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PRELIMINARY NOTE

SELECTIVITY IN THE ENE REACTION OF HEXAFLUOROTHIOACETONE. THE PREPARATION OF ALLYLIC SULFIDES.

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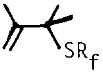
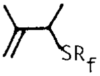
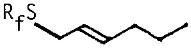
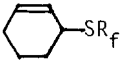
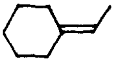
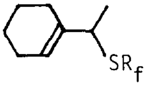
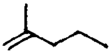
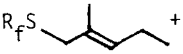
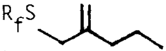
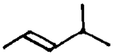
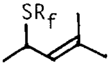
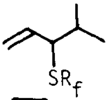
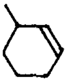
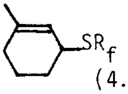
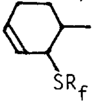
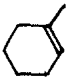
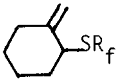
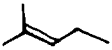
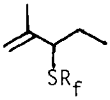
Snider's novel synthesis of allylmalonates [1], which employs the ene reaction of alkenes with hexafluorothioacetone (HFTA) as a key step in the allylic functionalization reaction, prompts us to record our own detailed work in this area on the selectivity of the ene reaction with HFTA [2]. In general, the selectivity is as expected: $\equiv CH > {=}CH_2 > -CH_3$. However, total selectivity is not observed even in some simple systems, and steric or conformational effects, rather than the type of hydrogen abstracted, may alter the anticipated selectivity.

The pioneering work of Middleton and co-workers [3] has demonstrated HFTA to be a highly reactive and unique compound. Unfortunately, the difficulty of preparation of HFTA, its ease of dimerization and its toxicity have impeded the use of this interesting material in organic synthesis. However, the ready availability of tetrakis (trifluoromethyl)-1,3-dithietane (1) from hexafluoropropene, and the "insitu" generation of HFTA from 1 via reaction with fluoride ion [5], has provided a convenient synthetic entry into the chemistry of HFTA. Initially, Middleton demonstrated the ene reaction of HFTA with a few selected olefins [6]. Similar work was later reported by Ishikawa via "insitu" generation of HFTA in the presence of olefin [5]. However, the limited selection of olefinic substrates by these workers did not elucidate the selectivity of the ene reaction with HFTA nor the factors which govern any selectivity. In conjunction with other interests in the chemistry of HFTA [7], we have examined this ene reaction with a variety of olefins. Table I summarizes some of this work and illustrates some of the controlling factors in allylic sulfide production.

TABLE I

Ene reactions of HFTA[a]

Entry	Alkene	Ene Product(s)	Yield[b,c]
1.			72
2.			41
3.			66[d]
4.			52
5.			59
6.		 + (2.7)  (1)	55[d,e]
7.		 + (4.5)  (1)	50[e]
8.		 + (4.2)  (1)	45[f]
9.			65
10.			58

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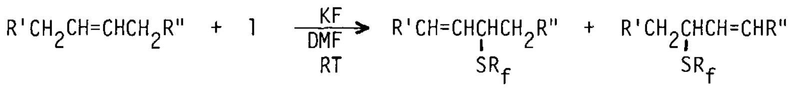
a. Alkene (2-4 moles), KF(1.5-4 moles), 1 (1 moles) were reacted for 24 hours in DMF at room temperature. b. Isolated yields. c. All products were completely characterized by ^{19}F, ^{1}H, ^{13}C NMR, IR, and mass spectral analysis. d. Stereochemistry of the allylic sulfide tentatively assigned. e. Ratio of products determined from ^{1}H NMR. f. Ratio of products determined by glpc.



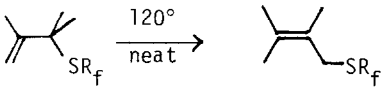
$$R'CH_2CH{=}CHCH_2R'' + 1 \xrightarrow[\text{RT}]{\text{KF, DMF}} R'CH{=}CH\underset{SR_f}{C}HCH_2R'' + R'CH_2\underset{SR_f}{C}HCH{=}CHR''$$

$R_f = -CH(CF_3)_2$

When only one type of allylic carbon-hydrogen bond is available (Entries 1-4), the reaction is straight forward and only one ene product is possible. However, entries 5 and 6 allow the comparison of allylic CH_2 vs. CH_3. In the cyclic system only abstraction of CH_2 occurs in ene product formation, whereas in reaction 6 abstraction from both CH_2 and CH_3 occurs to give a mixture of isomeric ene products. Similarly, in entry 7, the comparison of CH vs. CH_3, and in entry 8 the comparison of CH vs. CH_2, can be made. Again, the selectivity of tertiary hydrogen abstraction is noted, however, a significant amount of allylic abstraction from CH_3 or CH_2 is observed. Consequently, on the basis of entries 1-8, the observed selectivity is $CH>CH_2>CH_3$ and one would conclude that abstraction of hydrogen occurs predominately from the most highly substituted carbon.

Entries 9 and 10, however, pointedly demonstrate the pitfalls of such a gross generalization based on the type of hydrogen abstracted. In these systems (9-10), selective abstraction occurs on the methyl group - not on the methylene group. We believe this reversal of selective abstraction is a reflection of the steric hindrance encountered in the approach of HFTA. If one looks at models, the allylic sulfides (from 9-10) result from the approach of HFTA to the least hindered face of the molecule - which leads to formation of the carbon-sulfur bond at the least substituted end of the double bond with concomitant abstraction of hydrogen from the methyl group. Consequently, it appears that in highly substituted olefins that steric hindrance to HFTA becomes the predominant factor in controlling the allylic sulfide formation. Indeed, formation of the carbon-sulfur bond at the least substituted olefinic carbon may be the predominant factor in all cases, as is also observed in entries 2, 5, 6, 7, 8. Additional work is needed to clarify this point.

A note of caution in the use of the ene reaction for the preparation of allyl malonates should be made. If the ene reaction gives only one allylic sulfide - and if the allylic sulfide is stable to the carbene reaction - the novel allylic functionalization proposed by Snider will undoubtedly work well. However, where the ene reaction is not totally selective (Entries 6-8), the resultant mixture of sulfides will lead to a mixture of allylmalonates. Like Snider, we have also observed the thermal rearrangement of the ene product to the more stable thermodynamic isomer as shown below. Since the conditions of the thermal isomerization are similar to those of the carbene reaction, functionalization may result from the thermodynamic isomer and/or the kinetic isomer [8]. In more complex systems this problem may lead to a mixture of allylmalonates. Therefore, only those ene reactions which give only one allylic sulfide which is stable to the carbene conditions will lead to isomerically pure allylmalonates.



95% conversion after 24 hrs.

100% conversion after 3 days

Acknowledgement

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7 12th Regional Midwest ACS Meeting (Kansas City), 1976. Abstracts, pg. 56.

8 In Snider's paper [1], Rxs. 3 and 4 give products from the thermodynamic isomer only, whereas Rx. 6 gives products from both the kinetic and thermodynamic isomer.