CHAPTER 1

THE ALLYLIC TRIHALOACETIMIDATE REARRANGEMENT

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CONTENTS

INTRODUCTION

Sigmatropic rearrangements of allylic systems have found wide application in organic synthesis, with carbon-carbon bond forming rearrangements such as the Cope and Claisen rearrangements being particularly well known. The sigmatropic rearrangement of allylic imidates (also known as the "aza-Claisen" or "Claisen-imidate" rearrangement) offers a valuable entry into the preparation of protected allylic amines. Conversion of an imidate to the amide is essentially irreversible, with the transformation of the imidate to the amide being exothermic by about 15 kcal/mol.[1,2] Since the discovery of the thermal allylic imidate rearrangement in 1937,[3] a number of systems have been investigated for the practical preparation of allylic amines by this route, including urethanes, isourethanes, formimidates, benzimidates, isoureas and carbonimidothioates. However, it was the discovery and development of the rearrangement of allylic trichloroacetimidates that overwhelmingly demonstrated the widespread utility of this synthetic method (Eq. 1).[4-6]

$$\text{(Eq. 1)}$$

The [3,3]-sigmatropic rearrangement of allylic trichloroacetimidates (now generally referred to as the Overman rearrangement) or trifluoroacetimidates can be conveniently carried out either thermally or with Hg(II) or Pd(II) catalysis. The scope of the rearrangement is such that primary, secondary, and tertiary allylic amides are readily accessible, thus providing entry into a wide variety of nitrogen-containing products including amino sugars, nucleotides, amino acids, peptides, and various nitrogen heterocycles. In addition, the Overman rearrangement has found extensive application in the total synthesis of natural products. The recent development of chiral Pd(II) catalysts to promote asymmetric allylic trichloroacetimidate rearrangements with good enantioselectivity bodes well for the continued broad application of this amine synthesis.[7-9]

This chapter is limited to the discussion of allylic trichloro- and trifluoroacetimidate rearrangements. Several relevant reviews have appeared regarding the allylic imidate rearrangement,[10] the use of allylic imidates in organic synthesis,[11] Hg(II)- and Pd(II)-catalyzed [3,3]-sigmatropic rearrangements,[12] enantioselective rearrangement of allylic imidates,[13,14] and the preparation of allylic amines.[15] Trichloroacetimidates of propargylic alcohols also undergo thermal [3,3]-sigmatropic rearrangement, giving *N*-acylamino-1,3-dienes as a result of tautomerization of the

initially formed allenyl trichloroacetamide (Eq. 2).[16] This more limited transformation is not reviewed in this chapter.

(Eq. 2)

MECHANISM

Thermal Rearrangements

The concerted nature of the allylic trichloroacetimidate rearrangement has been established by examination of thermodynamic parameters, solvent effects, regioselection, and stereoselection. Activation parameters for the thermal rearrangement of the trichloroacetimidate of geraniol (Eq. 3) are consistent with a [3,3]-sigmatropic rearrangement, with the large negative change in entropy being similar to that observed for Cope and Claisen rearrangements.[6] An intermediate is not detected, even in cases where a highly delocalized allylic carbocation would result from the ionization of the trichloroacetimidate, as in the rearrangement of the trichloroacetimidate of cinnamyl alcohol.[6] The observed regiochemical outcome of the allylic trihaloacetimidate rearrangement also lends support to the representation of this transformation as an essentially concerted process. For allylic trichloroacetimidates, the thermal rearrangement occurs with complete allylic oxygen-to-nitrogen transfer; the product arising from ionization and recombination, formal [1,3]-rearrangement, is rarely observed.[17] As discussed in more detail shortly, solvent and substituent effects support the development of some charge separation in the transition state.

$$\Delta H^{\ddagger} = 24 \text{ kcal/mol}$$
$$\Delta S^{\ddagger} = -19 \text{ eu}$$

(Eq. 3)

The thermal allylic trihaloacetimidate rearrangement follows first-order kinetics,[6,18] with an assortment of steric and electronic substituent effects influencing the rate of the reaction. Alkenes having E double bonds tend to react more quickly than Z alkenes, a difference embodied in the $\Delta H^{\ddagger}$-term for reaction of the E and Z isomers of imidate **1**.[18] The rearrangement is facile for a wide variety of allylic alcohols, with doubly allylic alcohols reacting at room temperature, tertiary alcohols generally reacting at 80° ($t_{1/2} \sim 1$ hour), and primary alcohols reacting the least quickly ($t_{1/2} \sim 1$ hour at 140°).[6] These reactivity trends are attributed to stabilization of posi-

tive charge developed on the oxygen-bearing carbon in the transition state.[6] A five-fold rate enhancement is observed in changing the solvent from xylenes to nitrobenzene in the rearrangement of the trichloroacetimidate of geraniol at 132°. This finding is consistent with the postulated charge development in the transition state, that is, partial negative charge on the electronegative $HN=C(CCl_3)O$ fragment and partial positive charge on the all-carbon allyl fragment.[6] One observation is not readily rationalized by this model: the apparent increase in rate seen when para electron-withdrawing substituents are present in the rearrangement of cinnamyl substrates **2** shown in Eq. 4.[19]

E $\Delta H^{\ddagger} = 25.6$ kcal/mol
Z $\Delta H^{\ddagger} = 28.3$ kcal/mol

1

(Eq. 4)

2

The excellent stereoselectivity of the allylic trihaloacetimidate rearrangement is typical of suprafacial [3,3]-sigmatropic processes, as complete transfer of chirality is a hallmark of this reaction. Thus, the trichloroacetimidate of (*R,E*)-4-phenyl-3-buten-2-ol rearranges to give the (*R,E*)-trichloroacetamide **4** with no loss of enantiomeric purity, an outcome which can be rationalized as arising from the preferred chair-like transition structure **3** (Eq. 5).[20]
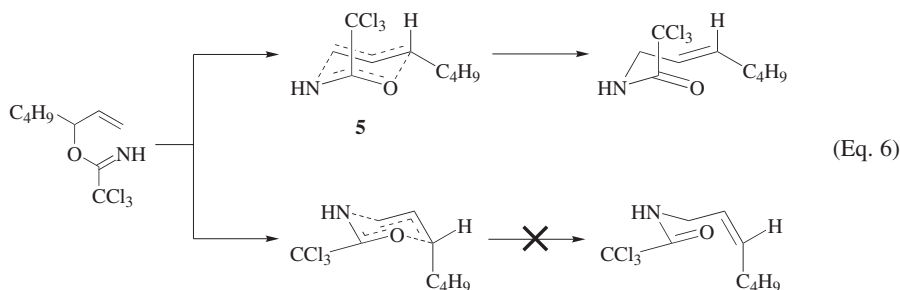

3

4

(Eq. 5)

High selectivity for forming the E stereoisomer of the product is seen in rearrangements of virtually all trihaloacetimidates of secondary allylic alcohols, including trisubstituted allylic alcohols such as 4-methyl-3-penten-2-ol,[6,21–23,81] and E and Z disubstituted allylic alcohols.[24–26] For example, rearrangement of the trichloroacetimidate of 1-hepten-3-ol proceeds to give a 92% yield of the E isomer by transition state structure **5** having the *n*-butyl group in the preferred equatorial position (Eq. 6).[6]

(Eq. 6)

As a result of the suprafacial nature of the rearrangement and the chair-like topography, either enantiomer of an E allylic amine can be prepared from the appropriate enantiomer of the starting allylic alcohol or from a configurationally related pair of alkene stereoisomers. An example of the latter strategy is shown in Eqs. 7 and 8.[24]

xylenes, 140°   (35% from alcohol)   (Eq. 7)

xylenes, 140°   (45% from alcohol)   (Eq. 8)

The allylic trichloroacetimidate rearrangement has not been the subject of *ab initio* or DFT theoretical studies. Early MNDO-PM3 semi-empirical molecular orbital calculations of the rearrangement of the trichloroacetimidate of allyl alcohol suggest an ion pair reaction pathway.[18] In this study, an ion pair transition state is calculated to have an enthalpy of formation of 11 kcal/mol, more than 9 kcal/mol lower than the calculated enthalpy of formation for the transition state of the [3,3]-sigmatropic pathway. Nevertheless, experimental evidence is fully consistent with a concerted sigmatropic rearrangement pathway.

Metal-Catalyzed Rearrangements

The rearrangement of allylic trihaloacetimidates can also be induced by using metal catalysts, thus lowering the temperature required for rearrangement and sometimes leading to higher yields, cleaner reactions and/or better stereocontrol. Many allylic trichloroacetimidates, ranging from simple allylic trichloroacetimidates to highly functionalized substrates, rearrange rapidly in the presence of Pd(II) or Hg(II) catalysts. Although the first reports employed $Hg(O_2CCF_3)_2$,[4] soluble complexes

of $PdCl_2$ emerged as the most useful metal catalysts.[27–31] Rate accelerations are large (10^{12} is estimated for 1 M $Hg(O_2CCF_3)_2$),[4] allowing many Pd(II)- and Hg(II)-catalyzed trichloroacetimidate rearrangements to be carried out at room temperature.

A cyclization-induced rearrangement mechanism in which the metal coordinates to the allylic double bond to bring about antarafacial intramolecular nucleophilic attack by the imidate nitrogen is believed to be involved in Pd(II)- or Hg(II)-catalyzed rearrangements (see Scheme 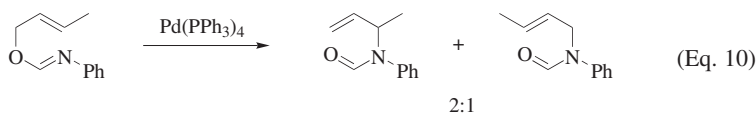1).[4,12,32] This mechanism is closely related to the mechanism originally proposed by Henry[33,34] for Pd(II)-catalyzed allylic acetate rearrangements and subsequently by Overman for $PdCl_2$-catalyzed Cope rearrangements.[35]

Scheme 1

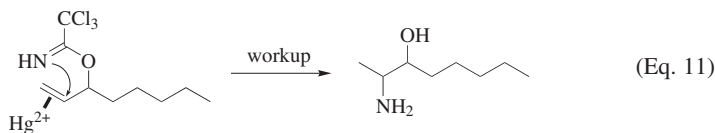A cyclization-induced rearrangement mechanism rationalizes the complete 1,3 oxygen-to-nitrogen transfer that is observed in Hg(II)- and Pd(II)-catalyzed rearrangements such as depicted in Eq. 9.[28] In contrast, rearrangements of allylic *N*-phenylformimidates and *N*-phenylbenzimidates catalyzed by Pd(0) complexes provide mixtures of products resulting from formal [1,3]- and [3,3]-sigmatropic

(Eq. 9)

rearrangements that undoubtedly involve the formation of Pd-π-allyl intermediates (Eq. 10).[36]
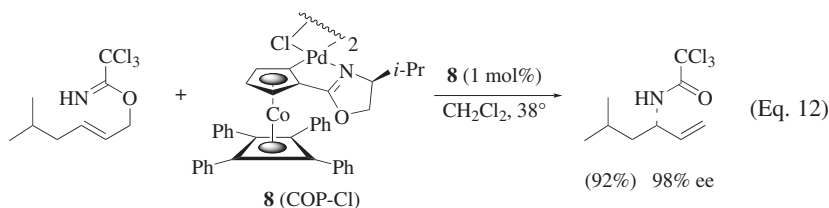

$$\text{(Eq. 10)}$$

2:1

Reactivity trends also support the cyclization-induced rearrangement mechanism for metal-catalyzed allylic trichloroacetimidate rearrangements. For example, substitution at the internal carbon of the allyl double bond (C2) slows the rate of the Pd(II)-catalyzed rearrangement, presumably as a result of the difficulty of generating a tertiary carbon-palladium sigma bond.[32] The limited scope of the Hg(II)-catalyzed process also provides support for a cyclization-induced rearrangement mechanism. Allylic substrates in which alkene substitution does not strongly favor intramolecular nucleophilic attack by the imino nitrogen at the allyl terminus (C3) fail to rearrange or rearrange in low yields under Hg(II) catalysis. Thus, for trichloroacetimidates containing terminal vinyl units, the 2-amino alcohol can be obtained after basic hydrolysis (Eq. 11).[4] This latter limitation is also seen in Pd(II)-catalyzed rearrangements as no reports exist of successful catalyzed rearrangements of allylic imidates containing terminal vinyl units.

$$\text{(Eq. 11)}$$

The suprafacial nature and high E stereoselectivity of Pd(II)-catalyzed rearrangements also implicate a cyclization-induced mechanism. Collapse of the most stable chair conformation of intermediate **7** of Eq. 9 predicts the observed stereochemical outcome, just as in corresponding thermal rearrangements. For example, palladium-catalyzed rearrangement of dioxolane **6** gives the trichloroacetamide product with exclusive E geometry and complete transfer of chirality (Eq. 9).[28]

Given the direct involvement of the metal, the potential exists for asymmetric induction by a chiral metal complex in the rearrangement of prochiral allylic imidates. Not surprisingly, the development of suitable chiral metal catalysts has been a focus of intensive recent research in this area. Early results suggest that allylic trichloroacetimidates are generally unsuitable substrates for palladium-catalyzed asymmetric rearrangements, either resulting in poor yields, poor stereoselectivity or both.[37–39] However, recent reports demonstrate that di-μ-chlorobis[(η^5-(S)-($_pR$)-2-(2'-(4'-isopropyl)oxazolinylcyclopentadienyl-1-C, 3'-N))-(η^4-tetraphenylcyclobutadiene)-cobalt]dipalladium (**8**, COP-Cl) and related Pd(II) complexes are excellent catalysts for asymmetric rearrangements of E allylic trichloroacetimidates and N-aryl trifluoroacetimidates, e.g., Eq. 12.[7–9]

(Eq. 12)

8 (COP-Cl)

(92%)   98% ee

SCOPE AND LIMITATIONS

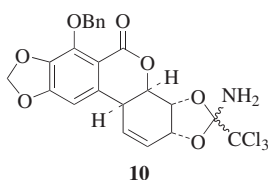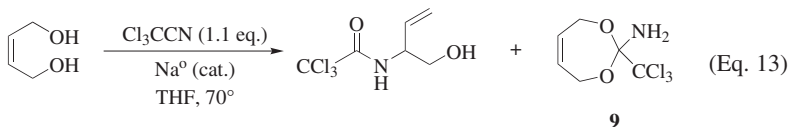### Preparation and Stability of Allylic Trihaloacetimidates

Preparation of Allylic Trichloroacetimidates. The ease of preparation of trichloroacetimidates is a major reason for the broad synthetic utility of the allylic trichloroacetimidate rearrangement. The Pinner synthesis of imidates, wherein an alcohol is condensed with a nitrile in the presence of one or more equivalents of a strong mineral acid, is not suitable for preparing allylic imidates because ionization to the allylic cation and subsequent Ritter reaction typically occurs.[11] However, allylic trihaloacetimidates can be prepared conveniently by a base-catalyzed method first presented by Cramer.[40,41] Thus, addition of a mixture of the allylic alcohol and 5–20% of its alkoxide to an ether solution of trichloroacetonitrile at low temperature provides the trichloroacetimidate in isolated yields generally greater than 85%.[4,6,42,43] Although many allylic trichloroacetimidates can be purified by silica gel chromatography or vacuum distillation, such purification is frequently bypassed as crude trichloroacetimidates commonly can be used directly in the subsequent rearrangement step.

A wide variety of bases can be used to generate the alkoxide, with alkali metal hydrides often selected.[6,44–46] More recently, the addition of allylic alcohols to trichloroacetonitrile in dichloromethane or other aprotic solvents in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), employed either catalytically[47] or in excess,[48–50] has been the method of choice for preparing allylic trichloroacetimidates. A direct comparison of potassium hydride to DBU in the preparation of aromatic trichloroacetimidates showed that catalytic DBU gave improved yields.[50]
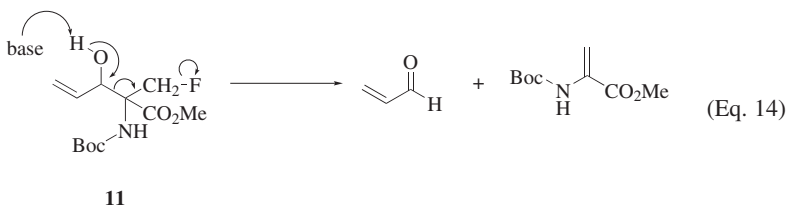
Limitations to the preparation of allylic trichloroacetimidates are rare. Primary allylic alcohols are converted readily to the corresponding trichloroacetimidates at or below room temperature. Although these conditions also succeed with many secondary and tertiary alcohols, some hindered alcohols require more forcing conditions. For example, the reaction of (*R,E*)-4-methylhexa-3,5-dien-2-ol with trichloroacetonitrile requires the addition of 18-crown-6 to the potassium hydride/alcohol mixture and long reaction times.[51] The synthesis of trichloroacetimidate derivatives of cyclic tertiary alcohols, for example 1-vinylcyclopentanol and 1-vinylcyclohexanol, is reported to be problematic,[52] however such imidates have been sucessfully prepared and rearranged.[6,52–54]

An unusual obstruction to the preparation of the trihaloacetimidate is seen when a nucleophilic functional group is proximal to the alcohol. For example, attempted

formation of the monotrichloroacetimidate of *cis*-2-butene-1,4-diol by reaction with 1.1 equivalents of trichloroacetonitrile provides instead the dioxepin **9** in 84% yield (Eq. 13). Although heating **9** in *tert*-butylbenzene at 175–180° for 1.5 hours gives the desired rearrangement product in 80% yield,[55] rearrangement of such ortho-amides is not always successful. For example, efforts to force the [3,3]-sigmatropic rearrangement of orthoamide **10** (formed in 85% yield from the precursor diol) failed to produce the product of allylic rearrangement.[56]

(Eq. 13)

9

10

The presence of fluoro functionality in the allylic alcohol can prevent successful formation of the trichloroacetimidate, although only in rare situations where the fluoro substituent is suitably positioned. For example, efforts to prepare the trichloro-acetimidate of fluoro alcohol **11** led to either Grob fragmentation (Eq. 14) or no reaction.[57] Likewise, 1,1,1-trifluoro-2-phenylbut-3-en-2-ol failed to react with tri-chloroacetonitrile, presumably because of low nucleophilicity of the alkoxide.[58]
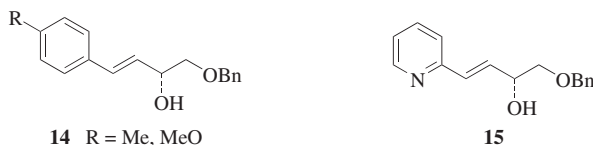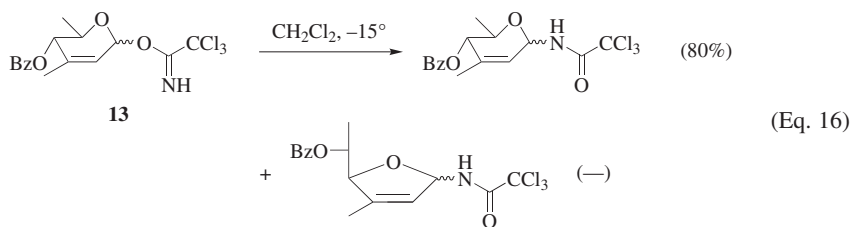

(Eq. 14)

11

Preparation of Allylic Trifluoroacetimidates. The preparation of allylic tri-fluoroacetimidates is complicated by the fact that trifluoroacetonitrile is a gas at room temperature and pressure.[1] Initial procedures for preparing allylic trifluo-roacetimidates involved deprotonation of a THF solution of the allylic alcohol with 20 mol% of *n*-butyllithium followed by addition of an excess of a freshly-prepared THF solution of trifluoroacetonitrile at −78°.[60] More recently, a "one-pot" proce-dure was developed in which trifluoroacetonitrile is generated in situ by the reaction of trifluoroacetamide with oxalyl chloride, dimethyl sulfoxide, and triethylamine.[61] A mixture of DBU and the allylic alcohol is then added to the crude trifluoroace-tonitrile solution, providing the trifluoroacetimidates in good yields (54–92%).[62]

