

## Reaction of 4-Ethoxy-2-(2,3,3-trichloro-1-nitro-2-propenylidene)benzazetine with Methyl- and Phenyllithium\*

V. I. Potkin, V. A. Knizhnikov, A. A. Yanuchok, and R. V. Kaberdin

Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus,  
ul. Surganova 13, Minsk, 220072 Belarus  
fax: (017)284 1679; e-mail: ifoch@ifoch.bas-net.by

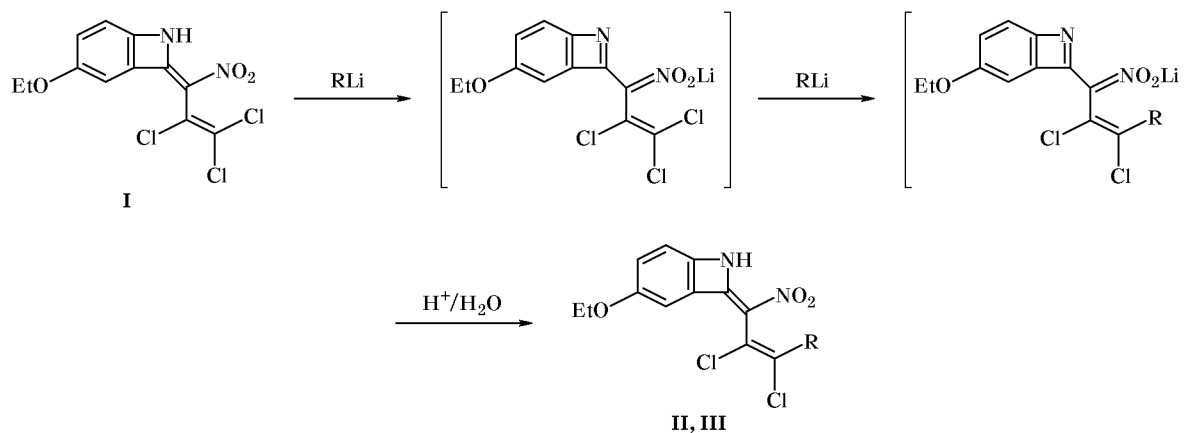
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**Abstract**—The reactions of 4-ethoxy-2-(2,3,3-trichloro-1-nitro-2-propenylidene)benzazetine with methyl- and phenyllithium at a ratio of 1:2 result in replacement of one chlorine atom and formation, respectively, of 4-ethoxy-2-(2,3-dichloro-3-methyl-1-nitro-2-propenylidene)benzazetine and 4-ethoxy-2-(2,3-dichloro-1-nitro-3-phenyl-2-propenylidene)benzazetine in 45 and 52% yield. With excess phenyllithium (reactant ratio 1:5), a mixture of products is formed due to replacement of one, two, and three chlorine atoms by phenyl groups. An analogous reaction with methylolithium is nonselective.

We recently described a new convenient procedure for building up difficultly accessible benzazetine derivatives [1] starting from azolyl-substituted halonitrodienes [2]. We have found that heating of 1-azolyl-1-arylamino-2-nitrotrihalobutadienes (where azolyl = 1-benzotriazolyl, 1-triazolyl-, and 3,5-dimethyl-1-pyrazolyl) in proton-donor solvents leads to formation of 2-(2,3,3-trichloro-1-nitro-2-propenyl-

dene)benzazetines containing a methyl, methoxy, ethoxy, or butoxy group in position 4. Studies of the reaction of the resulting benzazetines with N-, O-, and S-nucleophiles (such as amines and sodium alkoxides and thiolates) showed the low reactivity of chlorine atoms in nucleophilic vinyl substitution. These reactions involved the side-chain nitro group and afforded the corresponding salts of *aci*-nitro compounds. In

Scheme 1.



II, R = Me; III, R = Ph.

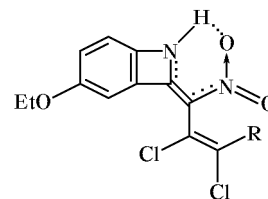
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continuation of our studies on the chemical properties of benzazetines we examined reactions of one of the synthesized benzazetine derivatives, 4-ethoxy-2-(2,3,3-trichloro-1-nitro-2-propenylidene)benzazetine (**I**), with methyl- and phenyllithium. There are very limited published data on reactions of organolithium reagents with compounds possessing a trichlorovinyl group [3].

