isopropyl alcohol the compound melted at 126–127.5°. Other thiazoles, prepared by this procedure, are listed in Table I.

From 16.4 g. (0.1 mole) of 2-bromothiazole[4] and 21.4 g. (0.2 mole) of benzylamine[26b] in 75 ml. of either cumene or xylene, refluxed for 72 hours and isolated by a modification of Method B, there was obtained 1.8 g. (9.5%) of 2-benzylaminothiazole, m.p. 117–121°. The compound, recrystallized three times from isopropyl alcohol, melted at 127.5–128.5° and showed no depression in melting point when mixed with product obtained by Method A.

N,N-Diethyl-N′-(2-thiazolyl)-ethylenediamine.[10] **Method B.**—A solution of 8.2 g. (0.05 mole) of 2-bromothiazole and 11.6 g. (0.10 mole) of 2-diethylaminoethylamine in 12 g. of pyridine was refluxed for 3.5 hours. After cooling to room temperature, 100 ml. of water was added. The mixture was saturated with potassium carbonate and then extracted several times with ether. The combined ether extracts were dried over anhydrous potassium carbonate and the solvent removed. Distillation of the residue *in vacuo* gave 6.0 g. (60%) of a light yellow oil, b.p. 112–115° (0.4 mm.).

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BROOKLYN 10, NEW YORK

[CONTRIBUTION FROM DEPARTMENT OF CHEMISTRY, COLLEGE OF LIBERAL ARTS AND SCIENCES, TEMPLE UNIVERSITY]

A New Approach to 3-Indolecarboxaldehyde

BY FLOYD T. TYSON AND JOHN T. SHAW

The number of steps required in heretofore published syntheses of 3-indolecarboxaldehyde led to a search for a shorter method involving more readily available materials. Investigation of this problem has yielded two new methods: one method involves the use of carbon monoxide at elevated pressures with a salt of indole, and the second method is a modification of the N-methylformanilide synthesis. Of particular import is the possible applicability of the pressure reaction to other compounds of reactivity comparable to indole.

In the former preparations of 3-indolecarboxaldehyde, the reactivity of the 3-position in indole has been evidenced by the variety of methods used to place the formyl group in this position, one of the most recent being the N-methylformanilide[1] synthesis. Other well-known reactions have been used to accomplish this end: the Reimer–Tiemann[2] reaction, a modified Gattermann[3] aldehyde synthesis, a modified Claisen[4] reaction and the Grignard reaction.[5] The preparation of 3-indolecarboxylic acid by a reaction between indolemagnesium iodide and carbon dioxide[6] suggested that possibly the metal salts of indole might be sufficiently reactive with carbon monoxide under suitable conditions to yield the desired aldehyde.

An appropriate solvent for the reaction was found to be commercial dimethylformamide, although pyridine or excess indole can be used, but with decreased yields. The influence of various reaction conditions may be summarized as follows: Over the pressure and temperature ranges investigated, 47 to 480 atmospheres and 25 to 200°, respectively, the optimum conditions were found to be 480 atmospheres at 135 to 150° for a bomb of total void 120 ml., half-full of liquid reactants. The yield of aldehyde was 57%, based upon the potassium salt of indole. Using the optimum conditions cited above, potassium indole gave 24% higher yield than sodium indole, and 48% higher than lithium indole. This latter result might have been expected as the increase in atomic weight of the metal would tend to make the nitrogen metal bond more ionic and increase the tendency toward desirable electronic shifts. Use of indole or indolemagnesium bromide, the latter in diethyl ether, gave negative results. The presence of a slight amount of excess potassium amide or the use of very dry dimethylformamide, was found to influence the yield favorably. It was found that there was no correlation between pressure drop of carbon monoxide and the amount of aldehyde formed, the latter always being less than the equivalent amount of carbon monoxide consumed. In the absence of carbon monoxide there was no yield of aldehyde, all other conditions of the reaction being identical. The synthesis may prove to be applicable to other compounds of reactivity comparable to indole such as pyrrole, imidazole and pyrazole, since the metallic salts of these compounds are known, the anions of which like that of indole, are thought to be stabilized by resonance.

