Pyrolysis Products of Some Pyrazolinodiazepines: Homodiazepines and Pyrazolopyridines

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Pyrolysis at 150°C of the 1-pyrazolinodiazepines **1a,b**, **3a**, and **3c** gave mainly the expected homodiazepines **4a**–**c** with a high reaction rate. Pyrolysis of the 2-pyrazolinodiazepines **2b**–**d** required higher temperatures (170–180°C) and longer reaction times leading to the formation of tarry residues. From these homodiazepines **4b**–**d** and pyrazolopyridines **8b,c**, **9b,c**, and **10b,c** could be isolated in moderate to poor yields only. Rather unexpected trace amounts of the bicyclic methylenecyclopropane derivative **11** were isolated from the pyrolysis of **2d**, besides the expected isomeric homodiazepine **4d**.

Pyrolyse-Produkte von Pyrazolinodiazepinen: Homodiazepine und Pyrazolopyridine

Die Pyrolyse der 1-Pyrazolinodiazepine **1a,b**, **3a** und **3c** bei 150°C führte mit hoher Geschwindigkeit zu den erwarteten Homodiazepinen **4a**–**c**. Pyrolyse der 2-Pyrazolinodiazepine **2b**–**d** benötigte höhere Temperaturen (170–180°C) und längere Reaktionszeiten, wobei jedoch teerartige Rückstände entstanden. Aus diesen konnten die Homodiazepine **4b**–**d** sowie die Pyrazolopyridine **8b,c**, **9b,c** und **10b,c** in mäßigen bis schwachen Ausbeuten isoliert werden. Überraschend war die Isolierung von winzigen Mengen des bicyclischen Methylencyclopropan-Derivats **11** aus den Pyrolyseprodukten von **2d** neben dem erwarteten Homodiazepin **4d**.

Recently we obtained a series of pyrazolinodiazepines by 1,3-dipolar cycloadditions of diazoalkanes to 1*H*-1,2-diazepines[1]. These reactions proved to be site specific, since only the Δ^4 double bond of the diazepine educts underwent cycloaddition. The regioselectivity of these cycloadditions was usually high, favouring adducts **1** in preference to adducts **3**, except in those cases where steric crowding led to a decrease in regioselectivity, as predicted also by quantum chemical considerations[1].

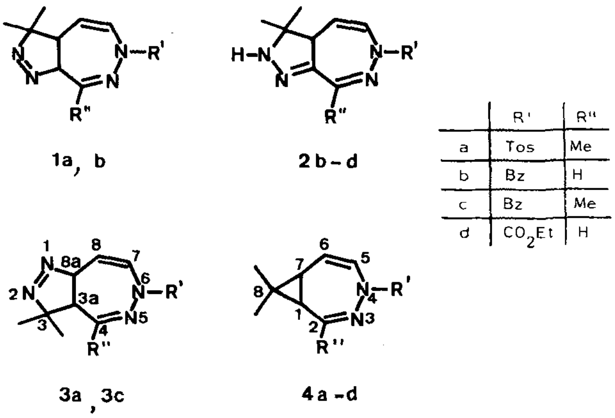
We describe herein some pyrolytic properties of pyrazolinodiazepines **1**–**3** which have been obtained by cycloaddition reactions of 2-diazopropane to some 1,2-diazepines[1].

At the outset we were aiming at preparing the homodiazepines **4**, some of which had already been described[2]. However, the product distribution, after pyrolysis of the adducts, proved to be more complex than we had anticipated. Therefore we examined the reaction mixtures more closely and were able to isolate, in addition to the expected homodiazepines **4**, some new heterocyclic compounds, and in particular pyrazolopyridines **8**, **9**, and **10**. Compounds **9** and **10** proved to be of considerable interest as starting material for the synthesis of the corresponding cyclopropapyridines[3].

Homodiazepines

Pyrolysis of the two regioisomeric 1-pyrazolinodiazepines **1a** and **3a**[1] led as expected to the same homodiazepine **4a** (Scheme 1) as deduced from the ^{1}H-NMR spectra (Table 1). Similar results were obtained starting from 1-pyrazolinodiazepine **1b**, a direct adduct[4], and from **3a** and **3c**, two inverse adducts[4], as well as from the direct 2-pyrazolinodiazepines **2b**, **c** and **d** (vide infra).

Scheme 1



	R'	R''
a	Tos	Me
b	Bz	H
c	Bz	Me
d	CO_2Et	H

In some cases pyrolysis of pyrazolinodiazepines led to tarry mixtures which contain several compounds besides the expected homodiazepines **4a**–**d**. Furthermore, the temperature of the pyrolytic treatment is a critical parameter. For example, pyrolysis of **1b** at 105°C led to the isomeric 2-pyrazolinodiazepine **2b** as the major product (50%), followed by the expected homodiazepine **4b** (32%). At least three additional compounds were also formed during this process; only 5-isopropyldiazepine **5b** (11%), which is an isomer of **4b** (Scheme 2), was isolated. Whereas **2b** is formed by prototropy from **1b** – of which it is an isomer – homodiazepine **4b** and diazepine **5b** obviously result from a multistep process in which the diradical **A** is the most likely intermediate[5].