When the reaction was performed in diethyl ether at 20–25°C with the reactants taken at a ratio of 2:1 (RLi–benzazetine), one terminal chlorine atom in the trichlorovinyl group was replaced by methyl or phenyl group to give 2-(2,3-dichloro-3-methyl-1-nitro-2-propenylidene)-4-ethoxybenzazetine (**II**) and 2-(2,3-dichloro-1-nitro-3-phenyl-2-propenylidene)-4-ethoxybenzazetine (**III**), respectively, in 45 and 52% yield (Scheme 1). With a smaller amount of organolithium compound, the reaction was not complete, and the mixture contained unchanged initial compound **I**. Presumably, the reaction involves reversible transformation of the nitro group into *aci*-nitro form which gives the corresponding lithium salt (as was observed previously in the reaction of **I** with sodium alkoxides and thiolates [2]). Next follows replacement of the terminal chlorine atom. Treatment of the mixture with water or dilute hydrochloric acid leads to decomposition of the *aci*-nitro salt and regeneration of the initial heterocyclic system.

According to the  $^1\text{H}$  NMR and TLC data, products **II** and **III** are single isomers. However, we failed to reliably establish their configuration on the basis of the spectral data. In the  $^1\text{H}$  NMR spectra of **II** and **III**, signals from aromatic protons of the benzazetine fragment appear as three doublets in the region  $\delta$  7.1–7.8 ppm. The NH proton gives a broadened singlet at  $\delta$  12.6 ppm, and protons of the ethoxy group give a triplet at  $\delta$  1.4 ppm (3H,  $\text{CH}_3$ ) and a quadruplet at  $\delta$  4.1 ppm ( $\text{CH}_2\text{O}$ ). The singlet at  $\delta$  1.70 ppm in the

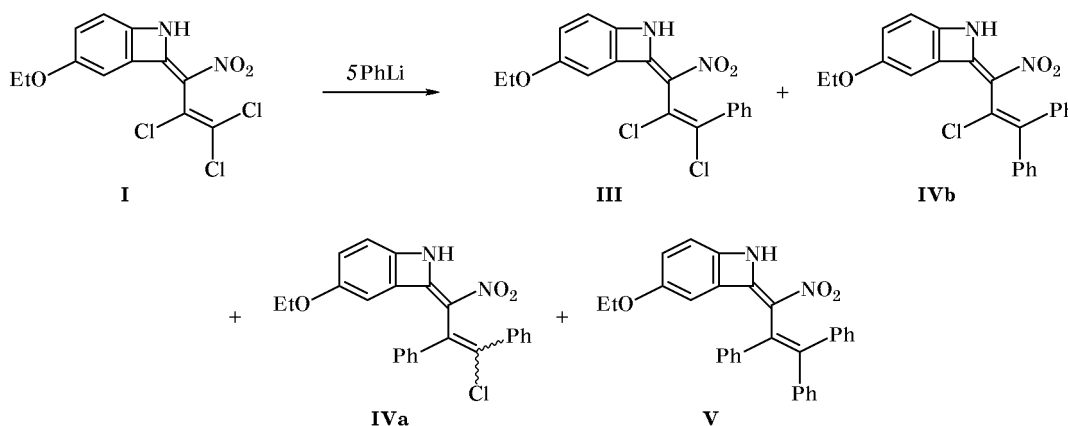
spectrum of **II** belongs to the terminal methyl group, and the phenyl group in **III** gives a multiplet in the region of  $\delta$  7.4 ppm. Compounds **II** and **III** show in the IR spectra symmetric and antisymmetric vibration bands of the nitro groups at 1353 and 1529  $\text{cm}^{-1}$  (**II**) and 1362 and 1530  $\text{cm}^{-1}$  (**III**). The bands at 1573, 1625 (**II**) and 1492, 1601  $\text{cm}^{-1}$  (**III**) were assigned to C=C stretching vibrations. The absorption at 1650  $\text{cm}^{-1}$  indicates a partial double character of the C–N bond due to conjugation and intramolecular interaction between the nitro group and NH proton. This band in the spectrum of phenyl derivative **III** is stronger than in the spectrum of **II**.



The mass spectra of **II** and **III** contained the molecular ion peaks with an isotope ratio of 100:65, indicating the presence of two chlorine atoms:  $m/z$  314 (**II**) and 376 (**III**) (calculated on  $^{35}\text{Cl}$  [4]).

