

SHORT
COMMUNICATIONSUnprecedented [2+2]-Cyclodimerization of 1-Aza-1,3,4-trienes:
First Representative of 3,4-Diisopropylidenecyclobutane-
1,2-dicarbimidothioatesN. A. Nedolya^a, O. A. Tarasova^a, A. I. Albanov^a, I. A. Ushakov^a, and L. Brandsma^b^a *Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences,
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Received October 13, 2006

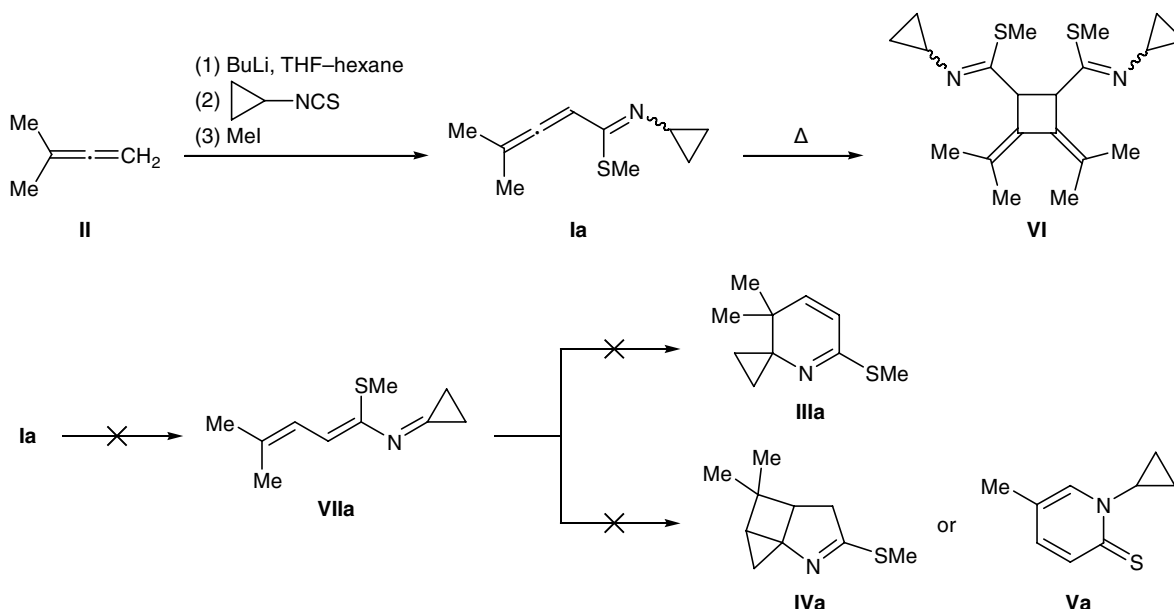
DOI: 10.1134/S1070428007030268

Allenecarbimidothioates (1-aza-1,3,4-trienes) of the general formula $R^1R^2C=C=C(R^3)C(SR^4)=NR^5$ have recently become accessible due to development of a novel and simple procedure for their preparation by reaction of lithiated allenes and alkynes with isothiocyanates [1, 2]; these compounds are unique and universal precursors of various carbo- and heterocyclic structures [1–12], from four-membered (cyclobutenes and thietanes [3]) to five- (pyrroles, dihydropyrroles, thiophenes, and dihydrothiophenes [4, 5]), six- (pyridines, dihydropyridines, and quinolines [4, 6–11]), and

