**Synthesis of α-Allenic Esters (Acids)**

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**Abstract:** This article focuses on the synthesis of α-allenic esters (or alkane-2,3-dienoates) and their corresponding acids, but does not claim to present all of the synthetic methods of this type of compounds. A brief account dealing with the asymmetric synthesis of α-allenic esters is also presented.

1 **Introduction**

α-Allenic esters (acids) are valuable synthetic targets because they represent important building blocks for several purposes including the total synthesis of biologically active compounds. On the other hand, their reactivity, enhanced by the electron-withdrawing groups, makes these compounds valuable candidates to explore a large panel of reactions such as reactions with nucleophiles and cycloaddition reactions ([2+2], Diels–Alder, 1,3-dipolar cycloadditions etc.). Despite many reviews and papers dealing with allenes, the synthesis of α-allenic esters (acids) has received little attention. This article will present the principle methods giving access to α-allenic esters (acids) as well as a brief account of the most recent methodologies developed for the asymmetric synthesis of α-allenic esters (acids).

2 **Synthesis of α-Allenic Esters (Acids)**

2.1 **From Propargyl Derivatives**

In 1950, Wotiz reported that the Grignard reagent derived from propargyl bromides could be carbonated with dry ice in modest yields to give α-allenic acids contaminated with the corresponding acetylenic derivatives. These reaction conditions did not allow the preparation of pure butane-2,3-dienoic acid, but the latter could be isolated in nearly quantitative yield by isomerization of but-3-ynoic acid with dilute ethanolic potassium carbonate solution. The same reaction could be carried out with the corresponding acetylenic ester leading this time to an α-allenic ester in modest yield (Scheme 1).

![Scheme 1](image)

Transition metal-mediated carbonylation reactions have been applied to propargyl chlorides (bromides) to generate α-allenic acids (esters). For example, Ni(CO)₄ was used as a catalyst in the early 1950s. More recently, a very efficient conversion of α-haloalkynes into α-allenic acids in the presence of Ni(CN)₃ under phase-transfer conditions was reported (Scheme 2).

![Scheme 2](image)
It has also been shown that propargyllithium alanates or lithium borates react with gaseous carbon dioxide to yield α-allenic esters slightly contaminated with the corresponding acetylenic derivatives. Another metalation reaction was carried out on allyl 1-methoxycarbonyl propargyl ethers with t-BuLi or LDA to afford, after addition of methanol, α-allenic esters (Scheme 4).

More recently, the preparation of monocarboxylate surrogates of allenic dicarboxylates (diesters) was achieved via a base-catalyzed isomerization of propargyl esters (Scheme 5).

2.2 From Palladium-Catalyzed Reactions of Propargyl Compounds

In 1986, Tsuji et al. reported that propargyl carbonates could undergo smooth palladium-catalyzed decarboxylation-carbonylation reactions to give allenylpalladium complexes which react with carbon monoxide in alcohol to exclusively afford α-allenic esters (Scheme 6).

Consequently, the palladium(0)-catalyzed reaction was applied to several different substrates including allenyl and propargyl halides, tertiary propargyl alcohols using a Pd(II) complex, cyclic alkynyl carbonates, propargyl mesylates, alkynyl oxiranes, and alkynyl dioxolanones (Scheme 7).

The availability of propargyl derivatives makes the palladium-catalyzed reaction a method of choice for the synthesis of α-allenic esters and thus, promotes their synthetic utility.

2.3 From Horner–Wadsworth–Emmons and Wittig Reactions

In 1961, Wadsworth and Emmons showed that α-allenic esters can be prepared by treating a phosphonate carbanion with a ketene. Two years later, Bestmann et al. reported that acid chlorides reacted with resonance-stabilized phosphorane in the presence of a second equivalent of phosphorane to give α-allenic esters in good yields. These first results were followed by numerous articles in which the reactivity of ketenes and acid chlorides toward Wittig and Horner–Wadsworth–Emmons reagents were extensively studied. For example, ketene, trimethylsilylketene as well as bis(alkoxy carbonyl)ketenes underwent an olefination reaction with stabilized phosphorus ylides to give the corresponding α-allenic ester (Scheme 8).

Very often the Wittig reaction was used, and the substitution of the phosphoranes (or phosphonium salts) as well as the substitution of the acid chlorides were extensively studied in order to obtain functionalized α-allenic esters. For example, mono and dialkyl-N-phthalimidyl.
alkenyl-, 25 α-(phenylchalcogeno)acid chlorides 26 as well as bromoylides 27 were utilized (Scheme 9).

On the other hand, in order to avoid the use of ketenes (and of acyl chlorides), acids activated with halogenopyridium salts 28 or as BHT ester derivatives 29 were reacted with phosphonium salts and/or with phosphoranes to cleanly afford α-allenic esters (Scheme 10).

2.4 Sigmatropic Rearrangements

[3,3] Sigmatropic Rearrangement

Ester derived from prop-2-ynyl vinyl ether undergoes a Claisen rearrangement to yield α-allenic ester in good yield (Scheme 11).

[2,3] Sigmatropic Rearrangement

Thio-, 31 sulfinyl-, 31–33 sulfonyl-, 31,33 and phosphoryl-substituted 33 α-allenic esters were prepared starting from propargyl alcohols which undergo a [2,3] sigmatropic rearrangement after addition of the appropriate sulfonyl/ sulfinyl chloride or chlorophosphite (Scheme 12).

