Stereoselective Cyclizations and Rearrangements in Vinyl Radicals Promoted by Regioselective Sulfanyl Radical Addition to Enynes

Pier Carlo Montevecchi* and Maria Luisa Navacchia

Dipartimento di Chimica Organica "A. Mangini", Università di Bologna, Viale Risorgimento 4, I-40136 Bologna, Italy

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Regioselective radical addition of 4-cyanotoluenethiol (**1a**) to enynes **3**−**6** leads to vinyl radicals **7**−**10** that can undergo five- or six-membered cyclization onto styrene or terminal double bonds in competition with 5-*exo* cyclization onto the aryl ring. The latter affords spiro-cyclohexadienyl radical intermediates which can either be trapped by 2-cyanoisopropyl radicals or give 1,4-aryl migration products. Regioselective radical addition of phenethanethiol (**1b**) to enynes **3**−**6** gives radicals **11**−**14** which undergo five- or six-membered cyclization onto the alkene double bond; the stereoelectronically disfavored 6-*exo* cyclization can compete with intermolecular hydrogen abstraction and (to a small extent) with 1,5-hydrogen migration. The 5- and 6-(*π*-*exo*)*exo* cyclization of vinyl radicals **7**, **9**, **11**−**13** is highly stereoselective and exclusively or predominately affords products deriving from the (*Z*)-isomers. Stereochemical evidence indicates that the six-membered *endo*-cyclization products **30** and **50** could derive from a direct 6-*endo* cyclization of (*E*)-radicals (*E*)-**10** and (*E*)-**14** rather than from a 5-*exo* cyclization/ring expansion process. Sulfanyl radical addition to enynes **3**−**5** is highly regioselective to the terminal triple bond. In contrast, reaction of thiols **1a**,**b** with enyne **6** leads to products deriving from sulfanyl radical addition to both the CC triple and double bond. This behavior is accounted for by assuming that sulfanyl radical addition to the alkyne triple bond is not reversible, while the addition to the alkene double bond is. Vinyl radical **10** affords product **33** by a rare 1,4-hydrogen migration/fragmentation process.

Vinyl radicals can be readily generated in several ways, most of these involving addition to the alkyne triple bond[1] of carbon-centered[2] and heteroatom-centered radicals (including sulfanyl,[3] stannyl,[4] silyl,[5] germyl,[6] or selenyl[7] radicals).

In the last few years we have been particularly interested in the chemistry of vinyl radicals generated by sulfanyl radical addition to alkynes,[8] which we have considered from both a synthetic and a mechanistic standpoint. Vinyl radicals display a large variety of reactivity: they can readily undergo 5- or 6-*exo* cyclization onto carbon−carbon double and triple bonds,[9] and aromatic[2f−k,8b,c,10] and heteroaromatic[8e] rings, while the 5-*endo* cyclization onto alkene double bonds[8f] and aromatic rings[8b] is preferred with linear α-phenyl-substituted radicals. Moreover, vinyl radicals can undergo 1,5-radical translocation toward an activated methylene by intramolecular hydrogen migration.[8f,11] We have recently reported a sequential radical process involving a 1,5-radical translocation of vinyl radicals as the key step.[8f]

It appears that no data are presently available concerning the competition between the different cyclization

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(1) For reviews on radical addition to the alkyne triple bonds see: (a) Chatgilialoglu, C.; Ferreri, C. Radical Addition involving CC Triple Bonds. In *The Chemistry of Triple-bonded Functional Groups*; Patai, S., Ed.; J. Wiley: New York, 1994; Suppl. C2, Vol. 2, Chapter 16. (b) Curran, D. P. Radical Addition Reactions. *Comprehensive Organic Synthesis*; Pergamon Press: Oxford, U.K., 1991; Vol. 4, Chapter 4.1.

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(3) For a review on sulfanyl radical addition to the alkyne triple bond see: Chatgilialoglu, C.; Guerra, M. *Supplement S: The Chemistry of Sulfur-containing Functional Groups*; Patai, S.; Rappoport, Z., Eds.; J. Wiley: Chichester, 1993, Chapter 8. See also ref 8 and references cited therein.

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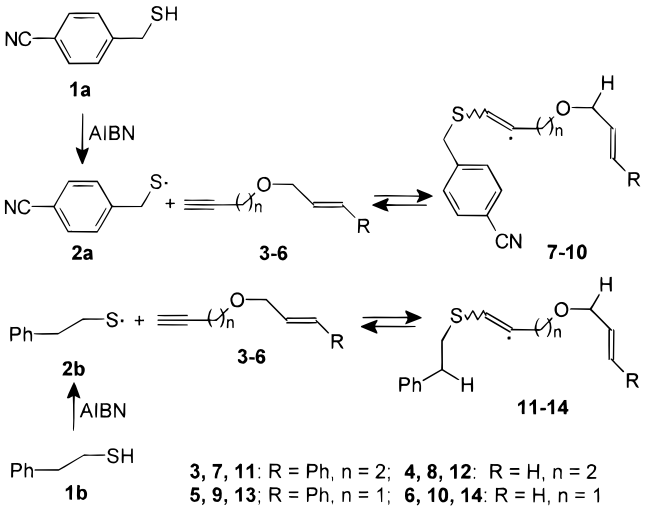
Scheme 1



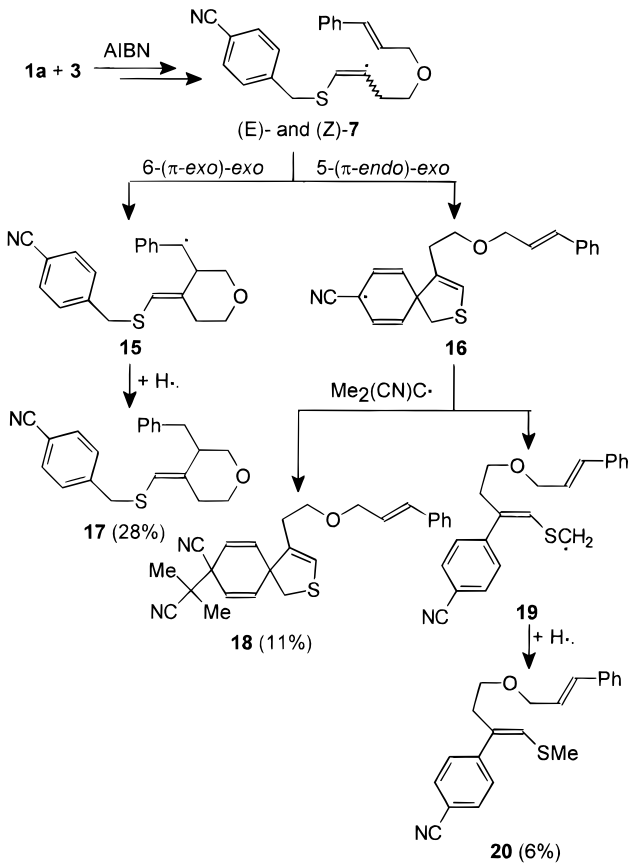
modes (five- or six-membered, *exo* or *endo*) onto different radicophilic moieties and the intramolecular hydrogen migration. With the aim of reaching this goal we planned a study of the fate of vinyl radicals generated by addition of methanesulfanyl radicals **2** (having suitable α-radicophilic substituents) to alkynes carrying radicophilic moieties in 5- or 6-position. We report herein results obtained from the radical addition of thiols **1a**,**b** to the alkynyl ethers **3**−**6**. We reasoned that the regioselective addition[12] of AIBN-generated sulfanyl radicals **2a**,**b** to the alkyne triple bond of **3**−**6** would lead to radicals **7**−**14**, from which 5- (or 6)-*exo* cyclization onto the terminal (or the styrene) double bond might occur in competition with the 5-*exo* cyclization onto the aryl ring (see radicals **7**−**10**) and the radical migration toward the α-oxy allylic methylene and the benzylic methylene (for radicals **11**−**14**)[13] (Scheme 1).

Results and Discussion

Reactions of thiols **1a**,**b** with the alkynyl ethers **3**−**6** were generally carried out under conditions of method A and/or method B, as described in the Experimental Section. According to method A, a benzene solution of thiol **1a,b** containing a 2-fold excess of ether **3**−**6** and 0.1 mol equiv of AIBN was refluxed for 3 h. Following method B, a benzene solution of thiol **1a**,**b** was slowly added over 3 h with a syringe pump to a boiling benzene solution containing a 2-fold excess of the appopriate alkyne **3**−**6** and equimolar amounts of AIBN. In both cases the reaction mixtures were washed with 10% aqueous NaOH to separate the unreacted thiol **1a**,**b** and then chromatographed on silica gel column. In all cases thiol **1a**,**b** was generally recovered in 10−40% yield after acidification of the aqueous layer.

