removal of the volatile solvents a residue of 1-nitro-2-*p*-acetamidophenylamino-2-imidazolinium chloride remained; yield 842 mg. (92.4%). This compound melted with decomposition at 189° and gave a deep green color in the Franchimont test using dimethylaniline. It gave a positive test for chlorine with aqueous silver nitrate solution. An aliquot was converted into the picrate (m.p. 178° with decomposition) in the usual manner.

Anal. Calcd. for $C_{17}H_{16}N_8O_{10}$: C, 41.38; H, 3.45; N, 22.72. Found: C, 41.61; H, 3.44; N, 22.46.

A portion of 500 mg. (0.00167 mole) of the 1-nitro-2-*p*-acetamidophenylamino-2-imidazoline hydrochloride was dissolved in 10 cc. of cold 10% sodium hydroxide solution. After it had remained at room temperature for 15 minutes, it was acidified to *p*H 1 with 10% aqueous hydrochloric acid solution. The crude product (m.p. 194° with decomposition) was removed by filtration and washed with water; yield 382 mg. (81.3%). One crystallization from ethanol raised the melting point to 204° with decomposition and it did not depress the melting point of an authentic sample of N-β-nitraminoethyl-N'-*p*-acetamidophenylurea[4] on admixture.

OTTAWA, CANADA

[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

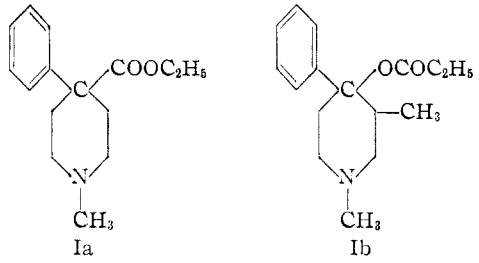
Synthesis of 4,4-Diphenyl-1-methylpiperidine[1]

BY NATHAN SPERBER, MARGARET SHERLOCK AND DOMENICK PAPA

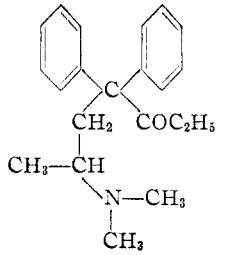
RECEIVED OCTOBER 13, 1952

4,4-Diphenyl-1-methylpiperidine has been synthesized by several procedures based on the dialkylation of diphenylmethane with substituted β-ethyl halides. Subsequent cyclization of the dialkylated products to the piperidine ring system was studied.

In recent years, a number of structures representing various fragments of the morphine molecule have been synthesized and tested for analgesic activity.[2] Among these structural types, several compounds derived from 4-phenyl-1-methylpiperidine; *i.e.*, ethyl 4-phenyl-1-methylpiperidine-4-carboxylate (Ia)[3] and *dl*-1,3-dimethyl-4-phenyl-4-propionoxypiperidine (Ib),[4] possess high analgesic activity and are in clinical use under the trade names Demerol and Nisentil, respectively. In our



Ia Ib



Ic

investigations on analgesic agents, 4,4-diphenyl-1-methylpiperidine (VI) was synthesized to determine whether the introduction of a second phenyl group into the 4-phenyl-1-methylpiperidine moiety would yield a compound with pronounced analgesic activity.[5] In this respect VI has in common with Amidone (Ic)[6] a *gem*-diphenyl group and may be considered a hybrid structure of types Ia and Ic. Structurally, VI is also closely related to the recently described 1-methyl-4,4-diphenyl-3-piperidone, a cyclic analog of Amidone.[7]

The simplest approach to VI appeared to be the alkylation of diphenylmethane with N,N-bis-(β-chloroethyl)-benzylamine[8] with the formation of 4,4-diphenyl-1-benzylpiperidine. However, this reaction gave only the linear product N,N-bis-(3,3-diphenylpropyl)-benzylamine. Several closely related synthetic routes were then studied which depended upon the dialkylation of diphenylmethane with ethyl halides possessing functional groups in the β-position followed by cyclization of the dialkylated products.

Diphenylmethylpotassium[9] was treated with β-bromoethyl ethyl ether in liquid ammonia to give 3,3-diphenyl-1-ethoxypropane (II). Alkylation of II with β-dimethylaminoethyl chloride yielded 5-ethoxy-3,3-diphenyl-N,N-dimethylamylamine (III) and cleavage of the ethoxy group gave the corresponding carbinol IV. The reaction of IV with thionyl chloride gave 4,4-diphenyl-1,1-dimethylpiperidinium chloride (V), which on sublimation *in vacuo* yielded 4,4-diphenyl-1-methylpiperidine (VI).[10]

(1) Presented in Abstract before the Division of Medicinal Chemistry at the 122nd Meeting of the American Chemical Society, Atlantic City, N. J., September, 1952.

(2) For a discussion of this subject, see J. Lee, A. Ziering, L. Berger and S. D. Heineman, in "Jubilee Volume Emil Barell," Reinhardt, Basle, 1946, p. 264; L. Small, *Ann. N. Y. Acad. Sci.*, **51**, 12 (1948); F. Bergel and A. L. Morrison, *Quart. Rev. Chem. Soc.*, **2**, 349 (1948); J. Lee, in "Medicinal Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 438.