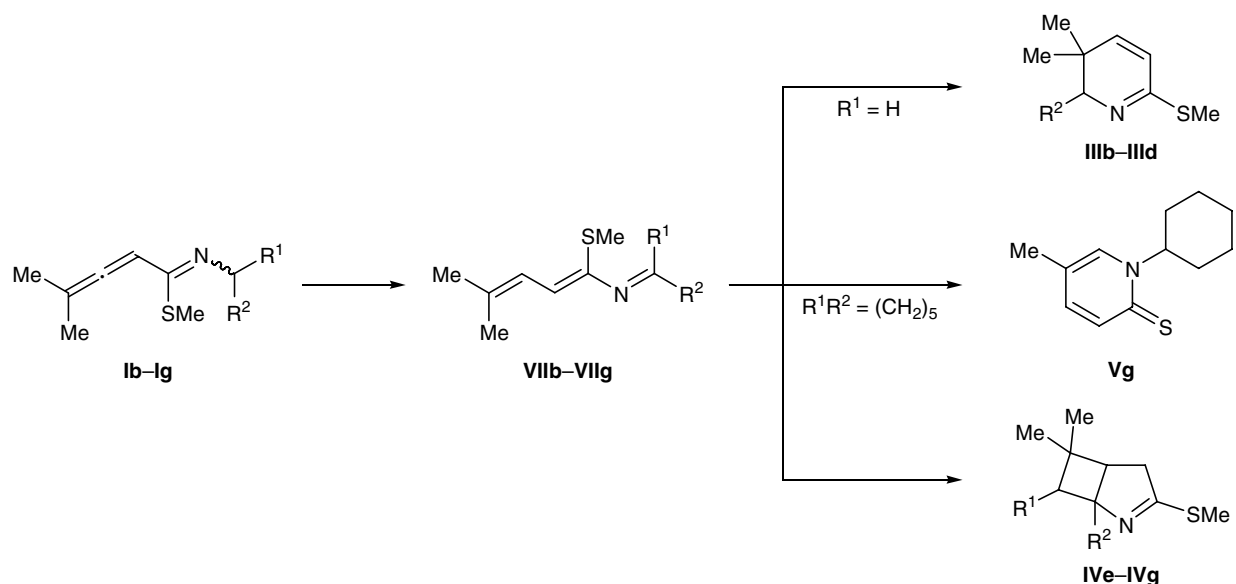
seven-membered systems (azepines and dihydroazepines [12]).

1-Aza-1,3,4-triene **Ia** was prepared as a mixture of *E* and *Z* isomers (~9:1) [13] in almost quantitative yield by reaction of γ -lithiated 3-methylbuta-1,2-diene (**II**) and cyclopropyl isothiocyanate (Scheme 1). Unlike azatrienes **Ib–Ig** (Scheme 2) obtained from allene **II** and methyl, ethyl, 2-(vinylloxy)ethyl, isopropyl, cyclopentyl, and cyclohexyl isothiocyanates, heating of compound **Ia** gave neither 2,3-dihydropyridine **IIIa** [7, 8] nor 8-azatricyclo[3.3.0.0^{1,3}]oct-7-ene **IVa** [5, 7]

Scheme 1.



Scheme 2.



I, III, VII, $R^1 = R^2 = H$ (**b**), $R^1 = H, R^2 = Me$ (**c**), $R^1 = H, R^2 = CH_2=CHOCH_2$ (**d**), $R^1 = R^2 = Me$ (**e**), $R^1R^2 = (CH_2)_4$ (**f**), $R^1R^2 = (CH_2)_5$ (**g**); **IV**, $R^1 = H, R^2 = Me$ (**e**), $R^1R^2 = (CH_2)_3$ (**f**), $R^1R^2 = (CH_2)_4$ (**g**).

nor pyridinethione **Va** [10]; therefore, we were able to perform its additional purification by vacuum distillation (yield ~90%).

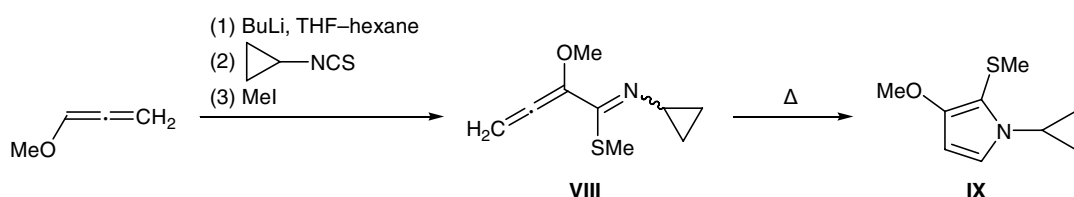
On prolonged storage even at reduced temperature, 1-aza-1,3,4-triene **Ia** was transformed with a conversion of ~45% (according to the 1H NMR data) into previously unknown dimethyl N,N' -dicyclopropyl-3,4-diisopropylidencyclobutane-1,2-dicarbimidothioate (**VI**). Obviously, compound **IV** was formed via intermolecular [2+2]-cycloaddition of **Ia**, which was not observed previously for 1-aza-1,3,4-triene systems. In contrast to known allenes [14], the cyclization of **Ia** followed exclusively the "head-to-head" pattern (1,2-addition), as shown by the 1H and ^{13}C NMR spectra (the ^{13}C NMR spectra were recorded both with decoupling from protons and without it), including ^{13}C 2D INADEQUATE, NOESY, HSQC, and HMBC techniques. [2+2]-Cycloaddition of allenes is usually promoted by photochemical or (more rarely) thermal activation (150–200°C), and it leads to the formation of isomer mixtures (especially in thermally induced reactions). In our case, the process occurs under very

