Synthesis of *N*-allenylazoles from azoles and propargyl chloride or 1,2,3-trichloropropane in one preparative step

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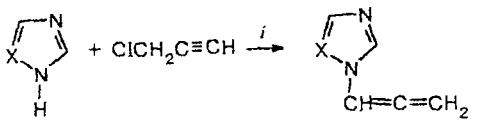
Reactions of imidazole and 1,2,4-triazole with propargyl chloride and its more accessible equivalent, 1,2,3-trichloropropane, in the superbasic KOH—DMSO system have been studied. The reactions afford the corresponding *N*-allenylazoles in one preparative step.

Key words: *N*-allenylazoles, imidazole, 1,2,4-triazole, propargyl chloride, 1,2,3-trichloropropane, KOH—DMSO system.

Among allene derivatives of azoles, only *N*-allenylimidazole and allenylpyrazole have been described in the literature. These compounds were obtained in 20% and 10% yields by the reaction of the corresponding heterocyclic derivatives with propargyl bromide in the $NaNH_2/NH_3$ (liquid) system followed by isomerization of the resulting *N*-(prop-2-ynyl)azole into allene in the presence of alumina pretreated by KNH_2 in liquid ammonia.[1]

The use of the superbasic catalytic system, KOH—DMSO, which markedly facilitates nucleophilic substitution, dehydrohalogenation, and prototropic isomerization,[2,3] allowed us to develop a simple and efficient procedure for the synthesis of *N*-allenylpyrroles from pyrroles and propargyl chloride[4—6] or its more accessible equivalents, *viz.*, 2,3-dichloroprop-1-ene[5,7] and 1,2,3-trichloropropane (TCP),[5,8] in one preparative step.

The subsequent studies, whose results are reported in the present paper, have shown that other azoles, namely, imidazole (**1a**) and 1,2,4-triazole (**1b**), react with propargyl chloride similarly to pyrrole to give *N*-allenylazoles **2a,b**:



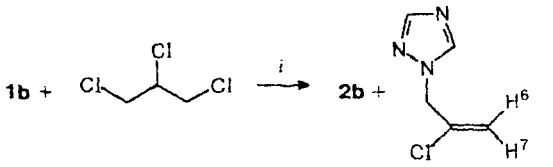
1a,b **2a,b**

X = CH (**1a**, **2a**), N (**1b**, **2b**)

i. KOH/DMSO, 25—40 °C, 30—50 min

Products **2a,b** are soluble in water. To isolate them from aqueous DMSO, they were extracted with chloroform, and the resulting extracts were repeatedly washed with water in order to remove the DMSO that passed into chloroform and cannot be separated by distillation. Removal of the solvent and evacuation of the residue at 1 Torr (30 min, ~20 °C) gave the products in the following yields: **2a**, 73%, **2b**, 46%; the yields of the distilled compounds were 46 and 31% (purity 98 and 97%), respectively. In both cases, non-distillable polymeric residues were left. The IR and ^1H NMR spectra recorded for samples of **2a,b** before and after distillation were virtually identical. This suggests that these compounds polymerize during distillation, and this substantially decreases their yields. These losses can be avoided by using *N*-allenylazoles **2a,b** *in situ*.

The reaction of 1,2,4-triazole (**1b**) with TCP carried out similarly to the reactions involving pyrrole and 2-phenylpyrrole[5,8] in which only *N*-allenylpyrroles were obtained in 50 and 62% yields, afforded a mixture of allene **2b** and *N*-(2-chloroprop-2-enyl)-1,2,4-triazole (**3**) in a ratio of 55 : 45 and in 38 and 23% yields (according to the ^1H NMR spectrum), respectively. The attempt to dehydrochlorinate propene **3** by heating the mixture of **2b** and **3** in the KOH (calcined)—DMSO system to 50 °C in order to obtain pure allene **2b** was unsuccessful. The ratio of **2b** to **3** did not change (see Experimental).



i. KOH/DMSO, 40—50 °C, 45 min

3

However, when a more concentrated (30% instead of 17%) suspension of KOH in DMSO is used, even with ordinary ($KOH \cdot 0.5\ H_2O$) rather than calcined KOH, and when the concentration of azole is 1.43 mol L^{-1}

