1,3-DIPOLAR CYCLOADDITION OF DIAZOMETHANE TO SUBSTITUTED 3-(2-FURYL)ACRYLONITRILES*

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1,3-Dipolar cycloaddition of diazomethane to substituted 2-X-3-(2-furyl)acrylonitriles and the dependence of its course on the molar ratio of components was studied. The reaction takes place exclusively at the double bond under formation of 1-pyrazolines the further fate of which is determined by the nature of the substituent X (X = CN, $COOCH_3$, 4-$NO_2C_6H_4$) and by the reaction temperature.

1,3-Dipolar cycloaddition of diazomethane to substituted acrylonitriles takes place at the double bond under formation of 1-pyrazolines[1-4]. Hirao and Kato[5] described the cycloaddition of diazomethane to nitrile group in 3-(5-nitro-2-furyl)acrylonitrile. Our investigation concerns the effect of substituents and of components ratio on the reaction of diazomethane with substituted acrylonitriles.

Reaction of the *E*-isomer of ethyl 3-(2-furyl)-2-cyanoacrylate[6] (*Ia*) with diazomethane in the molar ratio 1 : 0·8 affords 1-pyrazoline *II* which is unstable and decomposes to methyl 3-(2-furyl)-2-cyanocrotonate (*IIIa*). Comparison of ^{1}H-NMR spectra of thus obtained compound *IIIa* with the mixture of *E*- and *Z*-isomers obtained by isomerization[7] of the compound *IIIa* revealed that *IIIa* has *E*-configuration. Similar course was observed in the reaction of 2-furylidenemalononitrile (*Id*) and 5-bromo-2-furylidenemalononitrile (*Ie*) with diazomethane in the molar ratio 1 : 0·8 which afforded low yields of the corresponding methyl-substituted derivatives *IIId* and *IIIe*. A twofold increase in the amount of diazomethane in the reaction mixture resulted only in higher yields of compounds *IIId* and *IIIe*. Reaction of diazomethane with *Ia* in the molar ratio 1 : 2 and with *IIIa* in the ratio 1 : 1 at 0°C afforded the 1-pyrazoline *IVa*. The addition to methyl 3-(5-bromo-2-furyl)-2-cyanoacrylate (*Ib*) in the ratio 1 : 2 proceeded analogously and gave the corresponding 1-pyrazoline *IVb*. When the addition of diazomethane was carried out at room temperature, 2-pyrazoline *Va* was isolated. The synthesized 1-pyrazolines *IVa* and *IVb* are unstable compounds which contain an active methylene group. In the presence of triethylamine they

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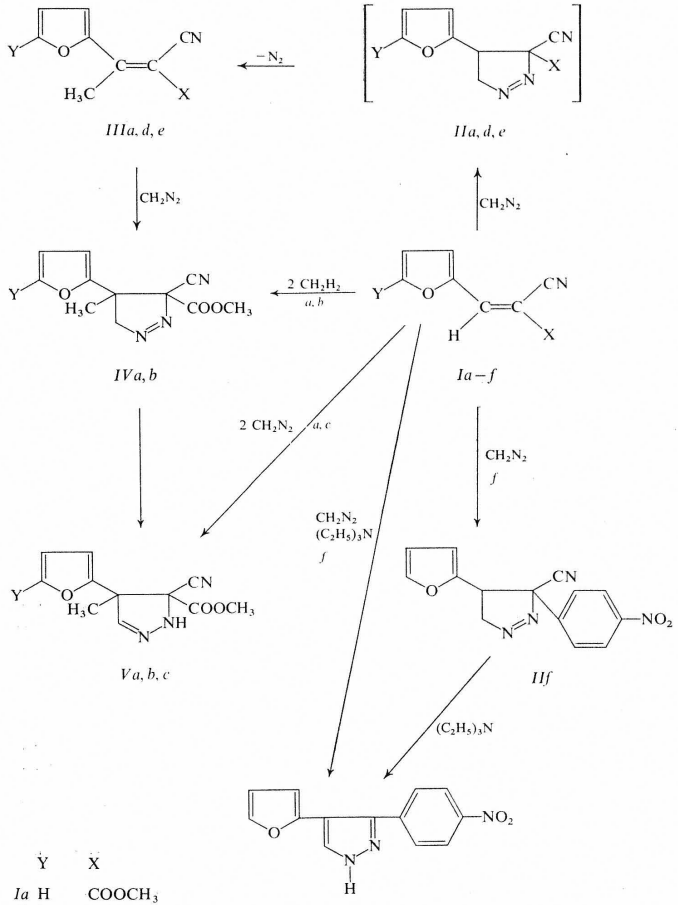

