calcium chloride) was passed in for four hours. After filtration from the catalyst, the xylene was distilled in a vacuum; the residual product was obtained in the form of a pale yellow oil which solidified when stirred. The aldehyde, washed with a little low-boiling petroleum ether, was obtained in the form of fine, white needles melting at 101°; yield 16.5 g. When the product was recrystallized from methyl alcohol, the melting point was unchanged. The compound is soluble in most of the organic solvents; recrystallization from alcohol is wasteful. The product gave a positive aldehyde test with Schiff reagent. It was further characterized by analysis and preparation of the oxime and hydrazone.

Anal. Calcd. for $C_{21}H_{18}O$: C, 88.1; H, 6.3. Found: C, 87.9; H, 6.4.

β,β,β-Triphenylpropionaldoxime.—Triphenylpropionaldehyde, 5 g., hydroxylamine hydrochloride, 4 g., and sodium bicarbonate, 5 g., were added to 50 ml. of 95% alcohol and 8 ml. of water and the mixture was refluxed. After an hour the hot solution was filtered and diluted with boiling water to faint turbidity. A white crystalline precipitate formed, which was collected, washed with warm water and dried in a vacuum desiccator; yield 4.6 g., recrystallized from ethanol, m. p., 190.5–191° (cor.).

Anal. Calcd. for $C_{21}H_{19}NO$: N, 4.64. Found: N (Dumas), 4.75.

Triphenylpropionaldehyde Hydrazone.—A mixture of 5.7 g. of triphenylpropionaldehyde, 5 g. of recently fused and powdered barium oxide, 6 g. of hydrazine hydrate (90%) and 25 ml. of absolute ethanol was refluxed for ten hours. The alcohol was removed by distillation in a vacuum. The residue was extracted with ether and the latter evaporated in a stream of dry air. A white crystalline solid remained; yield 4.2 g. The hydrazone was found to be soluble in the usual organic solvents. It was best purified by means of fractional crystallization from ether; m. p., 92°.

Anal. Calcd. for $C_{21}H_{20}N_2$: N, 9.3. Found: N (Dumas), 9.4.

When the hydrazone in benzene solution at 5° was shaken with yellow mercuric oxide for several hours, there resulted, after filtration and removal of the solvent, a pale yellow oil which solidified gradually. The product was extracted with ether and a small amount of white, insoluble material remained; m. p. 189–192°. This was identified as triphenylpropionaldazine by comparison with an authentic sample of the latter. The crude reaction products from this and other similar experiments were found by test to contain no diazo compound. No definite product other than the aldazine was isolated.

Synthesis of β,β,β-Triphenylpropionaldazine.—When β,β,β-triphenylpropionaldehyde hydrazone, 0.45 g., and triphenylpropionaldehyde, 0.43 g., were refluxed in ether solution for an hour, a white solid precipitated from the solution. This was collected, washed thoroughly with boiling ether, and dried; m. p. 190–191°.

Anal. Calcd. for $C_{42}H_{36}N_2$: N, 4.9. Found: N (Dumas), 5.1.

Summary

Decompositions of α-diazo-γ,γ,γ-triphenylpropane are found to result in the formation of products to be anticipated from intermolecular rather than intramolecular transformations. This is in contrast to the behavior of the lower homolog, diazo-β,β,β-triphenylethane. The thermal decomposition of the diazopropane yields, principally, β,β,β-triphenylpropionaldehyde azine, and its decomposition in the presence of acetic or benzoic acid gives, respectively, γ,γ,γ-triphenylpropyl acetate or benzoate. It is recognized that some of the evidence may not exclude absolutely the possibility of intramolecular rearrangement but none of the observations appears definitely to support such a conclusion. Reference is made to structural factors affecting the stability of certain compounds containing the β,β,β-triphenylethyl group.

