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A novel thermal rearrangement of allenic imidothioates. Formation of iminocyclobutenes

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Abstract—Allenic imidothioates, $H_2C{=}C{=}C(Ph)C(SMe){=}NR$ (R = Me, *t*-Bu, Ph) have been obtained in good yields by reaction of 1,3-dilithiated 1-(2-propynyl)benzene with isothiocyanates and successive addition of *t*-butyl alcohol and methyl iodide. Heating the imidothioates at ~120 °C gave an iminocyclobutene as the only isolated product (if R = *t*-Bu), a ~4:6 mixture of a 2,3-dihydropyridine and an iminocyclobutene (if R = Me) or a 3:1 mixture of a quinoline and an iminocyclobutene (if R = Ph).

1. Introduction

Previously,[1–4] we reported that the imidothioates $H_2C{=}C{=}C(R^1)C(SLi){=}NR^2$, obtained by regioselective reaction of isothiocyanates with allenic lithium compounds, can serve as intermediates for the synthesis of a variety of heterocyclic compounds. While under *nucleophilic* conditions intramolecular attack of the thioate moiety on the allenic system leads to thiophene or dihydrothiophene rings, the formation of 2,3-dihydropyridines, pyrroles, quinolines or cyclobutanopyrrolines from the *S-alkylated* products $H_2C{=}C{=}C(R^1)C(S\text{-alkyl}){=}NR^2$ can be effected by *thermal* rearrangement or under the catalytic action of copper(I) halides (in the case of pyrroles).

The recent extension[5] of our investigations to reactions between dilithiated acetylenes and isothiocyanates led to unexpected and highly interesting results. Reaction of a 1,3-dilithiated alkyne, for example, 1,3-dilithiated 2-propynylbenzene **1**, with 1 equiv of an isothiocyanate, followed by successive addition of *t*-butyl alcohol, potassium *t*-butoxide in DMSO and methyl iodide afforded, depending upon the nature of the isothiocyanate, an iminocyclobutene, iminothietane or thiophene as the only product or as a mixture of two or all of these compounds. It was assumed, and in the meantime confirmed,[6] that the products were formed under nucleophilic conditions, that is, by tandem reactions including nucleophilic addition, base-promoted cyclisation and methylation.

We now report the facile synthesis of the hitherto unknown azatrienes **2** and their conversion into iminocyclobutenes **5** by a novel, *thermal* reaction.

Azatrienes **2** were obtained in excellent yields by addition of the isothiocyanate to a solution of 1,3-dilithiated 2-propynylbenzene **1**, followed by successive protonation with *t*-butyl alcohol and reaction with methyl iodide. Apparently, the lithium *t*-butoxide formed in the protonation reaction does not cause the previously reported cyclisations of intermediates with the acetylenic or allenic system under more strongly basic conditions.[5,6]

The procedure for the thermal rearrangement of **2** involved refluxing a solution of it in toluene for 10–30 min. In the cases R = Me and Ph a mixture of **5** and 2,3-dihydropyridine **6** or **5** and quinoline **7**, respectively, was obtained. If R = *t*-Bu, **5** was the only product (Scheme 1).

Keywords: 2-Propynylbenzene; Isothiocyanates; Allenyl imidothioates; Cyclobutenes; Dihydropyridines; Quinolines; Dilithiation; Electrocyclisation.
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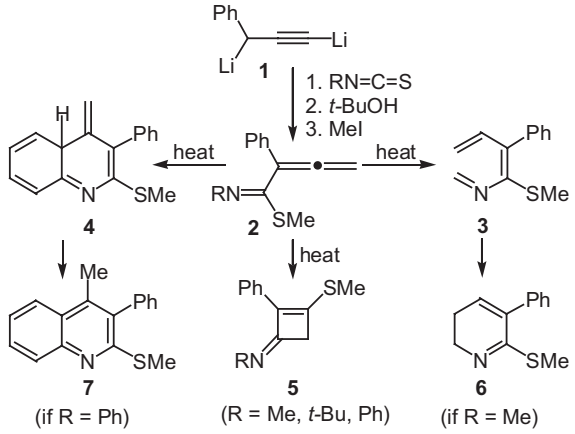


Scheme 1.

