

# Action of 1,2-Diamines and *o*-Aminophenols on 1-Alkyl-3-carboxyindole-2-acetic Acid Anhydrides. Preparation of New Ring Systems

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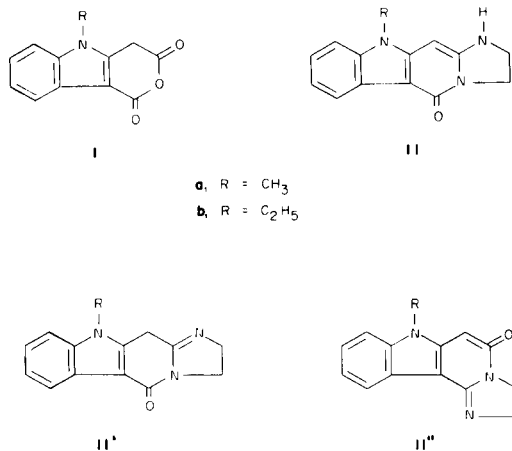
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1-Alkyl-3-carboxyindole-2-acetic acid anhydrides (I) react with ethylenediamine and with *o*-phenylenediamine to give directly 10-alkylimidazo[3,2:1',2']pyrido[4,5-*b*]indol-5(1*H*)-ones (II) and 5,6-dihydro-5-alkyl-13*H*-indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazol-13-one (V), respectively. However, anhydrides I react with *o*-aminophenol and with *o*-aminothiophenol to give carboxyindole-acetanilide derivatives IX, which can be cyclised to indolo[2',3':4,5]pyrido[2,1-*b*]benzoxazolone and indolo[2',3':4,5]pyrido[2,1-*b*]benzthiazolone (XI). Some derivatives of II and V were prepared to help in elucidating the structures.

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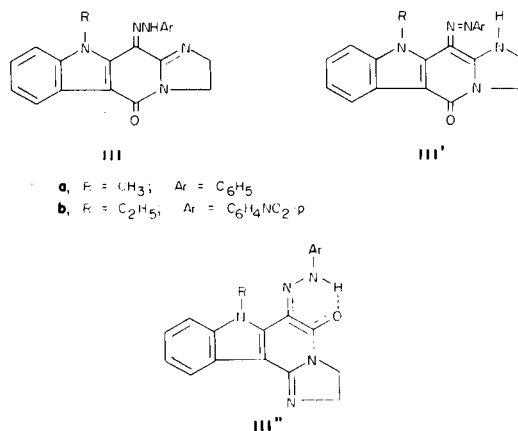
It has been found by Trofimov (1) that 1-alkyl-3-carboxyindole-2-acetic acid anhydrides (I) react with primary amines to give 1-alkyl-3-carboxyindole-2-acetanilide derivatives. We would like here to report on the reaction of anhydrides I with ethylenediamine, *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol. The reaction products of I with the latter three amino compounds yield new ring systems.

When anhydrides I were heated with ethylenediamine at 170° for 15 minutes, there were obtained 2,3-dihydro-10-alkylimidazo[3,2:1',2']pyrido[4,5-*b*]indol-5(1*H*)-ones (II).



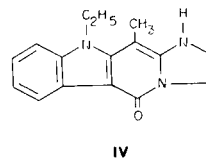
The assignment of structure II, and not II' or II'', to the reaction products is based on the facts that, (a) the ir spectrum of IIb showed bands at 1640 cm<sup>-1</sup> (C=O) and 3280 cm<sup>-1</sup> (NH), (b) the nmr spectrum (DMSO-d<sub>6</sub>) of IIb showed signals at  $\delta$  1.30 ppm (triplet, 3H, CH<sub>3</sub>),  $\delta$  4.0 ppm (m, 7H, 3CH<sub>2</sub> + NH), 5.75 ppm (s, 1H, ethylenic proton), and (c) CO absorption appeared at the same wave length in the ir spectra of both IIb and its coupling product (see below).

Compounds II coupled with arenediazonium salts in pyridine to yield the 4-arylazo derivatives, more properly represented as the arylhydrazones III.



