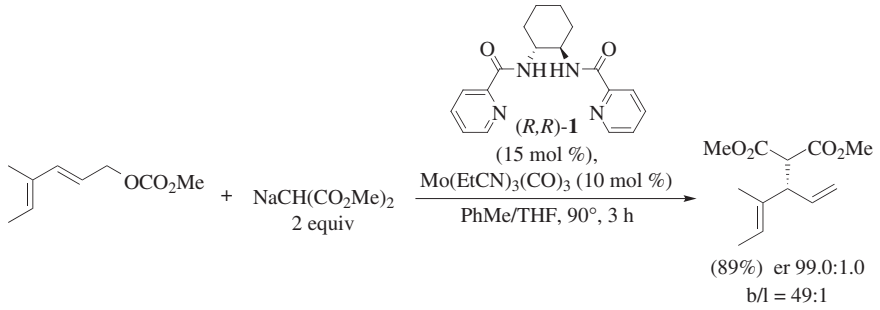


Dimethyl 2-[(*R*)-1-Methyl-2-propenyl]propanedioate [Allylation of a Malonate with an Alkyl-Substituted Allylic Carbonate].[21] A solution of ligand (*S,S,S,S*)-**57** (9.8 mg, 0.025 mmol) and $Mo(EtCN)_3(CO)_3$ (5.9 mg, 0.017 mmol) in freshly distilled THF (0.7 mL) was degassed and then stirred at 70° in an ampule with a J-Young valve under argon for 1 h. A solution of sodium dimethyl malonate [prepared from dimethyl malonate (40 mg, 0.3 mmol) and NaH (5.3 mg, 0.22 mmol) in THF (1.0 mL) at rt] and (*E*)-2-butenyl methyl carbonate (22.1 mg, 0.17 mmol) were then added to the reaction mixture. The solution was again degassed and then stirred at 70° for 24 h. After cooling to rt, H_2O (3 mL) was added. The mixture was extracted with Et_2O (3 ×15 mL), the combined extracts were washed with brine (5 mL) and dried ($MgSO_4$), and the solvent was evaporated. The resulting oil was purified by silica gel chromatography (pentane/BuOMe, 10:1) to afford 25.7 mg (81% yield) of a 9:1 mixture of products (*R*)-**60** and **61** as a colorless oil: R_f 0.35 (hexane/EtOAc, 4:1); GC (Restek Trx-1701, 30 m, 60–120°, 2°/min, 60 kPa H_2) t_R 23.2 (**60**), 27.4 ((*E*)-**61**), 28.1 ((*Z*)-**61**); GC (Chiraldex γ-CD-TA, 30 m, 50–100°, 1°/min, 90 kPa H_2) t_R 33.4 ((+)-(*R*)-**60**), 34.7 ((−)-(*S*)-**60**), 41.7 ((*E*)-**61**), 44.2 ((*Z*)-**61**).

Isomer **60**: The er (98.5:1.5) and the regioselectivity were determined by GC; $[\alpha]_D^{20}$ + 19.4 (*c* 0.76, $CHCl_3$; determined using a sample with er 96.5:3.5); IR (film) 3082, 2956, 2852, 1739, 1643, 1436, 1268, 1200, 1153, 1022, 921, 802 cm^{-1}; ^1H

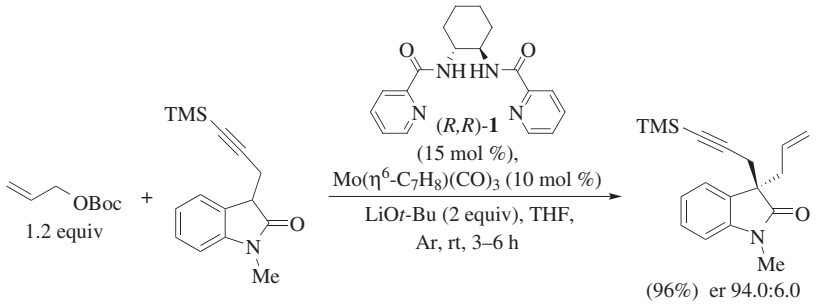
NMR (300 MHz) δ 5.77 (ddd, J = 17.1, 10.2, 8.0 Hz, CH), 5.13–5.00 (m, CH_2), 3.74 (s, MeO), 3.71 (s, MeO), 3.32 (d, J = 9.0 Hz, CHCO), 2.97–2.94 (m, MeCH), 1.10 (d, J = 6.8, Me); ^{13}C NMR (75 MHz) δ 168.7 (C=O), 168.7 (C=O), 139.7 (CH), 115.6 (CH_2), 57.6 (*C*HCO), 52.4 (MeO), 52.3 (MeO), 38.1 (Me*C*H), 18.1 (Me); EIMS (*m*/*z*): $[M + H]^+$ 187 (0.5), 155 (6), 127 (100), 111 (32), 101 (28), 95 (42). Anal. Calcd for $C_9H_{14}O_4$: C, 57.97; H, 7.63. Found: C, 58.05; H, 7.57.

Isomer (*E*)-**61**: IR (film) 2955, 1736, 1437, 1268, 1231, 1154, 1023, 968 cm^{-1}; ^{1}H NMR (300 MHz) δ 5.61–5.49 (m, CH), 5.42–5.31 (m, CH), 3.75 (s, 2 MeO), 3.41 (t, J = 7.5 Hz, CH), 2.57 (m, CH_2), 1.64 (dd, J = 6.1, 1.0 Hz, Me); ^{13}C NMR (75 MHz) δ 169.2 (C=O), 128.4 (CH), 126.2 (CH), 52.4 (MeO), 51.9 (CH), 31.9 (CH_2), 17.8 (Me); EIMS (*m*/*z*): M^+ 186 (10), 154 (8), 132 (43), 126 (55), 123 (57), 111 (100), 101 (25), 95 (31).



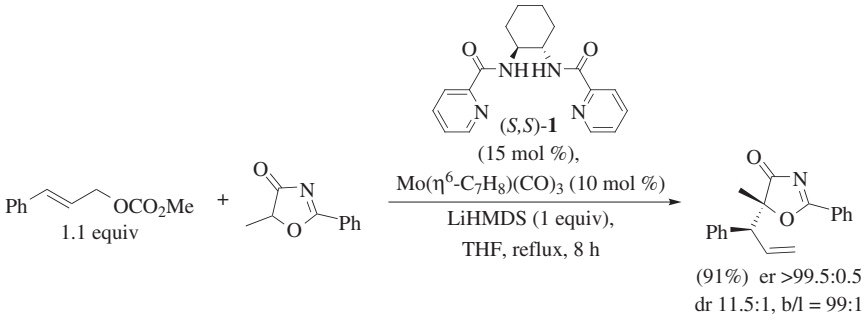
Dimethyl 2-[3-(*S*,*E*)-4-Methylhexa-1,4-diene]propanedioate [Allylation of a Malonate with a Dienylic Carbonate].[49] *Thorough degassing was performed since the catalyst is sensitive to oxygen*. The reaction vessel containing $Mo(EtCN)_3(CO)_3$ (7.5 mg, 0.022 mmol) and ligand (*R*,*R*)-**1** (10.7 mg, 0.035 mmol) was evacuated and flushed with nitrogen three times and then toluene (1 mL, degassed with argon) was added. The mixture was heated at 60° for 1 h. *Note: The resultant catalyst solution should be very dark red to almost black. If the solution turned to brown, the catalyst has become deactivated and the reaction should be abandoned*. A THF solution (1 mL) of the nucleophile prepared from dimethyl malonate (63.2 mg, 0.48 mmol) and sodium hydride (60% oil dispersion, 17.4 mg, 0.44 mmol) and (*E*,*E*)-4-methylhexa-2,4-dienyl methyl carbonate (37 mg, 0.217 mmol) was added at rt and the resultant mixture was heated at 90° for 3 h. Work-up (dilution with Et_2O and washing with water) and silica gel chromatography (petroleum ether/Et_2O, 8:1) provided 43.8 mg (89% yield) of the title product: HPLC (Daicel AD column, heptane/*i*-PrOH, 99:1) $t_R(+)$ (major) 34.93 min, $t_R(-)$ (minor) 43.46 min; IR (neat) 1740, 1638, 1435, 1318 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.71 (ddd, J = 17.2, 10.1, 8.1 Hz, 1H), 5.35 (q, J = 6.4 Hz, 1H), 5.07 (d, J = 17.2 Hz,

1H), 5.04 (d, J = 10.1 Hz, 1H), 3.70 (d, J = 10 Hz, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.43 (dd, J = 11.4, 8.1 Hz, 1H), 1.60–1.52 (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 168.59, 136.93, 133.94, 121.71, 116.50, 54.95, 52.64, 52.33, 13.39, 13.29; HRMS (m/z): M^+ calcd for $C_{12}H_{18}O_4$, 226.1205; found, 226.1206.



(*R*)-3-Allyl-1-methyl-3-(3-(trimethylsilyl)prop-2-ynyl)indolin-2-one [Allylation of an Alkyloxindole].[56] *Preparation of the active catalyst solution*: A solution of ligand (*R*,*R*)-**1** (0.015 mmol) and Mo(η^6-C_7H_8)$(CO)_3$ (0.01 mmol) in freshly distilled and degassed THF (0.3 mL) was stirred at 60° in a sealed pyrex test tube under argon atmosphere. The solution turned deep purple after 3–5 min, indicating successful generation of the active catalyst. Further heating caused a black precipitate and decomposition to occur. The active catalyst is very sensitive to oxygen and moisture and should be used immediately after generation. *Preparation of the nucleophile*: A pyrex test tube containing 0.1 mmol of the oxindole was transferred to the dry box and LiO*t*-Bu (0.2 mmol) was added. The test tube was sealed, taken out of the dry box, and degassed THF (0.7 mL) was added. The resulting solution was stirred for 5 min before the solution of the active catalyst was added via cannula, followed by the addition of allyl *tert*-butyl carbonate (0.12 mmol) via a syringe. The resulting solution was stirred at rt under argon for 3–6 h until TLC indicated complete consumption of the starting oxindole. The reaction mixture was then concentrated and purified through silica gel to give the desired product (96% yield, er 94.0:6.0) as a colorless oil: Chiral HPLC (AD column, heptane/*i*-PrOH, 90:10, 6 mL/min) t_R (major) 6.55 min, t_R (minor) 7.22 min; $[\alpha]_D^{20}$ – 78.8 (*c* 2.1, $CHCl_3$); IR (film) 2958, 2178, 1716, 1613, 1493, 1469, 1376, 1250, 842 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dd, J = 7.5, 1.5 Hz, 1H), 7.28 (dt, J = 7.5, 1.5 Hz, 1H), 7.07 (dt, J = 7.5, 1 Hz, 1H), 6.82 (d, J = 7.5, 1H), 5.45–5.31 (m, 1H), 5.02 (dm, J = 16 Hz, 1H), 4.90 (dm, J = 16 Hz, 1H), 3.20 (s, 3H), 2.77–2.70 (m, 2H), 2.61 (dd, J = 7, 16 Hz, 1H), 2.52 (d, J = 16 Hz, 1H), 0.57 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.5, 143.6, 132.2, 131.2, 128.1, 123.6, 122.3, 118.8, 107.7, 78.2, 74.1,

51.2, 40.0, 27.1, 26.1, 3.5; HRMS-EI (*m*/*z*): calcd for $C_{18}H_{23}NOSi$, 297.1549; found, 297.1559.