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[1] The trifluoroacetonitrile can be generated from trifluoroacetamide by dehydration with phosphorus pentoxide.[59]

Stability of Allylic Trihaloacetimidates. Primary allylic trihaloacetimidates are quite robust. However, if the alcohol is more substituted, trihaloacetimidate derivatives become susceptible to acid-catalyzed ionization at elevated temperatures to form trihaloacetamide and, initially, the corresponding allylic cation. For example, the bis-trichloroacetimidate **12** failed to undergo rearrangement, with imidate cleavage taking place instead (Eq. 15).[52] As will be discussed in more detail subsequently, addition of an acid scavenger such as potassium carbonate can minimize this decomposition pathway, allowing some rearrangements to take place that were previously unsuccessful.[63]

(Eq. 15)

12

The [1,3]-rearrangement product arising from dissociation-recombination is rarely observed, however such products are formed exclusively upon attempted Overman rearrangement of pyranoside **13** (Eq. 16).[64] The failed rearrangements of the trichloroacetimidates of aromatic allylic alcohols **14** and **15** are also attributed to the instability of the trichloroacetimidate,[65] although other cinnamyl substrates have been rearranged in high yields.[20,65,66]

(Eq. 16)
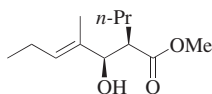
14 R = Me, MeO   **15**

In some cases, the stability of the imidate can be enhanced by manipulation of the structural features of the allyl substrate. Thus, while trichloroacetimidate **16a**[21] is unstable and fails to rearrange, replacement of the terminal methyl group (R^1) with a sterically more demanding phenyl or isopropyl group apparently enhances the imidate stability to a level that the rearrangement takes place in good yields

(60–98%).[21] The tendency of the trichloroacetimidate of β-hydroxy ester **17** to elim-
inate to form a dienyl ester is overcome by reduction to diol **18** followed by forma-
tion of the bis-trichloroacetimidate and rearrangement to give the desired acetamide
(Eq. 17).[67] However, such an alternative route generally appears not to be required.
For example, the series of structurally similar alcohols **19** are converted to the cor-
responding trichloroacetimidates and rearrange without incident.[22] Moreover, the
rearrangement of the trichloroacetimidate derived from the unsaturated β-hydroxy
ester **20** is reported to proceed in 100% yield.[23]

OMOM

16
R^1 = Me (**a**), Ph, i-Pr
R^2, R^3 = n-Bu, Me, Ph, Et

(Eq. 17)

1. Cl$_3$CCN, DBU
2. xylene, 138°

(73% from alcohol **18**)

17   **18**

X = F, Cl, Me
R = Me, i-Pr, Bn

19   **20**

Thermal Rearrangements of Allylic Trihaloacetimidates

   Reaction Conditions: Temperature, Solvent, and Additives.   Thermal re-
arrangements of allylic trihaloacetimidates are carried out conveniently by dissolv-
ing the imidate in an aprotic solvent at ~0.1 M and heating the solution at reflux.
Typically, trichloroacetimidates of primary allylic alcohols rearrange at 138–140°
(refluxing xylene) in the range of 4–24 hours. Trichloroacetimidates derived from
secondary alcohols rearrange at lower temperatures (110°, refluxing toluene) or in
shorter reaction times (often in 1–5 hours). Tertiary trichloroacetimidates typically
rearrange within a few hours at 80° (refluxing benzene). As noted previously, re-
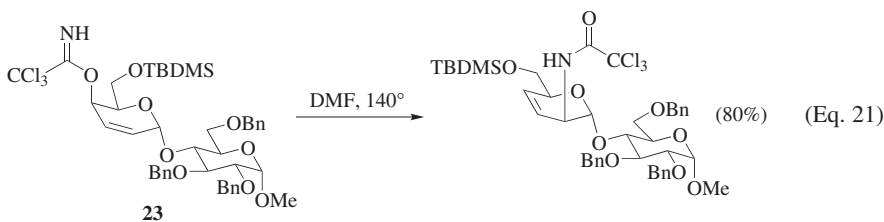arrangements of trichloroacetimidates of doubly allylic alcohols take place at tem-

peratures at or below 0°. For example, the preparation of trichloroacetimidate **21** under normal conditions (addition of the alkoxide/alcohol mixture to trichloroacet-onitrile at −5° to 0°) yields the trienylamide rearrangement product directly (Eq. 18).[6] In general, rearrangements of allylic trifluoroacetimidates are carried out under similar conditions (see later discussion).

(Eq. 18)

Although allylic trichloroacetimidate rearrangements can be effected under sol-vent-free conditions by preadsorbing the alcohol onto KF-alumina, reacting this mixture with trichloroacetonitrile, and then allowing the rearrangement to take place at room temperature,[68] the vast majority of thermal rearrangements are run in a sol-vent at reflux. Frequently the impact of the solvent is related to its reflux tempera-ture. Thus, various cinnamyl trichloroacetimidates do not rearrange at a convenient rate in refluxing chloroform, toluene or THF, whereas refluxing xylenes give the re-arrangement products in good to high yields (Eq. 19).[19] Similarly, *tert*-butylbenzene (bp 169°) proved to be a convenient solvent for the rearrangement of imidate **22**; in refluxing xylene the reaction failed to go to completion in a convenient time span (Eq. 20).[69]

(Eq. 19)

(Eq. 20)

In some cases the polarity of the solvent appears to play an important role. For example, attempted rearrangement of dissacharide trichloroacetimidate **23** in re-fluxing xylenes at 140° for 5.5 hours gives the allylic trichloroacetamide product in only a 27% yield, whereas switching to *N,N*-dimethylformamide (with the reaction run at essentially the same temperature) increases the yield to 80% (Eq. 21).[70] The increase in yield in this example likely reflects a faster rate of rearrangement in the
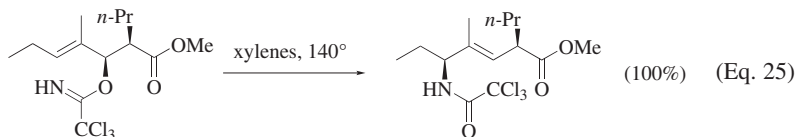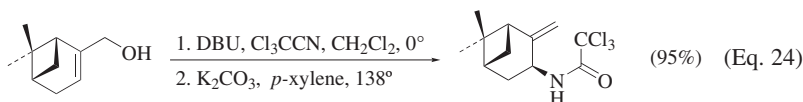
(80%)   (Eq. 21)

more polar solvent DMF, and perhaps less acid-catalyzed decomposition of the im-
idate in this Lewis basic solvent.

Acid-catalyzed decomposition of the allylic trichloroacetimidate is typically the
problematic reaction pathway that competes with allylic rearrangement. As a result,
the addition of sodium or potassium carbonate can dramatically increase the yield of
the rearrangement product.[63] For example, rearrangement of trichloroacetimidate **24**
in refluxing *para*-xylene in the absence of potassium carbonate yields trichloroac-
etamide **25** in 74% yield from the starting allylic alcohol, whereas the yield is 90%
when the rearrangement step is conducted in the presence of K_2CO_3 (2 mg/mL sol-
vent, Eq. 22).[63] An even more dramatic improvement is seen in the rearrangement
of the tetrahydropyridine derivative **26**. Attempts to carry out this rearrangement in
several solvents (THF, toluene, or chlorobenzene) give low yields (0–50%); how-
ever, upon addition of K_2CO_3 the rearrangement is accomplished in refluxing
chlorobenzene in 95% yield (Eq. 23).[71]

without K_2CO_3 (74% from alcohol)
with K_2CO_3   (90% from alcohol)

(Eq. 22)

(Eq. 23)

Scope.   Allylic trihaloacetimidates of primary, secondary, and tertiary allylic
alcohols—both cyclic and acyclic—can be prepared and undergo Overman re-
arrangement in good yields with few limitations. Representative examples are shown
in Eqs. 24–28.[23,52,60,63,72–75]

(95%) (Eq. 24)

(100%) (Eq. 25)

(71%) (Eq. 26)

(Eq. 27)

(Eq. 28)

The Halogen Substituents. The halogen substituent on the imidate plays an important role, not only in facilitating the synthesis of the rearrangement precursor, but also in increasing the rate of rearrangement. While thermal allylic rearrangements of several types of imidates are known, the presence of the electron-withdrawing CCl_3 or CF_3 group on the imidate leads to a more facile rearrangement. For example, formimidates and benzimidates require higher temperatures and/or longer reaction times than trihaloacetimidates to effect their allylic transposition.[10]

Trifluoroacetimidates in some cases rearrange slightly faster than the corresponding trichloroacetimidates. This rate enhancement, found to be approximately two-fold in one study,[75] can result in increased product yields. For example, the rearrangement of trichloroacetimidate **27** proceeds slowly in refluxing xylenes, with accompanying decomposition of the imidate under these conditions resulting in a poor yield of allylic trichloroacetamide **28** (Eq. 29). Switching to trifluoroacetimidate **29** results in doubling the yield of the allylic amide product (Eq. 30).[76]

$$\text{(Eq. 29)}$$

$$\text{(Eq. 30)}$$

However, higher rearrangement yields are not universally observed when trifluoroacetimidates are employed. For example, rearrangement of the trifluoroacetimidate of 2,4-hexadien-1-ol proceeds under thermal conditions to provide the dienyl trifluoroacetamide in low yield (Eq. 31),[60] whereas thermal rearrangement of the trichloro analogue gives the analogous rearrangement product in 63% yield (73% in the presence of K_2CO_3).[63] In another recent study, several trifluoroacetimidates were found to rearrange more slowly and in lower yields than their trichloro congeners. Results obtained for the geranyl to linalyl conversion are shown in Eq. 32.[62]

$$\text{(Eq. 31)}$$

X = F (35%)
X = Cl (63%)

$$\text{(Eq. 32)}$$

X = F   16 h (69%)
X = Cl   4 h (90%)

Carbon Skeleton. The allylic carbon skeleton, particularly substitution at the α carbon, plays a large role in determining what temperature is required for allylic trihaloacetimidate rearrangements. However, there are only a few reports where structural features present insurmountable difficulties in carrying out the rearrangement.

In most cases, difficulties can be overcome by increasing the reaction temperature. We have already discussed the fact that higher reaction temperatures are required as electron-releasing α substituents are replaced by hydrogen, with $130-160°$ typically being required for primary allylic imidates and $80°$ or less for tertiary allylic analogues.

Steric effects at the imidate γ carbon can also play a role. In comparing the rearrangement of the ortho- and para-substituted aromatic imidates **30**, the para-substituted substrate is found to rearrange more quickly, and in higher yield, than the ortho isomer. This outcome is attributed to steric encumbrance to C–N bond formation in the latter case (Eq. 33).[19]

(Eq. 33)

para   12 h (82%)
ortho   24 h (30%)

The geometry of the alkene affects both the temperature required for trihaloacetimidate rearrangements and the yields observed. Allylic trihaloacetimidates having a Z 1,2-disubstituted double bond typically require slightly higher temperatures to promote their allylic reorganization than their E counterparts.[24,25] Presumably in part for this reason, many fewer examples of allylic trihaloacetimidate rearrangements are reported in the Z series. For example, the E trichloroacetimidate **31** rearranges in useful yield (Eq. 34), whereas the Z stereoisomer is noted to rearrange with "significantly more byproducts".[77] However, a few Z disubstituted allylic trichloroacetimidates are reported to rearrange in high yield. For example, the rearrangement of the secondary trichloroacetimidates **32** proceeds in good yields in refluxing xylenes (Eq. 35).[78]

(Eq. 34)

1:1 (55% from alcohol)

(74-79% from alcohol)

(Eq. 35)

32
R = *n*-Bu, *i*-Pr, Ph

Numerous trisubstituted allylic trihaloacetimidates having a second substituent at either the β or γ carbon undergo thermal rearrangement in useful yields. Three representative examples are shown in Eq. 36–38.[79–81]

(Eq. 36)

(78% from alcohol)

(51% from alcohol)   (Eq. 37)

(84%)   (Eq. 38)

Cyclic Substrates.   Rearrangements of allylic trihaloacetimidates in which the allyl unit is embedded in a ring can be challenging as the transition state conformation required for rearrangement is higher in energy than that of acyclic counterparts. If the ring is not large, the oxygen of the imidate must adopt a quasi-axial orientation to bring the imidate nitrogen and distal alkene carbon within bonding distance. This feature is illustrated in the cyclohexenyl series in Eq. 39. Moreover, in a half-chair transition structure, a destabilizing syn-pentane interaction would exist between the starred atoms in **33**. This interaction would be avoided in a twist-boat transition structure.

33

(Eq. 39)

Because the trihaloacetimidate must adopt a high-energy conformation to undergo rearrangement, cyclic allylic imidates are particularly prone to decompose at the elevated temperatures required to promote their sigmatropic rearrangement. The addition of K_2CO_3 to thwart acid-catalyzed decomposition of the allylic imidate can be particularly critical in these cases as illustrated in the rearrangement of imidate **34** (Eq. 40).[63]

$$[K_2CO_3]$$
$$o\text{-dichlorobenzene, } 165°$$

without K$_2$CO$_3$ (7%)
with K$_2$CO$_3$ (56%)

(Eq. 40)

34

If additional steric impediments exist, rearrangements of six-membered cyclic substrates can be low-yielding. For example, the additional 1,3-diaxial interaction (between O and C) brought about by the gem dimethyl group in trichloroacetimidate **35** is believed to be responsible for the low rearrangement yields realized in this case (Eq. 41);[6] this situation is not improved by adding K$_2$CO$_3$.[63]

toluene, 110°

(10-43% from alcohol)

(Eq. 41)

35

The deleterious effect of adding an additional 1,3-diaxial interaction is also seen in the rearrangements shown in Eq. 42 and Eq. 43. Thus, while cyclohexenyl tri-

K$_2$CO$_3$ (cat.)
xylene, 138°

(95% from alcohol)

36

(Eq. 42)

K$_2$CO$_3$ (cat.)
xylene, 138°

37

(Eq. 43)

(0%)

38

chloroacetimidate **36** rearranges in high yield at 138°, the attempted rearrangement of stereoisomeric imidate **37**, which would suffer a 1,3-diaxial O–O interaction if the imidate is oriented quasi-axially,[96] yields none of the rearrangement product **38**.

Instead, the starting imidate is recovered in 35% yield.[82] Under some circumstances, interactions of this type can completely subvert the rearrangement process (Eq. 44).[83]

(Eq. 44)

Many pyranose[45,64,70,84–86] and furanose[18,53,54,87] substrates have been subjected to the Overman rearrangement with good success, but rearrangements of unsaturated pyranose substrates having the $1\alpha,4\alpha$ configuration are problematic. For example, the $2\beta,5\alpha$-trichloroacetimidate **39** rearranges stereospecifically in refluxing xylenes in 80% yield, whereas the $2\alpha,5\alpha$ isomer **40** (R = Me) rearranges much more sluggishly (Eqs. 45, 46).[86] Although these results are ascribed to a more sterically congested transition state in the reaction of isomer **40**, the loss of anomeric stabilization in transition structure **41** is more likely the origin of this difference. However, examples exist where pyranose substrates having the $1\alpha,4\alpha$ configuration do rearrange in moderate yield. For example, heating **40** (R = Et) at 165° in *ortho*-dichlorobenzene in the presence of K_2CO_3 gives the trichloroacetamide in 56% yield.[63]

(80% from alcohol)   (Eq. 45)

(Eq. 46)

Successful Overman rearrangements of dissaccharides have been reported, particularly in cases where the energetically favored half-chair conformation of the unsaturated pyranose places the trichloroacetimidate in an axial orientation. Such an example is shown in Eq. 21.[70]

Substituent Effects and Problematic Substituents.   Allylic trihaloacetimidate rearrangements are impacted by the electronic effects of substituents attached to carbons 2 and 3 of the allylic system. Electron-releasing substituents can favor the rearrangement. For example, reaction of the secondary dihydrofuryl alcohol **42** with trichloroacetonitrile at 0° leads directly to the rearranged trichloroacetamide **43** in 78% yield (Eq. 47); the intermediate imidate derivative is not observed.[88]

(Eq. 47)

The presence of electron-withdrawing groups at the distal alkene carbon can be problematic. For example, the trifluoromethylated allylic alcohol **44** undergoes imidate formation without incident, however allylic rearrangement fails (Eq. 48).[58] Some allylic trichloroacetimidates in which the double bond is part of an α,β-unsaturated carbonyl system fail to undergo Overman rearrangement, for example, dienyl ester **45**. The presence of the electron-withdrawing ester is shown to be the problem, as the structurally similar THP-protected dienol **46** rearranges without incident (Eq. 49).[89]

(Eq. 48)

45

(Eq. 49)

The problem in these examples is likely competitive 1,4-addition of the imidate nitrogen to the α,β-unsaturated carbonyl functionality. For example, when unsaturated ester **47** is heated in refluxing toluene, [3,3]-sigmatropic rearrangement is not observed, but instead oxazoline **48** is formed (Eq. 50). As in the previous example, this side reaction is circumvented by reducing the ester to the alcohol, protecting the alcohol, then carrying out the rearrangement with the protected alcohol congener.[29]

(Eq. 50)

Regioselectivity

If the trihaloacetimidate is positioned proximal to two different double bonds, two regioisomeric dienyl trichloroacetamides can be formed. In cases of this type, little selectivity is observed. For example, conversion of 5,9-dimethyl-1,4,8-deca-triene-3-ol to its trichloroacetimidate derivative results in a 60:40 mixture of regioi-someric trichloroacetamides upon rearrangement (Eq. 51).[6] In the case of the trichloroacetimidate derived from 1,4-hexadien-3-ol, a slight preference for reaction at the more highly substituted alkene is observed (Eq. 52).[90]

(Eq. 51)

(Eq. 52)

An interesting example in which regioisomers result from participation of the double bond of a heteroaromatic system is known. Thus, attempted rearrangement of the imidazole trichloroacetimidate **49** leads to the desired product **50** in relatively low yield, with the major product arising from competitive rearrangement at the 4,5 double bond of the imidazole ring (Eq. 53).[91] This limitation is not seen with related aromatic substrates and may arise in the imidazole case by an ionization-recombination pathway as the trityl-protected nitrogen is perfectly situated to stabi-lize the derived allyl cation.

