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Pyrrolo[3,2,1-*jk*]carbazole **1a**, the previously unreported 16π -electron parent compound, has been synthesized by treatment of pyrrolo[3,2,1-*kl*]phenothiazine **2a** with a 1:1 mixture of bis(1,5-cyclooctadiene)nickel(0) and 2,2'-bipyridyl. An unequivocal assignment of the ^1H nmr spectrum of **1a** was made by decoupling experiments and by comparison with the ^1H nmr spectrum of 1,9-dideuteriopyrrolo[3,2,1-*jk*]carbazole **1b**. Meta-stable ion studies, exact mass measurements and the dideuterioderivative **1b** were utilized to investigate the electron impact induced fragmentation of **1a**.

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Since tetracyclic systems containing a phenothiazine or dibenz[*b,f*]azepine moiety are important precursors for the synthesis of conformationally restricted tranquilizers and antidepressants [3,4], we have recently prepared a series of these compounds by means of a modified Bischler synthesis [5]. Cyclization of the *N*-acetaldehydes of phenothiazine, dibenz[*b,f*]azepine, 10,11-dihydrodibenz[*b,f*]azepine and diphenylamine readily gave the tetracyclic systems pyrrolo[3,2,1-*kl*]phenothiazine **2a**, indolo[1,7-*ab*][1]benzazepine **3**, 6,7-dihydroindolo[1,7-*ab*][1]benzazepine **4** and 1-phenylindole **5** by treatment with molecular sieves. However, attempted preparation of **1a** by cyclization of carbazole-9-acetaldehyde failed and the starting material remained intact under those conditions. After reflux for two days in toluene no cyclized product was detectable, but 2,4-dicarbazole-9-yl-2-butenal had been formed instead [5]. In connection with the preparation of the tetracyclic compounds we undertook a study of the electron impact promoted mass spectral fragmentations of **2a**, **3**, and **4** and 1,2,6,7-tetrahydroindolo[1,7-*ab*][1]benzazepine-1-one [6,7]. In all cases a heteroaromatic ion believed to have a pyrrolocarbazolium structure appeared. To test

this hypothesis it was essential to have access to a sample of **1**. Since it could not be prepared by the route we had used to prepare the other compounds, we attempted to use the appealing method of Eisch and co-workers [8,9]. They have extensively studied the desulfurization of sulfur heterocycles by nickel(0) complexes and have reported the conversion of phenothiazine into carbazole [8].

We have now used their method successfully and isolated **1** in good yield after treatment of **2a** with an excess of a 1:1 mixture [10] of bis(1,5-cyclooctadiene)nickel(0) and 2,2'-bipyridyl. Only traces of *N*-phenylindole were formed according to a glc analysis of the reaction mixture. We interpret the unsuccessful ring closure reaction of carbazole-

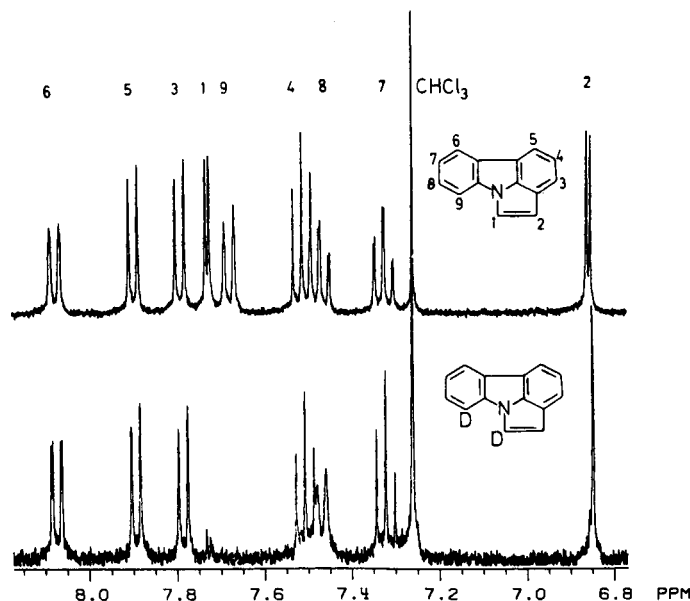
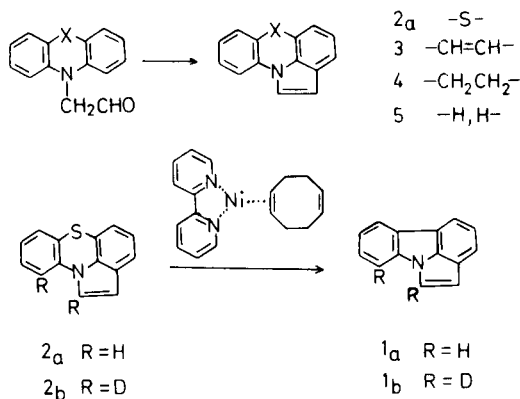