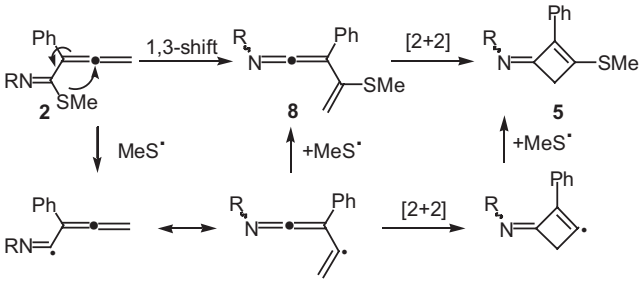
The routes from **2** to **6** or from **2** to **7** may be visualised, in analogy with previously published thermal reactions,[1–4] as a successive 1,5-H shift and electrocyclisation of intermediate **3** or an electrocyclisation of **2** followed by aromatisation of **4**, respectively.

Yields of **5b** (R = *t*-Bu) or combined yields of **5a** (R = Me) and **6** or **5c** (R = Ph) and **7** were ~50% or at least 87%, and the ratios of the product mixtures ~4:6 or ~1:3, respectively. The product mixtures could be successfully separated into the components by crystallisation or by column chromatography. It seems that at higher temperatures the relative amount of **5** increases to some extent: if **2** (R = Me) was added to refluxing DMSO (~185 °C), the product mixture of **5a** and **6** had a ratio of ~6:4, the combined yield being the same as in the case of heating in toluene under reflux. At temperatures below 100 °C (refluxing benzene) the conversion of **2** proceeded much more slowly.

The formation of iminocyclobutenes **5** from azatrienes **2** cannot proceed via **6** or **7**, as after prolonged heating the relative amounts of **5** did not increase. It should be pointed out that these four-membered ring systems have never been obtained from azatrienes $H_2C{=}C{=}C(R^1)$-C(S-alkyl)$=NR^2$ in which R^1 is OR, SR, CH_2NR_2 or alkyl.

This novel thermal rearrangement of allenyl imidothioates **2** into cyclobutenes **5** may proceed via an intramolecular 1,3-transfer of the methylthio group with formation of intermediate **8**, followed by intramolecular [2+2]-cycloaddition. Alternative routes involve C–S bond cleavage with formation of radicals, followed by their recombination and subsequent [2+2] cycloaddition (Scheme 2). However, heating of the S-*n*-Bu analogue of **2** (R = Me) in the presence of hydroquinone did not result in a change of the ratio of the corresponding analogue of **5** and the 2,3-dihydropyridine derivative. Refluxing a mixture of the same analogue and MeSSMe did not lead to replacement of SBu by SMe in the iminocyclobutene.

These results may be considered to disfavour the radical mechanism and not necessarily the 1,3-shift mechanism.



Scheme 2.

The shift of the MeS group towards the central carbon atom of the allenic system may be explained by the electron-withdrawing properties of the phenyl group. Analogues of **2** having OR, SR or alkyl groups instead of Ph do not undergo this type of rearrangement.[1–4]

Summarising, we can state that a convenient method for the synthesis of 2-phenyl-2,3-butadieneimidothioates **2** has been developed. Their conversion into iminocyclobutenes **5** represents a novel thermal rearrangement, taking place as the only reaction (if R = *t*-Bu) or is accompanied by the rearrangement leading to 6-(methylthio)-5-phenyl-2,3-dihydropyridine **6** (if R = Me) or to 2-(methylthio)-3-phenylquinoline **7** (if R = Ph).