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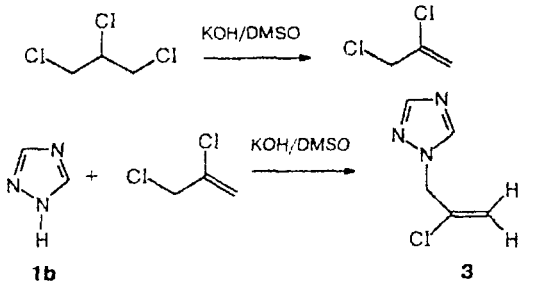
(instead of 0.5 mol L^{-1}), and the azole : TCP : KOH · 0.5 H_2O ratio is 0.05 : 0.06 : 0.26, the reaction carried out at 45—50 °C for 30 min gives allenes **2a,b** in 47 and 36% yields (for distilled products) and with purities of 98% (2% the propargyl isomer) and 94% (6% the propargyl isomer), respectively. In the latter case, we were not able to increase the content of allene even by adding Bu^tOK (45 mmol per 50 mmol azole **1b**) to the reaction mixture and by heating it to 50 °C.[6]

Based on our results, the formation of the stable propene **3** from **1b** and TCP in a dilute KOH—DMSO suspension can be explained by assuming that, when there is no enough KOH to abstract two HCl molecules from TCP, the 1,2,4-triazole anion,[9] which is more nucleophilic than the pyrrolate anion, substitutes a chlorine atom in the intermediate 2,3-dichloro-1-propene.



1b **3**

This fact is evidence in favor of the mechanism of allenylation of azoles with TCP that includes initial dehydrochlorination of TCP to propargyl chloride followed by nucleophilic replacement of the chlorine atom in it by the triazolate anion.

The reaction of azoles with TCP in the KOH—DMSO system, which makes it possible to synthesize *N*-allenylazoles in one preparative step, can become important in the chemistry of heterocyclic compounds, because it makes *N*-allenylazoles accessible for studies and practical applications.

N-Allenylazoles **2a,b** are colorless liquids with a strong smell; they turn dark and polymerize in air at room temperature, but are stable when stored under an inert atmosphere at a temperature below −20 °C. Their structures were determined by IR and ^1H NMR spectra and the composition was confirmed by elemental analysis.

Experimental

^1H NMR spectra were recorded on Jeol FX-90Q (89.95 MHz) and Tesla BS-567A (100 MHz) specrometers in $CDCl_3$ using HMDS as the internal standard. IR spectra were recorded on a Specord 75 IR spectrophotometer in thin films.

Anhydrous DMSO containing less than 0.2% water and prepared by distillation over Bu^tOK at 3—6 Torr was used in the experiments. Calcined KOH was obtained by keeping ordinary KOH (KOH · 0.5 H_2O) at 450 °C for 4 h.

N*-Allenylimidazole (2a).** ***A. At 27—30 °C, propargyl chloride (5.59 g, 75 mmol) was added with stirring over a period of 15 min to a mixture of imidazole (2.55 g, 37.5 mmol) and powdered KOH · 0.5 H_2O (8.4 g, 131 mmol) in 75 mL of DMSO. The mixture was stirred for an additional 35 min; during this period, the temperature decreased from 35 to 25 °C. Then the reaction mixture was poured into 150 mL of water and extracted with chloroform (5×30 mL), and the extract was washed with water (5×15 mL) to remove DMSO and dried with $CaCl_2$. The chloroform was evaporated *in vacuo* under a pressure of 120—121 Torr (~20°C), and the residue (2.97 g; containing 98% **2a** according to ^1H NMR; yield 75%) was distilled with hydroquinone at 10 Torr to give 1.91 g of compound **2a**, b.p. 92 °C, purity 98%, yield 47%, n_D^{20} 1.5628. Found (%): C, 67.91; H, 5.60; N, 26.45. $C_6H_6N_2$. Calculated (%): C, 67.92; H, 5.66; N, 26.42. ^1H NMR, δ: 5.51 (d, 2 H, CH_2=); 6.87 (t, 1 H, —CH=, ^4J = 6.5 Hz); 7.53 (s, 1 H, H-2); 7.03, 7.96 (s, 2 H, H-3, H-5). IR: ν (C=C=C) 1960 cm^{-1} (w).

B. At 45—50 °C, TCP (8.85 g, 60 mmol) was added with stirring over a period of 10 min to a mixture of imidazole (3.45 g, 51 mmol) and KOH · 0.5 H_2O (16.8 g, 263 mmol) in 35 mL of DMSO; the mixture was stirred for an additional 20 min; during this period, the temperature decreased from 50 to 35 °C. The reaction mixture was poured into 100 mL of water and extracted with chloroform (5×30 mL), and the extract was washed with water (5×15 mL) and dried with $CaCl_2$. The chloroform was removed at 120—121 Torr (~20 °C), and the residue (3.54 g) was distilled to give 2.62 g of product **2a**, b.p. 73—75 °C (3 Torr), purity 98%, yield 47%, polymeric residue 0.8 g.

