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PYRROLOINDOLES.
17.* SYNTHESIS AND CONDENSATION REACTIONS OF BENZO[e]PYRROLO[3,2-g]INDOLE-2,9-DICARBOXYLIC ACID DICHLORIDE

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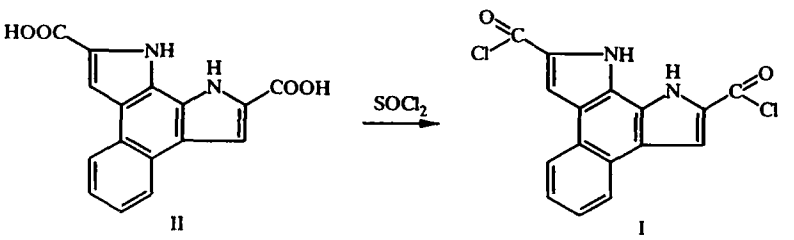
1H,10H-benzo[e]pyrrolo[3,2-g]indole-2,9-dicarboxylic acid dichloride has been synthesized and condensed with amines and phenols to give the corresponding diamides and activated diesters. The mass spectra of the dichloride and several diamides have been investigated.

We have previously [2] reported the synthesis and reactions of benzo[e]pyrrolo[3,2-g]indole dihydrazides. With the aim of preparing α-substituted benzopyrroloindoles we have now synthesized 1H,10H-benzo[e]pyrrolo[3,2-g]indole-2,9-dicarboxylic acid dichloride (I) and studied its reactivity.

Dichloride I is prepared by treatment of 1H,10H-benzo[e]pyrrolo[3,2-g]indole-2,9-dicarboxylic acid (II) with thionyl chloride.



II I

The IR spectrum of I shows a characteristic indole NH group stretching band at 3370 cm^{-1} and a strong band for the absorption of the C=O group at 1750, 1665 cm^{-1}.

In the PMR spectrum of I the lowest field, broad signal at 11.83 ppm is assigned to the protons of the N−H group. The signals for the 3-H and 8-H protons appear as a doublet at 7.74 ppm. The protons of the naphthalene ring form two signals as a double doublet with typical ortho- and meta- spin spin couplings $J_{4,5}$ = 9.32 and $J_{4,6}$ = 6.22 Hz.

The reactivity of dichloride I was studied under acceptor catalyzed condensation conditions with amines and phenols. The use of an excess of the amines is dictated by the need to take up the evolved acid. Condensation with anthranilic acid, sulfanilamide, and dimethylamine needs the addition of triethylamine (TEA) as catalyst in order to increase the yield of the amides (to 65-75%). Hence we were able to prepare the α,α'-disubstituted benzopyrroloindoles III-XI.

The synthesized amides III-XI are insoluble in ether and weakly soluble in THF and N-methylmorpholine which prevents the reduction of diamide X with lithium aluminium hydride. Reduction of a suspension of X with $LiAlH_4$ in THF [3] gives only unchanged starting amide.

We have synthesized the novel benzopyrroloindole diesters XII-XIV by condensation of the dichloride I with phenols. The reaction proceeds smoothly in the presence of TEA.

*For Communication 16 see [1].

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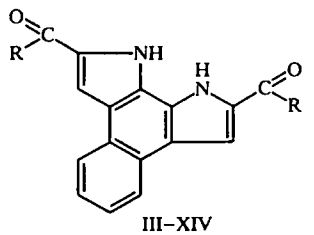
TABLE 1. UV and IR Spectral Data for Compounds III-XIV

