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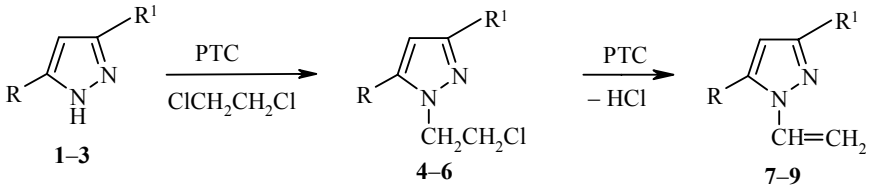
SYNTHESIS OF N-VINYLPYRAZOLES

O. S. Attarian, S. G. Matsoyan, and S. S. Martirosyan

A method is proposed for the alkylation of pyrazoles with dichloroethane in water in the presence of the phase-transfer catalyst benzyltriethylammonium chloride (TEBAC). It was shown that dehydrochlorination of the corresponding N-(β-chloroethyl)pyrazoles in water under conditions of phase-transfer catalysis proceeds smoothly with the formation of N-vinylpyrazoles in 80-90% yield.

Keywords: N-vinylpyrazoles, alkylation, dehydrochlorination, phase-transfer catalysis.

In the present work the N-alkylation of pyrazole (**1**), 3(5)-methylpyrazole (**2**), and 3,5-dimethylpyrazole (**3**) with dichloroethane (DCE) and the dehydrochlorination of the obtained 1-(β-chloroethyl)pyrazoles **4-6** has been carried out with the aim of synthesizing N-vinylpyrazoles.



1–3 **4–6** **7–9**

1, **4**, **7** R = R^1 = H; **2**, **5**, **8** R = H, R^1 = Me, R = Me, R^1 = H; **3**, **6**, **9** R = R^1 = Me

Attempts to carry out the reaction under standard conditions (water–benzene–NaOH–TEBAC) did not lead to the desired result. The alkylation of compounds **1-3** occurs slowly with low yields of products (Table 1). It turned out however that the yields were sharply increased if benzene was excluded from the reaction medium [1-5], replacing it with an excess of reagent.

Investigations showed that the ease of alkylation depends strongly on the basicity of the pyrazole. The introduction of an electron-donating substituent (Me) into the molecule of pyrazole **1** increases the electron density at the "pyrrole" nitrogen atom, as a result of which deprotonation is hindered and the base is consumed in the elimination of dichloroethane. Thus on alkylation of pyrazole **1** (pK_b 2.53) the substitution product is isolated predominantly and in the case of 3(5)-methylpyrazole **2** (pK_b 3.55) and 3,5-dimethylpyrazole **3** (pK_b 4.38) vinyl chloride is also formed in significant amounts (Table 1). Consequently on alkylation of compound **3** a 7-fold excess of alkali is necessary, since the main portion of it is consumed by the competing β-elimination of dichloroethane.

It must also be mentioned that a 5 to 7-fold excess of dichloroethane is necessary to obtain optimal yields on alkylation of compounds **1-3**. Reduction of this amount does not lead to bisalkylation since DCE is rapidly dehydrochlorinated and the alkylation process stops due to the absence of base.

Institute of Organic Chemistry, National Academy of Sciences of the Republic of Armenia, Erevan 375091; e-mail: MVM@lx2.yerphi.am. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 533-536, April, 2005. Original article submitted March 14, 2003.

TABLE 1. Alkylation of Pyrazoles **1-3** by Dichloroethane in Water*

Compound	pK_b	Dichloroethane (mol)	NaOH (mol)	Yield of compounds **4-6**, %	Yield of vinyl chloride (mol)
1	2.53	0.3	0.15	70.0	—
		0.5	0.15	80.0	0.02
		0.5	0.15	45.0*[2]	—
		0.5	0.15	4.15*[3]	—
2	3.55	0.3	0.2 + 0.2	60.0	—
		0.5	0.25	40.0	0.10
		0.5	0.2 + 0.1	68.0	—
		0.5	0.2 + 0.2	80.0	—
		0.5	0.2 + 0.2	45.0*[2]	—
3	4.38	0.5	0.25	25.0	0.16
		0.5	0.2 + 0.2	50.0	—
		0.5	0.2 + 0.25 + 0.25	78.0	—
		0.5	0.2 + 0.25 + 0.25	40.0*[2]	—

* Pyrazole 0.1 mol, TEBAC catalyst 0.0052 mol, 70°C, 2-4 h.
*[2] H_2O + benzene.
*[3] Without catalyst.

In the presence of DCE the rates of bisalkylation and HCl elimination from the obtained β-chloroethylpyrazoles **4-6** are superseded by the rate of alkylation of the pyrazoles (Fig. 1), consequently the products of monoalkylation may be isolated in yields of 75-80%. The IR and ^{1}H NMR spectra of the β-chloroethylpyrazoles **4-6** are given in Table 2.

