An unexpected pathway of the reaction of lithiated 1,1-dimethylallene with isopropyl isothiocyanate

L. Brandsma,[a] N. A. Nedolya,[b]* A. C. T. H. M. van der Kerk,[c] W. Heerma,[c] E. T. H. G. Lutz,[d] R.-J. de Lang,[a] A. V. Afonin,[b] and B. A. Trofimov[b]

[a]*Preparative Organic Chemistry Department, Utrecht University,*
Padualaan 8, 3584 CH, Utrecht, The Netherlands
[b]*Irkutsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences,*
1 ul. Favorskogo, 664033 Irkutsk, Russian Federation.
Fax: 007 (395 2) 35 6046
[c]*Department of Mass Spectrometry, Utrecht University, Utrecht,*
The Netherlands
[d]*Department of IR Spectroscopy, Utrecht University, Utrecht,*
The Netherlands

The reaction of lithiated 1,1-dimethylallene with isopropyl isothiocyanate gives 3a,4,5,5a-tetrahydro-4,4,5a-trimethyl-2-methylthio-3*H*-cyclobuta[*b*]pyrrole resulting from cyclization of the intermediate 2,7-dimethyl-4-methylthio-3-azaocta-2,4,6-triene.

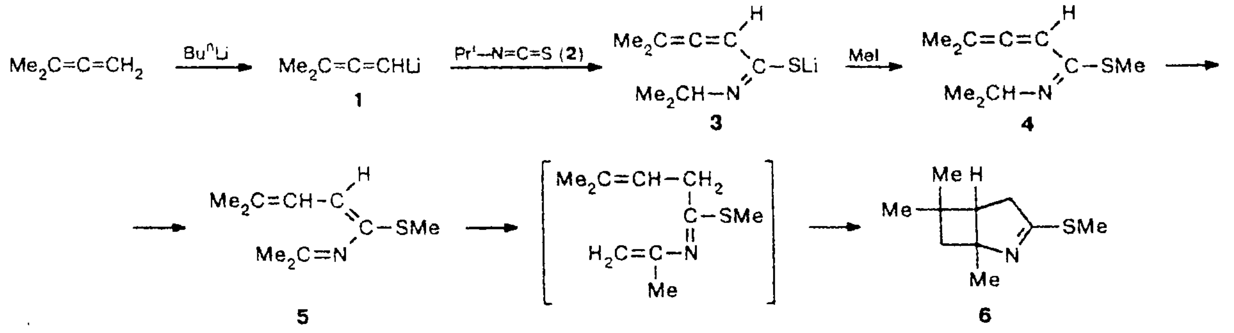
Key words: isopropyl isothiocyanate, 1,1-dimethylallene, butyllithium, lithiation, alkylation, azatrienes, 3a,4,5,5a-tetrahydro-4,4,5a-trimethyl-2-methylthio-3*H*-cyclobuta[*b*]pyrrole.

Up to now, the reactions of organometallic compounds with isothiocyanates have been used to prepare thioamides.[1,2] Recently, we synthesized for the first time pyrroles[3,4] and 5,6-dihydropyridines[3–5] by the reaction of isothiocyanates with lithiated allene and acetylene derivatives. The addition of 3,3-dimethylallen-1-yllithium (**1**) to phenyl isothiocyanate is a fundamentally new method for the synthesis of quinolines.[6]

The replacement of phenyl isothiocyanate in the reaction with **1** by isopropyl isothiocyanate (**2**) leads to a novel and unexpected result, *i.e.*, the formation of 3a,4,5,5a-tetrahydro-4,4,5a-trimethyl-2-methylthio-3*H*-cyclobuta[*b*]pyrrole (**6**) (a possible reaction pathway is shown in Scheme 1).

The initially formed azatriene **4** isomerizes quantitatively to azatriene **5** during distillation. We have also observed prototropic isomerization of 3,5,6-azatrienes of type **4** to 2,4,6-azatrienes of type **5** in the reactions of lithiated allene and acetylene derivatives with ethyl, isopropyl, and cyclohexyl isothiocyanates.[5] Thermolysis of conjugated azatriene **5** gives compound **6** in a high yield. The structures of compounds **4**, **5**, and **6** were determined by the data of elemental analysis, IR spectroscopy, ^1H and ^{13}C NMR spectroscopy, and GC/MS.