Compound	IR Spectrum, ν, cm^{-1}				UV Spectrum, λ_{max}(log ε)
	NH	amide I	amide II	SO_2, NO_2	
III	3320, 3270	1660	1520	–	204(4,70), 234(4,59), 240(4,62), 253(4,55), 272(4,79), 288(4,73), 355(4,78), 368(4,78)
IV	3425, 3280	1680	1540	–	205(4,85), 242(4,69), 273(4,38), 290(4,39), 357(4,50), 374(4,50)
V	3370, 3340	1650	1535	–	227(4,41), 236(4,48), 251(4,48), 266(4,57), 280(4,58), 333(4,51), 350(4,50)
VI	3410...3230	1600	1510	–	210, 238, 250, 269, 280, 342, 350
VII	3370, 3230	1645	1580	–	209, 229, 237, 249, 267, 278, 338, 350
VIII	3450...3330	1600	1520	–	238(4,37), 281(4,21), 348(4,17), 370(4,31), 398(4,32)
IX	3210...3100	1680, 1660 sh	1540	1320, 1120	210, 236, 266, 278, 352
X	3330	1620	–	–	227, 237, 250, 268, 279, 337, 349
XI	3450, 3250	1665	1570	–	210, 237, 250, 268, 279, 341, 350
XII	3420	1700(C=O)		–	212, 230, 238, 246, 268, 281, 351, 368
XIII	3390	1740(C=O)		1300, 1540	217, 234, 250, 270, 280, 354, 366
XIV	3440	1750(C=O)		1310, 1550	239(4,41), 249(4,39), 269(4,36), 279(4,31), 357(4,11)

TABLE 2. PMR Spectra of Certain Compounds in DMSO-D_6

Compound	Chemical shift, δ, ppm							Spin-spin coupling, Hz
	1-H, 10-H	N−H_{amide}	3-H, 8-H	4-H, 7-H	5-H, 6-H	2'-H, 6'-H	3'-H, 5'-H	
I	11,83 br. s	—	7,72 d	8,29 dd	7,46 dd	—	—	J_{13} = 2,19, J_{45} = 9,32, J_{46} = 6,22
III	11,95 br. s	10,28 s	8,06 br.s	8,21 m	7,54 m	7,58 d, 7,12 m (4'-H)	7,40 m	$J_{2'3'}$ = 8,04
IV	12,0 br. s	10,50 s	8,15 s	7,55 br. s	8,20 br.s	7,93 d	7,50 d	$J_{2'3'}$ = 8,04
V	11,63 br. s	7,89 s	7,61 s	7,45 br.s	8,11 br.s	1,79...2,14 (Ad)		—
VIII	12,01 br. s	11,90 br. s	7,70 d	8,17 m	7,44 m	8,16m, 6'-H, 7,60m 4'-H	8,72m,3'-H, 7,16m,5'-H	J_{13} = 1,47
X	11,78 br. s	—	7,62 s	8,31 dd	7,44 dd	3,25 s (CH_3)		J_{45} = 6,2, J_{46} = 3.1
XI	11,90 br. s	10,63 br.s NH(α), 10,93 br.s NH(β)	7,93 s	8,17 dd	7,53 dd	8,88 d	8,01 d	J_{45} = 8,5, J_{46} = 5,12, J_{23} = 8,11
XII	12,17 br. s	—	8,33 s	8,47 m	7,55 m	—	—	—
XIII	12,54 br. s	—	8,16 s	8,42 br. s	7,54 br.s	7,72 d	8,40 d	$J_{2'3'}$ = 8,40
XIV	12,6 br. s	—	8,24 d	8,44 m	7,55 m	8,06 d (6'-H)	8,95 d (3'-H), 18,73 dd (5'-H)	J_{13} = 1,83, $J_{3'5'}$ = 2,56, $J_{5'6'}$ = 9,13

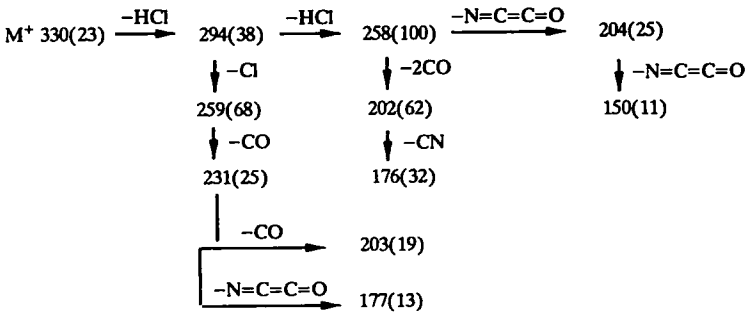


III–XIV

III R = C_6H_5NH; IV R = *p*-ClC_6H_4NH; V R = AdNH; VI R = piperazinyl;
VII R = methylpiperazinyl; VIII R = *o*-$HO_2CC_6H_4NH$; IX R = *p*-$H_2NSO_2C_6H_4NH$; X R = $N(CH_3)_2$;
XI R = 4-pyridyl -CONHNH; XII R = C_6Cl_5O; XIII R = *p*-$NO_2C_6H_4O$; XIV R = 2,4-$(NO_2)_2C_6H_3O$