(Eq. 53)

Stereochemistry

Chiral Secondary Imidates: Chirality Transfer.   High stereoselection is a hallmark of the trihaloacetimidate rearrangement. Self-immolative[92] transfer of chi-rality was first demonstrated in the rearrangement of *(R)*-1-methyl-3-phenyl-2*E*-

propenyl trichloroacetimidate, which proceeds smoothly to give the corresponding secondary benzylic trichloroacetamide with complete transfer of chirality (Eq. 5).[20]

There are numerous other examples of this reliable transposition of chirality. Three are shown in Eqs. 54–56.[24,26,93]

$$\text{(Eq. 54)}$$

$$\text{(Eq. 55)}$$

$$\text{(Eq. 56)}$$

Diastereoselectivity Arising from Stereocenters Outside the Pericyclic Arena. The impact of chirality external to the six-centered electrocyclic framework varies widely. The conformational flexibility of the substrate and the temperature for the rearrangement influence the observed degree of diastereoselection. For example, no stereocontrol is achieved in the rearrangement of the chiral allylic dioxolane **31** in refluxing xylenes (Eq. 34).[77] Likewise, rearrangement of trichloroacetimidate **51** at 140° yields a 1.6 : 1 mixture of diastereomeric amides (Eq. 57).[30] As will be discussed later, Pd(II)-catalyzed rearrangements of substrates of this type typically proceed with high stereoselectivity.[30,94]

$$\text{(Eq. 57)}$$

Allylic trihaloacetimidate rearrangements of more conformationally constrained systems often proceed with substantial diastereoselectivity, however. Thus, trifluoroacetimidate **52** rearranges to give an excellent yield of epimeric amides **53** and **54** with 10:1 diastereoselectivity (Eq. 58). The trichloroacetimidate analogue of **52** is reported to rearrange over a period of 30 hours in 47% yield with no diastereoselectivity.[95] No explanation for this surprising difference has been advanced.

$$ \text{(Eq. 58)} $$

52   **53**   (95%) 10:1   **54**

Rearrangement of the exo-allylic trichloroacetimidate **24** takes place selectively from the face opposite the dioxolane substituent, which would be oriented quasi-axially[96] to give amide **25** as a single stereoisomer in excellent yield on a 20 gram scale (Eq. 22).[49] This product is a key intermediate in the synthesis of (–)-5,11-dideoxytetrodotoxin. Excellent stereoselectivity also is observed in the rearrangement of the E and Z propenyl trichloroacetimidates **55** and **56** (Eqs. 59 and 60). In both reactions, rearrangement occurs from the same alkene face to provide opposite epimers at the new nitrogen-bearing stereocenter.[53]

xylene, 138°   (90%)   (Eq. 59)

55

xylene, 138°   (≈100%)   (Eq. 60)

56

Geometry of the New Double Bond.   As discussed earlier in the context of favored chair transition structures for allylic trihaloacetimidate rearrangements, a common feature of the [3,3]-sigmatropic rearrangement of secondary allylic trihalo-

acetimidates is transposition to generate a new E double bond. Although extremely high E stereoselectivity is typically seen, some examples of moderate stereoselection have been reported. For example, in the rearrangement of a series of trichloroacetimidates of alkyl-substituted α-hydroxyphosphonates, the product is obtained as a mixture of E and Z isomers, with the Z isomer typically accounting for $\sim$13% of the product mixture (Eq. 61).[97]

(Eq. 61)

(86%)   87:13

Low stereoselectivity is seen in allylic trichloroacetimidate rearrangements of chiral tertiary allylic alcohols when the two α substituents are of similar size, as the two possible chair transition structures are of similar energy. For example, rearrangement of the trichloroacetimidate of linalool at 80° provides a 60:40 mixture of geranyl and neryl trichloroacetamides (Eq. 62).[6]

(Eq. 62)

(83%)   E:Z   60:40

Catalyzed Rearrangements of Allylic Trihaloacetimidates

Catalysis of trichloroacetimidate rearrangements by mercuric trifluoroacetate was disclosed in the inaugural report of this transformation.[4] Whereas the thermal rearrangement of the trichloroacetimidate of (E)-2-hexen-1-ol requires refluxing *meta*-xylene (138°) for nine hours to give the allylically rearranged trichloroacetamide in 81% yield, this allylic amide is formed in similar yield within minutes in THF at 0° in the presence of 10 mol% of mercuric trifluoroacetate. This mercury(II) complex is estimated to increase the rate of the rearrangement by a factor greater than 1×10^{12}.[6] Similar rate accelerations are realized in the presence of soluble complexes of PdCl$_2$, which have emerged as the most generally useful catalysts for allylic trihaloacetimidate rearrangements. An early example was reported in 1980,[11] although Pd(II)-catalysis of allylic trihaloacetimidate rearrangements was not studied in detail until several years later.[28]

The utility of the metal-catalyzed rearrangement is limited by the propensity of the catalyst to promote elimination to form dienes and trichloroacetamide, occasioned by competitive coordination of the catalyst to the allylic trichloroacetimidate

nitrogen. In general, primary allylic trihaloacetimidates containing trans 1,2-disub-stituted double bonds rearrange in good yields in the presence of Hg(II) or Pd(II) catalysts. Fewer examples exist of successful rearrangements of secondary allylic trihaloacetimidates; however, several high-yielding examples are known with Pd(II) catalysts.[25,28,29] Complete suprafacial transfer of chirality is a hallmark of catalyzed versions of the rearrangement, as it is of the thermal variant. Diastereoselection in rearrangements of chiral, δ-substituted, allylic trihaloacetimidates can be signifi-cantly enhanced in the presence of PdCl$_2$ catalysts. Of potentially greater signifi-cance, useful asymmetric Pd(II) catalysts have been developed quite recently.[7–9]

General Conditions. The rearrangement of allylic trichloroacetimidates with mercuric trifluoroacetate is carried out using 10–30 mol% of this catalyst in THF, e.g., Eq. 63. Hg(II)-catalyzed rearrangements can take place at temperatures as low as $-60°$, with yields often being high for primary substrates.[6]

More recently, Pd(II) complexes have been the catalysts of choice, with excellent outcomes being achieved at room temperature using 4–8 mol% of the soluble bis(acetonitrile) or bis(benzonitrile) complexes of PdCl$_2$ in aprotic solvents such as THF or toluene. Palladium acetate and palladium trifluoroacetate have also been employed, although rarely.[25] Pd(II)-catalyzed allylic trichloroacetimidate rearrange-ments typically take place in a few hours at or below room temperature, as exempli-fied by the conversion of trichloroacetimidate **57** to amide **58** (Eq. 64).[28]

There is a single report of trichloroacetimidate rearrangements being promoted by halogen electrophiles, specifically *N*-bromosuccinimide (NBS) and *N*-iodosuc-cinimide. For example, the E allylic phosphonate trichloroacetimidate **59** is trans-formed to the rearrangement product **60** in moderate yield at room temperature in the presence of one equivalent of NBS (Eq. 65). In contrast, the Z isomer reacts slowly under identical conditions to give oxazoline **61** (Eq. 66).[66,2]

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[2] The reported yield in Eq. 66 is after hydrolysis to the hydroxamide.

$$(Eq.\ 66)$$

61

Scope. Although metal-catalyzed allylic trihaloacetimidate rearrangements take place under milder conditions than their thermal counterparts, the scope of the catalyzed rearrangement is much more limited. Trichloroacetimidates are typically used and give higher yields than the less nucleophilic trifluoroacetimidates,[62] a result expected for a cyclization-induced rearrangement mechanism. Primary trichloroacetimidates containing trans 1,2-disubstituted double bonds are the best substrates for metal-catalyzed rearrangements, typically undergoing rearrangement in good yields using either $PdCl_2(RCN)_2$ or $Hg(O_2CCF_3)_2$ catalysts.[6,27,62,94] Substitution on the allylic double bond impedes the metal-induced rearrangement. For example, the rearrangement of the trichloroacetimidate of geraniol (**62**, Eq. 67) under thermal conditions provides linalyl trichloroacetamide in 90% yield (Eq. 32), whereas this product is formed in only 66% yield in the presence of $PdCl_2(MeCN)_2$.[62] There have been no reports of successful metal-catalyzed rearrangements of substrates having a substituent on the internal allylic alkene carbon.

62

$$(Eq.\ 67)$$

More highly functionalized primary allylic trichloroacetimidates often have proven to be resistant to metal catalysis. For example, the ribose-derived imidate **63** fails to yield any rearrangement product in the presence of $PdCl_2(MeCN)_2$ or $Hg(O_2CCF_3)_2$.[98] This result should be contrasted with the successful rearrangement of this imidate under thermal conditions (xylene at 137° in the presence of two percent di(*tert*-butyl)-*para*-cresol; Eq. 68). Similarly, xylose derivative **64** (Eq. 69) fails to rearrange under catalysis by either Pd(II) or Hg(II) species, although again its rearrangement is successfully realized thermally (xylene at 200°).[95]

63

thermal X = Cl (84% from alcohol)
thermal X = F (45% from alcohol)
metal-catalyzed X = Cl, F (0%)

$$(Eq.\ 68)$$

64

thermal (93%)
metal-catalyzed (0%)

(Eq. 69)

An interesting example is shown in Eq. 70, where failure to observe [3,3]-sigmatropic rearrangement arises from an alternate reaction pathway of a Pd(II)-olefin complex. In this case, attempted rearrangement of **65** using PdCl$_2$(MeCN)$_2$ gives a 58% yield of cyclopropane derivative **67**. This product is postulated to derive from **66**, which would arise if intramolecular attack by the imidate on the nascent Pd(II)–olefin complex took place at the proximal alkene carbon (5-exo, rather than 6-endo cyclization).[98]

65

PdCl$_2$(MeCN)$_2$ (5 mol%)

THF, rt

66

67

(Eq. 70)

Although there are no examples of high-yielding rearrangements of secondary allylic trichloroacetimidates using Hg(O$_2$CCF$_3$)$_2$ as the catalyst, several successful PdCl$_2$-catalyzed rearrangements of secondary allylic trichloroacetimidates containing trans 1,2-disubstituted double bonds are known (see the following section). However, this catalyzed transformation is limited to secondary substrates of this specific type. For example, attempted PdCl$_2$-catalyzed rearrangement of the cis secondary trichloroacetimidates **68** failed due to competing elimination to form the corresponding dienes and trichloroacetamide,[25] an outcome also observed with Z trichloroacetimidates **69**.[78] Low yields (<30%) were also reported for rearrangements of secondary allylic trichloroacetimidates containing trans 1,2-disubstituted double bonds using Pd(OAc)$_2$ as the catalyst; elimination was again the major reaction pathway.[25] Consistent with these observations, there are no reports of successful catalytic rearrangements of cyclic secondary allylic trichloroacetimidates nor secondary allylic trichloroacetimidates containing trisubstituted double bonds.

R^1	R^2
Me	n-Bu
i-Pr	n-Bu
i-Bu	i-Bu

R
n-Bu
i-Pr
Ph

68   **69**

Stereoselectivity.   *Chiral Secondary Imidates: Chirality Transfer.*   Although metal-catalyzed rearrangements of secondary allylic trihaloacetimidates are limited to substrates containing trans 1,2-disubstituted double bonds, such rearrangements of chiral imidates proceed with excellent transfer of chirality. For example, Pd(II)-catalyzed rearrangement of trichloroacetimidate **6** proceeds with complete suprafacial diastereoselection to give the trichloroacetamide in high yield (Eq. 9).[28] In one reaction, the milder conditions associated with Pd(II) catalysis lead to enhanced selectivity when compared to the thermal counterpart. For example, thermal rearrangement of chiral trichloroacetimidate **70** (Eq. 71) at 110° (refluxing toluene) takes place with 7% loss of enantiomeric purity.[29] In contrast, the Pd(II)-catalyzed version of this rearrangement occurs with no loss of enantiomeric purity. As is seen in analogous thermal rearrangements, high E stereoselectivity is observed in forming the new 1,2-disubstituted double bond of the allylic trichloroacetamide products, see, e.g., Eqs. 64 and 71.

$$\xrightarrow[\text{benzene, rt}]{\text{PdCl}_2(\text{PhCN})_2\ (10\ \text{mol\%})}$$

(72%)

(Eq. 71)

70

Chiral Primary Imidates: Diastereoselectivity.   A number of examples of chiral, δ-substituted trichloroacetimidates rearranging with enhanced stereoselectivity in the presence of PdCl$_2$ catalysts have been reported. For example, thermal rearrangement of trichloroacetimidate **71** in refluxing xylene provides the anti and syn stereoisomeric allylic amides in moderate yield and a mediocre 3 : 2 ratio (Eq. 72).[99] In

71   **I**   **II**

(Eq. 72)

I:II	Conditions	
3:2	p-xylene, 138°	(54%)
1:7	PdCl$_2$(PhCN)$_2$ (10 mol%), THF, rt	(71%)

R =

72

contrast, rearrangement of **71** with either $PdCl_2(MeCN)_2$ or $PdCl_2(PhCN)_2$ takes place with much improved diastereoselectivity, providing the 3,4-anti isomer as the major product. This product results from preferential cyclization of the imidate nitrogen from the si face of the alkene. The authors suggest that this transition structure is favored because it allows coordination of the Pd(II) catalyst to the double bond to occur away from the bulky *tert*-butyldiphenylsilyl protecting group, as depicted in **72**.[99,3]

Several examples show high stereoselectivity in the synthesis of anti vicinal diamines by diastereoselective Pd(II)-catalyzed rearrangements of allylic trichloroacetimidates having a Boc-protected amine substituent at the δ position. For example, rearrangement of **73** in the presence of $PdCl_2(MeCN)_2$ gives exclusive formation of the anti isomer (the syn isomer was undetected; Eq. 73). In contrast, thermal rearrangement of the same substrate gives a 62:38 mixture of the anti:syn products.[30] Coordination of the palladium to the adjacent Boc-protected nitrogen, as depicted in **74**, is invoked to rationalize the stereoselection.

73   *anti:syn* 99:1

(48% from alcohol)

(Eq. 73)

74

In a related example, potential chelation of a Pd(II) catalyst to a δ-alkoxy or δ-siloxy substituent was examined and found to have no impact. The rearrangement results summarized in Eq. 74 lead to the conclusion that diastereoselection, which can be as high as 10:1, results solely from steric effects.[100]

(Eq. 74)

R	I:II	
Me	1.4:1	(63%)
MOM	6.2:1	(58%)
BOM	9.95:1	(57%)
OTBDMS	10:1	(61%)

[3] This intermediate is drawn incorrectly in the original paper; i.e. the configuration shown at C4 is incorrect.

Asymmetric Catalysis. The success of Pd(II) catalysis for allylic trichloroacet-imidate rearrangements naturally has led to research on the development of asymmetric Pd(II) catalysts. Early studies employing cationic Pd(II) complexes suggested that allylic trichloroacetimidates were not viable substrates for asymmetric catalysis, as attempts to carry out such transformations were plagued by competing elimination reactions, slow reaction rates, and low enantioselectivities.[101] The first two of these difficulties were ascribed to competitive strong complexation of the small, basic trichloroacetimidate nitrogen to the hard palladium center.[102] Consequently, success in developing asymmetric Pd(II) catalysts for allylic imidate rearrangements was realized initially with less strongly coordinating *N*-arylimidates.[101] Whereas high enantioselectivities can be realized with substrates of this type, for example Eq. 75,[39] transformation of the amide products to the corresponding allylic amines is not high yielding. A wide variety of chiral, enantiopure Pd(II) complexes have been shown to catalyze allylic rearrangements of *N*-arylimidates,[8,37,39,101,103–105] although a survey of these studies is outside the scope of this review. Reviews of early developments in this area have appeared.[14,102]

(Eq. 75)

N-Anisyltrifluoroacetimidates are more attractive substrates for catalytic asymmetric allylic imidate rearrangements as their allylic *N*-anisyltrifluoroacetamide products can be converted to the parent allylic amines in good yield. An initial survey of six asymmetric Pd(II) complexes for catalyzing the rearrangement of **76** to **79** identified the cationic ferrocenyl oxazoline palladacyclic complex **75** (Eq. 75),

(Eq. 76)

and the related cationic and neutral palladacyclic catalysts **77**, **78**, and **8** (COP-Cl) containing a chiral oxazoline substituent and a planar chiral cyclopentadienyl(η^4-''' tetraphenylcyclobutadiene)cobalt fragment, as effective catalysts for this transformation (Eq. 76).[8] Subsequent deprotection of the *N*-anisyltrifluoroacetamide **79** to form (*R*)-3-amino-1-hexene is accomplished in 73% yield. Cis allylic *N*-anisyltrifluoroacetimidates are converted also in good yield and high ee to the corresponding secondary *N*-anisyltrifluoroacetamides using the cobalt oxazoline palladacycle (COP) catalysts (Eq. 77). Incorporation of small amounts of tertiary amines, typically *i*-Pr$_2$NEt, minimizes acid-catalyzed decomposition of the starting imidates in rearrangements that employ the trifluoroacetate-bridged catalysts **75** and **77**, which are

generated in situ by reaction of the corresponding halide-bridged dimers with excess silver trifluoroacetate.

77 X = O$_2$CCF$_3$
8 X = Cl (COP-Cl)

78

$$\text{catalyst (5 mol\%)} \atop i\text{-Pr}_2\text{NEt (20 mol\%), CH}_2\text{Cl}_2\text{, rt}$$

(Eq. 77)

catalyst		% ee
77	(76%)	96
8	(99%)	96

In a recent publication, the neutral chloride-bridged dimer COP-Cl (**8**) was shown to be an excellent catalyst for asymmetric rearrangement of trans 1,2-disubstituted allylic trichloroacetimidates, thus providing the first truly useful catalytic asymmetric method for transforming prochiral allylic alcohols to enantioenriched allylic amines and their analogues, e.g., Eq. 78.[7] Although the scope and limitations of this method are not well explored at this point, a variety of oxygen functionality is well tolerated. Some nitrogen functional groups appear to be also well tolerated, e.g. Eq. 79. However, the allylic rearrangement is prevented (at least at 38°) by tertiary amine functionality at C6, secondary amine functionality at either C6 or C12, or a thio ether substituent at C6 of the (*E*)-2-alkenyl trichloroacetimidate starting material. This method is limited to the rearrangements of allylic trichloroacetimidates containing trans 1,2-disubstituted double bonds as analogous cis substrates rearrange only slowly in the presence of COP-Cl.

$$\text{COP-Cl (}\mathbf{8}\text{, 5 mol\%)} \atop \text{CH}_2\text{Cl}_2\text{, 38°}$$

(82%) 96% ee   (Eq. 78)

$$\text{COP-Cl (}\mathbf{8}\text{, 5 mol\%)} \atop \text{CH}_2\text{Cl}_2$$

(Eq. 79)

R	Temp.		% ee
(CH$_2$)$_3$NBn(Boc)	38°	(96%)	95
(CH$_2$)$_9$NBn$_2$	rt	(82%)	97

The more soluble monomeric COP-hexafluoroacetylacetonate complex **78** allows a wider variety of solvents to be employed and higher catalyst concentrations, and correspondingly higher catalysis rates, to be achieved.[9] One example is shown in Eq. 80.

$$\text{(94\%) 91\% ee} \qquad \text{(Eq. 80)}$$

APPLICATIONS TO SYNTHESIS

Overview

The chief significance of the allylic trihaloacetimidate rearrangement lies in the many uses of the allylic trichloroacetamide products. Foremost among these uses is ready access to allylic amines. The trichloroacetyl group is typically removed from allylic trichloroacetamides using either NaOH in mixed organic–aqueous solvent systems, strong mineral acids, or methanolic $NaBH_4$. One potential advantage of employing trifluoroacetimidates in this allylic rearrangement is the ready cleavage of the trifluoroacetyl group under mildly basic conditions.[106]

The trichloroacetyl group has also been exploited to accomplish subsequent elaborations of rearrangement products. For example, the trichloroacetyl group has been used to initiate radical cyclizations; as a precursor of guanidines, carbodiimides, and ureas; and to regulate facial selectivity in the addition of various reagents to the allylic double bond.

Preparation of Allylic Amines

Overman rearrangements have been employed to prepare a broad range of allylic amines for many diverse uses. For instance, a number of selective enzyme inhibitors have been prepared in this way. Examples include a variety of 2-(2-thienyl)allyl-amines, synthesized for studies of the inhibition of dopamine β-hydroxylase,[107] and dienyl amino acid **81**, an inhibitor of 4-aminobutyrate-2-oxoglutarate aminotransferase.[89] This latter agent is prepared in four steps from dienyl trichloroacetamide **80** (Eq. 81), whose synthesis by allylic trichloroacetimidate rearrangement is summarized in Eq. 49.

$$\text{(Eq. 81)}$$

An example of the application of this rearrangement to the preparation of novel classes of biologically important nitrogen compounds is seen in the synthesis of

γ-aminophosphonic acids, for example **83** (Eq. 82).[97] Refluxing 6N HCl was employed to hydrolyze the trichloroacetamide and phosphonic ester functionalities of **82** in good yield.

82 (91%)

(Eq. 82)

83 (88%)

A variety of amino sugars, including both monosaccharides and disaccharides, has been prepared using the Overman rearrangement as the key step. In many of these syntheses, the trihaloacetimidate rearrangement is employed to install the amino functionality with high stereocontrol.[45,70,85,108,109] In one approach, the trihaloacetimidate rearrangement is carried out on a carbohydrate framework, as exemplified by the example shown in Eq. 83. This tactic has been employed widely, with several examples of the rearrangement stage of these amino sugar constructions being highlighted earlier in Scope and Limitations (cyclic substrates).