2. Preparation of allenic imidothioates 2

To a solution of 2-propynylbenzene (5.8 g, 50 mmol) in THF (110 mL) a solution of *n*-BuLi (110 mmol) in hexane (68 mL) was added at −100 °C over ~1 min. The solution was stirred at 10–12 °C for 10 min, then cooled to −90 °C and a solution of the isothiocyanate (50 mmol) in THF (5 mL) was added in one portion. After being stirred for 5 min at ~−65 °C (in the case of MeNCS or PhNCS) or for 10 min at ~−50 °C (in the case of *t*-BuNCS), a mixture of *t*-BuOH (4 g, 54 mmol) and Et_2O (~2 mL) was added at −55 °C. MeI (15 g, 105.6 mmol) was added in one portion at ~−40 °C followed by stirring for ~2 h at room temperature, then a saturated aqueous solution of NH_4Cl was added with vigorous stirring. After extraction with Et_2O, drying over $MgSO_4$, the organic solution was concentrated under reduced pressure, while keeping the bath temperature below 30 °C. The remaining product was subjected to flash chromatography over a ~2 cm layer of Al_2O_3 (Et_2O/light petroleum, 1:3 v/v). Final concentration of the eluate under reduced pressure (in the last stage a vacuum of 1–4 torr was applied) at a bath temperature below 30 °C afforded the substantially pure (by NMR) imidothioates **2a–c** as mixtures of *syn* and *anti* isomers.

2.1. Methyl *N*-methyl-2-phenyl-2,3-butadienimidothioate 2a

Yield 82%; purity ~95%; mobile brownish liquid; $[n]_D^{22}$ 1.6064. ^1H NMR (400 MHz, $CDCl_3$, δ values in

ppm relative to HMDS): major isomer −2.35 (s, SMe), 3.15 (s, NMe), 5.25 (s, $=CH_2$), 7.18 (t, $^3J = 7.2$ Hz, H-*p*), 7.25 (m, 2H-*o*, 2H-*m*); minor isomer 2.21 (s, SMe), 3.32 (s, NMe), 5.31 (s, $=CH_2$), 7.25 (m, H-*p*, 2H-*m*), 7.35 (d, $^3J = 7.7$ Hz, 2H-*o*); 3:1 ratio; ^{13}C NMR (100 MHz, $CDCl_3$): major isomer 13.02 (SMe), 40.88 (NMe), 80.11 ($=CH_2$), 104.22 (=*C*-Ph), 125.64 (2C-*o*), 127.26 (C-*p*), 128.58 (2C-*m*), 131.61 (C-*i*), 161.09 (C=N), 206.23 (=C=); minor isomer 14.80 (SMe), 40.17 (NMe), 80.27 ($=CH_2$), 106.33 (=*C*-Ph), 125.90 (2C-*o*), 127.26 (C-*p*), 128.46 (2C-*m*), 133.13 (C-*i*), 162.35 (C=N), 207.78 (=C=).

2.2. Methyl *N*-(*tert*-butyl)-2-phenyl-2,3-butadienimidothioate 2b

Yield 80%; purity ~90%; mobile brownish liquid.

2.3. Methyl *N*-2-diphenyl-2,3-butadienimidothioate 2c

Yield 70%; purity ~99%; light-yellow crystals.

3. Thermal rearrangement of 2

The imidothioate **2** (3 g) and toluene (5 mL) were mixed at rt and the solution subsequently heated to reflux for 30 min (in the case of **2a**,**b**) or for 10 min (for **2c**). After removal of the solvent under reduced pressure, the residue (if R = Me or *t*-Bu) was analysed by NMR, then distilled under high vacuum. Compound **5b** was purified by crystallisation from light petroleum. Iminocyclobutene **5a** was isolated from the mixture with **6** by crystallisation from light petroleum. Concentration of the mother liquor gave **6** contaminated with some **2a**. Cyclobutene **2c** and quinoline **7** were isolated in high purity by column chromatography (Al_2O_3, 1:3 Et_2O/light petroleum).

3.1. 6-(Methylthio)-5-phenyl-2,3-dihydropyridine 6

Yield ~55%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (m, 3-CH_2), 2.26 (s, SMe), 3.66 (t, $^3J_{CH_2CH_2N} = 8.2$ Hz, NCH_2), 6.25 (t, $^3J_{CH_2CH} = 4.5$ Hz, =CH), 7.30 (narrow m, Ph); ^{13}C NMR: δ 12.98 (SMe), 22.23 (C-3), 47.16 (C-2), 127.87 (C-4, 2C-*m*), 128.55 (2C-*o*), 132.63 (C-*p*), 136.08 (C-5), 137.57 (C-*i*), 163.85 (C-6).

