Radical Addition to Isonitriles: A Route to Polyfunctionalized Alkenes through a Novel Three-Component Radical Cascade Reaction

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The reaction of aromatic disulfides, alkynes, and isonitriles under photolytic conditions affords polyfunctionalized alkenes—β-arylthio-substituted acrylamides or acrylonitriles—in fair yields through a novel three-component radical cascade reaction. The procedure entails addition of a sulfanyl radical to the alkyne followed by attack of the resulting vinyl radical to the isonitrile. A fast reaction, e.g., scavenging by a nitro derivative or β-fragmentation, is necessary in order to trap the final imidoyl radical, since addition of vinyl radicals to isonitriles seems to be a reversible process. The stereochemistry of the reaction is discussed, particularly with respect to the stereochemical outcome of related hydrogen abstraction reactions by the same vinyl radicals. The lower or even inverted preference for either geometrical isomer observed in our cases with respect to that encountered in hydrogen abstraction reactions is explained in terms of transition-state interactions and/or isomerization of the final imidoyl radical. The latter possibility is supported by semiempirical calculations, which show that the spin distribution in the imidoyl radical can allow rotation of the adjacent carbon−carbon double bond prior to β-fragmentation.

Introduction

Radical addition to isonitriles dates back to the 1960s, when Shaw and Saegusa discovered the isonitrile−nitrile isomerization mediated by methyl[1a] or stannyl radicals.[1b] Until recent years, this reaction has been studied both from a mechanistic and a synthetic point of view,[2] especially as an approach to nitriles[2i] or a deamination method.[2f,j]

Only since 1991 have radical reactions with isonitriles been successfully employed in the synthesis of heterocyclic compounds.[3] In his pioneering work,[3a] Curran carried out several 4 + 1 annulations using isonitriles as geminal radical acceptor/radical donor synthons: this strategy allowed the synthesis of cyclopenta-fused quinolines and provided easy access to the antitumor agents of the camptothecin family.[3b,e,h,i,l,n] Almost in the same years, Bachi performed studies on the free-radical cyclization of alkenyl and alkynyl isonitriles, thus accomplishing the syntheses of pyrroline and pyroglutamate derivatives.[3c,f,g] He also achieved the stereo-[3j] and enantioselective syntheses[3k,m] of (±)- and (−)-α-kainic acid through radical cascade reactions involving isonitriles bearing suitable unsaturated side chains.

Our long interest in the chemistry of imidoyl radicals[4] recently led us to develop new synthetic strategies for the generation of those intermediates via radical addition to isonitriles. Quinoxaline derivatives have thus been synthesized by addition of cyano-substituted vinyl,[4h] alkyl,[4l] and sulfanyl[4l] radicals to aromatic isonitriles. Of special interest was our vinyl radical-mediated cyclopenta-fused quinoxaline production,[4h] since it provided the first trimolecular version of the radical addition, tandem cyclization strategy. This finding seemed worthy of further investigations since three-component radical

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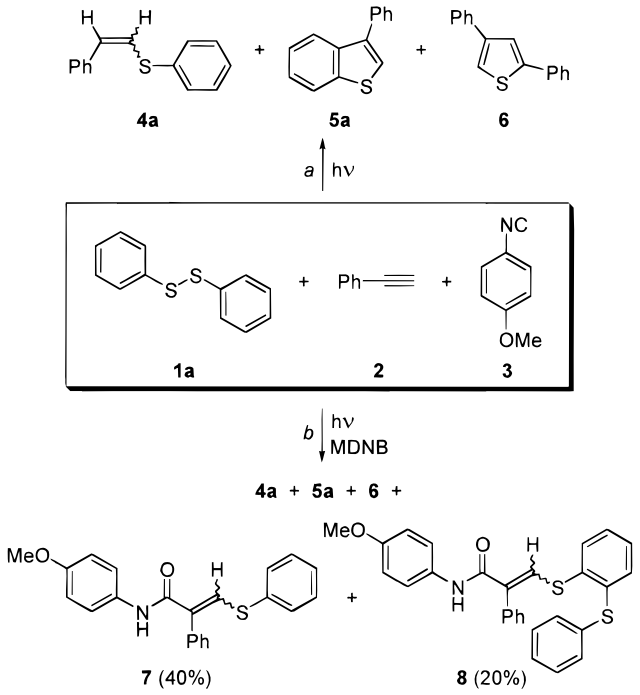
reactions, besides being quite rare,[5] are potentially very powerful synthetic strategies. Indeed, they might provide access to polyfunctionalized molecules—or polyfused cyclic compounds—from very simple, easily accessible—often commercially available—starting materials.

In light of the fair propensity of vinyl radicals to add to isonitriles,[4h] we were prompted to exploit these reactions in search of other synthetically useful three-component procedures. Toward this purpose, the generation of vinyl radicals in the presence of isonitriles was carried out through regioselective addition of sulfanyl radicals to alkynes.[6] Sulfanyl radicals in turn were produced by light-induced homolytic cleavage of the corresponding disulfides. The usual hydrogen abstraction from thiols was not considered, since thiols are known to be highly efficient scavengers of vinyl radicals. Here we are pleased to report that irradiation of aromatic disulfides in the presence of suitable alkynes and isonitriles can actually result in a novel three-component radical cascade reaction involving initial addition of a sulfanyl radical to the alkyne and subsequent addition of the ensuing vinyl radical to the isonitrile.[7]

Results and Discussion

The first experiment was carried out by UV irradiation of a benzene solution (40 mL) of commercially available diphenyl disulfide **1a** (0.5 mmol) and phenylacetylene **2** (5 mmol) and easily accessible 4-methoxyphenyl isonitrile **3** (10 mmol).[8] Benzene proved to be the best reaction solvent. Reactions carried out in methylene chloride, methanol, or hexane were characterized by lower yields and/or longer reaction times. Comparable yields but longer reaction times were obtained by performing the experiments in more concentrated solutions.[9] Unexpectedly, the reaction afforded only products **4a**, **5a**, and **6**, derived from **1a** and **2** with no intervention of the isonitrile (Scheme 1, reaction *a*). This curious outcome, quite unpredictable in light of our previous results,[4h] led us to repeat the experiment in the presence of a radical scavenger to trap some reaction intermediate. Indeed, when the same reagents were allowed to react under identical conditions in the presence of *m*-dinitrobenzene (MDNB) we obtained again minor amounts of the above compounds together with amides **7** and **8** in ca. 60% overall yield (Scheme 1, reaction *b*). Structure **8** was assigned on the basis of the X-ray structure determined for another byproduct obtained from analogous, previously reported photolyses of disulfides and isonitriles.[4l,10]

Scheme 1



This result can be rationalized according to the reaction pathway shown in Scheme 2. Fast addition of a sulfanyl radical to the alkyne gives vinyl radical **9**; subsequent addition of **9** to isonitrile **3** generates imidoyl radical **10**. In the absence of MDNB, radical **10** cannot evolve rapidly into other intermediates;[11] since the addition of **9** to **3** is likely to be reversible,[12] it rather prefers to give back vinyl radical **9**, which is responsible for the formation of compounds **4a**, **5a**, and **6**.[13] On the other hand, in the presence of MDNB, imidoyl **10** is efficiently trapped by

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(7) Under these conditions, the only side reaction is the isonitrile—nitrile self-isomerization (see: Casanova, J., Jr.; Werner, N. D.; Schuster, R. E. *J. Org. Chem.* **1966**, *31*, 3473). Since the isonitrile was present in a large excess, this reaction did not significantly affect the reaction outcome; however, it occurred quite remarkably only in the case of very long reaction times.

(8) Isonitriles can be readily synthesized in very good yields by conversion of the corresponding amines into formamides and subsequent dehydration with phosphorus oxychloride (Wolber, E. K. A.; Schmittel, M.; Rüchardt, C. *Chem. Ber.* **1992**, *125*, 525).

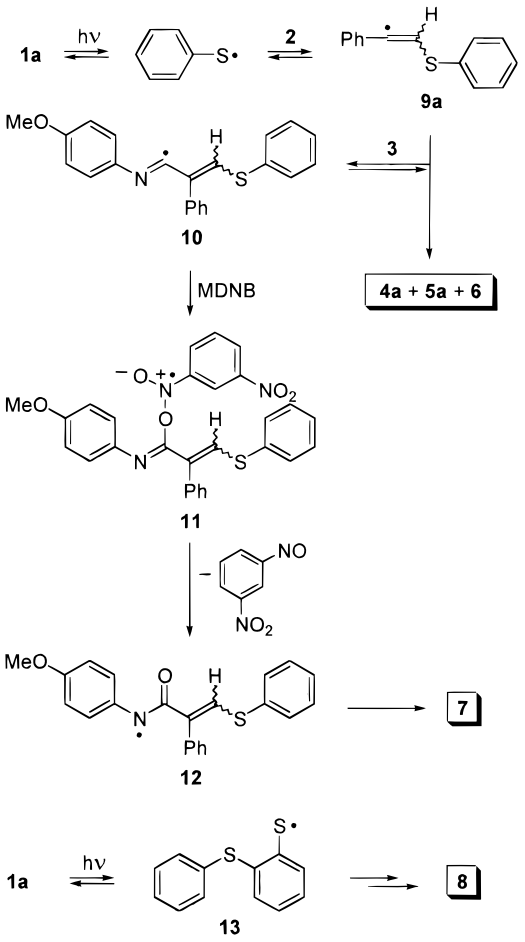
(9) This is consistent with the disulfide dissociation equilibrium, which is shifted towards the reagent by lowering the dilution. Synthetically useful reactions with photolytically generated sulfanyl radicals are therefore usually carried out at high dilutions.