(56% from alcohol)   (Eq. 83)

In another construction of amino sugars, the rearrangement step is carried out on an acyclic substrate, with cyclization to form the carbohydrate occurring at a later stage. An early example, the preparation of (±)-*N*-(trichloroacetyl)vancosamine (**84**), is shown in Eq. 84.[51] This strategy has been applied also to the synthesis of several aminocarbasugar derivatives,[27,110] as in preparation of the conduramine analogue **85** (Eq. 85).[27]

84

(Eq. 84)

(Eq. 85)

Given the promise of nucleoside analogues as therapeutic agents, much effort has been devoted to their synthesis, with trihaloacetimidate rearrangements being central steps in several approaches. For example, the dideoxyribose **43** has been prepared in 78% yield from the allylic alcohol precursor, placing the amino group in the correct position for subsequent construction of the appropriate heterocylic substituent (Eq. 47).[88] Allylic rearrangement of trichloroacetimidate **86** is a central step in the synthesis of a series of 5′-branched 5′-aminothymidines (Eq. 86).[98] This example illustrates the mild removal of the trichloroacetyl group by reaction of allylic trichloroacetamide **87** with ethanolic NaBH$_4$ at room temperature.

(Eq. 86)

Allylic trichloroacetimidate rearrangements have been central to the synthesis of several peptide analogues. For example, a range of dipeptide olefin isosteres has been synthesized in a study of parathyroid hormone receptor activation by analogues of the *N*-terminal fragment of the natural hormone. These dipeptide isosteres were accessed by the sequence exemplified in Eq. 87.[22] Numerous other dipeptide isosteres have been prepared using allylic trichloroacetimidate rearrange-

ments.[22,23,25,67,111,112] In an additional example, the modified opioid pentapeptide **88** is prepared from an allylic alcohol precursor as summarized in Eq. 88.[196]

(Eq. 87)

(Eq. 88)

88

Trichloroacetimidate rearrangements have been used in the synthesis of a wide variety of α-amino acids, for example, the Boc-protected β,γ-unsaturated α-amino acid **89** (Eq. 89).[29,86] A more common sequence for assembling α-amino acids introduces the carboxylic acid by oxidative cleavage of the allylic double bond.[113] Use of such a strategy to prepare the biologically important 1-aminocyclopropanecarboxylic acid in high overall yield from allylic alcohol precursor **90** is summarized in Eq. 90.[31]

(Eq. 89)

89

$$\text{(Eq. 90)}$$

90   (89%)   (87%)

Enantiopure amino acids have been accessed in this way using several strategies. In one method, a diastereoselective allylic imidate rearrangement is orchestrated on a chiral, enantiopure template. An example that employs a carbohydrate scaffold to synthesize (*S*)-(2-^{2}H)glycine is shown in Eq. 91.[53] A second example, where a δ-methoxymethyl substituent regulates face selectivity in the key allylic imidate rearrangement, is summarized in Eq. 92.[21]

(97%)

$$\text{(Eq. 91)}$$

$$\text{(Eq. 92)}$$

R^1	R^2	R^3	
i-Pr	Me	*n*-Bu	(85%)
i-Pr	Me	Et	(81%)
i-Pr	Ph	Me	(70%)

Another tactic couples direct construction of enantioenriched, chiral secondary allylic alcohols with oxygen-to-nitrogen chirality transfer. In the example shown in Eq. 93, catalytic asymmetric vinylation of benzaldehyde provides **91**, which is transformed in 83% overall yield without loss of enantiomeric purity into trichloroacetyl-protected amino acid **92**.[114]

$$\text{(Eq. 93)}$$

91 96% ee   (90%) 96% ee   **92** (92%)

A third appealing strategy exploits asymmetric catalysis to access directly the chiral, enantioenriched allylic trichloroacetamide. For example, the differentially protected S α-amino ester **94** is prepared without loss of enantiopurity from allylic trichloroacetamide **93** (Eq. 94), which in turn is prepared by a COP-Cl catalyzed allylic trichloroacetimidate rearrangement (see Eq. 78).[7]

$$93 \text{ 96\% ee} \qquad\qquad 94 \text{ 96\% ee} \qquad (58\%) \qquad \text{(Eq. 94)}$$

Other Direct Uses of Allylic Trihaloacetamides

Because trichloromethyl is a competent leaving group, allylic trichloroacetamides can be directly converted to congeneric ureas, carbodiimides, and guanidines.[115] One example of this chemistry, which was developed by Isobe and co-workers during their studies of the total synthesis of tetrodotoxin and analogues, is illustrated in Eq. 95; see Eq. 22 for the preparation of the starting allylic trichloroacetamide **25**.

$$\textbf{25} \qquad (75\%) \qquad\qquad (79\%) \text{ (2 steps)} \qquad \text{(Eq. 95)}$$

A variety of heterocycles have been assembled from products of allylic trihaloacetimidate rearrangements, employing the double bond as a partner in ring-closing metatheses,[116] or involving the double bond in other C–C bond-forming ring constructions.[90,117–122] A clever strategy of this type which requires no additional manipulation of the allylic trichloroacetamide functionality has been used to prepare a series of γ-lactams.[72] In this case, ring construction is accomplished by an atom transfer radical cyclization (Eq. 96).

$$(71\%) \qquad \text{(Eq. 96)}$$

The potential for functionalization of the double bond to be directed by the nearby trichloroacetamide group has also been exploited. The trichloroacetamide group is particularly effective in promoting syn dihydroxylation as a result of the strong propensity of the N-H bond to participate in hydrogen bonding.[93,123,124] This strategy has been employed in syntheses of several amino sugars as exemplified in the preparation of talosamine (Eq. 97).[125,126]

talosamine

(Eq. 97)

However, the trichloroacetyl group proves to be a hindrance in attempted Sharpless oxyamination of allylic trichloroacetamide **95**, a finding attributed to the "suppressing influence of an electronegative substituent".[45] Conversion of the trichloroacetyl group to the acetate followed by oxyamination with chloramine T and osmium tetroxide yields the desired product **96** in 39% yield from the precursor allylic amide (Eq. 98).[45]

95 (68%)   **96**

(Eq. 98)

Applications in the Total Synthesis of Natural Products

(±)-Acivicin. Syntheses of the antitumor, antimetabolites (±)-acivicin and (±)-bromoacivicin take advantage of the trichloroacetimidate rearrangement's residual allylic functionality to elaborate the heterocyclic acivicin framework through a 1,3-dipolar cycloaddition. The crucial building block in this synthesis is vinyl glycine, for which, at the time, no other efficient preparation was available. Thermal rearrangement of the trichloroacetimidate derivative **97** of *cis*-2-butene-1,4-diol is used to prepare the vinyl glycine fragment **98** (Eq. 99).[55,69]

$$X = Cl \ \text{acivicin}$$
$$X = Br \ \text{bromoacivicin}$$

(Eq. 99)

97   **98** (84%)

(+)-Lactacystin.   The application of the trichloroacetimidate rearrangement to the synthesis of (+)-lactacystin exemplifies the utility of this reaction for constructing tertiary carbinyl amine stereocenters. The starting material for the synthesis, D-glucose, provides the chiral template for the rearrangement, giving allylic trichloroacetamides **99** as a 4.8:1 mixture of diastereomers in 60% yield from the starting allylic alcohol (Eq. 100). After acidic cleavage of the acetonide, these epimers are separated and the major stereoisomer is processed in two steps to pyrrolidine imide **100**. Treatment of intermediate **100** with NaBH$_4$ in methanol at 0° removes both the *N*-trichloroacetyl and *O*-formyl groups to provide late stage lactacystin precursor **101**.[127] A similar strategy is employed to synthesize (–)-sphingofungin E.[47,128]

99 (60% from alcohol)   dr = 4.8:1

100   **101**   (+)-lacticystin

(Eq. 100)

(±)-Pancratistatin.   The reliable suprafacial transfer of chirality of trichloroacetimidate rearrangements was exploited in the synthesis of (±)-pancratistatin. Although it was initially hoped that diol **102** would react with trichloroacetonitrile at the less-hindered allylic oxygen center, orthoamide **10**, formed as a mixture of diastereomers, was the only product produced. Unfortunately, this intermediate stubbornly refused to undergo thermal [3,3]-sigmatropic rearrangement (Eq. 101).[56]

(85%)   (Eq. 101)

102   **10**

However, benzyl-protected congener **103** is converted to the late-stage ($\pm$)-pancratistatin precursor **104** upon heating at 100–105° under high vacuum (Eq. 102).

$$\text{(Eq. 102)}$$

COMPARISON WITH OTHER METHODS

The importance of allylic amines in synthesis has led to the development of many methods for their synthesis, several of which take advantage of allylic alcohols as starting materials. Although various attractive methods have been developed, few match the breadth, regiocontrol, and stereocontrol of the trihaloacetimidate rearrangement. The ease by which the trihaloacetyl group can be removed to release the free allylic amine further distinguishes the trihaloacetimidate rearrangement from related methods. A recent review summarizes some of these methods as well as other syntheses of allylic amines.[15] This section covers the more significant developments since that review, including other rearrangement methods, aminolysis of allylic electrophiles, allylic amination of alkenes, hydroamination of alkynes and dienes, and addition of vinyl nucleophiles to imine derivatives.

Other Allylic Rearrangements

In addition to the imidate group, several functional groups are suitable for preparation of allylic amines by [3,3]-sigmatropic rearrangement. Allylic urethanes,[129] isoureas,[130] cyanates,[131] thioimidates,[132,133] and sulfamates[134] were explored early on as potential candidates for the sigmatropic transformation of allylic alcohols into allylic amines.[10] More recently, rearrangements of allylic *N*-benzoyl benzimidates and allylic phosphorimidates have been studied.[101,135] Each of these methods exhibits some limitations, either in the preparation of the rearrangement precursors, conditions required for the rearrangement, scope of the rearrangement, or difficulties encountered in subsequent hydrolysis of the protected amine products. At this point, none of the aforementioned alternatives to the trihaloacetimidate rearrangement has been developed into a broadly useful method for preparing allylic amines.

Thioiminocarbonates have found some application in the synthesis of allylic nitrogen derivatives.[136] However, in a direct comparison, trichloroacetimidate rearrangement of **105** is found to be the preferred method for preparation of the amine **106** (Eq. 103). Rearrangement of thioiminocarbonate **107** gives rearrangement product **108** in low yield (Eq. 104), whereas heating **105** in refluxing xylene provides the desired amine in high yield after mild hydrolysis to remove the trichloroacetyl group.[137]

105 → **106** (Eq. 103)

1. xylene, 138°
2. NaOH (6N), EtOH, H$_2$O, rt

(80%)

107 → **108** (Eq. 104)

toluene, xylene or DMF, 140°

A method for converting an allylic alcohol to the corresponding amine with retention of configuration that involves two sequential [3,3]-sigmatropic rearrangement steps is used in the synthesis of an ansamycin.[138] In this study, thionocarbamate **109** is not isolated, but rearranges spontaneously upon its formation at room temperature to give the allylically-transposed thiocarbamate product in 90% yield from the starting allylic alcohol (Eq. 105). This intermediate is then transformed in two

109 → (90%)

rt

1. NH$_3$
2. KOBu-*t*
3. BrCN

(Eq. 105)

→ **110** (83%)

steps to the allylic thiocyanate, which also rearranges spontaneously providing allylic isothiocyanate **110** in 83% yield.

Allylic amine derivatives are also available from allylic alcohols by [2,3]-sigmatropic rearrangements of allylic selenimides[139,140] and allylic selenonium ylides.[141] These promising methods also exhibit the potential for asymmetric induction. For example, rearrangement of chiral, enantioenriched allylic selinimide **111** takes place in situ to yield the allylic carbamate (Eq. 106). Enantiomeric excesses of up to 93% are achieved in some related reactions when the substituent on nitrogen is a *para*-toluenesulfonyl group.[140]

(Eq. 106)

Allylic sulfoximines undergo either thermal or Pd(II)-catalyzed rearrangement to yield *N*-protected allylic amines. Although the thermal process gives a mixture of isomers, presumably by a dissociation-recombination mechanism,[142] Pd(II)-catalyzed rearrangement of allylic sulfoximine **112** takes place readily with transposition of the double bond to give rearrangement product **113** in 80% overall yield (Eq. 107).[143,144]

(Eq. 107)

Other Routes to Allylic Amines

Amination of Allylic Electrophiles.   The most straightforward preparation of allylic amines is unquestionably direct allylation of nitrogen with an allylic electrophile. However, this approach is often compromised by the propensity for di- and triallylation. This problem can be circumvented by delivery of the nitrogen atom in protected form as in the Gabriel synthesis.

An area of intense recent study is the transition-metal-catalyzed reaction of amines with allylic electrophiles.[15] A variety of allyl acetates, carbonates, halides, and even allylic alcohols are converted to allylic amines in this way, with the most widely used catalysts to date being complexes of palladium. When a π-allyl palladium intermediate is unsubstituted at one end, the amine generally attacks

at this terminus to give a trans unbranched allylic amine. Recently, complexes of rhodium,[145-147] ruthenium,[148,149] iridium,[150-153] and palladium[154] have been shown to catalyze allylic aminations favoring reaction at the more hindered allyl terminus to give the branched allylic amine product (Eq. 108).[147] However, regioselectivity is typically diminished when there is branching α to the leaving group. These discoveries open up the opportunity to accomplish such aminations in enantioselective fashion,[150,153-156] providing a highly attractive route to enantioenriched allylic amines (Eq. 109).[150,155,156]

(Eq. 108)

(Eq. 109)

C–H Activation. Direct substitution of an allylic C–H bond of an alkene by nitrogen is a very attractive route to allylic amines. This chemistry is generally associated with ene reactions of N=N species[157] or nitrene addition followed by rearrangement to the allylic amine.[158] Several approaches of these types have met with success, although yields are generally moderate and these methods at present are limited in scope. Thus, the ene reaction of diethyl-azodicarboxylate with alkenes provides good yields (77–95%) of allylic amine adducts (Eq. 110).[157] Efforts to introduce asymmetry into the reaction using di-(–)-menthyl diazodicarboxylate meet with moderate success; however, removal of the menthol chiral auxiliary is difficult.[159] Iron[160,161] and manganese[158] complexes have also been used to successfully introduce nitrogen at the allylic position of alkenes, although yields are modest.

(Eq. 110)

Hydroamination. The application of transition metal catalysis to the synthesis of allylic amines by hydroamination of dienes[162] and alkynes (Eq. 111)[163] holds considerable promise. At this point, the scope of this approach is largely unexplored. Mixtures of regioisomeric products are not uncommon in the hydroamination of dienes, including variable trans/cis ratios of the allylic amine product, depending

upon the reaction conditions.

$$Ph\!\!=\!\!=\ +\ H\!-\!N\!\!\begin{array}{c}Bn\\Bn\end{array}\ \xrightarrow[\substack{PhCO_2H\ (10\ mol\%)\\dioxane,\ 100°}]{Pd(PPh_3)_4\ (5\ mol\%)}\ Ph\diagdown\!\!\diagup\!\!\diagdown_{N}\!\!\begin{array}{c}Bn\\Bn\end{array}\ (98\%)\qquad \text{(Eq. 111)}$$

Addition of Vinyl Nucleophiles to Imine Derivatives. Much progress has been recorded in recent years in the synthesis of amines by the addition of organometallic reagents to imines and their derivatives, with several recent reviews summarizing this progress.[164,165] When the nucleophile is vinylic, an allylic amine or a derivative results. An example, illustrating the synthesis of enantioenriched allylic amines, is shown in Eq. 112.[166]

$$\equiv\!\!-C_6H_{13}\ \xrightarrow[\substack{H_2O,\ CH_2Cl_2,\ 0°}]{Cp_2ZrCl_2\ (cat.),\ Me_3Al}\ \left[Me_2Al\diagup\!\!\diagdown\!\!\diagup_{C_6H_{13}}\right]\ \xrightarrow[]{}$$

(Eq. 112)

reagent: $p\text{-Tol}\overset{O}{\underset{}{\overset{\|}{S}}}{-}N\overset{}{\underset{H}{=}}\!\!\diagdown Ph$, $-15°$

$$p\text{-Tol}\overset{O}{\underset{}{\overset{\uparrow}{S}}}\!\!\diagdown_{NH}\underset{Ph}{\diagup}\!\!\diagdown\!\!\diagup_{C_6H_{13}}\ \xrightarrow[\substack{Amberlyst\ IR\text{-}120}]{MeOH,\ rt}\ \underset{Ph}{\overset{NH_2}{\diagup}}\!\!\diagdown\!\!\diagup_{C_6H_{13}}$$

(80%)   (90%) 79% ee

EXPERIMENTAL CONDITIONS

General Comments

An attractive aspect of the Overman rearrangement is its experimental simplicity. Typically the intermediate allylic trichloroacetimidate is not purified, but rearranged directly under either thermal or metal-catalyzed conditions. Despite the progress that has been made in the area of metal catalysis, the thermal rearrangement of allylic trihaloacetimidates is so reliable and convenient that most applications employ these conditions. A wide variety of non-nucleophilic solvents can be used in the imidate preparation and rearrangement steps. Dry solvents (commercial quality) are typically acceptable, and should be employed to minimize hydrolysis of the trichloroacetimidate intermediate.

Preparation of Allylic Trichloracetimidates

Bases promote the addition of alcohols to trichloroacetonitrile. Two general conditions are commonly employed for preparing allylic trichloroacetimidates: catalytic or stoichiometric amounts of 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU),[91,108] or catalytic quantities of a metal alkoxide that is generated in situ by reaction of the allylic alcohol with 5–20 mol% of NaH, KH, sodium metal, or *n*-BuLi. Sodium hydride is employed most commonly in the latter procedure with diethyl ether or

THF being used as the solvent and deprotonation being carried out at temperatures from $0°$ to $-15°$. If the alkoxide is generated, it is important to use only catalytic quantities: although the equilibrium constant for generating trichloroacetimidates from the addition of alcohols to trichloroacetonitrile is high, the corresponding equilibrium of an alkoxide and trichloroacetonitrile to form the trichloroacetimidate conjugate base is much less favorable. Dichloromethane has commonly been the solvent when DBU is used as a base, although other dry aprotic solvents could likely be utilized. When DBU is used, it is employed catalytically (10 mol%) or used in excess.

In the alkoxide-catalyzed procedure, the order of addition of the reagents is variable. For secondary and tertiary alcohols, the preferred order of addition is to slowly transfer the alcohol/alkoxide solution by cannula into a solution of trichloroacetonitrile,[6] although the reverse order of addition has been employed without adverse effects.[137,167] The formation of trichloroacetimidates from primary alcohols is best carried out by adding trichloroacetonitrile to the alcohol/alkoxide mixture.

In the DBU-promoted process, the order of addition of the base does not play a critical role: DBU can be pre-mixed with the alcohol,[26,49] added to the alcohol as a mixture with the trichloroacetonitrile,[47,108] or added sequentially with trichloroacetonitrile (first DBU, followed by trichloroacetonitrile). Use of DBU allows unhindered allylic trichloroacetimidates to be formed at low temperatures (down to $-78°$), although temperatures around $-35°$ to $0°$ are most common.

Allylic trichloroacetimidates are reasonably stable to standard purification methods, such as either vacuum distillation or silica gel chromatography. Nonetheless, they are almost always used with minimal purification. For example, after extractive workup and quick passage through a plug of silica gel, the solvent is removed and the crude imidate is redissolved in the rearrangement solvent for heating to reflux. Allylic trichloroacetimidates often undergo partial hydrolysis during slow chromatography on silica gel; this is not observed if Davisil grade silica gel (W.R. Grace & Co.) is used.