2.5 From Organometallic Reagents

The reaction of allenyl organometallic reagents with carbon dioxide yielded the corresponding α-allenic acids (Scheme 13). 34

2.6 From Acetylenic Derivatives

The isomerization of methyl tetrolate was achieved in the presence of lithium isopropylcyclohexylamine (LiICA) to yield the corresponding α-allenic ester. 35

However, these isomerization reactions cannot be efficiently applied to other substrates because further isomer-
ization could take place to give either nonconjugated acetylenic esters or dienes.\textsuperscript{37}

To eliminate this problem Franck-Neumann et al. showed that electrophilic acetylenes could be cleanly transformed into dicarbonyl(methylcyclopentadienyl)manganese complexes which underwent a base-catalyzed isomerization to give, exclusively after decomplexation, \(\alpha\)-allenic esters in good yields. No isomerization products were detected (Scheme 15).\textsuperscript{38}

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\text{Scheme 15}
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2.7 From \(\beta\)-Keto Esters and \(\omega\)-Keto Esters

\(\alpha\)-Allenic esters can be obtained from \(\beta\)-keto esters when the latter are treated with hydrazine (to give 5-pyrazolones) followed by an oxidation reaction [thallium(III) nitrate or lead(IV) tetracetate].\textsuperscript{39,40} The same reaction sequence was utilized to obtain cyclic allenic esters with a ring size of 9–12 carbon atoms (Scheme 16).\textsuperscript{41}

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\text{Scheme 16}
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We have reported that the treatment of acetylenic \(\omega\)-keto esters, bearing a three or four carbon–carbon bond spacer located between the cycloalkanone moiety and the electrophilic triple bond, with TBAF led to functionalized \(\alpha\)-allenic esters (Scheme 17).\textsuperscript{42,43}

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\text{Scheme 17}
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2.8 Via Flash Vacuum Thermolysis (FVT)

In order to obtain preparative amounts of methyl buta-2,3-dienoate, the pyrolysis of 3-methylene cyclobutane-1,2-dicarboxylate proved to be an efficient method (Scheme 18).\textsuperscript{44}

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\text{Scheme 18}
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The FVT of substituted trimethylsilyloxy butadiene yields \(\alpha\)-allenic acids after hydrolysis (Scheme 19).\textsuperscript{45}

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\text{Scheme 19}
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We have reported that the FVT of aminobicyclo[2.1.0]pentane derivatives led stereospecifically to macrocycles containing an \(E\)-double bond and an \(\alpha\)-allenic ester, the intermediate probably being a \(\beta\)-aminoacrylate (Scheme 20).\textsuperscript{46}

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\text{Scheme 20}
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Consequently, we have also shown that flash vacuum thermolysis of unsaturated \(\beta\)-amino esters smoothly led to \(\alpha\)-allenic esters without traces of the corresponding dienes (Scheme 21).\textsuperscript{47}

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\text{Scheme 21}
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2.9 From \(\text{gem}\)-Difluorocyclopropene

The synthesis of steroidal allenic esters was achieved by a formic acid hydrolysis of the \(\text{gem}\)-difluorocyclopropene group followed by the addition of 2-chloro-1,1,2-trifluoromethylamine to afford an allenic fluoride which was treated with sodium methoxide in methanol (Scheme 22).\textsuperscript{48}

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\text{Scheme 22}
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From Methylenecyclobutanone

The photolysis of methylenecyclobutenone in the presence of benzophenone or oxygen afforded an $\alpha$-allenic ester resulting from the cycloaddition reaction of the methoxyketene intermediate (Scheme 23).49

From Octafluoroisobutene

The cesium fluoride-catalyzed reaction of ethyl phenylacetate with octafluoroisobutene led to the corresponding 1,1-bis(trifluoromethyl)-3-phenyl-3-ethoxycarbonylallene in good yield and thus, expand the scope of the available methods for the synthesis of electrophilic allenes (Scheme 24).50

From $\alpha$-Allenic Alcohols

The microbial oxidation of $\alpha$-allenic alcohols by a bacterium *Pseudomonas aeruginosa* (ATCC’ 17504) afforded the corresponding $\alpha$-allenic acids (Scheme 25).51

3 Asymmetric Synthesis of $\alpha$-Allenic Esters

In 1973, Rossi and Diversi published an excellent review dealing with the synthesis of chiral allenes and, especially chiral $\alpha$-allenic esters (acids).52 Since that time, many articles have been devoted to the preparation of chiral allenes with high enantiomeric purity. Among them, the enantioselective elimination of chiral selenoxides,53 the asymmetric Horner–Wadsworth–Emmons reaction and the asymmetric Wittig reactions still play an important role and prove to be very useful.54 For example, the chiral phosphonoacetate A as well as the chiral phosphorus ylide B were efficiently utilized to synthesize optically active $\alpha$-allenic esters (Figure 1).55,56

Enantioenriched allenic esters could also be obtained through Pd(0)-catalyzed propargyl rearrangement of optically active propargyl mesylates (Scheme 26).57

More recently, the samarium(II) iodide-mediated reduction of secondary and primary propargyl phosphates afforded regio- and enantioselectively allenic esters through dynamic kinetic protonation without chirality transfer (Scheme 27).58

4 Conclusion

Numerous methods are presently available for the regio-, enantio- and stereoselective synthesis of $\alpha$-allenic esters (acids). Since the pioneering methods, much refinement has been achieved and it is now possible to choose between several synthetic routes depending on the synthetic...
goal. Moreover, optically pure electrophilic allenes are now readily available. Nevertheless, the synthesis of α-allenic esters (acids) is not a straightforward process and new methods that provide an easy access to such electrophilic compounds are still of interest.

References