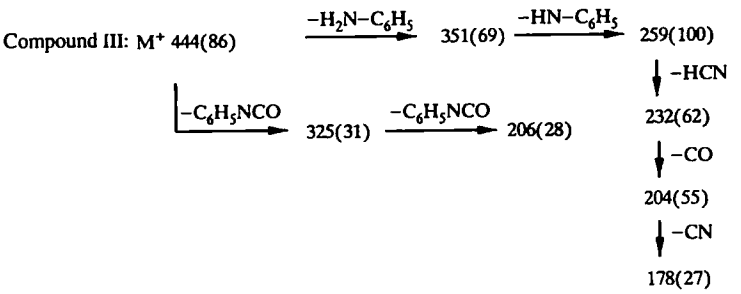
The IR absorption spectra of the diamides III-XI (Table 1) show stretching vibrations for the N–H group and bands characteristic of amide groups.

Interesting results were obtained when analyzing the mass spectra of the dichloride I and of several diamides. The mass spectrum of I shows a molecular ion M^+ peak of comparatively low intensity. In the first two stages there occur consecutive eliminations of two molecules of hydrogen chloride. The $[M\text{-}HCl\text{-}HCl]^+$ ion formed is the most intense in the spectrum. Further fragmentation of this ion at 258* (100%) occurs similarly by two pathways. An important difference from known schemes for fission of indoles is the occurrence of a loss of N=C=C=O (fission of the pyrrole ring). The spectrum shows another route for fission of the $[M-HCl]^+$ ion (294) to form the ion at 259 (68). Formation of this ion also plays an important role in the fragmentation of diamides III, IV, and X. The most likely scheme for fission of compound I bearing in mind all of these spectral peaks is as shown:

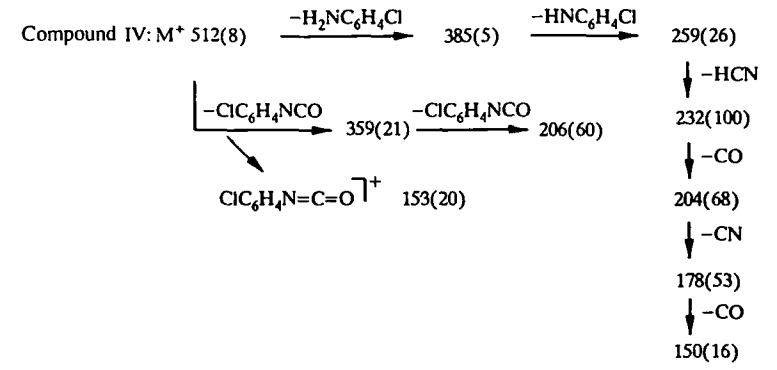


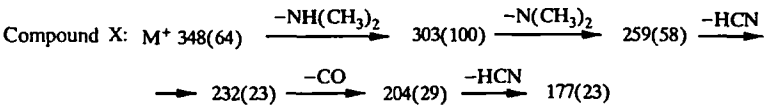
An interesting fragmentation occurs for the molecular ions of diamides III, IV, and X. After fission of the bonds at both carbonyl groups due to elimination of the corresponding parts or molecules there is formed a fragment with mass 259 which has maximum or high peak intensity and further undergoes consecutive loss of HCN and CO groups. The mass spectra of diamides III and IV also includes a process of elimination of arylisocyanates from the molecular ions. Fission of the arylisocyanate ion at 119 (compound III) and 153 (compound IV) is registered via the appearance of discrete peaks.

Fragmentation Scheme



*Here, and subsequently, m/z values are give for the peaks.