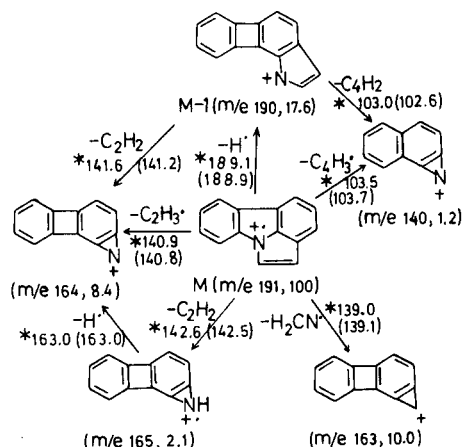
Figure. ^1H nmr spectra of pyrrolo[3,2,1-*jk*]carbazole (**1a**) and 1,9-dideuteriopyrrolo[3,2,1-*jk*]carbazole (**1b**) in deuteriochloroform.

9-acetaldehyde in terms of steric strain in the cyclization transition state. Apparently the nickel-promoted reaction can succeed in relatively strained systems and can provide us with a valuable method for conversion of even more complex strained phenothiazine derivatives of pharmacological interest into the corresponding carbazole series.

The assignment of the ^1H nmr spectra of **1a** was made from decoupling experiments in combination with comparison of the spectrum of 1,9-dideuteriopyrrolo[3,2,1-*jk*]-phenothiazine **2b** which had been prepared by metalation and subsequent deuteration of **2a** [11]. The well separated doublet at 6.86 ppm and doublet of doublets at 7.73 with a coupling constant of 3.1 Hz were assigned to the 1- and 2-protons, respectively [12]. The assignment of the 3-spin system is based on the existence of a long range coupling of 0.5 Hz between the 1- and 5-protons. Irradiation of the 1-proton results in a doublet of doublets from the 5-proton due to coupling to the 4-proton ($J = 7.4$ Hz) and to the 3-proton ($J = 0.5$ Hz). The assignment of the 4-spin system is primarily based on comparison with the spectra of **1b** and also on decoupling experiments. A comparison of the chemical shifts reveals that all of the hydrogens in the spectrum of the planar molecule **1a** appear at lower fields than the corresponding hydrogens in **2a**, **3** or **4** [13] and that the hydrogens in carbazole and the corresponding hydrogens in the 4-spin system of **1a** have almost identical chemical shift values [14].