(10) Leardini, R.; Nanni, D.; Zanardi, G. *Eur. J. Org. Chem.*, **2000**, 707. Analogous compounds were always obtained, generally in small amounts, in all of the subsequent reactions (see the Experimental Section).

(11) At least one fate was in principle conceivable—and expected—for imidoyl radical **10**, i.e., six-membered cyclization onto the *S*-phenyl ring. In fact, it has been reported that imidoyls can give 1,6-ring closure onto aromatic rings, at least under oxidative conditions (see ref 4b). Under the present conditions this process is probably slow and it cannot compete with the α-fragmentation reaction giving back the isonitrile and the vinyl radical. Another possibility was the trap of radical **10** by another sulfanyl radical to give an *N*-bis(arylthio)methylene derivative. These products were actually obtained in low to moderate yields by reacting isonitriles and disulfides in the absence of alkynes or hydrogen donors, but they were never observed in the present study.

(12) Although data on the reversibility of radical addition to isonitriles—as well as homolytic fragmentations providing vinyl radicals—are not available in the literature, we found evidence that, at least with particularly stable radicals, this reaction is likely to be reversible (see ref 4j). Further support to a reversible radical addition to isonitriles will be reported below.

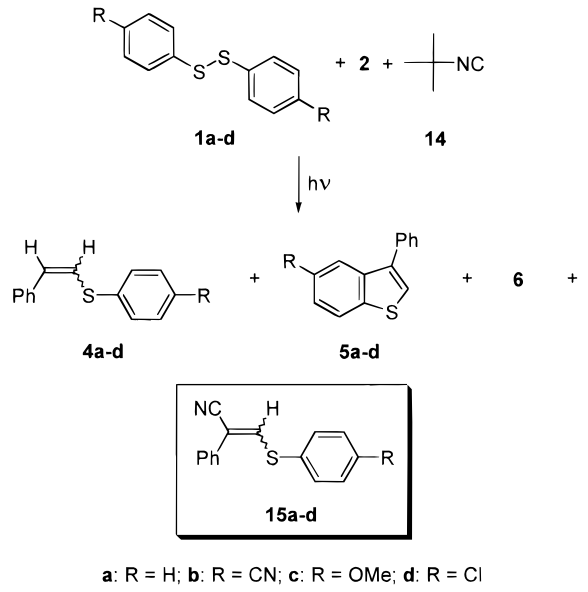
Scheme 2



the scavenger, giving the intermediate **11**;[14] fragmentation of **11** followed by hydrogen abstraction of amidyl radical **12** affords the final amide **7**. An identical mechanism can explain the formation of amide **8** starting from sulfanyl radical **13**, which is formed by ortho-selective photo-Fries rearrangement of the starting disulfide **1a**.[4l,10]

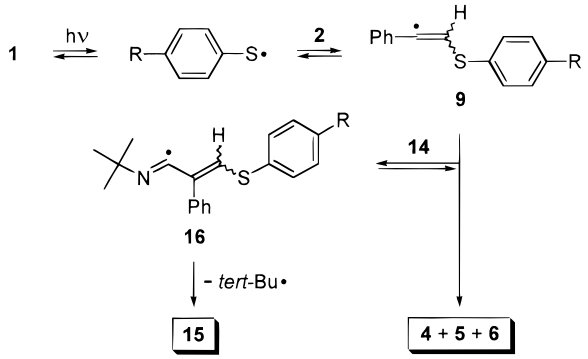
This result was particularly encouraging, since the reaction afforded—in fair overall yield—compounds derived from a selective three-component radical cascade reaction.[15] In addition, the reaction provided a one-pot procedure for the synthesis of potentially interesting polyfunctionalized alkenes from three simple molecules. On this basis, we were prompted to explore the synthetic

Scheme 3



a: R = H; **b**: R = CN; **c**: R = OMe; **d**: R = Cl

Scheme 4



potential of this reaction by employing a different isonitrile, which might lead to an imidoyl radical capable of undergoing a fast evolution without the intervention of any additional fourth component (e.g., MDNB). The subsequent reactions were therefore carried out with commercially available *tert*-butyl isonitrile (**14**). Indeed, this is known to afford imidoyl radicals that undergo quite fast β-scission with release of a *tert*-butyl radical and formation of a nitrile.[1a,b,2a−c,e,h−j,4g,16]

When **1a** (0.5 mmol), **2** (5 mmol), and **14** (10 mmol) were allowed to react under the usual conditions, the unsaturated nitrile **15a** was produced in satisfactory yield (46%),[17] in addition to minor amounts of compounds **4a** (17%), **5a** (2%), and **6** (21%) (Scheme 3). Nitrile **15a** occurred as a mixture of the *E*- and *Z*-isomer, whose relative ratio was originally 4.5:1, but it became 6.7:1 upon chromatographic separation. The reaction mechanism is outlined in Scheme 4. As before, tandem addition of sulfanyl radical to phenylacetylene and reaction of the resulting vinyl radical with the isonitrile give imidoyl radical **16**. This intermediate is efficiently "trapped" by β-fragmentation with loss of *tert*-butyl radical—a pathway that is precluded to imidoyl radical **10**—and it is thus responsible for the formation of nitrile **15**. Molecules with

(13) All of these compounds have been commonly observed in the reactions between sulfanyl radicals and phenylacetylene (see ref 6a,b). However, since we did not use thiols as a source of sulfanyl radicals, we were quite astonished to obtain the hydrogen-abstraction product **4a** in significant amounts. In our reaction, one of the possible hydrogen-atom sources could be tentatively identified as the cyclohexadienyl radicals involved in the formation of compound **5a**.

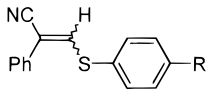
(14) For trapping of radicals by nitro groups resulting in oxygen-transfer reactions from the nitro moiety to the radical center, see, for example: Topiwala, U. P.; Luszniak, M. C.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1185.

(15) It is worth noting that the literature has reported several examples of both sulfanyl radical addition to isonitriles (see refs 2a,d,g and 4l) and imidoyl radical addition to alkynes (see ref 4a,c,h and: Dan-oh, Y.; Matta, H.; Uemura, J.; Watanabe, H.; Uneyama, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1497). Therefore, one could envisage an alternative reaction pathway including sulfanyl radical addition to **3** followed by reaction of the resulting α-thio-imidoyl radical with **2** to give a vinyl radical. Cyclization of the latter intermediate onto the isonitrile aryl ring could lead to a quinoline derivative. Nevertheless, this kind of product was never observed under any experimental conditions.

(16) Ohta, H.; Tokumaru, K. *J. Chem. Soc., Chem. Commun.* **1970**, 1601.

(17) A large excess of isonitrile is essential to trap the vinyl radical efficiently. When we used 5 mmol of **14**, the yield dropped to 15%.

Table 1. Yields of Compounds 4−6, and 15 Obtained in the Reactions of Disulfides 1a−d with 2 and 14[a,b]



15a-d

	R	*t* (h)	**4** (%)	**5** (%)	**6** (%)	**15** (%, *E*/*Z*)
a	H	72	17	2	21	46, 4.5:1
b	CN	7	8	12	8	60, 2.5:1
c	OMe	30	9	9	7	45, 4:1
d	Cl	24	8	12	9	60, 3.7:1

[a] Products **4**−**6** were usually obtained as mixtures, and yields were determined by GC and/or NMR analysis. [b] Yields of **15** are for the pure compound obtained after column chromatography; the *E*/*Z* ratio was determined by GC analysis prior to column chromatography.

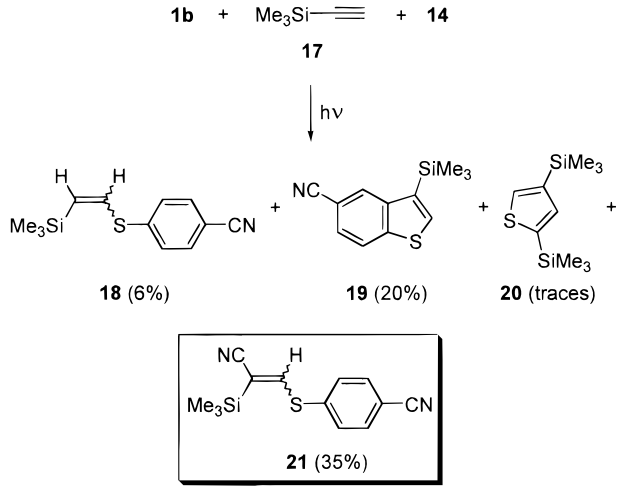
a **15**-like structure are potentially very interesting, since they combine the functionalities of α,*β*-unsaturated nitriles and vinyl sulfides, both of considerable importance in organic synthesis.[18] Moreover, the specific skeleton of **15**—a *β*-thio-substituted acrylonitrile—has been successfully employed in the syntheses of fungicides, herbicides, and insecticides,[19] cephalosporin derivatives,[20] and push−pull dienes for nonlinear optics applications,[21] and it is considered a notable building block for a wide range of natural or biologically active compounds.[22]

The reaction was repeated with various aromatic disulfides and alkynes (Table 1). The formation of nitrile **15** was favored by electron-withdrawing disulfide substituents: indeed, with R = CN or Cl a good yield of **15** (60%) was obtained. Furthermore, any R group was found to lower reaction times remarkably. This effect was particularly notable with disulfide **1b**, whose reaction was about 10 times faster than that of disulfide **1a**. Therefore, reactions with further alkynes were normally studied with disulfide **1b**.