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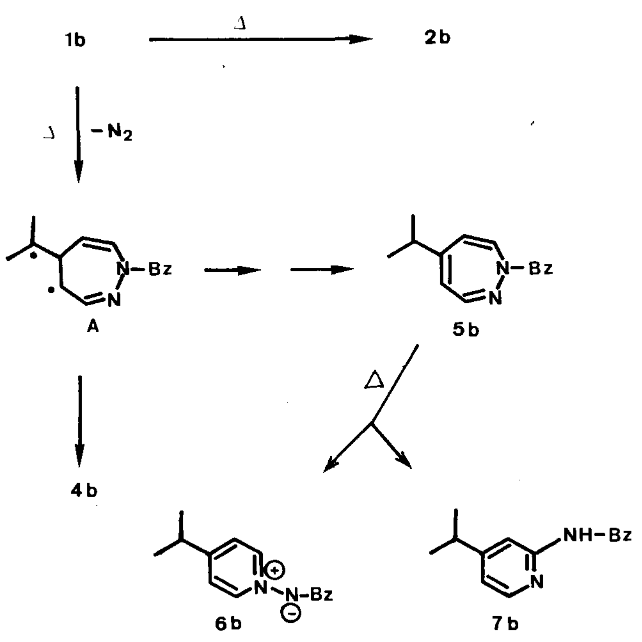
Table 1. ^{1}H-NMR spectra of homodiazepines **4a**–**d**, data of *N*-substituents are omitted [60 MHz; $CDCl_3$; δ (ppm); *J* (Hz); int. standard TMS]

	H-1	R''	H-5	H-6	H-7	CH_3	CH_3
4a	1.63 m	2.00 s (CH_3-2)	6.83 d J=9.5	5.00 ddd J=9.5;2.5;2.0	1.63 m	1.26 s CH_3-8	0.75 s CH_3-8
4b	1.76 m	6.93 t J=2.0 (H-2)	7.23 m	5.23 ddd J=10;3;2.5	1.76 m	1.33 s CH_3-8	0.90 s CH_3-8
4c	1.70 m	1.96 s (CH_3-2)	7.16 m	5.23 ddd J=9.5;2.5;2.5	1.70 m	1.33 s CH_3-8	0.93 s CH_3-8
4d [2]	1.72 m	6.98 t J=2.0 (H-2)	6.93 dd J=9; 1.0	4.99 ddd J=9;2;1.5	1.72 m	1.32 s CH_3-8	0.88 s CH_3-8

Scheme 2

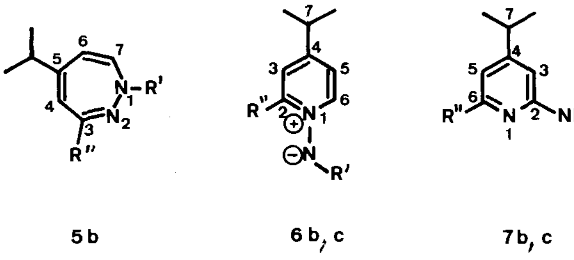


Pyrolysis of **1b** at 150°C led to an immediate and explosive evolution of nitrogen with a product distribution different to that observed at 105°C. Homodiazepine **4b** turned out to be the major product (70%), whereas the 2-pyrazolinodiazepine **2b** is but a minor one (9%). Instead of affording diazepine **5b**, its pyridine isomers **6b** and **7b** were formed. Furthermore, at least two very minor products, neither of which were isolated nor identified, appeared.

The assumption that **5b** is the precursor of **6b** and **7b** could easily be substantiated: by heating **5b** up to 150°C these two pyridine derivatives were indeed formed. Thermally induced ring contraction of 1-substituted 1,2-diazepines have been described by several authors to lead to pyridine isomers analogous to **6b** and **7b**. These rearrangements proceed most likely via diazanorcaradiene intermediates[6-8].

Pyrolysis at 150°C of the inverse 1-pyrazolinodiazepine **3c** leads also in good yield (71%) to the corresponding homodiazepine **4c** (Table 1), the minor reaction products having not been isolated.

Scheme 3



	R'	R''
b	COPh	H
c	COPh	CH_3

From the results presented so far as well as from those discussed below it is obvious that direct and inverse 1-pyrazolinodiazepines are the best precursors to the corresponding homodiazepines. Furthermore, a pyrolysis temperature of 150°C (instead of 105°C) leads to better homodiazepine yields. At even higher temperatures, the yields of homodiazepine formation decrease, most likely a result of the fact that some reaction products decompose to give tarry residues.

Pyrazolopyridines[9]

In order to obtain homodiazepines **4b** and **4c** the corresponding 2-pyrazolinodiazepines had to be pyrolyzed at higher temperatures (170–180°C) and over a longer period of time. As a consequence formation of tar increased and the yields of **4b** and **4c** decreased. Quite interestingly though, pyrazolopyridines **8**, **9**, and **10** were formed. It should be noted that these three compounds did not appear during the relatively short pyrolysis periods of 1-pyrazolinodiazepines, at least not in sizable amounts.

Structural determinations of these pyrazolopyridines follow in a straightforward manner from their ^1H-NMR spectra (see Experimental) and from their ^{13}C-NMR data (Tables 2, 3). An X-ray analysis of **9b** corroborated these spectroscopic analyses (vide infra).

The formation of the pyrazolopyridines **8**–**10** from **2** is best explained by assuming the following reaction cascade (Scheme 5):

i) H_2 orbital symmetry allowed 1,4-elimination of **2** leading to the pyrazolodiazepine **B**.