IIIa, d, e *IIa, d, e*

IVa, b *Ia–f*

Va, b, c *IIf*

VIf

	Y	X
Ia	H	$COOCH_3$
Ib	Br	$COOCH_3$
Ic	NO_2	$COOCH_3$
Id	H	CN
Ie	Br	CN
If	H	$C_6H_4NO_2$

rearrange in acetonitrile at room temperature to 2-pyrazolines *Va* and *Vb*. Methyl 3-(5-nitro-2-furyl)-2-cyanoacrylate (*Ic*) reacts with diazomethane in the molar ratio 1 : 2 at 0°C to give 1-pyrazoline *IVc* which rearranges directly in the absence of triethylamine in the reaction medium into 2-pyrazoline *Vc*. In contrast to the previous cases in which the intermediate 1-pyrazoline *II* was not proved or isolated, the reaction of diazomethane with 3-(2-furyl)-2-(4-nitrophenyl)acrylonitrile afforded a stable 1-pyrazoline, *IIf*. Thanks to its stability we were not able to prove the existence of 3-(2-furyl)-2-(4-nitrophenyl)crotononitrile in the reaction mixture. In acetonitrile, in the presence of triethylamine, *IIf* is isomerised to 2-pyrazoline and splits off hydrogen cyanide, affording 4-(2-furyl)-3-(4-nitrophenyl)pyrazole (*VIf*). The compound *VIf* was also prepared from *If* by the action of diazomethane in the presence of triethylamine.

On the basis of our results we may suggest the pertinent reaction scheme. The first step is represented by a 1,3-dipolar cycloaddition of diazomethane to the double bond, leading to 1-pyrazolines, analogously as described in the literature[3,4]. The structure of these products was confirmed by ^{1}H-NMR spectra (INDOR, ABX system) of the stable 1-pyrazoline *IIf*. The unstable 1-pyrazolines *II* are stabilised by rearrangement of the β-hydrogen leading to substituted cronotononitrile derivatives *IIIa,b,c* or to ethylidenemalononitriles *IIId,e*. Reaction of *Ia,b,c* with an excess of diazomethane affords the 1-pyrazolines *IVa,b,c*. The compounds *IVa*, *IVb* are more stable than the 1-pyrazolines *II*. The last reaction step is then the isomerisation of 1-pyrazolines *IVa*, *IVb* and *IVc* to the corresponding 2-pyrazolines *Va,b,c*.

EXPERIMENTAL

IR spectra were measured on a UR 20 (Zeiss) spectrophotometer, UV spectra on a UV-VIS Specord spectrometer. ^{1}H-NMR spectra were taken on a BS 487 C (80 Hz) instrument and mass spectra on a MS 902S (AEI Manchester) mass spectrometer. Melting points were determined on a Koffler block. Starting compounds were prepared according to ref.[6,8].

Reaction of Diazomethane with 2-X-3-(5-Y-2-Furyl)acrylonitriles

A) A mixture of *Ia* (1 g; 5·6 mmol), ether (50 ml) and diazomethane (0·19 g; 4·5 mmol) was allowed to stand for 10 days at −5°C. The solvent was distilled off *in vacuo* and the residue was chromatographed on a silica gel column using ethyl acetate–n-heptane (1 : 1) mixture as eluant. First fractions afforded crude methyl (*E*)-3-(2-furyl)-2-cyanocrotonate (*IIIa*) which on crystallization from ethanol melted at 85–86°C (in accord with ref.[7]); yield 0·35 g (40·3%).

B) A mixture of *Id* (1 g; 7·0 mmol), ether (50 ml) and diazomethane (0·59 g; 14·0 mmol) was treated as described in the above experiment and afforded 0·95 g (86·2%) of 1-(2-furyl)ethylidenemalononitrile (*IIId*), m.p. 76–77°C. For $C_9H_6N_2O$ (158·2); [M^+] 158 *m/e*; calculated: 68·35% C, 3·82% H, 17·71% N; found: 68·38% C, 3·66% H, 17·61% N. UV spectrum: (ethanol) λ_{max} 208 nm (log ε 3·85), 249 (3·44), 345 (4·37); IR spectrum (KBr): 2229 cm^{-1} (C≡N); ^{1}H-NMR spectrum (CCl_4), δ: 2·54 ppm (s, 3 H, CH_3), 6·65 (q, J = 2 Hz, J = 4 Hz, 1 H, $C_{(4)}$—H furan), 7·45 (d, J = 4 Hz, 1 H, $C_{(3)}$—H furan), 7·70 (d, J = 2 Hz, 1 H, $C_{(5)}$—H furan).