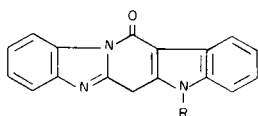
The assignment of structure III to the coupling products is based on the facts that, (a) the uv spectrum of IIIa showed an absorption maximum at 412 nm, similar to hydrazones which are known to exhibit strong absorption at wave lengths higher than 320 nm (2) and (b)  $\nu$  C=O in IIb and IIIa occurs at identical positions ( $\sim$  1640 cm<sup>-1</sup>). If compound IIIa had structure III'' it would reveal a large downward shift in  $\nu$  C=O due to conjugation and strong chelation between the hydrazone hydrogen and the C=O group (3).

Methylation of IIb with methyl iodide in aqueous ethanolic sodium carbonate yielded 2,3-dihydro-10-ethyl-11-methylimidazo[3,2:1',2']pyrido[4,5-*d*]indol-5(1*H*)-one (IV).



The ir spectrum of IV showed bands at 1645 cm<sup>-1</sup> (CO) and 3310 cm<sup>-1</sup> (NH).

Similarly, the anhydrides I reacted with *o*-phenylenediamine at 200° to give 5,6-dihydro-5-alkyl-13*H*-indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazol-13-ones (V) (a new ring system).

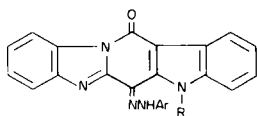


V

- a, R = CH<sub>3</sub>  
b, R = C<sub>2</sub>H<sub>5</sub>

The structure of Va, which was taken as example, was inferred from the facts that, (a) the ir spectrum showed absorption at 1625 cm<sup>-1</sup> (CO) and no absorption in the NH region, (b) the nmr spectrum (DMSO-d<sub>6</sub>) showed signals at δ 4.1 ppm (s, 3H, CH<sub>3</sub>), δ 4.82 (s, 2H, CH<sub>2</sub>) and at δ 7.68 (m, 8H, Ar-H), and (c) the carbonyl absorption in the ir spectra of Va and their phenylhydrazone and phenylmethylene derivatives were nearly at the same wave lengths (see below).

Compounds V coupled with arenediazonium salts in pyridine to give 5,6-dihydro-5-alkyl-13*H*-indolo[2',3':4,5]-pyrido[1,2-*a*]benzimidazole-6,13-dione 6-arylhydrazones (VI).

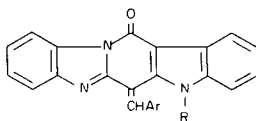


VI

- a, R = CH<sub>3</sub>; Ar = C<sub>6</sub>H<sub>4</sub>Cl-*p*  
b, R = CH<sub>3</sub>; Ar = C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>-*p*  
c, R = C<sub>2</sub>H<sub>5</sub>; Ar = C<sub>6</sub>H<sub>5</sub>  
d, R = C<sub>2</sub>H<sub>5</sub>; Ar = C<sub>6</sub>H<sub>4</sub>Cl-*p*

The structure of VIa (as example) was inferred from the facts that the uv spectrum showed absorption at 420 nm and the ir spectrum showed CO absorption at 1630 cm<sup>-1</sup>.

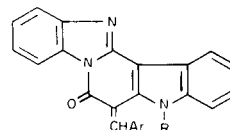
Compound V condensed with 2,4-dichlorobenzaldehyde in refluxing acetic acid in presence of anhydrous fused sodium acetate to yield 5,6-dihydro-5-alkyl-13*H*-6-(2,4-dichlorophenylmethylene)indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazol-13-one (VII).



VII

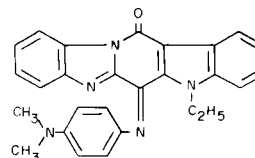
- a, R = CH<sub>3</sub>; Ar = C<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>(2,4)  
b, R = C<sub>2</sub>H<sub>5</sub>; Ar = C<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>(2,4)

The ir spectrum of VIIa showed carbonyl absorption at 1630 cm<sup>-1</sup> with no shift from that of Va. If compound Va had an angular structure, the CO group of its phenylmethylene derivative (VII'') would be conjugated with C=C double bond, a combination which is known to lower the stretching frequency of the CO group (4).



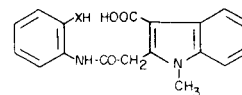
VII''

Compound Vb also reacted with *p*-nitrosodimethylaniline to give the 12-arylimino derivative VIII.