Table 2. ^{13}C-NMR spectra of pyrazolopyridines **8b**–**10b** [20.1 MHz; $CDCl_3$; δ (ppm); *J* (Hz); int. standard TMS]

	C-3	C-3a	C-4	C-5	C-7	C-7a	CH_3-C_3	C=0
9b	90.06 S_7 $^2J_{CH}\simeq5$	158.02 Sm $^3J=3.6$ $^3J_{H_7}=4.5$	106.73 Dd $^1J=175$ $^3J_{NH}=4.8$	152.14 Sd $^3J_{H7}=11.5$ $^2J_{H_4}<1$	141.71 Ds $^1J=186,4$	149.82 St $^2J_{H_7}=5.5$ $^3J_{H_4}=5.5$	21.73 Qq $^1J=132$ $^3J=5$	166.17 Sm
8b	92.30 S_7 $^2J=4.5$	154.39 Sm $^3J_{H_7}=8$ $^3J_{H_5}=5$	117.63 Dd $^1J=175$ $^2J_{H_5}=6$	143.27 Dt $^1J=196$ $^3J_{H_7}=5.5$ $^2J_{H_4}=5.5$	138.04 Dd $^1J=200$ $^3J_{H_5}=5.5$	152.43 Sdd $^2J_{H_7}=8$ $^3J_{H_4}=2$	21.25 Qq $^1J=134$ $^3J=5$	170.78 St $^3J=4$
10b	90.42 S_7 $^3J=5$	154.47 Sdd $^3J_{H_5}=8$ $^3J_{H_7}=5$	116.34 Ddd $^1J=167$ $^2J_{H_5}=9$ $^4J_{H_7}=2$	149.68 Ddd $^1J=182$ $^3J_{H_7}=11$ $^2J_{H_4}=5$	143.67 Dd $^1J=186$ $^3J_{H_5}=11$	151.78 St $^2J_{H_7}=5$ $^3J_{H_4}=5$	21.51 Qq $^1J=131$ $^3J=5$	

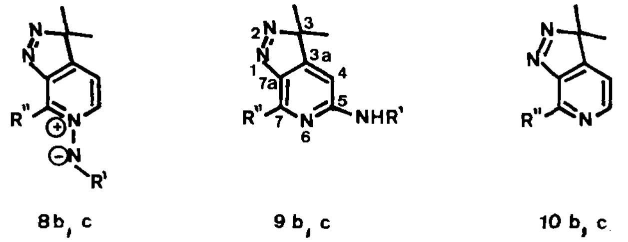
Table 3. ^{13}C-NMR spectra of pyrazolopyridines **8c**–**10c** [20.1 MHz; $CDCl_3$; δ (ppm); *J* (Hz); int. standard TMS]

	C-3	C-3a	C-4	C-5	C-7	C-7a	CH_3-C_3	CH_3-C_7	C=0
9c	89.83 S_7 $^2J=4$	158.06 S_7 $^3J=3$	104.23 Dd $^1J=175$ $^3J_{NH}=4$	151.32 Ss	151.69 Sq $^2J_{CH_3}=6$	148.18 Sdq $^3J_{H_4}=6$ $^3J_{CH_3}=3$	21.83 Qq $^1J=132$ $^3J=5$	19.46 Qs $^1J=129$	165.85 Sm
8c	92.88 S_7 $^2J=4.5$	154.74 Sd_7 $^3J_{H_5}=8$ $^3J_{CH_3}=4$	115.16 Dd $^1J=156$ $^2J_{H_5}=5$	145.27 Dd $^1J=194$ $^2J_{H_4}=6.5$	149.91 Sdq $^2J_{CH_3}=7$ $^3J_{H_5}=6$	151.96 Sdq $^3J_{H_4}=6$ $^3J_{CH_3}=4$	21.10 Qq $^1J=134$ $^3J=4$	14.45 Qs $^1J=134$	169.91 St $^3J=3$
10c	90.47 Sm	154.74 Sm $^3J_{H_5}\simeq7$	114.02 Dd $^1J=167$ $^2J_{H_5}=5$	149.14 Dd $^1J=180$ $^2J_{H_4}=4$	153.42 Sm $^3J_{H_5}\simeq14$	150.32 S	21.55 Qq $^1J=132$ $^3J=5$	19.96 Qs $^1J=130$	

ii) Ring contraction of the diazepine moiety of **B** to the diazanorcaradiene **C**, a reaction which has been described several times[6-8].

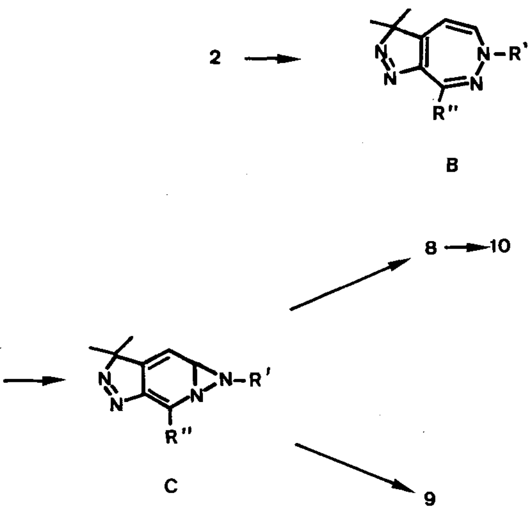
iii) **C** may then undergo ring-opening to **8** and **9**; **8** is subsequently thermolyzed to give **10**.

