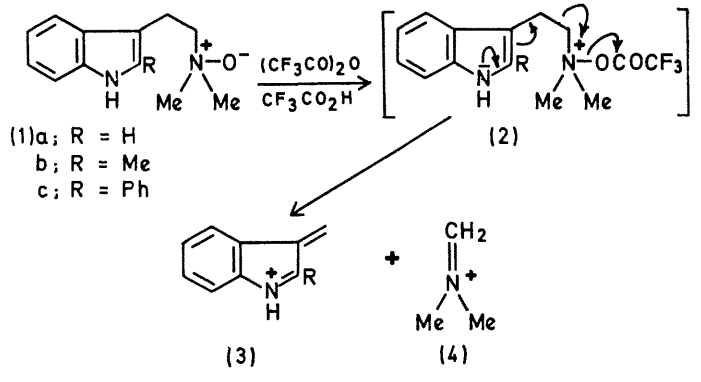
The Fragmentation of *NN*-Dimethyltryptamine Oxide and Related Compounds: a Possible Implication in Indole Alkaloid Biosynthesis

By ALAIN AHOND, ADRIEN CAVÉ, CHRISTIANE KAN-FAN, YVES LANGLOIS, and PIERRE POTIER*
(*Institut de Chimie des Substances Naturelles, C.N.R.S., 91-Gif-sur-Yvette, France*)

Summary A modified Polonovski reaction on *NN*-dimethyltryptamine oxide and related compounds leads to products of fragmentation; the possible role of this new reaction in indole alkaloid biosynthesis is emphasized.

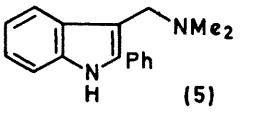
IT has recently been shown that certain γδ-unsaturated *N*-oxides, on treatment with trifluoroacetic anhydride (modified Polonovski reaction) undergo ready N–O bond cleavage which leads to fragmentation products.[1-4]

This new reaction has now been applied to *NN*-dimethyltryptamine oxide (**1a**) and related compounds (**1b**) and (**1c**). The course of the reaction of (**1a**) with trifluoroacetic anhydride was followed by n.m.r. spectroscopy: a trifluoroacetic acid solution of (**1a**) was treated with 2 equiv. of trifluoroacetic anhydride; the reaction was complete within 3 min.; the n.m.r. signals were consistent with the presence, in the medium, of (**4**).[2,4a] The presence of (**4**) was demonstrated after reduction of the reaction medium (Zn/CF_3CO_2H or Pt/H_2) and steam distillation by the isolation of trimethylamine (as hydrochloride or picrate, yield *ca.* 60%). The presence of (**3**) was shown by the isolation, after alkaline hydrolysis followed by $LiAlH_4$ reduction, of skatole (yield *ca* 1%).†

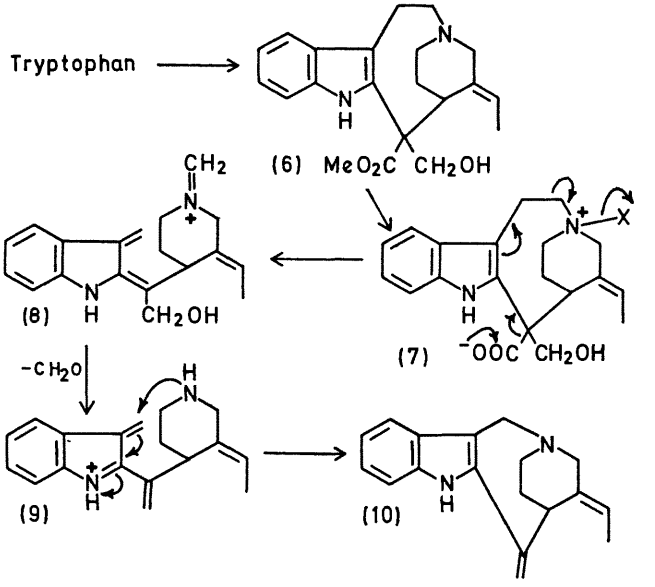


With the aim of trapping the versatile ion (**3**), the same reaction has been carried out on (**1b**): an equivalent fragmentation occurred and the products were similarly characterized. The yield of 2,3-dimethylindole obtained was, again, of the order of 1%. However, when (**1c**) was treated in the same manner, (**4**) was formed again, but, after alkaline hydrolysis (10% aqueous KOH), (**5**)[5] was obtained with *ca.* 15% overall yield.

This result is easily rationalized on the basis of: (i) fragmentation of the intermediate (**2**; R = Ph), giving rise to (**3**; R = Ph) and (**4**); (ii) Michael-type addition of dimethylamine [from hydrolysis of (**4**)] on to (**3**; R = Ph). The immonium salt (**3**; R = Ph) is probably more stabilized than (**3**; R = H or Me) because of the presence of a phenyl group on C-2 of the indole nucleus.



This type of fragmentation reaction may well be relevant in the biosynthesis of certain indole alkaloids *e.g.* that of apparicine (**10**). This is formed from tryptophan *via* stemmadenine (**6**)[6] and a Scheme indicating the further transformation of the latter is shown here. A phosphoxyammonium, or equivalent group, could replace trifluoroacetoxyammonium as a leaving group in this reaction.



SCHEME

(*Received, March 9th*, 1970; *Com.* 326.)

† This very low yield is most probably due to the high reactivity of the ion (**3**) to which many other reaction pathways are accessible.

[1] A. Cavé, C Kan-Fan, P. Potier, and J. Le Men, *Tetrahedron*, 1967, **23**, 4681.
[2] A. Ahond, A. Cavé, C. Kan-Fan, H.-P. Husson, J. de Rostolan, and P. Potier, *J. Amer. Chem. Soc.*, 1968, **90**, 522.
[3] H.-P. Husson, J. de Rostolan, Y. Pépin, P. Potier, and J. Le Men, *Tetrahedron*, 1970, **26**, 147.
[4] A. Ahond, A. Cavé, C. Kan-Fan, and P. Potier, *Bull. Soc. chim. France*, in the press.
[5] M. Julia, R. Melamed, and R. Gombert, *Ann. Inst. Pasteur*, 1965, **109**, 343.
[6] J. P. Kutney, V. R. Nelson, and D. G. Wigfield, *J. Amer. Chem. Soc.*, 1969, **91**, 4278, 4279.