VIII

On the other hand attempts to fuse the anhydrides I with *o*-aminophenol or *o*-aminothiophenol to obtain compounds with structures similar to II and V were unsuccessful, but on refluxing the anhydride I (R = CH<sub>3</sub>) with *o*-aminophenol or *o*-aminothiophenol in anhydrous dioxan, compounds IX were obtained.

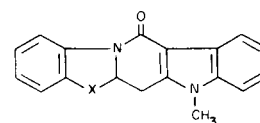
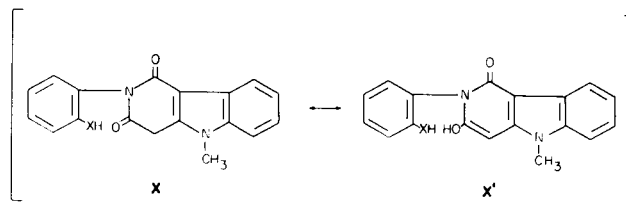


IX

- a, X = O  
b, X = S

The structure of IX was inferred from the facts that, (a) the ir spectrum of IX (a and b) showed broad peaks at 1640 cm<sup>-1</sup> (CO) and 3100 cm<sup>-1</sup> (NH, OH), and (b) the anhydrides I react with primary amines to give 1-alkyl-3-carboxyindole-2-acetanilide derivatives (I).

Compounds IXa and IXb underwent ring-closure on heating with acetic anhydride to give 5-methylindolo[2',3':4,5]pyrido[2,1-*b*]benzoxazol-13(5*H*)-one (XIa) and 5-methylindolo[2',3':4,5]pyrido[2,1-*b*]benzthiazol-13(5*H*)-one (XIb), respectively. This ring closure may have occurred *via* the intermediate X which enolises to X' before further cyclisation.



- a, X = O  
b, X = S

Table I

5,6-Dihydro-5-alkyl-13*H*-indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazole-6,13-dione 6-Arylhydrazones

Compound	Mp	Yield %	Solvent	Formula	C	Analysis %		ir cm <sup>-1</sup>
						Calcd./Found	N	
VIa (a)	298	75	Ethylene glycol	C <sub>24</sub> H <sub>16</sub> ClN <sub>5</sub> O	67.67	3.78	16.46	3300 (NH) 2850 (CH) 1630 (CO)
					67.80	3.88	16.50	
VIb	290	78	Ethylene glycol	C <sub>25</sub> H <sub>19</sub> N <sub>5</sub> O	74.07	4.72	17.28	3325 (NH) 2900 (CH) 1625 (CO)
					74.00	4.70	17.10	
VIc	160	80	Ethanol	C <sub>25</sub> H <sub>19</sub> N <sub>5</sub> O	74.07	4.72	17.28	3250 (NH) 2850 (CH) 1630 (CO)
					74.27	4.90	17.20	
VI d	215	70	Dioxane	C <sub>25</sub> H <sub>18</sub> ClN <sub>5</sub> O	68.24	4.12	15.93	3300 (NH) 2820 (CH) 1630 (CO)
					68.40	4.40	15.95	

(a) Uv (dioxane): 420 nm ( $\epsilon$  28,000), 256 (6000).

The ir spectra of X (a and b) showed CO absorption at 1640 cm<sup>-1</sup> and no absorption in NH region.

### EXPERIMENTAL

Melting points were taken on a Kofler apparatus and are uncorrected. Infrared (ir) spectra were determined as potassium bromide pellets with a Perkin-Elmer Infracord 137 instrument. The nmr spectra were determined with a Perkin-Elmer R 12 A instrument. Ultraviolet (uv) spectra were obtained in dioxan solution with a Perkin-Elmer spectrophotometer 402.

#### 2,3-Dihydro-10-alkylimidazo[3,2:1',2']pyrido[4,5-*b*]indol-5(1*H*)-one (II).

A mixture of 0.1 mole of the anhydride I and 0.12 mole of ethylenediamine was gently heated in an oil bath, the temperature was raised gradually and kept at 170° for 10 minutes and then cooled. The products which separated were crystallised to give II.

Compound IIa was crystallised from acetic acid in 75% yield, mp 350°; ir: 3300 (NH), 2920 (CH), 1640 cm<sup>-1</sup> (CO).

*Anal.* Calcd. for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O: C, 70.27; H, 5.47; N, 17.58. Found: C, 70.2; H, 5.9; N, 12.42.

