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REGIO- AND SITE-SELECTIVE ACTIVATION OF CARBON-CARBON DOUBLE BONDS TO NUCLEOPHILIC REAGENTS. CYCLOPROPANATION OF VINYLSELENONES WITH ACTIVE METHYLENE COMPOUNDS

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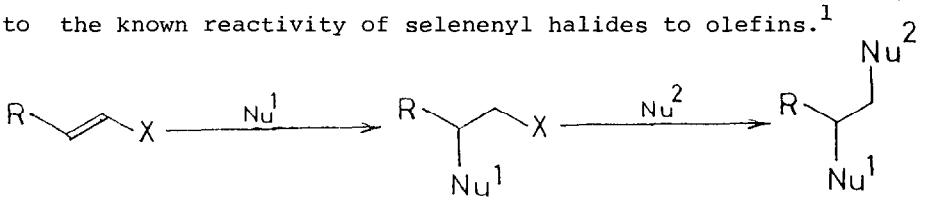
Summary: Treatment of vinylselenones with active methylene compounds in basic media leads to the formation of cyclopropanes in excellent yields via an addition-substitution reaction.

Olefinic linkages have occupied important positions in organic synthesis; electron-rich olefins undergo addition reactions with electrophilic reagents, whereas certain nucleophiles react with electron-deficient ones to give conjugate addition products. However, few examples have been reported up to now on introduction of two nucleophiles to each carbon of an olefin. We describe here selective formation of cyclopropanes on terminal olefinic bonds via an addition-substitution process with nucleophiles.

The transformation depicted in Scheme I will be envisioned if a substituent X on a C=C bond is not only an electron-withdrawing group, but acts also as a good leaving group enough to be substituted with another nucleophile. Organoselenium substituents of higher oxidation level seem to satisfy these requirements because of their electronegative character as well as lability of carbon-selenium bond. Another attractive feature to use selenium compounds is that regio- and site-selective activation of a terminal C=C bond may be feasible due to the known reactivity of selenenyl halides to olefins.[1]



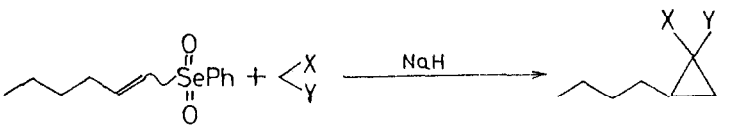
(Scheme I)

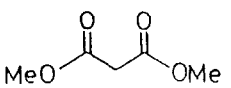
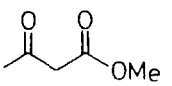
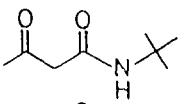
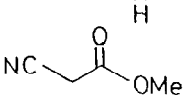
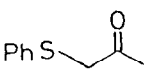
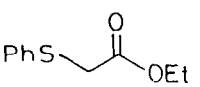
Studies on this line led us to the finding that vinyl selenoxides react with lithium enolates to yield the corresponding cyclopropyl ketones.[2] However, activation of a C=C bond with seleninyl group seems to be insufficient for addition of reagents of lower nucleophilicities such as active methylene compounds; the corresponding cyclopropane was isolated in only poor yield from the reaction of a phenyl vinyl selenoxide with lithio diethyl malonate.

Various examinations revealed that reactivity of a C=C bond to such a nucleophile has been greatly improved by a selenonyl group to form a cyclopropane ring on that linkage with high efficacy. Thus, 1-hexenyl phenyl selenone[3,4] was treated with an equimolar amount of sodio dimethyl malonate in THF at room temperature. Usual workup of the reaction mixture followed by silica gel column chromatography afforded the cyclopropyl compounds[5,6] in 92% yield. Various kinds of active methylene compounds can also be used equally well for this transformation (see Table 1).

In addition to activation of a neighboring C=C bond to nucleophiles, a selenonyl group appears to enhance the acidity of vinyl proton, which sometimes results in undesired side reactions such as decomposition to the corresponding acetylene.[7] For example, anions of less acidic substrates usually give less satisfactory results (run 7 of Table 1). Such a feature disfavors use of selenones for preparation of cyclopropyl ketones,[8] and vinyl selenoxides should be used complementally.