C) A mixture of *Ie* (1 g; 4·5 mmol), ether (70 ml) and diazomethane (0·38 g; 9·0 mmol) was treated as described in the experiment *A*) and afforded 1·00 g (84·3%) of 1(-5-bromo-2-furyl)-ethylidenemalononitrile (*IIIe*), m.p. 130–131°C. For $C_9H_5BrN_2O$ (237·1); $[M^+]$ 236/238 *m/e*; calculated: 45·60% C, 2·13% H, 11·82% N, 33·79% Br; found: 45·50% C, 2·02% H, 11·64% N, 33·88% Br UV spectrum (ethanol): λ_{max} 214 nm (log ε 4·02), 253 (3·51), 355 (4·44); IR spectrum (KBr): 2229 cm^{-1} (C≡N); ^{1}H-NMR spectrum (CCl_4), δ: 2·54 ppm (s, 3 H, CH_3), 6·54 (d, J = = 4 Hz, 1 H, $C_{(4)}$—H furan), 7·47 (d, J = 4 Hz, 1 H, $C_{(3)}$—H furan).

D) A mixture of *Ia* (1 g; 5·6 mmol), ether (50 ml) and diazomethane (0·47 g; 11·3 mmol) was kept at −5°C for 10 days. The solvent was distilled off *in vacuo* and the residue was crystallized from a mixture of ether and light petroleum, affording 1·06 g (80·5%) of 3-methoxycarbonyl-3-cyano-4-methyl-4-(2-furyl)-1-pyrazoline (*IVa*), m.p. 78–80° (dec.). For $C_{11}H_{11}N_3O_3$ (233·2); $[M^+ - 282]$ 205 *m/e*; calculated: 56·65% C, 4·75% H, 18·02% N; found: 56·62% C, 4·84% H, 17·81% N. UV spectrum (ethanol): λ_{max} 222 nm (log ε 4·03), 331 (3·30); IR spectrum (KBr): 1751 cm^{-1} (C=O), 2231 (C≡N); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 1·50 ppm (s, 3 H, CH_3), 3·93 (s, 3 H, OCH_3), 4·70 (d, J = 18 Hz, 1 H, CH_2 1-pyrazoline), 5·31 (d, J = = 18 Hz, 1 H, CH_2 1-pyrazoline), 6·38 (m, 2 H, $C_{(3,4)}$—H furan), 7·48 (m, 1 H, $C_{(5)}$—H furan).

E) A mixture of *Ib* (1 g; 3·9 mmol), ether (70 ml) and diazomethane (0·33 g; 7·8 mmol) was treated as described in the procedure *D*). Yield 1·13 g (92·3%) of 3-methoxycarbonyl-3-cyano-4-methyl-4-(5-bromo-2-furyl)-1-pyrazoline (*IVb*), m.p. 93–95°C (dec.). For $C_{11}H_{10}BrN_3O_3$ (312·3); $[M^+ - 28]$ 283/285 *m/e*; calculated: 42·33% C, 3·23% H, 13·46% N, 25·59% Br; found: 42·44% C, 2·99% H, 13·23% N, 25·68% Br. UV spectrum (ethanol): λ_{max} 288 nm (log ε 4·12), 388 (3·42); IR spectrum (KBr): 1765 cm^{-1} (C=O), 2225 (C≡N); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 1·53 ppm (s, 3 H, CH_3), 3·93 (s, 1 H, OCH_3), 4·71 (d, J = 19 Hz, 1 H, CH_2 1-pyrazoline), 5·35 (d, J = 19 Hz, 1 H, CH_2 1-pyrazoline), 6·41, 6·43 (d, d, J = 3·7 Hz, 1 H, 1 H, $C_{(3,4)}$—H furan).