(*R*)-5-Methyl-5-[(*S*)-(1-phenyl)-2-propenyl]-2-phenyloxazol-4(5*H*)-one [Allylation of an Oxazolidine-4-one].[38] A solution of ligand (*S*,*S*)-**1** (4.9 mg, 0.015 mmol) and $Mo(CO)_3(\eta^6\text{-}C_7H_8)$ (2.8 mg, 0.01 mmol) in freshly distilled and degassed THF (0.5 mL) was gently refluxed under argon in a pyrex test tube sealed with a rubber septum until a deep purple color developed (5–10 min). A separate tube containing 5-methyl-2-phenyloxazol-4(5*H*)-one (0.1 mmol) was evacuated and flushed with argon three times and anhydrous, degassed THF (0.5 mL) was added, followed by dropwise addition of a freshly prepared solution of LiHMDS (1 M in THF; 0.1 mL, 0.1 mmol) with stirring at 0°. The solution was stirred for 5–10 min and the resulting nucleophile was added to the catalyst. (*E*)-3-Phenyl-2-propenyl methyl carbonate (0.11 mmol) was then added at 60° using a syringe. The reaction mixture was heated at reflux for 8 h and was then poured onto a 1 N solution of 1:1 KH_2PO_4/K_2HPO_4 (pH 7, 8 mL). Dichloromethane (15 mL) was added, the phases were separated, the aqueous phase was extracted with CH_2Cl_2, and the combined organic phases were dried ($MgSO_4$). After evaporation of the solvent a crude oil was obtained which was purified by chromatography (silica gel, petroleum ether/EtOAc, 90:10, R_f 0.23), affording 26.5 mg of the desired product (91% yield, er >99.5:0.5, branched/linear 99:1, dr 11.5:1). Major diastereomer: HPLC (Daicel Chiralpac AD column, heptane/*i*-PrOH, 99:1, 1 mL/min, 254 nm): t_R (1) 27.5 min, t_R (2) 34.1 min; IR (neat) 2924, 2853, 1754, 1603, 1547, 1451, 1356, 1149, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.26–8.23 (m, 2H), 7.74–7.7 (m, 1H), 7.59–7.55 (m, 2H), 7.4–7.28 (m, 5H), 5.99 (ddd, J = 17, 10, 8.8 Hz, 1H), 5.21–5.00 (m, 2H), 3.79 (d, J = 8.8 Hz, 1H), 1.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.6, 185.3, 137.8, 135.2, 133.6, 130.0, 129.0, 128.9, 128.7, 127.5, 125.7, 119.8, 90.2, 56.2, 21.2. Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.66; H, 6.71; N, 4.02.

TABULAR SURVEY

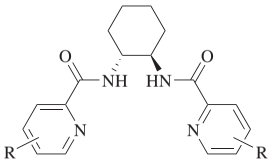
The literature has been reviewed up to June 2012. The tables are divided according to the nucleophiles. Entries are ordered by increasing carbon count of the allylic

substrate, excluding carbon atoms in the leaving group and typical protecting groups. Where (+) or (−) is used instead of (*R*) or (*S*), the author did not report an absolute configuration for the product. The absolute configuration of the product varies in some entries with subtables; in these cases one enantiomer is drawn with (*R*) or (*S*) marked on the structure and the associated subtable should be consulted for the absolute configuration of the product for each set of conditions. Unspecified yields, enantiomeric ratios, and absolute configurations are denoted by (—).

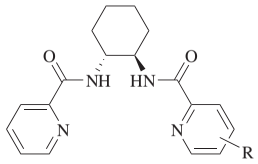
The following abbreviations that are not in the list of standard abbreviations published by the *Journal of Organic Chemistry* are used in the tables.

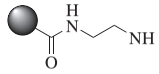
BSA	*N*,*O*-bis(trimethylsilyl)acetamide
C_7H_8	cycloheptatriene
Mes	1,3,5-trimethylbenzene
MW	microwave irradiation
PMP	4-methoxyphenyl
Ts	4-toluenesulfonyl
W	watt

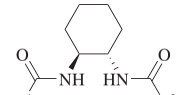
CHART 1. LIGANDS USED IN TABLES



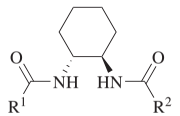
	R
1a	H
1b	2-Me
1c	4-MeO
1d	2-MeO
1e	4-*t*-Bu
1f	4-O_2N
1g	4-Cl
1h	2-Br
1i	4-pyrrolidinyl
1j	5-HO



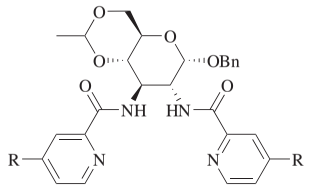
	R
2a	4-MeO
2b	4-Cl
2c	4-pyrrolidinyl
2d	4-$NH(CH_2)_2NH_2$
2e	



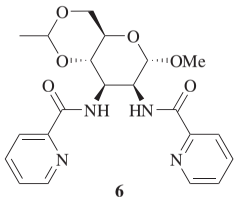
	R^1	R^2
3a	2-pyridinyl	*t*-Bu
3b	2-pyridinyl	Ph
3c	4-pyrimidinyl	4-pyrimidinyl



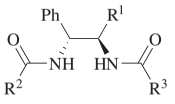
	R^1	R^2
4a	Ph	Ph
4b	2-pyridinyl	3-pyridinyl
4c	2-pyridinyl	2-quinolyl
4d	2-quinolyl	2-quinolyl



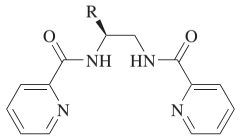
	R
5a	H
5b	Cl



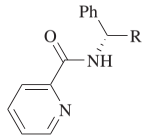
6



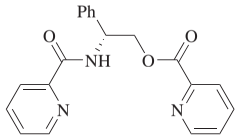
	R^1	R^2	R^3
7a	Ph	2-pyridinyl	2-pyridinyl
7b	H	2-pyridinyl	2-pyridinyl
7c	H	2-pyridinyl	Ph
7d	H	Ph	2-pyridinyl



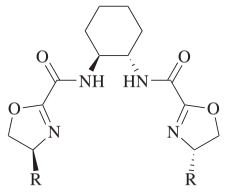
	R
8a	*i*-Pr
8b	Bn
8c	*t*-Bu



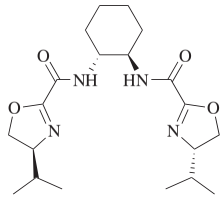
	R
9a	MeO_2C
9b	Me



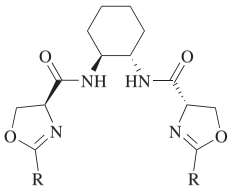
10



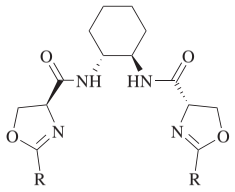
	R
11a	*i*-Pr
11b	*t*-Bu



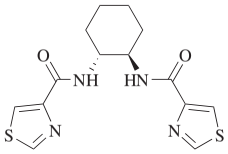
12



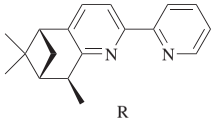
	R
13a	*n*-Pr
13b	*i*-Pr
13c	Ph



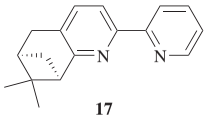
	R
14a	*n*-Pr
14b	*i*-Pr
14c	*t*-Bu
14d	Ph



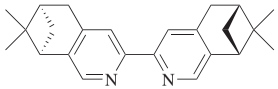
15



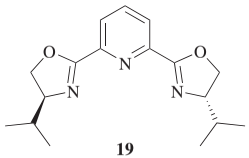
	R
16a	H
16b	Me



17

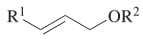
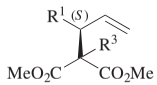
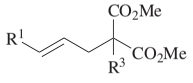


18

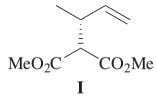
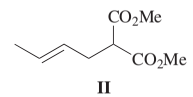


19

TABLE 1. ALLYLATION OF MALONATES

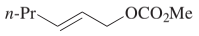
Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_4  $NaR^3C(CO_2Me)_2$	Ligand (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF, 70°	 +  **I** **II**	

R^1	R^2	R^3	Ligand	Time (d)	**I** + **II**	**I**/**II**	er **I**	Config.	
Me	MeO_2C	H	*ent*-**1a**	1	(85)	5:1	97.0:3.0	(*R*)	21
Me	MeO_2C	H	**11a**	1	(88)	1.5:1	97.0:3.0	(*R*)	21
Me	MeO_2C	H	**11a**[a]	5	(80)	1.5:1	96.5:3.5	(*R*)	21
Me	MeO_2C	H	**11b**	1.5	(79)	2.2:1	90.0:10.0	(*R*)	21
Me	MeO_2C	H	**12**	5	(53)	0.6:1	63.0:37.0	(*S*)	21
Me	MeO_2C	H	**13a**	1	(81)	9:1	98.5:1.5	(*R*)	21
Me	MeO_2C	H	**13b**	1.5	(81)	9:1	97.5:2.5	(*R*)	21
Me	MeO_2C	H	**13c**	5	(73)	5:1	87.0:13.0	(*R*)	21
Me	MeO_2C	H	**14a**	2	(80)	11:1	98.0:2.0	(*S*)	21
Me	MeO_2C	H	**14b**	1	(86)	7:1	96.0:4.0	(*S*)	21
Me	MeO_2C	H	**14c**	2	(85)	1.5:1	50.0:50.0	—	21
Me	MeO_2C	H	**14d**	3	(76)	7:1	92.5:7.5	(*S*)	21
Me	MeO_2C	H	**19**	2	(69)	1.5:1	50.0:50.0	—	120
MeO	Ac	Me	*ent*-**1a**	1	(60)	>20:1	87.0:13.0	(+)	21
MeO	Ac	Me	**13a**	1	(52)	6:1	81.0:19.0	(+)	21
MeO	Ac	Me	**13b**	1	(72)	5:1	83.0:17.0	(+)	21
MeO	Ac	Me	**14a**	1	(38)	5:1	81.5:18.5	(–)	21
MeO	Ac	Me	**14b**	1	(54)	13:1	88.0:12.0	(–)	21
MeO	Ac	Me	**14c**	1	(35)	3:1	60.5:39.5	(–)	21

 $NaCH(CO_2Me)_2$ — **13a** (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF, 70°, 1 d —  +  **I** **II** — 21

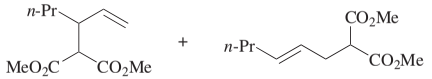
I + **II** (83), **I**/**II** = 5:1, er **I** 90.0:10.0 (*R*)

C_6



$NaCH(CO_2Me)_2$

Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
THF, 70°

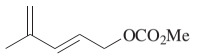


I + **II**

21

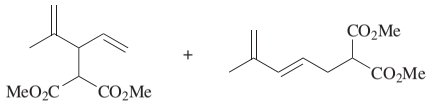
Ligand	Time (d)
ent-**1a**	1.5
13a	2
13b	2.5
14a	1.5
14b	1.5

