Generation of Iminyl Radicals through Sulfanyl Radical Addition to Vinyl Azides

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Received April 11, 1997[⊗]

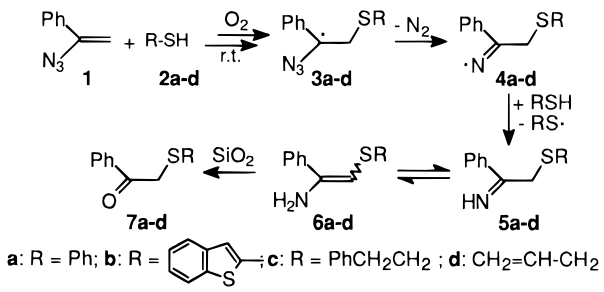
Benzenethiol and 2-benzo[*b*]thiophenethiol undergo almost instantaneous reaction with α-azidostyrene and 1-azido-*trans*-stilbene in benzene, at room temperature, to give corresponding *β*-sulfanylated imines and enamines in virtually quantitative yield. With α-azidostyrene, phenethyl and allyl mercaptan are found to react in a similar fashion, but to rates very much lower. Results are interpreted in terms of radical-chain reactions involving intermediacy of 2-sulfanyliminyl radicals which could result from sulfanyl radical attack at the azide *β*-carbon followed by nitrogen extrusion by the ensuing radical adduct.

Alkane- and arenethiols are well known to react with alkenes under radical conditions to give 2-sulfanylalkyl radicals arising from reversible addition of transient sulfanyl radicals to the carbon−carbon double bond.[1] The radical addition is normally governed by the stability of the ensuing carbon radical, though steric factors can play a significant role. We report herein novel radical-chain reactions of thiols with vinyl azides that form intermediate iminyl radicals through sulfanyl radical addition at the *β*-carbon and disclose unprecedented instances of homolytic substitution of S_H2' type at a vinylic azido nitrogen. Generation of iminyl radicals is of interest especially in view of very recent reports of their utility in synthetic radical chemistry. Iminyl radicals have been proved to exhibit intramolecular cyclization reactions onto double bonds[2−4] and aromatic rings[2] as well as fragmentation reactions[4] to give nitrile products. These species have been formerly generated by thermolysis or photolysis of various N-substituted imine derivatives,[2] by addition of carbon radicals to nitriles[5] and, very recently, using radical-chain reactions of Bu_3SnH with sulfanylimines[3], *N*-benzotriazolylimines,[4] and xanthic hydrazones.[6]

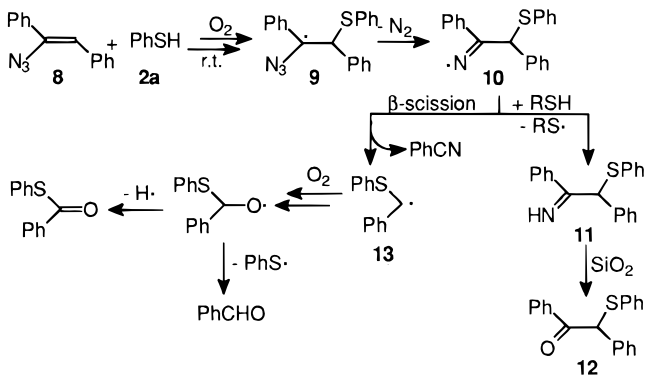
Results and Discussion

Treatment of α-azidostyrene (**1**) (0.1 M) in dry benzene, at room temperature, with 1 equiv of benzenethiol (**2a**) resulted in immediate evolution of nitrogen which virtually ceased within ca. 5 min. TLC analysis showed the absence of the starting azide and apparent formation of a single product, which was shown by ^{1}H NMR spectroscopy to be a 80:20 mixture of the sulfanylated enamine **6a** and its tautomer **5a**. Column chromatography on silica gel furnished their hydrolysis product, the *β*-keto sulfide **7a**, in almost quantitative yield (Scheme 1). The azide **1** similarly reacted with 2-benzo[*b*]thiophenethiol (**2b**), being rapidly (and quantitatively) converted into the corresponding 80:20 mixture of tautomers **6b** and **5b** which were isolated as keto sulfide **7b** upon subsequent column chromatography (Scheme 1). Analogous reaction also occurred with phenethyl mercaptan (**2c**) though it proceeded much more slowly. In fact, even after 10 days reaction time column chromatography isolated significant amounts of unchanged azide (10%) in addition to the expected sulfide **7c** (40%) as the only identifiable product (Scheme 1). Similar to the azide **1**, under comparable conditions 1-azido-*trans*-stilbene (**8**) was smoothly transformed by benzenethiol **2a** into the fairly stable enamine **11**, which could be isolated in 75% yield along with minor amounts (10%) of the derived keto sulfide **12** (Scheme 2). Instead, a different behavior was exhibited by *β*-azidostyrene and 2-azido-3-phenylpropene. These azides in

Scheme 1



Scheme 2



[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1997.