Scheme 4



	R'	R''
b	COPh	H
c	COPh	CH_3

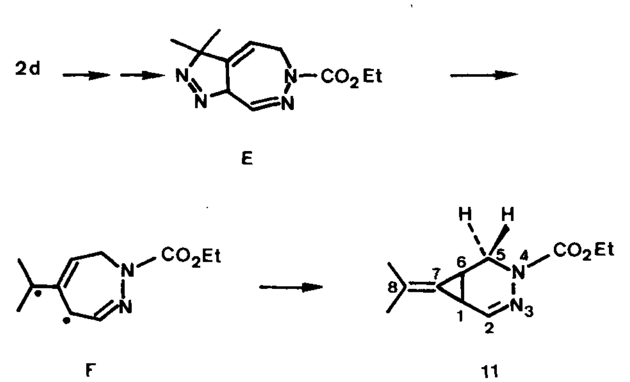
Scheme 5



Pyrazolopyridines **9** and **10**, which had been obtained in moderate to poor yields only (see above), are the obvious precursors for the photolytic synthesis of the corresponding cyclopropapyridines[3]. They could also be prepared, albeit in no better yields, by heating for example **2b** in pyridine solution in the presence of 1 equiv. of tosyl chloride. Thermolytic elimination (induced by pyridine at 180°C) of *p*-toluenesulfenic acid was supposed to give the postulated pyrazolodiazepine **Cb**. This assumption turned out to be reasonable since compounds **8b**, **9b**, and **10b** were isolated in this experiment.

Eventually, pyrolysis of the 2-pyrazolinodiazepine **2d** led also to a tarry mixture, from which the expected homodiazepine **4d** (17%)[2] as well as pyrazolopyridine **10a** (26%) (see above) could be isolated. Quite unexpectedly, an isomer of homodiazepine was also formed, though in poor yield (4%). The spectroscopic data for this isomer matches the bicyclic methylene-cyclopropane structure **11**. Its structural elucidation follows from its ^1H- and ^{13}C-NMR spectroscopic data (see Experimental). In particular the presence of only one olefinic hydrogen atom is noticed whereas three sp^2 carbon atoms appear in addition to the carbonyl moiety. In order to interprete the formation of **11** two base-induced double bond shifts of **2d** to the pyrazolinodiazepine **E** may be postulated. Thermal expulsion of a nitrogen molecule from **E** would then lead to the short-lived trimethylenemethane diradical **F** which gives ultimately **11** (Scheme 6).

Scheme 6



Trimethylenemethane diradicals have been studied extensively[10]. They are known to arise from photolysis[11] or thermolysis[12] of 4-alkylidene-1-pyrazolines and to close the ring to the corresponding alkylidenecyclopropane(s)[11].

Crystal Structure Analysis of 9b

The crystal data of **9b** ($C_{15}H_{14}N_4O$), which were determined at 295 K, are as follows: triclinic; space group $P\bar{1}$; $Z = 4$; $a = 9.360(18)$, $b = 12.778(25)$, $c = 12.864(25)$ Å; $\alpha = 92.60°$, $\beta = 90.07°$, $\gamma = 111.51°$; $V = 1430$ Å^3; $D_c = 1.24$ g cm^{-3}; $\lambda = 1.5418$ Å; 4113 reflections were measured of which 2728 with $I > 3\sigma(I)$ were used for the solution by direct methods. Final R factor = 0.048. For intramolecular bond lengths see Figure 1[13].

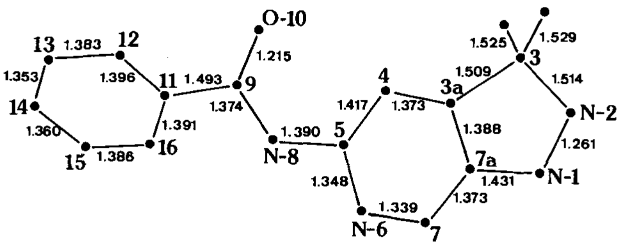


Figure 1. X-ray crystallography of **9b**: interatomic distances

As will be seen in a forthcoming publication[14], the geometrical parameters associated with the pyridine moiety of **9b** are of some interest when compared to those of the corresponding cyclopropapyridine. In particular, a shortening of the C3a–C7a bond length is expected which is indeed observed[3].

Conclusion

Whereas pyrolysis of type **1** and type **3** 1-pyrazolinodiazepines led to good, even excellent, yields of the corresponding homodiazepines **4**, pyrolysis of 2-pyrazolinodiazepines **2** always gave mixtures of homodiazepines **4** and somewhat unexpectedly the pyrazolopyridines **8**–**10**. It is possible that flash-vacuum pyrolysis may lead to better overall yields, to less tarry mixtures, and to a more simple product distribution. Unfortunately, the 2-pyrazolinodiazepines **2** were not amenable to sublimation, not even under a vacuum of 10^{-4} Torr.