I + **II**	**I**/**II**	er **I**	Config.
(80)	8:1	99.0:1.0	(+)
(69)	2:1	98.0:2.0	(+)
(54)	2:1	93.0:7.0	(+)
(84)	8:1	99.0:1.0	(–)
(83)	8:1	98.5:1.5	(–)



$NaCH(CO_2Me)_2$

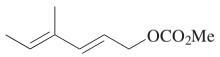
1a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°, 3 h



I + **II** (81), **I**/**II** = 8.1:1, er **I** 90.0:10.0

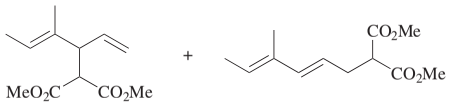
49

C_7



$NaCH(CO_2Me)_2$

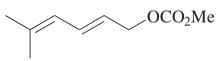
Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°



49

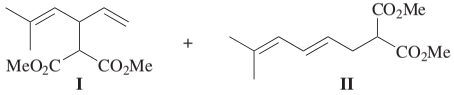
Ligand	Time (h)
1a	3
7a	6

I + **II**	**I**/**II**	er **I**
(89)	49:1	99.0:1.0
(87)	15.7:1	98.5:1.5



$NaCH(CO_2Me)_2$

Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°, 2 h

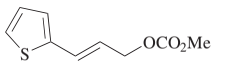
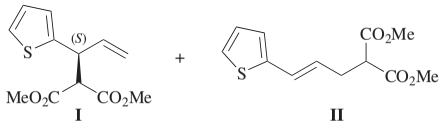


49

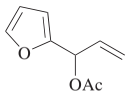
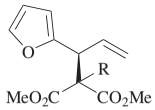
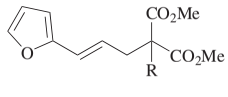
Ligand
1a
3c

I + **II**	**I**/**II**	er **I**
(96)	15.7:1	93.0:7.0
(94)	15.7:1	95.5:4.5

TABLE 1. ALLYLATION OF MALONATES (*Continued*)

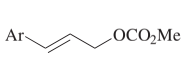
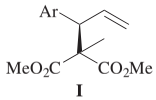
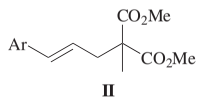
Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7 	$NaCH(CO_2Me)_2$	Ligand (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), THF, 60°, 5 h	 **I** + **II**	118

Ligand	I + II	I/II	er I	Config.
7b	(68)	10:1	95.0:5.0	(*S*)
8a	(87)	18:1	96.0:4.0	(*R*)

	$NaRC(CO_2Me)_2$	**1a** (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF	 **I** +  **II**	32

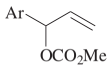
R	Temp	Time (h)	I + II	I/II	er I	Config.
Me	rt	18	(54)	99:1	97.5:2.5	(*S*)
Me	reflux	2	(65)	32:1	93.5:6.5	(*S*)
allyl	rt	12	(50)	99:1	99.0:1.0	(*S*)

C_{7-9}

	$NaMeC(CO_2Me)_2$	Ligand (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF, reflux	 **I** +  **II**	

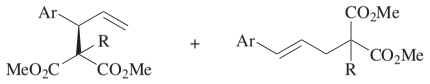
Ar	Ligand	Time (h)	I + II	I/II	er I	Config.	
2-furyl	**1a**	2	(71)	32:1	98.5:1.5	(*S*)[b]	32
Ph	**1a**	4	(67)	24:1	99.0:1.0	(*R*)[b]	32
Ph	**7b**	12	(37)	4:1	86.5:13.5	(*R*)	118
Ph	**8b**	10	(32)	10:1	78.5:21.5	(*S*)	118

C_{7-13}



$NaRC(CO_2Me)_2$

1a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
THF, reflux, 2 h

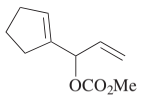


32

Ar	R
2-thienyl	Me
2-thienyl	H
2-pyridinyl	Me
2-pyridinyl	H
1-naphthyl	H

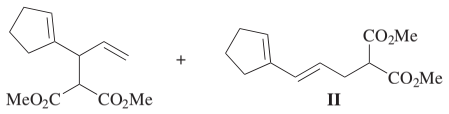
I + **II**	**I**/**II**	er **I**	Config.
(71)	13:1	87.5:12.5	(*S*)
(78)	19:1	94.0:6.0	(*S*)
(71)	5:1	97.0:3.0	(*S*)
(69)	8:1	98.0:2.0	(*S*)
(82)	99:1	93.5:6.5	(*S*)

C_8



$NaCH(CO_2Me)_2$

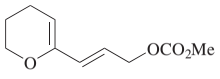
Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°



49

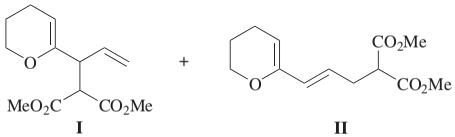
Ligand	Time (h)
1a	2
3c	1.5

I + **II**	**I**/**II**	er **I**
(94)	11.5:1	93.5:6.5
(88)	13.3:1	93.0:7.0



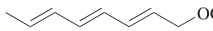
$NaCH(CO_2Me)_2$

1a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°, 1.5 h



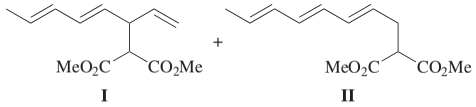
49

I + **II** (93), **I**/**II** = 13.3:1, er **I** 98.0:2.0



$NaCH(CO_2Me)_2$

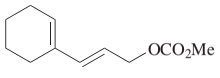
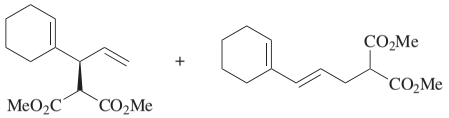
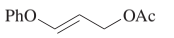
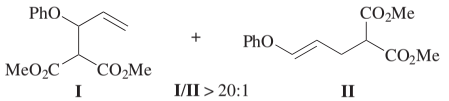
1a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°, 3 h



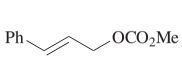
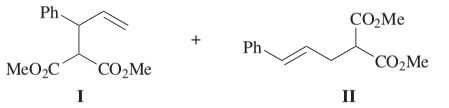
49

I + **II** (81), **I**/**II** = 10.1:1, er **I** 99.0:1.0

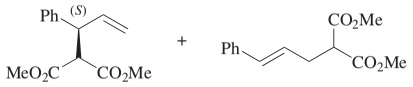
TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	$NaCH(CO_2Me)_2$	**7b** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), THF, 60°, 24 h	 **I** + **II** **I + II** (59), **I/II** = 5.5:1, er **I** 93.0:7.0 (*S*)	118
	$NaCH(CO_2Me)_2$	**8a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), THF, 60°, 24 h	**I + II** (61), **I/II** = 6.2:1, er **I** 93.5:6.5 (*R*)	118
	$NaCH(CO_2Me)_2$	**1a** (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), PhMe/THF, 80–90°, 3 h	**I + II** (91), **I/II** = 11.5:1, er **I** 97.0:3.0	49
	$NaCH(CO_2Me)_2$	Ligand (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF, 70°	 **I** **I/II** > 20:1 **II**	21

Ligand	Time (d)	**I + II**	er **I**	Config.
ent-**1a**	2	(79)	96.5:3.5	(–)
13a	2	(79)	99.0:1.0	(–)
13b	2	(78)	97.5:2.5	(–)
14a	1.5	(81)	96.5:3.5	(+)
14b	2	(75)	98.0:2.0	(+)

	$NaCH(CO_2Me)_2$	*ent*-**1a** (15 mol %), $Mo(CO)_6$ (10 mol %), PhMe, 85°, 8–12 h	 **I** + **II** **I + II** (80), **I/II** = 19:1, er **I** 99.5:0.5	119

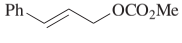
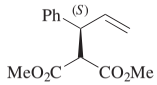
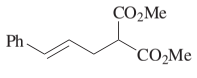
$NaCH(CO_2Me)_2$ Ligand (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF

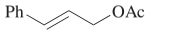


I **II**

Ligand	Temp (°)	Time	**I + II**	**I/II**	er **I**	Config.	
1a	rt	3 h	(70)	49:1	99.5:0.5	(*S*)	32
1a	reflux	3 h	(88)	32:1	99.5:0.5	(*S*)	32
3a[c]	—	—	(95)	30:1	99.0:1.0	(*R*)	19
3b[c]	—	—	(90)	60:1	99.0:1.0	(*R*)	19
ent-**4a**[c]	—	—	(35)	1:1	62.0:38.0	(*R*)	19
ent-**4b**[c]	—	—	(93)	46:1	99.5:0.5	(*R*)	19
4c	—	—	(29)	19:1	99.0:1.0	(*S*)	19
4d	—	—	traces	—	—	—	19
7a[c]	—	—	(95)	19:1	99.5:0.5	(*S*)	19
7b	60	4 h	(63)	8:1	96.0:4.0	(*S*)	118
7b[c]	60	4 h	(65)	8:1	96.0:4.0	(*S*)	118
7c	60	24 h	(21)	12:1	89.0:11.0	(*S*)	118
7d[c]	60	24 h	(51)	9:1	94.5:5.5	(*S*)	28
8a	60	12 h	(68)	32:1	99.0:1.0	(*R*)	118
8b	60	4 h	(69)	13:1	94.5:5.5	(*R*)	118
8c[c]	60	72 h	(64)	13:1	79.5:20.5	(*R*)	28
9a	60	3 h	(57)	1:1	52.5:47.5	(*R*)	28
9b	60	2 d	(47)	2:1	63.5:36.5	(*R*)	28
10[c]	60	1 d	(29)	1:1	55.0:45.0	(*S*)	28
11a	70	0.5 d	(86)	14:1	99.5:0.5	(*R*)	21
13a	70	1 d	(83)	6:1	99.0:1.0	(*R*)	21
ent-**1a**	48	—	(>90)	35:1	98.5:1.5	(*R*)[d]	35

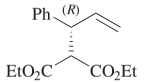
TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)				Refs.
C_9  $NaCH(CO_2Me)_2$	Ligand (5 mol %), $Mo(CO)_6$ (4 mol %), BSA, THF, MW	 **I** +  **II**				
Ligand	Temp/Power	Time (min)	**I + II**	**I/II**	er **I**	Config.	
1a	200 W	5	(71)[e]	19:1	99.0:1.0	(*S*)	33
1a	200 W	6	(82)[e]	19:1	99.0:1.0	(*S*)	33
1a	160°	6	(80)	19:1	99.0:1.0	(*S*)	34
1b	200 W	5	(30)[e]	13:1	89.5:10.5	(*S*)	33
1c	200 W	4	(88)	41:1	>99.5:0.5	(*S*)	33
1c	200 W	5	(89)	39:1	>99.5:0.5	(*S*)	33
1d	160°	6	(0)	—	—	—	34
1e	200 W	5	(46)[e]	13:1	99.0:1.0	(*S*)	33
1f	200 W	5	(7)[e]	16:1	98.5:1.5	(*S*)	33
1f	200 W	8	(32)[e]	16:1	98.5:1.5	(*S*)	33
1f	150 W	15	(37)[e]	16:1	98.5:1.5	(*S*)	33
1g	165°	6	(89)	74:1	98.0:2.0	(*S*)	34
1h	160°	6	(0)	—	—	—	34
1i	170°	12	(91)	88:1	98.0:2.0	(*S*)	34
1j	160°	6	(0)	—	—	—	34
2a	160°	6	(90)	98:1	98.5:1.5	(*R*)	33
2b	160°	6	(89)	74:1	98.5:1.5	(*R*)	33
2c	160°	6	(89)	75:1	99.5:0.5	(*R*)	33
2d	160°	12	traces	—	—	—	33
2e	160°	30	(82)	35:1	98.5:1.5	(*R*)	33
5a	160°	6	(90)[f]	49:1	99.5:0.5	(*R*)	61
5a	160°	6	(35)[g]	8:1	99.5:0.5	(*R*)	61
5b	160°	6	(42)[e]	12:1	93.5:6.5	(*R*)	61
6	160°	6	(41)[e]	5:1	70.0:30.0	(*S*)	61



