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THE STRUCTURE OF SKATOLE DIMER.
NEW REACTIONS OF INDOLINE DERIVATIVES

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IN connection with our work on the determination of the base strengths of indole derivatives,[1] it became of importance to study the dimers which some of these compounds form in acidic solutions. While structure I was definitely proved for indole dimer,[2] no recent data were available on skatole dimer, although its structure had been a matter of dispute between Oddo,[3] who proposed a pentacyclic formula, and Schmitz-Dumont,[4] who favoured instead the more likely formulation II, but did not give a real proof for it. A structure similar to that of diindole (I) was evidently impossible for diskatole, but III seemed to be a possible alternative for II, on the basis of our results on the comparative basicities of indole and its methyl derivatives.[1] We have now succeeded in proving that III is the structure of diskatole. In a recent paper No-

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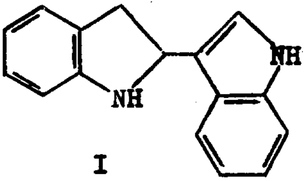
[1] G. Berti, A. Da Settimo and D. Segnini, Ricerca Sci. **30**, 1057 (1960).

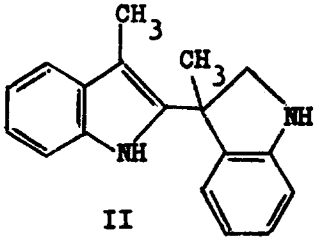
[2] H.F.Hodson and G.F.Smith, J. Chem. Soc. 3544 (1957).

[3] B. Oddo, Gazz. Chim. Ital. **43**, 898 (1933).

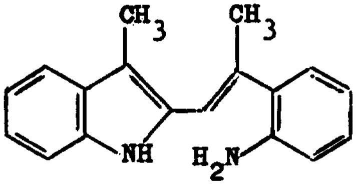
[4] O. Schmitz-Dumont, Liebigs Ann. **514**, 267 (1934).



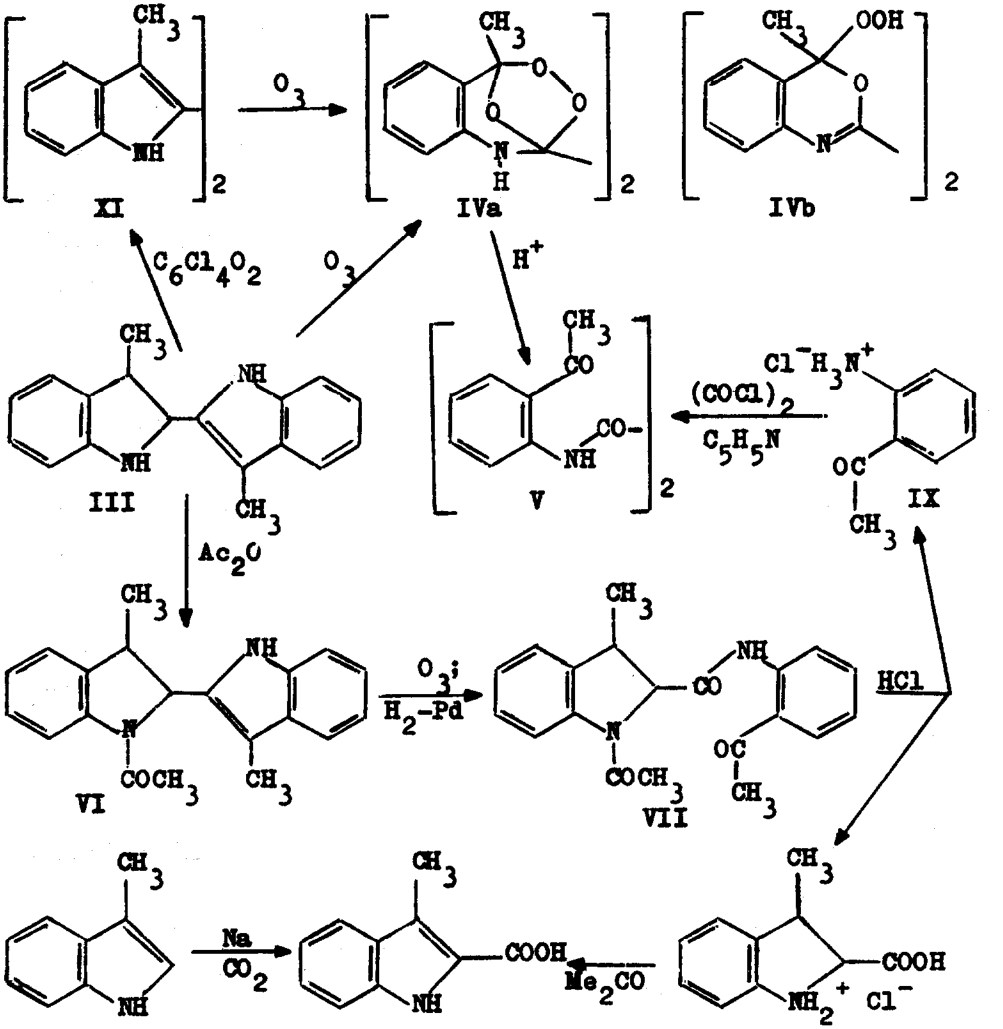
I



II



IV


XI
O_3
IVa
IVb
$C_6Cl_4O_2$
O_3
H^+
III
V
$(COCl)_2$
C_5H_5N
IX
Ac_2O
VI
O_3; H_2-Pd
VII
HCl
Na
CO_2
X
Me_2CO
VIII

land and Hammer [5] mentioned that they had been privately informed by G.F. Smith and A.E. Walters, that diskatole has structure III, but did not give any detail on how this was demonstrated. As some unusual reactions were encountered during our work, we are reporting briefly on our proofs of structure.

