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ALLYLIC FUNCTIONALIZATION: THE PREPARATION OF ALLYLMALONATES

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The allylic functionalization of olefins with formation of a new carbon-carbon bond is a potentially valuable synthetic method. Our approach to this process, modelled after the SeO_2 oxidation, involves an ene reaction followed by a [2,3] sigmatropic rearrangement to allow allylic functionalization with overall retention of double bond position.[1] We describe here a 3-step preparation of allylic malonates from alkenes. The ene reaction of alkenes with hexafluorothioacetone (HFTA) generated in situ provides the corresponding allyl hexafluoropropyl sulfides in good yield. Reaction of these sulfides with dicarbomethoxycarbene gives ylides which rearrange to allyl(hexafluoropropylthio)malonates. Desulfurization of these leads to allylic malonates which are difficult to prepare from alkenes by other methods (see Figure 1).[2]

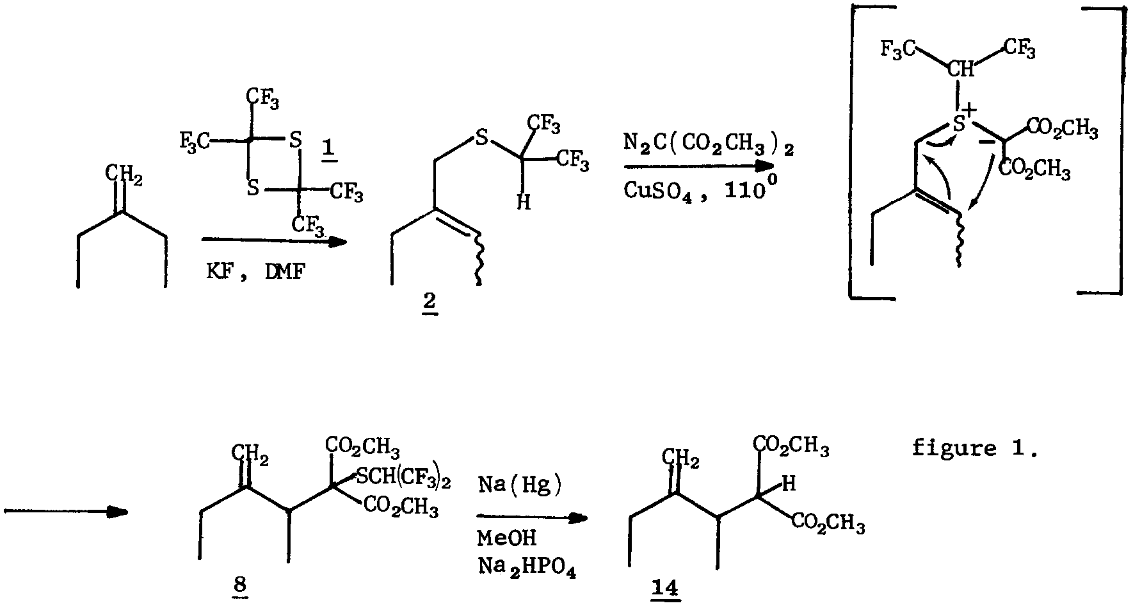


figure 1.

HFTA is known to undergo rapid ene reactions at -80° with a variety of olefins.[3] Unfortunately, HFTA is difficult to make, very unstable and highly toxic. Recent reports indicate that tetrakis(trifluoromethyl)-1,3-dithietane(1), which is readily available[4] can be converted to HFTA in situ by treatment with anhydrous potassium fluoride for 2 days at 25°.[5] It has been reported that HFTA generated in this manner forms [2+2] adducts with cyclohexene rather than the ene adduct.[5] However, the reported NMR data for this compound is consistent with the expected ene adduct. We have investigated the reaction of HFTA generated in situ with a wide variety of alkenes and find that in all cases ene adducts are formed in good yield (see Table 1).