EXPERIMENTAL

Monitoring of the course of a reaction and of the purity of the compounds was carried out on Silufol UV-254 plates. IR Spectra were obtained on a UR-20 instrument in Vaseline oil and UV spectra on a Specord spectrophotometer using ethanol solvent. PMR Spectra were recorded on a WP-200 SY instrument with TMS internal standard. Mass spectra were taken on a Ribermag R-10-10 chromato-mass spectrometer with an ionization energy of 70 eV and direct introduction of samples into the ion source.

1H,10H-Benzo[e]pyrrolo[3,2-g]indole-2,9-dicarboxylic Acid Dichloride (I). A suspension of 1H,10H-benzo[e]-pyrrolo[3,2-g]indole-2,9-dicarboxylic acid (II, 0.3 g, 1 mmole) and thionyl chloride (10 ml) was refluxed with stirring for 5 h. The reaction mixture was cooled to 35-40°C and the precipitate was washed several times with absolute ether and dried *in vacuo*. Yield 0.24 g (90%). Yellow crystals, mp 240-241°C. R_f 0.77 (benzene-ether, 3:1). Found, %: C 58.4; H 2.8; N 8.5; Cl 21.1. $C_{16}H_8N_2Cl_2O_2$. Calculated, %: C 58.1; H 2.4; N 8.5; Cl 21.2.

2,9-Di(phenylcarboxamido)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (III). Aniline (1.2 ml, 0.01 mole) in dioxane (5 ml) was added to a solution of the dichloride I (0.1 g, 0.3 mmole) in absolute dioxane (15 ml) and the product was stirred for 30 min at room temperature. The reaction mixture was poured into a mixture of HCl and water (1:1). The precipitated crystals were filtered off, washed with water, and dried. Compound III was purified on a silica gel column using pentane-ether eluent (1:2). Yield 0.06 g (63%). Cream crystals, mp 328°C (decomp.). R_f 0.80 (benzene–acetone, 3:1). Found, %: C 75.5; H 4.4; N 12.6. $C_{28}H_{20}N_4O_2$. Calculated, %: C 75.5; H 4.5; N 12.6.

2,9-Di(p-chlorophenylcarboxamido)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (IV). Prepared similarly to compound III from the dichloride I (0.1 g, 0.3 mmole) and p-chloroaniline (0.1 g, 1.2 mmole). Yield 0.11 g (73%), mp 166-167°C. R_f 0.58 (ammonia–propan-2-ol, 1:5). Found, %: C 65.6; H 3.1; N 10.7; Cl 13.5. $C_{28}H_{18}Cl_2N_4O_2$. Calculated, %: C 65.5; H 3.5; H 10.9; Cl 13.8.

2,9-Di(adamantylcarboxamido)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (V). Aminoadamantane (0.6 g, 4 mmole) in dioxane (10 ml) was added to a solution of I (0.3 g, 1 mmole) in dioxane (20 ml). The reaction mixture was stirred for 1 h at 70°C. The solution was cooled and the precipitated crystals were filtered off, washed with absolute ether, and dried. Yield 0.34 g (68%). Yellow crystals, mp 283-284°C. R_f 0.63 (benzene–acetone, 4:1). Found, %: C 76.8; H 6.7; N 9.7. $C_{36}H_{40}N_4O_2$. Calculated, %: C 77.1; H 7.2; N 10.0.

2,9-Di(piperazino-N-carbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (VI). Obtained similarly to compound V from I (0.05 g, 0.15 mmole) and piperazine (0.1 g, 1 mmole). Yield 0.04 g (67%). Yellow colored crystals, mp 339°C (decomp.). Found, %: C 66.8; H 6.3; N 19.1. $C_{24}H_{26}N_6O_2$. Calculated, %: C 67.0; H 6.0; N 19.5.

2,9-Di(p-methylpiperazino-N-carbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (VII). Obtained similarly to III from I (0.1 g, 0.3 mmole) and p-aminomethylpiperazine (0.2 ml) in dioxane (15 ml). The precipitated crystals were filtered off,

washed with ether, and dried in an inert gas atmosphere. Yield 0.09 g (60%), mp 240°C (from alcohol with ether, decomp.). Found, %: C 64.1; H 6.6; N 22.4. $C_{26}H_{32}N_8O_2$. Calculated, %: C 63.9; H 6.6; N 22.0.