Preparation of Allylic Trifluoroacetimidates

The preparation of allylic trifluoroacetimidates first requires generation of trifluoroacetonitrile, a colorless gas (bp $= -64°$). In early studies, trifluoroacetonitrile was generated by the vigorous dehydration of trifluoroacetamide using phosphoric pentoxide.[75] After passing gaseous trifluoroacetonitrile through a sequence of traps and scrubbers, an excess of trifluoroacetonitrile is condensed to prepare an ethereal solution for subsequent addition to a solution of the alcohol/alkoxide at $-78°$. The alkoxide is typically generated by the action of *n*-BuLi (20 mol%) on the alcohol in THF at $0°$ or below. A more convenient "one-pot" procedure for preparing allylic trifluoroacetimidates generates trifluoroacetonitrile in situ from trifluoroacetamide by reaction with oxalyl chloride and DMSO.[168]

Thermal Rearrangements of Allylic Trihaloacetimidates

As discussed in the Scope and Limitations section, the thermal rearrangement is somewhat faster in solvents of higher polarity. Nevertheless, high-boiling hydrocarbon solvents such as toluene and xylenes have been employed most widely. The crude allylic trichloroacetimidate typically is dissolved in the solvent of choice and

the rearrangement carried out at reflux. Some substrates require higher temperatures and these rearrangements can be carried out in a sealed tube. Alternatively, *ortho*-dichlorobenzene (bp 180°), decalin (bp 190°), *tert*-butylbenzene (bp 169°), or diphenyl ether (bp 259°) can be used to bring about the rearrangement. The concentration at which the thermal rearrangement is conducted appears to be of little importance: most rearrangements are run at about 0.1 M, although some have even been effected at high concentration or neat.

Unwanted decomposition of the allylic trichloroacetimidate by ionization to form trichloroacetamide and the corresponding allylic cation (and eventually diene byproducts) can be problematic when ionization of the allylic C–O σ-bond produces a particularly stable allylic cation, for example with tertiary allylic trichloroacetimidates. This side reaction is likely promoted by acidic impurities. A significant improvement to the rearrangement procedure is the inclusion of powdered anhydrous K_2CO_3, which scavenges acids and prevents the decomposition of the imidate.[63] The amount of K_2CO_3 added varies from a small amount (20 mol% relative to the crude allylic imidate) to a slight excess. Improvements in yield of up to 50% are reported;[63] in some cases, previously nonviable rearrangements are made possible.

Rearrangements of allylic trifluoroacetimidates are carried out under similar conditions. The time required for the rearrangement to proceed to completion may be reduced and/or the yield improved when trifluoroacetimidates, rather than their trichloro congeners, are employed.[75,95]

Metal-Catalyzed Rearrangements of Allylic Trichloroacetimidates

After the initial report that mercuric trifluoroacetate catalyzes the rearrangement of allylic trichloroacetimidates,[4] the catalysts that have been most successfully applied are Pd(II) complexes. The commercially available, or readily prepared,[169] bis(acetonitrile) and bis(benzonitrile) complexes of $PdCl_2$ are employed widely. These complexes are used at 4–10 mol% to effect the rearrangement of primary and secondary allylic trichloroacetimidates; reports of successful Pd(II)-catalyzed rearrangements of secondary imidates are rare. Tetrahydrofuran, toluene, and dichloromethane have been used as solvents, with rearrangements taking place at room temperature in a matter of hours.[27,28,30,62] Catalytic asymmetric rearrangements employing the catalyst COP-Cl (**8**) generally are carried out with catalyst loadings of 1–5 mol% in CH_2Cl_2.[7] The recently introduced COP-hexafluoroacetylacetonate complex **78** is more soluble allowing a wider variety of solvents to be employed and the reactions to be conducted at high substrate concentration (up to 2.6 M).[9] Catalytic asymmetric rearrangements of allylic trichloroacetimidates with the COP catalysts can be conducted at temperatures up to 60° without loss of enantioselectivity.

EXPERIMENTAL PROCEDURES

2,2,2-Trichloro-*N*-(3,7-dimethylocta-1,6-dien-3-yl)acetamide   (Alkoxide-Catalyzed Procedure for Preparing Allylic Trichloroacetimidates and Thermal Rearrangement of the Crude Imidate Intermediate).[43]   This preparation is described in *Organic Synthesis*.[43]

3,7-Dimethylocta-1,6-dien-3-amine (Basic Hydrolysis of an Allylic Trichloroacetamide to Form the Allylic Amine).[43]   This preparation is described in *Organic Synthesis*.[43]

(*Z*)-2-[(6*S*)-6-(2,2-Dimethyl-1,3-dioxolan-4-yl)-4-methylcyclohex-3-enylidene]ethyl 2,2,2-Trichloroacetimidate (Preparation of a Trichloroacetimidate using DBU).[49] To a cooled ($-35°$) solution of the allylic alcohol (18.5 g, 77.7 mmol) in dry CH_2Cl_2 (370 mL) was added DBU (13.9 mL, 93.2 mmol) followed by the dropwise addition of Cl_3CCN (9.35 mL, 93.2 mmol) over a period of 10 minutes. The reaction mixture was stirred at $-35°$ for 1 hour, then was quenched with NH_4Cl (saturated aqueous, 300 mL) and extracted with CH_2Cl_2. The combined organic extracts were washed with saturated NH_4Cl solution, dried (Na_2SO_4) and concentrated. The residue was dissolved in Et_2O and passed through a short column packed with anhydrous Na_2SO_4 and silica gel 60. The Et_2O was evaporated to yield the imidate as a light yellow oil: IR (KBr) 3345, 2983, 2931, 1661, 1455, 1370, 1289, 1072 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 1.33 (s, 3H), 1.41 (s, 3H), 1.64 (br s, 3H), 1.72 (br d, $J = 18$ Hz, 1H), 2.33 (br d, $J = 18$ Hz, 1H), 2.67 (br d, $J = 19$ Hz, 1H), 2.94–3.10 (m, 2H), 3.71 (dd, $J = 8$, 6.5 Hz, 1H), 4.10 (dd, $J = 8$, 6 Hz, 1H), 4.23 (dt, $J = 10$, 6.5 Hz, 1H), 4.77 (ddd, $J = 12$, 6, 2 Hz, 1H), 5.00 (ddd, $J = 12$, 8, 1 Hz, 1H), 5.38 (br s, 1H), 5.71 (ddd, $J = 8$, 6, 2 Hz, 1H), 8.25 (br s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 23.2, 25.3, 26.7, 32.3, 33.3, 39.8, 65.3, 68.6, 75.7, 91.5, 109.0, 118.2, 120.2, 131.1, 142.5, 162.7.

2,2,2-Trichloro-*N*-[(1*R*,6*S*)-6-(2,2-dimethyl-1,3-dioxolan-4-yl)-4-methyl-1-vinylcyclohex-3-enyl]acetamide (Thermal Rearrangement of a Trichloroacetimidate in the Presence of K$_2$CO$_3$).[49]   Powdered K_2CO_3 (1.2 g) was added to a

solution of the crude imidate (prepared as described in the previous procedure) in *para*-xylene (600 mL) and the mixture was heated at reflux with vigorous stirring for 20 hours. After cooling to room temperature, the mixture was filtered through a pad of Super-Cel and the precipitate was washed with toluene. The combined filtrates were concentrated and the residue was purified by column chromatography (SiO$_2$, 550 g, ether in hexane, 1:10 to 1:5) to yield the amide as colorless crystals (27.4 g, 92% from the alcohol): mp 100–102°; $[\alpha]_D^{27} = +70.2°$ (*c* 0.97, CHCl$_3$); IR (KBr) 3313, 2987, 2924, 1727, 1542, 1261, 1067 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 1.39 (s, 3H), 1.42 (s, 3H), 1.64–1.71 (m, 5H), 2.08 (td, *J* = 9, 7.5 Hz, 1H), 2.27 (d quintet, *J* = 17.5, 2.5 Hz, 1H), 3.37 (ddq, *J* = 17.5, 6, 1.5 Hz, 1H), 3.63 (dd, *J* = 9, 7.5 Hz, 1H), 4.03 (td, *J* = 9, 5.5 Hz, 1H), 4.10 (dd, *J* = 7.5, 5.5 Hz, 1H), 5.30 (dd, *J* = 17, 1 Hz, 1H), 5.32 (dd, *J* = 11, 1 Hz, 1H), 5.39 (m, 1H), 5.82 (dd, *J* = 17, 11 Hz, 1H), 9.21 (br s, 1H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 22.5, 26.2, 26.5, 30.0, 35.8, 44.3, 59.9, 68.8, 76.3, 93.8, 109.9, 116.0, 119.0, 130.8, 133.7, 160.4; HRMS (FAB) calcd for C$_{16}$H$_{22}$NO$_3$Cl$_3$ (M+H), 382.0743, found 382.0721.

(4*S*,5*S*)-4-(*tert*-Butyldimethylsiloxymethyl)-5-[(3*S*,4*S*,1*E*)-4-*tert*-butyldiphenylsiloxy-3-(2,2,2-trifluoroacetimidoyloxy)pentenyl]-2,2-dimethyl-1,3-dioxolane (Preparation of an Allylic Trifluoroacetimidate).[75] To a solution of the alcohol (0.25 g, 0.43 mmol) in THF (6 mL) at −78° was added *n*-butyllithium (1.6M in hexane; 0.29 mL, 0.46 mmol). The resulting solution was stirred for 1 hour whereupon a stream of trifluoroacetonitrile was allowed to bubble through the reaction mixture for five minutes. [The trifluoroacetonitrile was prepared by mixing powdered trifluoroacetamide (10 g, 88 mmol) with phosphorus pentoxide (24 g, 148 mmol) in a round-bottomed flask fitted with a nitrogen inlet and condenser. A polytetrafluoroethylene tube fitted to the condenser led to a trap cooled in an ice–salt mixture, then to a trap cooled in an ether–N$_2$ (liquid) mixture, and finally to a bath containing aqueous sodium hydroxide via a tube packed with calcium chloride. The reaction mixture was slowly heated to 150° and held at this temperature for 3 hours under a gentle stream of nitrogen gas. The trifluoroacetonitrile distilled out and was collected as a colorless liquid in the −100° ether/N$_2$ (liquid) trap.] The reaction was allowed to warm to room temperature over a period of 1 hour, then NH$_4$Cl (0.2 g, 3.6 mmol) was added and the reaction mixture was concentrated under reduced pressure. The product was purified by column chromatography (silica gel 60; petroleum ether in ether, 9:1): 81%; $[\alpha]_D^{23} = -5.7°$ (*c* 0.5, CHCl$_3$); IR (CHCl$_3$) 3360, 1680, 1470, 1430, 1380, 1200, 1170, 1112, 840 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.1 (s, 6H), 0.9 (s, 9H), 1.0 (d, *J* = 7 Hz, 3H), 1.1 (s, 9H), 1.45 (s, 6H), 3.74 (m, 3H), 4.2 (quintet, *J* = 6 Hz, 1H), 4.44 (m, 1H), 5.5 (t, *J* = 6 Hz, 1H), 5.85 (dd, *J* = 5, 6 Hz, 1H), 5.9 (dd, *J* = 16, 5 Hz, 1H), 7.3–7.8 (m, 10H), 8.2 (s, 1H).

(4S,5S)-4-(*tert*-Butyldimethylsiloxymethyl)-5-[(1R,4S,2E)-4-*tert*-butyl-diphenylsiloxy-1-(2,2,2-trifluoroacetylamino)pent-2-enyl]-2,2-dimethyl-1,3-dioxolane (Thermal Rearrangement of an Allylic Trifluoroacetimidate).[75] A solution of a portion of the trifluoroacetimidate prepared in the previous procedure (90 mg, 0.13 mmol) in xylene (2 mL) was degassed with argon and heated at reflux for 20 hours. The reaction mixture was then concentrated under reduced pressure and the residue was purified by column chromatography (silica gel 60, petroleum ether in ether, 15:1) to give the amide (74 mg, 82%): $[\alpha]_D^{23} = -50.6°$ (*c* 1.1, CHCl$_3$); IR (CHCl$_3$) 3420, 1730, 1530, 1480, 1470, 1430, 1370, 1170, 1110, 1080, 840 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.1 (s, 6H), 0.9 (s, 9H), 1.1 (s, 9H), 1.2 (d, J = 6 Hz, 3H), 1.4 (s, 6H), 3.7 (m, 2H), 3.85 (m, 1H), 4.0 (dd, J = 8, 2 Hz, 1H), 4.3 (quintet, J = 6 Hz, 1H), 4.67 (t, J = 7.5 Hz, 1H), 5.5 (dd, J = 16, 7 Hz, 1H), 5.75 (dd, J = 16, 6 Hz, 1H), 6.85 (d, J = 9 Hz, 1H), 7.3–7.8 (m, 10H). Anal. Calcd for C$_{35}$H$_{52}$F$_3$NO$_5$Si$_2$: C, 61.8; H, 7.7. Found: C, 61.5; H, 8.05.

Cinnamyl 2,2,2-Trifluoroacetimidate ("One-Pot" Procedure for the Preparation of an Allylic Trifluoroacetimidate).[62] Into a flame-dried three-necked round-bottomed flask was placed 2,2,2-trifluoroacetamide (734 mg, 3 mmol), DMSO (1.36 mL, 8.7 mmol), and CH$_2$Cl$_2$ (30 mL). The mixture was cooled to −75° whereupon oxalyl chloride (0.51 mL, 5.9 mmol) and triethylamine (2.5 mL, 18 mmol) were slowly added. The mixture was stirred at −78° for 30 minutes, then DBU (0.6 mL, 4 mmol) and cinnamyl alcohol (296 mg, 2.2 mmol) were added slowly by syringe. The reaction mixture was allowed to warm to room temperature over 10 hours, then the reaction was quenched by the addition of water. The aqueous layer was extracted (EtOAc), the combined organic layers washed with brine, dried (Na$_2$SO$_4$) and filtered. Purification by column chromatography (SiO$_2$, hexane in ethyl acetate, 10:1) and then Kugelrohr distillation afforded the product as a colorless oil (384 mg, 76%): bp 100–105°/0.9 mm; IR (neat) 3347, 3087, 3063, 3031, 2950, 2887, 1686, 1356, 1202, 1167, 1117, 1076, 967, 847, 747, 735, 693 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.94 (d, J = 6.3 Hz, 2H), 6.37 (td, J = 6.3, 16.1 Hz, 1H), 6.73 (d, J = 16.1 Hz, 1H), 7.26–7.29 (m, 1H), 7.32–7.36 (m, 2H), 7.40–7.43 (m, 2H), 8.23 (s, 1H); ^{13}C NMR (100 MHz, CDCl$_3$) δ 68.2, 115.6 (q, J = 280 Hz), 121.9, 126.7, 128.4, 128.6, 135.0, 136.0, 157.8 (q, J = 38.0 Hz); EI-HRMS: [M$^+$] calcd for C$_{11}$H$_{10}$F$_3$NO, 229.0714; found 229.0689.

(*3R*,*4S*)-4-*tert*-Butoxycarbonylamino-3-(trichloroacetylamino)-1-pentene (Pd(II)-Catalyzed Rearrangement of an Allylic Trichloroacetimidate).[30]   To a solution of the crude allylic trichloroacetimidate, prepared from 4.25 g (21 mmol) of the corresponding allylic alcohol, in THF was added $PdCl_2(MeCN)_2$ (552 mg, 2.13 mmol) under nitrogen. The reaction mixture was stirred at room temperature for 3 hours, whereupon the solvent was removed and the product (3.48 g, 48% from the alcohol) was isolated by column chromatography (silica gel 60, 4:1 toluene–ethyl acetate): ^{1}H NMR (CDCl$_3$) δ 1.21 (d, J = 7.0 Hz, 3H), 1.44 (s, 9H), 4.02 (m, 1H), 4.28 (m, 1H), 4.49 (d, J = 7 Hz, 1H), 5.34 (m, 2H), 5.73 (m, 1H), 8.73 (s, 1H); ^{13}C NMR (CDCl$_3$) δ 18.6, 28.7, 49.7, 60.2, 80.9, 93.3, 119.6, 131.7, 157.5, 161.9.

(*S*)-2,2,2-Trichloro-*N*-(1-propylallyl)acetamide (Catalytic Asymmetric Rearrangement of an Allylic Trichloroacetimidate).[170]   A round-bottomed flask fitted with a stirring bar was charged with (*E*)-2-hexenyl trichloroacetimidate (6.81 g, 28 mmol, prepared from (*E*)-2-hexenol in 99% yield using the DBU procedure and purified by filtration through a short column of Davisil-grade silica gel using 2% ethyl acetate–hexanes as eluent), (*S*)-COP-Cl (816 mg, 0.56 mmol), and dry methylene chloride (9.3 mL). The flask was sealed with a polyethylene stopper, the stopper secured to the flask with Parafilm, and placed in an oil bath preheated to 38°. After 24 hours, the solution was cooled to room temperature and concentrated using a rotary evaporator to yield a brown oil. This oil was purified by flash chromatography (Davisil-grade silica gel, 0.5% ethyl acetate:hexanes) to give after concentration 6.50 g (95%, 94% ee) of the S allylic trichloroacetamide product as a pale yellow oil: IR (neat) 3329, 2966, 2873, 1699, 1522, 1460, 1251 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.96 (t, J = 7.4 Hz, 3H), 1.35–1.47 (m, 2H), 1.55–1.69 (m, 2H), 4.39–4.47 (m, 1H), 5.19 (d, J = 10.5 Hz, 1H), 5.23 (d, J = 17.2 Hz, 1H), 5.80 (ddd, J = 17.0, 10.4, 5.6 Hz, 1H), 6.50 (broad s, 1H); ^{13}C NMR (CDCl$_3$) δ 13.7, 18.8, 36.6, 53.3, 92.8, 116.0, 136.7, 161.2; HRMS (CI-NH$_3$): (M–*n*-Pr) calcd for $C_5H_5Cl_3NO$, 199.9437; found 199.9436.

TABULAR SURVEY

The tabular survey in this chapter covers allylic trihaloacetimidate rearrangements reported from 1974 through April, 2004. [3,3]-Sigmatropic rearrangements of

other imidates are not included, nor are the [3,3]-sigmatropic rearrangements of propargylic alcohols. The tables are organized by substrate structure (the starting allylic alcohol) and are arranged on the basis of increasing carbon count of the alcohol, exclusive of protecting groups.[4] Secondary alcohols are separated into acyclic (Table 2A) and cyclic (Table 2B) substrates. Both thermal and metal-catalyzed conditions are included in the individual tables with the exception of Table 4, which presents examples of metal-catalyzed asymmetric trihaloacetimidate rearrangements.

For Tables 1–3 the yield presented is the overall yield for the two-step process (preparation of the imidate and subsequent rearrangement) unless otherwise noted. For Table 4 the yield is for the rearrangement step only. The highest yield is generally given in the case of multiple reports for the same rearrangement. A "(—)" entry indicates that no yield was reported.

The following abbreviations are used in the tables:

OAc	Acetate
Bn	Benzyl
Boc	*tert*-Butoxycarbonyl
BOM	Benzyloxymethyl
Bz	Benzoyl
Cbz	Carbobenzyloxy
DBPC	Di(*tert*-butyl)-*para*-cresol
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
MOM	Methoxymethyl
MPM	*para*-Methoxybenzyl
NIS	*N*-Iodosuccinimide
NBS	*N*-Bromosuccinimide
TBDMS	*tert*-Butyldimethylsilyl
TBDPS	*tert*-Butyldiphenylsilyl
THF	Tetrahydrofuran
THP	Tetrahydropyran
Tr	Trityl (triphenylmethyl)
Ts	*para*-Toluenesulfonyl

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[4] Generally, the methoxy group was not considered as a protecting group, hence anisole, for example, would be categorized as a C7 compound.