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Experimental

General: Pyrolysis experiments were performed in 100-ml screw-capped thick-glass vessels („Bombenrohre") which were equipped with pressure valves withstanding pressures of up to 20 atm$^{15)}$. Flash-chromatographic (FC) separations according to ref.$^{16)}$, silica gel (Merck 60; 230–400 mesh). – TLC: Alumina roll (Merck 60; F_{254}). – Microanalyses: *Service Central de Microanalyses* of the *Centre National de la Recherche Scientifique.* – Melting points: Büchi SMP-2 apparatus, not corrected. – UV spectra: Varian Techtron 635 spectrophotometer. – IR spectra: Perkin-Elmer 157 G spectrophotometer. – ^{1}H- and ^{13}C-NMR spectra: Varian T-60 (60 MHz) and Bruker WH 80 DS (80 MHz) instruments, Me_4Si internal reference. – Normal MS and high-resolution MS: LKB 100 and Thomson-Houston THN 208 mass spectrometers, respectively.

Starting Materials: The synthesis of pyrazolinodiazepines **1a, b**, **2b**–**d**, **3a**, and **3c** has already been described$^{1)}$.

2,8,8-Trimethyl-4-tosyl-3,4-diazabicyclo[5.1.0]octa-2,5-diene (**4a**)

a) *From the Direct Adduct* **1a**: Standard procedure: A 50-ml bombenrohr (see above) containing **1a** (0.40 g; 1.2 mmol), under argon, and containing a fast-rotating magnetic stirrer, was heated at 150°C in an oil bath, whereby a quick gas evolution occurred. After 10 min the reaction mixture was cooled to room temp. and separated by FC (ethyl acetate/cyclohexane 5:5), whereby only **4a** (least polar product, 189 mg; 51%) was isolated as colourless crystals, m.p. 123°C (*i*PrOH). – UV (EtOH): $\lambda_{\max}$ (ε) = 222 nm (13900), 255 (6900). – IR (KBr): 1670 cm^{-1}, 1655, 1595, 1350, 1170. – ^{1}H NMR: Table 1. – ^{13}C NMR ([D$_6$]DMSO): δ = 155.14 (Sqd, *J* = 10; 2 Hz, C-2), 144.34 (Sq, *J* = 6.5 Hz, C_p-arom.), 133.87 (St, *J* = 5 Hz, C_s-arom.), 129.63 (Ddq, *J* = 165; 6; 6 Hz, C_m-arom.), 128.22 (Dd, *J* = 168; 6 Hz, C_o-arom.), 128.08 (Dt, *J* = 180; 6 Hz, C-5), 109.27 (D, *J* = 161 Hz, C-6), 34.57 (S, C-8), 34.57 (Dm, *J* = 158 Hz, C-1), 28.28 (Dm, *J* = 160 Hz, C-7), 26.74 (Qm, *J* = 130 Hz, 8-CH$_3$), 25.69 (Q, *J* = 130 Hz, 2-CH$_3$), 21.00 (Qt, *J* = 128, 4.5 Hz, CH$_3$-arom.), 16.03 (Qm, *J* = 128 Hz, 8-CH$_3$).

$C_{16}H_{20}N_2O_2S$ (304.4) Calcd. C 63.13 H 6.62 N 9.20
Found C 63.1 H 6.8 N 9.4

b) *From the Inverse Adduct* **3a**: Same procedure as above using a 100-ml bombenrohr and **3a** (1.35 g; 4.49 mmol). **4a** was obtained (1.05 g; 85%) which was identical with the product described above.

Pyrolysis of 1-Pyrazoline Adduct **1b** *at 105°C: Formation of 2-Pyrazoline* **2b**, *of 4-Benzoyl-8,8-dimethyl-3,4-diazabicyclo[5.1.0]-octa-2,5-diene* (**4b**), *and of 1-Benzoyl-5-isopropyl-1H-1,2-diazepine* (**5b**): Standard procedure using **1b**$^{2)}$ (12 g; 44.8 mmol) which was heated to 105°C for 5 min in a 100-ml bombenrohr. Column chromatography (ethyl acetate/cyclohexane 3:7) gave three products in the following order of increasing retention time:

Homodiazepine **4b** (3.43 g; 32%) as colourless crystals, m.p. 59°C. – UV (EtOH): $\lambda_{\max}$ (ε) = 270 nm (9800), 235 (5200). – IR (CHCl$_3$): 1670 cm^{-1}, 1600, 1580. – ^{1}H NMR: Table 1.

$C_{15}H_{16}N_2O$ (240.3) Calcd. C 74.97 H 6.71 N 11.66
Found C 75.0 H 6.8 N 11.5

Isopropyldiazepine **5b** (1.21 g; 11%) as a yellow oil. – UV (MeOH): $\lambda_{\max}$ (ε) = 224 nm (13400). – IR (CHCl$_3$): 1655 cm^{-1}, 1640, 1610, 1360, 1350. – ^{1}H NMR (CDCl$_3$): δ = 7.30 (m, H-3), 6.10 (dd, *J* = 4, 2 Hz, H-4), 5.77 (dd, *J* = 8, 2 Hz, H-6), 6.50 (dd, *J* = 8 Hz, H-7), 2.43 (m, *J* = 7 Hz, C*H*Me$_2$), 1.10 (d, *J* = 7 Hz, 2 CH$_3$), 7.65 (m, H-arom.), 7.40 (m, H-arom.).