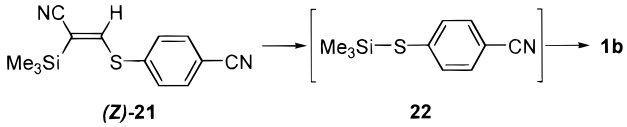
We first examined the use of trimethylsilylacetylene (**17**), which is known to react with sulfanyls to give vinyl radicals structurally analogous to those obtained with phenylacetylene.[23] As shown in Scheme 5, in this case the formation of nitrile **21** was significantly hindered by the competing intramolecular ring closure of the vinyl radical to give benzothiophene **19**. This behavior was somewhat expected, since α-trimethylsilyl-*β*-(phenylsulfanyl)vinyl radicals are reported to be much more prone to cyclize to benzothiophenes than α-phenyl-*β*-(phenylsulfanyl)vinyl radicals.[6b]

The acrylonitrile **21** was produced as a 2.5:1 mixture of the geometrical isomers in 35% overall yield. However, column chromatography of the crude led to isolate only a 10% yield of a 1:1 mixture[24] of (*Z*)- and (*E*)-**21**, together

Scheme 5



Scheme 6



with a 25% yield of the starting disulfide **1b**, which was initially shown by GC−MS analysis to be totally absent. Presumably, nitrile **21** was preferentially formed as the *Z*-isomer, which, under chromatographic conditions, could suffer extensive syn-elimination of transient aryl trimethylsilyl sulfide **22**; this eventually gave disulfide **1b** by subsequent decomposition (Scheme 6). The outcoming stereochemistry of nitrile **21**, as well as that of the above nitrile **15**, can be explained in terms of preferential trapping of linear 1-trimethylsilyl- and 1-phenyl-2-(arylsulfanyl)vinyl radicals by isonitrile **14** on the side opposite to the sulfanyl moiety (see below for further discussion).

To test the possibility that the low yield of **21** could be a result of steric hindrance between the trimethylsilyl group of the vinyl radical and the *tert*-butyl substituent of the incoming isonitrile, we carried out the same reaction in the presence of an isonitrile bearing a linear side-chain, i.e., *n*-dodecyl isonitrile (**24**). Unexpectedly, after 9 h—the same time needed for complete disappearance of the starting material in the analogous reaction with **14**—the reaction mixture contained major amounts of unreacted disulfide **1b** and small quantities of **18** and **19**: no trace of **21** was detected. Although not useful to throw more light on the reason **21** was obtained in low

(18) For the use of vinyl sulfides in organic synthesis, see: Cookson, R. C.; Parson, P. J. *J. Chem. Soc., Chem. Commun.* **1976**, 990. Ager, D. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1131. Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694.

(19) Frazza, E. J.; Rappoport, L. U.S. 3,271,408, 1966; *Chem. Abstr.* **1966**, *65*, 16975a. Strong, J. G. U.S. 3,828,091, 1974; *Chem. Abstr.* **1974**, *81*, 105054w.

(20) Carlo Erba S.p. A. Belg. 849,177, 1977; *Chem. Abstr.* **1978**, *88*, 190855v.

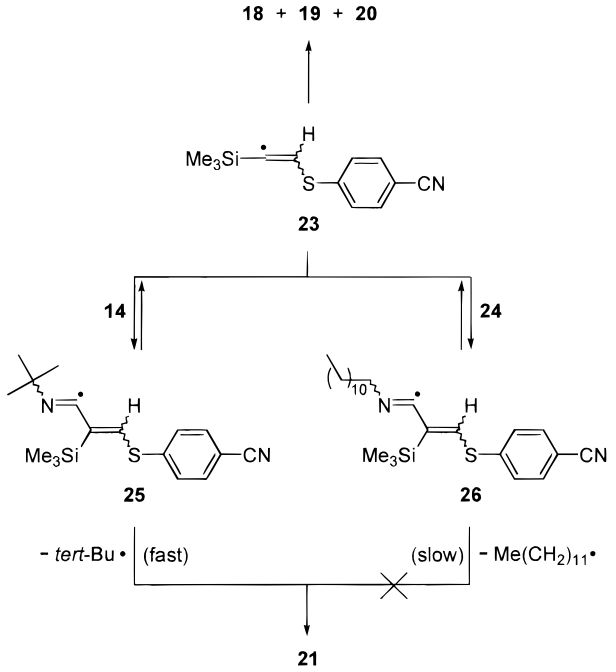
(21) Ono, N.; Matsumoto, K.; Ogawa, T.; Tani, H.; Uno, H. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1905.

(22) Bakuzis, P.; Bakuzis, M. L. F. *J. Org. Chem.* **1981**, *46*, 235. Aurich, H. G.; Quintero, J.-L. R. *Tetrahedron* **1994**, *50*, 3929.

(23) Griller, D.; Cooper, J. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1975**, *97*, 4269.

(24) In all of the reactions described in this paper, the alkene having the alkyne-derived group and the sulfanyl moiety on the same side of the C−C double bond is more stable than the other isomer. This was suggested by the silica-catalyzed isomerization observed during column chromatography and it was definitively proved by photolyses of each of the (supposed) less stable isomers in the presence of the corresponding disulfide. After 24 h under these conditions, they gave almost complete conversion to the alkene with the opposite configuration, due to reversible sulfanyl radical addition to the C−C double bond. See: (a) Kice, J. L. In *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973; Vol. II, pp 720−724. (b) Oswald, A. A.; Griesbaum, K.; Hudson, B. E., Jr.; Bregman, J. M. *J. Am. Chem. Soc.* **1964**, *86*, 2877. (c) Kampmeier, J. A.; Chen, G. *J. Am. Chem. Soc.* **1965**, *87*, 2608. (d) Heiba, E. I.; Dessau, R. M. *J. Org. Chem.* **1967**, *32*, 3837. It is worth noting that the most stable configuration is named *E* for the alkene obtained from phenylacetylene (and 1-hexyne, see below) but *Z* for that arising from trimethylsilylacetylene, due to the presence of the silicon atom instead of a carbon.

Scheme 7

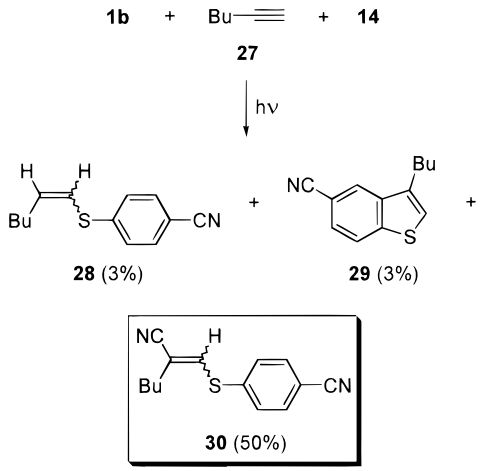


yields from **14**, this finding interestingly gave additional support to the above postulated reversible attack of vinyl radicals to isonitriles. As a matter of fact, there is no plausible reason to postulate very different reaction rates between vinyl radical **23** and the two alkyl isonitriles **24** and **14**. Even if we do, the fastest reaction should be that with **24** rather than the other one, since the linear side chain of **24** should minimize the steric hindrance in the transition state. Nevertheless, this reaction did not afford **21** at all. The only conceivable, meaningful difference between the two processes resides in the next step, i.e., the β-scission of the imidoyl radical, which furnishes either a *tert*-butyl—with **14**—or a primary alkyl radical—with **24**. Assuming a reversible addition step between vinyl radical **23** and the two isonitriles (Scheme 7), imidoyl radical **25** is rapidly consumed by the fast β-fragmentation with loss of a *tert*-butyl radical, thus driving the equilibrium toward nitrile **21**. On the contrary, the β-scission of imidoyl **26**, with loss of a primary carbon radical, cannot compete efficiently with the reverse reaction and the process exclusively affords—and in much longer times—products derived from vinyl radical **23**. In our opinion, the overall present and previous[4j] results strongly suggest that radical addition to isonitriles is a reversible process, at least when—like in the case of vinyls **9** and **23**—the attacking radicals possess a fair stability.