Scheme 1



Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 4, pp. 865—867, April, 1997.

Experimental

IR spectra were recorded on FT-IR and Perkin—Elmer 283 spectrophotometers in thin films. NMR spectra were obtained on Varian EM-390 (90 MHz, ~20% solutions in CCl_4, tetramethylsilane as the internal standard) and Bruker AC-300 (300 MHz for ^1H, 75 MHz for ^{13}C, ~20% solutions in $CDCl_3$, tetramethylsilane as the internal standard) spectrometers. GLC analysis was performed on a Varian 3400 gas chromatograph (flame ionization detector, a 15 m×0.53 mm capillary column, 1.5 μm DB-5, nitrogen as the carrier gas). GC/MS analysis was carried out on a JEOL AX-505 instrument (accelerating voltage 3 kV, emission current 100 mA, ionization energy 70 eV, helium as the carrier gas).

All operations were carried out in a nitrogen atmosphere. 1,1-Dimethylallene was synthesized by a known procedure,[7] and isopropyl isothiocyanate (2) was prepared by the reaction of isopropylamine with CS_2 and AcCl. Tetrahydrofuran was purified mechanically by treatment with dispersed KOH (~50 g L^{-1}) and by distillation over $LiAlH_4$ in the presence of benzophenone under nitrogen. Butyllithium (1.6 *M* a solution in hexane) was provided by the Chemetall company (Germany).

Reaction of 3,3-dimethylallen-1-yllithium (1) with isopropyl isothiocyanate (2) and methyl iodide. 1,1-Dimethylallene (4.9 g, 0.07 mol) was added to a solution of Bu^nLi (0.05 mol) in 70 mL of anhydrous THF and 35 mL of hexane cooled to −50 °C. The mixture was stirred for 1.5 h at −40 to −30 °C and cooled to −95 °C. Compound **2** (5.4 g, 0.05 mol) was added. The reaction mixture was warmed to −55 °C (over a period of ~25 min), and MeI (9.8 g, 0.07 mol) was added. The mixture was stirred for 10—15 min at 5 °C and diluted with ~50 mL of cold water. The organic layer was separated, the aqueous layer was extracted with ether, and the combined organic fraction was dried with potassium carbonate. The solvent was evaporated to give 8.51 g (93%) of 2,7-dimethyl-5-methylthio-6-azaocta-2,3,5-triene (**4**) containing a minor amount of azatriene 5 (judging from ^1H NMR) as a light labile liquid, n_D^{20} 1.5250. Found (%): C, 65.34; H, 8.98; N, 6.45; S, 17.57. $C_{10}H_{17}NS$. Calculated (%): C, 65.57; H, 9.29; N, 6.65; S, 17.49.

IR, ν/cm^{-1}: 1970 (C=C=C); 1605 (C=N); 1655 (C=C). ^1H NMR (90 MHz, CCl_4), δ: 5.86 (sept., 1 H, CH=); 1.82 (d, 6 H, $Me_2C=C$); 3.82 (sept., 1 H, CH); 1.12 (d, 6 H, $\underline{Me}_2CH$); 2.20 (s, 3 H, SMe).

Vacuum distillation of azatriene **4** gave 2,7-dimethyl-4-methylthio-3-azaocta-2,4,6-triene (**5**) (yield 90%), b.p. 80—85 °C (0.7 Torr), n_D^{20} 1.5610. Found (%): C, 65.73; H, 9.11; N, 6.54; S, 17.20. $C_{10}H_{17}NS$. Calculated (%): C, 65.57; H, 9.29; N, 6.65; S, 17.49. MS, *m/z*: 183 $[M]^+$, 168 $[M-Me]^+$, 136 $[M-SMe]^+$, 127 $[M-Me_2C=N]^+$.

