[Contribution from the Department of Chemistry, State University of Iowa]

# PREPARATION OF $\alpha,\beta,\beta$-TRIPHENYLETHYLAMINE AND $\beta,\gamma,\gamma$-TRIPHENYLPROPYLAMINE

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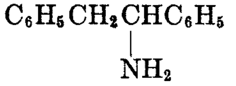
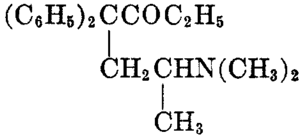
$\alpha,\beta$-Diphenylethylamine (I) derivatives have received a considerable amount of attention in the past as possible analgetics (1) and cancer-inhibiting compounds (2). The structure of the new and very powerful analgetic, Amidone (II), suggested that the analgetic behavior of these compounds might be enhanced by the introduction of another phenyl group on the $\beta$-carbon atom of $\alpha,\beta$-diphenylethylamine (I). The synthesis of the simplest amine, $\alpha,\beta,\beta$-triphenylethylamine (III), having this structure is reported in this paper. In the course of the work, $\beta,\gamma,\gamma$-triphenylpropylamine (IV) was also prepared as the hydrochloride.



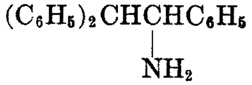
$$C_6H_5CH_2\underset{\displaystyle NH_2}{\underset{|}{C}}HC_6H_5$$

I



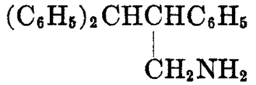
$$(C_6H_5)_2\underset{\displaystyle \underset{\displaystyle \underset{\displaystyle CH_3}{|}}{CH_2CHN(CH_3)_2}}{\underset{|}{C}}COC_2H_5$$

II



$$(C_6H_5)_2CH\underset{\displaystyle NH_2}{\underset{|}{C}}HC_6H_5$$

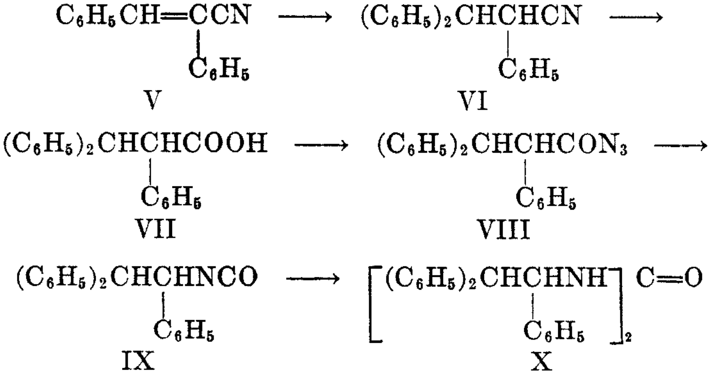
III



$$(C_6H_5)_2CH\underset{\displaystyle CH_2NH_2}{\underset{|}{C}}HC_6H_5$$

IV

$\alpha,\beta,\beta$-Triphenylethylamine (III) was prepared successfully by a Leuckart reaction on phenyl benzhydryl ketone. Proof for the structure of this product was the thermal decomposition of its hydrochloride into triphenylethylene and ammonium chloride.



$$\underset{\text{V}}{C_6H_5CH{=}\underset{\displaystyle C_6H_5}{\underset{|}{C}}CN} \longrightarrow \underset{\text{VI}}{(C_6H_5)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCN} \longrightarrow$$

$$\underset{\text{VII}}{(C_6H_5)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCOOH} \longrightarrow \underset{\text{VIII}}{(C_6H_5)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCON_3} \longrightarrow$$

$$\underset{\text{IX}}{(C_6H_5)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HNCO} \longrightarrow \underset{\text{X}}{\left[(C_6H_5)_2CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HNH\right]_2C{=}O}$$

Other methods of synthesis tried and found unsuccessful were dependent on $\alpha,\beta,\beta$-triphenylpropionitrile (VI) as a starting material. An attempt to prepare this compound (VI) by the reduction of α,β-diphenylcinnamonitrile failed with the usual catalysts, and gave β,γ,γ-triphenylpropylamine (IV) with platinized Raney nickel (3). The nitrile (VI) was obtained by the addition of phenylmagnesium bromide to α-phenylcinnamonitrile (V) (4) and was converted by acid hydrolysis to α,β,β-triphenylpropionic acid (VII). The preparation of α,β,β-triphenylethylamine (III) from this acid (VII) by a Curtius reaction failed because of the difficulty encountered in hydrolyzing the intermediate isocyanate (IX). Alkali and acid converted this compound (IX) to the urea (X) while alcohol had no effect.

The two amines (III, IV) showed analgetic behavior only at a toxic level.