In principle the conditions of method A should favor intermolecular hydrogen abstraction reactions, since thiols are good hydrogen donors. Vice versa, the conditions of method B should be preferred for trapping radical

Scheme 2



intermediates by 2-cyanopropyl radicals owing to the high AIBN concentration employed. However, in these cases more complex reaction mixtures were generally obtained.

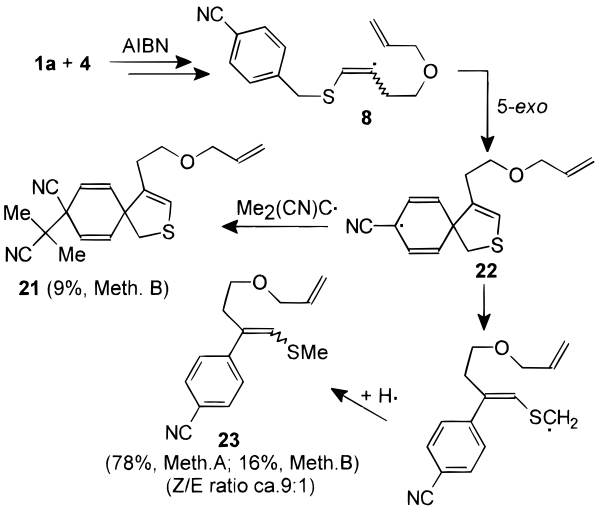
Reaction of thiol **1a** with butynyl ether **3** was carried out under method B conditions. Chromatography of the resulting reaction mixture allowed for the separation of the pyran **17** (28%), the methyl sulfide **20** (6%), and the spiro-compound **18** (11%) (Scheme 2). The pyran **17** and the sulfide **20** were obtained as pure stereoisomers. The *Z* configuration for **20** was postulated on the basis of our previous evidence on the 1,4-aryl migration toward vinyl radicals.[8c] The *E* configuration for the pyran **17** was established by NOE measurements. Compounds **17**, **18**, and **20** were derived from vinyl radical intermediate **7** through two competitive processes. 6-*Exo* cyclization of radical (*Z*)-**7** onto the styrene double bond led to benzyl radical **15**, and then to the pyran **17** by hydrogen abstraction, while 5-*exo* cyclization of radical (*E*)-**7** onto the aromatic ring led to the spiro-cyclohexadienyl radical **16**. This radical could either be trapped by 2-cyanopropyl radicals, leading to the spiro-compound **18**, or undergo fragmentation of the spiro-ring leading to the thiomethyl radical **19** and then to the 1,4-aryl migration product **20** by subsequent hydrogen abstraction. We have previously reported examples of 1,4-aryl migrations toward vinyl radicals,[8c] although at that time the intermediacy of cyclohexadienyl radicals was only postulated. The present formation of the coupling product **18** strongly supports our previous claim.

Although the overall yields from the reaction of **1a** with **3** are not quite satisfactory, it appears that the 5-*exo* cyclization onto the aromatic ring and the 6-*exo* cyclization onto the styrene double bond occur at comparable rates. These two cyclization modes compete favorably

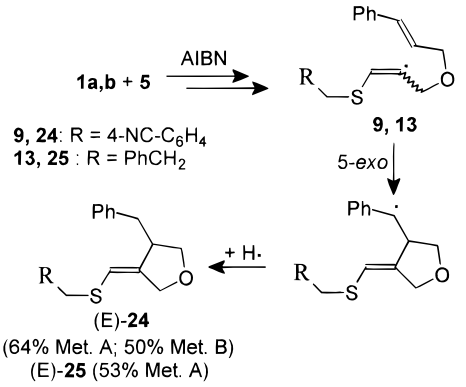
(12) It is well known that radical species, including arenesulfanyl (Broka, C. A.; Reichert, D. E. C. *Tetrahedron Lett.* **1987**, *28*, 1503), selenyl (ref 7d), and stannyl radicals (ref 16a) promote the cyclization of enynes by regioselective addition to the CC triple bond. These radicals facilely add to both CC double and triple bonds of enynes leading to alkyl and vinyl radical intermediates. The reason for the regioselective addition is the greater reversibility of radical addition to alkenes compared with alkynes (see ref 1a).

(13) Preliminary results have been previously reported; see: Montevecchi, P. C.; Navacchia, M. L. *Tetrahedron Lett.* **1996**, *37*, 6583.

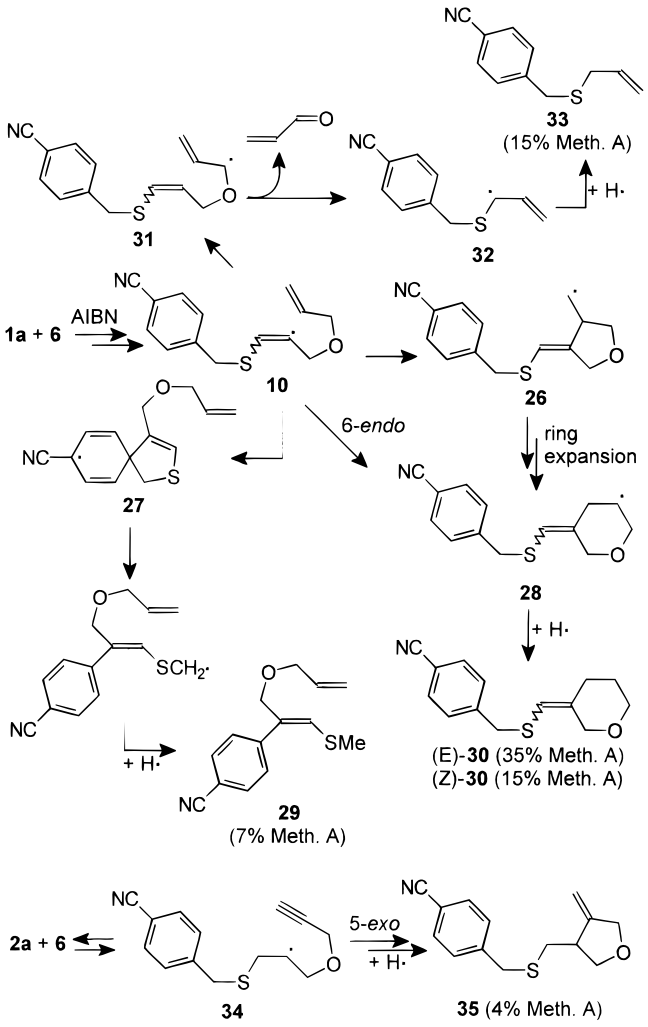
Scheme 3



Scheme 4



Scheme 5



with both the intermolecular hydrogen abstraction and the 1,5-hydrogen migration from the α-oxy allylic methylene.

Thiol **1a** was let to react with ether **4** under conditions of both methods A and B to give exclusively products **21** and **23** deriving from radical **8** through 5-*exo* cyclization onto the aromatic ring (Scheme 3). In this case as well no products deriving from radical **8** by intermolecular hydrogen abstraction or hydrogen migration were obtained. Moreover, we did not detect any product derived from radical **8** by 6-*exo* cyclization onto the terminal CC double bond. The scarce tendency of the terminal double bond to undergo 6-*exo* cyclization can be ascribed to both stereoelectronic effects, which favor the 5-*exo* cyclization,[15] and to thermodynamic effects, which favor the cyclization onto the styrene double bond with formation of a stable benzyl radical.

The importance of stereoelectronic effects is clearly evidenced by the reaction of thiol **1a** with ether **5**, which gave only the tetrahydrofuran **24** under method A and B conditions (64% and 50% yields, respectively) (Scheme 4). Compound **24** (as pyran **17**) was obtained as pure (*E*) isomer through 5-*exo* cyclization of radical intermediate (*Z*)-**9**. The *E* configuration was established by NOE measurements. Vinyl radical intermediate **9** seems incapable of undergoing competitive 5-*exo* cyclization onto the aromatic ring.