(1) For a recent review on sulfanyl radical additions to alkenes see: Chatgilialoglu, C.; Guerra, M. *Supplement S: The Chemistry of Sulfur-containing Functional Groups*; Patai, S., Rappoport, Z., Eds.; J. Wiley: Chichester, 1993; Ch. 8.

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(4) Kaim, L. E.; Meyer, C. *J. Org. Chem.* **1996**, *61*, 1556.

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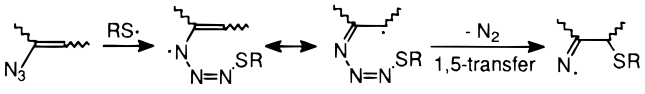
(6) Callier-Doublanchet, A.-C.; Quiclet-Sire, B.; Zard, S. Z. *Tetrahedron Lett.* **1995**, *36*, 8791. LeTadic-Biadatti, M.-H.; Callier-Doublanchet, A.-C.; Horner, J. H.; Quiclet-Sire, B.; Zard, S. Z.; Newcomb, M. *J. Org. Chem.* **1997**, *62*, 559.

S0022-3263(97)00691-9 CCC: $14.00

Scheme 3



the presence of benzenethiol (**2a**) were slowly consumed over ca. 24 h to give intractable product mixtures.

The above findings suggest that the thiols **2a**−**c** could add to the vinyl azides **1** and **8** by a radical-chain mechanism involving intermediate β-sulfanyliminyl radicals **4**, **10**. These intermediates probably arose from initial addition of transient sulfanyl radicals (produced by spontaneous reaction of corresponding thiols with oxygen) to the β-vinylic carbon followed by β-elimination of nitrogen from the benzyl radical adducts **3**, **9** (Schemes 1 and 2). In principle, the postulated iminyl radicals **4**, **10** might have alternately resulted from sulfanyl radical addition to the terminal nitrogen that would form a fairly resonance-stabilized triazenyl radical (Scheme 3). Azides are known to undergo homolytic attack at either end of the azido function.[7] However, sulfanyl radical addition at β-carbon is strongly suggested by the much higher reactivity of azides **1** and **8** with respect to β-azidostyrene and 2-azido-3-phenylpropene which would result from a comparatively higher stability of α-azidobenzyl than α-azidoalkyl radicals.

The primary intervention of benzenesulfanyl radicals was substantiated by the finding that the reaction of benzenethiol (**2a**) with α-azidostyrene (**1**) was inhibited in carefully degassed benzene solution. Further support came by reacting benzenethiol (**2a**) with the azide **1** in the presence of phenylacetylene, that is known to smoothly add the thiol **2a** by a free-radical process.[8] Usual treatment of thiol **2a** (0.5 equiv) with the azide **1** (1 equiv) in the presence of increasing amounts of phenylacetylene (5, 10, and 20 equiv) led to the formation of the adducts **5a**, **6a**, and the expected thiol/alkyne *Z*- and *E*-styrene adducts [PhSCH=CHPh]. In agreement with the common intervention of benzenesulfanyl radicals, the relative proportions of **5a**, **6a** to the styrene adducts were found to decrease roughly linearly with the increasing alkyne concentration (the ratios of **5a**, **6a** to the thiol/alkyne adducts, as determined by ^{1}H NMR spectroscopy, were respectively 28:1, 12:1, and 6:1).

Sound support to the postulated occurrence of the iminyl radical **10** was lended by reacting the azide **8** in the presence of a very low thiol **2a** concentration, which was achieved by adding the thiol (1 equiv) by a syringe pump over 3 h. Under these circumstances, column chromatography, besides the compounds **11** and **12** (15% overall yield), separated benzonitrile (20%), phenyl thiobenzoate (15%), and trace amounts of benzaldehyde (Scheme 2). Evidently, the intermediate **10** could exhibit competing β-scission to give the benzyl radical **13** that led to the thiobenzoate and benzaldehyde by further reaction with oxygen (Scheme 2).