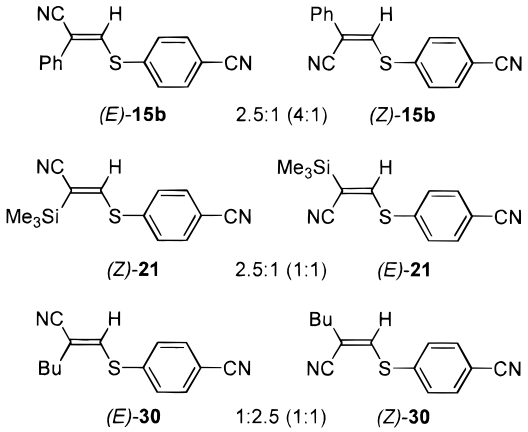
Much better results were obtained by reacting disulfide **1b** and isonitrile **14** with 1-hexyne (**27**). This reaction afforded small amounts of byproducts **28** and **29** (3% each)—2,4-di-*n*-butylthiophene analogous to **6** and **20** was not detected at all—together with a good 50% yield of nitrile **30** (Scheme 8). In this case, a low yield of **29** was expected on the basis of the reported low propensity of α-alkyl-β-(phenylsulfanyl)vinyl radicals to cyclize to benzothiophenes.[6b]

Having shown that the three-component radical cascade reaction can be efficiently applied to alkynes with very different properties, in the next section we shall deal with a detailed mechanistic discussion about the stereochemical outcome of the reaction itself. As a matter of fact, the stereochemistry of the reactions of β-(arylsulfanyl)vinyl radicals with isonitriles differs significantly from the analogous reactions of those radicals with hydrogen donors.

Scheme 8



Scheme 9



First, let us summarize the results obtained with the three alkynes (Scheme 9). The reactions carried out with phenyl- (**2**) and trimethylsilylacetylene (**17**) afforded predominantly the alkenes arising from approach of the isonitrile to the side of the vinyl radical opposite to the sulfanyl group (*E* for the former and *Z* for the latter alkyne). Confining the discussion to alkyne **2** for sake of simplicity—the reaction with **17** suffers from decomposition problems of the major product—the two isomers were identified by mp and spectral data comparison between each of the two alkenes obtained in the reaction of disulfide **1d**, partially separable by column chromatography, and authentic samples of compounds (*E*)-**15d** and (*Z*)-**15d**.[25] Identification was then extended to products **15a**−**c** on the basis of spectral analogies and assuming that no substantial change in the stereochemical outcome could be produced by changing the disulfide substituent. In addition, an NOE experiment was carried out on the presumed compound (*E*)-**15c**, which was unique to show sufficiently separated resonances in the aromatic region. By irradiating the two ortho protons of the α-phenyl ring, we observed an exclusive positive effect on the signals of the two vicinal meta protons, whereas no effect at all was

(25) Rappoport, Z.; Topol, A. *J. Chem. Soc., Perkin Trans. 2* **1975**, 982.

noticed for the vinylic proton. The *E*/*Z* ratio increased slightly during the reaction, as proved by GC−MS analyses performed at regular times, and, for compounds **15**, it showed a remarkable enhancement after column chromatography (Scheme 9, values in parentheses).

The major production of the *E*-isomer was consistent with the results of previous reactions of a hydrogen donor with *β*-(arylsulfanyl)vinyl radicals.[6a] α-Phenylvinyl radicals have been suggested to be linear *π*-radicals,[26] and to minimize steric hindrance, a hydrogen donor approaches an α-phenyl-*β*-(arylsulfanyl)vinyl radical from the side trans to the sulfanyl moiety, yielding the corresponding alkene—under kinetic control—in a 1:9 *E*/*Z* ratio. This approach seems to be additionally favored by significant bonding interactions occurring between the unpaired electron and the sulfur orbitals.[6a] This behavior should be substantially imitated also when the scavenger is an isonitrile and, as the isocyano group is at least as encumbering as the thiol group, we should expect for nitriles **15** an *E*/*Z* ratio of ca. 9:1 or even a little higher.[27] On the contrary, although we could not perform our reactions under perfect kinetic control, we can definitely say that in our case the *E*-isomer was actually still the major product, but the *E*/*Z* ratio was quite low, i.e., only 2.5−4.5:1. In addition, since for nitrile **15** the thermodynamically and kinetically favored isomers are the same compound (*E*)-**15**,[24] the little isomerization that occurred during the reaction and altered the isomer ratio with respect to the one obtainable under kinetic control caused the *E*/*Z* ratio to increase rather than decrease. Therefore, we can reasonably conclude that, under absolute kinetic control, the *E*/*Z* ratio should be even lower than that observed and, thus, far away from what was expected.

Even more interesting were the results obtained from 1-hexyne **27**. With this alkyne, the reaction is brought about by α-alkyl-*β*-(arylsulfanyl)vinyl radicals, which—unlike the linear α-phenyl-substituted analogues—are bent and rapidly interconverting *σ*-radicals.[26] The choice of an incoming scavenger is again dictated by steric factors: if the reaction is dominated by the steric hindrance between the α- and *β*-group of the vinyl radical, then a hydrogen donor enters on the same side of the sulfanyl group, giving the (*E*)-alkene; otherwise, it approaches the opposite side, yielding the *Z*-isomer. It is worth pointing out that with **27** the hydrogen-abstraction reaction follows the latter pathway affording the reduction product in a 1:9 *E*/*Z* ratio, thus perfectly resembling the result obtained with α-phenyl-substituted vinyl radicals.[6a] This means that also with 1-hexyne the product distribution is governed by steric interactions in the transition state between the *β*-substituent and the incoming scavenger. The negligible steric hindrance between the α- and *β*-substituent of the vinyl radical, compared with that between the *β*-group and the isonitrile moiety, is also supported by the stability of compound (*E*)-**30** that, like in the case of nitriles **15**, is thermodynamically favored with respect to its (*Z*)-counterpart. This is an additional point that let us predict an approach of the isonitrile from the side opposite to the sulfanyl group.

As far as our reaction with **27** is concerned, the (*E*)-**30**/(*Z*)-**30** ratio was not only low beyond any expectation, but, additionally, the kinetically favored product was (*Z*)-**30** instead of the predicted (*E*)-isomer. As the matter of fact, when the reaction was stopped after 8 h, i.e., much before complete conversion of the starting material, the measured (*E*)-**30**/(*Z*)-**30** ratio was 1:2.5. The ratio changed to 1:1.3 and 1:1 at the end of the reaction and after column chromatography, respectively, since—like in the case of the other nitriles—the *E*-isomer is the more stable and thence considerable *Z*/*E* isomerization occurred during the reaction and chromatographic separation. The assignment of the *Z*-structure to the kinetic product (the major isomer at early reaction times) was made on the basis of NOE measurements carried out on a pure sample of presumed (*Z*)-**30** obtained after chromatographic workup. Irradiation on the allylic methylene signals caused a marked enhancement of the vinyl proton.

Thus, the markedly decreased ratio of the (*E*)- and (*Z*)-nitriles **15** and the inversion of the expected stereochemistry for nitrile **30** clearly indicate that the scavenging of *β*-(arylsulfanyl)vinyl radicals by isonitriles and/or the stereochemical fate of the resulting imidoyl radicals are governed by more complicated factors than those involved in analogous hydrogen abstraction reactions.

The stereochemical outcome of our reactions might be explained in terms of possible vinyl radical—isonitrile interactions in the transition state. Since carbon radicals are well-known to attack intermolecularly the sulfur atom of aryl sulfides to give sulfuranyl radicals[28]—and isonitriles can be considered diradical species in their geminal radical acceptor/radical donor behavior—it would not be unreasonable to postulate that in the transition state the incoming isonitrile might interact not only with the vinyl-radical carbon but also with the sulfur atom (Scheme 10). This effect could direct the approach of the isonitrile to the same side of the sulfanyl group, thus partially balancing steric hindrance. Due to the significant intramolecular bonding interactions between the unpaired electron and the sulfur orbitals,[6a] the three-center interaction could be slightly important in the reactions of radical **9**. On the contrary, this is likely to be quite significant in the case of radical **31**, where the intramolecular overlap is instead unimportant. This hypothesis would lead to predict not only a low *E*/*Z* ratio for the alkene products in the reactions with phenylacetylene but also a marked preference for the *Z*-isomer with 1-hexyne, which is consistent with our experimental data.

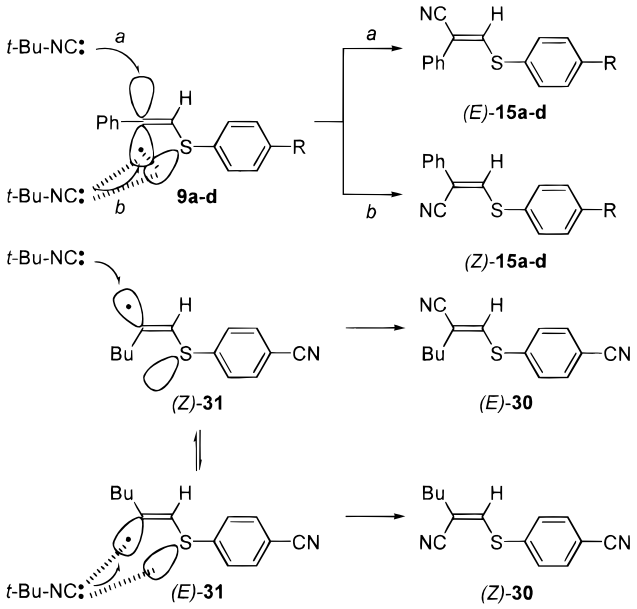
A different approach to rationalize the product distribution is to consider the geometry and electronic structure of the imidoyl radical arising from addition of the vinyl radical to the isonitrile (Scheme 11). In the absence

(26) (a) Singer, L. A.; Chen, J. *Tetrahedron Lett.* **1969**, 4849. (b) Bennett, J. E.; Howard, J. A. *Chem. Phys. Lett.* **1971**, *9*, 460. (c) Ito, O.; Omori, R.; Matsuda, M. *J. Am. Chem. Soc.* **1982**, *104*, 3934. (d) Giese, B.; Lachhein S. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 768. (e) Giese, B.; Gonzales-Gomez, J. A.; Lachhein, S.; Metzger, J. O. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 479. (f) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969. (g) Curran, D. P.; Kim, D. *Tetrahedron* **1991**, *47*, 6171. (h) Journet, M.; Malacria, M. *Tetrahedron Lett.* **1992**, *33*, 1892. (i) Journet, M.; Malacria, M. *J. Org. Chem.* **1992**, *57*, 3085.