2,9-Di(anthranyl-N-carbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (VIII). A solution of anthranilic acid (0.04 g, 0.3 mmole) in dioxane (5 ml) was added to a solution of I (0.05 g, 0.15 mmole) in absolute dioxane (8 ml). Triethylamine (1-2 drops) was added with stirring to the reaction mixture and the product held for 30 min. The precipitated yellow crystals were filtered off, washed with absolute ether, and dried. Yield 0.06 g (75%), mp 191°C (decomp.). Found, %: C 67.6; H 4.0; N 9.4. $C_{30}H_{20}N_4O_6$. Calculated, %: C 67.7; H 3.8; N 10.2.

2,9-Di(benzenesulfonamidocarboxamido)-1H,10H-benzo[e]pyrrolo[3.2-g]indole (IX). Obtained similarly to VIII from I (0.05 g, 0.15 mmole) and p-aminobenzenesulfonamide (0.05 g, 0.3 mmole). Yield 0.06 g (67%). Compound IX is a red colored powder, mp 308°C (decomp.). Found, %: C 55.6; H 3.5; N 13.9; S 10.1. $C_{28}H_{22}N_6O_6S$. Calculated, %: C 55.5; H 3.7; N 14.0; S 10.6.

2,9-Di(dimethylcarboxamido)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (X). Obtained similarly to VIII from dichloride I (0.1 g, 0.3 mmole)and aqueous dimethylamine solution (33%, 3 ml). Yield 0.07 g (70%), mp 320°C (decomp.). R_f 0.63 (ethanol). Found, %: C 69.3; H 5.9; N 15.6. $C_{20}H_{20}N_4O_2$. Calculated, %: C 69.0; H 6.0; N 16.1;

2,9-Di(isonicotinoylhydrazidocarbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (XI). Prepared similarly to III from I (0.2 g, 0.6 mmole) and isonicotinoylhydrazine (0.17 g, 1 mmole). The precipitated crystals were filtered off, washed with absolute ether, and dried in an inert gas atmosphere. Yield 0.27 g (90%), mp 230°C (decomp.). R_f 0.48 (ammonia–propan-2-ol, 1:3). Found, %: C 63.2; H 4.0; N 21.5. $C_{28}H_{20}N_8O_4$. Calculated, %: C 63.2; H 3.8; N 21.1.

2,9-Di(pentachlorophenoxycarbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (XII). Obtained from dichloride I (0.1 g, 0.3 mmole) and pentachlorophenol (0.16 g, 0.6 mmole), similarly to VIII. Compound XII was precipitated by absolute ether. Yield 0.12 g (60%), mp 299°C (decomp.). Found, %: C 42.3; H 1.3; N 2.9; Cl 44.6. $C_{28}H_8Cl_{10}N_2O_4$. Calculated, %: C 42.5; H 1.0; N 3.5; Cl 44.9.

2,9-Di(p-nitrophenoxycarbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (XIII). Obtained similarly to VIII from I (0.1 g, 0.3 mmole) and p-nitrophenol (0.08 g, 0.6 mmole). Compound XIII is precipitated by absolute ether. Yield 0.1 g (63%), mp 168-169°C. Found, %: C 62.9; H 3.0; N 10.3. $C_{28}H_{16}N_4O_8$. Calculated, %: C 62.7; H 3.0; N 10.4.

2,9-Di(2,4-dinitrophenoxycarbonyl)-1H,10H-benzo[e]pyrrolo[3,2-g]indole (XIV). Obtained similarly to VIII from dichloride I (0.1 g, 0.3 mmole) and 2,4-dinitrophenol (0.11 g, 0.6 mmole). Yield 0.14 g (70%), mp 245-246°C. R_f 0.67 (propan-2-ol–ammonia, 1:2). Found, %: C 53.4; H 2.3; N 13.6. $C_{28}H_{14}N_6O_{12}$. Calculated, %: C 53.7; H 2.2; N 13.4.

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