

ADDITION OF SULFINYLATED AND SULFONYLATED CARBON CENTERED RADICALS TO ALKENES AND ENOLETHERS

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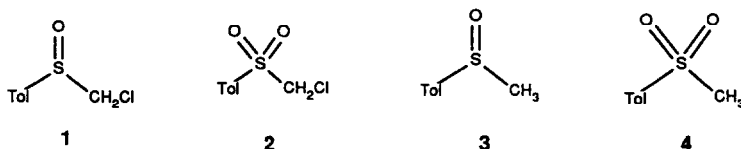
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Summary: (*p*-Tolylsulfonyl)- and (*p*-tolylsulfinyl)methyl radicals reacted with electron rich olefins like vinylsilane, enolethers and silylenolethers in the presence of Bu_3SnH to give addition products. Cyclization of sulfonylated and sulfinylated radicals proceeded in good yield and high *trans* stereoselectivity in the case of enolethers.

Most of the recent developments in the field of radical chemistry are in connection with nucleophilic radicals¹. The use of electrophilic radicals for chain reactions is highly desirable since it will open new synthetic approach to fonctionalized molecules. Substitution by electron withdrawing groups is required for the activation of the electrophilic² character of carbon centered radicals. To that effect, we have used sulfinyl and sulfonyl groups. This choice was governed by the two following reasons:

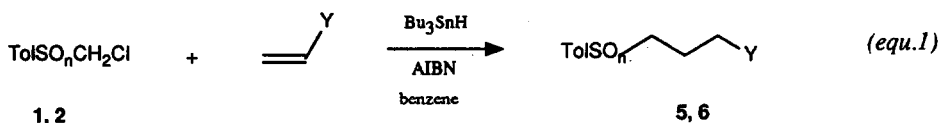
- ESR study of sulfonylated radicals indicates that they are not stabilized by the sulfur fonction and for sulfinylated radicals less than 6 % spin delocalization was observed³, therefore we can expect them to be very reactive. This aspect is corroborated by the observation of very fast intramolecular cyclizations of sulfonylated radicals^{4,5}.
- the radical precursors are easy to prepare (even in enantiomerically pure form for the sulfinyl derivative).

The generation of the radicals was possible from the corresponding chlorides⁶ (1 and 2 for example) by treating them with AIBN/ Bu_3SnH in refluxing benzene. It is worth noting that under these conditions, (*R*)-1⁷ was reduced in a quantitative yield to (*S*)-3 without racemization at the sulfur center.

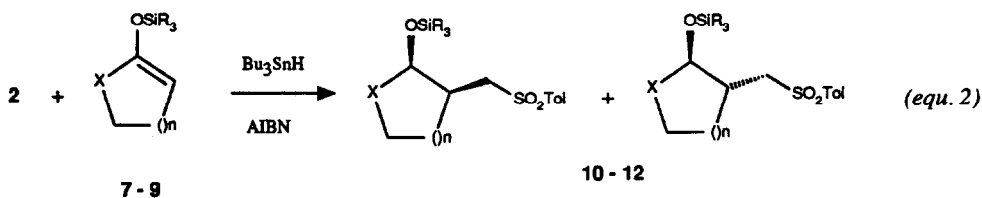


Reactions between the radicals derived from 1 and 2 with olefins in the presence of Bu_3SnH are described in the equation 1. No reaction was observed with 1-octene. Activation of the olefin with a trimethylsilyl or an ethoxy group was sufficient to obtain the adduct 5 and 6 in 45 % and 40 % yield respectively¹⁰. Products of direct reduction 3 and 4 were isolated as single side products.

The use of enolethers as substrates for addition of electrophilic radicals was further investigated. The presence of a β -substituant on the olefin completely inhibits the addition. For example, no addition product was isolated when the reaction was performed with dihydropyrene. To overcome this problem, it was necessary to use the most nucleophilic silylenolether (equ. 2). Trimethylsilyloxycyclopentene and -cyclohexene reacted cleanly with 2 to give the addition products 10 and 11 respectively in good yields as a mixture of *cis* and *trans* isomers. Silylketenacetals were also good substrates for this reaction. For example, the reaction of 2 with 9 gave the acetal 12 with a slight preference for the *trans* isomer (*trans/cis* 2:1).



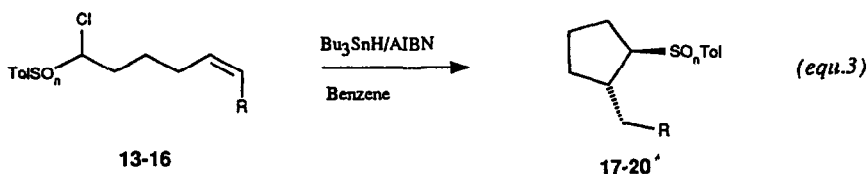
n	Y	product	yield
1, 2	C ₆ H ₁₃	-	-
1	Si(CH ₃) ₃	5	45 %
2	OC ₂ H ₅	6	40 %



substrate	X	n	SiR ₃	product	yield	cis/trans
7	CH ₂	1	TMS	10	41 %	1 : 1
8	CH ₂	2	TMS	11	55 %	2 : 3
9	O	2	TBDMS	12	47 %	1 : 2