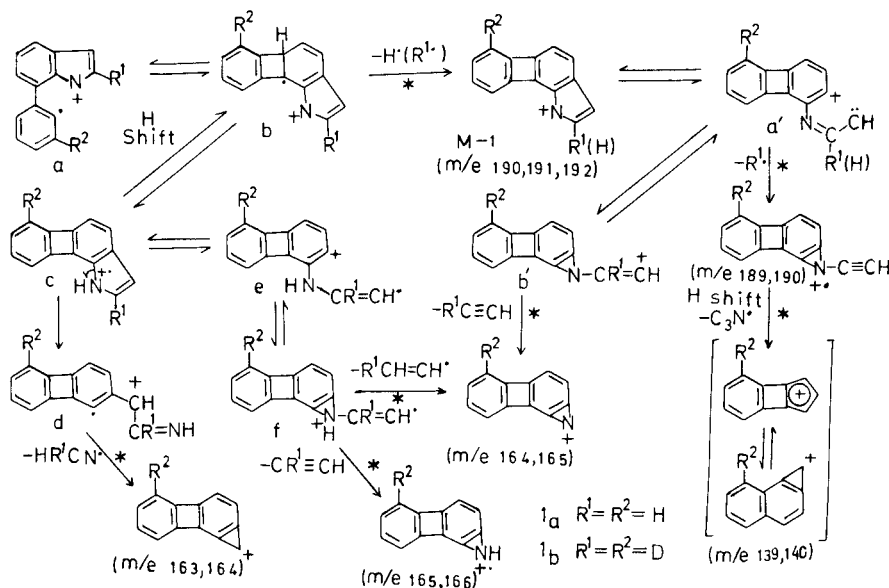
Because of its aromatic nature, **1a** yields a characteristically simple mass spectrum. The base peak, as expected, is the molecular ion (**M**) at m/e 191 and there is a relatively intense doubly charged ion at m/e 95.5 (relative intensity

16%). Other weakly to moderately intense ions are observed at m/e 190 (**M-1**), 164 and 163. Primary fragmentation routes for the **M** and **M-1** ions, elucidated with the aid of metastable ion studies, are shown in Scheme 1. Elemental compositions of the fragment ions were confirmed by exact mass measurements.



Scheme 1

Exact measurements (Table 1) indicate that the fragment ions at m/e 164 and 165 have elemental compositions $\text{C}_{12}\text{H}_6\text{N}$ and $\text{C}_{12}\text{H}_7\text{N}$, respectively, and not the isoelectronic C_{13}H_8 and C_{13}H_9 . These ions are therefore formed by losses of ethylene radical ($\text{C}_2\text{H}_3\cdot$) from **M** or acetylene from **M-1** (m/e 164) and by expulsion of acetylene from **M** (m/e 165). Since m/e 165 is an odd electron ion it is not very abundant. Our previous ascertainment that, in the electron im-



Scheme 2

parent spectrum of pyrrolophenothiazine, the fragment ion of *m/e* 165 with apparent composition $C_{13}H_9$, was formed

Table 1
Exact Mass Measurements

Ion	Empirical Formula	Calcd.	Observed
M ⁺	$C_{14}H_9N$	191.0734	191.0731
M-1	$C_{14}H_8N$	190.0657	190.0695
M-2	$C_{14}H_7N$	189.0579	189.0610
M-C ₂ H ₂	$C_{12}H_7N$	165.0578	165.0614
M-C ₂ H ₃	$C_{12}H_6N$	164.0500	164.0551
M-H ₂ CN	$C_{13}H_7$	163.0547	163.0541
M-C ₄ H ₂	$C_{10}H_6N$	140.0502	140.0501

by successive expulsions of sulfur followed by cyanide radical from the molecular ion [7] must therefore be incorrect. Other fragmentation pathways for M involve expulsion of H₂CN and C₄H₃ radicals to form fragment ions at *m/e* 163 and 140 respectively.

Proposed mechanisms for the fragmentation of the M and M-1 ions and for the formation of *m/e* 139 from the M-2 ion are outlined in Scheme 2. The spectrum of the deuterio derivative **1b** lends considerable support to these proposals. Thus, it is suggested that scission of the carbon-nitrogen bond of M occurs to give intermediate ion **a**, which rearranges to **b**. Ion **b** can either lose a hydrogen atom to give M-1 or experience a hydrogen atom shift to form **c**. Carbon-nitrogen bond scission in **c** provides ion **d**, which can then expell H₂CN radical giving *m/e* 163. An ion at *m/e* 164 with the elemental composition C₁₃H₈D in the spectrum of **1b** indicates that HDCN radical has been lost from the molecular ion. Alternatively, the carbon-carbon bond of **c** may cleave to form ion **e**, which can then rearrange to the aziridinium ion radical **f**. Expulsions of ethylene radical and acetylene from **f** give *m/e* 164 and 165, respectively. Peaks at *m/e* 165 and 166 in the spectrum of **1b** are consistent with the loss of a single deuterium atom in each of these transformations.