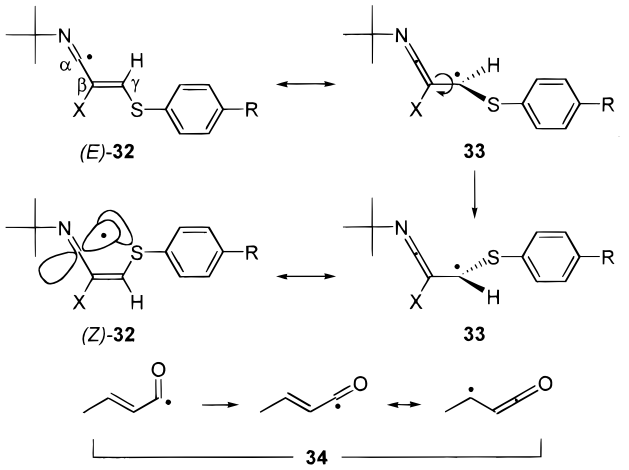
(27) Calculations of both molar volume and parachor for thiol and isocyano groups gave slightly greater values for the latter moiety. On this occasion, to avoid confusion, we would like to point out that the *E*/*Z* convention overturns passing from hydrogen abstraction products **4**, **18**, and **28** (ref 6a) to our nitriles.

(28) Sulfuranyl radicals are assumed to be true intermediates in intramolecular cyclizations onto diarylsulfide moieties; see: Leardini, R.; Pedulli, G. F.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Chem. Commun.* **1985**, 1390 and references therein. See also: Kampmeier, J. A.; Evans, T. R. *J. Am. Chem. Soc.* **1966**, *88*, 4096. Beckwith, A. L. J.; Boate, D. R. *J. Chem. Soc., Chem. Commun.* **1986**, 189. Franz, J. A.; Roberts, D. H.; Ferris, K. F. *J. Org. Chem.* **1987**, *52*, 2256.

Scheme 10



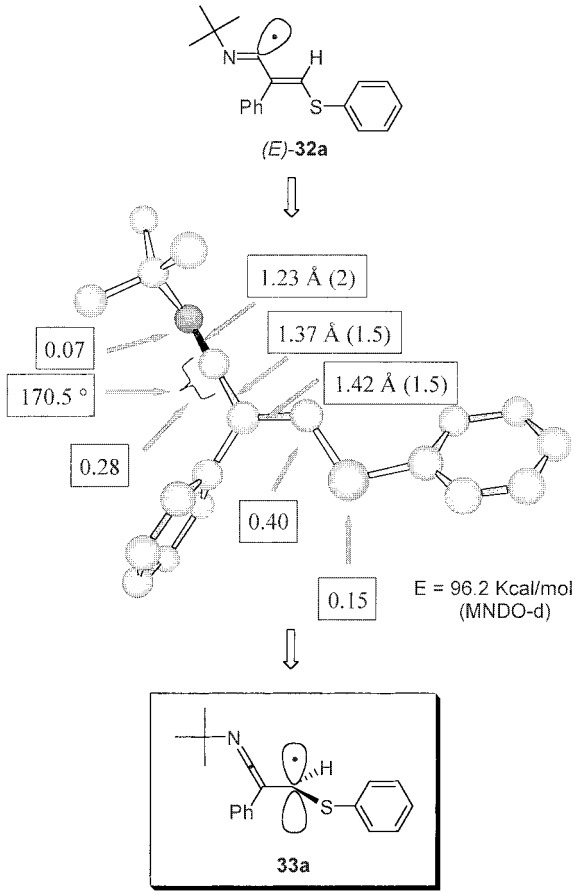
Scheme 11



of significant interactions in the transition state other than steric hindrance, adduct **32** could be preferentially formed in its predicted *E*-configuration. Nevertheless, before undergoing β-fragmentation, (*E*)-**32** might equilibrate to some extent to the *Z*-isomer through rotation around the virtually single $C_\beta-C_\gamma$ bond of the contributing resonance structure **33**. Imidoyl radical (*Z*)-**32** could be the thermodynamically preferred isomer due to some intramolecular bonding interactions between the unpaired electron and the sulfur orbitals, which should be even more effective than in vinyl radical **9** (see above). Very recently, some isoelectronic α,β-unsaturated acyl radicals **34** have been described in terms of analogous mesomeric structures (Scheme 11).[29]

Since no data have been so far reported concerning the geometry and electronic structure of α,β-unsaturated imidoyl radicals, semiempirical MNDO-d calculations[30] were performed on radicals **32** (**a**: R = H, X = Ph; **b**: R = H, X = Me). Generally, imidoyls are σ-radicals with a

Scheme 12



bent geometry at the radical center,[2d,g,31] but recent studies have suggested that—like in the case of the isoelectronic vinyl radicals[26b,e]—their geometry and delocalization degree of the unpaired electron may depend on the substitution pattern, i.e., the α-group and particularly the nitrogen substituent.[32]

Both energy and equilibrium geometry of radical (*E*)-**32a** were first optimized. The results shown in Scheme 12 indicate that a bent geometry (120°) at the radical center was transformed into a quasilinear arrangement (170.5°) of the N=C−C moiety. In addition, the order of the $C_\alpha-C_\beta$ and $C_\beta-C_\gamma$ bonds was changed to 1.5 from 1 and 2, respectively, with the latter bond slightly longer than the former, however. Finally, the estimated spin density showed a maximum on the C_γ atom (0.40) instead of the starting C_α carbon (0.28), with some distribution also on the nitrogen (0.07) and sulfur (0.15) atoms. These data are more consistent with structure **33a** rather than the initial imidoyl **32a**. The energies and equilibrium geometries were then calculated for the other radicals (*Z*)-**32a**, (*E*)-**32b**, and (*Z*)-**32b**, and the rotation barriers were estimated for both pairs of radical configurations (6.0 and 5.7 kcal/mol, respectively, Scheme 13). Finally, from the kinetic data previously reported for β-fragmentations of analogous *N-tert*-butyl-substituted imidoyls,[2g] we estimated a value of ca. 8−10 kcal/mol for the activation energy concerning release of the *tert*-butyl

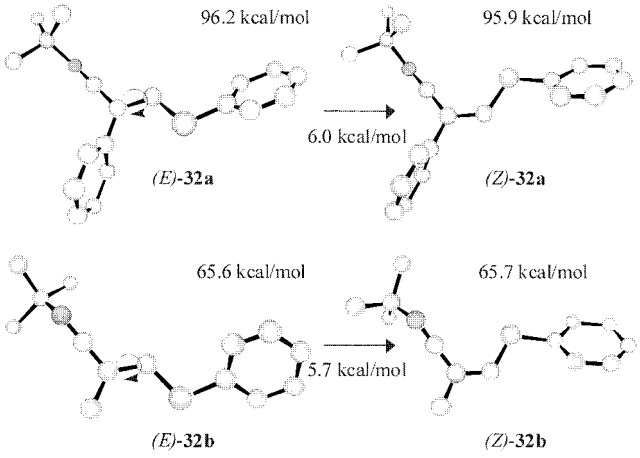
(29) De Boeck, B.; Herbert, N.; Pattenden, G. *Tetrahedron Lett.* **1998**, *39*, 6971. De Boeck, B.; Pattenden, G. *Tetrahedron Lett.* **1998**, *39*, 6975.

(30) The choice of MNDO-d parametrization was made to better take into account the possible involvement of sulfur d-orbitals.

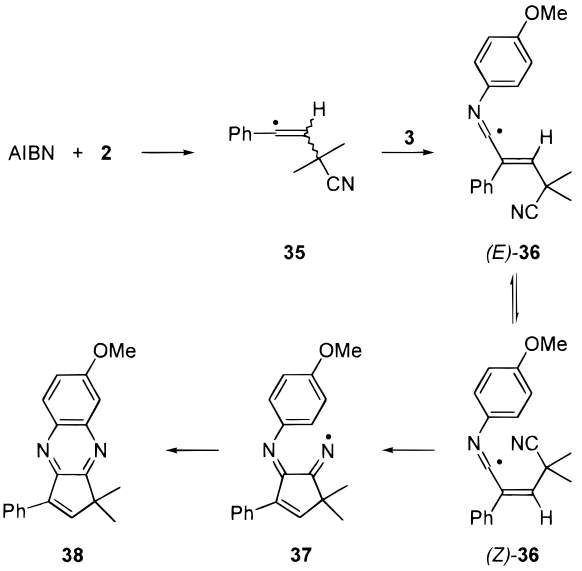
(31) Danen, W. C.; West, C. T. *J. Am. Chem. Soc.* **1973**, *95*, 6872.