Cyclizations of sulfonylated and sulfynylated radicals were examined for alkenes (13-14) and enoethers (15-16). Compound 14 was prepared from (5-hexenyl)*p*-tolylsulfoxide 22 by chlorination according to Yamakawa's procedure⁷. The sulfone 13 was obtained by alkylation of 2 with 1-bromohexene. Compound 13 was treated with AIBN /Bu₃SnH in refluxing benzene and the cyclopentane derivative 17 was isolated in 72 % yield as a *trans/cis* (84:16) mixture of isomers. The tricyclic sulfone 21 was also formed in 22 % yield as a 3:2 mixture of isomers. This side product is formed by a double cyclization of the initial radical. Such a rearrangement followed by SO₂ elimination was reported by Clive and Boivin⁵. The sulfoxide 14 gave, under the same reaction conditions, the cyclopentane derivative 18 in 40 % yield as a mixture of four isomers⁸. Oxidation of the crude product with mCPBA gave 17 as a *trans/cis* 86:14 mixture. The sulfone 21 was also formed in 42 % yield (79:21 mixture of isomers). The radical precursors 15 and 16 were prepared by alkylation of 2 and 1 with the bromide 23 in 77 % and 64 % yield respectively. With both substrates (15 and 16), the cyclization was very fast and high yielding under standard conditions. It was possible to add tributyltinhydride (1.1 equivalent) immediately at the beginning of the reaction (no slow addition technique

required). The sulfone **19** was isolated as a single *trans* isomer. The sulfoxide **20** was a 1:1 mixture of isomers. Oxidation of this mixture with mCPBA gave a single product identical to the sulfone **19**, proving that the cyclisation reaction was *trans* selective but not selective in respect to the sulfur atom. The high *trans* selectivity which prevails in the formation of **19** and **20** is attributed to steric interactions and electronic repulsion between the oxygen at the sulfur and the enolether oxygen, thus destabilizing the transition state of type A in relation to B (R = OCH₃). The transition states are drawn according to *Spellmeyer* and *Houk*⁹ for the 1-methyl-5-hexenyl radical cyclization (only the chair conformation are shown). In the case of sulfone **13** and sulfoxide **14** (R = H), steric interactions and dipolar repulsion are smaller, and some *cis* product is formed.



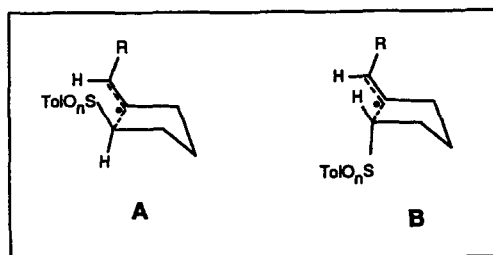
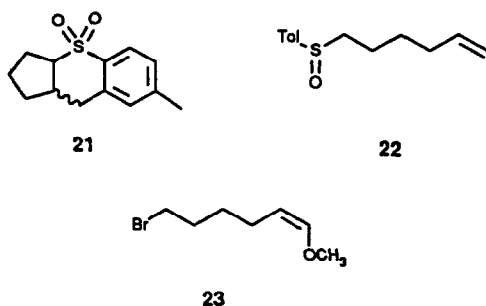
precursor	n	R	product ^{a)}	yield	trans/cis ^{b)}
13	2	H	17	72 %	84 : 16
14	1	H	18^{c)}	40 %	86 : 14 ^{d)}
15	2	OCH ₃	19	82 %	> 95 : 5
16	1	OCH ₃	20^{c)}	94 %	> 95 : 5 ^{d)}

a) Reaction conditions: a solution of 2 mmol chloride, 2.1 mmol Bu₃SnH and 10 mg AIBN is treated according to note 10

b) GC ratios, DB-1 (30 m), 250 °C.

c) 1:1 mixture of diastereomers relative to the sulfur center.

d) Determined after oxidation with mCPBA of the crude product to the corresponding sulfone.



In conclusion, the inter- and intramolecular addition of sulfonylated and sulfinylated radicals to electron rich alkenes is achieved in good yield and should be of valuable interest in the synthesis of natural products. For instance, the use of enolethers opens a route to flexible and bifunctionalized products with good stereoselectivity in the most favorable cases.

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Notes and references

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8. The cyclization reaction was not diastereoselective with respect to the chiral sulfur center.
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10. Typical procedure: a solution containing 1 mmol of the chloride, 5 mmol of the olefin, 1.3 mmol Bu_3SnH and 10 mg AIBN in 10 ml benzene is heated under reflux. The reaction is followed by tlc and 10 mg AIBN are added every 5 h until completion of the reaction. The solvent was evaporated and the residue dissolved in ether, stirred for 2 h with 2 g KF and 0.5 ml H_2O , dried over MgSO_4 , filtrated and evaporated to give the crude product.

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