$C_{15}H_{16}N_2O$ Calcd. 240.1263 Found 240.1267 (MS)

2-Pyrazolinodiazepine **2b**$^{1)}$ (6.0 g; 50%), m.p. 122°C$^{1)}$.

Pyrolysis of **1b** *at 150°C. Formation of Homodiazepine* **4b**, *of 2-Pyrazoline* **2b**, *of 2-(Benzoylamino)-4-isopropylpyridine* (**7b**), *and of 4-Isopropylpyridinium-1-benzamidate* (**6b**): Standard procedure as above using **1b** (4.0 g; 14.9 mmol) which was heated to 150°C for 45 min in a 100-ml bombenrohr. Column chromatography (ethyl acetate/cyclohexane from 3:7 to 8:2) led to the separation of four products (besides some other compounds which were neither isolated nor characterized) in the following order of increasing polarity:

4b (2.5 g; 70%) and **2b** (0.32 g; 9%).

Isopropylpyridine **7b** (50 mg; 1.4%), oil. – IR (CHCl$_3$): 3400 cm^{-1}, 2960, 1675, 1610, 1420. – ^{1}H NMR (CDCl$_3$): δ = 8.4 (d, *J* = 1.5 Hz, H-3), 6.95 (dd, *J* = 5.5; 1.5 Hz, H-5), 8.1 (d, *J* = 5.5 Hz, H-6), 3.0 (m, *J* = 6.5 Hz, C*H*Me$_2$), 1.35 (d, *J* = 6.5 Hz, 2 CH$_3$), 9.5 (s, NH), 8.0 (m, H-arom.), 7.5 (m, H-arom.).

$C_{15}H_{16}N_2O$ Calcd. 240.1263 Found 240.1264 (MS)

Pyridinium Ylide **6b** (40 mg; 1.1%), m.p. 128.5°C. – UV (MeOH): $\lambda_{\max}$ (ε) = 305 nm (5900), 260 (7200), 230 (16300). – IR (KBr): 2960 cm^{-1}, 1620, 1598, 1550, 1445, 1330. – ^{1}H NMR (CDCl$_3$): δ = 8.7 (d, *J* = 7 Hz, H-2, -6), 7.4 (m, H-3, -5), 3.05 (m, *J* = 6.5 Hz, C*H*Me$_2$), 1.30 (d, *J* = 6.5 Hz, 2 CH$_3$), 8.2 (m, H-arom.), 7.4 (m, H-arom.).

$C_{15}H_{16}N_2O$ (240.3) Calcd. C 74.97 H 6.71 N 11.65
Found C 74.9 H 6.6 N 11.7

Thermal Isomerisation of Diazepine **5b** *to the Pyridine Derivatives* **6b** *and* **7b**: Standard procedure using **5b** (340 mg, 1.42 mmol) under argon in a round-bottomed flask which was heated to 150°C for 20 min. Crystallisation of the crude reaction mixture gave mainly **6b** (300 mg, 88%) as colourless needles, m.p. 128°C. The mother liquors were shown by ^{1}H NMR to contain mainly **7b**.

4-Benzoyl-2,8,8-trimethyl-3,4-diazabicyclo[5.1.0]octa-2,5-diene (**4c**): Standard procedure using **3c**$^{1)}$ (640 mg, 2.26 mmol) which was heated to 150°C for 10 min in a 50-ml bombenrohr under argon. Homodiazepine was obtained by FC of the reaction mixture (ethyl acetate/cyclohexane 1:1) and purified by kugelrohr distillation at 70°C/10^{-2} Torr. Compound **4c** (410 mg, 71%) was obtained as colourless crystals, m.p. 66–68°C. – UV (EtOH): $\lambda_{\max}$ (ε) = 274 nm (9100), 220 (shoulder). – IR (CHCl$_3$): 1660 cm^{-1}, 1600, 1580. – ^{1}H NMR (CDCl$_3$): δ = 7.76–7.16 (H-arom. and H-5), 5.23 (ddd, *J* = 9.5; 2.5; 2.5 Hz, H-6), 1.96 (s, 2-CH$_3$), 1.70 (m, H-1 and H-7), 1.33 (s, 8-CH$_3$), 0.93 (s, 8-CH$_3$).

$C_{16}H_{18}N_2O$ (254.3) Calcd. C 75.56 H 7.13 N 11.02
Found C 75.4 H 7.1 N 11.0

Pyrolysis of **2b** *at 170°C. Formation of Homodiazepine* **4b**, *of N-(3,3-Dimethyl-3H-pyrazolo[3,4-c]pyridin-5-yl)benzamide* (**9b**), *of 3,3-Dimethyl-3H-pyrazolo[3,4-c]pyridine* (**10b**), *and of 3,3-Di-*

methyl-3H-pyrazolo[3,4-c]pyridinium-6-benzamidate (**8b**): Standard procedure using **2b** (10 g; 37.3 mmol) which was heated to 170°C for 3 h in a 100-ml bombenrohr. The black-coloured reaction mixture was separated by column chromatography (300 g silica gel; ethyl acetate/cyclohexane gradient elution going from 3:7 to 2:8 ratios) and led to four compounds which appeared in the following order of increasing polarity:

Homodiazepine **4b** (1.34 g; 15%), colourless crystals, m.p. 59°C.