Compound IIb was crystallised from ethanol (80% yield), mp 235°; ir: 3280 (NH), 2940 (CH), 1640 cm<sup>-1</sup> (CO); <sup>1</sup>H-nmr (deuteriodimethylsulfoxide):  $\delta$  1.3 (triplet, 3H), 4.0 (m, 7H), 5.75 (s, 1H).

*Anal.* Calcd. for C<sub>15</sub>H<sub>15</sub>N<sub>2</sub>O: C, 71.12; H, 5.96; N, 16.60. Found: C, 70.90; H, 6.1; N, 16.50.

#### 2,3-dihydro-10-alkylimidazo[3,2:1,2,2<sub>a</sub>]pyrido[4,5-*b*]indole-5,11-dione 11-Arylhydrazones (III).

##### General Procedure.

About 2 g of II was dissolved in 40 ml of pyridine, cooled in an ice bath, and treated with an equimolecular amount of the appropriate diazotised amine, prepared by the diazotisation of the calculated amount of the corresponding amine in 10 ml of hydrochloric acid with sodium nitrite solution. The mixture was left for one hour and then poured into cold water. The precipitate was collected, dried, and crystallised from the proper solvent to give III. Compound IIIa was crystallised from nitrobenzene in 85% yield, mp 260°; ir: 3320 (NH), 2860 (CH), 1645 cm<sup>-1</sup> (CO); uv (dioxane): 412 nm ( $\epsilon$  35,500), 320 (11,500).

*Anal.* Calcd. for C<sub>20</sub>H<sub>17</sub>N<sub>5</sub>O: C, 69.94; H, 4.99; N, 20.41. Found: C, 70.0;

H, 5.0; N, 20.33.

Compound IIIb was crystallised from DMF in 72% yield, mp 284°. *Anal.* Calcd. for C<sub>21</sub>H<sub>18</sub>N<sub>5</sub>O<sub>3</sub>: C, 62.68; H, 4.51; N, 20.89. Found: C, 62.60; H, 4.70; N, 20.67.

#### 2,3-Dihydro-10-ethyl-11-methylimidazo[3,2:1',2']pyrido[4,5-*b*]indol-5(1*H*)-one (IV).

A suspension of 0.01 mole of I in 50 ml of 10% sodium carbonate solution and 20 ml of ethanol was treated with 1.56 g (0.011 mole) of methyl iodide. The whole was refluxed for 3 hours, diluted with water, and cooled. The solid that separated was filtered off and crystallised from ethanol to give colourless crystals of IV, mp 220°, yield 52%; ir: 3310 (NH), 2950 (CH), 1640 cm<sup>-1</sup> (CO).

*Anal.* Calcd. for C<sub>16</sub>H<sub>17</sub>N<sub>3</sub>O: C, 71.88; H, 6.40; N, 15.73. Found: C, 71.72; H, 6.50; N, 15.70.

#### 5,6-Dihydro-5-alkyl-13*H*-indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazol-13-one (V).

A mixture of 0.1 mole of I and 0.11 mole of *o*-phenylenediamine was powdered, and heated in an oil bath at 140-160° for 1 hour. The resulting product was washed thoroughly with ethanol to give V. Compound Va was crystallised from ethanol in 68% yield, mp 202°; ir: 2850 (CH); 1625 cm<sup>-1</sup> (CO); <sup>1</sup>H-nmr (deuteriodimethylsulfoxide):  $\delta$  4.1 (s, 3H, CH<sub>3</sub>), 4.82 (s, 2H, CH<sub>2</sub>), 7.4-7.9 (m, 8H, Ar-H).

*Anal.* Calcd. for C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>O: C, 75.24; H, 4.56; N, 14.64. Found: C, 75.40; H, 4.70; N, 14.51.

Compound Vb was crystallised from acetic acid in 75% yield, mp 218°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>13</sub>N<sub>3</sub>O: C, 75.74; H, 5.02; N, 13.95. Found: C, 75.90; H, 5.10; N, 13.85.

#### 5,6-Dihydro-5-alkyl-13*H*-indolo[2',3':4,5]pyrido[1,2-*a*]benzimidazole-6,13-dione 6-Arylhydrazones (VI).

##### General Procedure.

About 2 g of V was dissolved in 40 ml of pyridine, cooled in an ice bath and treated with an equimolecular amount of appropriate diazotised amine. The mixture was left for 1 hour and then poured into water. The precipitate was collected, dried, and crystallised from the proper solvent. See Table I.

