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REACTION OF PYRIDO[1,2-a]BENZIMIDAZOLE AND
TETRAHYDROPYRIDO[1,2-a]BENZIMIDAZOLE WITH ACETYLENEDICARBOXYLIC ESTER

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Previously unknown polynuclear condensed systems with bridgehead nitrogen atoms have been obtained by treating acetylenedicarboxylic ester with pyrido[1,2-a]-benzimidazole and tetrahydropyrido[1,2-a]benzimidazole.

We have developed a convenient method for the synthesis of pyrido[1,2-a]benzimidazole (I) [1] allowing us to expand studies of its properties. With the aim of obtaining new polynuclear condensed heterocyclic compounds with bridging nitrogen atoms we have turned to reactions of pyridobenzimidazole (I) (and the derived tetrahydropyrido[1,2-a]benzimidazole) with acetylenedicarboxylic ester (ADCE).

Both of these compounds can be regarded as 1,2-disubstituted benzimidazoles. Thus their reaction with ADCE can be the same as benzimidazole [2] but with the formation of more complex heterocycles.

The reaction of pyrido[1,2-a]benzimidazole (I) with ADCE in benzene takes place quantitatively at 20°C. In addition, adducts are formed with two and three molecules of ADCE and are separated using column chromatography. The first of these is red, crystalline material

TABLE 1. PMR Spectral Parameters for II, IV-VI

Com- pound*	Chemical shifts,† δ , ppm										CH ₃ O	J, Hz
	1-H	2-H	3-H	4-H	5-H	6-H	7-H	8-H	10-H	11-H		
II	6,65	7,50	7,08	7,41	9,12	8,02	8,56	7,80	—	—	3,26; 3,37; 3,488; 3,492	(1—2) 7,5; (1—3) 1,2; (1—4) 0,4; (2—3) 7,5; (2—4) 1,2; (3—4) 7,5; (5—6) 6,0; (5—7) 1,4; (5—8) 0,7; (6—7) 7,8; (6—8) 1,5; (7—8) 8,0
V	6,69	7,03	7,03	6,69	3,67	2,01	1,53	1,53	—	—	3,71; 3,73; 3,78; 4,02	—
VI	6,90	7,10	7,10	6,90	3,85	1,98	2,45	—	5,47	5,91	3,49; 3,65; 3,69; 3,82	$^3J_{10,11}=5$
IV	7,69	7,23	7,21	7,28	4,07	2,11	2,02	3,09	—	—		

*For IV-VI, the chemical shifts for the methylene protons are assigned as the center of the corresponding multiplets.

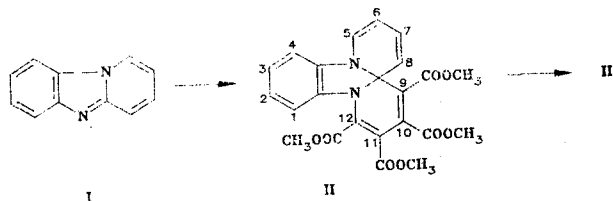
†Benzene ring protons 1H-4H, nitrogen ring protons 5H-8H, 10H, 11H.

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whose color is apparently due to the poly-conjugated molecular system. The structure of this material was shown by PMR spectroscopy to be 9,10,11,12-tetra(carbomethoxy)bis-pyrido[1,2-a:2',1'-b]benzimidazole (II). Assignment of all of the PMR signals can be made for II by means of double resonance and by comparison with the parameters for the starting pyridobenzimidazole I [1] (Table 1). The PMR spectrum of II shows two four-spin systems for the protons of the dihydropyridine and the benzene fragments in the molecule with characteristic parameters. The large increments for the chemical shifts of protons 1 and 3 to high field (1.26 and 0.42 ppm, respectively, when compared with I [2]) are due to the change in hybridization of the imidazole nitrogen atom from sp^2 in I to sp^3 in II. The presence of the quaternary carbon atom (C_{9a} in II) is shown by a ^{13}C NMR signal at δ 79.5 ppm.

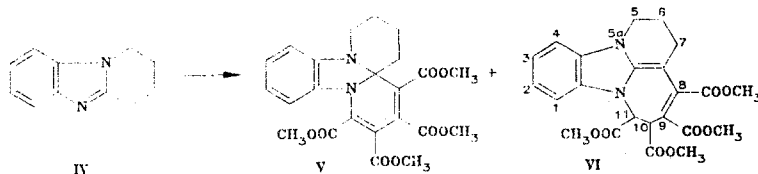
The second adduct (III), formed in significantly larger quantities, is a yellow crystalline material with PMR and ^{13}C NMR data in conflict with one another and not permitting an unequivocal structural assignment. Detailed NMR parameters for III will be reported after x-ray investigation.

The studied reaction occurs in two stages. Adduct II is initially formed and this reacts with a third molecule of ADCE to give III. Direct reaction of isolated II with ADCE gives III in 90% yield.



The adducts are also produced from the reaction of tetrahydropyrido[1,2-a]benzimidazole (IV) with ADCE. The basic product of the reaction (an analog of II) is the red, crystalline 5,6,7,8-tetrahydro-9,10,11,12-tetra(carbomethoxy)bispypyrido[1,2-a:2',1'-b]benzimidazoline (V).

In significantly smaller yield there is also obtained the yellow crystalline 5,5a,6,7,10,11-hexahydro-8,9,10,11-tetra(carbomethoxy)pyrido[1,2-a]azepino[2',1'-b]benzimidazoline (VI).