Thiol **1a** reacted with ether **6** to give products **29**, **30**, **33**, and **35** (Scheme 5). Reaction products **29** and **30** arose from vinyl radical **10** by competitive cyclization onto the aromatic ring and the terminal double bond, respectively. Methyl sulfide **29** was expected to derive from 5-*exo* cyclization onto the aromatic ring and subsequent fragmentation of intermediate spiro-radical **27**, while the pyran **30** might be derived from either 6-*endo* and/or 5-*exo* cyclization onto the terminal double bond. In this latter case, the *exo* radical **26** would afford the *endo* radical **28** through a well known ring-expansion process.[8c,15c,d,16] Pyran **30** was obtained in both (*E*) and (*Z*) configurations, with a ca. 2:1 (*E*)/(*Z*) ratio. The actual configurational structure was established for the (*E*) isomer by NOE measurements.

The rearranged sulfide **33** was initially believed[13] to derive from radical **10** through initial 1,4-hydrogen migration leading to the translocated radical **31**. Subsequent carbon−oxygen bond cleavage (with loss of acrolein) would afford the allyl radical **32** and then **33** by hydrogen abstraction. Analogues 1,4-hydrogen migration/C−O fragmentation processes have been recently reported.[17] However, we observed that the homologous

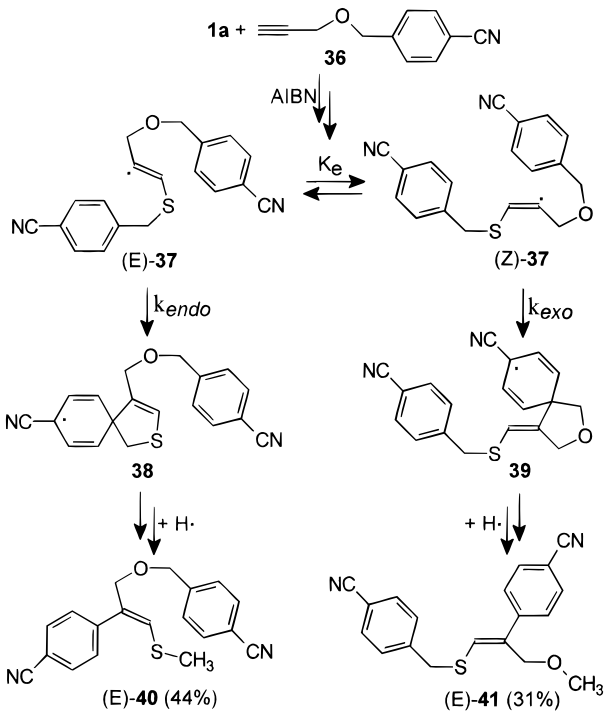
(14) Compound (*Z*)-**23** was contaminated by minor amounts of its (*E*)-isomer [*Z*/*E* ratio ca. 9:1] probably deriving from a postisomerization process.

(15) (a) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. (b) Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980,** 482. (c) Crich, D.; Fortt, S. H. *Tetrahedron Lett.*, **1987**, *28*, 2895. (d) Stork, G.; Mook, R *Tetrahedron Lett.*, **1986**, *27*, 4529.

(16) (a) Stork, G.; Mook, R. *J. Am. Chem. Soc.* **1987**, *109*, 2829. (b) Beckwith, A. L. J.; O'Shea, D. M. *Tetrahedron Lett.* **1986**, *27*, 4525.

(17) Crich, D.; Sun, S.; Brunckova, J. *J. Org. Chem.* **1996**, *61*, 605; Hart, D. J.; Kuzmich, D *J. Chin. Chem. Soc.* **1995**, *42*, 873.

Scheme 6



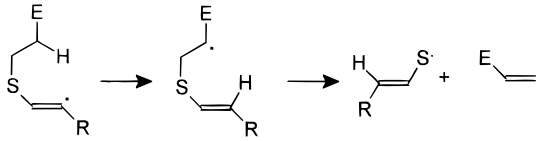
vinyl radical **8** did not undergo any 1,5-hydrogen migration (see Scheme 3), even though this process (much more feasible than the corresponding 1,4-hydrogen migration[18]) would lead to an α-oxy allyl radical analogous to the translocated radical **31**. This observation led us to claim that the loss of acrolein, with concomitant formation of the stable α-thio-substituted allyl radical **32**, might be the driving force of the entire process. On this basis we might consider the possibility that a one-step, concerted mechanism takes place leading to **32** from **10**; that is, the 1,4-hydrogen migration might be favored by the concomitant carbon−oxygen bond cleavage.

Compound (*Z*)-**30** was contaminated by a minor product which was likely the tetrahydrofuran **35** [80:20 (*Z*)-**30**/**35** ratio](Scheme 5). Compound **35** could be derived from competitive sulfanyl radical **2a** addition to the carbon−carbon double bond of ether **6** followed by 5-*exo* cyclization onto the CC triple bond of the resulting alkyl radical **34**. The nonregioselective sulfanyl radical promoted cyclization of the enyne **6** will be discussed later.

The above results indicate that the cyclization onto the styrene double bond predominates over the cyclization onto both the terminal double bond and the aromatic ring; these latter reactions occur at comparable rates. However, it should be noted that the cyclization onto the aromatic ring is *π-endo*, while the cyclization onto the CC double bond is *π-exo*; these cyclization modes might have different stereoelectronic demands, also in light of the fact that different heteroatoms (oxygen and sulfur) are present in the *exo* and *endo* chains of radicals **7**−**10**.

To evaluate this point we investigated the fate of radical **37** which was expected to cyclize onto both aryl rings to an extent only depending on the different stereoelectronic demands (Scheme 6). The reaction of thiol **1a** with alkynyl ether **36** carried out under conditions of method A furnished a mixture of the rearranged

Scheme 7



products **40** and **41** in a 59:41 ratio (75% overall yield). Both products **40** and **41** were obtained in a stereoselctive fashion as pure (*E*) stereoisomers; the actual configurations were assigned by NOE measurements. This finding led us to suggest that the methyl ether (*E*)-**41** was derived from stereoselective *π-exo* cyclization of radical (*Z*)-**37** followed by scission of the spiro-ring of radical **39**, while the methyl sulfide (*E*)-**40** was the expected product from *π-endo* cyclization of radical (*E*)-**37** (Scheme 6). Since α-alkyl-substituted vinyl radicals exist as rapidly interconverting (*E*) and (*Z*) isomers,[1a] the [**41**]/[**40**] ratio depends on k_{exo} and k_{endo} values as well as on the *E*/*Z* equilibrium constant, K_e, through the equation [**41**]/[**40**] = $K_e k_{exo}/k_{endo}$. The observed slight preference of the *π-endo* cyclization mode ($K_e k_{exo}/k_{endo} = 0.69$) might result from the fact that (*E*) radicals could be preferred at the equilibrium ($K_e < 1$) rather than from more favorable stereoelectronic conditions.

In all cases examined, we did not find any products deriving from radicals **7**−**10** by hydrogen abstraction nor any products deriving from radicals **7**, **8** by 1,5-hydrogen migration, even though the 1,5-hydrogen migration from an activated methylene toward vinyl radicals is a feasible process. In particular, we have previously reported[8f] that *β*-ethanesulfanyl-substituted vinyl radicals carrying a suitable activating group in *δ* position smoothly undergo a 1,5-hydrogen migration/fragmentation process. This reaction leads to alkenesulfanyl radicals and alkene by C−S bond scission of the new translocated radicals (Scheme 7). Thus, in order to study the competition between the 1,5-hydrogen migration and the five- and six-membered cyclization onto the CC double bond, the fate of radicals **11**−**14**, which were generated by reacting thiol **1b** with alkynyl ethers **3**−**6** under method A conditions, was considered.