There is described a feasible method for the preparation of β,β,β-triphenylpropionitrile; there are presented syntheses of γ,γ,γ-triphenylpropylamine its hydrochloride, chloroplatinate, nitrate and nitrite; of ethyl N-γ,γ,γ-triphenylpropyl carbamate, the corresponding crystalline nitrosocarbamate, and α-diazo-γ,γ,γ-triphenylpropane; and of β,β,β-triphenylpropionaldehyde, its oxime, hydrazone and azine. Evidence is cited for the persistence of the carbon skeleton in certain transformations involving the diazo compound.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY]

The Action of Grignard Reagents upon β,β,β-Triphenylpropionitrile. Stability of the Triphenylethyl Grouping[1]

BY R. L. GARNER AND LESLIE HELLERMAN

The properties of certain compounds containing as a substituent the β,β,β-triphenylethyl grouping afford presumptive evidence regarding a rather remarkable degree of stability or non-reactivity in this configuration. The pertinent observations are considered to be related to the inductive effect of the unsymmetrically substituted, electron-attracting phenyl groups, connoting a significant degree of "deactivation"[2] in the methylene grouping vicinal to the triphenylmethyl group. Cumulative evidence includes (1) certain reactions of α-diazo-γ,γ,γ-triphenylpropane, leading to non-rearranged products of its decomposition[2]; and (2) marked resistance to the action of powerful oxidizing reagents (*e. g.*, hot chromic acid) of α,α,α-triphenylethane, β,β,β-triphenylpropionic acid and β,β,β-triphenylpropionitrile.[3] In addition, β,β,β-triphenylethylamine is much less readily attacked by oxidizing reagents under various conditions[4] than are such amines as benzylamine and benzohydrylamine.[5] Most convincing, however, are the clear-cut observations recorded

(1) Submission of this paper has been delayed for some years; compare ref. 2.

(2) Hellerman and Garner, THIS JOURNAL, **68**, 819 (1946).

(3) Ref. 2, p. 819; Kuntze-Fechner, *Ber.*, **36**, 473 (1903).

(4) Hellerman, THIS JOURNAL, **68**, 825 (1946).

(5) Hellerman and Sanders, *ibid.*, **59**, 1742 (1927).

herein which concern addition reactions of organomagnesium halides to β,β,β-triphenylpropionitrile, resulting in high yields of the corresponding ketimine salts.[6] This is shown, for example, for the reactions involving phenylmagnesium and ethylmagnesium bromides.

$$(C_6H_5)_3CCH_2CN + RMgBr \longrightarrow (C_6H_5)_3CCH_2C(=NMgBr)R$$

$$(C_6H_5)_3CCH_2C(=NMgBr)R + H_2O \xrightarrow[(NH_4Cl)]{} (C_6H_5)_3CCH_2C(=NH)R + MgBrOH$$

These results appear noteworthy inasmuch as the alkyl and aralkyl cyanides are known to have an "acidifying" action upon Grignard reagents as a result of which only relatively low yields of ketimines or ketones may be anticipated in these cases; in such reactions acetonitrile affords little or no ketone, and benzyl cyanide gives, after hydrolysis of the reaction mixtures, a low yield (*ca.* 3%) of benzylphenylketimine or desoxybenzoin, in contrast to high yields obtainable when benzonitriles are employed.[6]

It would appear therefore that in processes of this type, also, the β,β,β-triphenylethyl group, acting "as a unit" and preserving its identity in these addition reactions of β,β,β-triphenylpropionitrile, is possessed of marked stability in the sense discussed above. There is displayed here little or none of the acidic quality commonly observed with nitriles with the substituent grouping, $-CH_2CN$.