CATALYSTS USED IN TABLE 4
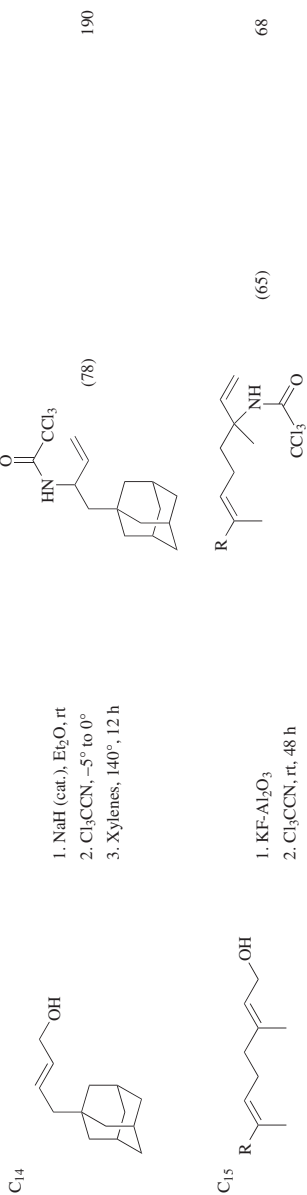
TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₃	1. NaH (cat.), Et₂O 2. Cl₃CCN, <0° to rt 3. Xylene, 140°, 12 h	(50)	6, 4, 113
C₄	1. NaH (cat.), Et₂O 2. Cl₃CCN, <0° to rt 3. Xylene, 140°, 12 h	(83)[a] **I**	4, 118, 171, 172, 173
	1. NaH (cat.), THF 2. Cl₃CCN 3. Hg(O₂CCF₃)₂ (20 mol%), THF, 0° to rt, 1 h	**I** (69)	6
	1. KF-Al₂O₃ 2. Cl₃CCN, rt, 48 h	**I** (85)	68
	1. Na⁰ (cat.), THF 2. Cl₃CCN, −23° 3. t-BuC₆H₅, 169°, 1 h	(50)	69, 55
	1. Na⁰ (cat.), 0° 2. Cl₃CCN (2.2 eq.), rt 3. 180-185°, 1 h	(46)	174, 55
	1. NaH (cat.), Cl₃CCN, THF, 0° to rt, 2.5 h 2. C₁₀H₁₈, 190°, 12 h	R BnOCH₂ (—)[b] HOCH₂ (—)[b]	117

54

62, 113

62

116

68

31

62

62

(86)

(71)

(36)

(65)

(89)^d

(61)

(60)

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, Et$_2$O, −15 to 0°
3. Xylenes, 150° (sealed tube), 52 h

1. F$_3$CCN, DBU, CH$_2$Cl$_2$, −78° ^{c}
2. Xylenes, 150° (sealed tube), 68 h

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, 0°
3. Xylenes, 140°

1. KF–Al$_2$O$_3$
2. Cl$_3$CCN, rt, 48 h

1. NaH (cat.)
2. Cl$_3$CCN
3. Toluene, 100°, 48 h

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, Et$_2$O, −15 to 0°
3. Xylenes, 150° (sealed tube), 23 h

1. F$_3$CCN, DBU, CH$_2$Cl$_2$, −78° ^{c}
2. Xylenes, 150° (sealed tube), 96 h

C$_5$

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_5$			
TBDMSO—OTBDMS	1. DBU, Cl$_3$CCN, 0°	OTBDMS **I** / OTBDMS **II** 3:1 (71)	100
	2. PdCl$_2$(MeCN)$_2$ (10 mol%), THF, rt, 5 h		
NHBoc—OH	1. NaH (cat.), Et$_2$O	**I** + **II**	30
	2. Cl$_3$CCN, rt		
	3. Conditions	Conditions — I:II	
		o-xylene, 140°, 25 h — 62:38 (82)	
		PdCl$_2$(MeCN)$_2$ (6-8 mol%), MeCN, rt, 3 h — >99:1 (46)	
TBDMSO—NHBoc	1. NaH (cat.), Et$_2$O	**I** + **II** NHBoc / NHBoc I:II 99:1 (57)[a]	30
	2. Cl$_3$CCN, rt		
	3. PdCl$_2$(MeCN)$_2$ (6-8 mol%), MeCN, rt, 3 h		
C$_6$			
OH	1. NaH (cat.), Et$_2$O	**I** (72)	6, 4, 117, 118, 120, 175, 173
	2. Cl$_3$CCN		
	3. Xylenes, 140°, 12 h		
OH	1. NaH (cat.), Et$_2$O	**I** (62)	6
	2. Cl$_3$CCN, 0° to rt		
	3. Hg(O$_2$CCF$_3$)$_2$ (10 mol%), THF, 25 min		

89

51

63

60, 75

30

30

(77)

(100)

I (73)

$(35)^a$

I:II 99:1 $(62)^a$

I:II 99:1 $(45)^a$

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, 0° to rt
3. Xylenes, 140°, 20 h

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, −15° to rt, 4 h
3. Xylenes, 140°, 12 h

1. DBU, CH$_2$Cl$_2$, 0°
2. Cl$_3$CCN, CH$_2$Cl$_2$, 0°, 1 h
3. K$_2$CO$_3$, p-xylene, 138°, 13 h

1. n-BuLi (cat.), THF, −78° to 0°
2. F$_3$CCN (excess), THF, −78° to rt
3. Xylenes, 140°, 9.5 hr

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, rt
3. PdCl$_2$(MeCN)$_2$ (6-8 mol%),
   MeCN, rt, 3 h

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN, rt
3. PdCl$_2$(MeCN)$_2$ (6-8 mol%),
   MeCN, rt, 3 h

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$	1. NaH (cat.), Et$_2$O, 15° 2. Cl$_3$CCN, Et$_2$O, –15° to rt 3. Xylenes, 140°, 48 h	(28) + (27)	77, 176
	1. NaH (cat.), Et$_2$O, 15° 2. Cl$_3$CCN, Et$_2$O, –15° to rt 3. Xylenes, >140°, 48 h^e	(—) + (—)	77
C$_7$	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. Xylenes, 140°	(—)	172
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. Xylenes, 140°	(62)	177
	1. NaH (cat.) 2. Cl$_3$CCN 3. *p*-Xylenes, 140°, 24 h	I + II I:II 3:2 (45)	99

58

99

113

30

98

98

1. NaH (cat.)
2. Cl$_3$CCN
3. PdCl$_2$(RCN)$_2$ (10 mol%), THF, rt, 3 h

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN
3. Xylenes, 140°

1. NaH (cat.), Et$_2$O
2. Cl$_3$CCN
3. PdCl$_2$(MeCN)$_2$ (6-8 mol%), MeCN, rt, 3 h

1. NaH (cat.), Et$_2$O, 0°, 5 min
2. Cl$_3$CCN, 0° to rt, 45 min
3. DBPC (2%), xylenes, 137°, 13 h

1. NaH (cat.), THF, 0°, 15 min
2. F$_3$CCN, −78°, 20 min
3. DBPC (2%), xylenes, 137°, 81 h

R	I:II
Me	1:6 (54)
Ph	1:7 (59)

(63)

I:II 99:1 (49)^a

(72) dr = 1.1:1

(64) dr = 1.5:1

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_7$			
	1. NaH (cat.), Et$_2$O, 0°, 5 min 2. Cl$_3$CCN, 0° to rt 3. DBPC (%), xylenes, 137°	dr = 1:1 % DBPC 0 (23)^a 2 (84)^a	98
	1. NaH (cat.), THF, 0°, 15 min 2. F$_3$CCN, −78°, 20 min 3. DBPC (2%), xylenes, 137°, 81 h	(45) dr = 1.2:1	98
	1. DBU, Cl$_3$CCN, 0° 2. PdCl$_2$(MeCN)$_2$ (10 mol%), THF, rt, 5 h	I + II I:II 2.2:1 (52)	100
C$_8$			
	1. NaH (cat.), Et$_2$O, 0° 2. Cl$_3$CCN, 0°, 1 hr 3. Xylenes, 140°, 48 h	(65)	178
	1. NaH (cat.) 2. Cl$_3$CCN 3. Toluene, 110°	(75)^a	179
	1. DBU, CH$_2$Cl$_2$, −10° 2. Cl$_3$CCN, −10°, 1 h 3. Na$_2$CO$_3$, *p*-xylene, 138°	(trace)	19

51

27

79

79

1. DBU (cat.), Cl_3CCN, CH_2Cl_2, rt
2. Xylenes, 140°, 24 h

1. DBU (cat.), Cl_3CCN, CH_2Cl_2, 0°
2. $PdCl_2(MeCN)_2$ (8 mol%),
   toluene, rt, 12 h

1. DBU (cat.), Cl_3CCN, CH_2Cl_2, 0°
2. Toluene (sealed tube), 140°

1. DBU (cat.), Cl_3CCN, CH_2Cl_2, 0°
2. Toluene (sealed tube), 140°

(—)

(69)

I   +   **II**

I + II

R^1	R^2	Time	**I:II**	
Me	MOMO	3 d	1.0:8.3	(78)
$BnOCH_2$	MeO	6.5 d	6.3:1.0	(64)
Me	BnO	2 d	1.0:5.4	(71)
$MPMOCH_2$	BnO	2.5 d	5.0:1.0	(69)

I + II

R^1	R^2	Time	**I:II**	
Me	MOMO	3 d	1.3:1.0	(73)
$MPMOCH_2$	BnO	1.5 d	1.0:9.0	(65)

61

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_8$	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, 0° 2. K$_2$CO$_3$, xylenes, 140°, 140 h	(60) + (14)	128
	1. NaH (cat.), Et$_2$O, 0° 2. X$_3$CCN 3. Xylenes, 200°	**I** + **II**	95
	1. NaH (cat.) 2. Cl$_3$CCN 3. Toluene, 110°	(51)	80
C$_9$	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, 0° 2. K$_2$CO$_3$, xylenes, 140°	**I** + **II**	47, 180

X	E/Z	Time	I:II
Cl	E	30 h	50:50 (22)
F	E	2 h	42:58 (93)
Cl	Z	30 h	50:50 (25)
F	Z	2 h	9:91 (95)

E/Z	R	Time	I:II
E	MOM	—	5:1 (65)
E	Bn	60 h	7:1 (90)
Z	MOM	—	1:4 (49)
Z	Bn	—	1:5 (70)

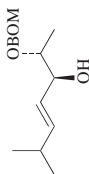| Reagent conditions	Product	References
1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Xylenes, 140°, 6 h	**I** (92)	4, 6, 60, 62, 68, 112, 113, 115, 116, 118, 120, 122, 171, 173,175, 177, 181, 182
1. KF-Al₂O₃ 2. Cl₃CCN, rt, 48 h	**I** (78)	68
1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Hg(O₂CCF₃)₂ (40 mol%), THF, 0° to rt, 1 h	**I** (39)	4, 6
1. n-BuLi (cat.), Et₂O 2. F₃CCN, THF, −78° 3. Xylenes, 140°, 5 h	(81)ᵃ	60, 62
1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Xylenes, 140°	(—)	115
1. NaH, CH₂Cl₂, −6° 2. Cl₃CCN, CH₂Cl₂, −6° 3. o-Dichlorobenzene, 165°, 6 h	(53)	84, 85

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_9$	1. NaH (cat.), Et$_2$O, −15° 2. Cl$_3$CCN, −15° to rt 3. Toluene, 150° (sealed tube), 89 h	**I** + **II** E/Z **I:II** E 2.7:1.0 (—) Z 5.0:1.0 (—) 1:1 4.8:1 (60)	79, 87, 127
C$_{10}$	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, 0° to rt 3. Xylenes, 140°	(62)	113
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. Xylenes, 190° (sealed tube), 4 h	(80)	183
	1. DBU, CH$_2$Cl$_2$, −10° 2. Cl$_3$CCN, −10°, 1 h 3. Na$_2$CO$_3$, *p*-xylene, 138°, time	 R Time H 24 h (89) *p*-F 12 h (84) *p*-Cl 12 h (82) *o*-Cl 24 h (30)	19, 116^f
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, <0° to rt 3. *m*-Xylene, 138°, 6 h	**I** (67–74)	4, 6, 42, 43, 62, 63, 68, 115, 184, 185

1. DBU, CH$_2$Cl$_2$, 0° 2. Cl$_3$CCN, CH$_2$Cl$_2$, 0°, 1 h 3. K$_2$CO$_3$, p-xylene, 138°, 13 h	**I** (84)	63
1. KF-Al$_2$O$_3$ 2. Cl$_3$CCN, rt, 48 h	**I** (69)	68
1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. Hg(O$_2$CCF$_3$)$_2$ (20 mol%), THF, $-78°$ to rt, 1 h	**I** (63–73)	4, 6
1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. PdCl$_2$(MeCN)$_2$, THF, rt, 4 h	**I** (66)	62
1. n-BuLi (cat.), THF, 0° to $-78°$ 2. F$_3$CCN, THF, $-78°$ to rt, 1 h 3. Xylenes, 140°, 9.5 h	 **I** (70)	60, 75
1. F$_3$CCN, DBU, CH$_2$Cl$_2$, $-78°$ ^{c} 2. PdCl$_2$(MeCN)$_2$, THF, rt, 16 h	**I** (19)	62
1. DBU, CH$_2$Cl$_2$, 0° 2. Cl$_3$CCN, CH$_2$Cl$_2$, 0°, 0.5-1 h 3. [K$_2$CO$_3$], p-xylene, 138°, 13-15 h	 *without K$_2$CO$_3$* (72) *with K$_2$CO$_3$* (95)	63
1. NaH (cat.), THF 2. Cl$_3$CCN 3. Xylenes, 130°, 5 h	 (72) 1:1 exo:endo	186

65

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{10}	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, Et$_2$O 3. Xylene, 140°, 12 h	(60)	179
C_{11}	1. DBU, CH$_2$Cl$_2$, –10° 2. Cl$_3$CCN, –10°, 1 h 3. Na$_2$CO$_3$, *p*-xylene, 138°, time	 R Time Me 24 h (72) CF$_3$ 12 h (89) MeO 24 h (trace)	19
	1. NaH (cat.), Et$_2$O, 0° 2. Cl$_3$CCN, Et$_2$O 3. Toluene, 110°, 5 h	(45) dr = 1:1	187, 188
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, rt 3. PdCl$_2$(MeCN)$_2$ (6-8 mol%), MeCN, rt, 3 h	 I + II I:II 99:1 (43)[a]	30
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN 3. Xylenes, 140°	I (56)	115

189, 63

63

94

94

1. DBU, CH$_2$Cl$_2$
2. Cl$_3$CCN, CH$_2$Cl$_2$
3. K$_2$CO$_3$, p-xylene, 138°

I (93)

1. DBU, CH$_2$Cl$_2$, 0°
2. Cl$_3$CCN, CH$_2$Cl$_2$, 0°, 0.5-1 h
3. [K$_2$CO$_3$] Xylenes, 140°, 13-15 h

without K$_2$CO$_3$ (37)^g
with K$_2$CO$_3$ (62)^h

CCl$_3$

OTBDMS

1. NaH (cat.), THF, 0°
2. Cl$_3$CCN, 0° to rt
3. Xylenes, 140°, 24 h

dr = 55:45 (52)

CCl$_3$

Boc·N
H

1. NaH (cat.), THF, 0°
2. Cl$_3$CCN, 0° to rt
3. Conditions

CCl$_3$

Boc·N
H

Conditions	
I$_2$, rt, 48 h	(0)^i
NBS, THF	(—)^j
Hg(O$_2$CCF$_3$)$_2$, NaBH$_4$	(—)^j

OH

OTBDMS

OH

Boc·N
H

TABLE 1. REARRANGEMENTS OF TRIHALOACETIMIDATES OF PRIMARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₁			
	1. NaH (cat.), THF, 0° 2. Cl₃CCN, 0° to rt 3. Pd(OAc)₂ (6.4 eq.), THF, rt, 4 h	(44)	94
	1. NaH (cat.), THF 2. Cl₃CCN 3. Xylenes, 130°, 5 h	(48) 1:1 exo:endo	186
C₁₁₋₁₂	1. DBU, Cl₃CCN, 0° 2. PdCl₂(MeCN)₂ (10 mol%), THF rt, 5 h	I + II	100

R	I:II	
Me	1.4:1	(63)
MOM	6.2:1	(58)
BOM	9.95:1	(57)
OTBDMS	10:1	(61)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₁₄	1. NaH (cat.), THF, rt, 15 min 2. Cl₃CCN, 0° to rt, 45 min 3. DBPC (2%), xylene, 137°, 44 h	(84) dr = 1:1	98

68

C$_{14}$

1. NaH (cat.), Et$_2$O, rt
2. Cl$_3$CCN, −5° to 0°
3. Xylenes, 140°, 12 h

(78)

190

C$_{15}$

1. KF-Al$_2$O$_3$
2. Cl$_3$CCN, rt, 48 h

(65)

68

R = H only.

---

^{a} This is the yield for rearrangement only.

^{b} The trichloroacetamide products were hydrolyzed and the amine hydrochloride salts were obtained in "very high yields" from the corresponding alcohol.

^{c} Trifluoroacetonitrile was generated in situ from trifluoroacetamide by reaction with dimethylsulfoxide/oxalyl chloride.

^{d} Heating at 140° (xylene reflux) led to decomposition. Several other variables (solvent, microwave irradiation) were tried with poor success.

^{e} This, the Z isomer, required higher temperatures and produced "significantly more byproducts" than its E counterpart.

^{f} R = H only.

^{g} In addition to the desired product, a 32% yield of 2,2-dimethyl-4-(5-methyl-2-vinylphenyl)-1,3-dioxolane (a product of aromatization) was obtained.

^{h} Ten percent of the starting imidate was recovered.

^{i} Attempted rearrangement resulted in either no reaction or a mixture of several products.
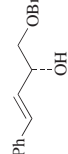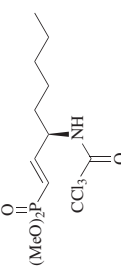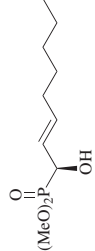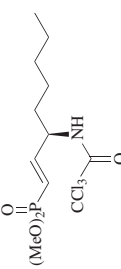
^{j} Several products were obtained.

