

solution was added 25 ml. of concentrated ammonium hydroxide. The ammoniacal solution was allowed to stand seventy hours in a stoppered flask at room temperature and then concentrated to a gummy residue. The crude material was triturated with an ethanol-ether solution and the tan, granular solid which separated was collected and recrystallized from warm ethanol. The yield of the amide was 1.1 g. (65%), m.p. 144–145°.

*Anal.* Calcd. for  $C_8H_{11}N_3O$ : C, 46.5; H, 8.5; N, 32.6. Found: C, 46.2; H, 8.8; N, 32.6.

**2-Piperazinecarboxylic Acid Hydrazone (IX).**—A mixture consisting of 0.80 g. (0.0051 mole) of VII, 1.0 ml. of hydrazine hydrate (100%) and 10 ml. of dry ethanol was refluxed for 15 hours. The volatile material was then removed at reduced pressure and steam-cone temperature leaving a semi-crystalline residue which solidified when triturated with two 10-ml. portions of dry ether; 0.70 g. (95%). An analytical sample that was recrystallized twice from hot benzene had a m.p. 100–101°.

*Anal.* Calcd. for  $C_8H_{12}N_4O$ : C, 41.7; H, 8.3; N, 38.8. Found: C, 42.0; H, 8.5; N, 38.2.

**Dehydrogenation of 2-Piperazinecarboxamide (X).**—A sublimation tube equipped with inlet and outlet tubes was charged with a mixture of 0.040 g. (0.00031 mole) of 2-piperazinecarboxamide and 0.040 g. of palladium-on-charcoal (5%). The sublimation apparatus was set upright in a Wood metal-bath and the system was swept with nitrogen (an atmosphere of nitrogen was maintained by means of a slight positive pressure, ca. 40 mm., during the course of the reaction). When the temperature of the metal-bath reached 290°, gas was evolved and the temperature was regulated between 290–305° until the evolution of gas ceased. The crystalline sublimate which formed on the sides of the tube during the dehydrogenation was collected and triturated with small portions of ether and acetone, m.p. 173–183° (micro-stage melting block). The infrared absorption spectrum of this material is shown in Fig. 1.

**Acknowledgment.**—The authors wish to thank Mr. L. Brancone and staff for the analytical results and Mr. W. Fulmor for the infrared absorption measurements.

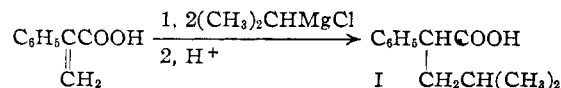
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## The Reaction of Isopropylmagnesium Chloride with Atropic, Tropic and $\alpha$ -Phenylisocaproic Acids

By F. F. BLICKE AND HAROLD ZINNES

RECEIVED JULY 5, 1955

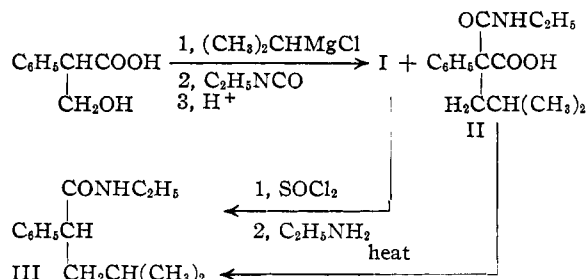
The interaction of isopropylmagnesium chloride with crotonic acid by 1,4-addition has been described.<sup>1</sup> It has now been found that this Grignard reagent reacts with atropic acid in a similar manner. When the  $\alpha,\beta$ -unsaturated acid was refluxed with a solution of isopropylmagnesium chloride and the resulting mixture was hydrolyzed,  $\alpha$ -phenylisocaproic acid (I) was obtained in 72% yield. This acid



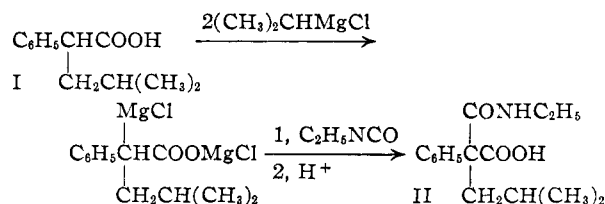
was found to be identical with the  $\alpha$ -phenylisocaproic acid obtained by hydrolysis of  $\alpha$ -phenylisocapronitrile according to the method of Bodroux and Taboury.<sup>2</sup>

Compound I was also produced in 51% yield when tropic acid was treated with isopropylmagne-

sium chloride and the mixture was hydrolyzed. When ethyl isocyanate was added to the reaction mixture before hydrolysis there was obtained, in addition to I (25% yield), a 40% yield of  $\alpha$ -(ethylcarbamyl)- $\alpha$ -phenylisocaproic acid (II). The structure of II was established by its conversion, by decarboxylation, into the same  $\alpha$ -phenyl-N-ethylisocaproamide (III) which was formed by successive treatment of I with thionyl chloride and ethylamine. These reactions indicate that tropic acid may have undergone initial dehydration to atropic acid under the influence of the Grignard reagent.<sup>3</sup>



Compound II was also prepared by an Ivanov reaction from compound I and ethyl isocyanate.



