Notes

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Tomoyoshi Komai : Synthesis of Bis(2-methyl-2-indolin-3-one)

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It was shown by the writer[1] that ethyl indoxylate was reduced with lithium aluminum hydride to form two kinds of yellow crystals, one of which melted at 209~210° (decomp.) (A) and the other at 192~193°(decomp.) (B). The former, which had a molecular formula $C_{18}H_{16}ON_2$, was proved to be 2-methyl-2-(2′-methylindyl-3′)pseudoindoxyl (I) as suggested by Witkop.[2] The structure of the latter (B) with a molecular formula $C_{18}H_{16}O_2N_2$ was assumed to be bis(2-methyl-2-indolin-3-one) (II), and this paper deals with the synthesis of (II) and its identification with (B).

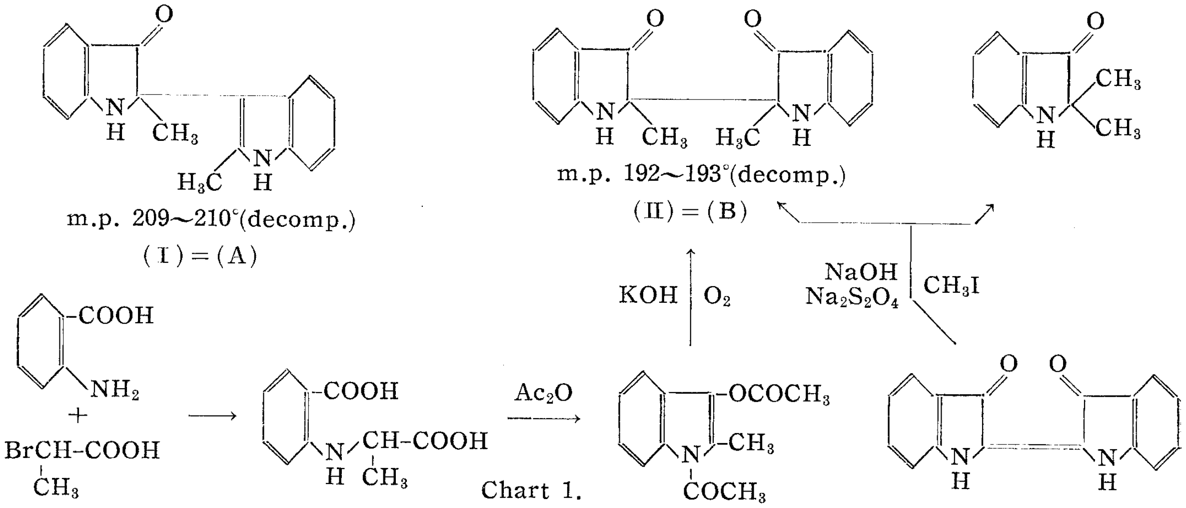

Chart 1.

In the literature there are found two ways to synthesize bis(2-methyl-2-indolin-3-one). Alphen[3] reported a method of obtaining a compound having the structure (II), as shown in Chart 1. Starting from anthranilic acid, N,O-diacetyl-2-methylindoxyl was prepared, which on further oxidation in alkaline medium by air, was condensed to give bis(2-methyl-2-indolin-3-one), m.p. 174°. When the experiment was followed the yellow crystals obtained melted at 192~193° with decomposition, after repeated recrystallization and proved to be identical with the compound (B) by mixed fusion. Madelung[4] obtained the so-called dimethylindigo white, which is a dimethylated bis(2-indolin-3-one), by the methylation of indigo white with dimethyl sulfate under alkaline conditions, but the positions of the two methyl groups in this compound were not clarified. The same author, however, described that benzyl chloride converts indigo white into bis(2-benzyl-2-indolin-3-one) under alkaline condition. Hence, when methyl halide is used in place of benzyl chloride, it is expected that a compound corresponding to (II) would be obtained. Indigo was reduced with sodium hydrosulfite and sodium hydroxide and the indigo white in the solution was methylated with methyl iodide. On purification of the products through alumina chromatography two kinds of yellow crystals, $C_{18}H_{16}O_2N_2$, m.p. 192~193°(decomp.), and $C_{10}H_{11}ON$, m.p. 88~88.5°, were isolated.