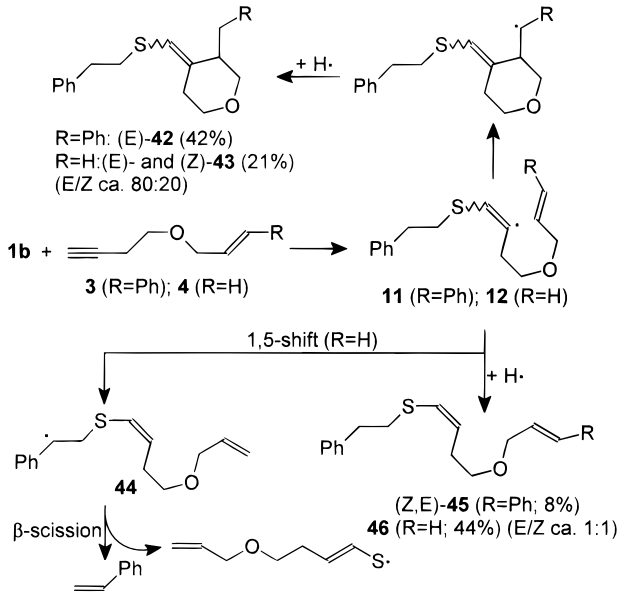
The reaction of thiol **1b** with ether **3** gave products (*E*)-**42** (42%) and **45** (8%). Product **45** is expected from vinyl radical **11** through hydrogen abstraction. This reaction can compete, although to a minor extent, with the 6-*exo* cyclization onto the styrene double bond leading to pyran **42** (Scheme 8). On the other hand, the reaction with ether **4** afforded major amounts of the hydrogen abstraction product **46** (44%) in addition to minor amounts of the 6-*exo* cyclization product **43** (21%), as a result of the lesser reactivity of the terminal double bond with respect to the styrene double bond (Scheme 8). Pyran **42**, analogous to the cyclization products **17** and **24**, was obtained in a high stereoselective fashion as an (*E*) stereoisomer,[19] while radical **12** gave a 80/20 mixture of isomeric (*E*)- and (*Z*)-**43**. The actual configurational structure for pyran **43** was established for the (*E*) isomer by NOE measurements.

No product deriving from radicals **11** or **12** through 1,5-hydrogen migration could be separated by column

(18) 1,4-Hydrogen migrations are very rare. For examples see: Brunton, G.; Griller, D.; Barclay, L. R. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 6803. Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085. Wallace, T. J.; Gritter, R. J. *J. Org. Chem.*, **1961**, *26*, 5256.

(19) The (*E*) configuration of the 6-(*π-exo*)*exo* cyclization product **42** and the 5-(*π-exo*)*exo* product **25** was attributed on the basis of the general evidence provided by related cyclization products **17**, **24**, and **43**, whose (*E*) configurations were assigned by NOE measurements.

Scheme 8



chromatography. However, GC-MS analysis of the reaction mixture of **1b** with **4** detected formation of styrene which was expected from the translocated radical **44** through C−S bond cleavage (Scheme 8).

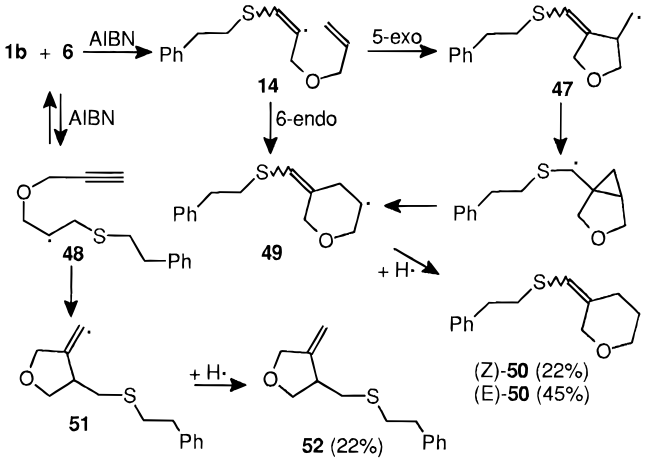
However, it would appear that the hydrogen abstraction reaction and, to a lesser extent, the 1,5-hydrogen migration can only compete with the stereoelectronically disfavored 6-*exo* cyclization. In fact, thiol **1b** reacted with ether **5** to give compound (*E*)-**25** (53%) as the only identifiable reaction product (Scheme 4). Compound (*E*)-**25** was obtained in a highly stereoselective fashion by radical (*Z*)-**13** through 5-*exo* cyclization onto the styrene double bond.[19]

Similarly, reaction of thiol **1b** with the ether **6** gave the pyran **50** (67%) as the only product deriving from radical **14**. The pyran **50** resulted from cyclization onto the terminal double bond through intermediacy of the six-membered *endo*-radical **49**. The latter, analogous to the *endo*-radical **28** (see Scheme 5), might be formed either by a 5-*exo* cyclization followed by ring expansion of resulting *exo*-radical **47** or by a 6-*endo* cyclization. Pyran **50** was obtained in both (*E*) and (*Z*) configurational forms with a ca. 2:1 (*E*)/(*Z*) isomeric ratio. The actual configurational structure was established for the (*E*) isomer by NOE measurements.

The reaction of **1b** with **6** furnished product **52** (22%) in addition to pyran **50**. Product **52**, analogous to **35**, could be the result of sulfanyl radical addition to the CC double bond of ether **6** and subsequent 5-*exo* cyclization of the resulting alkyl radical **48** onto the terminal alkyne triple bond (Scheme 9).

Regioselectivity of Sulfanyl Radical Addition to Enynes. Sulfanyl radical addition to the employed enynes was generally found to be regioselective to the CC triple bond, but with ether **6** a marked nonregioselectivity was observed. This behavior can be accounted for on the basis of the general evidence reported in the literature for the sulfanyl radical addition to CC double and triple bonds. To our knowledge no kinetic data have

Scheme 9



been reported on alkanesulfanyl radical addition to alkynes, and little is known about alkanesulfanyl radical addition to alkenes.[20] However, even though no comparative data are available for alkanesulfanyl radicals, results reported for arenesulfanyl radical addition to 1-pentyne and 1-hexene indicate that alkylacetylenes and terminal alkenes react with sulfanyl radicals nearly at the same rate.[21] Both sulfanyl radical addition to alkenes and alkynes are reversible, but the reversibility is less important for alkynes. Ito and co-workers[21] estimated the absolute rate constants k_1 and k_{-1} by measuring the arenesulfanyl radical decay in the presence of alkenes (and alkynes) and oxygen. The k_{-1} values for the addition to terminal alkenes not having electron acceptor substituents was found to be ca. 100 times greater than k_1. In contrast, the addition to terminal alkynes was not found to be reversible under the conditions employed. The importance of the C−S bond cleavage should strongly diminish on passing from arenethiyl to alkanethiyl radicals as a result of the increased C−S bond strength (the C−SPh bond is 10 kcal/mol weaker than the C−SAlk bond[22]). On this basis, it can be assumed that alkanesulfanyl radical addition to enynes occurs in a nonreversible fashion to the CC triple bond, and in a reversible fashion to the CC double bond. Thus, products deriving from the latter reaction are expected only if the resulting alkyl radical can react before equilibrating. This is the case for radicals **34** and **48** (see Schemes 5 and 9), which can undergo a facile 5-*exo* cyclization onto the CC triple bond.

Stereoselectivity of the (*π*-*exo*) Vinyl Radical Cyclization.[23] As mentioned above, the (*π*-*exo*)*exo* five-membered cyclization products **24** and **25** (see Scheme 4), as well as the (*π*-*exo*)*exo* six-membered products **17** and **42** (see Schemes 2 and 8), were obtained as pure (*E*) stereoisomers. These products were derived from stereoselective cyclization of vinyl radicals (*Z*)-**7**, -**9**, -**11**, -**13**. Moreover, the rearranged compound **41** was obtained as pure (*E*) isomer which was derived from radical (*Z*)-**37** by stereoselective 5-(*π*-*exo*)*exo* cyclization onto the aryl ring (see Scheme 6). The apparent incapability of radicals (*E*)-**7**, -**9**, -**11**, -**13**, -**37** to undergo (*π*-*exo*)*exo* cyclization can be ascribable to steric repulsion which

(20) In particular, the absolute rate of addition of butanesulfanyl radicals to cyclopropylethylene and 1-octene (McPhee, D. J.; Campredon, M.; Lesage, M.; Griller, D *J. Am. Chem. Soc.* **1989**, *111*, 7563) and 1-pentene (Sivertz, C. *J. Phys. Chem.* **1959**, *63*, 34) have been reported.

(21) Ito, O.; Omori, R.; Matsuda, M. *J. Am. Chem. Soc.* **1982**, *104*, 3934.

(22) Benson, S. W. *Chem. Rev.* **1978**, *78*, 23.