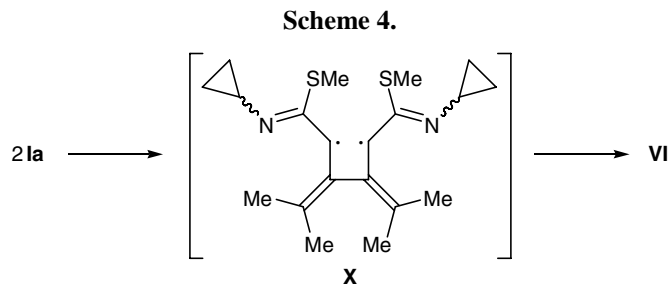
mild conditions (in the dark at reduced temperature) and is characterized by high regioselectivity.

Presumably, among the two possible pathways, cyclodimerization of azatriene **Ia** is considerably more favorable from the viewpoint of thermodynamics than [1,5]-sigmatropic rearrangement into 2-aza-1,3,5-triene **VIIa** (precursor of cyclic structures **IIIa–Va**) containing a strained N-cyclopropylidene fragment. It should be noted that 1-aza-1,3,4-triene **VIII** synthesized from cyclopropyl isothiocyanate and α -lithiated methoxyallene undergoes thermal cyclization to produce exclusively 3-methoxy-2-methylsulfanyl-1-cyclopropyl-1H-pyrrole (**IX**) (Scheme 3). No cycloadduct analogous to **VI** was detected in the reaction mixture.

Presumably, thermal [2+2]-cycloaddition of 1-aza-1,3,4-triene **Ia**, as well of simpler allenes, is not a concerted process. It is likely to include two steps. In the first of these, rupture of two π -bonds gives rise to one new σ -bond with formation of diradical intermediate **X**, and the subsequent recombination of **X** yields final product **VI** (Scheme 4).

Scheme 3.





Thus we have discovered one more transformation pathway of highly reactive azapolyene systems that are readily available from accessible polyunsaturated carb-anions and isothiocyanates [1–12] in a single preparative stage. As a result, tetrasubstituted polyfunctional cyclobutane derivatives having carbimidothioate, alkylidene, and cyclopropyl fragments are obtained.

Methyl *N*-cyclopropyl-4-methylpenta-2,3-dien-imidothioate (Ia). 3-Methylbuta-1,2-diene (**II**), 8 g (57 mmol), was added under stirring to a solution of 59 mmol of butyllithium in a mixture of 37 ml of hexane and 50 ml of THF, maintained at -75°C . The mixture was stirred for 15 min at -60 to -50°C and cooled to -100°C , and a solution of 3.9 g (53 mmol) of cyclopropyl isothiocyanate in 10 ml of diethyl ether was quickly added. The mixture was stirred for ~ 10 min at -60 to -40°C , 12 g (83 mmol) of methyl iodide was added, and the mixture was allowed to warm up to 20°C and treated first with water and then with diethyl ether (2×50 ml). The extracts were combined and dried over potassium carbonate, and the solvent was distilled off on a rotary evaporator. Yield 9.4 g (98%). ^1H NMR spectrum (CCl_4), δ , ppm: 6.05 m (1H, CH=), 3.10 m (1H, NCH), 2.10 s (3H, SMe), 1.82 d (6H, $\text{Me}_2\text{C}=\text{C}$), 0.75 m (4H, 2CH_2). By vacuum distillation we isolated 8.65 g ($\sim 90\%$) of azatriene **Ia** containing 97% of the main substance (GLC data), bp $\sim 70^{\circ}\text{C}$ (~ 0.2 mm), $n_D^{20} = 1.5554$.

Repeated distillation of a 3.9-g sample of the product stored for a long time in a freezer gave 1.8 g of compound **Ia** with bp $93\text{--}96^{\circ}\text{C}$ (~ 1 mm), $n_D^{21} = 1.5531$. IR spectrum (film), ν , cm^{-1} : 414, 432, 563 sh, 582, 671, 730, 766, 807, 836 sh, 902, 950, 1015, 1039, 1055 sh, 1110, 1172, 1190 sh, 1235, 1310, 1360, 1377 sh, 1416, 1445, 1596 v.s (C=N), 1957 s (C=C=C), 2857, 2922, 2985, 3006, 3089, 3174. ^1H NMR spectrum, δ , ppm: *E* isomer (fraction $\sim 90\%$): 6.15 sept (1H, CH=, $^5J = 3.0$ Hz), 3.14 t.t (1H, NCH, $^3J_{CB} = 6.9$, $^3J_{CA} = 3.6$ Hz), 2.17 s (3H, SMe), 1.79 d (6H, $\text{Me}_2\text{C}=\text{C}$, $^5J = 3.0$ Hz), 0.80 m (2H, CH_2), 0.75 m (2H, CH_2); *Z* isomer (fraction $\sim 10\%$): 5.78 sept (1H,

