213. *The Action of Ephedrine on Benzaldehyde.*

By WILLIAM DAVIES.

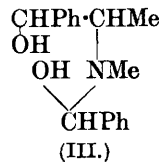
THE oxidation of ephedrine (I) by aqueous solutions of alkaline reagents such as potassium permanganate or potassium ferricyanide gives the substance "benzalephedrine," m. p. 72—73°, to which Schmidt (*Arch. Pharm.*, 1914, **252**, 89) assigns formula (II). The benzaldehyde first formed in the oxidation condenses with unchanged ephedrine, as Schmidt (p. 97) showed by the direct action of benzaldehyde on ephedrine in the presence of aqueous alkali. The evidence he adduced for formula (II) is that the compound is basic, is resolved into its components by warm mineral acids, and decolorises bromine in chloroform.

Modern ideas of induced activation make the existence of such an active methyl group in ephedrine very improbable. An alternative structure is that of 2 : 5-*diphenyl*-3 : 4-*dimethyltetrahydro-oxazole* (IV), which can be found *via* the intermediate compound (III). Ephedrine is sufficiently basic to condense almost quantitatively with benzaldehyde without the addition of alkali. The compound produced (m. p. 73·5°) has the general properties of tetrahydro-oxazoles, does not contain hydroxyl or an imino-group, and is saturated. There can moreover be no doubt that the compound (m. p. 65°) which Schmidt (*loc. cit.*, p. 97) produced from ψ-ephedrine and benzaldehyde is an oxazole derivative stereoisomeric with (IV).

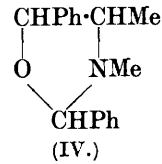
Adrenaline also can be made to react with benzaldehyde with the loss of water, but the product is difficult to obtain in a pure state.

$OH{\cdot}CHPh{\cdot}CH(NHMe){\cdot}CH_3$ (I.)

$OH{\cdot}CHPh{\cdot}CH(NHMe){\cdot}CH{:}CHPh$ (II.)



(III.)



(IV.)

EXPERIMENTAL.

2 : 5 - *Diphenyl* - 3 : 4 - *dimethyltetrahydro* - *oxazole*.—Merck's pure ephedrine hydrochloride (m. p. 216—220°) is converted into the free base (m. p. 35—39°), which is mixed (0·6470 g. ; 1 mol.) with benzaldehyde (0·42 c.c. : 5% excess of 1 mol.) and heated over a flame for a few seconds until water suddenly separates. The product, after being heated on the water-bath for ¼ hour, is allowed to crystallise (m. p. 67—69°), and is then obtained from dilute alcohol as colourless needles or platelets, m. p. 73·5°, which are very soluble in cold light petroleum (b. p. 40—60°) and moderately easily soluble in cold alcohol. This compound has all the properties of the " benzalephedrine," m. p. 72—73°, described by Schmidt (*loc. cit.*) (Found : C, 80·3; H, 7·3; *M*, by Rast's method, 256, 254. $C_{17}H_{19}ON$ requires C, 80·6; H, 7·5%; *M*, 253).

The hydroxy- and the imino-group are shown to be absent by the inertness of the compound to (a) phenyl *iso*cyanate and (b) an ethereal solution of methylmagnesium iodide. The absence of a double bond is shown by the fact that the compound does not decolorise dilute permanganate solution during at least a minute at room temperature or at 80°. This is a much more trustworthy test for unsaturation than the use of bromine in chloroform (Schmidt, *loc. cit.*).

THE UNIVERSITY OF MELBOURNE. [*Received, April 25th*, 1932.]