We expected that application of a larger amount of organolithium reagent will lead to replacement of two or three chlorine atoms. However, the reaction with excess methyl lithium was not selective, and we obtained a complex mixture of products and a considerable amount of tars. The reaction with phenyllithium was more selective. Using 3 mol of PhLi per mole of **I** we succeeded in isolating from the reaction mixture product **IV** which, according to the  $^1\text{H}$  NMR data, contained two phenyl groups: the intensity ratio of aromatic and aliphatic protons was 13 ( $\text{H}_{\text{arom}}$ ): 2 ( $\text{CH}_2\text{O}$ ): 3 ( $\text{CH}_3$ ). The same also follows from the

Scheme 2.



elemental analysis data. Analysis of the  $^1\text{H}$  NMR spectrum shows that product **IV** is a mixture of two regioisomers **IVa** and **IVb**, for the observed signal multiplicity exceeds that expected for an individual isomer, as well as for a mixture of *cis/trans* isomers of 2,3-diphenyl derivative **IVa**. Presumably, replacement of the second chlorine atom occurs not only at  $\text{C}^3$  but also at  $\text{C}^2$ . Isomers **IVa** and **IVb** have similar physical properties, and we failed to separate them.

By reaction of benzazetine **I** with 5 equiv of phenyllithium we obtained a complex mixture of products, and the reaction was accompanied by strong tarring. The products were separated by column chromatography on silica gel. We thus isolated mono-substituted compound **III** (yield 10%), disubstituted derivatives **IVa** and **IVb** (12%), and 8% of compound **V**. The latter, according to the spectral data and elemental analysis, is the product of replacement of three chlorine atoms in **I**.

In the  $^1\text{H}$  NMR spectrum of **V** we observed signals from the ethoxy group at  $\delta$  1.3 ppm (t,  $\text{CH}_3$ ) and 4.1 ppm (q,  $\text{CH}_2\text{O}$ ), a multiplet in the region  $\delta$  6.8–8.1 ppm from the phenyl protons, and a broadened singlet at  $\delta$  10.3 ppm from the NH proton. The intensity ratio of the aromatic and aliphatic proton signals is 18 ( $\text{H}_{\text{arom}}$ ):2 ( $\text{CH}_2\text{O}$ ):3 ( $\text{CH}_3$ ), indicating the presence of three phenyl groups in the molecule. The IR spectrum of **V** contained bands belonging to symmetric and antisymmetric vibrations of the nitro group at 1387 and 1518  $\text{cm}^{-1}$ . Stretching vibrations of the C=C bonds give rise to absorption at 1495, 1578, and 1599  $\text{cm}^{-1}$ . A partially double character of the C–N bond due to conjugation in the system and intramolecular interaction  $\text{N–H}\cdots\text{O}=\text{N}$  follows from the position of the corresponding band (1655  $\text{cm}^{-1}$ ). The mass spectrum of **V** lacks molecular ion peak but contains fragment ion peaks formed by elimination of phenyl groups, ethoxy group, and alkyl fragments.

## EXPERIMENTAL

The IR spectra were recorded in KBr on a Protege-460 spectrophotometer. The  $^1\text{H}$  NMR spectra were obtained on a Tesla 576A instrument in  $\text{CDCl}_3$ ; the chemical shifts were measured relative to TMS. The mass spectra (50 eV) were obtained on an MKh-1320 high-resolution mass spectrometer.

**2-(2,3-Dichloro-3-methyl-1-nitro-2-propenyli-dene)-4-ethoxy-1,2-dihydrobenzazete (II)**. To a suspension of 0.34 g (1 mmol) of 4-ethoxy-2-(2,3,3-trichloro-1-nitro-2-propenyli-dene)-1,2-dihydrobenzazete (**I**) in 30 ml of dry diethyl ether we added under argon

2.1 ml of a 1 N ether solution of methyllithium, and the mixture was stirred for 10 h at 20–25°C. It was then decomposed with water, and the ether layer was separated and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the product was isolated by column chromatography on silica gel (100/160  $\mu\text{m}$ ), eluent hexane–ether, 2:1. Yield 0.14 g (45%). mp 164–165°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1353, 1529 ( $\text{NO}_2$ ); 1573, 1625 (C=C); 3250 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.70 s (3H,  $\text{CH}_3$ ); 1.4 t (3H,  $\text{CH}_3$ ); 4.1 q ( $\text{CH}_2\text{O}$ ); 7.36 d.d, 7.45 d, and 7.73 d (3H,  $\text{C}_6\text{H}_3$ ); 12.6 br.s (NH). Mass spectrum,  $m/z$  (for  $^{35}\text{Cl}$ ): 314 [ $M^+$ ], 299 [ $M^+ - \text{CH}_3$ ], 264 [ $M^+ - \text{CH}_3\text{Cl}$ ], 229 [ $M^+ - \text{CH}_3 - 2\text{Cl}$ ]. Found, %: C 49.30; H 4.07; Cl 22.11; N 9.08.  $\text{C}_{13}\text{H}_{12}\text{Cl}_2\text{N}_2\text{O}_3$ .  $M^+$  314. Calculated, %: C 49.54; H 3.84; Cl 22.50; N 8.89.  $M$  315.16.