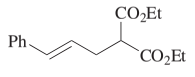
$NaCH(CO_2Et)_2$

11a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %)



I

\+



II

21

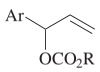
Solvent	Temp (°)	Time (d)	**I** + **II**	**I**/**II**	er **I**	Config.
THF	70	5	(38)	9:1	99.0:1.0	(*R*)
PhMe	110	3	(84)	10:1	98.5:1.5	(*R*)

$NaCH(CO_2Et)_2$

Ligand–$Mo(CO)_4$ (20 mol %),
$SnCl_4$, NaH, 1,4-dioxane,
80°, 24 h

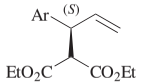
I + **II**

Ligand	**I** + **II**	**I**/**II**	er **I**	Config.	
16a	(52)	6.1:1	61.0:39.0	(*S*)	120
16b	(0)	—	—	—	
17	(33)	6.7:1	54.0:46.0	—	
18	(42)	3.5:1	56.0:44.0	(*R*)	



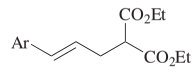
$NaCH(CO_2Me)_2$

Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
THF



I

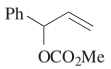
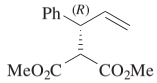
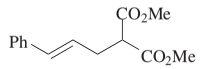
\+



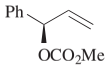
II

Ar	R	Ligand	Temp (°)	Time (h)	**I** + **II**	**I**/**II**	er **I**	Config.	
Ph	Me	**1a**	rt	3	(61)	32:1	98.5:1.5	(*S*)	32
Ph	Me	**1a**	reflux	3	(70)	13:1	96.0:4.0	(*S*)	32
Ph	Me	**3a**	—	—	(88)	28:1	94.0:6.0	(*R*)	19
Ph	Me	**3b**[c]	—	—	(90)	53:1	96.0:4.0	(*R*)	19
Ph	Me	**7b**	60	4	(72)	12:1	94.0:6.0	(*S*)	118
Ph	Me	**8a**	60	12	(59)	38:1	98.5:1.5	(*R*)	118
Ph	Me	**8b**	60	4	(68)	13:1	87.0:13.0	(*R*)	118
Ph	Me	**13a**	70	24	(83)	6:1	92.0:8.0	(*R*)	21
3-$O_2NC_6H_4$	*t*-Bu	**1a**[h]	67	24	(94)	100:0	98.0:2.0	(*R*)	65

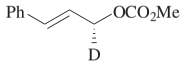
TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	$NaCH(CO_2Me)_2$	Ligand (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %)  **I** **I + II** (—) +  **II**	35

Ligand	Solvent	Temp (°)	**I/II**	er **I**	Config.[d]
ent-**1a**	THF	48	25:1	93.5:6.5	(*R*)
ent-**1a**	PhMe	60	46:1	98.0:2.0	(*R*)
ent-**1a**[i]	PhMe	90	32:1	98.5:1.5	(*R*)
ent-**1a**	MeCN	48	23:1	91.5:8.5	(*R*)
ent-**1a**	tetrahydropyran	48	30:1	96.0:4.0	(*R*)
ent-**1a**	tetrahydropyran	80	18:1	95.0:5.0	(*R*)
ent-**1a**	$ClCH_2CH_2Cl$	75	40:1	97.5:2.5	(*R*)
ent-**1a**	*i*-PrOAc	48	23:1	95.0:5.0	(*R*)

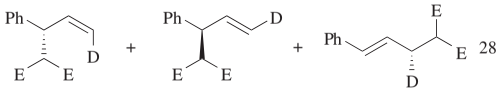
	$NaCH(CO_2Me)_2$	Ligand (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %) **I + II** (—)		35

Ligand	Solvent	Temp (°)	**I/II**	er **I**	Config.[d]
1a	THF	48	55:1	99.5:0.5	(*S*)
1a	PhMe	60	65:1	99.75:0.25	(*S*)
1a	MeCN	48	36:1	99.0:1.0	(*S*)
ent-**1a**	THF	48	12:1	85.0:15.0	(*R*)
ent-**1a**	PhMe	60	32:1	95.0:5.0	(*R*)
ent-**1a**	MeCN	48	8:1	72.0:28.0	(*R*)



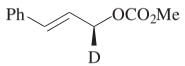
$NaCH(CO_2Me)_2$

8a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
THF, 60°, 20 h



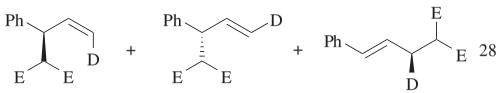
I er >97.5:2.5 **II** er >97.5:2.5 **III** 28

E = CO_2Me, **I** + **II** + **III** (—), **I/II/III** = 83.2:6.0:10.8



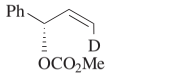
$NaCH(CO_2Me)_2$

8a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
THF, 60°, 20 h



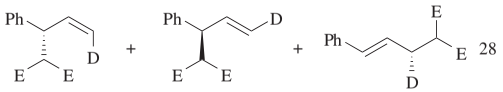
I er 70.0:30.0 **II** er >97.5:2.5 **III** 28

E = CO_2Me, **I** + **II** + **III** (—), **I/II/III** = 4.1:89.5:6.4



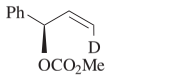
$NaCH(CO_2Me)_2$

8a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
THF, 60°, 20 h



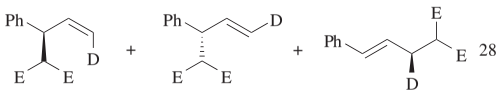
I er >97.5:2.5 **II** er >97.5:2.5 **III** 28

E = CO_2Me, **I** + **II** + **III** (—), **I/II/III** = 97.3:1.3:1.4



$NaCH(CO_2Me)_2$

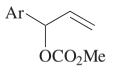
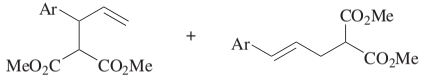
8a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
THF, 60°, 20 h



I er 70.0:30.0 **II** er 93.5:6.5 **III** 28

E = CO_2Me, **I** + **II** + **III** (—), **I/II/III** = 7.6:84.0:8.4

TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate		Conditions	Product(s) and Yield(s) (%)	Refs.
C_9				
 Ar = Ph	$NaCH(CO_2Me)_2$	*ent*-**1a** (15 mol %), $Mo(CO)_6$ (10 mol %), PhMe, 85°, 8–12 h	 **I** + **II** (76), **I/II** = 13:1, er **I** 98.0:2.0	119

		Ligand (5 mol %), $Mo(CO)_6$ (4 mol %), BSA, THF, MW, 165°, 6 min	**I + II**	Ligand	**I + II**	**I/II**	er **I**	Config.	
Ar = Ph	$NaCH(CO_2Me)_2$			**1a**	(76)	13:1	98.0:2.0	(*S*)	34
				1g	(89)	69:1	93.0:7.0	(*S*)	34
				5a	(82)	8:1	98.0:2.0	(*R*)	61

Ar = 3-FC_6H_4 $NaCH(CO_2Me)_2$ *ent*-**1a** (15 mol %), Mo complex (10 mol %)[j] **I + II**

Mo Complex	Solvent	Time (h)[j]	Temp (°)	**I + II**	**I/II**	er **I**	Config.	
$Mo(CO)_6$	PhMe	0.75	85	(77)[k]	19:1	97.5:2.5	—	119
$Mo(CO)_6$	PhMe	4	85	(84)	19:1	98.5:1.5	—	119
$Mo(CO)_6$	PhMe	15	85	(91)[k]	11.5:1	94.5:5.5	—	119
$Mo(CO)_6$	THF	2	65	(86)[k]	11.5:1	96.0:4.0	—	119
$Mo(CO)_6$	THF	4	65	(83)[k]	8:1	96.0:4.0	—	119
$Mo(CO)_6$	THF	4	rt	(33)[k]	5.3:1	98.0:2.0	—	119
$Mo(CO)_6$	DMF	4	85	(55)[k]	6.1:1	93.5:6.5	—	119
$Mo(CO)_6$	DME	4	80	(90)[k]	5.7:1	97.5:2.5	—	119
$Mo(CO)_6$	DCE	4	80	(36)[k]	24:1	99.0:1.0	—	119
$Mo(EtCN)_3(CO)_3$	PhMe	0.5	85	(84)[k]	13.6:1	97.5:2.5	—	119
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$	PhMe	0.5	85	(87)[k]	24:1	98.0:2.0	—	119
$Mo(CO)_6$	PhMe	4	85	(91)[k]	19:1	98.5:1.5	—	119
$Mo(EtCN)_3(CO)_3$	THF	0.5	65	(88)[k]	9:1	95.5:4.5	—	119
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$	THF	0.5	65	(81)[k]	7.3:1	94.0:6.0	—	119
$Mo(CO)_6$	THF	4	65	(83)[k]	8.1:1	95.5:4.5	—	119
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$	THF	—	48	(—)	15:1	94.0:6.0	(*R*)[d]	35
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$	PhMe	—	75	(—)	30:1	98.0:2.0	(*R*)[d]	35

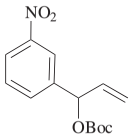
Ar = 4-ClC_6H_4 | $NaCH(CO_2Me)_2$ | *ent*-**2e** (5 mol %), $Mo(CO)_6$ (4 mol %), BSA, MW, 160°, 30 min | **I + II**

Solvent	**I + II**	**I/II**	er **I**	Config.	
THF	(95)	27:1	74.0:26.0	(*R*)	67
THF/PhMe (1:1)	(98)[e]	24:1	88.0:12.0	(*R*)	
THF/PhMe (1:9)	(76)[e]	25:1	94.5:5.5	(*R*)	

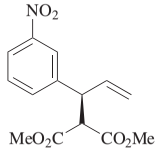
Ar = 4-FC_6H_4

$NaCH(CO_2Me)_2$ | Ligand (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), THF | **I + II**

Ligand	**I + II**	**I/II**	er **I**	Config.	
1a	(84)	10:1	97.0:3.0	(*S*)	
7a	(93)	13:1	98.0:2.0	(*S*)	19
7b	(92)	6:1	95.5:4.5	(*S*)	
7c	(43)	9:1	88.5:11.5	(*S*)	
7d	(72)	8:1	95.0:5.0	(*S*)	

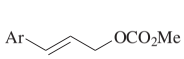


$NaCH(CO_2Me)_2$ | Ligand (15 mol %), $Mo(CO)_6$ (10 mol %), THF, MW, 180°, 20 min