Since 3-indolecarboxaldehyde is appreciably soluble in dimethylformamide or aqueous solutions thereof, it is removed from the reaction mixture either by refluxing with sodium hydroxide or by distillation under reduced pressure. In both syntheses the 3-indolecarboxaldehyde was converted to the 3-indolalacetophenone[7] for identification purposes.

Experimental

3-Indolecarboxaldehyde Preparation by Reaction of Potassium Indole with Carbon Monoxide.—An Aminco autoclave, #406-35BX3, of 120 ml. void, fabricated with 18-8 stainless steel, with heater and shaker was used for the pressure reactions with carbon monoxide. Into a 3-necked 100-ml. flask, fitted with a suitable mineral oil trap and containing 50 ml. of liquid ammonia with a 2″ suspended iron nail, was added 4.0 g. (0.103 mole) of potassium. After completion of reaction which was evidenced by disappearance of the blue color of the potassium solution, 11.7 g. (0.10 mole) of indole was added. The excess ammonia was removed by evaporation and the remaining potassium indole heated to about 170° for 0.25 hour. (Potassium hydroxide[8] could have been used to prepare potassium indole also.) The flask was allowed to cool to room temperature under dry nitrogen after which 45 ml. of anhydrous dimethylformamide, dried by boiling with calcium hydride, was added.

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(2) A. Ellinger, *Ber.*, **39**, 2515 (1906).

(3) W. J. Boyd and W. Robson, *Biochem. J.*, **29**, 555 (1935).

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(6) R. Majima, *Ber.*, **55**, 3865 (1922).

(7) R. B. Van Order and H. G. Lindwall, *J. Org. Chem.*, **10**, 128 (1945).

(8) R. Weissgerber, *Ber.*, **43**, 3520 (1910).

The flask was warmed slightly to aid solution and the material was transferred as quickly as possible to the autoclave. (In order to facilitate transfer of the material into the autoclave, it is found best to break the unmelted material into small pieces and to pour the mixture of liquid and solid into the autoclave, thus decreasing the period of preliminary heating.) The flask was washed with 5 ml. more of anhydrous dimethylformamide to make the transfer complete. The autoclave was flushed with dry nitrogen and quickly closed after which it was filled with carbon monoxide up to a pressure of 415 atmospheres, the temperature being 33°. The autoclave was then heated to 150° and shaken for 4.0 hours at this temperature. Upon cooling, the autoclave contents were diluted with a liter of water, and after standing for a few minutes, 22.5 g. of sodium hydroxide was added and the mixture refluxed for 2.0 hours, dimethylamine being given off copiously. The mixture was then steam distilled to remove unreacted indole and the residue was diluted to approximately 3 liters with water, charcoal added, heated to reflux and filtered. The filtrate was cooled to room temperature and placed in the refrigerator overnight. The product was filtered, washed several times with water and dried, 8.0 g. This latter filtrate was concentrated to 500 ml. and then cooled, whereupon 0.3 g. more of the product separated. The reaction mixture can be processed in an alternate manner. The mixture from the bomb was placed in a 100-ml. Claisen flask and distilled at 12 mm. pressure. After collecting 40–45 ml. of the solvent boiling in the range 48° to 52°, the distilling flask was allowed to cool leaving a viscous residue. Fifty ml. of water was added and the mixture heated, the viscous mass reacted slowly with the water to give a brown-colored precipitate. The mixture was further diluted to 1 liter and steam distilled to remove any indole present. The remaining steps were the same as above; yield 8.3 g., 57% of the theoretical; 193–195°, mixed melting point with an authentic sample, 193–195°; conversion of the product to the 3-indolalacetophenone[7] gave a m.p. of 165.5–166.5°, lit. 166–167°.[7]