(23) For a recent monograph of stereoselective radical reactions see: Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH Publishers: New York, 1996.

occurs in the transition state between the radicophilic moiety (styrene double bond or aromatic ring) and the β-substituent. Support for our claim arose from the evidence that vinyl radical **12** can undergo 6-(π-*exo*)*exo* cyclization onto the terminal double bond in both (*Z*) and (*E*) configurations leading to (*E*)- and (*Z*)-**43**, respectively, in a 80:20 ratio (see Scheme 8). The formation of minor amounts of the (*Z*) isomer (*Z*)-**43** is consistent with the minor steric demand of the terminal CC double bond with respect to the styrene double bond (and the aromatic ring), which allows radical **12** to cyclize in the (*E*) configuration as well, although to a minor extent.

In contrast, the formal six-membered *endo*-cyclization onto the terminal CC double bond products **30** and **50** (see Schemes 5 and 9) were obtained in a stereoselective mode as 2:1 (*E*)/(*Z*) mixtures. In light of the evidence provided above which indicates that the (π-*exo*)*exo* cyclization is largely preferred for (*Z*)-vinyl radicals, this finding seems inconsistent with a mechanism leading to **30** and **50** by initial 5-(π-*exo*)*exo* cyclization followed by ring-expansion (see Schemes 5 and 9). In fact, in this case we would expect either complete nonstereoselectivity or (if transannular bond scission is fast enough to compete with rotation around the CC single bond) predominance of the (*Z*) isomer. Vice versa, the observed stereoselectivity might be accounted for by assuming that a 6-(π-*exo*)*endo* cyclization occurs. In our opinion no steric hindrance should be expected between the radicophilic double bond and the β-substituents for this cyclization mode; thus, the cyclization rates of the (*E*) and (*Z*) radicals should be equalized. In this assumption the observed predominance of the (*E*) isomers (*E*)-**30** and (*E*)-**50** would parallel the predominance at the equilibrium of the more stable (*E*)-vinyl radicals (*E*)-**10** and (*E*)-**14** with respect to their (*Z*)-isomers. However, our suggestion deserves further attention, since there is abundant evidence in the literature that vinyl radical cyclizations lead to thermodynamically more stable 6-*endo* radicals through ring-expansion of kinetically preferred 5-*exo* radicals.[8c,15d,16]

Conclusions

Regioselective radical addition of thiols **1a**,**b** to enynes **3**−**6** leads to vinyl radicals **7**−**14**, suitable for the study of the competition between cyclization onto different radicophilic groups and inter- or intramolecular hydrogen abstraction reaction. The results obtained from vinyl radicals **7**−**10** indicate that the five-membered cyclization onto the styrene double bond predominates over the six-membered *endo*-cyclization onto the terminal double bond as well as the 5-*exo* cyclization onto the 4-cyanophenyl ring. This last reaction affords spiro-cyclohexadienyl radical intermediates which can either be trapped by 2-cyanoisopropyl radicals or give 1,4-aryl migration products by fragmentation of the spiro-ring. Moreover, 5-*exo* cyclization onto the 4-cyanophenyl ring and 6-*exo* cyclization onto the styrene double bond occur at comparable rates; both largely predominate over the 6-*exo* cyclization onto the terminal double bond.

Cyclizations onto the aromatic ring and the double bond occur in a (π-*endo*) and a (π-*exo*) mode, respectively. Evidence has been provided that these two cyclization modes have comparable stereoelectronic demands, as shown by radical **37** (see Scheme 6) which furnished the 5-(π-*endo*)*exo* and the 5-(π-*exo*)*exo* products **40** and **41** in a 59:41 ratio.

Results obtained from radicals **11**−**14** indicate that the intermolecular hydrogen abstraction can only compete with the stereoelectronically disfavored 6-*exo* cyclization onto the styrene bond (to a minor extent) and onto the terminal double bond (to a major extent). Some evidence has been provided which indicates that the 1,5-hydrogen migration from a benzylic group can compete with the reaction onto the terminal double bond.

The six-membered *endo*-cyclization products **30** and **50**, deriving from radicals **10** and **14** (Schemes 5 and 9), might be formed either by a 5-*exo* cyclization/ring expansion process or by a direct 6-*endo* cyclization. However, stereochemical evidence appears to be inconsistent with the 5-*exo* cyclization/ring expansion process. In fact, pyrans **30** and **50** were obtained predominantly in the (*E*) configuration, which arose by cyclization of (*E*)-radicals (*E*)-**10** and (*E*)-**14**. A preferred 5-*exo* cyclization of (*E*)-radicals (*E*)-**10** and (*E*)-**14** is not consistent with the general behavior exhibited by vinyl radicals **7**, **9**, **11**−**13**, and **37** which undergo exclusive (or predominant) 5- or 6-(π-*exo*)*exo* cyclization in the (*Z*)-configuration due to steric repulsion occurring in the transition state between the *exo* double bond (or the aryl ring) and the β-substituent.

Sulfanyl radical addition to enynes **3**−**5** is highly regioselective to the terminal triple bond. In contrast, reaction of thiols **1a**,**b** with enyne **6** led to products deriving from sulfanyl radical addition to both the CC triple and double bond. This peculiar behavior is accounted for by assuming that sulfanyl radical addition to the alkyne triple bond is not reversible, while the addition to the alkene double bond is. The only route opened for alkyl radicals deriving from addition to the alkene double bond of **3**−**5** appears to be β-scission leading to starting enyne and sulfanyl radical. In contrast, sulfanyl radical addition to enyne **6** gives alkyl radicals **34** and **48** which can undergo a facile 5-*exo* cyclization onto the alkyne triple bond.

Experimental Section

Starting Materials. Thiol **1a**[8c] was prepared as previously described. Thiol **1b** is commercially available. Propynyl ethers **5**,[24] **6**,[25] and **36** were obtained in ca. 80% yields by heating in a sealed tube a THF solution (50 mL) of sodium propargylate (50 mmol) (prepared from equimolar amounts of propargyl alcohol and sodium hydride in anhydrous THF) and the appropriate commercially available bromide (*trans*-cinnamyl bromide, allyl bromide, and 4-cyanobenzyl bromide, respectively) at 80 °C for 8 h. Butynyl ethers **3** and **4** were similarly prepared from sodium but-3-yn-1-oate. [**3**: ^{1}H NMR δ (200 MHz) 2.0 (1H, t, J = 2.6 Hz), 2.50 (2H, dt, J_d = 2.6 Hz, J_t = 7.0 Hz), 3.60 (2H, t, J = 7.0 Hz), 4.20 (2H, br d, J = 6.0 Hz), 6.30 (1H, dt, J_d = 16 Hz, J_t = 6.0 Hz), 6.65 (1H, br d, J_d = 16.0 Hz), 7.2−7.45 (5H, m); MS *m*/*z* (rel inten) 186 (M^+, 10), 185 (10), 117 (100), 115 (45), 105 (100). Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58; O, 8.60. Found: C, 83.95; H, 7.55. **4**: ^{1}H NMR δ (200 MHz) 1.96 (1H, t, J = 2.6 Hz), 2.50 (2H, dt, J_t = 7.0 Hz, J_d = 2.6 Hz), 3.60 (2H, t, J = 7.0 Hz), 4.05 (2H, br d, J = 6 Hz), 5.20 (1H, br d, J = 10 Hz), 5.30 (1H, br d, J = 15 Hz), 5.92 (1H, ddt, J_1 = 15 Hz, J_2 = 10 Hz, J_t = 6 Hz); MS *m*/*z* (rel inten) 110 (M^+, 2), 79 (20), 71 (20), 41 (100), 39 (60). Anal. Calcd for $C_7H_{10}O$: C, 76.32; H, 9.15; O, 14.58. Found: C, 76.5; H, 9.20. **36**: ^{1}H NMR δ (200 MHz) 2.48 (1H, t, J = 2 Hz), 4.20 (2H, d, J = 2 Hz), 4.60 (2H, s), 7.40 (2H, d, J = 8.5 Hz), 7.60 (2H, d, J = 8.5 Hz); MS *m*/*z* (rel inten) 171

(24) Trost, B. M.; Edstrom, E. D.; Carter-Petillo, M. B. *J. Org. Chem.* **1989**, *54*, 4489.

(25) Fellous, R.; Rabin, J. P.; Lizzani-Cuvelier, L.; Luft, R. *Bull. Chem. Soc. Fr.* **1974**, 923.

(M^+, 10), 170 (20), 132 (95), 130 (60), 117 (60), 116 (95), 104 (75), 39 (100). Anal. Calcd for $C_{11}H_9NO$: C, 77.17; H, 5.30; N, 8.18; O, 9.35. Found: C, 77.3; H, 5.32; N, 8.15].