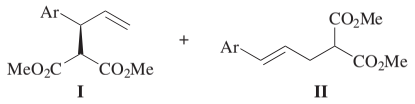


Ligand		er	Config.	
ent-**1a**	(92)	97.0:3.0	(*S*)	65
ent-**1c**	(94)	97.0:3.0	(*S*)	

C_{9-10}



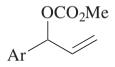
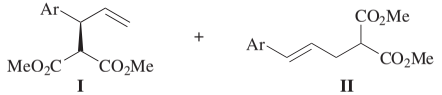
$NaCH(CO_2Me)_2$, $CH_2(CO_2Me)_2$ | Ligand (5 mol %), $Mo(CO)_6$ (4 mol %), BSA, THF, MW, 165°, 6 min



I + **II** 34

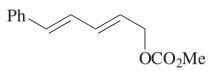
Ar	Ligand	**I + II**	**I/II**	er **I**
4-ClC_6H_4	**1a**	(51)	32:1	98.0:2.0
4-ClC_6H_4	**1g**	(86)	47:1	95.0:5.0
4-$CF_3C_6H_4$	**1a**	(50)	11:1	99.5:0.5
4-$CF_3C_6H_4$	**1g**	(66)	22:1	98.0:2.0
4-$MeOC_6H_4$	**1a**	(59)	51:1	99.0:1.0
4-$MeOC_6H_4$	**1g**	(79)	57:1	97.0:3.0

TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{9-10}  $NaCH(CO_2Me)_2$	**Ligand** (5 mol %), $Mo(CO)_6$ (4 mol %), BSA, THF, MW, 165°, 6 min	 **I** **II**	34

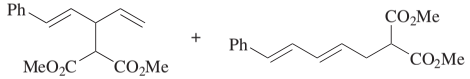
Ar	Ligand	I + II	I/II	er I
4-ClC_6H_4	**1a**	(78)	26:1	98.0:2.0
4-ClC_6H_4	**1g**	(70)	34:1	87.0:13.0
4-$CF_3C_6H_4$	**1a**	(48)	10:1	99.0:1.0
4-$CF_3C_6H_4$	**1g**	(52)	20:1	95.0:5.0

C_{11}



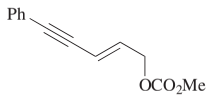
$NaCH(CO_2Me)_2$

7a (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), PhMe/THF, 80–90°, 3 h



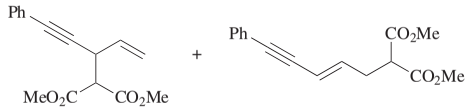
I **II** 49

I + **II** (95), **I/II** = 6.1:1, er **I** 99.0:1.0



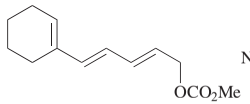
$NaCH(CO_2Me)_2$

1a (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), PhMe/THF, 80–90°, 3 h



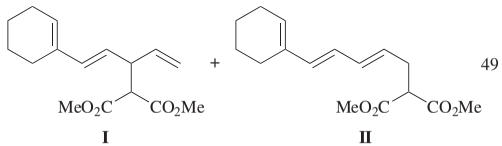
I **II** 49

I + **II** (—), **I/II** = 5.3:1, er **I** 99.5:0.5



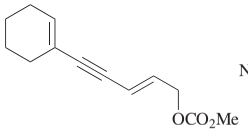
$NaCH(CO_2Me)_2$

1a (15 mol %), $Mo(EtCN)_3(CO)_3$ (10 mol %), PhMe/THF, 80–90°, 2 h



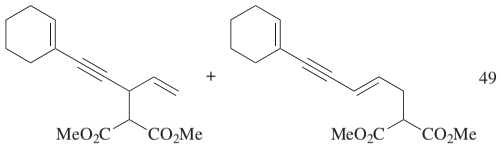
I **II** 49

I + **II** (70), **I/II** = 11.5:1, er **I** 98.5:1.5



$NaCH(CO_2Me)_2$

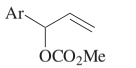
1a (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°, 3 h



I + **II** (—), **I**/**II** = 7.3:1, er **I** 99.5:0.5

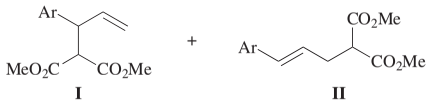
49

C_{13}



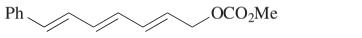
$NaCH(CO_2Me)_2$

1a (15 mol %), $Mo(CO)_6$ (10 mol %),
PhMe, 85°, 8–12 h



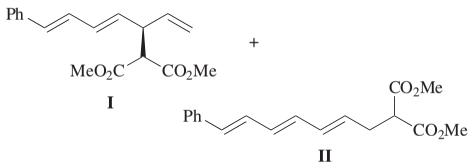
Ar	**I** + **II**	**I**/**II**	er **I**
4-*t*-BuC_6H_4	(76)	15.7:1	97.0:3.0
1-naphthyl	(80)	49:1	98.0:2.0

119



$NaCH(CO_2Me)_2$

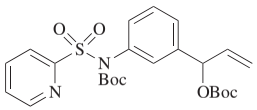
Ligand (15 mol %),
$Mo(EtCN)_3(CO)_3$ (10 mol %),
PhMe/THF, 80–90°



Ligand	Time (h)	**I** + **II**	**I**/**II**	er **I**	Config.
1a	3.5	(68)	6.1:1	>99.5:0.5	(*R*)
7a	4	(58)	5.3:1	98.5:1.5	(*R*)

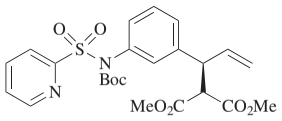
49

C_{14}



$NaCH(CO_2Me)_2$

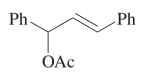
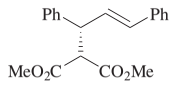
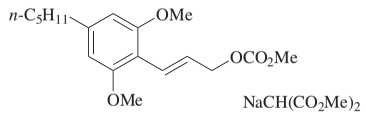
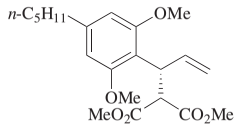
1a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
THF, 67°



(95) er 97.0:3.0 (*S*)

65

TABLE 1. ALLYLATION OF MALONATES (*Continued*)

Allyl Compound and Malonate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{15}  $NaCH(CO_2Me)_2$	Ligand–$Mo(CO)_4$ (20 mol %), $SnCl_4$, NaH, 1,4-dioxane, 80°, 24 h		120
C_{16}  $NaCH(CO_2Me)_2$	*ent*-**1a** (7.5 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (5 mol %),[l] THF, 65°, 30 h	 (95) er 97.0:3.0 (*R*)	48

Ligand		er	Config.
16b	(0)	—	—
18	(22)	55.0:45.0	(*R*)

[a] This reaction employed 3.8 mol % ligand and 2.5 mol % $Mo(EtCN)_3)(CO)_3$.

[b] The apparent change in configuration between the first 2 entries in the subtable is due to a change in substituent priorities.

[c] This reaction employed 10 mol % $Mo(\eta^6\text{-}C_7H_8)(CO)_3$.

[d] The opposite absolute streochemistry of the product was erroneously reported in ref. 35.

[e] The yield was determined by gas chromatography.

[f] This reaction employed 11 mol % ligand and 10 mol % $Mo(CO)_6$.

[g] This reaction employed 4.4 mol % ligand.

[h] This reaction employed $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ as the catalyst.

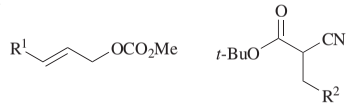
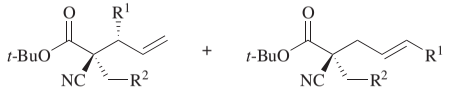
[i] This reaction employed $Mo(CO)_6$ as catalyst precursor.

[j] The catalyst was activated for 2–4 h at 65–90° prior to the catalytic reaction.

[k] The yield was determined by HPLC.

[l] The use of 15 mol % **1a** and 10 mol % Mo complex afforded the product in 95% yield and er 97.5:2.5.

TABLE 2. ALLYLATION OF CYANO ESTERS

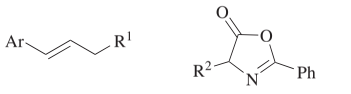
Allyl Compound and Cyano Ester	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{3-11} 	**1c** (15 mol %), $Mo(CO)_6$ (10 mol %), NaH (10 mol %), BSA (2 eq), THF, 60°, 17 h	 **I** + **II**	52

R^1	R^2	**I + II**	**I/II**	dr **I**	er **I**
H	Me	(99)	—	—	99.5:0.5
H	Et	(96)	—	—	99.0:1.0
2-thienyl	Et	(93)	>20:1	>20:1	99.0:1.0
Ph	Me	(96)	>20:1	16.8:1	96.5:3.5
Ph	Et	(93)	>20:1	12:1	97.5:2.5
Ph	Ph	(95)	>20:1	>20:1	>99.5:0.5
Ph	Bn	(93)	>20:1	>20:1	99.0:1.0
Ph	$Me(CH_2)_5$	(98)	>20:1	15.7:1	99.5:0.5
Ph		(91)	>20:1	6.5:1	98.0:2.0
Ph	MeO	(79)	>20:1	>20:1	94.0:6.0
4-BrC_6H_4	Et	(92)	>20:1	13.7:1	98.5:1.5
4-FC_6H_4	Et	(>99)	>20:1	20:1	95.5:4.5
4-$MeOC_6H_4$	Et	(85)	>20:1	12.2:1	94.5:5.5
4-$O_2NC_6H_4$	Et	(83)	>20:1	11.1:1	96.0:4.0
3,5-$Br_2C_6H_3$	Et	(94)	>20:1	14.0:1	98.5:1.5
3,5-$Br_2C_6H_3$	4-BrC_6H_4	(89)	>20:1	>20:1	99.5:0.5
3-(*N*-Boc)indolyl	Et	(>99)	>20:1	11:1	98.5:1.5

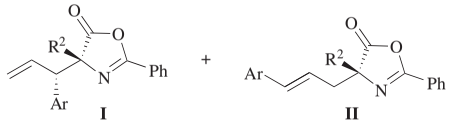
TABLE 3. ALLYLATION OF α-IMINO ESTERS AND α-IMINO LACTONES

Allyl Compound and α-Imino Ester or Lactone	Conditions	Product(s) and Yield(s) (%)	Refs.