3-Indolecarboxaldehyde by Reaction of Dimethylformamide on Indole in the Presence of Phosphorus Oxychloride.—To a flask protected from atmospheric moisture, fitted with a mechanical stirrer, and containing 1.18 mole of dimethylformamide cooled to −5°, 30.68 g. (0.2 mole) of phosphorus oxychloride was added with stirring so that the temperature did not rise above 10°. After completion of addition, 11.7 g. (0.10 mole) of indole was added in portions at temperature 23–27° followed by additional stirring at 25° for 0.5 hour. Then 40 g. of finely divided calcium carbonate was added to the mixture and the temperature gradually was raised to 30–35° whereupon the heat of reaction kept the temperature rising slowly, the external source of heat being removed. The temperature should be controlled by cooling of the flask with ice from time to time in order that the temperature reaches 55–60° in approximately 0.5 hour. The mixture was then cooled externally to 10° with ice and 200 ml. of a 30% solution of sodium acetate was poured into the flask with stirring, followed by dilution with water to 1.0 liter. After addition of 47.2 g. (1.18 moles) of sodium hydroxide, the mixture was refluxed for 3 hours, dimethylamine evolved copiously. The mixture was then steam-distilled to remove any unreacted indole and then diluted to 3.5 liters with water, heated to reflux, filtered, the filtrate being treated as above; yield 10.4 g. representing 72% of the theoretical; m.p. 193–195°, mixed m.p. with authentic sample, 193–195°; the product was converted to 3-indolalacetophenone,[7] m.p. 165.5–166.5°, lit. 166–167°.

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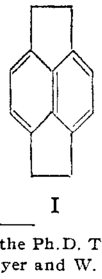
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF WASHINGTON]

The Synthesis of Pyracene[1]

BY A. G. ANDERSON, JR., AND ROBERT H. WADE

An attempted synthesis of pyracene *via* 5-acenaphtheneacetic acid is presented and the failure to effect ring closure of the acid to 1-pyracenone is briefly discussed. The synthesis of pyracene from 1-indanone is reported.

The synthesis of 1,2-dihydrocyclopenta[fg]acenaphthene or pyracene (I) was first attempted by Mayer and Kaufmann[2] in 1920 and since that time a number of workers have investigated the preparation of compounds containing two five-membered rings fused to the opposite *peri*-positions of naphthalene. The literature dealing with these studies has been summarized by Kloetzel and Chubb[3] who synthesized 1,2-dihydrocyclopenta[cd]fluoranthene or 1,2-benzpyracene (II) and found it to be a stable compound.



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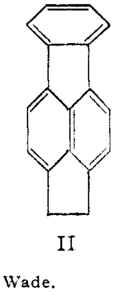
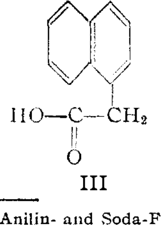


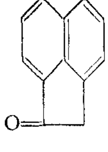
II

In this paper are reported first, the preparation of 5-acenaphtheneacetic acid (III) and our unsuccessful attempts to convert this acid to 1-pyracenone (IV) and second, the successful synthesis of pyracene from 1-indanone (V).

Since the treatment of the chloride or bromide of 1-naphthaleneacetic acid with aluminum chloride yields 1-acenaphthenone,[4] the cyclization of 5-acenaphtheneacetic acid (III) to 1-pyracenone (IV) seemed worthy of attempt.[5] Indeed, Mayer



III



IV

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[1] From the Ph.D. Thesis of Robert H. Wade.

[2] F. Mayer and W. Kaufmann, *Ber.*, **53**, 289 (1920).

[3] M. C. Kloetzel and F. L. Chubb, THIS JOURNAL, **72**, 150 (1950).

[4] Bad. Anilin- and Soda-Fabr., German Patent 230,237 (Oct. 23, 1909).

[5] The work of Kloetzel and Chubb (reference 3), wherein the analogous 3-fluorantheneacetyl chloride resisted cyclization, was reported after this portion of our work had been completed.