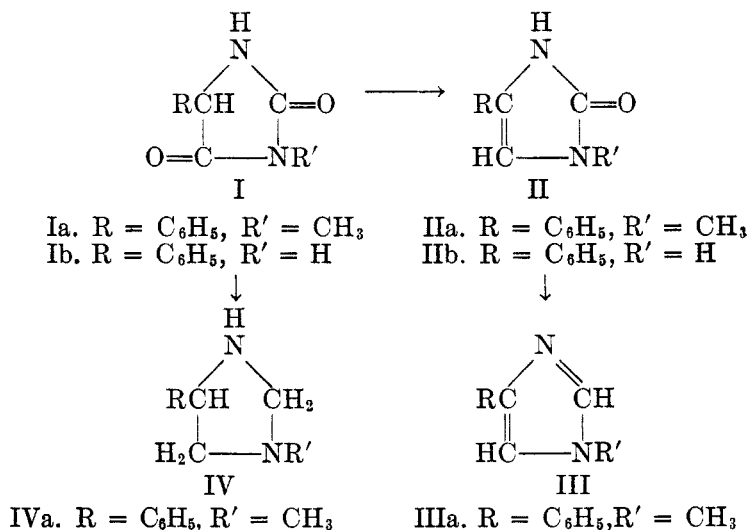


## THE ACTION OF LITHIUM ALUMINUM HYDRIDE ON 3-METHYL-5-PHENYLHYDANTOIN AND 5-PHENYLHYDANTOIN

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During investigations on the properties of hydantoins in these laboratories the reduction of these compounds with lithium aluminum hydride (1) was studied. The hydantoin nucleus (I) possesses two amide-type linkages, each of which is subject to reduction. Partial reduction may lead to an imidazolone (II) or an imidazole (III).<sup>1</sup> Complete reduction of both carbonyls leads to an imidazolidine (IV).<sup>2</sup>



We have found it possible to reduce selectively the carbonyl groups of certain hydantoins to type II compounds. Thus, when 3-methyl-5-phenylhydantoin (Ia) was treated dropwise with an ether solution of lithium aluminum hydride and allowed to stand overnight, it was converted to the 2(3H)-imidazolone (IIa) in good yield.

It was difficult to cause the 2-carbonyl group to undergo reaction. However, by prolonged refluxing of IIa with the reagent, a small amount of the imidazole (IIIa) could be obtained. The melting point of this product was in agreement with that reported by Hazeldine (5).

The completely reduced imidazolidine could be obtained from the methyl-phenylhydantoin by altering the conditions of reaction. On treating Ia with an excess of lithium aluminum hydride under Soxhlet conditions, IVa was obtained in fair yield.

<sup>1</sup> Compare the reduction of oxindoles by Julian and Printy (2).

<sup>2</sup> Compare the reduction of 2-pyrrolidone derivatives (3, 4).

When 5-phenylhydantoin (Ib) was subjected to the same conditions used to prepare IIa, the corresponding 4-phenyl-2(3H)-imidazolone (IIb) was obtained.

Assignment of the 2(3H)-imidazolone structure to the compounds described was made primarily on the basis of the following data: IIa was reduced catalytically with platinum oxide (6) to a compound whose analytical values agreed with those calculated for 4-cyclohexyl-1-methyl-2-imidazolidone. Furthermore, reduction with palladium black yielded a compound corresponding to 1-methyl-4-phenyl-2-imidazolidone. Reduction of IIb with palladium black in a similar manner gave 4-phenyl-2-imidazolidone, the melting point of which agreed with that reported by Kanewskaja (7) as well as by Cook (8). When this known compound was methylated, the 1-methyl-4-phenyl-2-imidazolidone obtained was shown to be identical with the product obtained from IIa.

The structure of the imidazolidine (IVa) was demonstrated by benzoylation, which resulted in ring rupture and formation of  $N^1, N^2$ -dibenzoyl- $N^2$ -methyl-1-phenylethylenediamine.

### EXPERIMENTAL<sup>3</sup>

*1-Methyl-4-phenyl-2(3H)-imidazolone (IIa).* To a stirred suspension of 19 g. (0.1 mole) of 3-methyl-5-phenylhydantoin in 300 cc. of anhydrous ether was added a solution of 3.8 g. (0.1 mole) of lithium aluminum hydride in 400 cc. of anhydrous ether so that a constant reflux rate was maintained. This addition required about three hours. Stirring was continued at room temperature for 16 hours; the complex was then decomposed by adding dilute hydrochloric acid followed by concentrated acid. The remaining precipitate was separated and recrystallized from ethyl alcohol. The yield was 11.5 g. (66%); m.p. 275–278°. Five grams of unreacted hydantoin could be isolated from the ether layer. No basic material was recovered from the acid layer.

*Anal.* Calc'd for  $C_{10}H_{10}N_2O$ : C, 69.0; H, 5.8; N, 16.1.