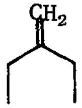
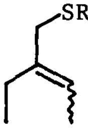
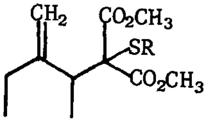
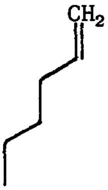
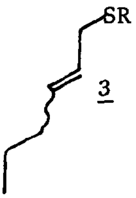
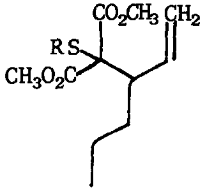
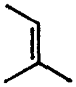
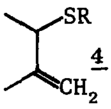
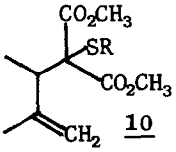
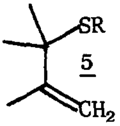
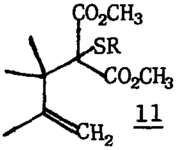
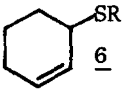
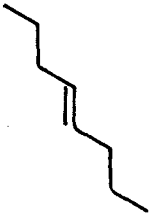
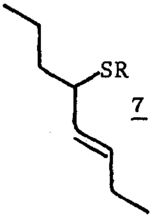
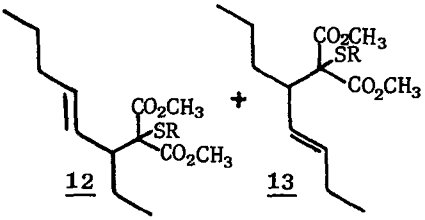
Allylic sulfides can be converted directly into ylides which undergo [2,3] sigmatropic rearrangement by reaction with diazo compounds under appropriate conditions.[6] Treatment of 2 with dimethyl diazomalonate and a catalytic amount of copper sulfate, neat, at 110° for 15 hours gives the expected rearrangement product 8 in 59% yield.[7] Under similar conditions 3 gives 9 in 55% yield. Desulfurization of 8 with excess 6% sodium amalgam in buffered methanol[8] for 2 hours at 25° gives the corresponding dimethyl allylmalonate 14 in 85% yield. Deactivated Raney Nickel[9] and aluminum amalgam also effect this transformation.

In the case of the non-primary sulfides 4 and 5, the malonates obtained, 10 and 11, appear to be derived from a [1,3] sigmatropic rearrangement of the sulfur ylide. An alternative mechanism is initial [1,3] sigmatropic rearrangement of 4 or 5 to give the primary allyl sulfide which undergoes a normal reaction with diazomalonate to give the observed products. It is known that the interaction of carbenes with sulfides is very sensitive to steric effects.[6,10] Steric interactions are especially important for these sulfides which are electron deficient and therefore unreactive towards carbenes. Allyl sulfides are also known to undergo [1,3] shifts at temperatures of 100-200° or with acid catalysis.[11] Heating 5 in benzene for 12 hours at 120° gives 45% recovered 5, 45% of the allylically rearranged species, 2,3-dimethyl-2-buten-1-yl hexafluoropropyl sulfide (15), and 10% 2,3-dimethyl-2-butene. The malonate 11 probably arises via the sulfide 15.

This route to allylic malonates should be of general synthetic utility. The products obtained generally have the less substituted double bond. This complements the reaction of malonate and similar nucleophiles with allylpalladium compounds which typically give alkylation at the less hindered position giving the more substituted double bond.[12]

We are currently investigating other synthetic applications of the now readily available hexafluoropropyl allylic sulfides.

TABLE 1. FUNCTIONALIZATION OF ALKENES

Expt.	Alkene	Ene Adduct[a] R = $CH(CF_3)_2$	Yield, %	Diazomalonate Adduct[b] R = $CH(CF_3)_2$	Yield, %
1		 2	90	 8	59
2		 3	70	 9	55
3		 4	65	 10	40[c,d,e]
4		 5	60	 11	40[c,d,e]
5		 6	43		
6		 7	86	 12 + 13	42[c,d]

a. Alkene(4 mmole), potassium fluoride (2 mmole) and dithietane 1 (1 mmole) are stirred for 4 days in 3 ml of DMF at 25°. b. Ene adduct, dimethyl diazomalonate (2 equiv) and copper sulfate(0.1 equiv) are heated neat at 115° for 15 hr. c. This compound undergoes a 1,3-allylic shift prior to formation of the sulfur ylide. d. In this reaction 4 equivalents of dimethyl diazomalonate are used. e. We are unable to detect any of the allylic isomer by examination of NMR spectra.

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12. In some cases allyl palladium species can be functionalized to give primarily the least substituted double bond.[2b]