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1) This Bulletin, **4**, 266(1956).

2) B. Witkop : J. Am. Chem. Soc., **73**, 713(1951).

3) J. v. Alphen : Rec. trav. chim., **61**, 888(1942) (Chem. Zentr., **1943**, II, 1875).

4) W. Madelung : Ber., **57**, 241(1924).

The former which was obtained in a poorer yield was proved to be identical with the compound (B), both by mixed melting point and comparison of their ultraviolet absorption curves. Another kind of yellow crystals, with molecular formula $C_{10}H_{11}ON$, obtained in the reaction of indigo white and methyl iodide, showed the same melting point with that of 2,2-dimethylpseudoindoxyl which had already been synthesized from indoxyl and methyl iodide.5) The ultraviolet absorption curve of this product was also in good agreement with that of *spiro*-cyclopentane-pseudoindoxyl as shown by Witkop.2)

Thus, the yellow compound(B), m.p. 192~193°(decomp.), one of the lithium aluminum hydride reduction products of ethyl indoxylate, was confirmed as bis(2-methyl-2-indolin-3-one) by identifing it with the synthetic specimen which was obtained by both Alphen's and the modified Madelung's methods.

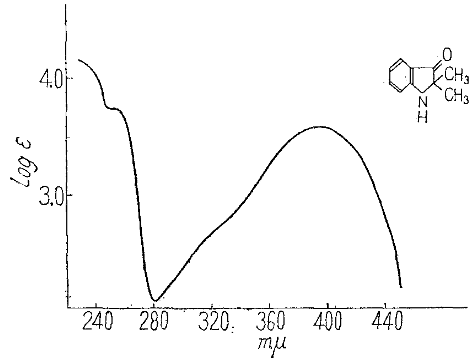

Fig. 1.

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Experimental

Action of Methyl Iodide on Indigo White—While shaking in H_2 atmosphere to prevent air oxidation, 10 g. of MeI was added slowly to a suspension of 2.5 g. of indigo in 40 cc. of water containing 3 g. NaOH and 3 g. $Na_2S_2O_4$. The shaking was continued for 100 hrs. After the reaction was complete the dark colored insoluble material was collected and dissolved in acetone, from which 0.5 g. of unreacted indigo was recovered as an insoluble matter. After removal of acetone, the residue was redissolved in benzene to remove any insoluble material. The product soluble in benzene solution was purified through an alumina column.

2,2-Dimethylpseudoindoxyl : From initial portions of the eluate, yellow crystals were obtained and recrystallized from ligroine to melt at 88~88.5°. Yield, ca. 300 mg. *Anal.* Calcd. for $C_{10}H_{11}ON$: C, 74.51, H, 6.88; N, 8.69. Found : C, 74.14; H, 7.70; N, 9.12.

Bis(2-methyl-2-indolin-3-one) : On evaporation, the latter portions of the eluate gave 100 mg. of yellow crystals which, after recrystallization from AcOEt, melted at 192~193°(decomp.), showing no depression when mixed with the compound, $C_{18}H_{16}O_2N_2$, obtained previously as the lithium aluminum hydride reduction product of ethyl indoxylate.1)

Action of Oxygen on O,N-Diacetyl-2-methylindoxyl—To the solution of 0.5 g. of 1,3-diacetylindoxyl in 30 cc. of EtOH was added a solution 0.3 g. of KOH in 20 cc. of water. When the mixture was shaken in O_2 atmosphere, the yellow color of the solution changed gradually into dark red and a fine crystalline product separated out. The product was collected and, after recrystallization from AcOEt, it melted at 192~193°(decomp.), undepressed on admixture with the compound, $C_{18}H_{16}O_2N_2$, obtained previously.

Summary

Bis(2-methyl-2-indolin-3-one) was synthesized from anthranilic acid and β-bromopropionic acid according to Alphen's method and also from indigo by reductive methylation. It was proved that this compound was identical with one of the products obtained from the reduction of ethyl indoxylate with lithium aluminum hydride.

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5) A. Estienne : Compt. rend., **225**, 124(1947) (C. A., **41**, 6885(1947)).