### Experimental

**$\alpha$ -Phenylisocaproic Acid (I) from Atropic Acid.**—Isopropylmagnesium chloride was prepared from 2.0 g. of magnesium, 10 cc. of isopropyl chloride and 80 cc. of ether. After the addition of 3.7 g. of atropic acid,<sup>4</sup> dissolved in 150 cc. of benzene, the material was refluxed for 18 hours. The mixture was hydrolyzed with ammonium chloride solution, the aqueous layer was separated and the ice-cold solution was made acidic to congo red. The solid precipitate weighed 3.4 g. (71%), m.p. and mixed m.p. 77–78° after recrystallization from petroleum ether (40–60°). Calcd. for  $C_{12}H_{16}O_2$ : neut. equiv., 192.3. Found: neut. equiv., 193.2.

**$\alpha$ -Phenylisocaproic Acid (I) from Tropic Acid.**—To the stirred isopropylmagnesium chloride solution obtained from 5.4 g. of magnesium, 25 cc. of isopropyl chloride and 100 cc. of ether, there was added 225 cc. of benzene and 8.3 g. of powdered tropic acid.<sup>6</sup> The mixture was refluxed for 18 hours. The product was isolated in the manner described above; yield 5.5 g. (57%), m.p. and mixed m.p. 77–78° after recrystallization from petroleum ether (40–60°).

**$\alpha$ -Phenyl- $\alpha$ -(ethylcarbamyl)-isocaproic Acid (II).** (A) **From Tropic Acid.**—Benzene (400 cc.) and then 16.6 g. of powdered tropic acid were added to the stirred solution obtained from 10.7 g. of magnesium, 50 cc. of isopropyl chloride and 200 cc. of ether. A solution of 25.9 g. of ethyl isocyanate in 100 cc. of benzene was added and the mixture was refluxed for 4 hours. After treatment of the material in the usual manner, the precipitated oily mixture of products was extracted with ether. The residue, obtained after removal of the ether, was triturated with cold

(3) In the study of a reaction between methyl tropate and phenylmagnesium bromide, A. McKenzie and E. R. Winton (*J. Chem. Soc.*, 840 (1940)) suggested that the initial reaction consisted of a dehydration of the tropate to methyl atropate.

(4) H. S. Raper, *J. Chem. Soc.*, 2558 (1923).

(5) Reference 2, m.p. 78–79°.

(6) F. F. Blicke, H. Raffelson and B. Barna, *This Journal*, **74**, 253 (1952).

(1) F. F. Blicke and Harold Zinnes, *This Journal*, **77**, 5399 (1955).

(2) F. Bodroux and F. Taboury, *Bull. soc. chim.*, [4] **7**, 668 (1910).

benzene. The solid material (10.6 g., 40%) melted at 108–110° dec. after recrystallization from diisopropyl ether.<sup>7</sup>

*Anal.* Calcd. for  $C_{16}H_{21}O_3N$ : C, 68.41; H, 8.04; neut. equiv., 263.3. Found: C, 68.51; H, 7.83; neut. equiv., 264.0.

The benzene wash solution was evaporated to dryness and the residue was extracted with 150 cc. of petroleum ether (30–40°). After removal of the solvent from the extract, there was obtained 4.8 g. (25%) of  $\alpha$ -phenylisocaproic acid, m.p. and mixed m.p. 77–78° after recrystallization from petroleum ether (40–60°).

(B) From  $\alpha$ -Phenylisocaproic Acid.—Isopropylmagnesium chloride, obtained from 1.6 g. of magnesium, 8 cc. of isopropyl chloride and 25 cc. of ether, was stirred, a solution of 5.7 g. of  $\alpha$ -phenylisocaproic acid in 150 cc. of benzene was added and the mixture was refluxed for 18 hours. Ethyl isocyanate (2.6 g.), dissolved in 50 cc. of benzene, was added and the mixture was refluxed for 4 hours. The mixture was treated in the manner described above; yield 1.1 g., m.p. and mixed m.p. 108–110° dec. after recrystallization from diisopropyl ether. Calcd. for  $C_{16}H_{21}O_3N$ : neut. equiv., 263.3. Found: neut. equiv., 263.8.

$\alpha$ -Phenyl-N-ethylisocaproamide (III).—When  $\alpha$ -phenyl- $\alpha$ -(ethylcarbamyl)-isocaproic acid (II) was heated in an oil-bath (125°) for 1 hour, carbon dioxide was evolved. The solidified residue was recrystallized from petroleum ether (30–40°); m.p. 64–66°.

*Anal.* Calcd. for  $C_{14}H_{21}ON$ : C, 76.67; H, 9.65. Found: C, 76.70; H, 9.56.

The amide also was prepared by successive treatment of I with thionyl chloride and aqueous ethylamine; m.p. and mixed m.p. 64–66° after recrystallization from petroleum ether (30–40°).