(32) Pareschi, P. Imidoyl Radicals: Spectroscopic Properties, Reactivity, and Use in the Synthesis of Heterocyclic Compounds. Ph.D. Thesis, University of Bologna, Italy, 1996, Chapter 1, in collaboration with J. C. Walton, University of St. Andrews, U.K.

Scheme 13



Scheme 14



radical from **32**-like intermediates. On this basis, it can be reasonably assumed that, under our experimental conditions, radicals **32** can exhibit fair rotation around the $C_\beta-C_\gamma$ in competition with the β-scission process. The lower barrier predicted for radical **32b** suggests that isomerization might be even more effective in the reaction carried out with 1-hexyne, which is consistent with the experimental data.

Although the above findings cannot afford a full explanation of the present stereochemical data, they strongly suggest that the structure of the α,β-unsaturated imidoyl radical can have a major influence on the configuration of the reaction products and it can thence considerably alter the expected, kinetically favored outcome. However, at this stage, concomitant or even alternative contribution of transition state interactions (Scheme 10) cannot be ruled out.

It is worth pointing out that the above theoretical data also serve to clarify some as yet unexplained behavior of the related imidoyl radical **36**. This was the key intermediate in the smooth formation of the cyclopenta-fused quinoxaline **38** (50% yield) by tandem 5-*exo*-*dig* cyclization onto the cyano group and subsequent six-membered ring closure of the resulting iminyl radical **37** onto the aromatic ring of the isonitrile (Scheme 14).[4h] At that time, we had no convincing explanation of the reasons why the radical intermediate **36** could undergo efficient cyclization on the nitrile moiety despite its kinetically predictable (and unfavorable) *E*-configuration. In light of the present data calculated for imidoyl radicals **32**, ready *E*/*Z* isomerization of **36** through rotation around the $C_\beta-C_\gamma$ bond—and thence approach of the radical center to the cyano group—now becomes plausible.

Conclusions

The photolytic reaction of disulfides with alkynes and isonitriles represents a novel three-component radical cascade reaction that proceeds by tandem addition of a sulfanyl radical to the alkyne and attack of the resulting vinyl radical to the isonitrile carbon atom to give an imidoyl radical. With aromatic isonitriles, a scavenger (e.g., MDNB) is needed to trap the produced imidoyl radical prior to back fragmentation to the vinyl precursor. With *tert*-butyl isonitrile, the imidoyl intermediate is "trapped" by a β-scission process resulting in release of a *tert*-butyl radical and production of a nitrile. This one-pot protocol affords fair yields of synthetically useful polyfunctionalized alkenes using disulfides, isonitriles, and alkynes with very different properties. Moreover, our present results suggest that vinyl radical addition to isonitriles is a reversible process: this fact is also supported by the reaction of disulfide **1b** and alkyne **17** in the presence of a nonbranched aliphatic isonitrile (**24**).

The stereochemical outcome of the three-component reactions differs significantly from that previously encountered with related hydrogen abstraction reactions of thio-substituted vinyl radicals. This could be the consequence of vinyl radical—isonitrile interactions in the transition state and/or fast *E*/*Z* isomerization of the eventual imidoyl radical. Support to the latter possibility was given by structure and spin-density data obtained by MNDO-d semiempirical calculations.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were recorded in deuteriochloroform using tetramethylsilane as an internal standard. Mass spectra (MS) and high-resolution mass spectra (HRMS) were performed by electron impact with a beam energy of 70 eV: relative intensities are given in parentheses. GC—MS analyses were carried out on a quadrupolar instrument equipped with a Quadrex capillary column (007, 25 m × 0.25 mm i.d.). The *E*/*Z* ratios for vinylic compounds were determined by a 60—260 °C temperature ramp with a rate of 10 °C/min, unless otherwise stated; the differences in retention times (Δ_{rt}) are given in seconds. IR spectra were recorded in film or chloroform solution. Column chromatography was carried out on 60-Å silica gel or basic aluminum oxide (70—230 mesh, activity 3) using light petroleum (40—70 °C) and a light petroleum/diethyl ether gradient (from 0 up to 100% diethyl ether) as eluant. UV photolyses of disulfides were performed with a Heraeus TQ 150 high-pressure mercury lamp (150 W). Previously reported reaction products were identified by spectral comparison and/or mixed mp determination with authentic specimens. The purity of new compounds was confirmed by HRMS and elemental analysis; in the case of inseparable mixtures of compounds, the purity was proved by the absence of any significant extraneous peak in the ^{1}H NMR spectra and/or by GC—MS analysis.

Diphenyl disulfide (**1a**), 4-methoxythiophenol, 4-chlorothiophenol, 4-hydroxybenzonitrile, *p*-anisidine, *n*-dodecylamine, phenylacetylene (**2**), *tert*-butyl isonitrile (**14**), trimethylsilylacetylene (**17**), 1-hexyne (**27**), and *m*-dinitrobenzene (MDNB) were commercially available. 4-[(4-Cyanophenyl)disulfanyl]-

benzonitrile (**1b**),[33] bis(4-methoxyphenyl) disulfide (**1c**),[34] and bis(4-chlorophenyl) disulfide (**1d**)[35] were prepared according to the literature. *N*-(4-Methoxyphenyl)formamide[36] and *N*-*n*-dodecylformamide[37] were synthesized from the corresponding amines by treatment with boiling formic acid.[36] 4-Methoxyphenyl isonitrile (**3**)[38] and *n*-dodecyl isonitrile (**24**)[39] were prepared from the corresponding formamides by reaction with diisopropylamine and phosphorus oxychloride in dichloromethane.[40]

Reactions of Disulfides with Alkynes and Isonitriles. General Procedure. A benzene (40 mL) solution of disulfide (0.5 mmol), alkyne (5 mmol), and isonitrile (10 mmol) in a quartz Erlenmeyer flask was kept at rt for 7−72 h under a nitrogen atmosphere and UV irradiation. Disappearance of the starting material was monitored by TLC and/or GC−MS analysis. After removal of the solvent, the residue was chromatographed. In each reaction, products are listed according to the elution order.

Reactions of 1a with 2 and 3. After 48 h, in the absence of MDNB, the reaction afforded, besides polymeric products and tarry material, a mixture (∼40%) of phenyl 2-phenylethenyl sulfide (**4a**),[6a] 3-phenylbenzo[*b*]thiophene (**5a**),[41] and 2,4-diphenylthiophene (**6**).[41] In the presence of MDNB (2 mmol), after 72 h, we obtained again, by chromatography on aluminum oxide, a first fraction containing **4a**, **5a**, and **6** (∼20%), followed by *N*-(4-methoxyphenyl)-2-phenyl-3-(phenylsulfanyl)-2-propenamide **7** (0.1 g, 38%) as a 1:1 *E*/*Z* mixture: oil; ^{1}H NMR (300 MHz) δ 4.03 (3 H, s), 4.04 (3 H, s), 7.09 (4 H, AA′BB′, J = 6.3 Hz), 7.30 (1 H, bs, NH, removed upon treatment with D_2O), 7.40 (1 H, s), 7.50−7.85 (24 H, m), 8.34 (1 H, s); ^{13}C NMR (50 MHz) δ 55.95, 114.65, 122.19, 122.27, 128.52, 129.04, 129.70, 129.83, 129.89, 129.93, 130.17, 130.31, 131.12, 131.40 (q), 131.50 (q), 131.60, 131.86 (q), 134.65 (q), 135.32 (q), 138.15 (q), 138.20 (q), 142.38, 145.43, 157.05 (q), 163.22 (q), 164.92 (q); MS *m*/*z* 361 (M^+, 56); HRMS calcd for $C_{22}H_{19}NO_2S$ 361.1137, found 361.1129. Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.87; S, 8.87. Found: C, 73.55; H, 5.33; N, 3.89; S, 8.84. A subsequent fraction contained *N*-(4-methoxyphenyl)-2-phenyl-3-[[2-(phenylsulfanyl)phenyl]sulfanyl]-2-propenamide **8** (0.05 g, 20%) as a 3:1 mixture of stereoisomers: oil; ^{1}H NMR (300 MHz) δ 4.03 (s, minor isomer), 4.04 (s, major isomer), 7.06−7.12 (d + d, J_1 = 8.2 Hz, J_2 = 7.6 Hz, A part of AA′BB′, both isomers), 7.25−7.90 (m); MS *m*/*z* 469 (M^+, 69); HRMS calcd for $C_{28}H_{23}NO_2S_2$ 469.1170, found 469.1191.

Reaction of 1a with 2 and 14. After 72 h, column chromatography of the reaction mixture gave a mixture of **4a**, **5a**, and **6** in a 1.7 (two isomers in a 0.6:0.4 ratio):0.1:2 ratio (38% overall yield), 2-phenyl-3-(phenylsulfanyl)-2-propenenitrile (**15a**) as a 6.7:1 *E*/*Z* mixture (4.5:1 before chromatography, 46% overall yield) [oil; ^{1}H NMR (200 MHz) δ 7.25−7.70 (11 H, m); MS *m*/*z* 237 (M^+, 100); HRMS calcd for $C_{15}H_{11}NS$ 237.0612, found 237.0625], and the presumable[41,10] photo-Fries rearrangement compound 2-phenyl-3-[[2-(phenylsulfanyl)phenyl]-sulfanyl]-2-propenenitrile (6%): oil; [^{1}H NMR (300 MHz) δ 7.05−7.70 (15 H, m); MS *m*/*z* 345 (M^+, 100); HRMS calcd for $C_{21}H_{15}NS_2$ 345.0646, found 345.0658. The *E*/*Z* ratio for compound **15a** was determined by GC with a rate of 8 °C/min (Δ_{rt} = 22).