Reaction Products. Reaction products were separated by Merck silica gel column chromatography (0.040−0.063 particle size) of the reaction mixtures by gradual elution with light petroleum ether (bp 40−70 °C)−diethyl ether. Yields were based on reacted thiol **1a**,**b**. Structural assignments generally came from ^{1}H NMR and MS spectral data in addition to elemental analysis. Elemental analysis was not performed for the spiro compound **18**, owing to the impossibility of obtaining a pure sample, nor for compounds **35** and **52** which were obtained as inseparable mixtures with (*Z*)-**30** and (*Z*)-**50**, respectively. Their identification arose from careful MS and ^{1}H NMR spectral analysis. ^{1}H NMR spectra were recorded at 200 (or 300 MHz) with Me_4Si as internal standard. Mass spectra were recorded with the electronic impact method.

Reactions of Thiols 1a,b with Alkynyl Ethers 3−6, 36. Method A. A benzene solution (25 mL) of the appropriate thiol **1a**,**b** (2 mmol), the appropriate ether **3**−**6**, **36** (4 mmol), and AIBN (0.2 mmol) was refluxed for 3 h. The reaction mixture was washed twice with NaOH 10% and once with water, the organic layer was dried over Na_2SO_4, and the solvent was evaporated off. The unreacted thiol **1a**,**b** was recovered by acidification of the aqueous layer and extraction with diethyl ether.

Method B. A benzene solution (5 mL) of thiol **1a** (2 mmol) was added over 4 h with a syringe pump to a boiling benzene solution (20 mL) of the appropriate alkynyl ether **3**−**6** (4 mmol) and AIBN (55 mg, 0.33 mmol). Further portions of AIBN (55 mg) were added after 1.5 and 3 h. The resulting reaction mixture was refluxed for an additional 1 h and then treated as described in method A.

From 4-Cyano-α-toluenethiol (1a) and Butynyl Phenylpropenyl Ether 3. Chromatography gave: **(*E*)-3-benzyl-4-[(4-cyano-α-tolylthio)methylidene]pyran (*E*)-17** [135 mg, 28% (method B)] [^{1}H NMR δ 2.4 (3H, m), 2.80 (2H, ABX system, J_{AB} = 12 Hz, J_{AX} = J_{BX} = 7 Hz; inner line separation 8 Hz), 3.4 (1H, m), 3.52 (2H, ABX system, J_{AB} = 11 Hz, J_{AX} = J_{BX} = 4 Hz; inner line separation 5 Hz), 3.73 (2H, s), 3.8 (1H, m), 5.50 (1H, s), 7.00−7.35 (7H, m), 7.55 (2H, d, J = 8.5 Hz). Irradiation at δ 5.50 caused an enhancement at δ 2.4 (allylic protons) and 2.8 (benzylic protons). MS *m*/*z* (rel inten) 335 (M^+, 20), 254 (25), 244 (100), 219 (20), 128 (95) 116 (95), 91 (55). Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18; O, 4.77; S, 9.56. Found: C, 75.40; H, 6.34; N, 4.16; S, 9.50.], **(*Z*)-3-(4-cyanophenyl)-4-(methylthio)but-3-en-1-yl (*E*)-3-phenylprop-2-en-1-yl ether (*Z*,*E*)-20** [27 mg, 6% (method B)] [^{1}H NMR δ 2.30 (3H, s), 2.75 (2H, t, J = 6.9 Hz), 3.45 (2H, t, J = 6.9 Hz), 4.10 (2H, br d, J = 5.5 Hz), 6.18 (1H, dt, J_d = 16 Hz, J_t = 5.5 Hz), 6.20 (1H, s), 6.54 (1H, br d, J = 16 Hz), 7.20−7.70 (9H, m); MS *m*/*z* (rel inten) 335 (M^+, 10), 188 (30), 137 (40), 117 (100). Anal. Calcd for $C_{21}H_{21}NOS$: C, 75.19; H, 6.31; N, 4.18; O, 4.77; S, 9.56. Found: C, 75.45; H, 6.28; N, 4.20; S, 9.60.] and **spiro-cyclohexadiene 18** [64 mg, 11% (method B)] [^{1}H NMR δ 1.50 (6H, s), 2.20 (2H, br t, collapsing to br s upon irradiation at δ 3.60), 3.15 (2H, s), 3.58 (2H, t, J = 7 Hz), 4.15 (2H, br d, J = 6.0 Hz), 5.90 (2H, d, J = 10 Hz), 6.08 (1H, br s), 6.18 (2H, d, J = 10 Hz), 6.27 (1H, dt, J_d = 15.9 Hz, J_t = 6.0 Hz; collapsing to doublet upon irradiation at δ 4.15), 6.60 (1H, br d, J = 15.9 Hz; collapsing to doublet upon irradiation at δ 4.15), 7.20−7.40 (5H, m); MS *m*/*z* (rel inten) 402 (M^+, 2), 335 (4), 296 (10), 232 (15), 219 (20), 116 (100). Thiol **1a** was recovered in ca. 30% yield.

From 4-Cyano-α-toluenethiol (1a) and Butynyl Propenyl Ether (4). Chromatography gave: **(*E*)-3-(4-cyanophenyl)-4-(methylthio)but-3-en-1-yl allyl ether (*E*)-23** (35 mg, 8% (method A); 5 mg, 2% (method B)] [^{1}H NMR δ 2.40 (3H, s), 2.88 (2H, t, J = 7 Hz), 3.52 (2H, t, J = 7 Hz), 3.95 (2H, br d, J = 6 Hz), 5.12 (1H, br d, J = 10 Hz), 5.20 (1H, br d, J = 16 Hz), 5.85 (1H, m, collapsing to dd, J_1 = 10 Hz, J_2 = 16 Hz upon irradiation at δ 3.95), 6.50 (1H, s), 7.40−7.70 (4H, A_2B_2 system); MS *m*/*z* (rel inten) 259 (M^+, 30), 202 (35), 188 (50), 41 (100). Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40; O, 6.17; S, 12.36. Found: C, 69.60; H, 6.60; N, 5.37; S, 12.40.]; **(*Z*)-3-(4-cyanophenyl)-4-(methylthio)but-3-en-1-yl allyl ether (*Z*)-23** (305 mg, 70% (method A); 70 mg, 18% (method B)] [^{1}H NMR δ 2.30 (3H, s), 2.72 (2H, t, J = 7 Hz), 3.40 (2H, t, J = 7 Hz), 3.90 (2H, br d, J = 6 Hz), 5.12 (1H, br d, J = 10 Hz), 5.20 (1H, br d, J = 16 Hz), 5.82 (1H, ddt, J_1 = 16 Hz, J_2 = 10 Hz, J_t = 6 Hz), 6.20 (1H, s), 7.40−7.70 (4H, A_2B_2 system); MS *m*/*z* (rel inten) 259 (M^+, 25), 202 (30), 188 (60), 41 (100). Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40; O, 6.17; S, 12.36. Found: C, 69.35; H, 6.58; N, 5.42 ; S, 12.30.]; **spiro-cyclohexadiene 21** [45 mg, 9% (method B)] [^{1}H NMR δ 1.55 (6H, s), 2.20 (2H, dt, J_d = 1.5 Hz, J_t = 6.5 Hz), 3.20 (2H, s), 3.55 (2H, t, J = 6.5 Hz), 4.00 (2H, br d, J = 6 Hz), 5.20 (1H, br d, J = 10 Hz), 5.30 (1H, br d, J = 15 Hz), 5.92 (2H, d, J = 9.5 Hz; superimposed to 1H, ddt, J_1 = 10 Hz, J_2 = 15 Hz, J_t = 6 Hz), 6.10 (1H, t, J = 1.5 Hz), 6.20 (2H, d, J = 9.5 Hz); MS *m*/*z* (rel inten) 326 (M^+, 20), 200 (40), 116 (60), 41 (100). Anal. Calcd for $C_{19}H_{22}N_2OS$: C, 69.90; H, 6.79; N, 8.58; O, 4.90; S, 9.82. Found: C, 69.65; H, 6.75; N, 8.61; S, 9.78.]. Thiol **1a** was recovered in ca. 15% yield (method A) and 25% (method B).