C_{7-11}



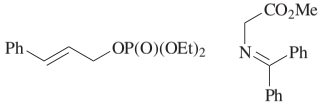
ent-**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LiHMDS, THF, 65°



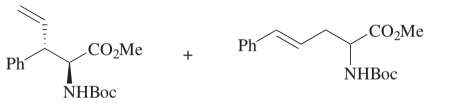
I + **II** — 37

Ar	R^1	R^2	Time (h)	**I**	dr **I**	er **I**	**II**
2-furyl	$MeOCO_2$	Me	4	(84)	>98:2	96.0:4.0	(4)
3-thienyl	$MeOCO_2$	Me	3	(84)	96:4	95.5:4.5	(—)
3-thienyl	$MeOCO_2$	Bn	3	(86)	>98:2	97.0:3.0	(—)
Ph	*t*-$BuOCO_2$	Me	—	(83)	96:4	99.5:0.5	(—)
Ph	$(EtO)_2PO_2$	Me	—	(80)	>98:2	99.5:0.5	(—)
Ph	$MeOCO_2$	Me	3	(92)	97:3	99.5:0.5	(—)
Ph	$MeOCO_2$	Bn	3	(92)	>98:2	98.0:2.0	(—)
Ph	$MeOCO_2$	$MeS(CH_2)_2$	4	(86)	>98:2	96.0:4.0	(6)
Ph	$MeOCO_2$	*i*-Bu	4	(85)	>98:2	98.0:2.0	(5)
Ph	$MeOCO_2$	*n*-Pr	3	(82)	>98:2	98.5:1.5	(6)
Ph	$MeOCO_2$	*i*-Pr	6	(76)	>98:2	98.0:2.0	(11)
2,4-$(MeO)_2C_6H_3$	$MeOCO_2$	Me	3	(89)	>98:2	95.0:5.0	(—)
2,4-$(MeO)_2C_6H_3$	$MeOCO_2$	Bn	3	(90)	>98:2	97.0:3.0	(—)

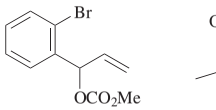
C_9



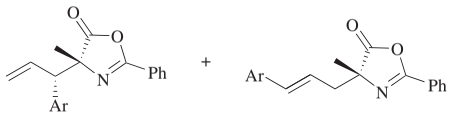
1. *ent*-**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LDA, THF, 0°
2. 1 N HCl
3. $(Boc)_2O$, Et_3N



I (67) dr 20:1, er 99.0:1.0 + **II** (33) — 37

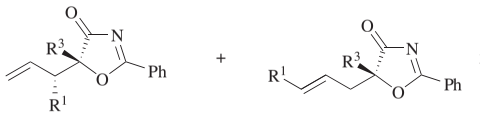


ent-**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LiHMDS, THF, 65°, 4 h



I (82) dr >98:2, er 92.5:7.5 + **II** (9) — 37

TABLE 4. ALLYLATION OF OXALACTIMS

Allyl Compound and Oxalactim	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-11} 	*ent*-**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), base, THF, 65°, 16 h	 **I** + **II**	38

R^1	R^2	R^3	Base	**I** + **II**	**I**/**II**	dr **I**	er **I**
$Me_2C{=}CH$	$MeOCO_2$	Me	LiHMDS	(77)	14:1	12:1	94.5:5.5
3-thienyl	$MeOCO_2$	*i*-Bu	LiHMDS	(89)	14:1	10:1	99.5:0.5
1-cyclohexenyl	$MeOCO_2$	Me	LiHMDS	(54)	12:1	12:1	99.0:1.0
Ph	$(EtO)_2PO_2$	Me	LiHMDS	(90)	7:1	8.1:1	98.0:2.0
Ph	$MeOCO_2$	Me	KHMDS	(88)	6.7:1	1.4:1	90.0:10.0
Ph	$MeOCO_2$	Me	NaHMDS	(80)	24:1	2.7:1	99.0:1.0
Ph	$MeOCO_2$	Me	LiHMDS	(91)	99:1	11.5:1	>99.5:0.5
Ph	$MeOCO_2$	*n*-Bu	LiHMDS	(86)	49:1	9:1	>99.5:0.5
Ph	$MeOCO_2$	allyl	LiHMDS	(97)	8:1	10:1	>99.5:0.5
Ph	$MeOCO_2$	*i*-Pr	LiHMDS	(70)	5.5:1	20:1	>99.5:0.5
Ph	$MeOCO_2$	*c*-C_6H_{11}	LiHMDS	(74)	9:1	12:1	>99.5:0.5
Ph	$MeOCO_2$	Bn	LiHMDS	(84)	>95:5	7.4:1	>99.5:0.5
2,4-$(MeO)_2C_6H_3$	$MeOCO_2$	Me	LiHMDS	(82)	12:1	18:1	>99.5:0.5

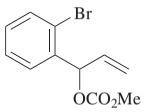
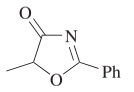
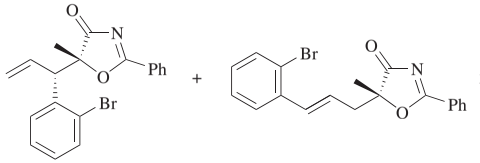
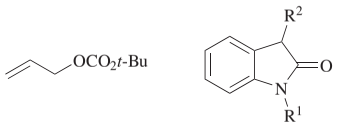
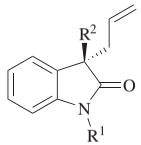
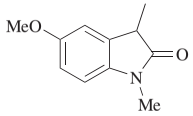
C_9  	*ent*-**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LiHMDS, THF, 65°, 16 h	 **I** + **II** (78), **I**/**II** = 27:1, dr **I** 24:1, er **I** 99.5:0.5	38

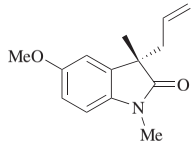
TABLE 5. ALLYLATION OF OXINDOLES

Allyl Compound and Oxindole	Conditions	Product(s) and Yield(s) (%)	Refs.
C_3 	**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LiO*t*-Bu (2 eq), THF, rt, 3–6 h		56

R^1	R^2		er
Me	Me	(98)	91.0:9.0
Me	Me	(99)	90.5:9.5
Bn	Me	(93)	87.5:12.5
Me	Bn	(95)	96.5:3.5
MOM	Bn	(95)	93.5:6.5
Bn	Bn	(92)	93.5:6.5
allyl	Bn	(99)	94.0:6.0
Me	*i*-Pr	(96)	95.5:4.5
Bn	*i*-Pr	(98)	92.5:7.5
Me	$NCCH_2$	(99)	96.5:3.5
allyl	$NCCH_2$	(98)	96.5:3.5
Me	2-(BocHN)$C_6H_4CH_2$	(96)	97.5:2.5
Bn	$Me_2C{=}CHCH_2$	(95)	90.0:10.0
Me	$MeC{\equiv}CCH_2$	(95)	90.0:10.0
MOM	$MeC{\equiv}CCH_2$	(96)	87.5:12.5
Bn	$MeC{\equiv}CCH_2$	(98)	87.0:13.0
Me	$TMSC{\equiv}CCH_2$	(96)	94.0:6.0
Me	$TBSO(CH_2)_2$	(94)	87.5:12.5



1a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
base, THF

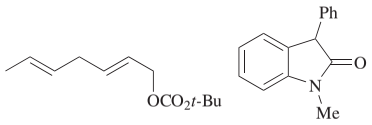


56

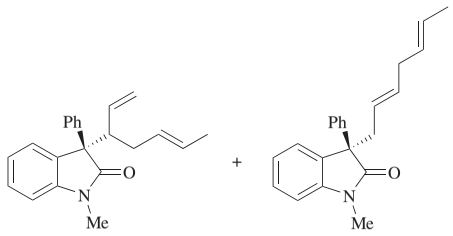
Base	Temp		er
KHMDS	67°	(—)	69.0:31.0
NaHMDS	67°	(—)	80.0:20.0
LiHMDS	67°	(75–92)	87.5:12.5–89.0:11.0
s-BuLi	67°	(—)	85.5:14.5
LiHMDS	rt	(45)	90.0:10.0
LiHMDS/LiO*t*-Bu	rt	(95)	90.5:9.5
LiHMDS (2 eq)	rt	traces	—
LiO*t*-Bu (2 eq)	rt	(95–98)	90.0:10.0–91.0:9.0
LiO*t*-Bu (2 eq)	4°	(95)	91.0:9.0
LiO*t*-Bu (2 eq)	–10°	(90)	86.5:13.5

65

C_7



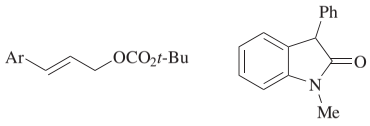
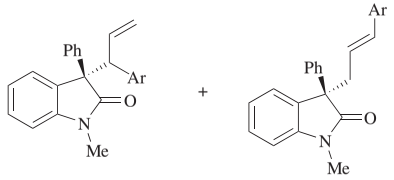
1a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
NaO*t*-Bu (1.1 eq), THF, 60°



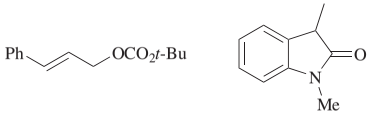
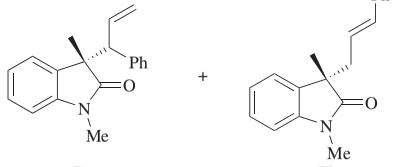
I + **II** (84), **I**/**II** = 6:1, dr **I** 6:1, er **I** 95.5:4.5

39

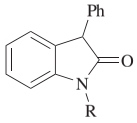
TABLE 5. ALLYLATION OF OXINDOLES (*Continued*)

Allyl Compound and Oxindole	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{7-9} 	**1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), NaO*t*-Bu (1.1 eq), THF, 60°	 **I** + **II**	39

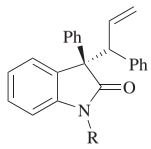
Ar	**I** + **II**	**I**/**II**	dr **I**	er **I**
2-furyl	(92)	12:1	6:1	95.5:4.5
2-thienyl	(88)	13:1	8:1	95.0:5.0
4-(TBSO)C_6H_4	(90)	19:1	8:1	94.5:5.5
2-(BocHN)C_6H_4	(89)	19:1	19:1	96.5:3.5
3,4-$Cl_2C_6H_3$	(87)	6:1	5.5:1	94.5:5.5

C_9 	Ligand **1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), LiO*t*-Bu (1 eq), THF, rt, 8 h	 **I** + **II**	45

I + **II** (—), **I**/**II** = 2:1, dr **I** 1.2:1, er **I** —

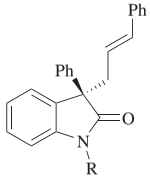


Ligand (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
base (1.1 eq), THF, 2–8 h



I

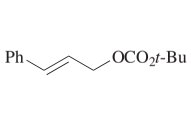
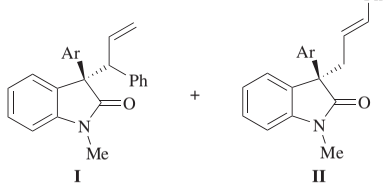
+



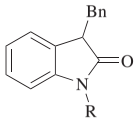
II

R	Ligand	Base	Temp	**I + II**	**I/II**	dr **I**	er **I**	
Boc	**1a**	NaO*t*-Bu	60°	(91)	5:1	5:1	96.5:3.5	39
MOM	**1a**	NaO*t*-Bu	60°	(90)	19:1	7:1	96.0:4.0	39
Bn	**1a**	NaO*t*-Bu	60°	(85)	17:1	9:1	95.0:5.0	39
Me	**1a**	NaO*t*-Bu	60°	(88)	18:1	8:1	96.0:4.0	39
Me	**1a**	NaO*t*-Bu	60°	(—)	16:1	—	—	45
Me	**1a**	LiO*t*-Bu	rt	(—)	4:1	8:1	97.5:2.5	45
Me	**1c**	LiO*t*-Bu	rt	(—)	2.5:1	5.5:1	—	45
Me	*ent*-**3c**	LiO*t*-Bu	rt	(—)	2.5:1	5:1	—	45
Me	**15**	LiO*t*-Bu	rt	(—)	4:1	7:1	—	45
Me	**7a**	LiO*t*-Bu	rt	(—)	1.2:1	3:1	—	45
Me	*ent*-**7d**	LiO*t*-Bu	rt	(—)	5:1	4:1	—	45
Me	**1a**	KO*t*-Bu	rt	(—)	10:1	5:1	97.0:3.0	45
Me	**1a**	NaO*t*-Bu	rt	(89)	16:1	9:1	96.0:4.0	45
Me	**1a**	NaO*t*-Bu	0°	(—)	16:1	9:1	96.0:4.0	45
Me	**1a**	NaO*t*-Bu	–78°	(40)	1:1	2:1	95.5:4.5	45