Pyrazolopyridine **9b** (1.50 g; 15%), colourless crystals, m.p. 179°C. – UV (EtOH): λ_{max} (ε) = 308 nm (20900), 284 (14200), 233 (12900). – IR (KBr): 3210 cm^{-1}, 3185, 1680, 1615, 1600, 1585. – ^{1}H NMR ($CDCl_3$): δ = 9.36 (s, NH), 8.92 (s, H-7), 8.66 (s, H-4), 7.96 (m, H-arom.), 7.60 (m, H-arom.), 1.60 (s, 2 CH_3). – ^{13}C NMR: Table 2.

$C_{15}H_{14}N_4O$ (266.3) Calcd. C 67.65 H 5.30 N 21.04
Found C 67.5 H 5.3 N 20.9

Pyrazolopyridine **10b** (1.0 g; 20%), colourless crystals, m.p. 108°C (hexane followed by sublimation). – UV (EtOH): λ_{max} (ε) = 348 nm (230), 270 (2600, shoulder), 242 (5900). – IR ($CHCl_3$): 1605, 1585 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 9.45 (s, H-7), 8.73 (d, J = 4.5 Hz, H-5), 7.48 (dd, J = 4.5; 1.0 Hz, H-4), 1.58 (s, 2 CH_3). – ^{13}C NMR: Table 2.

$C_8H_9N_3$ (147.2) Calcd. C 65.28 H 6.16 N 28.55
Found C 65.3 H 6.1 N 28.6

Ylide **8b** (400 mg, 4%), colourless crystals, m.p. 180–185°C (dec., $CHCl_3$/CCl_4). – UV (EtOH): λ_{max} (ε) = 335 nm (5500), 228 (16800), 364 (9300). – IR ($CHCl_3$): 1595, 1550 cm^{-1}. – ^{1}H NMR ($CDCl_3$): δ = 9.76 (s, H-7), 8.93 (dd, J = 6.5; 1.0 Hz, H-5), 8.2 (m, H-arom.), 7.66 (d, J = 6.5 Hz, H-4), 7.46 (m, H-arom.), 1.63 (s, 2 CH_3). – ^{13}C NMR ($CDCl_3$): Table 2.

$C_{15}H_{14}N_4O$ Calcd. 266.1168 Found 266.1171 (± 0.0008) (MS)

N-Tosylation of **2b** *Followed by Thermolysis in Pyridine Solution. Formation of Pyrazolopyridine Derivatives* **9b**, **10b**, *and* **8b**: A solution of **2b** (10.73 g; 40 mmol) and tosyl chloride (7.6 g; 40 mmol) in anhydrous pyridine (60 ml) was heated up to 180°C for 80 min in two 100-ml bombenrohrs under argon. Both vessels were then cooled to room temp. and the combined black-coloured solutions evaporated to dryness in vacuo. The residue was treated with brine (40 ml) and the resulting suspension extracted several times with CH_2Cl_2. These latter combined solutions were dried with $MgSO_4$ and evaporated to dryness in vacuo. The resulting crude reaction mixture was then separated by FC using a gradient elution technique as described above, whereby the following compounds were isolated:

Pyrazolopyridine **9b** (450 mg; 4.2%), m.p. 179°C (after sublimation at 145°C/0.5 Torr).

Pyrazolopyridine **10b** (850 mg; 14.5%), m.p. 110°C (after sublimation at 60°C/0.5 Torr).

Ylide **8b** (700 mg; 6.6%), m.p. 180–185°C (dec.).

Pyrolysis of 2-Pyrazoline Adduct **2c** *at 170°C. Formation of Homodiazepine* **4c**, *N-(3,3,7-Trimethyl-3H-pyrazolo[3,4-c]pyridin-5-yl)benzamide* (**9c**), *of 3,3,7-Trimethyl-3H-pyrazolo[3,4-c]pyridine* (**10c**), *of 3,3,7-Trimethyl-3H-pyrazolo[3,4-c]pyridinium-6-benzamidate* (**8c**), *and of 4-Isopropyl-2-methylpyridinium-1-benzamidate* (**6c**): Standard procedure using **2c** (10 g; 35.3 mmol) which was heated to 170°C for 3 h in a 100-ml bombenrohr. The black-coloured reaction mixture was separated by column chromatography (300 g silica gel, ethyl acetate/cyclohexane, gradient elution going from 3:7 to 2:8 ratios) and led to five compounds which appeared in the following order of increasing polarity:

Homodiazepine **4c** (1.1 g; 12%), m.p. 66–68°C.

Pyrazolopyridine **9c** (1.6 g; 16%) as colourless crystals, m.p. 196°C. – UV (EtOH): λ_{max} (ε) = 314 nm (20400), 283 (11100), 276 (10700, shoulder), 234 (14500). – IR (KBr): 3330 cm^{-1}, 1675, 1615, 1590, 1525. – ^{1}H NMR ($CDCl_3$): δ = 9.28 (s, NH), 8.45 (s, H-4), 8.00 (m, H-arom.), 7.56 (m, H-arom.), 2.93 (s, 7-CH_3), 1.56 (s, 2 CH_3). – ^{13}C NMR: Table 3.

