

An Unexpected Ring Opening–Ring Closure Reaction of 5-Azido-4-formylpyrazole

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5-Chloro-4-formyl-1-methylpyrazoles give 1-azidomethyl-4-cyanopyrazoles on reaction with an excess of sodium azide in dimethyl sulphoxide (DMSO), as a result of a ring opening–ring closure reaction; the crystal structure of the azidomethylpyrazole has been determined.

Heterocyclic azides often undergo ring opening and rearrangement reactions upon heating due to intermediate nitrene formation. In an attempt to prepare 5-azido-4-formylpyrazole by the reaction of 5-chloro-4-formyl-1,3-dimethylpyrazole (2)¹ with an excess of sodium azide in dimethyl sulphoxide (DMSO) at 80°C [N₂ (1 equiv.) was evolved during the reaction]. After addition of water and extraction with ether the sole reaction product (6) obtained from the ether extract was a crystalline compound, m.p. 72–73°C, with the elemental composition C₆H₆N₆.[†] This compound was stable, with decomposition first taking place at ca. 130°C. The ¹H and ¹³C n.m.r. spectra indicated the presence of a single uncoupled methine and methylene as well as a methyl group. The i.r. spectrum (KBr) showed the presence of one C≡N (ν 2240 cm⁻¹) and a benzylic N₃ (ν 2160, 2120, 2080 cm⁻¹). An X-ray structure determination[‡] confirmed the structure shown in Figure 1.

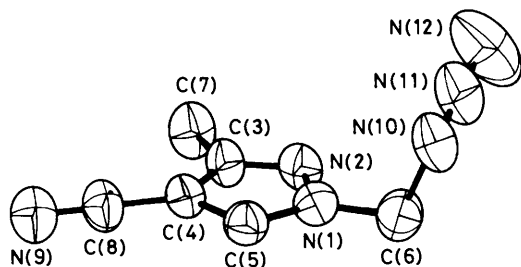
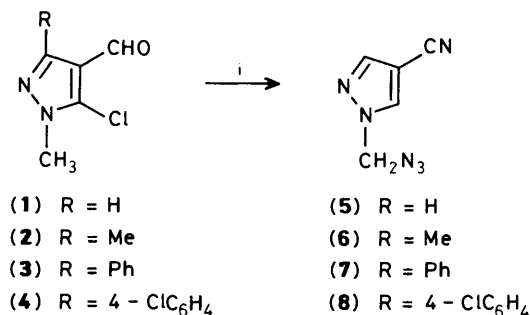


Figure 1. ORTEP drawing of (6) (50% probability ellipsoids). Selected bond lengths (Å) and angles (°): N(1)–N(2) 1.38(1), N(2)–C(3) 1.33(1), C(3)–C(4) 1.42(1), C(4)–C(5) 1.37(1), C(5)–N(1) 1.34(1), C(3)–C(7) 1.49(1), C(4)–C(8) 1.39(1), C(8)–N(9) 1.16(1), N(1)–C(6) 1.44(1), C(6)–N(10) 1.47(1), N(10)–N(11) 1.25(1), N(11)–N(12) 1.11(1); C(5)–N(1)–N(2) 112.9(7), N(1)–N(2)–C(3) 104.3(6), N(2)–C(3)–C(4) 110.8(8), C(3)–C(4)–C(5) 105.6(7), C(4)–C(5)–N(1) 106.5(7), N(1)–C(6)–N(10) 111.3(7), C(6)–N(10)–N(11) 113.2(9), N(10)–N(11)–N(12) 171(1).

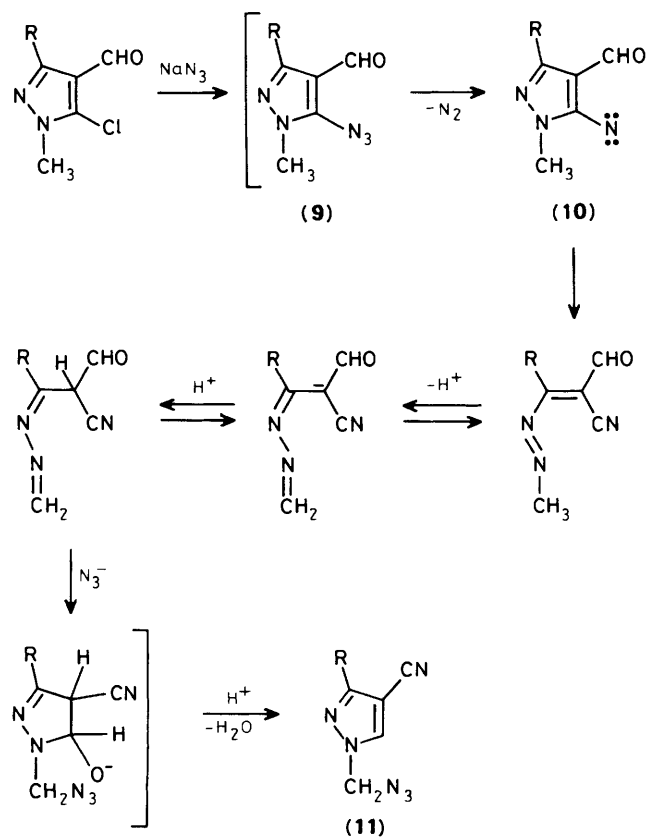
[†] All new compounds gave satisfactory elemental analysis ($\pm 0.4\%$ in C, H, and N).