A similar beahvior was instead not displayed by the iminyl congener **4a** under analogous high dilution conditions. Under such conditions also the radical **4a** could only undergo trapping by the thiol H-donor to give the above isomeric mixture of **5a** and **6a**.

In the present work we have also examined the reaction of the azide **1** with allyl mercaptan (**2d**) with the aim to find some evidence for intramolecular cyclization of the possible radical **4d** onto the adjacent sulfanyl double bond. Unfortunately such a reaction, while proving to be very much slow,[9] resulted in a complex product mixture from which only small amounts of the keto sulfide **7d** (7%) could be separated (Scheme 1).

In conclusion, we have shown that addition of sulfanyl radicals to the β-carbon of vinyl azides can interestingly lead to transient 2-sulfanyliminyl radicals, provided that the ensuing radical adducts be properly stabilized by an adjacent phenyl substituent. We have therefore disclosed a novel chemical behavior of vinyl azides that enlarges their versatile chemistry and synthetic usefulness.[10]

Experimental Section

Thiols **2a,c,d** were commercially available. Thiol **2b**,[11] α-azidostyrene **1**,[12] β-azidostyrene,[12] 2-azido-3-phenylpropene,[13] and 1-azido-*trans*-stilbene[13] **8** were prepared as described in the literature.

Known reaction products as the keto sulfides **7a**,[14] **7c**,[15] and **12**[16] and phenyl thiobenzoate[17] were identified on the basis of ^{1}H NMR and MS spectral data. Column chromatography was performed on Merck silica gel (0.040−0.063 particle size) by gradual elution with light petroleum (bp 40−70 °C)−diethyl ether. ^{1}H NMR spectra were recorded at 200 MHz in $CDCl_3$ solutions using Me_4Si as internal standard. Mass spectra were determined by the elctron impact method.

Reaction of Thiols 2a−d with α-Azidostyrene (1) and 1-Azido-*trans*-stilbene (8). The appropiate thiol (1 mmol) was added to a solution of azide (1 mmol) in dry benzene (10 mL), and the mixture was stirred at room temperature for the appropiate time. The solvent was removed, and the residue was normally analyzed by GC-MS and ^{1}H NMR and was then chromatographed on silica gel column.

From Benzenethiol (2a) and α-Azidostyrene (1). Upon addition of thiol **2a** immediate nitrogen evolution occurred. After ca. 5 min ^{1}H NMR analysis showed the exclusive presence of a mixture of the enamine **6a** and the imine **5a** in ca. 80:20 ratio [^{1}H NMR δ (**6a**) 4.40 (2H, br s), 5.25 (1H, s), 7.10−7.70 (10H, m); δ (**5a**) 4.20 (2H, s), 5.10 (1H, br s), 7.10−7.70 (10H, m); MS *m*/*z* 227 (M^+, 70), 226 (30) 104 (100)]. Chromatography gave the keto sulfide **7a** (220 mg, 96%). The reaction was repeated by adding slowly (3 h) with a syringe pump a solution of thiol **2a** (1 mmol) in benzene (5 mL) to the azide **1** (1 mmol) in benzene (10 mL). ^{1}H NMR analysis showed exclusive presence of the above isomeric mixture of **5a** and **6a**.

From 2-Benzo[*b*]thiophenethiol (2b) and α-Azidostyrene (1). Upon addition of thiol **2b** immediate nitrogen evolution occurred. After ca. 5 min ^{1}H NMR analysis showed the exclusive presence of the enamine **6b** and the imine **5b** in ca. 80:20 ratio [^{1}H NMR δ (**6b**) 4.50 (2H, br s), 5.30 (1H, s),

(7) Dang, H.-S.; Roberts, B. P. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1493, and references cited therein.

(8) Thiol **2a** quantitatively reacted with phenylacetylene (10 equiv) in benzene solution at room temperature over ca. 30 min to give a 90:10 *Z*/*E* mixture of styrene adducts [PhSCH=CHPh]. For a previous report of radical reactions of thiol **2a** with alkynes, including phenylacetylene, see: Benati, L.; Montevecchi, P. C.; Spagnolo, P. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2103, and references cited therein.-

(9) The lower reactivity of alkanethiols **2c,d** clearly resulted from their higher S−H bond strength.