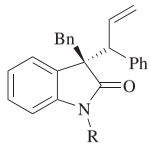
TABLE 5. ALLYLATION OF OXINDOLES (*Continued*)

Allyl Compound and Oxindole	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	Ligand (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), NaO*t*-Bu (1.1 eq), THF, 60°, 2–8 h	 **I** + **II**	39

Ar	Ligand	I + II	I/II	dr I	er I
4-FC_6H_4	**1a**	(90)	16:1	6:1	95.5:4.5
4-ClC_6H_4	**1a**	(88)	13:1	5.5:1	97.5:2.5
4-NCC_6H_4	**1a**	(84)	7:1	4.5:1	94.5:5.5
4-NCC_6H_4	**1c**	(85)	18:1	4:1	96.0:4.0
4-$MeOC_6H_4$	**1a**	(92)	18:1	8:1	96.0:4.0
4-$Me_2NC_6H_4$	**1a**	(87)	17:1	6:1	96.0:4.0
2-MeC_6H_4	**1a**	(90)	17:1	19:1	97.0:3.0
1-naphthyl	**1a**	(88)	15:1	19:1	97.5:2.5
2-naphthyl	**1a**	(90)	15:1	6:1	95.0:5.0
2-thienyl	**1a**	(90)	0:1	—	50.0:50.0
N-Me-3-indolyl	**1a**	(82)	0:1	—	—
2-Ph-5-thiazolyl	**1a**	(86)	0:1	—	—
3-Me-2-thienyl	**1a**	(95)	11:1	19:1	96.0:4.0
N-Me-2-Ph-3-indolyl	**1a**	(65)	9:1	19:1	97.0:3.0
2,4-Me_2-5-thiazolyl	**1a**	(84)	2.5:1	19:1	96.0:4.0
2,4-Me_2-5-thiazolyl	**1c**	(86)	16:1	19:1	96.5:3.5
2,4-Ph_2-5-oxazolyl	**1a**	(83)	16:1	19:1	98.0:2.0
N-Ts-3-indolyl	**1a**	(63)	10:1	19:1	98.5:1.5

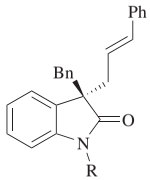


1a (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
base, THF, 60°, 2 h



I

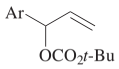
+

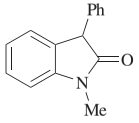


II

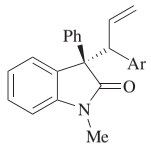
45

R	Base (eq)	I + II	I/II	dr I	er I
Me	NaO*t*-Bu (1)	(92)	2:1	1.2:1	96.0:4.0
AcO	NaO*t*-Bu (1)	(0)	—	—	—
2-pyridinyl	NaO*t*-Bu (1)	(89)	14:1	1:1	—
t-BuO_2C	NaO*t*-Bu (1)	(85)	12:1	3:1	99.0:1.0
EtO_2C	NaO*t*-Bu (1)	(86)	15:1	5:1	99.5:0.5
MeO_2C	NaO*t*-Bu (1)	(60)	15:1	7:1	99.0:1.0
MeO_2C	NaO*t*-Bu (0.1), BSA (1.2)	(88)	15:1	7:1	99.0:1.0
MeO_2C	NaO*t*-Bu (0.1), BSA (1.2)[a]	(83)	15:1	7:1	99.0:1.0



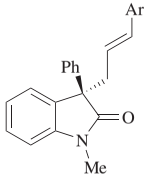


Ligand (15 mol %),
$Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %),
NaO*t*-Bu, THF, 60°, 2 h



I

+

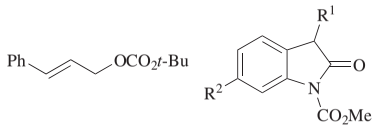
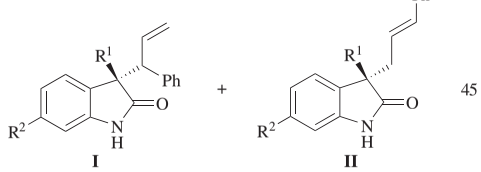


II

45

Ar	Ligand	I + II	I/II	dr I	er I
Ph	**1a**	(88)	10:1	6:1	91.0:9.0
Ph	**1c**	(85)	15:1	9:1	96.5:3.5
3,4-$Cl_2C_6H_3$	**1a**	(90)	6:1	5:1	90.0:10.0
3,4-$Cl_2C_6H_3$	**1c**	(87)	8:1	6:1	94.5:5.5
4-(TBSO)C_6H_4	**1a**	(89)	12:1	6.5:1	90.5:9.5
4-(TBSO)C_6H_4	**1c**	(89)	15:1	8:1	94.5:5.5

TABLE 5. ALLYLATION OF OXINDOLES (*Continued*)

Allyl Compound and Oxindole	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9 	1. **1a** (15 mol %), $Mo(\eta^6\text{-}C_7H_8)(CO)_3$ (10 mol %), NaO*t*-Bu (1 eq), THF, 60°, 2 h 2. NaOH/MeOH, 30 min	 **I** + **II**	45

R^1	R^2	**I** + **II**	**I**/**II**	dr **I**	er **I**
Me	H	(93)	>15:1	7:1	99.0:1.0
Et	H	(90)	>15:1	10:1	99.5:0.5
i-Pr	H	(90)	>19:1	>19:1	98.5:1.5
i-Pr	Cl	(87)	>15:1	>19:1	99.0:1.0
i-Pr	MeO	(90)	>15:1	>19:1	98.0:2.0
allyl	H	(89)	>15:1	8:1	99.5:0.5
$TBSO(CH_2)_2$	H	(83)	11:1	7:1	98.5:1.5
t-BuO_2CCH_2	H	(84)	12:1	4:1	98.5:1.5
Bn	H	(85)	>15:1	7:1	99.0:1.0

[a] This reaction employed 2.5 mol % $Mo(\eta^6\text{-}C_7H_8)(CO)_3$.

REFERENCES

[1] Trost, B. M.; Crawley, M. L. *Chem. Rev.* **2003**, *103*, 2921.
[2] Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258.
[3] Helmchen, G.; Kazmaier, U.; Förster, S. In *Catalytic Asymmetric Synthesis*, 3rd ed.; Ojima, I., Ed.; Wiley: Hoboken, 2010; pp 497–641.
[4] Poli, G.; Prestat, G.; Liron, F.; Kammerer-Pentier, C. *Top. Organomet. Chem.* **2012**, *38*, 1.
[5] Trost, B. M.; Crawley, M. L. *Top. Organomet. Chem.* **2012**, *38*, 321.
[5a] See reference 24.
[6] Moberg, C. *Top. Organomet. Chem.* **2012**, *38*, 209.
[7] Liu, W.-B.; Xia, J.-B.; You, S.-L. *Top. Organomet. Chem.* **2012**, *38*, 155.
[8] Kaiser, N.-F. K.; Bremberg, U.; Larhed, M.; Moberg, C.; Hallberg, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3596.
[9] Belda, O.; Moberg, C. *Acc. Chem. Res.* **2004**, *37*, 159.
[10] Pfaltz, A.; Lautens, M. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; pp 833–884.
[11] Trost, B. M. *Org. Process Res. Dev.* **2012**, *16*, 185.
[12] Brito, J. A.; Royo, B.; Gómez, M. *Catal. Sci. Technol.* **2011**, *1*, 1109.
[13] Malkov, A. V.; Baxendale, I. R.; Dvořák, D.; Mansfield, D. J.; Kočovský, P. *J. Org. Chem.* **1999**, *64*, 2737.
[14] Malkov, A. V.; Davis, S. L.; Baxendale, I. R.; Mitchell, W. L.; Kočovský, P. *J. Org. Chem.* **1999**, *64*, 2751.
[15] Malkov, A. V.; Spoor, P.; Vinader, V.; Kočovský, P. *J. Org. Chem.* **1999**, *64*, 5308.
[16] Hughes, D. L.; Lloyd-Jones, G. C.; Krska, S. W.; Gouriou, L.; Bonnet, V. D.; Jack, K.; Sun, Y.; Mathre, D. J.; Reamer, R. A. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5379.
[17] Krska, S. W.; Hughes, D. L.; Reamer, R. A.; Mathre, D. J.; Palucki, M.; Yasuda, N.; Sun, Y.; Trost, B. M. *Pure Appl. Chem.* **2004**, *76*, 625.
[18] Krska, S. W.; Hughes, D. L.; Reamer, R. A.; Mathre, D. J.; Sun, Y. *J. Am. Chem. Soc.* **2002**, *124*, 12656.
[19] Trost, B. M.; Dogra, K.; Hachiya, I.; Emura, T.; Hughes, D. L.; Krska, S.; Reamer, R. A.; Palucki, M.; Yasuda, N.; Reider, P. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1929.
[20] Luft, J. A. R.; Yu, Z.-X.; Hughes, D. L.; Lloyd-Jones, G. C.; Krska, S. W.; Houk, K. N. *Tetrahedron: Asymmetry* **2006**, *17*, 716.
[21] Glorius, F.; Neuburger, M.; Pfaltz, A. *Helv. Chim. Acta* **2001**, *84*, 3178.
[22] Faller, J. W.; Linebarrier, D. *Organometallics* **1988**, *7*, 1670.
[23] Rubio, A.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1993**, *115*, 891.
[24] Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1982**, *104*, 5543.
[25] Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1987**, *109*, 1469.
[26] Dvořák, D.; Starý, I.; Kočovský, P. *J. Am. Chem. Soc.* **1995**, *117*, 6130.
[27] Lloyd-Jones, G. C.; Krska, S. W.; Hughes, D. L.; Gouriou, L.; Bonnet, V. D.; Jack, K.; Sun, Y.; Reamer, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 702.
[28] Malkov, A. V.; Gouriou, L.; Lloyd-Jones, G. C.; Starý, I.; Langer, V.; Spoor, P.; Vinader, V.; Kočovský, P. *Chem.—Eur. J.* **2006**, *12*, 6910.
[29] Lloyd-Jones, G. C.; Muñoz, M. P. *J. Labelled Cmpd. Radiopharm.* **2007**, *50*, 1072.
[30] Ward, Y. D.; Villanueva, L. A.; Allred, G. D.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1996**, *118*, 897.
[31] Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395.
[32] Trost, B. M.; Hachiya, I. *J. Am. Chem. Soc.* **1998**, *120*, 1104.
[33] Belda, O.; Kaiser, N.-F.; Bremberg, U.; Larhed, M.; Hallberg, A.; Moberg, C. *J. Org. Chem.* **2000**, *65*, 5868.
[33a] See reference 118.
[34] Belda, O.; Moberg, C. *Synthesis* **2002**, 1601.
[35] Hughes, D. L.; Palucki, M.; Yasuda, N.; Reamer, R. A.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 2762.
[36] Trost, B. M. *Chem. Pharm. Bull.* **2002**, *50*, 1.
[37] Trost, B. M.; Dogra, K. *J. Am. Chem. Soc.* **2002**, *124*, 7256.
[38] Trost, B. M.; Dogra, K.; Franzini, M. *J. Am. Chem. Soc.* **2004**, *126*, 1944.
[39] Trost, B. M.; Zhang, Y. *J. Am. Chem. Soc.* **2007**, *129*, 14548.
[40] Gouriou, L.; Lloyd-Jones, G. C.; Vyskočil, Š.; Kočovský, P. *J. Organomet. Chem.* **2003**, *687*, 525.
[41] Faller, J. W.; Sarantopoulos, N. *Organometallics* **2004**, *23*, 2179.
[42] Trost, B. M.; Hung, M.-H. *J. Am. Chem. Soc.* **1984**, *106*, 6837.