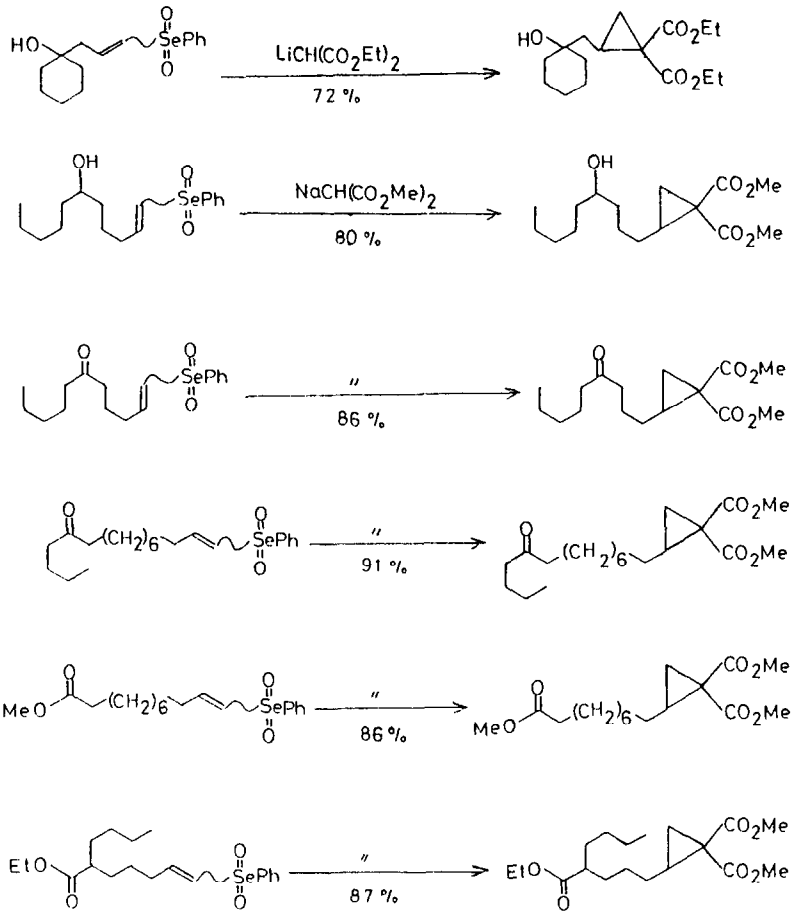
Table 1



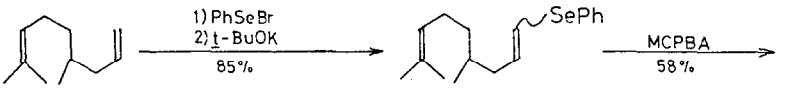
Run	Substrate	Reaction Condition	Yield,[c] %
1		r.t. 4hr	92(87)[d]
2		r.t. 1.5hr	77
3		r.t. 1.5hr	98
4		r.t. 1hr	91
5	CH_3NO_2	65°C 1hr	75
6		r.t. 1hr	83
7		r.t. 2.5hr	56

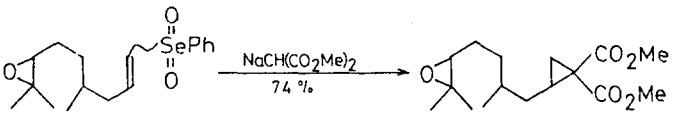
A copper catalyzed reaction of olefins with diazo compounds has been widely employed for this type of transformation,[5] but there exist serious drawbacks on the following two points; (i) use of an excess amount of an olefin is usually required for moderate success, and (ii) a range of its application suffers from severe limitation because oxygen-containing functional groups prevent the reaction.[5a]

Both of them have been overcome by the present method. In addition to circumvention of the first problem as described above, a good solution to the second one has also been observed with substrates bearing an alcohol, a ketone, or an ester group, which undergo this cyclopropanation cleanly.



Further, the following example has demonstrated site-selective activation of terminal olefins. When started from a diene, selenenylation takes place selectievly on the terminal C=C bond.[1] Although an internal one also undergoes oxidation to the oxirane during conversion of a selenide to the selenone, selective formation of cyclopropane ring has been executed on the parent terminal C=C bond under the reaction conditions where the oxirane survives.





Thus, high efficacy as well as various selectivities may broaden the synthetic utility of the present procedure.

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6) N. Kawabata and M. Tanimoto, *Tetrahedron*, 36, 3517 (1980). J. Ohishi, *Synthesis*, 690 (1980).
7) α-Elimination followed by proton transfer or β-elimination process may be conceivable. On α-deprotonation of vinyl selenides: S. Raucher and G. A. Koolpe, *J. Org. Chem.*, 43, 3794 (1978). H. J. Reich, W. W. Willis, Jr., and P. D. Clark, *ibid.*, 46, 2775 (1981).
8) For example, treatment of 1-dodecenyl phenyl selenone with lithium enolate of acetophenone led to the formation of the cyclopropane in 41% yield together with 1-dodecyne (19%).

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