[CONTRIBUTION FROM THE WILLIAM H. NICHOLS CHEMISTRY LABORATORY,
NEW YORK UNIVERSITY]

2-PHENYLINDOLE-3-ALDEHYDE AND CERTAIN OF ITS CONDENSATION PRODUCTS

R. C. BLUME[1] AND H. G. LINDWALL

Received November 30, 1945

The original purpose of this study was to accomplish the ring closure to the 4-position of indole-3-acrylic acid derivatives to yield compounds belonging to the benz[cd]indole ring system. While this objective was not realized, a number of condensation products were prepared.

The first attempt to prepare the substituted acrylic acid was by the condensation of malonic acid with 2-phenylindole-3-aldehyde (1) under Perkin conditions; this failed, as did attempts to condense these reagents using organic bases as catalysts. In the hope of obtaining the acrylic acid derivative indirectly, ethyl cyanoacetate and cyanoacetamide condensation products were prepared. However, hydrolytic treatment of these products regenerated the 2-phenylindole-3-aldehyde.

2-Phenylindole-3-aldehyde was oxidized by heating for two hours with 30% hydrogen peroxide. The resulting acid was not the expected 2-phenylindole-3-acid but N-benzoylanthranilic acid; this was proved by analysis and by comparison with an authentic sample. Other attempts to oxidize the aldehyde with less concentrated hydrogen peroxide or with alkaline potassium permanganate gave only smaller yields of benzoylanthranilic acid. It has been reported previously that 3-nitro-2-phenylindole (2), 1-hydroxy-2-phenylindole (3), and 3-nitroso-2-phenylindole (2) are oxidized by alkaline permanganate to give N-benzoylanthranilic acid. 2-Methylindole-3-aldehyde yields N-acetylanthranilic acid under these conditions (4). Angeli and Alessandri (5) ascribed this result to the hydroxymethylene form of the aldehyde.

2-Phenylindole-3-aldehyde fails to give a sodium bisulfite addition product or a positive fuchsin test. It does not give a silver mirror with Tollens reagent nor does it reduce Fehling solution. The failure of these characteristic aldehyde tests with indole-3-aldehyde has been reported (6). However, the successful preparation of the oxime, semicarbazone, and *p*-nitrophenylhydrazone have been reported (7).

EXPERIMENTAL

Ethyl 2-phenylindole-3-(α-cyano)acrylate (II). 2-Phenylindole-3-aldehyde (I) (2.2 g.; 0.01 mole) was refluxed for twenty minutes in a solution consisting of 6 cc. of isopropyl alcohol, 3 cc. of pyridine, 0.5 cc. of piperidine, and 1.5 cc. (0.012 mole) of ethyl cyanoacetate. Crystals separated after dilution with an equal volume of 70% alcohol. Recrystallized from 95% alcohol. (See Chart II).

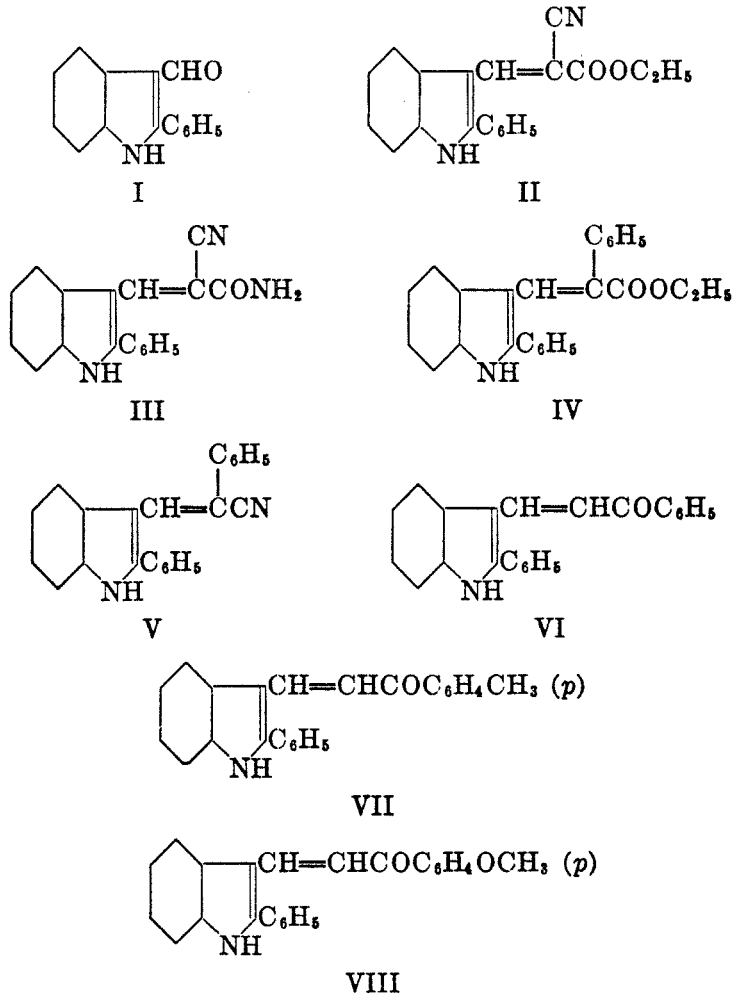
2-Phenylindole-3-(α-cyano)acrylamide (III). A mixture consisting of I (0.10 g.; 0.0045 mole), cyanoacetamide (0.1 g.), piperidine (0.25 cc.), and absolute alcohol (2.0 cc.) was

[1] Present address: E. I. DuPont de Nemours and Co., Waynesboro, Va.

heated on the steam-bath for one-half hour. The product which separated was recrystallized from 50% pyridine-alcohol.