Experimental

Preparation of Phenyl β,β,β-Triphenylethyl Ketimine Hydrochloride, $[(C_6H_5)_3CCH_2](C_6H_5)C{=}NH_2Cl$.—To phenylmagnesium bromide prepared from 6.12 g. of magnesium and 39.2 g. of bromobenzene in 100 ml. of dry ether, was added slowly 14 g. of finely powdered triphenylpropionitrile,[2] suspended in 125 ml. of ether. The solution was mechanically stirred and the usual precautions were taken to exclude moisture. The mixture was heated at the boiling point for four hours. It was then cooled to −5°, and the magnesium complex cautiously hydrolyzed by treatment with cracked ice and ammonium chloride at −5 to 5°. The reaction mixture was extracted rapidly with ether and the extracts dried at once, at −5°, by agitation with anhydrous sodium sulfate. The ether solution was separated from the sodium sulfate by filtration and the filtrate was saturated at 0° with dried hydrogen chloride gas. The white crystalline product was rapidly brought upon a filter, washed with dry ether, and placed in a vacuum desiccator over phosphoric anhydride and solid sodium hydroxide; yield, 12.8 g. (70%). The ketimine hydrochloride was readily soluble in dry chloroform from which it was precipitated by the addition of ligroin; m. p., with decomposition, 233–235°.

Anal. Calcd. for $C_{27}H_{24}NCl$: N, 3.52. Found: N (Dumas), 3.46.

Phenyl β,β,β-Triphenylethyl Ketimine.—The free ketimine was formed from its hydrochloride when the latter was suspended in ether and treated with dry ammonia gas. After filtration from ammonium chloride, the ether was evaporated in a stream of *dry* air. The evaporation was interrupted several times and the ketimine removed, affording a fractional crystallization; each fraction was dissolved in ether, filtered, and the solvent again evaporated; m. p., 156.5–157° (cor.).

Anal. Calcd. for $C_{27}H_{23}N$: N, 3.87. Found: N (Dumas), 3.85.

Preparation of Phenyl β,β,β-Triphenylethyl Ketone (Triphenylmethylacetophenone), $(C_6H_5)_3CCH_2COC_6H_5$.—When a concentrated ethanol (95%) solution of phenyl triphenylethyl ketimine hydrochloride was treated with a little concentrated hydrochloric acid and the mixture warmed upon a steam-bath, a white crystalline precipitate was formed. This was collected, washed with a little alcohol, and recrystallized from acetone; m. p. 169.5–170° (cor.). The ketone is almost insoluble in alcohol but is moderately soluble in acetone and methyl ethyl ketone.

Anal. Calcd. for $C_{27}H_{22}O$: C, 89.5; H, 6.1. Found: C, 89.3; H, 6.5.

Preparation of Ethyl β,β,β-Triphenylethyl Ketimine Hydrochloride, $[(C_6H_5)_3CCH_2](C_2H_5)C{=}NH_2Cl$.—To ethyl magnesium bromide prepared in the usual manner in ether solution from 14.3 g. of magnesium and 65.4 g. of ethyl bromide was added 28.3 g. of triphenylpropionitrile suspended in 150 cc. of dry xylene. The ether was distilled from the mixture and the latter refluxed for several hours at the boiling point. The mixture was cooled to −5° and the addition compound cautiously hydrolyzed with ammonium chloride and crushed ice. After extraction with ether, the ether–xylene solution was dried at 0° with anhydrous sodium sulfate, filtered, and the filtrate saturated with dry hydrogen chloride gas; the resulting white precipitate was quickly collected on a Buchner funnel, washed with dry ether, and placed at once in a vacuum desiccator over phosphoric anhydride, sodium hydroxide and paraffin; yield, 30.9 g. (88%). The practically pure product was further purified for analysis by means of precipitation with ether from a concentrated solution in absolute alcohol; dec. pt., 218–220° in a bath preheated to 200°. Hydrolysis of the salt yielded the corresponding ketone from which, in turn, there was obtained an oxime.

Anal. Calcd. for $C_{23}H_{24}NCl$: N, 4.0. Found: N, 4.1.

