Tetrahedron Letters, Vol 32, No 29, pp 3565-3568, 1991
Printed in Great Britain

0040-4039/91 $3 00 + 0(
Pergamon Press plc

SYNTHESIS OF 5-AMINO-4-CYANOPYRAZOLES VIA RING OPENING-RING CLOSURE OF 5-AZIDO-4-IMINOMETHYLPYRAZOLES

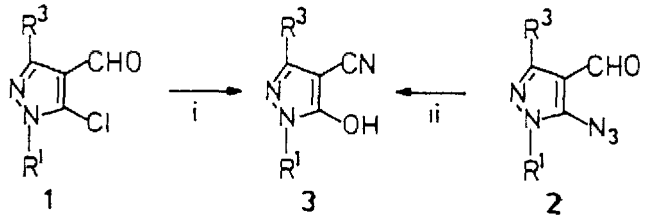
ISOLATION OF THE INTERMEDIATE

Wim Dehaen[a] and Jan Becher*[b]

[a]Department of Chemistry, University of Leuven,Celestijnenlaan 200F, B-3001 Heverlee, Belgium.
[b]Department of Chemistry, University of Odense, DK-5230 Odense M, Denmark.

Abstract: *5-Amino-4-cyanopyrazoles are prepared by thermolysis from 5-azido-4-iminomethylpyrazoles in fair yields. The reaction occurs via a ring opening-ring closure mechanism. The intermediate azocompound was isolated.*

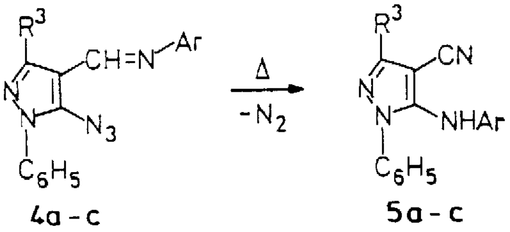
Heterocyclic azides are of interest because of their ability to form nitrenes[1]. In the course of our work[2] on 5-azidopyrazoles we observed[3] the formation of the hydroxynitriles **3** as side products in the reaction of 5-chloro-4-formylpyrazoles **1** with sodium azide in DMSO. Nitrile **3** was also formed by thermolysis of azide **2** in toluene[3]:



i: NaN_3, DMSO, heating. *ii.* Toluene, heating.

The initially formed nitrene ring opens to an azo compound, which then ring closes to give nitrile **3**. The formation of an azo intermediate is consistent with a general pattern for fragmentation of azoles[1,4].

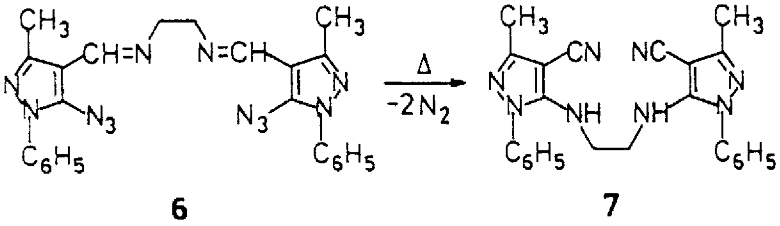
In the present work we have investigated the generality of this reaction scheme by thermolysing the readily available[5] imines **4**, which could be cleanly converted to the *o*-aminonitriles **5**[6] in high yields. The half life ($\tau_{1/2}$) of imines **4** in refluxing deuterochloroform were measured (^{1}H NMR) and the results summarised in the scheme:



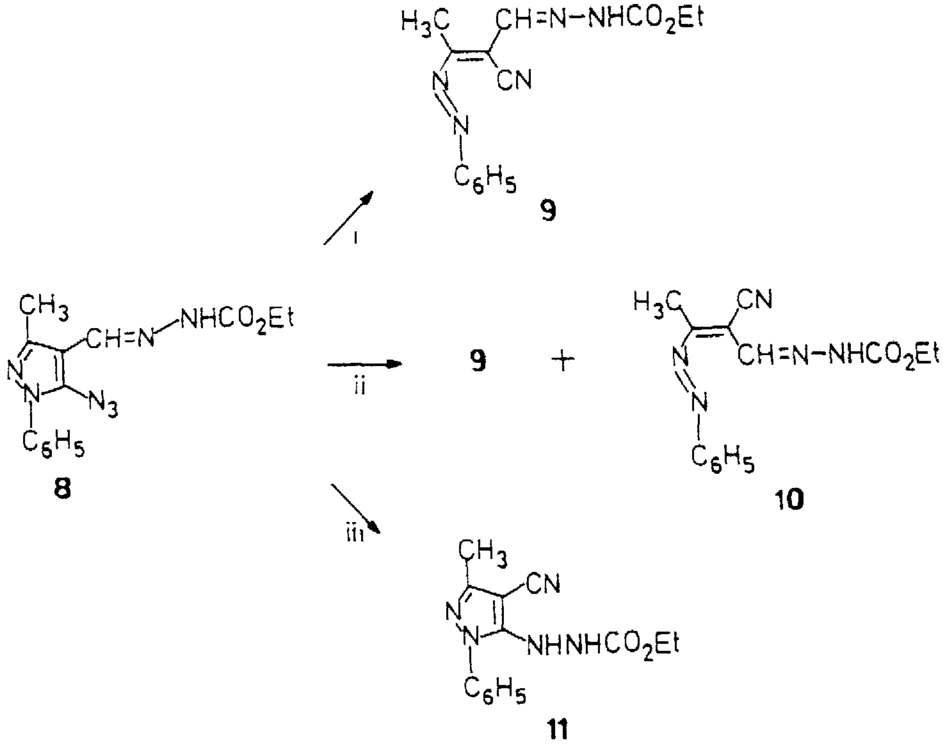
R^3	Ar	$\tau_{1/2}$ (hours)	Yield (%)
CH_3	4-CH_3-C_6H_4	3	83
C_6H_5	4-CH_3-C_6H_4	7	80
CH_3	4-CH_3O-C_6H_4	3	72

From this result it appears that the N-aryl moiety does not influence the rate of conversion, whereas the 3-substituent has some influence.