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₄	1. NaH (cat.), THF, 5°, 1 h 2. Cl₃CCN, THF, 0°, 2.5 h 3. Toluene, 110°, 2 h	(53)	121
C₅	1. KH (cat.) 2. Cl₃CCN 3. Xylenes, 140° 4. NaOH 5. (Boc)₂O	(71)	191
	1. KF-Al₂O₃ 2. Cl₃CCN, rt, 48 h	(90)	68
	1. KH, 18-crown-6, Et₂O, −15° 2. Cl₃CCN, Et₂O, −15° to rt, 4 h 3. Xylenes, 140°, 12 h	(≈35)	24
	1. KH, Et₂O, −15° 2. Cl₃CCN, Et₂O, −15° to rt, 4 h 3. Xylenes, 140°, 12 h	(≈45)	24
	1. DBU, Cl₃CCN, CH₂Cl₂, −35°, 35 min 2. Xylene, 140°, 22 h	E:Z 86:14 (61)	97
	1. n-BuLi (20 mol%) 2. F₃CCN, THF, −78° 3. Xylene, 140°	(93)[a]	60

C₆

1. KH, THF, Et$_2$O
2. Cl$_3$CCN
3. Toluene, 110°

(87)   126

1. NaH, Et$_2$O
2. Cl$_3$CCN, Et$_2$O, <0°
3. Xylene, 140°, 1 h

(74)   4, 6

1. NaH, Et$_2$O
2. Cl$_3$CCN, Et$_2$O, <0°
3. Hg(O$_2$CCF$_3$)$_2$ (30 mol%), THF, rt, 4 h

I   **I** (8)^b 4, 6

1. KH (cat.)
2. Cl$_3$CCN
3. Xylenes, 140°
4. NaOH
5. (Boc)$_2$O

(69)   191

1. NaH (1 eq.)
2. Cl$_3$CCN
3. Benzene, 80°, 1 h

(50)   81

1. NaH (cat.), hexane/Et$_2$O
2. Cl$_3$CCN, hexane/Et$_2$O
3. Xylenes, 140°, 1-3 h

(65)   183

1. Cl$_3$CCN, DBU, CH$_2$Cl$_2$, −35°, 40 min
2. Toluene, 110°, 10 h

(82)   E:Z 87:13   97

71

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_6$			
	1. DBU, Cl$_3$CCN 2. NBS (1 eq.), CHCl$_3$, 36 h	(53)[a, c]	66
	DBU, CH$_2$Cl$_2$, Cl$_3$CCN (2 eq.), 20°, 24 h	(22)	91
	1. KH (cat.), hexane/THF, –10° 2. Cl$_3$CCN, Et$_2$O, –10° to rt 3. Toluene, 110°, 3 h	**I** + **II** **I:II** 5:2 (84)	90
	1. NaH (cat.) 2. Cl$_3$CCN 3. *m*-Xylene, 139°	(40)	192
C$_7$			
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, Et$_2$O, <0° 3. Xylenes, 140°, 2.5 h	**I** (74)	4, 6
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, Et$_2$O, <0° 3. Hg(O$_2$CCF$_3$)$_2$ (30 mol%), THF, rt, 4 h	**I** (<5)[d]	4, 6

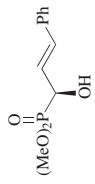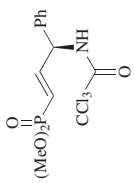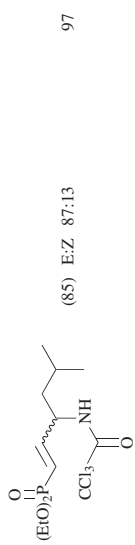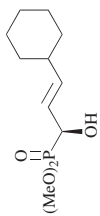| Reactant	Conditions	Product	Yield	Refs.
(heptenol, OH)	1. NaH (cat.), Et₂O 2. Cl₃CCN, Et₂O, <0° 3. Xylenes, 140°, 2.5 h	(CCl₃, NH, O)	(—)	72, 172
(t-Bu vinyl carbinol, OH)	1. KH (cat.) 2. Cl₃CCN 3. Xylenes, 140° 4. NaOH 5. (Boc)₂O	Boc-N-H	(68)	191
SiMe₃ (OH)	1. KH (cat.) 2. Cl₃CCN 3. Xylenes, 140° 4. NaOH 5. (Boc)₂O	Boc-N-H, SiMe₃	(52)	191
(diene, OH)	1. KH (cat.), 18-crown-6, Et₂O 2. Cl₃CCN, Et₂O, –15° to rt 3. Xylenes, 140°, 12 h	CCl₃, N, H, O	(89)	51
(dienol, OH)	1. KH (cat.), THF 2. Cl₃CCN, Et₂O, 0° to rt 3. Xylenes, 140°, 8 h	HN, CCl₃	(67)	193
MeN (OH)	1. NaH (cat.) 2. Cl₃CCN 3. [K₂CO₃], PhCl, 135°, 15 h	MeN, O, CCl₃, HN	*without K₂CO₃* (28) *with K₂CO₃* (52)	71
BnN (OH)	1. DBU, Cl₃CCN 2. K₂CO₃, PhCl, 135°, 5 h	BnN, O, CCl₃, HN	(85)	71

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_7			
	1. DBU, Cl$_3$CCN 2. Xylene, 140°	(—)	22
C_8			
	1. NaH (cat.), Et$_2$O 2. Cl$_3$CCN, Et$_2$O, –5° 3. PdCl$_2$(PhCN)$_2$ (5 mol%), THF, 1.5-3 h	(46)	28
	1. KH (cat.) 2. Cl$_3$CCN 3. Xylenes, 140° 4. NaOH 5. (Boc)$_2$O	(34)	191
	1. DBU, Cl$_3$CCN 2. Toluene, 110°, 20 h	**I** (92)^a 82% ee	29
	1. DBU, Cl$_3$CCN 2. PdCl$_2$(PhCN)$_2$ (10 mol%), benzene, rt	**I** (72)^a 88% ee	29

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₈			
	1. *n*-BuLi, THF, −78° 2. F₃CCN, −78° to rt 3. Xylenes, 140°, 20 h	(53)	75, 76
	1. NaH (cat.), Et₂O 2. Cl₃CCN, Et₂O, < −5° to rt 3. Toluene, 110°, 3 h	(75)	194
	1. NaH (cat.), Et₂O 2. Cl₃CCN, Et₂O, < 0° 3. Xylenes, 140°, 2.5 h	(61)	6
	1. DBU (1.2 eq.), Cl₃CCN, CH₂Cl₂, 0° to rt 2. K₂CO₃, *p*-Xylene, 140°	(74)	50
C₉			
	1. KH (cat.) 2. Cl₃CCN 3. Xylenes, 140° 4. NaOH 5. (Boc)₂O	(38)	191
	1. NaH (cat.), Et₂O, rt, 15 min 2. Cl₃CCN, −5°, 15 min 3. Toluene, 110°, 8 h	(48)	28
	1. NaH (cat.), Et₂O, rt, 15 min 2. Cl₃CCN, −5°, 15 min 3. PdCl₂(PhCN)₂ (4-5 mol%), THF, rt, 1.5-3 h	**I** (67)	28

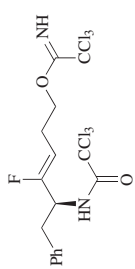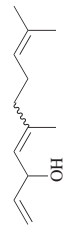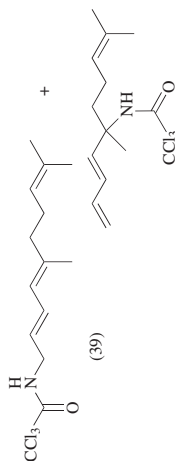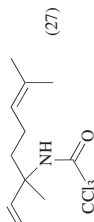| Substrate	Conditions	Product	Yield (%)
(starting allylic alcohol, acetonide)	1. NaH (cat.), Et$_2$O, rt, 15 min 2. Cl$_3$CCN, −5°, 15 min 3. PdCl$_2$(PhCN)$_2$ (4-5 mol%), THF, rt, 1.5-3 h	(44) CCl$_3$ trichloroacetamide product	28
(starting allylic alcohol, acetonide)	1. NaH (cat.), Et$_2$O, rt, 15 min 2. Cl$_3$CCN, −5°, 15 min 3. PdCl$_2$(PhCN)$_2$ (4-5 mol%), THF, rt, 1.5-3 h	(46) CCl$_3$ trichloroacetamide product	28
(EtO)$_2$P(=O) allylic alcohol	1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, −35°, 45 min 2. Toluene, 110°, 14 h	(80) CCl$_3$ product	97
(MeO)$_2$P(=O) furyl allylic alcohol	1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, −35°, 45 min 2. NIS, CH$_2$Cl$_2$, rt, 24 h	(65)[a] CCl$_3$ product	66
(MeO)$_2$P(=O) cyclohexenyl allylic alcohol	1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, −35°, 45 min 2. Toluene, 110°, 11 h	(83) E:Z 87:13 CCl$_3$ product	97
OBOM pyrrolidine-Boc allylic alcohol	1. n-BuLi (cat.), THF, 0° 2. F$_3$CCN, −78° to rt 3. Xylenes, 140°, 7 h	(30) CF$_3$ product	75

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_9$	1. *n*-BuLi (20 mol%) 2. F$_3$CCN, THF, −78° 3. Xylene, 140°	(92)	60
	1. DBU, Cl$_3$CCN 2. Xylenes, 140°	(—)	22
X = F, Cl			
C$_{10}$	1. NaH (cat.), Et$_2$O, rt, 15 min 2. Cl$_3$CCN, −5°, 15 min 3. Toluene, 110°, 8 h	(70)	20
	1. DBU, Cl$_3$CCN 2. NBS (1 eq.), CHCl$_3$, 24 h	(71)^d	66
	1. KH (cat.), THF 2. Cl$_3$CCN, THF, <0° 3. Xylenes, 140°	(49.5)	65
	1. DBU, Cl$_3$CCN 2. NBS (1 eq.), CHCl$_3$, 24 h	(55)$^{d, e}$	66

65

25

21

22

193

50

o (18.1)
m (15.5)
p (31.1)

(≈57)*f*

(>57)*g*

(—)

(68)

(70)

1. KH (cat.), THF
2. Cl₃CCN, THF, <0°
3. Xylenes, 140°

1. DBU, Cl₃CCN, CH₂Cl₂, –60°, 3 h
2. Xylenes, 140°, 12 h

1. DBU, Cl₃CCN, CH₂Cl₂, –78°, 1 h
2. Xylenes, 140°, 4 h

1. DBU, Cl₃CCN
2. Xylenes, 140°

1. KH (cat.), THF
2. Cl₃CCN, Et₂O, 0°
3. Xylenes, 140°, 8 h

1. DBU (20 mol%), Cl₃CCN,
   CH₂Cl₂, 0° to rt
2. Toluene, 110°

C₁₁

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{11}			
(TrO, Ph, OH structure)	1. DBU (20 mol%), Cl_3CCN, CH_2Cl_2, 0° to rt 2. Toluene, 110°	(72)	50
(TrO, aryl-R, OH structure)	1. DBU (20 mol%), Cl_3CCN, CH_2Cl_2, 0° to rt 2. Toluene, 110°	$\dfrac{\text{R}}{\begin{array}{l}o\text{-Br (71)}\\p\text{-Cl (68)}\\p\text{-F (81)}\end{array}}$	50
(TrO, cyclohexyl, OH structure)	1. DBU (1.2 eq.), Cl_3CCN, CH_2Cl_2, 0° to rt 2. K_2CO_3, p-Xylene, 140°	(66)	50
(OMOM, Ph, OTBDPS, OH structure)	1. NaH (cat.), Et_2O 2. Cl_3CCN, Et_2O, −5° to rt 3. Xylenes, 140°, 6 h	(70)	119
((MeO)$_2$P(O), Ph, OH structure)	1. DBU, Cl_3CCN, CH_2Cl_2, −35°, 30 min 2. Toluene, 110°, 24 h	(90) E:Z 90:10	97
((MeO)$_2$P(O), Ph, OH structure)	1. DBU, Cl_3CCN 2. NBS (1 eq.), $CHCl_3$, 24 h	(91)[a]	66

80

66

97

195

21

196

$(89)^a$

(85) E:Z 87:13

(—)

$(>59)^g$

(—)

Ph

O

O

N

n-Pr

CCl$_3$

O

HN

CCl$_3$

MOMO

n-Bu

HN

CCl$_3$

O

Ph

NH$_2$

(MeO)$_2$P

O

NH

O

CCl$_3$

(EtO)$_2$P

O

NH

O

CCl$_3$

1. DBU, Cl$_3$CCN
2. NBS (1 eq.), CHCl$_3$, 24 h

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$,
   –35°, 40 min
2. Toluene, 110°, 21 h

1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, 0°
2. Xylenes, 140°

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, –78°, 1 h
2. Xylenes, 140°, 4-10 h

1. NaH (cat.), Et$_2$O, 0°
2. Cl$_3$CCN, Et$_2$O
3. Xylenes, 140°, 14 h
4. NaOH (6 N), EtOH

(MeO)$_2$P

O

OH

(EtO)$_2$P
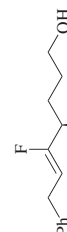
O

OH

Ph

O

O

N

n-Pr
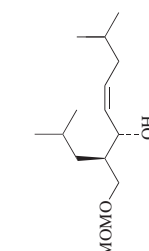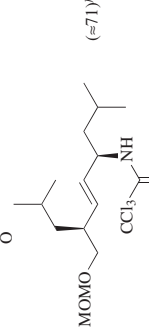
OH

C$_{12}$

MOMO

OH

Ph

OH

81

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (Continued)

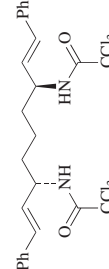| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{12}			
(Ph, cyclopropyl, OH)	DBU (cat.), Cl_3CCN, Et_2O, 0° to rt, 4 h	(93)	114
(TrO, CF_3-aryl, OH)	1. DBU (20 mol%), Cl_3CCN, CH_2Cl_2, 0° to rt 2. Toluene, 110°	(69)	50
(PhS, OH)	1. KH (cat.) 2. Cl_3CCN 3. Ethyl acetate, 77°, 12 h	(100)	51
(MOMO, OH)	1. DBU, Cl_3CCN, CH_2Cl_2, −60°, 3 h 2. Xylenes, 140°, 12 h	(≈68)^f	25
(F, Ph, OH)	1. NaH (cat.), THF 2. Cl_3CCN (2 eq.), Et_2O 3. Xylenes, 140°	(73)	67, 183
(OH)	1. KH (cat.), THF 2. Cl_3CCN, Et_2O, −5° to 0° 3. rt	(39) + (27)	6

82

97

23

23

23

44

114

(89) E:Z 86:14

(100)^a

(—)

(—)

(81)

(64)

OMe

Bn

OMe

Bn

Ph

Ph

THPO

Ph

n-Pr

n-Pr

n-Pr

CCl$_3$

CCl$_3$

CCl$_3$

CCl$_3$

CCl$_3$

NH

HN

HN

HN

HN

N

N

O

O

O

O

O

O

O

O

O

O

O

H

(i-PrO)$_2$P

(i-PrO)$_2$P

THPO

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, −35°, 55 min

2. Toluene, 110°, 19 h

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, rt

2. Xylenes, 140°, 18 h

1. DBU, F$_3$CCN, CH$_2$Cl$_2$, −196° to rt

2. Xylenes, 140°, 18 h

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, rt

2. Xylenes, 140°, 18 h

1. NaH (cat.), Et$_2$O, 0°

2. Cl$_3$CCN, 0° to rt

3. Xylenes, 140°, 2 h

1. KH (cat.), Cl$_3$CCN, 0° to rt

2. Toluene, 110°

OMe

Bn

Ph

Ph

n-Pr

n-Pr

n-Pr

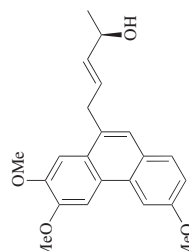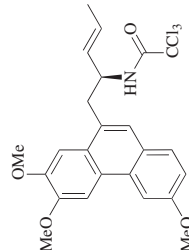THPO

OH

OH

OH

OH

OH

OH

O

N

N

O

O

O

C$_{13}$

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

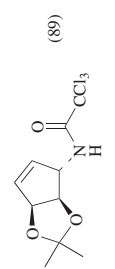| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_{13}	1. NaH (cat.), Et_2O, 0° 2. Cl_3CCN, Et_2O 3. Xylenes, 140°, 14 h 4. NaOH, EtOH	(67)	196
	1. KH (cat.), Cl_3CCN, 0° to rt 2. Toluene, 110°	(90)	114
	1. DBU (1.2 eq.), Cl_3CCN, CH_2Cl_2, 0° to rt 2. K_2CO_3, *p*-xylene, 140°	(68)	50
	1. KH (cat.), Cl_3CCN, 0° to rt 2. Toluene, 110°	(66)	114
	1. NaH (cat.), Et_2O, 0° 2. Cl_3CCN, Et_2O 3. Xylenes, 140°, 14 h 4. NaOH, EtOH	(83)	196
	1. NaH 2. Cl_3CCN 3. Xylenes, 140°	(73)	197
	1. DBU, Cl_3CCN, CH_2Cl_2, –60°, 3 h 2. Xylenes, 140°, 12 h	(≈71)^f	25

22

21

114

21

26

114

(—)

(>66)^g

(96)

(>93)^f

(81)

(83)

1. DBU, Cl$_3$CCN
2. Xylenes, 140°

1. DBU, Cl$_3$CCN, –78°, 1 h
2. Xylenes, 140°, 4 h

1. KH (cat.), Cl$_3$CCN, 0° to rt
2. Toluene, 110°

1. DBU, Cl$_3$CCN, –78°, 1 h
2. Xylenes, 140°, 4 h

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, –5°
2. Xylenes, 140°, 7 h

1. KH (cat.), Et$_2$O, rt, 15 min
2. Cl$_3$CCN, Et$_2$O, 0° to rt
3. Toluene, 110°, 1-2 h

C$_{15}$

C$_{18}$

C$_{19}$

TABLE 2A. REARRANGEMENTS OF TRIHALOACETIMIDATES OF ACYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_{21}$	1. KH (cat.), Et$_2$O, rt, 15 min 2. Cl$_3$CCN, Et$_2$O, 0° to rt 3. Toluene, 110°, 1-2 h	(65)^h	114
C$_{22}$	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, 0°, 2 h 2. Toluene, 110°, 12 h	(92)	198

^{a} This is the yield for rearrangement only.

^{b} This is the NMR yield; elimination was the major reaction.

^{c} Product was obtained in 86% crude yield on a 4 gram scale.

^{d} This is the NMR yield.

^{e} Rearrangement of the Z isomer gave 71% yield of the 5-exo-oxazoline halocyclization product.

^{f} Attempted catalysis with Pd(II) or Hg(II) led only to low (≈20-30%) yields of the desired product accompanied by diene formation from elimination of trichloroacetamide.

^{g} Attempted catalysis with Pd(II) or Hg(II) led only to diene formation from elimination of trichloroacetamide.

^{h} Standard rearrangement conditions led to recovery of 27% of the mono trichloroacetamide, which was recycled to provide a 65% combined yield of the desired bis(allylic trichloroacetamide).