Preparation of Methyl β,β,β-Triphenylethyl Ketimine Hydrochloride, $[(C_6H_5)_3CCH_2](CH_3)C{=}NH_2Cl$.—To methylmagnesium iodide prepared in ether solution from 11.8 g. of magnesium and 71.0 g. of methyl iodide there was added 28.3 g. of triphenylpropionitrile dissolved in 300 ml. of dry xylene. The ether was distilled and the xylene solution, mechanically stirred, was refluxed slowly for five hours. The mixture, cooled to −5°, was hydrolyzed with ice and ammonium chloride and extracted at once with ether. The extracts were dried at −5°, and the hydrochloride prepared by the general method already described. There was appreciable mechanical loss; yield 20.5 g., dec. pt. 210°, in a bath preheated to 205°.

Anal. Calcd. for $C_{22}H_{22}NCl$: N, 4.2. Found: N, 4.1.

Preparation of Methyl β,β,β-Triphenylethyl Ketone (1,1,1-Triphenylbutanone-3), $(C_6H_5)_3CCH_2COCH_3$.—When methyl triphenylethyl ketimine hydrochloride was warmed in the presence of ethanol (95%) and hydrochloric acid, the ketone precipitated as white needles, soluble in acetone but almost insoluble in alcohol. It was recrystallized from methyl ethyl ketone; m. p. 141° (cor.).[7]

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.9; H, 6.7. Found: C, 88.1, 88.5; H, 6.8, 6.8.

Methyl-β,β,β-triphenylethyl Ketoxime, $(C_6H_5)_3CCH_2C(=NOH)CH_3$.—Methyl β,β,β-triphenylethyl ketone, 24 g., hydroxylamine hydrochloride, 8.4 g., and sodium hydroxide, 6.4 g., in 250 ml. of ethanol (95%) and 50 ml. of water were refluxed for an hour. The solution was filtered and diluted with hot water to a faint turbidity. The crystalline oxime gradually precipitated; yield, 24.9 g.;

(6) Compare Moureu and Mignonac, *Compt. rend.*, **156**, 1801 (1913); *Ann. chim.*, **14**, 322 (1930).

(7) Conant and Scherp, THIS JOURNAL, **53**, 1943 (1931), prepared the substance by another method.

after purification by crystallization from alcohol, m. p. 117–117.5° (cor.).

Anal. Calcd. for $C_{22}H_{21}NO$: N, 4.1. Found: N (Dumas), 4.3.

α-Methyl-γ,γ,γ-triphenylpropylamine Hydrochloride, $(C_6H_5)_3CCH_2CH(CH_3)NH_3Cl$.—Methyl triphenylethyl ketoxime, 8.3 g., and 50 ml. of absolute ethanol were placed in a flask fitted with a reflux condenser protected from moisture, and clean sodium, 4.5 g., was added; the reduction was permitted to proceed briskly. The reaction was completed by heating; residual sodium was destroyed with ethanol, and the mixture was acidulated with hydrochloric acid. After ethanol was removed in a vacuum, there remained a white salt which was collected, washed with water and dried; yield 8.5 g. The product was extracted with boiling ether and recrystallized from hot ethanol and ether; dec. pt. 256° (in a bath preheated to 250°).

Anal. Calcd. for $C_{22}H_{24}NCl$: N, 4.15. Found: N (Dumas), 4.10.

Urethan Derivative, $(C_6H_5)_3CCH_2CH(CH_3)NHCOOC_2H_5$.—To a suspension of 8.4 g. of the above amine hydrochloride in 100 ml. of water was added 3.8 g. of ethyl chlorocarbonate and 3.2 g. of sodium hydroxide. The mixture was vigorously shaken for half an hour, crushed in a mortar, and triturated thoroughly during which additional portions of ethyl chlorocarbonate and potassium carbonate were added; it was treated with excess sodium carbonate, collected, washed with warm, dilute hydrochloric acid and with hot water. It was dried and recrystallized from ligroin; yield 7.7 g.; m. p. 84.5–86° (cor.).

Anal. Calcd. for $C_{25}H_{27}NO_2$: N, 3.7. Found: N (Dumas), 3.7.