**2-(2,3-Dichloro-1-nitro-3-phenyl-2-propenyli-dene)-4-ethoxy-1,2-dihydrobenzazete (III)** was synthesized by the above procedure from compound **I** and phenyllithium. Yield 52%, mp 183–185°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1362, 1530 ( $\text{NO}_2$ ); 1492, 1601 (C=C); 3200 (NH).  $^1\text{H}$  NMR spectrum,  $\delta$ , ppm: 1.4 t (3H,  $\text{CH}_3$ ); 4.1 q ( $\text{CH}_2\text{O}$ ); 7.15 d.d, 7.25 d, and 7.72 d (3H,  $\text{C}_6\text{H}_3$ ); 7.40 m (5H,  $\text{C}_6\text{H}_5$ ); 12.6 br.s (NH). Mass spectrum,  $m/z$  ( $^{35}\text{Cl}$ ): 376 [ $M^+$ ], 299 [ $M^+ - \text{C}_6\text{H}_5$ ], 361 [ $M^+ - \text{CH}_3$ ], 331 [ $M^+ - \text{C}_2\text{H}_5\text{O}$ ], 264 [ $M^+ - \text{C}_6\text{H}_5 - \text{Cl}$ ], 229 [ $M^+ - \text{C}_6\text{H}_5 - 2\text{Cl}$ ]. Found, %: C 57.78; H 4.01; Cl 18.90; N 7.52.  $M^+$  376.  $\text{C}_{18}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_3$ . Calculated, %: C 57.31; H 3.74; Cl 18.80; N 7.43.  $M$  377.22.

Diphenyl-substituted derivatives **IVa** and **IVb** were synthesized in a similar way at a **I**-to-PhLi ratio of 1:3. Isomeric mixture **IVa/IVb** was isolated by column chromatography on silica gel (100/160  $\mu\text{m}$ ) using hexane–ether (1:1) as eluent. Yield 20%. Found, %: C 68.61; H 4.92; Cl 8.55; N 6.78.  $M^+$  418.  $\text{C}_{24}\text{H}_{19}\text{ClN}_2\text{O}_3$ . Calculated, %: C 68.81; H 4.57; Cl 8.46; N 6.69.  $M$  418.86.

**4-Ethoxy-2-(1-nitro-2,3,3-triphenyl-2-propenyli-dene)-1,2-dihydrobenzazete (V)**. To a suspension of 3.36 g (10 mmol) of compound **I** in 100 ml of dry diethyl ether we added under argon 51 ml of a 1 N solution of phenyllithium in ether, and the mixture was stirred for 17 h at 20–25°C. The mixture was then decomposed with 10% hydrochloric acid, and the ether layer was separated and dried over magnesium sulfate. The solvent was removed under reduced pressure, and the product was isolated by column chromatography on silica gel (100/160  $\mu\text{m}$ ), using hexane–ether (1:1) as eluent. Yield 0.37 g (8%), mp 204–206°C. IR spectrum,  $\nu$ ,  $\text{cm}^{-1}$ : 1387, 1518

(NO<sub>2</sub>); 1495, 1578, 1599 (C=C); 250 (NH). <sup>1</sup>H NMR spectrum, δ, ppm: 1.3 t (3H, CH<sub>3</sub>); 4.1 q (CH<sub>2</sub>O); 6.8–8.1 m (18H, H<sub>arom</sub>); 10.3 br.s (1H, NH). Mass spectrum, *m/z* (<sup>35</sup>Cl): 445 [*M*<sup>+</sup>–CH<sub>3</sub>], 415 [*M*<sup>+</sup>–C<sub>2</sub>H<sub>5</sub>O], 383 [*M*<sup>+</sup>–C<sub>6</sub>H<sub>5</sub>], 354 [*M*<sup>+</sup>–C<sub>6</sub>H<sub>5</sub>–C<sub>2</sub>H<sub>5</sub>], 306 [*M*<sup>+</sup>–2C<sub>6</sub>H<sub>5</sub>], 229 [*M*<sup>+</sup>–3C<sub>6</sub>H<sub>5</sub>]. Found, %: C 78.50; H 5.47; N 6.04. [*M*<sup>+</sup>–CH<sub>3</sub>] 445. C<sub>30</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>. Calculated, %: C 78.24; H 5.25; N 6.08. *M* 460.51.

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