The molecule VI contains the fragment 9,10-dihydro-azepino[1,2-a]benzimidazole. Compounds of this type, obtained by reaction of benzimidazoles with ADCE have been described in [2].

A particular characteristic of the PMR spectrum of adduct VI is the presence of an isolated system of two methine protons with $\delta = 5.47$ and 5.91 ppm for C₍₁₀₎ and C₍₁₁₎, respectively (Table 1). The small vicinal spin-spin coupling for these protons ($^3J = 5$ Hz) is apparently due to the trans orientation of the carbomethoxy groups. It should also be mentioned that in the adducts V and VI the four spin system for the benzene ring protons has degenerate character on account of the virtual coincidence of 1H with 4H and of 2H with 3H. The 1H and 4H signals in V and VI are found at significantly higher field than those in IV, the highest shift being observed for 1H associated with the change in hybridization of the neighboring nitrogen atom. The signals for the methylene protons of the piperidine related rings in V and VI occur as complex multiplets.

The ^{13}C NMR spectra of V and VI clearly show signals for the methylene carbon atoms of the reduced heterocycles (corresponding to four and three carbons, respectively) as well as the tertiary carbons C₁₀ and C₁₁.

EXPERIMENTAL

PMR and ^{13}C NMR spectra (internal standard TMS) were measured on Bruker superconducting magnet instruments (WM-250 and WM-400) at 250 and 400 MHz for protons and 63 and 100.6 MHz for carbons, respectively. UV spectra were obtained on a Specord UV-VIS using ethanol solvent and IR spectra as KBr tablets. Mass spectra were run on a Varian MAT-44. Chromatography employed silica gel L 100/160 columns and applied layer Silufol grade UV 254 material.

9,10,11,12-Tetra(carbomethoxy)bispyrido[1,2-a:2',1'-b]benzimidazoline (II). A solution of I (0.4 g, 2.4 mmoles) and ADCE (1 g, 7 mmoles) in benzene (20 ml) was allowed to stand at 20°C for 5 h. After evaporation of benzene the residue was chromatographed (30 × 1 cm column). Initially, a mixture of ether and hexane (2:1) removed III (0.62 g, 44%) as yellow crystals with mp 151°C (with decomposition, from ether). R_f 0.36 (ether). Found: C 58.9; H 4.5; N 4.8%; M^+ 594. $C_{29}H_{26}N_2O_{12}$. Calculated: C 58.6; H 4.4; N 4.7%; M 594.

Subsequently adduct II (0.35 g, 33%) was eluted using ethyl acetate as red crystals, mp 171–172°C (from ethyl acetate). R_f 0.27 (mixture of ethyl acetate/alcohol, 3:1). ^{13}C NMR spectrum (DMSO- D_6): 79.5 ($C_{(sa)}$), 130.3 ($C_{(s)}$), 145.5 ppm ($C_{(s)}$); $J_{C5, H-5} = 189$ Hz. IR spectrum: 1750, 1720 cm^{-1} (CO). UV spectrum λ_{max} (log ϵ): 210 (4.40), 275 (4.05), 320 (4.00), 430 (3.80), 570 (sh) nm (3.20). Found: C 61.3; H 4.5; N 5.9%; M^+ 452. $C_{23}H_{20}N_2O_8$. Calculated: C 61.1; H 4.4; N 6.2%; M 452.

A solution of adduct II (0.1 g, 0.22 mmole) and ADCE (0.03 g, 0.24 mmole) in benzene (11 ml) was held for 2 h at 20°C. The residue was chromatographed to give III (0.12 g, 91%) with mp 150°C. A mixed melting point with the sample described above was not depressed.

5,6,7,8-Tetrahydro-9,10,11,12-tetra(carbomethoxy)bispyrido[1,2-a:2',1'-b]benzimidazoline (V) and 5,5a,6,7,10,11-Hexahydro-8,9,10,11-tetra(carbomethoxy)pyrido[1,2-a]-azepino[2',1'-b]-benzimidazoline (VI). A solution of IV (0.86 g, 5 mmoles) and ADCE (1.5 g) in benzene (25 ml) was stirred for 4 h at 20°C. The reaction product was column chromatographed (30 × 1 cm column) using a mixture of ether and hexane (1:1) as eluent. Adduct V (0.98 g, 43%) was obtained as red crystals with mp 176.5–178°C (ether) and $R_f = 0.78$ (ether). ^{13}C NMR spectrum ($CDCl_3$): 16.8 ($C_{(7)}$); 21.9 ($C_{(s)}$); 29.7 ($C_{(s)}$); 43.3 ($C_{(s)}$); 83.1 ($C_{(sa)}$); 103.5 ($C_{(4a)}$); 110.0 ($C_{(4)}$); 111.4 ($C_{(1)}$); 119.3 ($C_{(s)}$); 125.9 ($C_{(2)}$). UV spectrum λ_{max} (log ϵ): 219 (4.28), 260 (4.10), 327 (3.80), 465 nm (3.80). Found: C 60.7; H 5.3; N 6.3%; M^+ 456. $C_{23}H_{24}N_2O_8$. Calculated: C 60.5; H 5.3; N 6.1%; M 456.

Following this was obtained the yellow crystalline VI (0.28 g, 12%) with mp 196–198°C (ether) and $R_f = 0.3$ (identical solvent system). UV spectrum λ_{max} (log ϵ): 219 (4.30); 260 (3.97); 307 (3.62); 460 nm (4.80). Found: C 60.7; H 5.4; N 6.1%; M^+ 456. $C_{23}H_{24}N_2O_8$. Calculated: C 60.5; H 5.3; N 6.1%; M 456.

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