Summary

1. Evidence regarding a rather remarkable degree of stability, or non-reactivity, in the grouping $(C_6H_5)_3C-\overset{H}{\underset{H}{C}}-$, is afforded by several avenues of approach, including especially investigation of the reactions of β,β,β-triphenylpropionitrile and organomagnesium halides, which have been found to lead to the formation of the corresponding ketimine salts.

2. There have been prepared and characterized the following compounds, hitherto undescribed: the hydrochlorides of phenyl, ethyl, and methyl β,β,β-triphenylethyl ketimines; phenyl β,β,β-triphenylethyl ketimine; triphenylmethylacetophenone, methyl β,β,β-triphenylethyl ketoxime, α-methyl-γ,γ,γ-triphenylpropylamine hydrochloride, and its urethan derivative.

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[CONTRIBUTION FROM THE DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY, THE JOHNS HOPKINS UNIVERSITY]

The Oxidation of Compounds Possessing the Primary Amino Group. II. β,β,β-Triphenylethylamine[1]

BY LESLIE HELLERMAN

An important objective of these studies[2,3] has been to gain additional information concerning the mechanism or patterns of oxidation of certain primary amino compounds, as well as to try to discover some of the factors underlying apparent differences in behavior occasionally observed among this group in reactions involving oxidation. Despite careful studies in a number of laboratories there exists little clear-cut data on the controlled oxidation of the alkyl or aralkylamines, particularly when oxidizing reagents other than those of the peroxide type have been employed.[3]

In one segment of the field, of paramount importance especially to biochemistry, significant advances recently have been recorded. These concern the enzymatic oxidations of α-amino-acids of the *l*- and *d*-configuration,[4,5] yielding the corresponding ketoacids, most probably through hydrolysis of intermediate iminoketonic acids. The oxidizing substrate here is oxygen, and the catalysts, specific flavoenzymes; the partial reaction depicting oxidation of the aminoacid with preservation of its carbon skeleton[6] may be designated schematically

$$R-\overset{H}{\underset{NH_2}{C}}-COO^- \longrightarrow R-\overset{}{\underset{NH}{C}}-COO^- + 2H^+ + 2e \quad (1)$$

Thermodynamic reversibility has not been demonstrated, and no derivative of an imino intermediate, other than the ketoacid, has been isolated. No mention need be made here concerning many collateral studies, nor of other special processes, such as transamination. Studies in this laboratory concerning the enzymatic catalysis will be recorded elsewhere. Certain physiologically significant *amines*, *e. g.*, tyramine, are considered also to be oxidized to imino compounds in processes involving specific enzymes.[7]

In this paper are recorded observations concerning the oxidation of β,β,β-triphenylethylamine (I) the structural features of which suggested[2] its investigation. Collaterally, there are described certain transformations of N-chloro-β,β,β-tri-

(1) This investigation was completed some years ago. During initial experiments in the Department of Chemistry, The University of Chicago, the work gained much through the collaboration and interest of Dr. J. Elton Cole.

(2) Hellerman, THIS JOURNAL, **49**, 1735 (1927).

(3) Hellerman and Sanders, *ibid.*, **49**, 1742 (1927).

(4) Krebs, *Z. physiol. Chem.*, **217**, 191 (1933); **218**, 157 (1933).

(5) Warburg and Christian, *Biochem. Z.*, **298**, 150 (1938).

(6) In the course of non-enzymatic oxidations of the amino acids decarboxylation often is experienced; compare, for example, Langheld, *Ber.*, **42**, 392 (1909); Dakin, *J. Biol. Chem.*, **4**, 63 (1908); **5**, 405 (1909); *Biochem. J.*, **11**, 79 (1917); Herbst and Clarke, *J. Biol. Chem.*, **104**, 769 (1934); Van Slyke, Dillon, MacFayden and Hamilton, *J. Biol. Chem.*, **141**, 627 (1941).

(7) Compare Richter, *Biochem. J.*, **31**, 2022 (1937); Bernheim and Bernheim, *J. Biol. Chem.*, **123**, 317 (1938), and references therein.