Elimination of HCl from β-chloroethylpyrazoles **4-6** under the action of 50% aqueous solutions of KOH or NaOH [6-10] on using TEBAC as catalyst at 80°C is complete after 1.5 h. Yields of N-vinylpyrazoles **7-9** under the same conditions but without using catalyst were only 10%.

The rate of dehydrochlorination falls in the series **4** > **5** > **6** (Fig. 2). Such a difference may be explained by the difficulty of detaching the proton under the influence of electron-donating substituents.

TABLE 2. Characteristics of the Synthesized Compounds **4-6**

Compound	n_D^{20}	bp/mm Hg	IR spectrum, ν, cm^{-1} (ring)	^{1}H NMR spectrum (DMSO-d$_6$, 300 MHz), δ, ppm (*J*, Hz)	Literature
4	1.5021	43-48/3	1530	3.81 (2H, t, *J* = 6.0, NCH_2); 4.42 (2H, t, *J* = 6.0, CH_2Cl); 6.26 (1H, t, *J* = 2.2, H-4); 7.50 (1H, d, *J* = 2.4, H–3); 7.58 (1H, d, *J* = 2.0, H-5)	[11]
5	1.5030	55-60/1	1544	2.16 (3H, s, CH_3-3); 2.18 (3H, s, CH_3-5); 3.70 (2H, m, NCH_2); 4.38 (2H, m, CH_2Cl); 5.85 (1H, d, *J* = 2.0, H-5); 7.22 (1H, d, *J* = 2.0, H-3); 7.42 (1H, d, *J* = 2.3, H-5)	[11]
6	1.5010	60-65/1	1560	2.11 (3H, s, CH_3-3); 2.23 (3H, s, CH_3-5); 3.93 (2H, t, *J* = 6.0, NCH_2); 4.10 (2H, t, *J* = 6.0, CH_2Cl); 5.67 (1H, s, H-4)	[11]

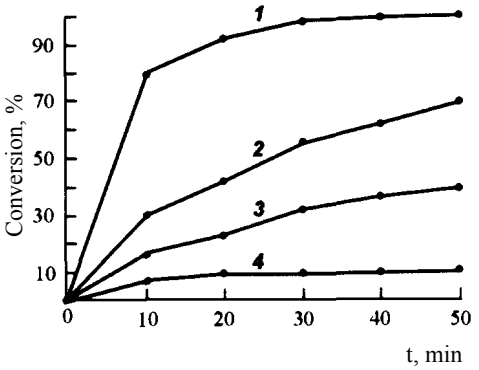


Fig. 1. Kinetic curves for the relationship of conversion and reaction time for alkylation with dichloroethane at 60°C: 1) pyrazole; 2) methylpyrazole; 3) 3,5-dimethylpyrazole; 4) bisalkylation of 3(5)-methylpyrazole (in the presence of dichloroethane reaction does not occur).

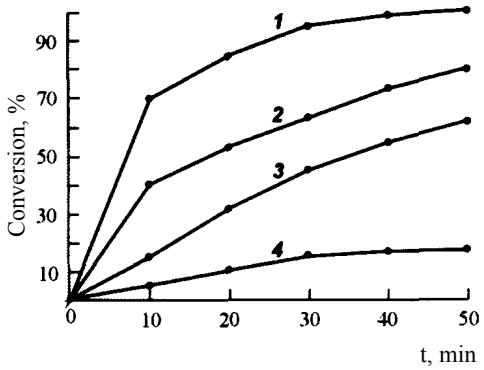


Fig. 2. Kinetic curves for the relationship of conversion and reaction time for dehydrochlorination at 60°C: 1) 1-(β-chloroethyl)pyrazole; 2) 1-(β-chloroethyl-3(5)-methylpyrazole; 3) 1-(β-chloroethyl)-3,5-dimethylpyrazole; 4) dehydrochlorination of 1-(β-chloroethyl)-3(5)-methylpyrazole in the presence of dichloroethane.

EXPERIMENTAL

1-(β-Chloroethyl)pyrazole (4). A mixture of pyrazole (**1**) (6.8 g, 0.1 mol), dichloroethane (49.5 g, 0.5 mole), sodium hydroxide (6.0 g, 0.15 mol), water (10 ml), and TEBAC (1.2 g, 0.0052 mol) was heated at 70-75°C for 2 h with vigorous stirring. After cooling to 20°C, water (50 ml) was added, the mixture was extracted with ether (100 ml), and the extract dried over $MgSO_4$. After removing the ether, the residue was distilled in vacuum. Compound **4** (10.5 g, 80%) was obtained.