Fragmentation of the M-1 ion is believed to involve carbon-carbon bond scission to give the intermediate ion **a'**, which can either expell a hydrogen atom to give *m/e* 189 or acetylene to give *m/e* 164. A metastable ion at *m/e* 101.9 indicates that the *m/e* 139 ion (C₁₁H₇) is derived from *m/e* 189 via expulsion of C₃N radical ($-C\equiv N-C\equiv C$). Similar rearrangement processes are apparently involved in the genesis of the *m/e* 140 ion (C₁₀H₆N) from M and M-1 (see Scheme 1).

EXPERIMENTAL

The ¹H nmr spectra were recorded on a Nicolet 360 WB spectrometer and the uv spectrum was recorded on a Perkin-Elmer 298 spectrometer.

The mass spectra were recorded on a Varian MAT 311A double focusing mass spectrometer at 70 eV. The samples were introduced by a direct inlet probe and were heated at a rate of about 450° in 200 seconds. The metastable ion spectra were obtained by focusing on the parent ion and scanning the electrostatic sector and magnetic fields in the first field free region of the spectrum at a rate such that the ratio E/B remained constant at a constant accelerating voltage. The high resolution spectra were recorded at a resolution of 7000 and processed with a Varian SS-200 data system. The temperature was raised manually to obtain the optimum spectrum. Compound purity was checked by tlc and gc (Varian model 3700) with fid.

Pyrrolo[3,2,1-*jk*]carbazole (**1a**).

A 50 ml round-bottomed flask fitted with a reflux condenser with a rubber septum was dried, flushed with nitrogen and charged with 1.8 mmole of bis(1.5-cyclooctadiene)nickel(0) and 1.8 mmoles of 2,2'-bipyridyl via syringe. Anhydrous degassed tetrahydrofuran, 5.0 ml, was added. Immediately a dark violet color appeared. Pyrrolo[3,2,1-*kl*]phenothiazine, 150 mg, 0.45 mmole, was introduced and the resulting mixture was magnetically stirred at 60° for 65 hours. After cooling, the mixture was filtered through a short neutral alumina column. The filtrate was then evaporated and purified by flash chromatography with toluene/hexane, 5/95, as eluent, giving 62 mg (72%) of pyrrolo[3,2,1-*jk*]carbazole as a white powder, mp 89-90°; nmr (deuteriochloroform): 8.08 (H-6), 7.90 (H-5), 7.79 (H-3), 7.73 (H-1), 7.68 (H-9), 7.51 (H-4), 7.47 (H-8), 7.32 (H-7), 6.86 (H-2), J_{H-1,H-2} = 3.1 Hz, J_{H-1,H-5} = 0.5 Hz, J_{H-3,H-4} = 7.4 Hz, J_{H-3,H-5} = 0.5 Hz, J_{H-4,H-5} = 7.4 Hz, J_{H-6,H-7} = 7.8 Hz, J_{H-6,H-8} = 1.2 Hz, J_{H-6,H-9} = 0.7 Hz, J_{H-7,H-8} = 7.8 Hz, J_{H-7,H-9} = 1.0 Hz, J_{H-8,H-9} = 8.0 Hz; ms (low resolution): *m/e* 192 (M+1, 15.9), 191 (M, 100), 190 (M-1, 17.6), 189 (4.3), 188 (2.2), 165 (2.1), 164 (8.3), 163 (10.0), 162 (1.8), 140 (1.2), 139 (1.0), 138 (1.4), 137 (1.5), 112 (1.1), 96 (2.5), 95.5 (M/2, 16.0), 95 (2.1), 94.5 (3.2), 88 (1.2), 87 (1.7), 86 (1.2), 82.5 (4.2), 82 (6.2), 81.5 (9.9), 81 (5.4), 75 (2.4), 74 (1.7), 63 (3.7), 62 (1.8), 61 (2.6), 55 (1.0), 51 (1.5), 50 (1.5); uv (methanol): max 218 nm (47,750), 255 (19,210), 265 (29,620), 272 (29,800), 276 (29,080), 306 (6,820), 331 (9,840); min 195 (27,800), 258 (19,030), 269 (21,540), 274 (24,950), 286 (2,440), 313 (6,750).