(10) For leading references on vinyl azide chemistry see: Hassner, A. *Acc. Chem. Res.* **1971**, *4*, 9. L'Abbè, G. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 775. Hassner, A. In *Azides and Nitrenes: Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic Press: London, 1984; ch. 2. Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297.

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(17) Mukaiyama, T.; Katsuyama, H. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 2703.

7.10−7.70 (10H, m); δ (**5b**) 4.20 (2H, s), 7.10−7.70 (10H, m); MS *m*/*z* 283 (M^+, 30)]. Chromatography gave the keto sulfide **7b** (270 mg, 95%). [^{1}H NMR δ 4.30 (2H, s), 7.20−7.70 (8H, m) 7.90 (2H, d, J = 8 Hz); MS *m*/*z* 284 (M^+, 40), 105 (100). Anal. Calcd for $C_{16}H_{12}OS_2$: C, 67.57; H, 4.25; O, 5.63; S, 22.55. Found: C, 67.80; H, 4.27; S, 22.6.]

From Phenethyl Mercaptan (2c) and α-Azidostyrene (1). The reaction mixture was stirred for 10 days, after which time chromatography gave unchanged azide (10%) and the keto sulfide **7c** (90 mg, 40%).

From Allyl Mercaptan (2d) and α-Azidostyrene (1). α-Azidostyrene **1** (1 mmol) was allowed to react with thiol **2d** (2 mmol) for 10 days, after which time chromatography gave unchanged azide (60%) and the keto sulfide **7d** (7%). [^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.20 (2H, d, J = 6 Hz), 3.80 (2H, s), 5.15 (1H, d, J = 9 Hz), 5.20 (1H, d, J = 16 Hz), 5.80 (1H, m; collapsing to dd, J_1 = 9 Hz, J_2 = 16 Hz upon irradiation at δ 3.2), 7.40−7.60 (3H, m), 8.0 (2H, d, J = 8 Hz); MS *m*/*z* 192 (M^+, 10), 105 (100). A satisfactory analytical sample of this compound was not obtained owing to the minute amounts available.]

From Benzenethiol (2a) and 1-Azido-*trans*-stilbene (8). After addition of thiol **2a** evident nitrogen evolution occurred for ca. 30 min, after which time TLC showed the absence of the starting azide. The solvent was removed, and the crude was treated with diethyl ether to give a white solid. This was filtered off and shown to be the enamine **11** (195 mg, 65%): m.p. 104−108 °C. [^{1}H NMR δ 4.7 (2H, br s), 6.4−6.9 (15H, m); MS *m*/*z* 303 (M^+, 100), 193 (40), 104 (45). Anal. Calcd for $C_{20}H_{17}NS$: C, 79.17; H, 5.65; N, 4.62; S, 10.57. Found: C, 79.0; H, 5.62; N, 4.6; S, 10.38.] Evaporation of the organic filtrate and chromatography of the residue furnished further enamine **11** (30 mg, 10%) along with the keto sulfide **12** (30 mg, 10%).

The reaction was repeated by adding the thiol **2a** in benzene (5 mL) with a syringe pump over 3 h. Chromatography gave, in addition to a 1:1 mixture of enamine **11** and ketone **12** (45 mg, 15% overall yield), benzonitrile (20 mg, 20%), benzaldehyde (trace amounts, detected by GC-MS analysis), phenyl thiobenzoate (30 mg, 15%), and unidentifiable material.

Reaction of Benzenethiol (2a) with α-Azidostyrene (1) in the Presence of Phenylacetylene. Following the general procedure, the thiol **2a** (0.5 mmol) was reacted with the azide **1** (1 mmol) in the presence of increasing amounts of phenylacetylene (5, 10, and 20 mmol). ^{1}H NMR analysis of the respective reaction mixture showed that in each case the tautomers **5a**, **6a**, and β-(phenylsulfanyl)styrene [PhSCH=CHPh] (as a ca. 90:10 mixture of the *Z*- and *E*-isomers)[8] had formed in relative ratio of 28:1, 12:1, and 6:1, respectively.

Acknowledgment. This work has been carried out in the frame of the "Progetto di Finanziamento Triennale Ateneo di Bologna". We also acknowledge financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) and CNR (Rome).

JO970691Q