CH=), 3.34 t.t (1H, NCH), 2.43 s (3H, SMe), 1.75 d (6H, $\text{Me}_2\text{C}=\text{C}$, $^5J = 3.0$ Hz), 0.89 m (4H, 2CH_2). ^{13}C NMR spectrum, δ_C , ppm: *E* isomer: 206.09 (C=C=C), 159.06 (C=N), 100.54 ($\text{Me}_2\text{C}=\text{C}$), 86.00 (CH=), 34.18 (NCH), 19.75 ($\text{Me}_2\text{C}=\text{C}$), 12.35 (SMe), 8.67 (CH_2); *Z* isomer: 206.54 (C=C=C), 157.76 (C=N), 98.8 ($\text{Me}_2\text{C}=\text{C}$), 93.93 (CH=), 36.04 (NCH), 19.93 ($\text{Me}_2\text{C}=\text{C}$), 16.01 (SMe), 9.01 (CH_2). Found, %: C 66.42; H 8.51; N 7.79; S 17.28. $\text{C}_{10}\text{H}_{15}\text{NS}$. Calculated, %: C 66.25; H 8.34; N 7.73; S 17.69.

Dimethyl *N,N'*-dicyclopropyl-3,4-diisopropylidene-cyclobutane-1,2-dicarbimidothioate (VI). The still residue obtained after distillation of azatriene **Ia**, 2.1 g (53.8 wt %) was a dark brown viscous liquid; it was subjected to flash chromatography on Al_2O_3 using petroleum ether as eluent to isolate compound **VI** as a light yellow viscous liquid. ^1H NMR spectrum, δ , ppm: 4.20 s (2H, CH), 3.07 m (2H, NCH), 2.13 s (6H, SMe), 1.90 s (6H, Me), 1.64 s (6H, Me), 0.75 m (8H, CH_2). ^{13}C NMR spectrum, δ_C , ppm: 165.79 (C=N), 132.22 (C=), 126.41 ($\text{Me}_2\text{C}=\text{C}$), 48.07 (CH), 33.72 (NCH), 22.15, 20.93 ($\text{Me}_2\text{C}=\text{C}$), 12.51 (SMe), 9.06 (CH_2), 8.62 (CH_2). Found, %: C 65.91; H 8.33; N 8.39; S 17.37. $\text{C}_{20}\text{H}_{30}\text{N}_2\text{S}_2$. Calculated, %: C 66.25; H 8.34; N 7.73; S 17.69.

The ^1H and ^{13}C NMR spectra were recorded on Bruker DPX-400 and AV-400 spectrometers at 400.13 and 100.61 MHz for ^1H and ^{13}C , respectively (samples were prepared as 5–10% solutions in CDCl_3 containing HMDS as internal reference), and on a Varian EM-390 instrument (90 MHz for ^{13}C ; $\sim 20\%$ solutions in CCl_4 ; internal reference tetramethylsilane). The IR spectra were measured on Bruker IFS-25, Perkin-Elmer-283, and Specord 75IR spectrometers from samples prepared as thin films or solutions in CCl_4 . Reaction mixtures and products were analyzed by GLC on a Varian 3400 chromatograph equipped with a flame ionization detector and a DB-5 capillary column ($15 \text{ m} \times 0.53 \text{ mm} \times 1.5 \mu\text{m}$); carrier gas nitrogen.

All operations were carried out under nitrogen. Liquid nitrogen was used as cooling agent. Tetrahydro-

furan was purified by treatment with dispersed potassium hydroxide (~50 g/l), followed by distillation over LiAlH₄ in the presence of benzophenone under nitrogen. 3-Methylbuta-1,2-diene (**II**) and cyclopropyl isothiocyanate were synthesized by the procedures described in [15] and [1], respectively. Butyllithium (a ~1.6 M solution in hexane) and the other reagents and solvents used were commercial products.

This study was performed under financial support by the Russian Foundation for Basic Research (project nos. 05-03-32578, 01-03-32698).

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