TABLE 2B. REARRANGEMENTS OF TRIHALOACETIMIDATES OF CYCLIC SECONDARY ALLYLIC ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₅	1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Xylene, 140°	(80)[a]	123
	1. DBU, Cl₃CCN, CH₂Cl₂, 0°, 10 min 2. Xylenes, 140°, 4 h	(89)	73, 74
C₆	1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Xylene, 140°	(69)	4, 6, 72, 93, 113, 199
	1. NaH (cat.), Et₂O 2. Cl₃CCN 3. Hg(O₂CCF₃)₂ (30 mol%), THF, 0° to rt, 1 h	I I (<5)[b]	4, 6
	1. DBU, Cl₃CCN, THF, rt, 1.5 h 2. K₂CO₃, xylene, 140°, 18 h	(95)[c] 95% ee	82, 200
	1. KH, Cl₃CCN, THF, rt, 1.5 h 2. Xylene, 140°, 4 h	(92)	201
	1. NaH (cat.) 2. Cl₃CCN (2 eq.), THF, 0° to rt 3. Xylene, 140°, 6 h	(56)	167

87

TABLE 2B. REARRANGEMENTS OF TRIHALOACETIMIDATES OF CYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

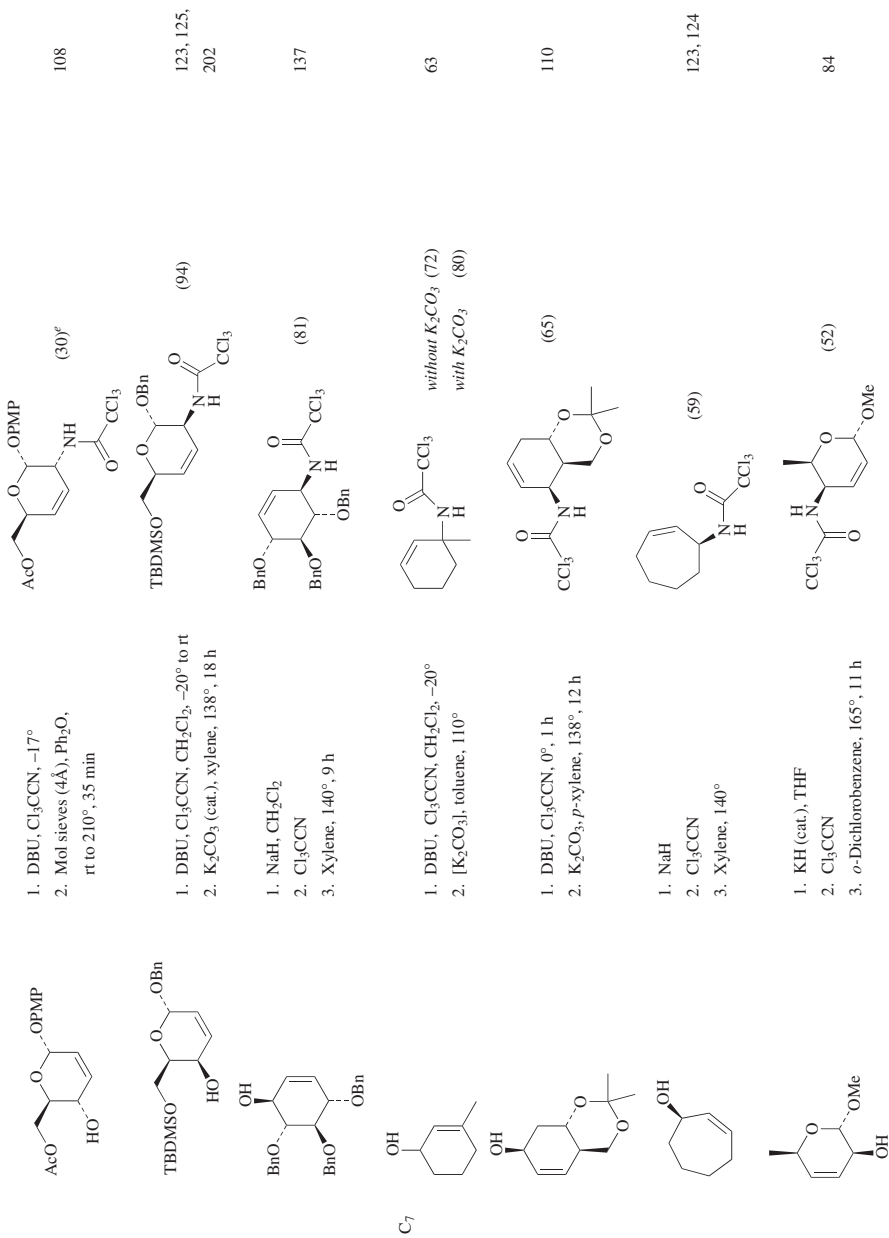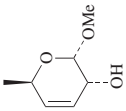| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C₆			
	1. NaH (cat.) 2. Cl₃CCN, Et₂O, 0°	(78)	88
	1. KH (cat.) 2. Cl₃CCN, –10° to rt 3. *o*-Dichlorobenzene, 165°, 8 h	(50)	85
	1. NaH 2. Cl₃CCN 3. Xylene, 138°	(80)	86
	1. NaH 2. Cl₃CCN 3. Xylene	(—)[d]	86
	1. NaH, CH₂Cl₂, rt 2. Cl₃CCN, CH₂Cl₂, 0° 3. *o*-Dichlorobenzene, 160°, 5 h	(68)	45
	1. DBU, CH₂Cl₂, 0° 2. Cl₃CCN, 0° 3. [K₂CO₃], *p*-xylene, 138°	*with or without* K₂CO₃ (85)	63, 93, 111, 202
	1. DBU, Cl₃CCN, –17° 2. Mol sieves (4Å), Ph₂O, rt to 210°, 35 min	(25)	108

C$_7$

1. DBU, Cl$_3$CCN, –17°
2. Mol sieves (4Å), Ph$_2$O,
   rt to 210°, 35 min

(30)^e

108

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, –20° to rt
2. K$_2$CO$_3$ (cat.), xylene, 138°, 18 h

(94)

123, 125, 202

1. NaH, CH$_2$Cl$_2$
2. Cl$_3$CCN
3. Xylene, 140°, 9 h

(81)

137

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, –20°
2. [K$_2$CO$_3$], toluene, 110°

without K$_2$CO$_3$ (72)
with K$_2$CO$_3$ (80)

63

1. DBU, Cl$_3$CCN, CH$_2$Cl$_2$, –20°
2. K$_2$CO$_3$, *p*-xylene, 138°, 12 h

(65)

110

1. NaH
2. Cl$_3$CCN
3. Xylene, 140°

(59)

123, 124

1. KH (cat.), THF
2. Cl$_3$CCN
3. *o*-Dichlorobenzene, 165°, 11 h

(52)

84

89

TABLE 2B. REARRANGEMENTS OF TRIHALOACETIMIDATES OF CYCLIC SECONDARY ALLYLIC ALCOHOLS (*Continued*)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_7$			
	1. KH (cat.), THF 2. Cl$_3$CCN 3. o-Dichlorobenzene, 165°, 6 h	(64)	84
	1. KH, CH$_2$Cl$_2$ 2. Cl$_3$CCN, –10° 3. o-Dichlorobenzene, 165°	(11)	85
	1. KH, CH$_2$Cl$_2$ 2. Cl$_3$CCN, –10° 3. o-Dichlorobenzene, 165°	(70)	85
	1. KH, CH$_2$Cl$_2$ 2. Cl$_3$CCN, –10° 3. o-Dichlorobenzene, 165°	(52)	85
	1. KH, CH$_2$Cl$_2$ 2. Cl$_3$CCN, –10° 3. o-Dichlorobenzene, 165°	(18)^f	85
	1. DBU (1.2 eq.), Cl$_3$CCN, CH$_2$Cl$_2$, –20° to rt 2. K$_2$CO$_3$, Ph$_2$O, 195°, 3 h	(63)	125

C_8

1. NaH (cat.), Et_2O
2. Cl_3CCN, Et_2O, –30° to –10°
3. Xylene, 133°, 6 h

(54)^g

203

1. NaH, CH_2Cl_2, 0°
2. Cl_3CCN, 0°, 6 h
3. K_2CO_3, o-dichlorobenzene, heat, 2 h

(46)

204

1. DBU, Cl_3CCN, CH_2Cl_2, 0°
2. [K_2CO_3], o-dichlorobenzene, 165°

without K_2CO_3   (7)
with K_2CO_3   (56)

63

C_9

1. DBU, Cl_3CCN, CH_2Cl_2, –20°
2. [K_2CO_3], toluene, 110°

without K_2CO_3   (10–43)
with K_2CO_3   (19)

4, 6
63, 93

1. NaH (cat.), Et_2O
2. Cl_3CCN
3. Hg(O_2CCF_3)_2 (20 mol%), THF, 0° to rt, 1 h

I   (20)^h

4
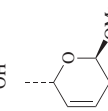
1. DBU (1 eq.), Cl_3CCN, CH_2Cl_2, 0°
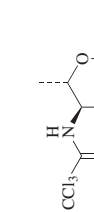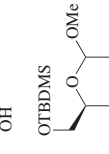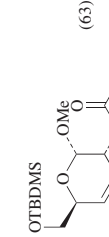2. o-Dichlorobenzene, 180°, 5 h

(69)

111

TABLE 2B. REARRANGEMENTS OF TRIHALOACETIMIDATES OF CYCLIC SECONDARY ALLYLIC ALCOHOLS (Continued)

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C10			
	1. DBU, Cl3CCN 2. K2CO3, xylene, heat	(75)[j]	93
	1. DBU, Cl3CCN 2. K2CO3, xylene, heat	(71)	93, 123, 202
	1. KH (cat.), Et2O 2. Cl3CCN, Et2O, −15° to 0°, 1.5 h 3. Toluene, 110°, 10 h	(35)	20
	1. KH (cat.), Et2O 2. Cl3CCN, Et2O, −15° to 0°, 1.5 h 3. Xylene, 140°, 8 h	(42)	20
	1. NaH (cat.), THF 2. Cl3CCN, Et2O, −5° to 0° 3. Hexane, 69°, 5 d	(20)	6, 5

92

205

70

70

108

(62)

(29)

(76)

(8)

C_{11-13}

1. NaH, Et_2O
2. Cl_3CCN
3. Toluene, 170°, 20 h

1. NaH, CH_2Cl_2
2. Cl_3CCN, rt, 24 h
3. Xylene, 140°, 24 h

1. NaH, CH_2Cl_2
2. Cl_3CCN, rt, 2.5 h
3. DMF, 140°, 6 h

1. DBU, Cl_3CCN, CH_2Cl_2, −17°, 15 min
2. Mol sieves (4Å), Ph_2O, 210°

TABLE 2B. REARRANGEMENTS OF TRIHALOACETIMIDATES OF CYCLIC SECONDARY ALLYLIC ALCOHOLS *(Continued)*

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
	1. NaH (cat.), THF, 0° 2. Cl_3CCN, 0° to rt, 2 h 3. 0.05-0.1 mm Hg, 100-105°, 1.2 h	(41)	56
C_{18}	1. NaH (cat.), THF, 66° 2. Cl_3CCN, THF, 0° to rt 3. Xylene, 160-170°, 3 h	(76)	206

[a] Previous reports[113] noted this substrate failed to rearrange successfully under similar conditions.

[b] NMR yield for rearrangement only.

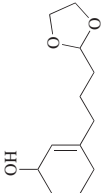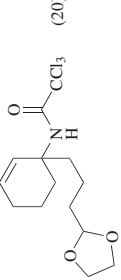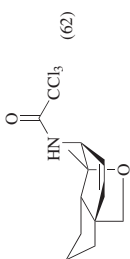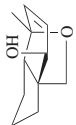[c] The (1S)-all-cis isomer did not successfully rearrange, giving instead a 34% yield of recovered acetimidate.

[d] This rearrangement was reported to be slow due to steric congestion in the transition state.

[e] The yield is 54% based on consumed imidate.

[f] Fifteen percent of the starting material was recovered.

[g] The β-epimer is incorrectly shown in paper; see *Tetrahedron*, **1981**, *37*, 4391.

[h] Yield for rearrangement only.

[i] Rearrangement of the enantiomer is reported.[123,202]

TABLE 3. REARRANGEMENTS OF TRIHALOACETIMIDATES OF TERTIARY ALLYLIC ALCOHOLS

Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C$_5$ [structure: OH]	1. NaH (cat.), THF 2. Cl$_3$CCN, Et$_2$O, <20°, 1 h 20 min 3. Toluene, 110°, 1 h	[structure: O=C–CCl$_3$ N–H amide] (71–82)	52, 72
C$_7$ [structure: cyclopentane with vinyl, OH]	1. NaH (cat.), THF 2. Cl$_3$CCN, Et$_2$O, <20° ^{a}	[structure H–N–CCl$_3$] (5)	52
C$_8$ [structure: cyclohexane with vinyl, OH]	1. KH (cat.), THF, rt 2. Cl$_3$CCN, Et$_2$O, –5° to 0°, 1.5 h 3. Benzene, 80°, 2 h	**I** [structure] (57)^b	6
	1. KH (cat.), THF, rt 2. Cl$_3$CCN, Et$_2$O, –5° to 0°, 1.5 h 3. Hg(O$_2$CCF$_3$)$_2$ (30 mol%), THF, rt, 4 h	**I** (<2)^c	6
[sugar structure with OH, D, H]	1. NaH 2. Cl$_3$CCN 3. Xylene, 140°, 36 h	[sugar structure with CCl$_3$, HN, D] (86)	53, 54
[sugar structure with OH, D, H]	1. NaH 2. Cl$_3$CCN 3. Xylene, 140°, 36 h	[sugar structure with CCl$_3$, HN, D] (—)	53, 54

TABLE 3. REARRANGEMENTS OF TRIHALOACETIMIDATES OF TERTIARY ALLYLIC ALCOHOLS (*Continued*)

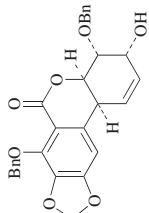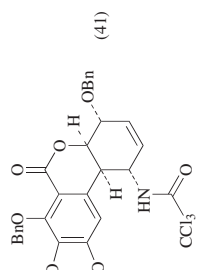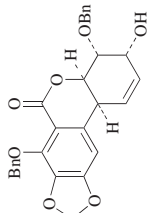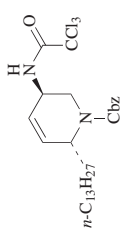| Substrate	Conditions	Product(s) and Yield(s) (%)	Refs.
C_9			
	1. NaH 2. Cl₃CCN 3. Xylene, 138°, 36 h	(≈68)	18, 53, 54, 207
	1. NaH 2. Cl₃CCN 3. Xylene, 138°, 36 h	(68)	18, 53, 54, 207
C_{10}	1. KH, THF 2. Cl₃CCN, Et₂O, –5° to 0°, 1.5 h 3. Benzene, 80°, 2 h	(83) E:Z = 60:40	6, 72, 208

[a] Imidate rearranged upon workup.

[b] The yield is 67% based on recovered starting material.

[c] This is the NMR yield; elimination was the major reaction.

TABLE 4. TRANSITION-METAL-CATALYZED ASYMMETRIC REARRANGEMENTS OF ALLYLIC TRIHALOACETIMIDATES

Refer to the chart at the beginning of the Tabular Survey for catalyst (bold numbers) structures.

Substrate	Conditions	Product(s), Yield(s) (%)^a, and % ee	Refs.
C$_4$	1. NaH, THF, 0° 2. p-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), i-Pr$_2$NEt (20 mol%), CH$_2$Cl$_2$, rt, 30 h	(90), 73	8
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, rt, 18 h	(84), 80	7
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, 38°, 18 h	(98), 96	7
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. *ent*-**1** (5 mol%), CH$_2$Cl$_2$, rt	(98), 96	7
C$_6$	1. DBU, Cl$_3$CCN 2. **5** (10 mol%), ClCH$_2$CH$_2$Cl, rt, 7 d	(4), 13^b	104
	1. NaH (cat.), Cl$_3$CCN, Et$_2$O 2. **6** (5 mol%), CH$_2$Cl$_2$, 40°	(20), 5	38, 102
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **6** (5 mol%), CH$_2$Cl$_2$, 40°, 6 d	(50), 43^b	39

TABLE 4. TRANSITION-METAL-CATALYZED ASYMMETRIC REARRANGEMENTS OF ALLYLIC TRIHALOACETIMIDATES (*Continued*)

Substrate	Conditions	Product(s), Yield(s) (%)[a], and % ee	Refs.
C$_6$			
(structure, OH)	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, temp, 18 h	**I** Temp rt (80), 94 38° (99), 95	7
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), THF, 50°, 8 h	**I** (94), 91	9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (1 mol%), MeCN, 50°, 22 h	**I** (91), 91	9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **3** (1 mol%), THF, 50°, 8 h	**I** (91), 95	9
(structure, OH)	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, 38°, 18 h	(17), 71	7
	1. NaH, THF, 0° 2. *p*-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), 1,8-bis(dimethylamino)-naphthalene, CH$_2$Cl$_2$, rt, 36 h	(71), 94	8
	1. NaH, THF, 0° 2. *p*-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), 1,8-bis(dimethylamino)-naphthalene, CH$_2$Cl$_2$, 23°, 36 h	(84), 84	8
(structure, AcO ... OH)	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, temp, 18 h	**I** Temp rt (74), 92 38° (97), 92	7

Substrate	Conditions	Product	Ref.
(structure: OH chain with 1,3-dioxolane)	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), THF, 50°, 8 h	**I** (95), 92	9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (1 mol%), MeCN, 50°, 24 h	**I** (93), 93	9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, rt, 18 h	**I** (structure with CCl$_3$, C=O, HN) (85), 95	7
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), THF, 50°, 9 h	**I** (80), 91	9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (1 mol%), MeCN, 50°, 29 h	**I** (86), 93	9
Bn–N(Boc) substrate with OH	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, temp, 18 h	(structure: Bn–N(Boc), CCl$_3$, C=O, HN) Temp rt (87), 95 38° (96), 95	7
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (1 mol%), CH$_2$Cl$_2$, 38°, 18 h	(92), 98	7
C$_7$ substrate with OH	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **2** (5 mol%), i-Pr$_2$NEt (20 mol%), CH$_2$Cl$_2$, rt, 30 h	**I** (structure with CCl$_3$, C=O, HN) (80), 92	8

TABLE 4. TRANSITION-METAL-CATALYZED ASYMMETRIC REARRANGEMENTS OF ALLYLIC TRIHALOACETIMIDATES (*Continued*)

Substrate	Conditions	Product(s), Yield(s) $(\%)^a$, and $\%$ ee	Refs.
C$_7$			
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), THF, 50°, 8 h		9
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (1 mol%), MeCN, 50°, 29 h	**I** (95), 95	9
	1. NaH, THF, 0° 2. p-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **1** (5 mol%), CH$_2$Cl$_2$, rt, 60 h	(88), 94	8
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, 38°, 18 h	(8), 73	7
	1. NaH, THF, 0° 2. p-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **1** (5 mol%), CH$_2$Cl$_2$, rt, 60 h	(58), 90	8
	1. NaH, THF, 0° 2. p-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), 20 mol % i-Pr$_2$NEt, CH$_2$Cl$_2$, rt, 30 h	**I** (67), 97	8
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **1** (5 mol%), CH$_2$Cl$_2$, 38°, 18 h	$(7)^c$	7

100

Substrate	Conditions	Product		Refs.
MeO₂C⟋⟋OH	1. DBU (cat.), Cl₃CCN, CH₂Cl₂, rt 2. **1** (5 mol%), CH₂Cl₂, rt, 18 h	MeO_2C ... CCl_3 NH	(73), 95	7
⟋OH (with O)	1. DBU (cat.), Cl₃CCN, CH₂Cl₂, rt 2. **1** (5 mol%), CH₂Cl₂, temp, 18 h	CCl_3 HN	Temp rt (80), 94 38° (98), 95	7
C₉ cyclohexyl-OH	1. DBU (cat.), Cl₃CCN, CH₂Cl₂, rt 2. **1** (5 mol%), CH₂Cl₂, 38°, 18 h	CCl_3 HN	(82), 96	7
C₁₁ Ph⟋OH	1. DBU (cat.), Cl₃CCN, CH₂Cl₂, rt 2. **1** (5 mol%), CH₂Cl₂, temp, 18 h	CCl_3 HN ... Ph	Temp rt (83), 96 38° (93), 93	7
Ph⟋OH	1. NaH, THF, 0° 2. p-MeOC₆H₄N=C(Cl)CF₃ 3. **1** (5 mol%), CH₂Cl₂, rt, 60 h	CF_3 O Ar–N ... Ph	(86), 93	8

TABLE 4. TRANSITION-METAL-CATALYZED ASYMMETRIC REARRANGEMENTS OF ALLYLIC TRIHALOACETIMIDATES (*Continued*)

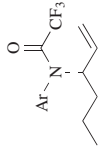| Substrate	Conditions	Product(s), Yield(s) (%)[a], and % ee				Refs.
C11						
Ph⌒⌒⌒OH	1. NaH, THF, 0° 2. *p*-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), *i*-Pr$_2$NEt (20 mol%), CH$_2$Cl$_2$, rt, 30 h	(80), 88				8
	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), solvent, 50°, time	Solvent	Time	% ee		9
		THF	6 h (93)	96		
		cyclohexane	12 h (88)	95		
		toluene	15 h (85)	97		
		acetone	9 h (95)	96		
		acetonitrile	9 h (93)	92		
Ph⌒⌒⌒OH	1. NaH, THF, 0° 2. *p*-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **1** (5 mol%), CH$_2$Cl$_2$, temp, 60 h	**I**	Temp			8
			rt (77), 97			
			38° (99), 96			
	1. NaH, THF, 0° 2. *p*-MeOC$_6$H$_4$N=C(Cl)CF$_3$ 3. **2** (5 mol%), *i*-Pr$_2$NEt (20 mol%), CH$_2$Cl$_2$, rt, 60 h	**I** (76), 96				8
C12						
Bn$_2$N(CH$_2$)$_9$⌒⌒OH	1. DBU (cat.), Cl$_3$CCN, CH$_2$Cl$_2$, rt 2. **4** (5 mol%), THF, 50°, 9 h	(98), 92				9

[a] Yields are for the rearrangement step only.

[b] Absolute configuration is not reported.

[c] Neither enantiomer excess nor configuration was determined.

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