A double rearrangement was also carried out, thus heating of the bisiminoethylene derivative **6** yielded the diaminodinitrile **7** in high yield, compounds of this type might be useful as starting materials for heterocyclic ligands:



During the decomposition of imine **4c** we observed formation of an unstable red coloured intermediate. This obviously points to an azo compound. Ethoxycarbonylhydrazone **8** is much more thermolabile than the imines **4** and **6** and the outcome of the reaction is strongly influenced both by solvent and reaction time. Thus heating of **8** at 60°C for 1 hour in chloroform gives 80% conversion to the azo compound **9**. At the same temperature in DMSO-d_6 we initially see (^1H NMR and TLC) the emergence of compound **9**[7]. Later the new isomer **10** appeared at the expense of **9** and after 2 hours all of the starting material **8** was consumed and a 40:60 mixture of **9** and **10** was obtained. Finally when the reaction was carried out in acetonitrile at 60°C we first observed the formation of a mixture of **9** and **10** followed by complete conversion to the cyanopyrazole **11** after 6 hours at 60°C. These results therefore confirm our previously proposed[2] mechanism:



i: $CHCl_3$, 60°C, 1 hour. *ii:* DMSO-d_6, 60°C, 2 hours. *iii:* CH_3CN, 60°C, 6 hours.

The results described here, opens up the possibility for related rearrangements in the same area. Further investigations are in progress.

Acknowledgement: A postdoctoral grant from Odense University to W. Dehaen is gratefully acknowledged.

References and notes

1. Azides and Nitrenes, E. F. V. Scriven Ed., **1984**, Academic Press.

2. J. Becher, K. Brøndum, N. Krake, K. Pluta, O. Simonsen, P. Molina and M. Begtrup, *J. Chem Soc. Chem. Commun.*, **1988**, 541.

3. J. Becher, K. Pluta, P. L. Jørgensen, N Krake and B. Falt-Hansen, unpublished results.

4. P. A. S. Smith, G. J. W. Green, M. D. Hajek and D. V. C. Awang, *J. Org. Chem.*, **1970**, *35*, 2215.

5. P. Molina, A. Arques, M. V. Vinader, J. Becher and K. Brøndum, *J. Org. Chem.*, **1988**, *53*, 4654.

6. For example: **5a**; mp 173°C (EtOH/H$_2$O); IR (KBr) 3276 (NH), 2218 (CN); ^{1}H NMR (CDCl$_3$) δ 2.35 (3H, s, CH$_3$), 2.45 (3H, s, CH$_3$), 5.90 (1H, s, NH, exchange D$_2$O), 6.92 (2H, d, J = 9 Hz, H$_{arom}$), 7.10 (2H, d, J = 9 Hz, H$_{arom}$), 7.35 - 7.60 (5H, m, H$_{arom}$); ^{13}C NMR (CDCl$_3$) δ 12.87 (CH$_3$, pyrazole), 20.66 (CH$_3$, aryl), 80.71 (C4, pyrazole), 113.46 (CN), 119.87, 124.32, 128.53, 129.62, 129.86, 133.78, 136.45, 137.04, 146.45, 151.98; Mass spectrum, *m/z*: 288 (M$^+$, 100), 272 (10), 141 (6), 91 (15), 77 (25); Peak match for C$_{18}$H$_{18}$N$_4$: 288.13749, Found: 288.13485; Anal. calcd. for C$_{18}$ H$_{18}$N$_4$1/2 H$_2$O: C, 72.71; H, 5.76; N, 18.84. Found: C, 72.56; H, 5.56; N, 18.70.

7. **9**; yield 60%, mp 172°C (CHCl$_3$/ether); IR (KBr) 2230 (CN), 1719 (CO), 1542, 1240 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 1.25 (3H, t, J = 8 Hz, CH$_3$), 2.22 (3H, s, CH$_3$), 4.20 (2H, q, J = 8 Hz CH$_2$O), 7.60 (3H, m, H$_{arom}$), 7.90 (2H, m, H$_{arom}$), 8.40 (1H, s, CH=N), 11.65 (1H, s, NH, exchange D$_2$O); ^{13}C NMR (DMSO-d$_6$) δ 11.23, 14.38, 113.62 (CN), 119.28 (CH$_3$-C=$\underline{\mathrm{C}}$), 123.45, 129.71, 133.18, 138.83, 151.96, 152.83 (CO), 163.04 (CH$_3$-$\underline{\mathrm{C}}$=C); Mass spectrum *m/z*: 285 (M$^+$, 17), 197 (16), 184 (34), 77 (100); Peak match for C$_{14}$H$_{15}$N$_5$O$_2$: 285.12257; Found: 285.1187; Anal. calcd. for C$_{14}$H$_{15}$N$_5$O$_2$: C, 58.93; H, 5.30; N, 24.55. Found: C, 58.54; H, 5.26; N, 24.66.

(Received in UK 30 April 1991)