N*-Allenyl-1,2,4-triazole (2b).** ***A. This compound was obtained similarly to compound **2a**, from azole **1b** (5.18 g, 75 mmol), calcined KOH powder (8 g, 300 mmol), and propargyl chloride (8.4 g, 112.5 mmol) in 150 mL of DMSO over a period of 30 min at 35—45 °C. The usual treatment with chloroform and water, drying with $CaCl_2$, and distillation gave 2.53 g of compound **2b**, b.p. 54 °C (1 Torr), purity 97%, yield 31%, n_D^{20} 1.5452 (polymeric residue 0.97 g). Found (%): C, 55.97; H, 4.69; N, 39.25. $C_5H_5N_3$. Calculated (%): C, 56.08; H, 4.67; N, 39.25. ^1H NMR, δ: 5.61 (d, 2 H, CH_2=); 7.10 (t, 1 H, —CH=, ^4J = 6.6 Hz), 8.16, 7.92 (both s, 2 H, H-3, H-5). IR: ν (C=C=C) 1960 cm^{-1} (w).

B. The compound was prepared similarly to **2a**, from **1b** (3.45 g, 50 mmol), KOH · 0.5 H_2O (16.8 g, 263 mmol), and TCP (8.85 g, 60 mmol) in 35 mL of DMSO at 35—50 °C over a period of 30 min. The usual workup and distillation gave 2.05 g of product **2b**, b.p. 56—60 °C (2 Torr), purity 94% (6% *N*-(prop-2-ynyl)-1,2,4-triazole), yield 36%, polymeric residue 1.6 g.

***N*-(2-Chloroprop-2-enyl)-1,2,4-triazole (3).** At 40—42 °C, TCP (11.6 g, 78.6 mmol) was added with stirring over a period of 15 min to a mixture of **1b** (3.45 g, 50 mmol) and calcined KOH powder (22.4 g, 400 mmol) in 100 mL of DMSO, and the mixture was stirred for an additional 30 min at 40—50 °C, cooled, and poured into 150 mL of water. The product was extracted with chloroform (5×30 mL), and the extract was washed with water (5×15 mL) and dried with $CaCl_2$. Removal of the chloroform followed by evacuation at 1 Torr (30 min, ~20 °C) gave 3.66 g of a reddish labile liquid that contained, according to ^1H NMR, 45% (1.65 g) compound **3** (yield 23%) and 55% (2.01 g) allene **2b** (yield 38%). Compound **3** was identified based on the ^1H NMR spectrum in which it accounts for the following signals (δ): 4.94 (br.s, 2 H, CH_2); 5.39 (br.s, 1 H, H-7); 5.47 (br.s, 1 H, H-6); 7.98 (s, 1 H, H-3); 8.23 (s, 1 H, H-5).

Attempts at dehydrochlorination of compound 3. A 45 : 55 mixture of compounds **3** and **2b** (2 g) was added to a stirred suspension of calcined KOH (2 g) in 10 mL of DMSO; the mixture was heated to 50 °C (~10 min) and diluted with 10 mL of water, the product was extracted with chloroform (5×10 mL), and the extract was washed with water and dried with $CaCl_2$. Removal of the chloroform followed by evacuation at 1 Torr (~20 °C) gave 0.95 g of a product; according to ^1H NMR, it consisted of **3** and **2b** in a 45 : 55 ratio.

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References

1. A. J. Hubert and H. Raimlinger, *J. Chem. Soc. (C)*, 1968, 606.
2. B. A. Trofimov, and A. I. Mikhaleva, *Zh. Org. Khim.*, 1996, **32**, 1127 [*J. Org. Chem.*, 1996, **32** (Engl. Transl.)].
3. B. A. Trofimov and A. I. Mikhaleva, *Heterocycles*, 1994, **37**, 1193.
4. O. A. Tarasova, B. A. Trofimov, A. I. Mikhaleva, M. V. Sigalov, and L. M. Sinegovskaya, *Zh. Org. Khim.*, 1991, **27**, 1798 [*J. Org. Chem. USSR*, 1991, **27** (Engl. Transl)].
5. O. A. Tarasova, L. Brandsma, and B. A. Trofimov, *Synthesis*, 1993, 571.
6. O. A. Tarasova, F. Taherirastgar, H. D. Verkruijsse, A. G. Mal'kina, L. Brandsma, and B. A. Trofimov, *Rec. Trav. Chim.*, 1996, **115**, 145.
7. O. A. Tarasova, A. I. Mikhaleva, T. L. Markova, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 1992, 125 [*Chem. Heterocycl. Compd.*, 1992 (Engl. Transl.)].
8. O. A. Tarasova, T. L. Markova, and B. A. Trofimov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 2161 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1991, **40**, 1918 (Engl. Transl.)].
9. A. F. Pozharskii, *Teoreticheskie osnovy khimii geterotsiklov* [*Theoretical Foundations of the Chemistry of Heterocyclic Compounds*], Khimiya, Moscow, 1985, 276 pp.

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