Reaction of 1b with 2 and 14. After 7 h, column chromatography of the reaction mixture afforded **6** (8%) and a mixture of 4-[[2-phenylethenyl]sulfanyl]benzonitrile (**4b**) (1:1 *E*/*Z* ratio) and 3-phenyl-1-benzothiophene-5-carbonitrile (**5b**) in a 2:3 ratio (20% overall yield, Δ_{rt} = 13). **4b**: MS *m*/*z* 237 (M^+, 100); HRMS calcd for $C_{15}H_{11}NS$ 237.0612, found 237.0628. **5b**: MS *m*/*z* 235 (M^+, 100); HRMS calcd for $C_{15}H_9NS$ 235.0456, found 235.0448. **4b** + **5b**: ^{1}H NMR (200 MHz) δ 6.46 (d, J = 10.6 Hz, (*Z*)-**4b**), 6.80 (d, J = 10.6 Hz, (*Z*)-**4b**), 6.82 (d, J = 15.3 Hz, (*E*)-**4b**), 6.96 (d, J = 15.3 Hz, (*E*)-**4b**), 7.24−7.73 (m), 7.99 (d, J = 8.4 Hz, **5b**), 8.22 (dd, J_1 = 1.3 Hz, J_2 = 0.8 Hz, **5b**).

Further elution gave 4-[[2-cyano-2-phenylethenyl]sulfanyl]-benzonitrile (**15b**) as a 4:1 *E*/*Z* mixture (2.5:1 before chromatography, 60% overall yield, Δ_{rt} = 30): mp = 124−126 °C (from light petroleum/benzene 70:30 v/v); ^{1}H NMR (200 MHz) δ 7.35−7.75 (m); ^{13}C NMR (50 MHz) δ 112.41 (q), 112.60 (q), 118.35 (q), 118.76 (q), 125.86, 127.47 (q), 128.51, 129.47, 129.74, 129.98, 130.10, 130.52, 130.80, 132.23 (q), 133.53, 133.62, 139.57, 139.91 (q), 141.97; MS *m*/*z* 262 (M^+, 100); HRMS calcd for $C_{16}H_{10}N_2S$ 262.0565, found 262.0577. Anal. Calcd for $C_{16}H_{10}N_2S$: C, 73.26; H, 3.84; N, 10.68; S, 12.22. Found: C, 73.59; H, 3.83; N, 10.61; S, 12.29.

Final elution gave presumably[41,10] 4-[[2-cyano-2-phenylethenyl]sulfanyl]-3-[(4-cyanophenyl)sulfanyl]benzonitrile (5%): oil; MS *m*/*z* 395 (M^+, 34); HRMS calcd for $C_{23}H_{13}N_3S_2$ 395.0551, found 395.0559.

Reaction of 1c with 2 and 14. After 30 h, column chromatography of the reaction mixture afforded a mixture of **4c**,[42] **5c**, and **6** in a 1 (two isomers in a 1:1 ratio):1:0.8 ratio (25% overall yield). **5c**: MS *m*/*z* 240 (M^+, 100); HRMS calcd for $C_{15}H_{12}OS$ 240.0608, found 240.0618. **4c** + **5c** + **6**: ^{1}H NMR (200 MHz) δ 3.79 (s, (*Z*)-**4c**), 3.82 (s, (*E*)-**4c**), 6.43 (d, J = 10.6 Hz, (*Z*)-**4c**), 6.53 (d, J = 10.6 Hz, (*Z*)-**4c**), 6.53 (d, J = 15.3 Hz, (*E*)-**4c**), 6.86 (d, J = 15.3 Hz, (*E*)-**4c**), 6.85−6.98 (m), 7.06 (dd, J_1 = 8.9 Hz, J_2 = 2.4 Hz, **5c**), 7.20−7.76 (m), 7.78 (d, J = 8.9 Hz, **5c**).

Further elution gave 3-[(4-methoxyphenyl)sulfanyl]-2-phenyl-2-propenenitrile (**15c**) as a 3.3:1 *E*/*Z* mixture (4:1 before chromatography, 45% overall yield, Δ_{rt} = 29): oil; ^{1}H NMR (300 MHz, benzene-d_6) δ 3.42 (s, (*Z*)-**15c**), 3.44 (s, (*E*)-**15c**), 6.75 (A part of AA′BB′, J = 9.1 Hz, (*E*)-**15c**), 6.80 (A part of AA′BB′, J = 9.1 Hz, (*Z*)-**15c**), 7.14−7.40 (m + B part of AA′BB′, J = 9.1 Hz, (*E*)-**15c**), 7.29 (s, (*E*)-**15c**), 7.87−7.93 (m, (*E*)-**15c**). A NOEDIF experiment was carried out on a fraction containing **15c** in a very high *E*/*Z* ratio by irradiating the two ortho protons of the unsubstituted α-phenyl ring (7.87−7.93 ppm); the experiment showed an exclusive positive effect (3.5%) on the signals of the two vicinal meta protons (7.30−7.37 ppm), whereas no effect at all was noticed for the singlet ascribable to the vinylic proton (7.29 ppm): MS *m*/*z* 267 (M^+, 100); HRMS calcd for $C_{16}H_{13}NOS$ 267.0718, found 267.0725. Anal. Calcd for $C_{16}H_{13}NOS$: C, 71.88; H, 4.90; N, 5.24; S, 11.99. Found: C, 72.05; H, 4.86; N, 5.26; S, 12.07.

A careful analysis of the final elution fractions showed that this reaction did not afford the photo-Fries rearrangement product.

Reaction of 1d with 2 and 14. After 24 h, column chromatography of the reaction mixture afforded a mixture of **4d**,[24b] **5d**,[43] **6**, and *tert*-butyl 4-chlorophenyl sulfide[44] in a 1.4 (2 isomers in a 1:0.8 ratio):2:1.4:1 ratio (35% overall yield).

Further elution gave 3-[(4-chlorophenyl)sulfanyl]-2-phenyl-2-propenenitrile (**15d**) as a 6.6:1 *E*/*Z* mixture (3.7:1 before chromatography, 60% overall yield, Δ_{rt} = 24), mp = 99−100 °C (from light petroleum/ethanol 70:30 v/v) (lit.[25] mp = 105−107 °C); comparison of spectral data of the two isomers of **15d** with those reported in the literature was essential to establish the absolute configurations of the major and minor isomer. (*E*)-**15d**: IR (film) ν_{max} (cm^{-1}) 3000, 2220 (CN), 1550, 1480, 1450, 1400, 1100, 1010, *865*, 810, 765, 695 [lit.[25] IR (KBr) ν_{max} (cm^{-1}) 2210 (CN), 1630, *865*; according to the authors, the band at 865 cm^{-1} is characteristic of the *E*-isomer; actually it was not observed in the IR spectrum of the minor isomer, see below]; ^{1}H NMR (300 MHz) δ 7.36−7.51 (8 H, m), 7.60−7.65

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(2 H, m) [lit.[25] ^{1}H NMR (60 MHz) δ 7.22−7.61 (m); one end of the resonance region is significantly shifted to lower fields for the *E*-isomer; this feature is clearly shown by the major isomer of **15d**, see also below]; MS *m*/*z* 273 (M^+ + 2, 25), 271 (M^+, 100), 236 (26), 203 (52), 159 (32), 155 (16), 108 (22), 75 (31) [lit.[25] MS *m*/*z* 273 (M^+ + 2, 36), 271 (M^+, 100), 270 (29), 236 (40), 203 (58), 159 (24), 143 (29), 108 (29)]; *Z*-**15d**: IR (film) ν_{max} (cm^{-1}) 3000, 2220 (CN), 1500, 1480, 1450, 1400, 1100, 1015, 810, 750, 700 [lit.[25] IR (KBr) ν_{max} (cm^{-1}) 2240 (CN), 1620]; ^{1}H NMR (300 MHz) δ 7.35−7.52 (10 H, m) [lit.[25] ^{1}H NMR (60 MHz) δ 7.25−7.53 (m)]; MS *m*/*z* 273 (M^+ + 2, 26), 271 (M^+, 100), 236 (25), 203 (51), 159 (33), 155 (16), 108 (25), 75 (38) [lit.[25] MS *m*/*z* 273 (M^+ + 2, 37), 271 (M^+, 100), 270 (30), 236 (28), 203 (44), 159 (31), 155 (25), 139 (36), 108 (27)].

Final elution gave traces of the presumable[41,10] photo-Fries rearrangement product, 3-([4-chloro-2-[(4-chlorophenyl)sulfanyl]phenyl]sulfanyl)-2-phenyl-2-propenenitrile, MS *m*/*z* 413 (M^+, 100); HRMS calcd for $C_{21}H_{13}Cl_2NS_2$ 412.9867, found 412.9875.