[43] Cameron, P. A.; Britovsek, G. J. P.; Gibson, V. C.; Williams, D. J.; White, A. J. P. *Chem. Commun.* **1998**, 737.
[44] Morales, D.; Navarro Clemente, M. E.; Pérez, J.; Riera, L.; Riera, V.; Miguel, D. *Organometallics* **2003**, *22*, 4124.
[45] Trost, B. M.; Zhang, Y. *Chem.—Eur. J.* **2010**, *16*, 296.
[46] Lehmann, J.; Lloyd-Jones, G. C. *Tetrahedron* **1995**, *51*, 8863.
[47] Shekhar, S.; Trantow, B.; Leitner, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 11770.
[48] Trost, B. M.; Dogra, K. *Org. Lett.* **2007**, *9*, 861.
[49] Trost, B. M.; Hildbrand, S.; Dogra, K. *J. Am. Chem. Soc.* **1999**, *121*, 10416.
[50] Kočovský, P.; Malkov, A. V.; Vyskočil, Š.; Lloyd-Jones, G. C. *Pure Appl. Chem.* **1999**, *71*, 1425.
[51] Trost, B. M.; Merlic, C. A. *J. Am. Chem. Soc.* **1990**, *112*, 9590.
[52] Trost, B. M.; Miller, J. R.; Hoffman, C. M., Jr. *J. Am. Chem. Soc.* **2011**, *133*, 8165.
[53] Kuhl, A.; Christopher, J. A.; Farrugia, L. J.; Kocienski, P. J. *Synlett* **2000**, 1765.
[54] Trost, B. M.; Lautens, M. *Organometallics* **1983**, *2*, 1687.
[55] Trost, B. M.; Lautens, M. *Tetrahedron* **1987**, *43*, 4817.
[56] Trost, B. M.; Zhang, Y. *J. Am. Chem. Soc.* **2006**, *128*, 4590.
[57] Trost, B. M.; Zhang, Y. *Chem.—Eur. J.* **2011**, *17*, 2916.
[58] Belda, O.; Moberg, C. *Coord. Chem. Rev.* **2005**, *249*, 727.
[59] Barnes, D. J.; Chapman, R. L.; Vagg, R. S.; Watton, E. C. *J. Chem. Eng. Data* **1978**, *23*, 349.
[60] Conlon, D. A.; Yasuda, N. *Adv. Synth. Catal.* **2001**, *343*, 137.
[61] Del Litto, R.; Benessere, V.; Ruffo, F.; Moberg, C. *Eur. J. Org. Chem.* **2009**, 1352.
[62] Glorius, F.; Pfaltz, A. *Org. Lett.* **1999**, *1*, 141.
[63] Conlon, D. A.; Jensen, M. S.; Palucki, M.; Yasuda, N.; Um, J. M.; Yang, C.; Hartner, F. W.; Tsay, F.-R.; Hsiao, Y.; Pye, P.; Rivera, N. R.; Hughes, D. L. *Chirality* **2005**, *17*, S149.
[64] Palucki, M.; Um, J. M.; Yasuda, N.; Conlon, D. A.; Tsay, F.-R.; Hartner, F. W.; Hsiao, Y.; Marcune, B.; Karady, S.; Hughes, D. L.; Dormer, P. G.; Reider, P. J. *J. Org. Chem.* **2002**, *67*, 5508.
[65] Trost, B. M.; Andersen, N. G. *J. Am. Chem. Soc.* **2002**, *124*, 14320.
[66] Ong, J.; Kerr, D. I. B. *CNS Drug Rev.* **2005**, *11*, 317.
[67] Belda, O.; Lundgren, S.; Moberg, C. *Org. Lett.* **2003**, *5*, 2275.
[68] Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003.
[69] Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813.
[70] Miyabe, H.; Takemoto, Y. *Synlett* **2005**, 1641.
[71] Guerrero Rios, I.; Rosas-Hernandez, A.; Martin, E. *Molecules* **2011**, *16*, 970.
[72] Prétôt, R.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 323.
[73] Kazmaier, U.; Stolz, D.; Krämer, K.; Zumpe, F. L. *Chem.—Eur. J.* **2008**, *14*, 1322.
[74] Lloyd-Jones, G. C.; Stephen, S. C. *Chem.—Eur. J.* **1998**, *4*, 2539.
[75] Fairlamb, I. J. S.; Lloyd-Jones, G. C.; Vyskočil, Š.: Kočovský, P. *Chem.—Eur. J.* **2002**, *8*, 4443.
[76] Minami, I.; Shimizu, I.; Tsuji, J. *J. Organomet. Chem.* **1985**, *296*, 269.
[77] Trost, B. M.; Lemoine, R. C. *Tetrahedron Lett.* **1996**, *37*, 9161.
[78] Trost, B. M.; Schroeder, G. M. *Chem.—Eur. J.* **2005**, *11*, 174.
[79] Braun, M.; Meier, T. *Synlett* **2005**, 2968.
[80] Nakoji, M.; Kanayama, T.; Okino, T.; Takemoto, Y. *Org. Lett.* **2001**, *3*, 3329.
[81] Franckevičius, V.; Cuthbertson, J. D.; Pickworth, M.; Pugh, D. S.; Taylor, R. J. K. *Org. Lett.* **2011**, *13*, 4264.
[82] Lloyd-Jones, G. C.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 462.
[83] See reference 46.
[84] Bartels, B.; García-Yebra, C.; Rominger, F.; Helmchen, G. *Eur. J. Inorg. Chem.* **2002**, 2569.
[85] Graening, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 17192.
[86] Helmchen, G.; Dahnz, A.; Dübon, P.; Schelwies, M.; Weihofen, R. *Chem. Commun.* **2007**, 675.
[87] Dahnz, A.; Helmchen, G. *Synlett* **2006**, 697.
[88] Spiess, S.; Welter, C.; Franck, G.; Taquet, J.-P.; Helmchen, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7652.
[89] Alexakis, A.; Polet, D. *Org. Lett.* **2004**, *6*, 3529.
[90] Bruneau, C.; Renaud, J.-L.; Demerseman, B. *Chem.—Eur. J.* **2006**, *12*, 5178.
[91] Renaud, J.-L.; Demerseman, B.; Mbaye, M. D.; Bruneau, C. *Curr. Org. Chem.* **2006**, *10*, 115.
[92] Matsushima, Y.; Onitsuka, K.; Kondo, T.; Mitsudo, T.; Takahashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 10405.
[93] Trost, B. M.; Fraisse, P. L.; Ball, Z. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1059.
[94] Hermatschweiler, R.; Fernández, I.; Pregosin, P. S.; Watson, E. J.; Albinati, A.; Rizzato, S.; Veiros, L. F.; Calhorda, M. J. *Organometallics* **2005**, *24*, 1809.
[95] Zhou, B.; Xu, Y. *J. Org. Chem.* **1988**, *53*, 4419.

[96] Evans, P. A.; Leahy, D. K. *Chemtracts: Org. Chem.* **2003**, 567.
[97] Plietker, B.; Dieskau, A.; Möws, K.; Jatsch, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 198.
[98] Ashfeld, B. L.; Miller, K. A.; Martin, S. F. *Org. Lett.* **2004**, *6*, 1321.
[99] Menard, F.; Chapman, T. M.; Dockendorff, C.; Lautens, M. *Org. Lett.* **2006**, *8*, 4569.
[100] Hayashi, T.; Okada, A.; Suzuka, T.; Kawatsura, M. *Org. Lett.* **2003**, *5*, 1713.
[101] Evans, P. A.; Uraguchi, D. *J. Am. Chem. Soc.* **2003**, *125*, 7158.
[102] Berkowitz, D. B.; Maiti, G. *Org. Lett.* **2004**, *6*, 2661.
[103] Begouin, J.-M.; Klein, J. E. M. N.; Weickmann, D.; Plietker, B. *Top. Organomet. Chem.* **2012**, *38*, 269.
[104] Yorimitsu, H.; Oshima, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 4435.
[105] Kacprzynski, M. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 10676.
[106] van Zijl, A. W.; Arnold, L. A.; Minnaard, A. J.; Feringa, B. L. *Adv. Synth. Catal.* **2004**, *346*, 413.
[107] Tissot-Croset, K.; Alexakis, A. *Tetrahedron Lett.* **2004**, *45*, 7375.
[108] Langlois, J.-B.; Alexakis, A.; *Top. Organomet. Chem.* **2012**, *38*, 235.
[109] Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796.
[110] Harutyunyan, S. R.; den Hartog, T.; Geurts, K.; Minnaard, A. J.; Feringa, B. L. *Chem. Rev.* **2008**, *108*, 2824.
[111] Hartwig, J. F.; Stanley, L. M. *Acc. Chem. Res.* **2010**, *43*, 1461.
[112] Jiang, K.; Peng, J.; Cui, H.-L.; Chen, Y.–C. *Chem. Commun.* **2009**, 3955.
[113] Trost, B. M.; Frederiksen, M. U. *Angew. Chem., Int. Ed.* **2005**, *44*, 308.
[114] Poulsen, T. B.; Alemparte, C.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 11614.
[115] Xue, D.; Chen, Y.-C.; Wang, Q.-W.; Cun, L.-F.; Zhu, J.; Deng, J.-G. *Org. Lett.* **2005**, *7*, 5293.
[116] Kubas, G. J.; Van Der Sluys, L. S. *Inorg. Synth.* **1990**, *28*, 29.
[117] Cotton, F. A.; McCleverty, J. A.; White, J. E. *Inorg. Synth.* **1990**, *28*, 45.
[118] Malkov, A. V.; Spoor, P.; Vinader, V.; Kočovský, P. *Tetrahedron Lett.* **2001**, *42*, 509.
[119] Palucki, M.; Um, J. M.; Conlon, D. A.; Yasuda, N.; Hughes, D. L.; Mao, B.; Wang, J.; Reider, P. J. *Adv. Synth. Catal.* **2001**, *343*, 46.
[120] Malkov, A. V.; Baxendale, I. R.; Bella, M.; Langer, V.; Fawcett, J.; Russell, D. R.; Mansfield, D. J.; Valko, M.; Kočovský, P. *Organometallics* **2001**, *20*, 673.