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Free-Radical Addition to Olefins of an H_2S Equivalent: Triphenylsilanethiol

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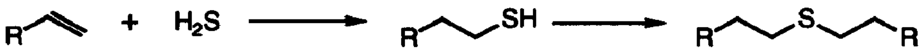
Abstract: The triphenylsilythiyl radical generated thermally (AIBN) or photochemically in the presence of an olefin yields the anti-Markovnikov H_2S adduct after deprotection by trifluoroacetic acid (TFA).

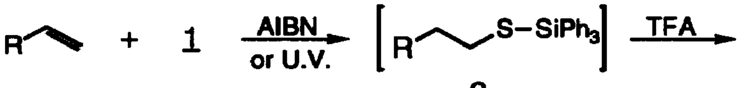
We have shown that Ph_3SiSH **1** can act as an H_2S equivalent in the ring opening of epoxides.[1] Easily prepared in one step from triphenylsilane and molecular sulfur,[2] this reagent appears to be of general use since it also behaves as a normal thiolate in S_n2 displacement,[3] or as H_2S in thioamide formation from nitriles[4] and thionation of ketones.[4]

Hydrogen sulfide adds to unsaturated systems by exposure to U.V. radiation or by the addition of a chemical initiator (peroxides, azo compounds, AIBN)[5] to yield thiols, which react further to sulfides (eq. 1) under the reaction conditions. This is a serious limitation to the synthetic scope of this reaction.



eq. 1

A few options can be envisioned to stop the reaction at the first addition. The use of a large excess of H_2S favors this reaction path.[6] From a more practical point of view, H_2S equivalents such as thiolacetic acid,[7] 2-tetrahydropyranethiol[8] and thiophosphonates of 1,1-binaphthol[9] will afford thiols after a deprotection step. We wish to report the use of **1** in free-radical addition reactions induced by an initiator (AIBN) and by U.V. light. This combined with a mild deprotection step allows the preparation of thiols having various functional groups in a one-pot reaction (eq. 2)



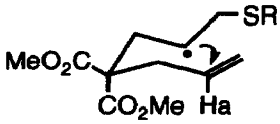
2

eq. 2

When a benzene solution of the desired olefinic substrate was refluxed in presence of 1 and AIBN for a determined period (table 1), one could detect by proton NMR the formation of intermediate 2 as a single regioisomer coming from an anti-Markovnikov addition. Removal of the protecting group was done under acidic conditions with TFA at room temperature and the free thiol isolated by flash chromatography. We also ran the reaction under U.V. light with the same substrates. Irradiation at 350 nm of a benzene solution of an olefin and 1 in a pyrex tube gave the same intermediate 2 as determined by proton NMR. Similar treatment of the reaction mixture with TFA afforded the deprotected thiol. In this case the adducts were not isolated and the yield was determined by NMR using an internal standard (dichloroethane or dibenzylether). There is no significant difference in yield between AIBN and light induced reaction. As can be seen in Table 1, the reaction conditions allowed the use of a variety of functional groups.

In general, 1 does not add to disubstituted olefins unless they are terminal or activated by ring strain (entries 7 and 9). Unstrained olefins, like cyclododecene (entry 11) and dihydropyran (entry 10), are not reactive enough. In the case of the norbornene derivative (entry 9), one equivalent of AIBN had to be used to ensure completion of the addition reaction. This reaction gave exclusively the exo thiol.

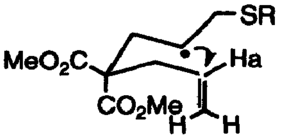
Diallylmalonate (entry 8) is a case where the radical formed from the addition of 1 was trapped in a 5 exo-trig fashion yielding the expected carbocyclic thiol in nearly quantitative NMR yield as a 4:1 mixture of cis and trans. The ratio was established by NOE experiments. The preference for the cis isomer can be rationalized by lesser steric repulsion 1,3 diaxial as well as by torsional strain favoring 3a over 3b and 3c.[10]



3a

↓

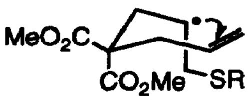
cis



3b

↓

trans



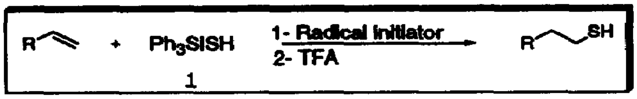
3c

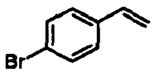
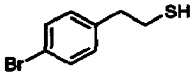
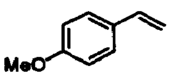
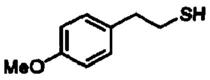
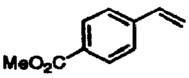
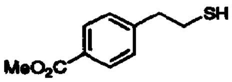
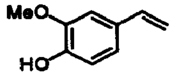
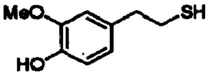
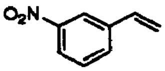
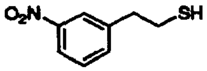
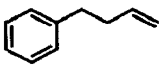
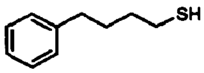
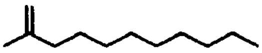
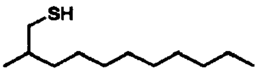
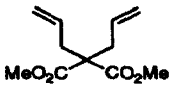
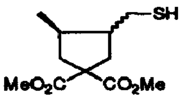
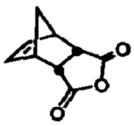
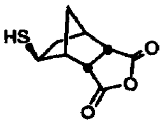
↓

trans

It is interesting to point out the relative unreactivity of certain functional groups that could stop the radical process, namely the aromatic halide (entry 1), the nitro group (entry 5) and especially the phenol (entry 4), well known to be a radical scavenger.

Table 1: Triphenylsilylthiyl radical addition of 1 to unsaturated compounds initiated by AIBN and UV light.[11]



Entry	Olefin	Product	Yield AIBN initiated	Time	Yield Light initiated	time
1-			74% (86%)[a]	1.5h	(92%)[a]	7h
2-			72% (85%)	1h	(86%)	15h
3-			37% (53%)	4h	(45%)	9h
4-			52% (64%)	1.5h	(65%)	8h
5-			58% (61%)	24h	(53%)	20h
6-			76% (86%)	15h	(89%)	6h
7-			56% (57%)	9h	(71%)	15h[b]
8-			80% (98%) cis/trans, 4/1	1.5h	(99%)	7h
9-			67% (93%)	15h	(96%)	24h[b]
10-	Dihydropyran	N.R.				
11-	Cyclododecene	N.R.				

a) yield in parenthesis determined by ^1H NMR using benzylether or dichloroethane as internal standard; all compounds gave satisfactory elemental analyses.

b) 5% of benzophenone was added to accelerate the reaction.

In conclusion, **1** can serve as an H_2S equivalent under radical conditions either thermally (AIBN) or photochemically initiated. The mild deprotection step (fluoride ion can also be used) allowed the presence of a wide variety of sensitive functional groups. We are currently exploring the use of triphenylsilylthiyl radical in other types of reactions.

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11. Typical conditions of AIBN initiated: olefin (1.4 mmoL), **1** (1.6 mmoL) and AIBN (0,4 mmoL) in 1.4 mL of benzene was refluxed until dissappearance of starting material. It was then cooled to room temperature and treated with 5 eq of TFA for c.a. 30 min. The solvent was removed and the thiol isolated by flash chromatography. Typical conditions for light initiated: the reagents in the same proportion are mixed in a pyrex tube at 1 cm away from a 350 nm U.V. lamp.

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