Reaction of 1b with 17 and 14. After 9 h, column chromatography of the reaction mixture afforded trimethyl-[4-(trimethylsilyl)-2-thienyl]silane[45] [MS *m*/*z* 228 (M^+, 13)]. Further elution gave a mixture of **18** and **19** in a 1 (2 isomers in a 0.9:0.1 ratio):3.5 ratio (26% overall yield, Δ_{rt} = 18); *E*-**18**: MS *m*/*z* 233 (M^+, 23); *Z*-**18**: MS *m*/*z* 233 (M^+, 20); HRMS calcd for $C_{12}H_{15}NSSi$ 233.0695, found 233.0701; **19**: MS *m*/*z* 231 (M^+, 9); HRMS calcd for $C_{12}H_{13}NSSi$ 231.0538, found 231.0531;[46] **18** + **19**: ^{1}H NMR (300 MHz) δ 0.09 (9 H, s, (*Z*)-**18**), 0.13 (9 H, s, (*E*)-**18**), 0.41 (9 H, s, **19**), 6.14 (1 H, d, J = 12.3 Hz, (*Z*)-**18**), 6.22 (1 H, d, J = 17.9 Hz, (*E*)-**18**), 6.65 (1 H, d, J = 17.9 Hz, (*E*)-**18**), 7.02 (1 H, d, J = 12.3 Hz, (*Z*)-**18**), 7.34−7.42 (4 H, A part of AA′BB′, (*E*)-**18** + (*Z*)-**18**, J_E = 8.3 Hz), 7.55 (1 H, dd, J_1 = 8.1 Hz, J_2 = 0.9 Hz, **19**), 7.56−7.62 (4 H, B part of AA′BB′, (*E*)-**18** + (*Z*)-**18**, J_E = 8.3 Hz), 7.66 (1 H, s, **19**), 8.02 (1 H, d, J = 8.1 Hz, **19**), 8.18 (1 H, d, J = 0.9 Hz, **19**).

Further elution yielded presumable 7-[(4-cyanophenyl)-sulfanyl]-3-(trimethylsilyl)-1-benzothiophene-5-carbonitrile [MS *m*/*z* 364 (M^+, 14)], 4-[[2-cyano-2-(trimethylsilyl)ethenyl]sulfanyl]benzonitrile (**21**) as a 1:1 *Z*/*E* mixture (2.5:1 before chromatography, 10% overall yield, Δ_{rt} = 32) [^{1}H NMR (300 MHz) δ 0.28 (9 H, s, (*Z*)-**21**), 0.40 (9 H, s, (*E*)-**21**), 7.50 (2 H, A part of AA′BB′, J = 8.3 Hz), 7.68 (2 H, B part of AA′BB′, J = 8.3 Hz), 7.80 (1 H, s, (*Z*)-**21**), 7.87 (1 H, s, (*E*)-**21**) [peak assignment was made on the basis of NMR analyses of fractions with different *Z*/*E* ratios]; MS *m*/*z* ((*Z*)-**21**) 258 (M^+, 23); MS *m*/*z* ((*E*)-**21**) 258 (M^+, 16); HRMS calcd for $C_{13}H_{14}N_2SSi$ 258.0647, found 258.0653], disulfide **1b** (25%), and trace amounts of the desilylation product 4-[[2-cyanoethenyl]sulfanyl]benzonitrile as a 3:1 isomer mixture [MS *m*/*z* 186 (M^+, 100); HRMS calcd for $C_{10}H_6N_2S$ 186.0252, found 186.0250]. Assuming that disulfide **1b** arises from decomposition of (*Z*)-**18**, the total yield of **18** is about 35% (25% and 10% for (*Z*)-**18** and (*E*)**18**, respectively, see the Results and Discussion).

Reaction of 1b with 17 and 24. After 9 h, TLC and GC−MS analyses of the reaction mixture revealed great amounts of starting material (at least 70%) together with small quantities of **18** and **19**. Nitriles **21** were absolutely absent.

Reaction of 1b with 27 and 14. After 24 h, column chromatography of the reaction mixture yielded a mixture of **28**, **29**, 4-(*tert*-butylsulfanyl)benzonitrile (**39**),[47] and presumably 4-[[2-phenyl-1-hexenyl]sulfanyl]benzonitrile (**40**) [the product arising from attack of the vinyl radical to the solvent benzene] in a 1 (two isomers in a 1:1 ratio, Δ_{rt} = 8):1:1:1.6 (2 isomers in a 1:0.3 ratio) ratio (14% overall yield). **28** (first isomer): MS *m*/*z* 217 (M^+, 37). **28** (second isomer): MS *m*/*z* 217 (M^+, 36); HRMS calcd for $C_{13}H_{15}NS$ 217.0925, found 217.0919. **29**: MS *m*/*z* 215 (M^+, 22); HRMS calcd for $C_{13}H_{13}NS$ 215.0769, found 215.0764. **40** (major isomer): MS *m*/*z* 293 (M^+, 57). **40** (minor isomer): MS *m*/*z* 293 (M^+, 67); HRMS calcd for $C_{19}H_{19}NS$ 293.1238, found 293.1241. **28** + **29** + **39** + **40**: ^{1}H NMR (300 MHz) δ 0.80−1.05 (m), 1.20−1.50 (m), 1.65−1.80 (m), 2.20−2.35 (m), 2.59 (t, J = 6.4 Hz), 2.77 (t, J = 6.5 Hz), 2.84 (t, J = 6.7 Hz), 6.04−6.22 (m, (*E*)-**28** + (*Z*)-**28**), 6.24 (s, **40** [major]), 6.40 (s, **40** [minor]), 7.20−7.64 (m), 7.72 (AA′BB′, J = 8.2 Hz), 7.92 (d, J = 8.2 Hz, **29**), 8.06 (br s, **29**).

Further elution gave 4-[[2-cyano-1-hexenyl]sulfanyl]benzonitrile (**30**) as a 1.1:1 *Z*/*E* mixture (1.3:1 before chromatography, 2.5:1 if the reaction is stopped after 8 h, 50% overall yield, Δ_{rt} = 5): oil. (*Z*)-**30**: ^{1}H NMR (300 MHz) δ 0.95 (3 H, t, J = 7.2 Hz), 1.32−1.45 (2 H, m), 1.52−1.67 (2 H, m), 2.37 (2 H, td, J_t = 7.5 Hz, J_d = 1.1 Hz), 6.90 (1 H, t, J = 1.1 Hz), 7.45 (2 H, A part of AA′BB′, J = 8.6 Hz), 7.65 (2 H, B part of AA′BB′, J = 8.6 Hz); MS *m*/*z* 242 (M^+, 61). (*E*)-**30**: ^{1}H NMR (300 MHz) δ 0.98 (3 H, t, J = 6.8 Hz), 1.30−1.50 (2 H, m), 1.50−1.70 (2 H, m), 2.35 (2 H, br t, J = 6.8 Hz), 7.15 (1 H, t, J = 0.8 Hz), 7.48 (2 H, A part of AA′BB′, J = 8.5 Hz), 7.67 (2 H, B part of AA′BB′, J = 8.5 Hz); MS *m*/*z* 242 (M^+, 61); HRMS calcd for $C_{14}H_{14}N_2S$ (*E*/*Z* mixture) 242.0878, found 242.0883. Anal. Calcd for $C_{14}H_{14}N_2S$ (*E*/*Z* mixture): C, 69.39; H, 5.82; N, 11.56; S, 13.23. Found: C, 69.62; H, 5.79; N, 11.60; S, 13.30. A NOEDIF experiment was carried out on a fraction containing pure (*Z*)-**30** by irradiating the two allylic protons (2.37 ppm); the experiment showed an exclusive positive effect (2%) on the signal of the vinylic proton (6.90 ppm).

Final elution gave traces of the presumable[41,10] photo-Fries rearrangement product, 4-[[2-cyano-1-hexenyl]sulfanyl]-3-[(4-cyanophenyl)sulfanyl]benzonitrile: oil; MS *m*/*z* 375 (M^+, 100); HRMS calcd for $C_{21}H_{17}N_3S_2$ (*E*/*Z* mixture) 375.0864, found 375.0879.

Semiempirical Calculations. Semiempirical calculations on radicals (*E*)-**32a**,**b** and (*Z*)-**32a**,**b** were carried out with the CS MOPAC routine included in the CambridgeSoft ChemOffice Pro 4.0 package. After a careful conformational search, the geometries of the open-shell intermediates were fully optimized following the MNDO-d parametrization. Geometries and energies for radicals (*E*)-**32a**,**b** and (*Z*)-**32a**,**b** are shown in Schemes 12 and 13. The rotation barrier for each couple of intermediates (Scheme 13) was calculated by determining the maximum of the energy profile for rotation of the $C_\beta-C_\gamma$ bond; this was obtained by calculating single point energies for a series of intermediates with decreasing $C_\alpha-C_\beta-C_\gamma-S$ dihedral angles.

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Supporting Information Available: Full IR and MS data for compounds **4b**, **5b**,**c**, **7**, **8**, **15a**−**c**, **18**, **19**, **21**, **28**−**30**, and **40** and photo-Fries rearrangement products. This material is available free of charge via the Internet at http://pubs.acs.org.

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