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Rearrangements and Cyclizations in Vinyl Radicals. Unusual Example of 1,4-Radical Translocation.

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Abstract. Vinyl radical **5** undergoes 5-*exo* cyclization onto the CC double bond in competition with the 5-*exo* cyclization onto the aryl ring. In addition, radical **5** exhibits an unusual 1,4-radical translocation/β-fragmentation process. In contrast, radical **4** exclusively undergoes 5-*exo* cyclization onto the benzene ring. This latter reaction leads to *spiro* radical intermediates which can either give the 1,4-aryl migration products or can be trapped by 2-cyano-*iso*-propyl radicals.

Depending on the reaction conditions, vinyl radicals can cyclize onto double[1a,b] and triple bonds[1b,2], aromatic[3] and heteroaromatics[4] rings or undergo 1,5-radical translocation.[5,6] With the aim of studying the competition between the different cyclization modes and the radical translocation reaction, we have undertaken an investigation of the radical addition of a number of radicophile β-containing sulfanyl radicals to a number of terminal alkynes carrying a radicophilic substituent in 5- or 6-position.

We report here preliminary results obtained from the 4-cyanophenylmethanesulfanyl radical **1** addition to alkynyl ethers **2** and **3** each having an alkene double bond as radicophilic group. Radicals **1** were generated from the corresponding 4-cyanotoluenethiol at different AIBN and thiol concentrations (Method A or Method B).[7] Vinyl radicals **4** and **5**, which result from regioselective addition of **1** to the alkyne moiety of **2** and **3**, respectively, could undergo 6-(or 5-*exo*) cyclization onto the alkene double bond in competition with the 5-*exo* cyclization onto the aryl ring and the hydrogen migration from the allylic methylene.

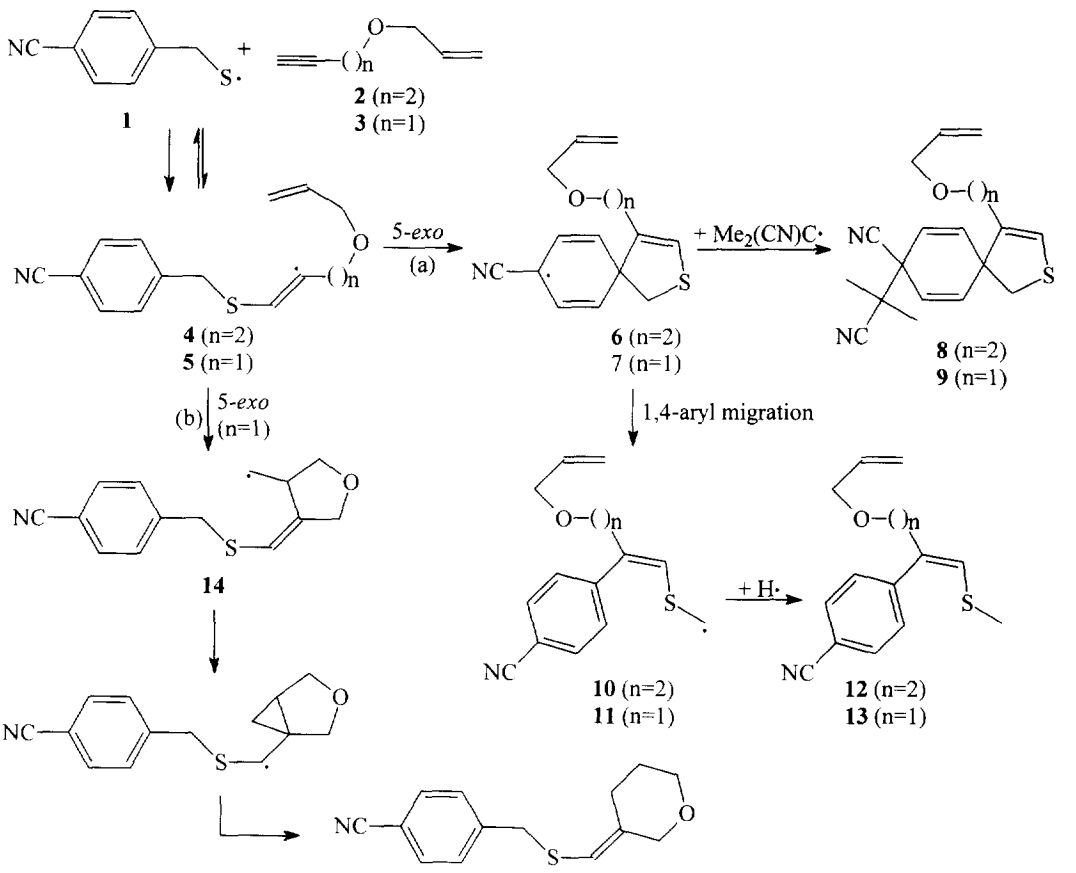
Sulfanyl radical addition to enines **2** and **3** to the alkyne triple bond is expected to be regioselective. In fact, although the sulfanyl radical[8] (and stannyl radical as well[9]) addition to the alkene double bond is faster than the analogous addition to the alkyne triple bond and while both reactions are reversible, β-sulfanyl- (and β-stannyl-) vinyl radicals are thermodinamically favored with respect to β-sulfanyl (and β-stannyl) alkyl radicals. Thus, products deriving from addition to the alkene double bond might be formed only if the resulting alkyl radicals react faster than vinyl radicals do.