IR, ν/cm^{-1}: 1575 (C=N); 1660 (C=C). ^1H NMR (300 MHz, $CDCl_3$), δ: 5.36 (d, 1 H, 6-CH=); 5.45 (d, 1 H, 5-CH=); 1.58 and 1.57 (both s, 3 H + 3 H, $Me_2C=C$); 1.99 and 1.71 (both s, 3 H + 3 H, $Me_2C=N$); 2.04 (s, 3 H, SMe). ^{13}C NMR, δ: 171.03 (2-C); 140.72 (4-C); 106.84 (5-C); 119.23 (6-C); 130.94 (7-C); 20.46 ($\underline{Me}C=N$, *cis*); 27.35 ($\underline{Me}C=N$, *trans*); 17.74 ($\underline{Me}C=C$, *cis*); 25.61 ($\underline{Me}C=C$, *trans*); 14.21 (SMe).

Heating compound 5 to ~220 °C for ~10 min followed by vacuum distillation gave 8.0 g (87.4%) of compound **6** with a purity of 96.6% (GLC); b.p. ~87 °C (15 Torr), 210—215 °C (760 Torr), n_D^{20} 1.5060. Found (%): C, 65.23; H, 9.19; N, 6.76; S, 17.00. $C_{10}H_{17}NS$. Calculated (%): C, 65.57; H, 9.29; N, 6.65; S, 17.49. MS, *m/z*: 183 $[M]^+$, 168 $[M-Me]^+$, 136 $[M-SMe]^+$, 127 $[M-Me_2C=CH_2]^+$, 112 $[127-Me]^+$.

IR, ν/cm^{-1}: 3153, 1586 (νC=N); 2997 (ν_{as}SMe); 2923 (ν_sSMe); 1282 (δSMe); 1061 (SMe); 2952 (ν_{as}Me). ^1H NMR (300 MHz), δ: 0.78 (s, 3 H, 4-Me); 1.04 (s, 3 H, 4-Me); 1.25 (s, 3 H, 5a-Me); 2.34 (s, 3 H, SMe); 1.69 and 1.78 (both d, 2 H, 5-CH_2); 2.14 (dd, 1 H, CH); 2.56 and 2.68 (both dd, 2 H, 3-CH_2). ^{13}C NMR, δ: 170.22 (C-2); 73.66 (5a-C); 13.61 (SMe); 49.96, 47.83, 41.40, 32.02, 29.67, 26.38, 24.36.

References

1. K. A. Petrov and L. N. Andreev, *Usp. Khim.*, 1969, **38**, 41 [*Russ. Chem. Rev.*, 1969, **38** (Engl. Transl.)].
2. L. Brandsma, in *Studies in Organic Chemistry. 34. Preparative Acetylenic Chemistry*, 2nd. Ed., Elsevier, Amsterdam, 1988, 100, 108, 299.
3. N. A. Nedolya, R.-J. de Lang, L. Brandsma, and B. A. Trofimov, *Abstr. of 11th Intern. Conf. on the Organic Synthesis*, Amsterdam, The Netherlands, 1996, 251.
4. L. Brandsma, B. Trofimov, N. Nedolya, and A. Mal'kina, *Abstr. of 17th Intern. Symp. on the Organic Chemistry of Sulfur*, Tsukuba, Japan, 1996, 234.
5. L. Brandsma, B. Trofimov, N. Nedolya, and A. Mal'kina, *Abstr. of 17th Intern. Symp. on the Organic Chemistry of Sulfur*, Tsukuba, Japan, 1996, 233.
6. L. Brandsma, N. A. Nedolya, R.-Zh. de Lang, and B. A. Trofimov, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 3024 [*Russ. Chem. Bull.*, 1996, **45**, 2873 (Engl. Transl.)].
7. L. Brandsma and H. D. Verkruijsse, in *Studies in Organic Chemistry. 8. Synthesis of Acetylenes, Allenes and Cumulenes. A Laboratory Manual*, Elsevier, Amsterdam, 1981, 190.

Received October 18, 1996;
in revised form December 10, 1996