$C_{16}H_{16}N_4O$ (280.3) Calcd. C 68.55 H 5.75 N 19.99
Found C 68.5 H 5.6 N 19.9

Pyrazolopyridine **10c** (1.3 g, 23%) as colourless crystals, m.p. 43–45°C. – UV (EtOH): λ_{max} (ε) = 350 nm (240), 283 (3500), 247 (5800). – IR ($CHCl_3$): 1610 cm^{-1}, 1585. – ^{1}H NMR ($CDCl_3$): δ = 8.61 (d, J = 5 Hz, H-5), 7.35 (d, J = 5 Hz, H-4), 3.10 (s, 7-CH_3), 1.58 (s, 2 CH_3). – ^{13}C NMR: Table 3.

$C_9H_{11}N_3$ (161.1) Calcd. C 67.05 H 6.88 N 26.05
Found C 67.2 H 7.1 N 25.7

Ylide **8c** (800 mg, 8%), colourless crystals, m.p. 170–172°C (dec.). – UV (EtOH): λ_{max} (ε) = 315 nm (3800, shoulder), 288 (21000). – IR (KBr): 1590 cm^{-1}, 1550, 1545. – ^{1}H NMR ($CDCl_3$): δ = 8.72 (d, J = 6.5 Hz, H-5), 8.16 (m, H-arom.), 7.40 (m, H-4 and H-arom.), 3.20 (s, 7-CH_3), 1.63 (s, 2 CH_3). – ^{13}C NMR: Table 3.

$C_{16}H_{16}N_4O$ Calcd. 280.1324 Found 280.1325 (MS)

Ylide **6c** (350 mg, 3.5%) colourless crystals, m.p. 129°C (after sublimation at 110°C/10^{-2} Torr). – UV (EtOH): λ_{max} (ε) = 296 nm (3800, shoulder), 260 (8700, shoulder), 233 (15000). – IR (KBr): 1620 cm^{-1}, 1590, 1550. – ^{1}H NMR ($CDCl_3$): δ = 8.46 (d, J = 6.5 Hz, H-6), 8.20 (m, H-arom.), 7.38 (m, H-3, -5 and H-arom.), 3.02 (sept, J = 6.5 Hz, H-7), 2.66 (s, 2-CH_3), 1.28 (d, J = 6.5 Hz, 2 CH_3).

$C_{16}H_{18}N_2O$ (254.3) Calcd. C 75.56 H 7.13 N 11.02
Found C 75.5 H 7.1 N 11.0

Pyrolysis of 2-Pyrazoline Adduct **2d** *at 170°C. Formation of Homodiazepine* **4d**, *of Pyrazolopyridine* **10a**, *and of Ethyl 7-(1-Methylethylidene)-3,4-diazabicyclo[4.1.0]hept-2-ene-4-carboxylate* (**11**): Standard procedure using **2d** (10 g; 42.3 mmol) which was heated to 170°C for 3 h in a 100-ml bombenrohr. The black-coloured reaction mixture was separated by column chromatography (300 g silica gel, ethyl acetate/cyclohexane gradient elution going from 3:7 to 2:8 ratios) and led to the isolation of three well-defined compounds only, which appeared in the following order of increasing polarity:

Homodiazepine **4d** (1.49 g, 17%) as a colourless oil[2].

Pyrazolopyridine **10a** (2.62 g, 26%) (see above).

Alkylidenecyclopropane **11** (360 mg, 4.1%) as a colourless oil. – UV (MeOH): λ_{max} (ε) = 251 nm (5000). – IR ($CHCl_3$): 1700 cm^{-1}, 1615, 1420, 1380, 1235, 1165, 1123. – ^{1}H NMR ($CDCl_3$): δ = 7.38 (d, J = 3 Hz, H-2), 4.40 (d, J = 12 Hz, H-5), 2.80 (dd, J = 12; 2 Hz, H-5), 2.5 (m, H-1), 2.05 (m, H-6), 1.80 (m, 2 8-CH_3), 4.25 (q, J = 7 Hz, OCH_2CH_3), 1.13 (t, J = 7 Hz, OCH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 154.84 (S, CO), 147.96 (D, J = 188 Hz, C-2), 126.06 (S, C-7), 116.26 (S, C-8), 61.47 (Tq, J = 152, 4 Hz, OCH_2CH_3), 36.83 (T, J = 147 Hz, C-5), 22.93 (Dm, J = 172 Hz, C-1), 21.26 (Qq, J = 131 Hz, 8-CH_3), 20.84 (Qq, J = 131 Hz, 8-CH_3), 17.82 (Qt, J = 130; 2 Hz, OCH_2CH_3), 13.14 (D, J = 172 Hz, C-6).

$C_{11}H_{16}N_2O_2$ (208.3) Calcd. C 63.44 H 7.74 N 13.45
Found C 63.5 H 7.8 N 13.5

CAS Registry Numbers

1a: 109152-70-7 / **1b**: 37928-40-8 / **2b**: 37928-41-9 / **2c**: 109241-72-7 / **2d**: 42067-20-9 / **3a**: 109182-02-7 / **3c**: 109182-03-8 / **4a**: 109152-72-9 / **4b**: 75073-03-9 / **4c**: 109152-73-0 / **4d**: 37928-44-2 / **5b**: 77134-05-5 / **6b**: 109152-75-2 / **6c**: 109152-79-6 / **7b**: 109152-74-1 / **8b**: 77134-14-6 / **8c**: 109152-78-5 / **9b**: 77134-13-5 / **9c**: 109241-73-8 / **10b**: 77134-15-7 / **10c**: 109152-77-4 / **11**: 77134-11-3

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