5,6-Dihydro-5-alkyl-13H-6-(2,4-dichlorophenylmethylene)indolo[2',3':4,5]-pyrido[1,2-a]benzimidazol-13-one (VII).

A mixture of 2 g of V, 3 g of anhydrous fused sodium acetate, 20 ml of acetic acid, and an equimolecular amount of 2,4-dichlorobenzaldehyde was refluxed for 3 hours. The reaction mixture was cooled and poured into cold water. The precipitate formed was collected, washed with water, and finally crystallised from ethanol. Compound VIIa was obtained in 76% yield, mp 300°; ir: 2850 (CH), 1630  $\text{cm}^{-1}$  (CO).

*Anal.* Calcd. for  $\text{C}_{25}\text{H}_{14}\text{Cl}_2\text{N}_3\text{O}$ : C, 67.71; H, 3.18; N, 9.49; Cl, 16.01. Found: C, 67.85; H, 3.27; N, 9.50; Cl, 16.00.

Compound VIIb, mp 155°, was obtained in 70% yield.

*Anal.* Calcd. for  $\text{C}_{26}\text{H}_{16}\text{Cl}_2\text{N}_3\text{O}$ : C, 68.26; H, 3.52; N, 9.19; Cl, 15.52. Found: C, 68.13; H, 3.70; N, 9.20; Cl, 15.72.

Condensation of V with *p*-Nitrosodimethylaniline.

*p*-Nitrosodimethylaniline (1.5 g, 0.01 mole) was added to a suspension of Vb (0.01 mole) in ethanol (100 ml) followed by one drop of piperidine and the reaction mixture was refluxed for 1 hour. The solution became violet in colour and compound VIII was separated and crystallised from benzene in 80% yield, mp 218°; ir: 2820 (CH), 1630  $\text{cm}^{-1}$  (CO).

*Anal.* Calcd. for  $\text{C}_{27}\text{H}_{23}\text{N}_5\text{O}$ : C, 74.80; H, 5.34; N, 16.17. Found: C, 74.88; H, 5.51; N, 16.20.

Reactions of Ia with *o*-Aminophenol and *o*-Aminothiophenol.

A mixture of 0.1 mole of Ia, 50 ml dioxane, and 0.1 mole of *o*-aminophenol or *o*-aminothiophenol, was refluxed for 3 hours. The mixture was cooled and poured into cold water. The solid that separated was filtered

off and dried. Compound IXa was crystallised from ethanol in 80%, mp 220°; ir: 3100 (broad, OH and NH), 1640  $\text{cm}^{-1}$  (CO).

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$ : C, 63.52; H, 4.73; N, 8.24; S, 9.41. Found: C, 63.60; H, 4.80; N, 8.25; S, 9.20.

Cyclisation of IX.

Two g of IXa or IXb in 12 ml of acetic anhydride was heated at 100° for 6 hours and cooled. The solid was collected and crystallised from acetic anhydride. Compound XIa was obtained in 60% yield, mp 250°; ir: 1640  $\text{cm}^{-1}$  (CO).

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}_2$ : C, 74.98; H, 4.19; N, 9.73. Found: C, 74.70; H, 4.02; N, 9.50.

Compound XIb was obtained in 80% yield, mp 235°; ir: 1640  $\text{cm}^{-1}$  (CO).

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{12}\text{N}_2\text{OS}$ : C, 71.04; H, 3.97; N, 9.21; S, 10.52. Found: C, 71.00; H, 4.00; N, 9.11; S, 10.41.

## REFERENCES AND NOTES

- (1) F. A. Trofimov, V. I. Ryabchenko and A. N. Grinev, *Khim. Geterotsykl. Soedin.*, 1343 (1975); *Chem. Abstr.*, **84**, 43754a (1976).
- (2) H. Y. Yao and P. J. Resnick, *J. Am. Chem. Soc.*, **84**, 3514 (1962).
- (3) M. I. Ali, A. A. El-Sayed and A. M. Abdel-Fattah, *J. Org. Chem.*, **37**, 3210 (1972).
- (4) L. J. Bellamy, "The Infrared Spectra of Complex Molecules", Methuen Ltd, London, 1967, p 136.