Anal. Calcd. for C₁₄H₉N: C, 87.93; H, 4.74; N, 7.32. Found: C, 87.85; H, 4.86; N, 7.28.

1,9-Dideuteriopyrrolo[3,2,1-*jk*]carbazole (**1b**).

This compound was prepared from **2b** according to the same procedure as for the preparation of **1a** giving **1b** in a 70% yield, mp 89-90°; ms (low resolution): *m/e* 195 (4.2), 194 (27.6), 193 (M, 100), 192 (40), 191 (10.9), 190 (3.5), 189 (1.4), 167 (1.8), 166 (5.8), 165 (10.4), 164 (6.7), 163 (2.0), 141 (1.4), 140 (1.3), 139 (1.7), 138 (1.6), 114 (1.2), 92 (4.2), 96.5 (M/2, 14.5), 96 (5.8), 95.5 (3.0), 89 (1.2), 87 (1.9), 86 (1.2), 83.5 (2.8), 83 (5.9), 82.5 (7.3), 82 (6.5), 81.5 (3.2), 76 (1.5), 75 (2.3), 74 (1.6), 70 (1.0), 69.5 (1.5), 69 (1.0), 64 (2.6), 63 (2.9), 62 (1.8), 61 (1.2), 52 (1.3), 51 (1.8), 50 (1.3).

Anal. Calcd. for C₁₄H₇D₂N: C, 87.03; H, 5.72; N, 7.25. Found: C, 86.99; H, 5.78; N, 7.21.

EXPERIMENTAL

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- [3] A. R. Martin, V. M. Paradkar, G. W. Peng, R. C. Speth, H. I. Hamamura and A. S. Horn, *J. Med. Chem.*, **25**, 865 (1980).
- [4] A. R. Martin, S. H. Kim, H. I. Yamamura and A. S. Horn, *ibid.*, **23**, 938 (1980).
- [5] A. Hallberg, D. Deardorff and A. Martin, *Heterocycles*, **19**, 75 (1982).
- [6] L. C. Vishwakarma, A. Hallberg, T. Dahlgren and A. R. Martin, *J. Heterocyclic Chem.*, **20**, 995 (1983).

- [7] L. C. Vishwakarma, A. Hallberg and A. R. Martin, *J. Heterocyclic Chem.*, **20**, 1199 (1983).
- [8] J. J. Eisch and K. R. Im, *J. Organometal. Chem.*, **139**, C 51 (1977).
- [9] J. J. Eisch, L. E. Hallenbeck and K. I. Han, *J. Org. Chem.*, **48**, 2963 (1983).
- [10] E. Dinjus, I. Gorski, E. Uhlig and H. Z. Walther, *Anorg. Allg. Chem.*, **422**, 75 (1976).
- [11] T. Dahlgren, A. Hallberg and A. R. Martin, *Heterocycles*, **20**, 33 (1983).
- [12] S. P. Hiremath and R. S. Hasmane, *Adv. Heterocyclic Chem.*, **15**, 277 (1973).
- [13] A. Hallberg, T. Dahlgren, A. Martin and K. Christiansen, *J. Heterocyclic Chem.*, **20**, 37 (1983).
- [14] A. Hallberg and A. R. Martin, *J. Heterocyclic Chem.*, **21**, 837 (1984).