According to our expectation, sulfanyl radical **1** addition to ether **2** occurred regioselectively to the CC triple bond affording the vinyl radical **4**. This latter exclusively underwent 5-(π-*endo*)*exo* cyclization onto the aromatic ring (Scheme 1). No 6-*exo* cyclization products onto the double bond, nor products ascribable to 1,5-hydrogen migration or intermolecular hydrogen abstraction, were formed. The 5-(π-*endo*)*exo* cyclization led to the *spiro*-cyclohexadienyl radical **6**, from which, under the reaction conditions of Method A, the 1,4-aryl migration product **12** (78%; ca. 1:1 E/Z mixture) was formed through fragmentation of the *spiro* ring and subsequent hydrogen abstraction by the resulting α-sulfanylmethyl radical **10**. Definite evidence of the intermediacy of the *spiro*-cyclohexadienyl radical **6** came from results obtained with Method B. Under these reaction conditions the *spiro*-radical **6** gave comparable amounts of the 1,4-aryl migration product **12** (16%;

ca.1:4 E/Z mixture) and the coupling product **8** (9%), which was derived from trapping of **6** by 2-cyano-*iso*-propyl radicals. We have previously reported[3a] examples of such 1,4-aryl migration towards alkenyl radicals, although at that time the intermediacy of *spiro*-cyclohexadienyl radicals was only postulated.

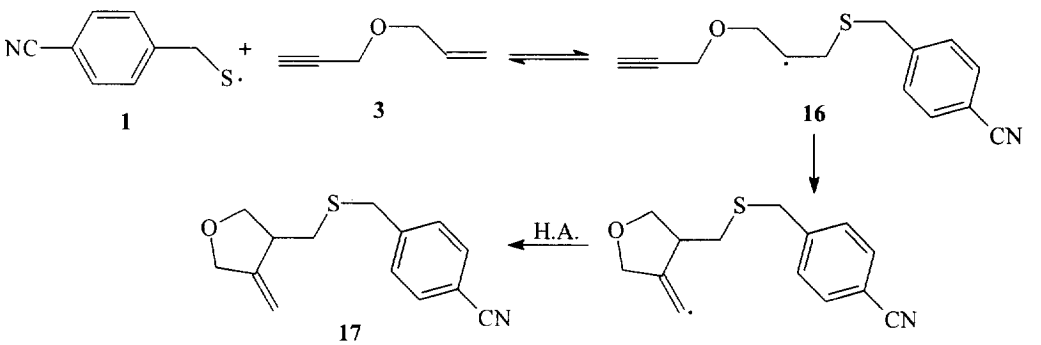
The failure to obtain products deriving from radical **4** through 6-*exo* cyclization onto the double bond could be attributable to stereoelctronic effects, which actually favor the 5-exo cyclization.[10] However, the 5-*exo* cyclization onto the aryl ring can also compete with the 5-*exo* cyclization onto the CC double bond, as evidenced by reaction of propynyl ether **3** with radicals **1**. In fact, the resulting vinyl radical **5**, under the reaction conditions of Method A, afforded major amounts of the pyran **15** (2:1 E/Z mixture) (50%) in addition to minor amounts of the 1,4-aryl migration product **13** (ca.1:1 E/Z mixture) (7%). Similar results were obtained with Method B. Products **9** and **13** were derived by 5-*exo* cyclization onto the aryl ring through intermediacy of the *spiro* radical **7**, whereas the pyran **15** was formed by 5-*exo* cyclization onto the CC double bond. The resulting alkyl radical **14** eventually gave the pyran **15** through a well-known ring expansion process (Scheme 1).