3.2. Methyl-*N*-[3-(methylthio)-2-phenyl-2-cyclobutenyliden]amine 5a

Yield 28%; yellow crystals; mp 90 °C. All spectral data are fully identical with those of the product described earlier.[5a]

3.3. *N*-(*tert*-butyl)-*N*-[3-(methylthio)-2-phenyl-2-cyclobutenyliden]amine 5b

Yield 49%; purity ~100% (NMR); yellow crystals; mp ~89 °C. The ^{1}H NMR spectrum showed inter alia the signal of the methylene protons at 3.57 ppm. Anal. Calcd for $C_{15}H_{19}NS$: C, 73.42; H, 7.80; N, 5.71; S, 13.07. Found: C, 72.98; H, 7.71; N, 5.89; S, 13.42%.

3.4. *N*-[3-(Methylthio)-2-phenyl-2-cyclobutenyliden]-*N*-phenylamine 5c

Yield 21%; light-brown crystals; mp 75 °C. Anal. Calcd for $C_{17}H_{15}NS$: C, 76.94; H, 5.70; N, 5.28; S, 12.08. Found: C, 77.08; H, 5.49; N, 5.18; S, 12.25%.

3.5. 4-Methyl-2-(methylthio)-3-phenylquinoline 7

Yield 66%; colourless crystals; mp 82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, C–Me), 2.55 (s, SMe), 7.24 (dd, $^3J = 7.2$ Hz, $^4J = 1.3$ Hz, 2H-*o*), 7.44 (m, 2H-*m*, H-*p*), 7.42 (ddd, $^3J = 8.3$ Hz, $^3J = 7.6$ Hz, $^4J = 1.2$ Hz, H-6), 7.61 (ddd, $^3J = 8.3$ Hz, $^3J = 7.6$ Hz, $^4J = 1.2$ Hz, H-7), 7.88 (br d, $^3J = 8.3$ Hz, H-5), 7.96 (br d, $^3J = 8.3$ Hz, H-8); ^{13}C NMR: δ 13.75 (SMe), 15.56 (C–Me), 124.94 (C-*p*), 125.14 (C-5), 125.85 (C-3), 128.04(C-8), 128.47 (C-8), 128.50 (C-*m*), 128.86 (C-7), 130.09 (C-*o*), 133.40 (C-9), 137.24 (C-*i*), 139.80 (C-4), 147.11 (C-10), 159.77 (C-2). Anal. Calcd for $C_{17}H_{15}NS$: C, 76.94; H, 5.70; N, 5.28; S, 12.08. Found: C, 77.03; H, 5.78; N, 5.27; S, 11.92%.

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References and notes

1. Nedolya, N. A. Novel Chemistry Based on Isothiocyanates and Polar Organometallics. Ph.D. Thesis; Utrecht University, The Netherlands, 1999.
2. Brandsma, L.; Nedolya, N. A.; Tarasova, O. A.; Trofimov, B. A. *Chem. Heterocycl. Compd. (N.Y.)* **2000**, *36*, 1241 [*Khim. Geterotsikl. Soedin*. **2000**, 1443].
3. Brandsma, L. *Eur. J. Org. Chem.* **2001**, 4569.
4. Brandsma, L.; Nedolya, N. A. *Synthesis* **2004**, 735.
5. (a) Brandsma, L.; Spek, A. L.; Trofimov, B. A.; Tarasova, O. A.; Nedolya, N. A.; Afonin, A. V.; Zinchenko, S. V. *Tetrahedron Lett.* **2001**, *42*, 4687; (b) Tarasova, O. A.; Brandsma, L.; Nedolya, N. A.; Afonin, A. V.; Ushakov, I. A.; Klyba, L. V. *Russ. J. Org. Chem.* **2003**, *39*, 1521; (c) Tarasova, O. A.; Brandsma, L.; Nedolya, N. A.; Ushakov, I. A.; Dmitrieva, G. V.; Koroteeva, T. V. *Zh. Org. Khim.* **2004**, *40*, 140.
6. Tarasova, O. A.; Nedolya, N. A.; Brandsma, L., unpublished results.