## EXPERIMENTAL[1]

*N-Formyl-α,β,β-triphenylethylamine.* A mixture of phenyl benzhydryl ketone (6.8 g.) (5) and ammonium formate (5.4 g.) was heated gradually to 180–190° and maintained there for seven hours. Additional 2.5-g. amounts of ammonium formate were added during the heating after three and five hours had elapsed. The resulting mixture was cooled, filtered, and the greater portion used in the next step. A small amount, when recrystallized from ethanol three times, formed needles melting at 184–185°.

*Anal.* Calc'd for $C_{21}H_{19}NO$: C, 83.69; H, 6.37.
Found: 83.64; H, 6.45.

*α,β,β-Triphenylethylamine hydrochloride.* The above N-formyl derivative was refluxed with concentrated hydrochloric acid for 1½ hours and the resulting precipitate filtered after cooling. The amine hydrochloride was purified by dissolving it in 25% ethanol and filtering off impurities. The filtrate was made alkaline and the amine extracted with ether and precipitated again as the hydrochloride. The white powder obtained weighed 5.5 g. (75%); m.p. 271.5–273°.

*Anal.* Calc'd for $C_{20}H_{20}ClN$: C, 77.51; H, 6.52.
Found: C, 77.96; H, 6.58.

The hydrochloride upon heating to 275–280° decomposed into triphenylethylene and ammonium chloride. Recrystallization from methanol gave crystals, m.p. 64–67°, which did not depress the melting point of triphenylethylene.

*β,γ,γ-Triphenylpropylamine hydrochloride.* A solution of α,β-diphenylcinnamonitrile (7.5 g.) (6) in dioxane (100 ml.) and 10 *N* sodium hydroxide (0.35 ml.) was reduced in the presence of platinized Raney nickel (3) (7.5 g.) with hydrogen under three atmospheres pressure. During the course of the reaction an additional 7.5 g. of catalyst and 0.5 ml. of 10 *N* alkali were added. The resulting mixture was filtered, acidified with hydrochloric acid, and the solution evaporated to 10 ml. Addition of ether precipitated the amine hydrochloride which, after three recrystallizations from a 1:2:3 mixture of absolute ethanol, ethyl acetate, and ether, melted at 269–272°; yield, 5.7 g. (76%).

*Anal.* Calc'd for $C_{21}H_{22}ClN$: C, 77.87; H, 6.85; N, 4.33; Cl, 10.95.
Found: C, 77.54; H, 6.65; N, 4.48; Cl, 10.87.

*α,β,β-Triphenylethyl isocyanate.* α,β,β-Triphenylpropionic acid (2.09 g.) (4) was converted into its acid chloride with thionyl chloride. The crude product was treated in acetone (30 ml.) at 0–8° with a solution of sodium azide (0.4 g.) in water (2 ml.) in the course of three minutes. Addition of water (25 ml.) gave the azide melting at 55–56° (d.) in a quantitative yield. The azide was not purified but was refluxed immediately in benzene (25 ml.) for four hours. Removal of the benzene gave the isocyanate which after one recrystallization from ethanol melted at 122–123°; yield, 1.5 g. (75%).

*Anal.* Calc'd for $C_{21}H_{17}NO$: C, 85.00; H, 5.73.
Found: C, 85.37; H, 6.13.

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[1] Melting points are corrected.

*sym-Di-(α,β,β-triphenylethyl)urea.* The isocyanate (0.6 g.) gave upon refluxing with either 10 ml. of 40% potassium hydroxide or 12 ml. of concentrated hydrochloric acid a mixture of the isocyanate and the *sym*-urea. The urea was separated by its greater solubility in alcohol. Recrystallization from alcohol gave crystals, m.p. 246–247°.

*Anal.* Calc'd for $C_{41}H_{36}N_2O$: C, 86.00; H, 6.34.

Found: C, 86.38; H, 6.73.

The isocyanate was not affected by refluxing with ethanol for three hours.

## SUMMARY

1. α,β,β-Triphenylethylamine hydrochloride was prepared by a Leuckart reaction on phenyl benzhydryl ketone.

2. β,γ,γ-Triphenylpropylamine hydrochloride was prepared by the reduction of α,β-diphenylcinnamonitrile using platinized Raney nickel as a catalyst.

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## REFERENCES

(1) (a) Dodds, Lawson, and Williams, *Nature*, **154**, 514 (1944); (b) McPhee, *J. Am. Chem. Soc.*, **68**, 624 (1946).

(2) Shear, First National Medicinal Chemistry Symposium, American Chemical Society, Ann Arbor, Michigan, 1948.

(3) Delepine and Horeau, *Bull. soc. chim.*, [5] **4**, 31 (1937); Delepine and Decombe, *Compt. rend.*, **222**, 90 (1946).

(4) Kohler, *Am. Chem. J.*, **35**, 386 (1906).

(5) Blitz, *Ber.*, **32**, 654 (1899).

(6) Bodroux, *Bull. soc. chim.*, [4] **9**, 758 (1911).