Found: C, 69.2; H, 5.7; N, 15.9.

*1-Methyl-4-phenylimidazole (IIIa).* A solution of 1.9 g. (0.051 mole) of lithium aluminum hydride was placed in a round-bottom flask and 3.0 g. (0.017 mole) of IIa was placed in a Soxhlet. Refluxing was continued for three weeks, but even after this extended period of time some of the imidazolone was still in the Soxhlet. The complex was decomposed in the usual manner, and the unreacted IIa removed by filtration. The acidic layer was made alkaline with sodium hydroxide and extracted with ether. The ether was removed, and the residue (0.5 g.) recrystallized from Skellysolve C; the product melted at 109.0–109.5° (5).

*Anal.* Calc'd for  $C_{10}H_{10}N_2$ : C, 75.9; H, 6.4; N, 17.7.

Found: C, 76.2; H, 6.5; N, 17.9.

*4-Cyclohexyl-1-methyl-2-imidazolidone.* Reduction of IIa with Adams' catalyst in glacial acetic acid under a hydrogen pressure of 30 pounds and recrystallization of the product from water gave material melting at 126°.

*Anal.* Calc'd for  $C_{10}H_{18}N_2O$ : C, 65.9; H, 10.0; N, 15.4.

Found: C, 65.9; H, 9.7; N, 15.3.

*1-Methyl-4-phenyl-2-imidazolidone.* Reduction of IIa as above except with palladium black catalyst gave a product melting at 131–133° (recrystallized from water).

*Anal.* Calc'd for  $C_{10}H_{12}N_2O$ : C, 68.2; H, 6.9; N, 15.9.

Found: C, 68.4; H, 6.7; N, 15.6.

*1-Methyl-4-phenylimidazolidine (IVa).* In a 3-neck flask equipped with a condenser, Soxhlet extractor, stirrer, and calcium-chloride tube were placed 100 cc. of anhydrous

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<sup>3</sup> Microanalyses by E. F. Shelberg and staff. Catalytic hydrogenations by M. Freifelder and G. R. Stone.

ether and 11.4 g. (0.3 mole) of lithium aluminum hydride. Nineteen grams (0.1 mole) of 3-methyl-5-phenylhydantoin was placed in the Soxhlet, and refluxing was carried out for 11 hours. The complex was decomposed as before. The layers were separated, and the acid layer made alkaline by adding sodium hydroxide. This was extracted several times with ether, and the ether solution dried over sodium sulfate. The ether residue was distilled at 88.5° (2 mm.). The yield was 7.0 g. (43%);  $n_D^{25}$  1.5200.

Anal. Calc'd for  $C_{10}H_{15}N_2$ : C, 73.6; H, 9.3; N, 17.2.

Found: C, 73.3; H, 9.4; N, 16.9.

*Benzoylation of IVa.* Two grams of the imidazolidine was treated with benzoyl chloride under Schotten-Baumann conditions. The precipitate of  $N^1, N^2$ -dibenzoyl- $N^2$ -methyl-1-phenylethylenediamine was recrystallized from 50% ethanol. The product melted at 122–123°.

Anal. Calc'd for  $C_{23}H_{22}N_2O_2$ : C, 77.1; H, 6.2; N, 7.8.

Found: C, 77.0; H, 6.0; N, 7.5.

*4-Phenyl-2(3H)-imidazolone (IIb).* The procedure described for IIa was used with 17.6 g. (0.1 mole) of 5-phenylhydantoin and 5.7 g. (0.15 mole) of lithium aluminum hydride. The product melted at 340–343° after recrystallization from alcohol.

Anal. Calc'd for  $C_9H_8N_2O$ : C, 67.5; H, 5.0; N, 17.5.

Found: C, 67.4; H, 4.9; N, 17.5.

*4-Phenyl-2-imidazolidone.* The catalytic reduction of IIb was carried out in the manner described for IIa, yielding material melting at 158–159° after recrystallization from water (7, 8).

Anal. Calc'd for  $C_9H_{10}N_2O$ : C, 66.6; H, 6.2; N, 17.3.

Found: C, 66.8; H, 6.3; N, 17.4.

*Methylation of 4-phenyl-2-imidazolidone.* 4-Phenyl-2-imidazolidone (0.13 g.) was methylated with methyl sulfate in alkaline 50% methanol in the usual manner. The product melted at 133–134°. The mixed melting point with 1-methyl-4-phenyl-2-imidazolidone prepared from IIa was 132–133°.

#### SUMMARY

Selective reduction of 5-phenylhydantoin and its 3-methyl derivative with lithium aluminum hydride yields the corresponding 2(3H)-imidazolones. Under different conditions the 3-methyl-5-phenylhydantoin was converted also to an imidazole and to an imidazolidine. Several new imidazole derivatives are described.

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