[‡] Crystal data for (6): C₆H₆N₆, *M* = 162.16, triclinic, space group *P* $\bar{1}$, *a* = 4.287(1), *b* = 8.966(3), *c* = 11.619(4) Å, α = 112.29(3), β = 98.68(3), γ = 91.81(3)°, *U* = 406.50 Å³, *D*_c = 1.33 g cm⁻³, *Z* = 2, *R* = 0.094, *R*_w = 0.101 for 512 observed reflections 2° < θ < 30°, *I* > 2.5 $\sigma(I)$, crystal size 0.03 × 0.20 × 0.29 mm. Mo-*K* α radiation, λ = 0.71069 Å. The structure was solved by direct methods using the SHELX76 system.³ Full matrix least squares refinement of non-H atoms and analysis of the structure were performed with the X-RAY-76 system.⁴ The positional H-parameters were calculated but not refined. Reflections with *I* ≤ 2.5 $\sigma(I)$ were included in the refinement process if *F*_c ≥ *F*_o. The final *R* index was rather high due to the low quality of the data set (only 512 out of 2340 measured reflections were regarded as observed). Maximum and minimum in final difference density map 0.52 and -0.33 e/Å³, respectively. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

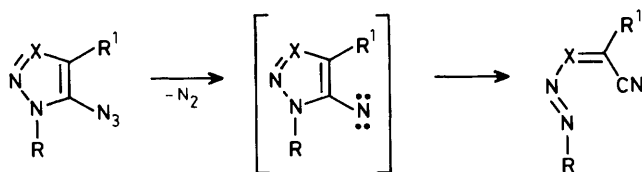
Reaction of the related chloroaldehydes (1), (3), and (4) also resulted in smooth formation of the 1-azidomethyl-4-cyanopyrazoles (5), (7), and (8) respectively in ca. 60% yields, confirming the generality of the reaction. In each case,



Scheme 1. Reagents and conditions: i, NaN₃ (1.5 molar excess), dimethyl sulphoxide (DMSO), heat 80–95°C, 4–5 h. (5) M.p. 83–84°C (water), (6) m.p. 70–71°C (water), (7) m.p. 86–87°C (water), and (8) m.p. 120–121°C (water-ethanol).



Scheme 2



Scheme 3

monitoring the reactions by t.l.c. revealed that the 5-azido-pyrazole (**9**) is probably an intermediate on the route to the final product (**11**), Scheme 2. In the case of chloroaldehyde (**1**) the intermediate (**9**) ($R = H$) was in fact isolated. The i.r. spectra of the compounds (**5**), (**7**), and (**8**) exhibited $C\equiv N$ and N_3 absorptions very similar to those of compound (**6**). Likewise, other analytical and spectral data confirmed the depicted structures.

On this basis it can be concluded that the new pyrazoles (**5**), (**6**), (**7**), and (**8**) probably have been formed *via* a nitrene (**10**) and an azo compound in which both the nitrile and the formyl moieties activate the *N*-methyl group towards attack by the nucleophilic azide anion. A mechanism which accounts for our observations is shown in Scheme 2.

A few related thermally induced ring openings of five membered heterocyclic azides are known in the triazole ($X = N$) and the pyrazole series ($X = CH$), all following the general reaction shown in Scheme 3.² In these cases where $R^1 \neq CHO$, ring closure of the initial reaction cannot take place resulting in the isolation of the ring opened product.

From the proposed reaction mechanism in Scheme 2 it can be presumed that related azoles may also undergo this new type of ring opening–ring closure reaction.

We thank the Danish Natural Science Research Council and the Thomas B. Thriges Foundation for the purchase of the X-ray diffraction equipment. A Danish Natural Science Research Council postdoctoral grant to K. Pluta, on leave from The Silesian School of Medicine, Sosnowiec, Poland, is gratefully acknowledged.

Received, 30th November 1987; Com. 1725

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