When a stream of ozonised oxygen was passed through a solution of diskatole in ethyl acetate, a stable ozonide (m. p. 160°) precipitated in 22% yield. Several cases of stable ozonides, derived from 2:3-disubstituted indoles, are known.[6-10] The analysis of our compound, however, showed that it was a diozonide, instead of the expected simple ozonide (found: C, 60.78; H, 4.89; N, 7.41. $C_{18}H_{16}O_6N_2$ requires:C, 60.67; H, 4.53; N, 7.86%). This result could have been explained by a structure of diskatole with two reactive double bonds, such as IV, a not completely unlikely hypothesis if one considers the structure of triindole.[11] However, it is known that diskatole

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[5] W.E. Noland and C.F. Hammer, J. Org. Chem. 25, 1525 (1960).

[6] P. Karrer and P. Enslin, Helv. Chim. Acta 32, 1390 (1949).

[7] C. Mentzer, D. Molho and Y. Berguer, Bull. Soc. Chim. Fr. 555 (1950).

[8] B. Witkop and J.B. Patrick, J. Amer. Chem. Soc. 74, 3855 (1952).

[9] B. Witkop, J.B. Patrick and H.M. Kissman, Ber. Dtsch. Chem. Ges. 85, 949 (1952).

[10] D.W.Ockenden and K. Schofield, J.Chem.Soc. 612 (1953).

[11] G.F. Smith, Chem. and Ind. 1451 (1954); W.E. Noland and W.C. Kuryla, J. Org. Chem. 25, 486 (1960).

forms a dinitroso derivative;[12] now we have found that it gives an alkali insoluble toluenesulphonamide, m.p. 193°, and, with an excess of methyl iodide, a quaternary iodide, with two methyl groups more than the starting compound (m.p. 204-206°; found: C, 57.29; H, 5.44. $C_{20}H_{23}N_2I$ requires: C, 57.42; H, 5.54%); all this proves the absence of a primary amino group and rules out structure IV.

When the ozonide was treated with acetic acid, or with sulphuric acid in tetrahydrofuran, it was transformed into compound V (m.p. 267-270°; found: C, 66.54; H, 4.97; N, 8.36. $C_{18}H_{16}O_4N_2$ requires: C, 66.66; H, 4.97; N, 8.64%), which was also prepared from o-aminoacetophenone and oxalyl chloride. The formation of V proved the structure IVa (or IVb [9]) for the ozonide and showed that the ozonisation of diskatole follows, at least in part, an unusual course, involving a dehydrogenation of the indoline ring by the ozone, 2:2'-diskatyl being a possible intermediate. The dehydrogenation is not caused by the oxygen mixed with the ozone, as diskatole was recovered unchanged after a two-hour treatment with oxygen; peroxides were not formed, in contrast with the behaviour of 2-phenylskatole.[8] The unknown 2:2'-diskatyl (XI) was easily prepared from diskatole with chloranil in benzene (m.p. 162-163°; found: C, 83.35; H, 6.26. $C_{18}H_{16}N_2$ requires: C, 83.04; H, 6.20%); it gave the same ozonide as diskatole, in 45% yield. Although the results described above pointed strongly to structure III for skatole dimer, we did not think it safe to base our proof only on

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[12] O. Schmitz-Dumont, K. Hamann and K.H. Geller, Liebigs Ann. **504**, 1 (1933).

a new reaction of low yield and unknown mechanism, which could even involve some rearrangement.

When the monoacetyl derivative of diskatole (VI) was ozonised, no stable ozonide was isolated (apparently, the abnormal reaction requires a free imino group in the indoline moiety); the ozonised solution was hydrogenated over palladium and compound VII was obtained in 70% yield (m.p. 126-127°; found: C, 71.39; H, 5.87. $C_{20}H_{20}O_3N_2$ requires: C, 71.41; H, 5.99%). It was hydrolysed by hydrochloric acid to a mixture of o-aminoacetophenone hydrochloride (IX) and of the hydrochloride VIII (m.p. 122°, sint. at 98°; found: C, 51.56; H, 6.38; N, 6.24. $C_{10}H_{11}O_2N.HCl.H_2O$ requires: C, 51.84; H, 6.09; N, 6.05%); the latter compound, when heated in vacuo at 80°, gave the free acid (m.p. 154-156°; found: C, 67.63; H, 6.40. $C_{10}H_{11}O_2N$ requires: C, 67.78; H, 6.26%), whose structure was proved through another unusual dehydrogenation reaction: the acid or its hydrochloride, dissolved in acetone, were transformed, after a few hours at room temperature, into another acid, m.p. 163-165°, which was shown to be skatole-2-carboxylic acid (X) by comparison of its infra-red spectrum with that of a sample prepared from skatole with sodium and carbon dioxide.[13] Structure III was thus definitely proved for the dimer of skatole. The facile dehydrogenations of indoline derivatives shown by reactions III → IVa (or IVb), III → XI and VIII → X, which should be due to a considerable gain in resonance stabilisation, caused by the formation of a new double bond, linking two unsaturated systems, deserve further study; work along these lines is in progress at present.

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[13] G. Ciamician and G. Magnanini, Ber. Dtsch. Chem. Ges. **21**, 1925 (1888).