Ethyl 2-phenylindole-3-(α-phenyl)acrylate (IV). Compound I (0.50 g.; 0.0023 mole), ethyl phenylacetate (1 cc.), and piperidine (1 cc.) were refluxed together for one-half hour. Dilution with alcohol, neutralization with acetic acid, and precipitation with water followed. The product was recrystallized from ethyl alcohol.

CHART I



2-Phenylindole-3-(α-phenyl)acrylonitrile (V). Compound I (0.50 g.; 0.0023 mole), benzyl cyanide (0.5 cc.), in 1 cc. of pyridine containing 3 drops of piperidine, were refluxed for six hours. Dilution with 4 cc. of alcohol and addition of water gave a yellow oil which slowly solidified. Recrystallized from alcohol containing ligroin.

β-(2-Phenylindolyl-3)-acrylophenone (VI). Compound I (1 g.; 0.0045 mole), 1 cc. of acetophenone, and 10 drops of piperidine were refluxed for ten minutes. The resulting oil was washed, while hot, with 25 cc. of hot 10% acetic acid. The residue was recrystallized from 15 cc. of alcohol.

p-Methyl-β-(2-phenylindolyl-3)-acrylophenone (VII). A mixture of I (0.50 g.), methyl *p*-tolyl ketone (1 cc.), and 1 cc. of piperidine was refluxed for one-half hour. To the resulting solution were added successively: 8 cc. of alcohol, 1 cc. of glacial acetic acid, and water to the point of cloudiness. The crystals, which formed were recrystallized from ethyl alcohol.

p-Methoxy-β-(2-phenylindolyl-3)-acrylophenone (VIII). A mixture of I (0.5 g.), *p*-methoxyacetophenone (0.50 g.), and 0.5 cc. of piperidine was refluxed for forty minutes. To the red melt were added successively: 3 cc. of alcohol, 1 cc. of glacial acetic acid, and water to the point of cloudiness. The product was recrystallized from ethyl alcohol.

CHART II

CONDENSATION PRODUCTS OF 2-PHENYLINDOLE-3-ALDEHYDE

WITH:[a]	PRODUCT	% YIELD	COLOR AND FORM	M.P. °C	ANAL.					
					Calc'd			Found		
					C	H	N	C	H	N
Ethyl cyanoacetate	(II) $C_{20}H_{16}N_2O_2$	89	Yellow needles	219–220	75.9	5.06	8.86	75.7	5.19	8.87
Cyanoacetamide	(III) $C_{18}H_{13}N_3O_2$	84	Yellow needles	292	75.3	4.53		75.0	4.59	
Ethyl phenylacetate	(IV) $C_{24}H_{21}NO_2$	52	Yellow needles	199–201	81.1	5.92	3.94	81.4	5.96	3.83
Benzyl cyanide	(V) $C_{23}H_{16}N_2$	76	Lemon-yellow needles	176–177[b]			8.75			8.73
Acetophenone	(VI) $C_{23}H_{17}NO$	67	Orange needles	170–171	85.5	5.26	4.34	85.4	5.60	4.36
Methyl *p*-tolyl ketone	(VII) $C_{24}H_{19}NO$	67	Orange platelets	200–201			4.15			4.15
p-Methoxyacetophenone	(VIII) $C_{24}H_{19}NO_2$	78	Orange prisms	176–177			3.97			3.82

[a] See Experimental Part for details of proportions, time of heating, etc.

[b] Partial sintering at 167°.

Oxidation of 2-phenylindole-3-aldehyde (I). Compound I (1 g.) was heated on the steam-bath with 20 cc. of 30% hydrogen peroxide for two hours. The cooled suspension was cautiously made alkaline with dilute sodium hydroxide. The alkaline solution was filtered and the N-benzoylanthranilic acid was precipitated by acidification with hydrochloric acid. After recrystallization from water and from benzene the product melted at 175–176.5°. Mixture with an authentic sample caused no lowering of the melting point.

Anal. Calc'd for $C_{14}H_{11}NO_3$: N, 5.81. Found: N, 5.74.

SUMMARY

1. Condensation products of 2-phenylindole-3-aldehyde with certain active methylene compounds have been prepared using basic catalysts.

2. 2-Phenylindole-3-aldehyde does not have the reducing properties characteristic of aldehydes.

3. Oxidation of 2-phenylindole-3-aldehyde with hydrogen peroxide yields N-benzoylanthranilic acid.

NEW YORK 53, N. Y.

REFERENCES

(1) MILLER AND ROBSON, *J. Chem. Soc.*, 1910 (1938).
(2) ANGELI AND ANGELICO, *Gazz. chim. ital.*, **30**(II), 277 (1901).
(3) FISCHER, *Ber.*, **29**, 2063 (1896).
(4) PLANCHER AND PONTI, *Atti accad. Lincei*, **16**(I), 130 (1907); *Chem. Abstr.*, **2**, 1147 (1908).
(5) ANGELI AND ALESSANDRI, *Atti accad. Lincei*, **23**(II), 93 (1914); *Chem. Abstr.*, **9**, 1322 (1915).
(6) VAN ORDER AND LINDWALL, *J. Org. Chem.*, **10**, 128 (1945).
(7) BLUME AND LINDWALL, *J. Org. Chem.*, **10**, 255 (1945).