F) A mixture of *Ic* (1 g; 4·5 mmol), tetrahydrofuran (100 ml) and diazomethane (0·38 g; 8·9 mmol) in ether was kept at −5°C for 10 days. The solvent was distilled off *in vacuo*, ethanol (20 ml) was added and the mixture was allowed to stand for 24 h at room temperature. The separated product was filtered and crystallized from ethanol, yielding 0·78 g (62%) of 4-methyl-4-(5-nitro-2-furyl)-5-cyano-5-methoxycarbonyl-2-pyrazoline (*Vc*), m.p. 151–153°C. For $C_{11}H_{10}$. N_4O_5 (278·2); $[M^+]$ 277 *m/e*; calculated: 47·49% C, 3·68% H, 20·14% N; found: 47·42% C, 3·42% H, 19·92% N. UV spectrum (ethanol): λ_{max} 221 nm (log ε 3·85), 227 (3·88), 307 (3·77); IR spectrum (KBr): 1362, 1537 cm^{-1} (NO_2), 1616 (C=N), 1776 (C=O), 2258 (C≡N), 3342 (N—H); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 1·85 ppm (s, 3 H, CH_3), 3·56 (s, 3 H, OCH_3), 6·89 (s, 1 H, $C_{(5)}$—H pyrazoline), 7·73 (s, broad, 1 H, N—H 2-pyrazoline), 7·42 (d, J = 4 Hz, 1 H, $C_{(3)}$—H furan), 7·74 (d, J = 4 Hz, 1 H, $C_{(4)}$—H furan).

G) A mixture of *If* (1 g; 4·2 mmol) tetrahydrofuran (50 ml) and diazomethane (0·35 g; 8·3 mmol) in ether was allowed to stand at −5°C for 10 days. Isolation of the product was the same as described in the procedure *F*) and afforded 0·84 g (71·3%) of 3-(4-nitrophenyl)-3-cyano-4-(2-furyl)-1-pyrazoline (*IIf*), m.p. 88–90°C (dec.). For $C_{14}H_{10}N_4O$ (282·3); $[M^+ - 28]$ 254 *m/e*; calculated: 59·57% C, 3·57% H, 19·85% N; found: 59·73% C, 3·51% H, 19·62% N. UV spectrum (ethanol): λ_{max} 207 nm (log ε 4·16), 217 (4·17), 262 (3·97), 291 (3·92); IR spectrum (KBr): 1354, 1538 cm^{-1} (NO_2), 1604 (C=C arom.), 2247 (C≡N); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 3·98 ppm (t, J = 8 Hz, 1 H, $C_{(4)}$—H 1-pyrazoline), 3·17 (q, J = 18 Hz, J = 8 Hz, 1 H, CH_2 1-pyrazoline), 5·50 (q, J = 18 Hz, J = 8 Hz, 1 H, CH_2 1-pyrazoline), 6·46 (m, 2 H, $C_{(4)}$—H, $C_{(3)}$—H furan), 7·56 (m, 1 H, $C_{(5)}$—H furan), 7·76 (d, J = 4 Hz, 2 H, $C_{(2)}$—H, $C_{(6)}$—H arom.), 8·37 (d, J = 4 Hz, 2 H, $C_{(3)}$—H, $C_{(5)}$—H arom.).

Isomerisation of 3-Methoxycarbonyl-3-cyano-4-methyl-4-(2-furyl)-1-pyrazoline (*IVa*)

A mixture of *IVa* (200 mg; 0·86 mmol), acetonitrile (3 ml) and triethylamine (1 drop) was allowed to stand at room temperature for 24 h. The solvent was evaporated *in vacuo* and the product was crystallized from ethanol, affording 154 mg (77%) of 4-methyl-4-(2-furyl)-5-cyano--5-methoxycarbonyl-2-pyrazoline (*Va*), m.p. 148—149°C. For $C_{11}H_{11}N_3O_3$ (233·2); $[M^+]$ 233 *m/e*; calculated: 56·65% C, 4·75% H, 18·02% N; found: 56·49% C, 4·99% H, 17·82% N. UV spectrum (ethanol): λ_{max} 222 nm (log ε 3·99); IR spectrum (KBr): 1621 cm^{-1} (C—N), 1745, 1767 (C=O), 2260 (C≡N), 3339 (N—H); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 1·49 ppm (s, 3 H, CH_3), 3·86 (s, 3 H, OCH_3), 6·75 (s, 1 H, $C_{(5)}$—H pyrazoline), 7·58 (s, broad, 1 H, N—H 2-pyrazoline), 6·40 (m, 2 H, $C_{(3,4)}$—H furan), 7·93 (m, 1 H, $C_{(5)}$—H furan).

