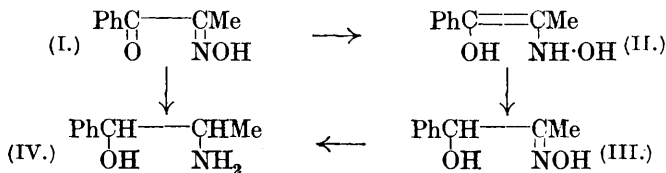


CLVII.—*Nor-dl-ephedrine and Nor-dl-ψ-ephedrine.*

By DONALD HOLROYDE HEY.

As previous attempts (this vol., p. 18) to obtain *nor-dl-ephedrine* and *nor-dl-ψ-ephedrine* (IV) from *isonitrosopropiophenone* (I) by direct reduction had proved unsatisfactory, attention was directed to the *oxime* of phenylacetylcarbinol (III): this on reduction with sodium amalgam in dilute acetic acid solution readily gave a viscous oil, which on treatment with hydrochloric acid gave *nor-dl-ephedrine* hydrochloride together with a small quantity of *nor-dl-ψ-ephedrine* hydrochloride. By introducing suitable modifications of the methods of obtaining phenylacetylcarbinol described in the literature the yield of this compound has been more than doubled, which therefore greatly improves the efficiency of this method of synthesis. A similar method, depending on the reduction of the oximes of ketonic alcohols of the type  $\text{OH}\cdot\text{CHPh}\cdot\text{COR}$ , has been recorded by Tiffeneau and Lévy (*Compt. rend.*, 1926, **183**, 969).



In the reduction of *isonitrosopropiophenone* (I), as carried out by Rabe (*Ber.*, 1912, **45**, 2166), in addition to a small quantity of the amino-alcohol (IV), a second compound was obtained, melting at  $112^\circ$ , which was described as the *oxime* of phenylacetylcarbinol (III). Hartung and Munch (*J. Amer. Chem. Soc.*, 1929, **51**, 2262) also observed the formation of a second compound, but only when *isonitrosopropiophenone* was reduced catalytically in the absence of hydrochloric acid. This compound melted at  $108\text{--}110^\circ$  and was not identified. The results of the present investigation give further support to Rabe's contention that the compound isolated by him was the *oxime* of phenylacetylcarbinol, which agrees in all its

properties with those of the oxime here described. The compound isolated by Hartung and Munch has also now been identified as the oxime of phenylacetylcarbinol. A specimen, kindly submitted by Dr. Hartung, produced no depression of melting point when mixed with the oxime described in this communication, and further observations by Dr. Hartung confirm this view. While there are many examples of the reduction of  $\alpha$ -oximino-ketones to amino-ketones, their reduction to oximino-alcohols is apparently very rare. However, the formation of this oxime in the reduction of *is*onitrosopropiophenone, though unusual, would not necessarily signify that the oximino-group is less susceptible to the action of the reducing agent than the carbonyl group (compare Hartung and Munch, *loc. cit.*), since it is not improbable that, under the conditions employed, the oxime is formed by molecular rearrangement of an intermediate hydroxylamino-alcohol (II).

#### EXPERIMENTAL.

*dl*-Mandelamide was prepared in excellent yield by the method of McKenzie and Wren (J., 1908, **93**, 310).

*Preparation of Phenylacetylcarbinol.*—By observing the following modifications in the methods of Wren (J., 1909, **95**, 1592) and of Tiffeneau and Lévy (*Bull. Soc. chim.*, 1925, **37**, 1247) the yields of phenylacetylcarbinol were increased to about 50% of the theoretical yield. Well-powdered *dl*-mandelamide (20 g.) was added very slowly to an excess of the Grignard reagent (7 mols.), well cooled in ice. The latter was prepared from 22 g. of magnesium, 140 g. of methyl iodide, and 250 c.c. of dry ether. When all the amide had been added, the mixture was kept at room temperature for 1 hour and then gently boiled under reflux for 12 hours. The solution, well cooled in ice, was decomposed by the gradual addition of ice and dilute sulphuric acid. No unchanged amide separated and the liberated phenylacetylcarbinol was extracted with ether and dried. It distilled as a pale yellow oil (9.5 g.) at 135—137°/24 mm. (Found : C, 71.8; H, 6.6. Calc. for  $C_9H_{10}O_2$  : C, 72.0; H, 6.7%). The semicarbazone, from boiling toluene, melted at 194°.

The 2 : 4-dinitrophenylhydrazone was prepared by warming an alcoholic solution of 2 : 4-dinitrophenylhydrazine and phenylacetylcarbinol. Orange needles separated on cooling, which after recrystallisation from alcohol melted at 170° (Found : N, 17.1.  $C_{15}H_{14}O_5N_4$  requires N, 17.0%).

The *oxime* of phenylacetylcarbinol was prepared by boiling under reflux for 2 hours a solution of 5 g. of the ketone, 2.6 g. of hydroxylamine hydrochloride, and 1.5 g. of sodium hydroxide in water with the addition of sufficient alcohol to make the solution homogeneous

at the temperature of boiling. When cold, the solution was acidified and the oxime was extracted repeatedly with ether and dried. Evaporation of the ether left an oily residue, which when kept in a vacuum deposited a crystalline solid (4 g.). Recrystallisation from hot water gave the oxime in white needles, m. p. 112.5° (Found : C, 65.55; H, 6.3; N, 8.4.  $C_9H_{11}O_2N$  requires C, 65.45; H, 6.7; N, 8.5%). A small quantity of a less soluble compound was also formed, which crystallised from alcohol in small white needles, m. p. 231°. This was in all probability phenylmethylglyoxime (Borsche, *Ber.*, 1907, 40, 740) (Found : N, 15.8. Calc. for  $C_9H_{10}O_2N_2$  : N, 15.7%).

*Reduction of Phenylacetylcarbinol Oxime.*—60 G. of 3% sodium amalgam were gradually added to a solution of the oxime (2 g.) in dilute acetic acid. After 6 hours, the mixture was made alkaline and extracted several times with ether. After drying over solid caustic potash, evaporation of the ether left a colourless viscous oil, which was dissolved in warm hydrochloric acid. The solid which separated on standing was recrystallised from absolute alcohol, nor-*dl*-ephedrine hydrochloride being obtained, m. p. 192° after a second recrystallisation (Found : Cl, 18.7. Calc. for  $C_9H_{13}ON, HCl$  : Cl, 18.9%). From the mother-liquor a small quantity of nor-*dl*- $\psi$ -ephedrine hydrochloride was obtained, which after several recrystallisations from absolute alcohol melted at 169° (Found : Cl, 18.9%) (compare Nagai and Kanao, *Annalen*, 1929, 470, 157).

THE UNIVERSITY, MANCHESTER.

[Received, April 7th, 1930.]

---