From 4-Cyano-α-toluenethiol (1a) and Propynyl Phenylpropenyl Ether (5). Chromatography gave **(*E*)-3-benzyl-4-[(4-cyano-α-tolylthio)methylidene]tetrahydrofuran (*E*)-24** [220 mg, 64% (method A); 250 mg, 50% (method B)] [^{1}H NMR δ 2.68 (ABX system, J_{AB} = 12 Hz, J_{AX} = 8.5 Hz, J_{BX} = 7 Hz; inner lines separation 6 Hz), 2.95 (1H, m), 3.6 (1H, dd, J_1 = 8.5 Hz, J_2 = 5.4 Hz), 3.8 (2H, s), 3.85 (1H, dd, J_1 = 8.5 Hz, J_2 = 7 Hz), 4.30 (2H, ABX system, J_{AB} = 14 Hz, J_{AX} = J_{BX} = 2 Hz; inner lines separation 2 Hz), 5.50 (1H, q, J = 2 Hz, collapsing to triplet upon irradiation at δ 2.95), 7.10−7.30 (5H, m), 7.35 (2H, d, J = 8.5 Hz), 7.60 (2H, d, J = 8.5 Hz). Irradiation at δ 5.50 caused an enhancement at δ 2.95 (allylic proton) and 2.68 (benzylic protons). MS *m*/*z* (rel inten) 321 (M^+, 10), 230 (25), 205 (10), 116 (100), 91 (40). Anal. Calcd for $C_{20}H_{19}NOS$: C, 74.73; H, 5.96; N, 4.36; O, 4.98; S, 9.97. Found: C, 74.50; H, 5.93; N, 4.34; S, 9.93.]. Thiol **1a** was recovered in ca. 45% yield (method A) and 20% (method B).

From 4-Cyano-α-toluenethiol (1a) and Propynyl Propenyl Ether (6). Chromatography gave **4-cyanobenzyl allyl sulfide 33** [40 mg, 15% (method A)] [^{1}H NMR δ 3.00 (2H, br d, J = 7 Hz), 3.70 (2H, s), 5.05 (1H, br d, J = 16.5 Hz), 5.15 (1H, br d, J = 10 Hz), 5.77 (1H, ddt, J_1 = 16.5 Hz, J_2 = 10 Hz, J_t = 7 Hz), 7.40 (2H, d, J = 8.5 Hz), 7.60 (2H, d, J = 8.5 Hz); MS *m*/*z* (rel inten) 189 (M^+, 30), 147 (45), 116 (100), 73 (50). Anal. Calcd for $C_{11}H_{11}NS$: C, 69.80; H, 5.86; N, 7.40; S, 16.94. Found: C, 69.60; H, 5.88; N, 7.37; S, 17.00.]; **(*Z*)-2-(4-cyanophenyl)-3-(methylthio)prop-2-en-1-yl allyl ether 29** [26 mg, 7% (method A)] [^{1}H NMR δ 2.32 (3H, s), 4.00 (2H, dt, J_d = 6 Hz, J_t = 1.5 Hz), 4.22 (2H, s), 5.20 (1H, dq, J_d = 10 Hz, J_q = 1.5 Hz), 5.26 (1H, dq, J_d = 15 Hz, J_q = 1.5 Hz), 5.90 (1H, ddt, J_1 = 15 Hz, J_2 = 10 Hz, J_t = 6 Hz), 6.45 (1H, s), 7.50−7.70 (4H, A_2B_2 system, J = 8.5 Hz). Minor peaks at δ 2.45 (s), 4.42 (s) and 6.80 (s) were assigned to the *E* isomer (*Z*/*E* ratio = 9:1); MS *m*/*z* (rel inten) 245 (M^+, 20), 188 (30), 71(60), 41(100). Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71; O, 6.52; S, 13.07. Found: C, 68.75; H, 6.18; N, 5.69; S, 13.10.]; a 4:1 mixture of **(*Z*)-3-[(4-cyano-α-tolylthio)methylidene]pyran (*Z*)-30** and (possible) 3-methylidene-4-[(4-cyano-α-tolylthio)methyl]tetrahydrofuran **35** [73 mg, 19% overall yield] [^{1}H NMR δ [(*Z*)-**30**] 1.60−1.70 (2H, m); 2.30 (2H, br t, J = 7 Hz; collapsing to broad singlet upon irradiation at δ 1.65), 3.70 (2H, t, J = 7 Hz, collapsing to singlet upon irradiation at δ 1.65), 3.82 (2H, s), 4.15 (2H, s), 5.62 (1H, br s), 7.40−7.60 (4H, A_2B_2 system, J = 9 Hz); ^{1}H NMR spectrum showed peaks at δ 4.20 (2H, br s, OCH_2C═), 3.95 (2H, m, OCH_2), 4.90 (1H, br s, ⟨C═CH_2), and 4.95 (2H, br s, ⟨C═CH_2) ascribable to product **35**; MS *m*/*z* (rel inten) 245 (M^+, 10), 129 (30), 116 (100)]; **(*E*)-3-[(4-cyano-α-tolylthio)methylidene]pyran (*E*)-30** [135 mg, 35% (method A)]: ^{1}H NMR δ 1.60−1.70 (2H, m); 2.33 (2H, br t, J = 7 Hz, collapsing to broad singlet upon irradiation at δ 1.65), 3.70 (2H, t, J = 7 Hz, collapsing to singlet upon irradiation at δ 1.65), 3.86 (2H, s), 3.95 (2H, s), 5.70 (1H, s), 7.40−7.60 (4H, A_2B_2 system, J = 9 Hz). Irradiation at δ 5.70 caused en enhancement at δ 3.95 (OCH_2C═). MS *m*/*z* (rel inten) 245 (M^+, 10), 129 (30), 116 (100). Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71;

O, 6.52; S, 13.07. Found: C, 68.75; H, 6.14; N, 5.73; S, 13.02.]. Thiol **1a** was recovered in 22% yield.

From Phenethanethiol (1b) and Butynyl Phenylpropenyl Ether (3). Chromatography gave **(*Z*)-4-(phenethylthio)but-3-en-1-yl (*E*)-3-phenylprop-2-en-1-yl ether (*Z*,*E*)-45** (30 mg; 8%) [^{1}H NMR δ 2.45 (2H, m), 2.90 (4H, s), 3.50 (2H, t, J = 6.5 Hz), 4.15 (2H, m), 5.60−5.76 (1H, m; collapsing to A part of an AB system upon irradiation at δ 2.40, J_{AB} = 11 Hz), 6.05 (1H, br d, collapsing to B part of an AB system upon irradiation at δ 2.45, J_{AB} = 11 Hz), 6.30 (1H, m, collapsing to A part of an AB system upon irradiation at δ 4.15, J = 15 Hz), 6.70 (1H, br d, collapsing to B part of an AB system upon irradiation at δ 4.15, J = 15 Hz), 7.10−7.40 (10H, m); MS *m*/*z* (rel inten) 324 (M^+, 10), 233 (30), 227 (40), 117 (50), 105 (100). Anal. Calcd for $C_{21}H_{24}OS$: C, 77.73; H, 7.46; O, 4.93; S, 9.88. Found: C, 77.90; H, 7.50; S, 9,84.] and **(*E*)-3-benzyl-4-[(phenethylthio)methylidene]pyran (*E*)-42** (160 mg, 42%) [^{1}H NMR δ 2.35−2.45 (3H, m), 2.8 (4H, br s), 2.9 (2H, m), 3.6 (3H, m), 3.90 (1H, dt, J_d = 10 Hz, J_t = 6.50 Hz), 5.60 (1H, s), 7.20−7.40 (10H, m); MS *m*/*z* (rel inten) 324 (M^+, 10), 233 (55), 105 (100), 91 (30). Anal. Calcd for $C_{21}H_{24}OS$: C, 77.73; H, 7.46; O, 4.93; S, 9.88. Found: C, 77.54; H, 7.42; S, 9.92.]. Thiol **1b** was recovered in ca. 40% yield.