Isomerisation of 3-Methoxycarbonyl-3-cyano-4-methyl-4-(5-bromo-2-furyl)-1-pyrazoline (*IVb*)

A mixture of *IVb* (200 mg; 0·64 mmol), acetonitrile (3 ml) and triethylamine (1 drop) was allowed to stand at room temperature for 24 h. The reaction mixture was worked up as described in the preceding experiment and afforded 182 mg (91%) of 4-methyl-4-(5-bromo-2-furyl)-5-cyano--5-methoxycarbonyl-2-pyrazoline (*Vb*), m.p. 150—151°C. For $C_{11}H_{10}BrN_3O_3$ (312·1); $[M^+]$ 310/312 *m/e*; calculated: 42·33% C, 3·20% H, 13·46% N, 25·59% Br; found: 42·17% C, 3·03% H, 13·45% N, 25·72% Br. UV spectrum (ethanol): λ_{max} 231 nm (log ε 4·01); IR spectrum (KBr): 1619 cm^{-1} (C=N), 1750, 1765 (C=O), 2258 (C≡N), 3338 (N—H); ^{1}H-NMR spectrum (hexa-(hexadeuterioacetone), δ: 1·51 ppm (s, 3 H, CH_3), 3·91 (s, 3 H, OCH_3), 6·68 (s, 1 H, $C_{(5)}$—H pyrazoline), 6·55 (s, 1 H, N—H 2-pyrazoline), 6·36, 6·38 (d, d, J = 3·6 Hz, 1 H, 1 H, $C_{(3,4)}$—H furan).

Transformation of 3-(4-Nitrophenyl)-3-cyano-4-(2-furyl)-1-pyrazoline (*IIf*) in the Presence of Triethylamine

A mixture of *IIf* (200 mg; 0·71 mmol), acetonitrile (3 ml) and triethylamine (1 drop) was allowed to stand at room temperature for 24 h. The product was isolated as described in the preparation of *Va*; yield 132 mg (72·9%) of 3-(4-nitrophenyl)-4-(2-furyl)pyrazole (*VIf*), m.p. 239—240°C. For $C_{13}H_9N_3O_3$ (255·2) calculated: 61·18% C, 3·55% H, 16·46% N; found: 61·23% C, 3·36% H, 16·45% N. UV spectrum (ethanol): λ_{max} 206 nm (log ε 4·17), 220 (4·13), 253 (4·11), 296 (3·94); IR spectrum (KBr): 1349, 1523 cm^{-1} (NO_2), 1616 (C=C arom.), 1632 (C=N), 3280 (N—H); ^{1}H-NMR spectrum (hexadeuterioacetone), δ: 6·35 ppm (d, J = 3·5 Hz, 1 H, $C_{(3)}$—H furan), 6·45 (q, J = 1 Hz, J = 3·5 Hz, 1 H, $C_{(4)}$—H furan), 7·50 (d, J = 1 Hz, 1 H, $C_{(5)}$—H furan), 7·86 (d, J = 9 Hz, 2 H, $C_{(3)}$—H, $C_{(5)}$—H arom.), 7·97 (d, J = 1 H, 1 H, $C_{(5)}$—H pyrazole), 8·22 (d, J = 9 Hz, 2 H, $C_{(2)}$—H, $C_{(6)}$—H arom).

3-(4-Nitrophenyl)-4-(2-furyl)pyrazole

A mixture of *If* (1 g; 4·2 mmol), acetonitrile (20 ml), diazomethane (0·35 g; 8·3 mmol) in ether, and triethylamine (3 drops) was kept at 5°C for 10 days. The solvent was evaporated *in vacuo* and the product (*VIf*) was crystallized from ethanol; m.p. 239—240°C. Yield 0·65 g (61%).

REFERENCES

1. Popp F. D., Catala A.: J. Org. Chem. *26*, 2738 (1961).
2. Bastus J., Castello J.: Proc. Chem. Soc., London *1962*, 216.
3. Hamelin J., Carrier R.: Bull. Soc. Chim. Fr. *1968*, 2162.
4. Kisch H., Polansky O. E., Schuster E.: Tetrahedron Lett. *1969*, 805.
5. Hirao I., Kato Y.: Bull. Chem. Soc. Jap. *45*, 2055 (1972).
6. Považanec F., Kováč J., Piklerová A.: Zb. Pr. Chemickotechnol. Fak. Slov. Vys. Šk. Tech. 1975, in press.
7. Černayová M., Kováč J., Rajniaková O.: This Journal, in press.
8. Považanec F., Kováč J., Piklerová A.: Zb. Pr. Chemickotechnol. Fak. Slov. Vys. Šk. Tech. 1975, in press.

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