(7) A positive qualitative test for nitrogen was obtained.

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## The Base-catalyzed Cleavage of 2,2-Dialkyl-1,3-diols

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The cleavage of a 1,3-diol by heating with a base was first observed by Nef<sup>1</sup> who heated the sodium salt of 1,3-propanediol at 150° and obtained a small amount of ethyl alcohol and hydrogen. He also heated the diol with an equimolar quantity of sodium hydroxide and obtained a complex mixture of products in which ethyl alcohol, propyl alcohol and acetic acid were identified. The alcohols were presumed to have been formed by the reduction of aldehydes, which were considered to be the primary cleavage products.

More recently, Searles<sup>2</sup> reported an analogous cleavage of 1,3-diols to carbonyl compounds and alcohols when heated at 200° with concentrated aqueous sodium or potassium hydroxide. A hydrogen-bonded cyclic intermediate was proposed to account for this cleavage.

The related base-catalyzed cleavages of  $\beta$ -dimethylaminopivalophenone methiodide,<sup>3</sup>  $\beta,\beta$ -dimethyl- $\alpha$ -tosyloxy- $\gamma$ -butyrolactone<sup>4</sup> and 3-bromo-2,2-dimethyl-1-propanol<sup>5</sup> also have been reported.

(1) J. U. Nef, *Ann.*, **335**, 302 (1904).

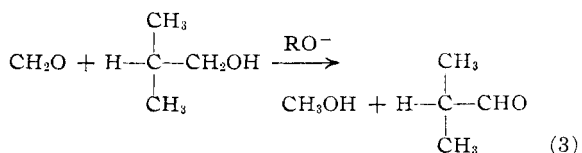
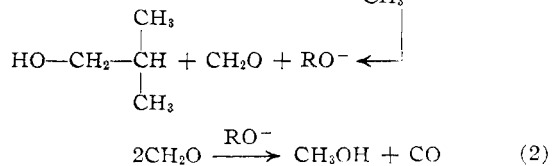
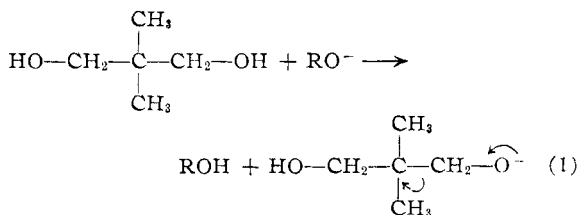
(2) S. Searles and E. K. Ives, Abstracts of Papers, 127th Meeting of the American Chemical Society, 1955, p. 24N.

(3) H. R. Snyder and J. H. Brewster, *THIS JOURNAL*, **71**, 1061 (1949).

(4) H. Bretschneider and H. Hass, *Monatsh.*, **81**, 945 (1950).

(5) S. Searles and M. J. Gortatowski, *THIS JOURNAL*, **75**, 3030 (1953).

We wish to report the base-catalyzed cleavage of some 2,2-dialkyl-1,3-diols, which bears a formal resemblance to the cleavages mentioned above. When 2,2-dimethyl-1,3-propanediol was heated with a catalytic amount of dissolved sodium (or with calcium oxide at a slightly higher temperature) cleavage of the diol occurred, presumably according to the scheme



The products isolated were isobutyl alcohol, methanol, carbon monoxide and isobutyraldehyde. The carbon monoxide and part of the methanol may have arisen from a Cannizzaro-like disproportionation of formaldehyde or from the base-catalyzed decomposition of the Tishchenko reaction product, methyl formate. The isobutyraldehyde may have arisen from an Oppenauer reaction between isobutyl alcohol and formaldehyde.

Similarly, 2,2-diethyl-1,3-propanediol with dissolved sodium gave 2-ethyl-1-butanol, methanol, carbon monoxide and 2-ethylbutyraldehyde, while 2-methyl-2-propyl-1,3-propanediol gave 2-methyl-1-pentanol, methanol, carbon monoxide and 2-methylvaleraldehyde. The high-boiling residues produced were not investigated.

2,2,4-Trimethyl-1,3-pentanediol, which is unsymmetrical, underwent base-catalyzed cleavage more readily than the propanediols described above. In this case cleavage occurred predominantly at the carbon atom bearing the secondary hydroxyl group and led to the formation of isobutyl alcohol and isobutyraldehyde, although small amounts of the products from cleavage at the primary carbinol carbon were isolated: namely, methanol, carbon monoxide and 2,4-dimethyl-3-pentanone. The 2,4-dimethyl-3-pentanone presumably came from the Oppenauer oxidation of the primary cleavage product, 2,4-dimethyl-3-pentanol, which was not isolated.

Under conditions similar to those which resulted in the cleavage of the 2,2-dialkyl-1,3-diols described above, 2-ethyl-1,3-propanediol, 1,3-propanediol and 1,3-butanediol showed only a negligible amount of decomposition.

The related ester, butyl hydroxypivalate, when heated in the presence of dissolved sodium, under-