From Phenethanethiol (1b) and Butynyl Propenyl Ether (4). Chromatography gave a ca. 1:1 mixture of **(*E*)-** and **(*Z*)-4-(phenethylthio)but-3-en-1-yl allyl ether (*E*)- and (*Z*)-46** (150 mg, 44%) [^{1}H NMR δ 2.40 (2H, q, J = 7 Hz), 2.45 (2H, q, J = 7 Hz), 2.90 (8H, br s), 3.42 (2H, t, J = 7 Hz), 3.48 (2H, t, J = 7 Hz), 3.95 (4H, br d, J = 6 Hz), 5.16 (2H, br d, J = 10.5 Hz), 5.25 (2H, br d, J = 16 Hz), 5.64 (2H, m, collapsing to 1H, d, J = 9.5 Hz and 1H, d, J = 15 Hz, upon irradiation at δ 2.42), 5.90 (2H, m), 6.00 (1H, br d; collapsing to doublet, J = 9.5 Hz, upon irradiation at δ 2.42) and 6.00 (1H, br d, collapsing to doublet, J = 15 Hz, upon irradiation at 2.42), 7.10−7.40 (10H, m); MS *m*/*z* (rel inten) 248 (M^+, 5), 143 (30), 105 (100), 41 (50). Anal. Calcd for $C_{15}H_{20}OS$: C, 72.54; H, 8.12; O, 6.44; S, 12.91. Found: C, 72.75; H, 8.15; S, 12.85.]; a ca. 80:20 mixture of **(*E*)- (*Z*)-3-methyl-4-[(phenethylthio)methylidene]pyran (*E*)- and (*Z*)-43** (75 mg; 21%) [MS *m*/*z* (rel inten) 248 (M^+, 90), 219 (20), 105 (100). Anal. Calcd for $C_{15}H_{20}OS$: C, 72.53; H, 8.12; O, 6.44; S, 12.91. Found: C, 72.45; H, 8.08; S, 12.95.]. Repeated column chromatography allowed for the separation of a fraction composed mainly of the (*E*)-isomer and a fraction containing a ca. 1:1 isomeric mixture. ^{1}H NMR (*E*-isomer) δ 1.0 (3H, d, J = 6.5 Hz, collapsing to singlet upon irradiation at δ 2.35), 2.23 (1H, ddd, J_1 = 13.5 Hz, J_2 = 9.5 Hz, J_3 = 4.8 Hz, collapsing to d_1d_2 upon irradiation at δ 3.5 and to d_1d_3 upon irradiation at δ 3.8), 2.35 (1H, m); 2.60 (1H, ddd, J_1 = 13.5 Hz, $J_2 = J_3$ = 4 Hz, collapsing to dd upon irradiation at δ 3.5 or 3.8), 2.90 (4H, s), 3.15 (1H, dd, J_1 = 10.5 Hz, J_2 = 8.3 Hz, collapsing to d, J = 10.5 Hz upon irradiation at δ 2.35), 3.50 (1H, ddd, J_1 = 12.5 Hz, J_2 = 9.5 Hz, J_3 = 4 Hz), 3.8 (2H, m) 5.64 (1H, s), 7.15−7.35 (5H, m). Irradiation at δ 5.64 caused an enhancement at δ 2.90 (PhCH_2CH_2), 2.35 (=CCH⟩) and 1.0 (*exo* methyl group). ^{1}H NMR (*Z*-isomer) δ 1.20 (3H, d, J = 6.5 Hz), 2.0 (1H, br d), 2.6 (1H, m), 2.8 (1H, m), 2.88 (4H, s), 3.3 (1H, m), 3.5 (1H, m), 3.75 (1H, m), 4.0 (1H, m), 5.65 (1H, s), 7.15−7.35 (5H, m)]; a product which was probably 4,4-Bis(phenethylthio)but-1-yl allyl ether (25 mg, 9%). Thiol **1b** was recovered in ca. 30% yield.

From Phenethanethiol (1b) and Propynyl Phenylpropenyl Ether (5). Chromatography gave **(*E*)-3-benzyl-4-[(phenethylthio)methylidene]tetrahydrofuran (*E*)-(25)** (200 mg, 53%) [^{1}H NMR δ 2.65 (1H, A part of an ABX system, J_{AB} = 13 Hz, J_{AX} = 8.5 Hz), 2.85 (1H, B part of an ABX system, J_{AB} = 13 Hz, J_{BX} = 6 Hz), 2.88 (4H, br s), 3.00 (1H, m), 3.65 (1H, A part of an ABX system, J_{AB} = 8.5 Hz, J_{AX} = 5 Hz), 3.90 (1H, B part of an ABX system, J_{AB} = 8.5 Hz, J_{BX} = 6 Hz), 4.35 (2H, ABX system, J_{AB} = 13 Hz, $J_{AX} = J_{BX}$ = 2 Hz, inner line separation 2 Hz), 5.60 (1H, q, J = 2 Hz), 7.1−7.4 (10H, m); MS *m*/*z* (rel inten) 310 (M^+, 15), 219 (40), 185 (20), 105 (100), 91 (40). Anal. Calcd for $C_{20}H_{22}OS$: C, 77.38; H, 7.14; O, 5.15; S, 10.33. Found: C, 77.60; H, 7.17; S, 10.30.]. Thiol **1b** was recovered in ca. 30% yield.

From Phenethanethiol (1b) and Propynyl Propenyl Ether (6). Chromatography gave a 50:50 mixture of **(*Z*)-3-[(phenethylthio)methylidene]pyran (*Z*)-50** and **3-α-[(phenethylthio)methyl]-4-methylidenetetrahydrofuran 52** (145 mg, 44% overall yield) [^{1}H NMR δ[(*Z*)-**50**)] 1.70 (2H, m); 2.34 (2H, dt, J_t = 6.5 Hz, J_d = 1.2 Hz), 2.90 (4H, br s), 3.72 (2H, t, J = 6 Hz, collapsing to singlet upon irradiation at δ 1.70), 4.22 (2H, s), 5.75 (1H, s), 7.20−7.40 (5H, m); δ(**52**) 2.70−2.90 (7H, m), 3.74 (1H, dd, J_1 = 8.8 Hz, J_2 = 5.6 Hz), 4.03 (1H, dd, J_1 = 8.8 Hz, J_2 = 7.0 Hz), 4.32 (2H, br s), 4.95 (2H, br s), 7.20−7.40 (5H, m); MS *m*/*z* (rel inten) 234 (M^+, 30), 152 (35), 129 (75), 105 (60), 97 (90), 83 (100)]; **(*E*)-3-[(phenethylthio)-methylidene]pyran (*E*)-50** (150 mg, 45%) [^{1}H NMRδ 1.70 (2H, m); 2.40 (2H, dt, J_t = 6 Hz, J_d = 1.2 Hz), 2.90 (4H, br s), 3.75 (2H, t, J = 6 Hz), 4.00 (2H, s), 5.80 (1H, s), 7.15 −7.40 (5H, m). Irradiation at δ 4.0 caused an enhancement at δ 5.8 (vinylic proton). MS *m*/*z* (rel inten) 234 (M^+, 25), 129 (70), 105 (40), 97 (100). Anal. Calcd for $C_{14}H_{18}OS$: C, 71.75; H, 7.74; O, 6.83; S, 13.68. Found: C, 71.55; H, 7.71; S, 13.73.]. Thiol **1b** was recovered in ca. 30% yield.

From 4-Cyano-α-toluenethiol (1a) and Propynyl 4-Cyanobenzyl Ether (36). Column chromatography gave a 59:41 mixture of **4-cyanobenzyl 3-(4-cyanophenyl)-4-(methylthio)prop-2-en-1-yl ether 40** and **4-cyanobenzyl 3-methoxy-2-(4-cyanophenyl)prop-1-en-1-yl sulfide 41** (310 mg, 75%) [^{1}H NMR δ(**40**) 2.35 (3H, s), 4.32 (2H, s), 4.58 (2H, s), 6.50 (1H, s), 7.30−7.70 (8H, m). Irradiation at δ 6.50 caused a 2% enhancement at δ 2.35 (CH_3S) and a 5% enhancement at δ 4.32 (=CHCH_2O). ^{1}H NMR δ(**41**) 3.30 (3H, s), 4.05 (2H, s), 4.38 (2H, s), 6.60 (1H, s), 7.40−7.70 (8H, m). Irradiation at δ 6.60 caused a 2% enhancement at δ 4.05 (CH_2S). MS *m*/*z* (rel inten) 320 (M^+, 30), 204 (45), 116 (100). Anal. Calcd for $C_{19}H_{16}N_2OS$: C, 71.22; H, 5.03; N, 8.74; O, 4.99; S, 10.01. Found: C, 71.50; H, 5.05; N, 8.70; S, 10.05.]. Thiol **1b** was recovered in ca. 35% yield.

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