Scheme 1



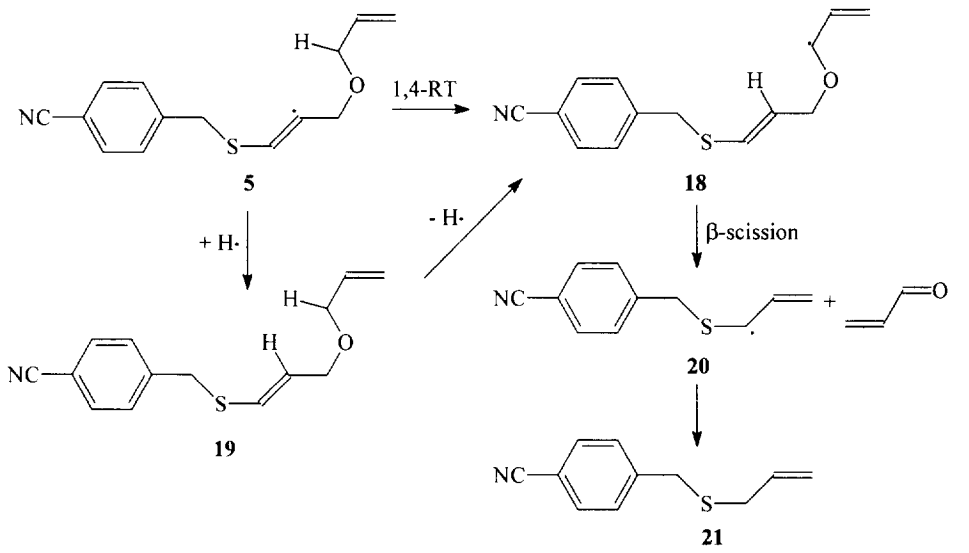
Sulfanyl radical addition to enine **3** is not completely regioselective. In fact, the pyran (Z)-**15** was found to be contaminated with minor amounts of the tetrahydrofuran **17** (5%) (Scheme 2). Its identification resulted from careful spectral analysis. ^{1}H NMR spectrum showed broad singlets at δ 4.90 and 4.95 (>C=C**H**$_2$) and δ 4.20 (-O-C**H**$_2$-C=) and a multiplet at δ 3.95 (-O-C**H**$_2$-CH<). The formation of **17** was accounted for assuming sulfanyl radical addition to the alkene double bond and subsequent cyclization of the resulting alkyl radical **16** onto the alkyne triple bond. From the assumption that β-sulfanylvinyl radicals **5** are thermodinamically favored with respect to β-sulfanylalkyl radicals **16**, we can infer that the 5-*exo* cyclization of the alkyl radical **16** onto the terminal alkyne triple bond and the 5-*exo*-cyclization of the vinyl radical **5** onto the terminal alkene double bond occur at comparable rates. This result is particularly relevant, because it has been reported[11] that the CC triple bond is less reactive than the CC double bond towards carbon centered radical addition.

Scheme 2



The reaction of ether **3** with sulfanyl radicals **1** afforded, besides the above products, the allyl aryl ether **21** (Method A 15%, Method B 6%). This product was probably derived from the translocated radical **18** through β-cleavage of the carbon-oxygen bond and loss of acrolein (Scheme 3).

Scheme 3



Radical **18** might arise from vinyl radical **5** through intramolecular 1,4-hydrogen migration towards the vinyl radicals. This should be a rare example of 1,4-hydrogen migration; only very few examples of such a process have been reported in the literature.[12] In particular, Crich and co.[13] have recently reported a similar reaction involving a 1,4-radical translocation from an alkyl radical followed by β-fragmentation of a carbon-oxygen bond. An alternative route to the translocated radical **18** might involve the intermediacy of the 1:1 adduct **19**. However, we found no traces of this possible adduct **19** under conditions of both Method A and B. An experiment carried out by using S-deuterated thiol led to inconclusive results, because no deuterium was incorporated by the allyl sulfide **21** neither in the vinylic position (as expected from an intramolecular 1,4-hydrogen migration) nor in any other position. Indeed, incorporation of deuterium in the allylic position was expected from both mechanisms. It seems that the allyl radical **20** abstracts a hydrogen atom from a scavenger different from the thiol. The question is still open at present.

Anyhow, it is really surprising that the radical **4** did not undergo analogous 1,5-radical translocation (intra- or inter-molecular), in spite of the fact that also in this case an α-oxy-substituted allyl radical should be formed.

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7. Method A: a benzene solution (20 mL) containing thiol (2 mmol), AIBN (0.2 mmol) and the appropriate alkyne (5 mmol) was refluxed for 3h. Method B: a benzene solution (5 mL) of thiol (2 mmol) was added within 3 h with a syringe pump to a boiling benzene solution of AIBN (1 mmol) and the appropriate alkyne 5 mmol). An additional amounts of AIBN (0.5 mmol) was added after 2 h. The resulting solution was refluxed for further 60 min.
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