1-(β-Chloroethyl)-3(5)-methylpyrazole (5). A mixture of 3(5)-methylpyrazole (**2**) (8.2 g, 0.1 mol), dichloroethane (49.5 g, 0.5 mol), sodium hydroxide (8.0 g, 0.2 mol), water (10 ml), and TEBAC (1.2 g, 0.0052 mol) was heated at 70-75°C for 2 h with vigorous stirring. After cooling to 20°C, further sodium hydroxide (8.0 g, 0.2 mol) and water (10 ml) were added and the mixture heated for a further 2 h (70-75°C). After cooling to 20°C, water (50 ml) was added, the mixture was extracted with ether (100 ml), and the extract dried over $MgSO_4$. After removing the ether, the residue was distilled in vacuum. A mixture (11.9 g, 82%) of the isomeric 1-(β-chloroethyl)-3-methylpyrazole and 1-(β-chloroethyl)-5-methylpyrazole was obtained (ratio of isomers was 60:40 according to GLC).

1-(β-Chloroethyl)-3,5-dimethylpyrazole (6). A mixture of 3,5-dimethylpyrazole (**3**) (9.6 g, 0.1 mol), dichloroethane (69.3 g, 0.7 mol), sodium hydroxide (8.0 g, 0.2 mol), water (10 ml), and TEBAC (1.2 g, 0.0052 mol) was heated at 70-75°C for 1 h with vigorous stirring. After cooling to 20°C, further sodium hydroxide (10.0 g, 0.25 mol) and water (10 ml) were added and heating continued for a further 2 h (70-75°C). Then sodium hydroxide (10.0 g, 0.25 mol) and water (10 ml) were added once again and the mixture was heated a further 2 h (70-75°C). After cooling to 20°C, water (100 ml) was added, the mixture was extracted with ether (100 ml), and the extract was dried over $MgSO_4$. After removing the ether, the residue was distilled in vacuum. 1-(β-Chloroethyl)-3,5-dimethylpyrazole (12.2 g, 77%) was obtained.

1-Vinylpyrazoles 7-9. A mixture of the appropriate 1-(β-chloroethyl)-pyrazole **4-6** (0.1 mol), base (NaOH or KOH) (0.2 mol), water (10 ml), TEBAC (1.2 g, 0.0052 mol), and hydroquinone was stirred vigorously at 80°C for 1.5 h. After cooling, water (50 ml) was added, the mixture was extracted with ether

(100 ml), and the extract dried over $MgSO_4$. After removing the solvent, the residue was distilled in vacuum to give the following.

1-Vinylpyrazole (7). Yield 7.5 g (80%); bp 63°C/50 mm Hg, n_D^{20} 1.5163 [12]. ^{1}H NMR spectrum (CCl_4), δ, ppm (*J*, Hz): 5.00 (1H, dd, *J* = 9.0 and *J* = 1.5, =CH_2); 5.52 (1H, dd, *J* = 15.8 and *J* = 1.5, =CH_2); 6.26 (1H, t, *J* = 2.2, H-4); 7.12 (1H, dd, *J* = 15.8 and *J* = 9.0, N–CH=); 7.50 (1H, d, *J* = 2.4, H-3); 7.58 (1H, d, *J* = 2.0, H-5).

3(5)-Methyl-1-vinylpyrazole (8). Yield 9.7 g (90%); bp 55-60°C/10 mm Hg, n_D^{20} 1.5160 [13]. ^{1}H NMR spectrum (CCl_4), δ, ppm (*J*, Hz): 2.16 (3H, s, CH_3-3); 2.18 (3H, s, CH_3-5); 4.76 (1H, dd, *J* = 9.3 and *J* = 1.5, =CH_2); 5.42 (1H, dd, *J* = 15.7 and *J* = 1.5, =CH_2); 5.85 (1H, d, *J* = 2.0, H-4); 6.92 (1H, dd, *J* = 15.7 and *J* = 9.3, N–CH=); 7.22 (1H, d, *J* = 2.0, H-3); 7.42 (1H, d, *J* = 2.3, H-5).

3,5-Dimethyl-1-vinylpyrazole (9). Yield 9.2 g (75%); bp 70°C/10 mm Hg, n_D^{20} 1.5180 [14]. ^{1}H NMR spectrum (CCl_4), δ, ppm (*J*, Hz): 2.11 (3H, s, CH_3-3); 2.23 (3H, s, CH_3-5); 4.42 (1H, dd, *J* = 9.5 and *J* = 1.5, =CH_2); 5.22 (1H, dd, *J* = 15.3 and *J* = 1.5, =CH_2); 5.67 (1H, s, H-4); 6.33 (1H, dd, *J* = 15.3 and *J* = 9.5, N–CH=).

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