(3) O. Eisleb and O. Schaumann, *Deut. med. Wochschr.*, **65**, 967 (1939).

(4) A. Ziering and J. Lee, *J. Org. Chem.*, **12**, 911 (1947).

(5) Shortly before this work was completed, L. O. Randall and G. Lehmann, *J. Pharmacol. Exp. Therap.*, **93**, 314 (1948), evaluated VI, along with several other series of compounds, and found it to be devoid of analgesic activity. However, no reference to the chemistry of the compound was given.

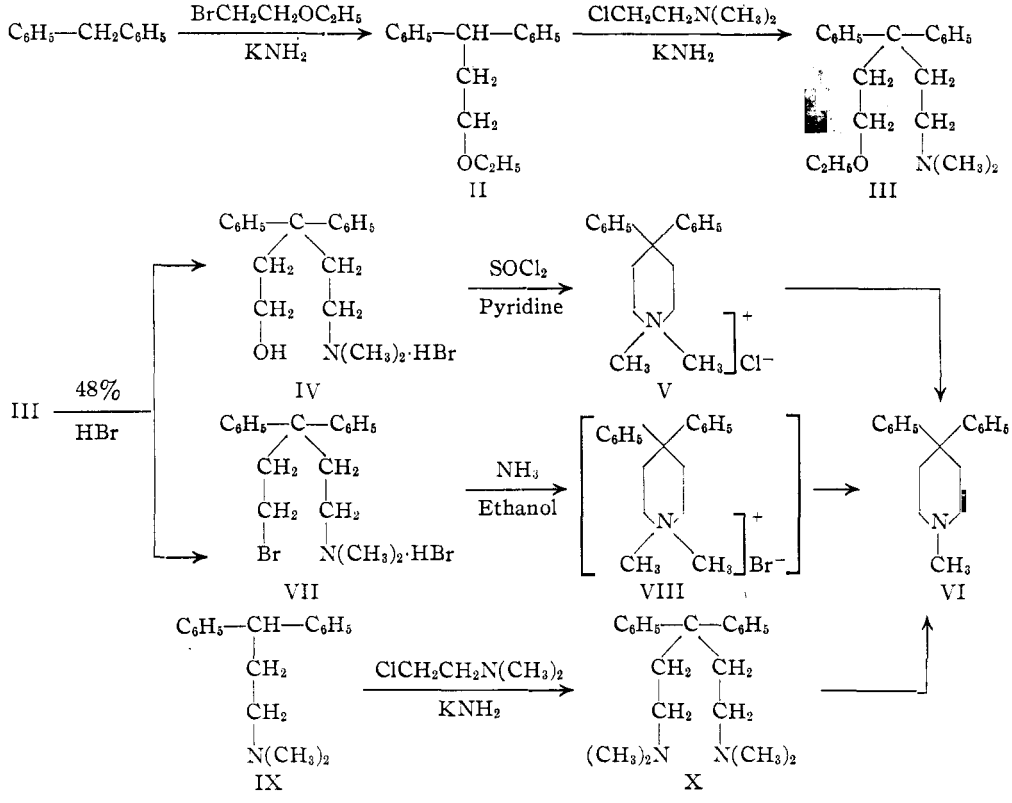
(6) M. Bockmühl and G. Ehrhart, *Ann.*, **561**, 52 (1949).

(7) F. F. Blicke and J. Krapcho, THIS JOURNAL, **74**, 4001 (1952).

(8) This approach was based on the procedure of O. Eisleb (*Ber.*, **74**, 1433 (1941)), who prepared 1-methyl-4,4-diphenylenepiperidine in good yield by the alkylation of fluorene with bis-(β-chloroethyl)-methylamine and sodamide.

(9) R. S. Yost and C. R. Hauser, THIS JOURNAL, **69**, 2325 (1947).

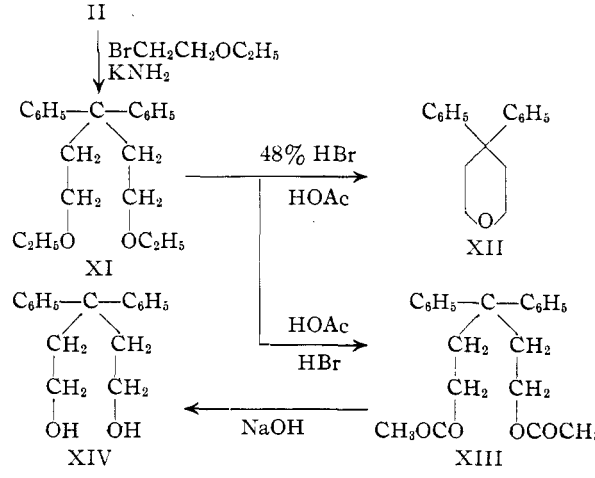
(10) This reaction is based on the method of O. Hieronimus, Dissertation, Berlin, 1938, as described in the chapter by F. F. Blicke, "Organic Reactions," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 324. A similar type of cyclization to a piperidinium salt, followed by the removal of methyl bromide to yield the corresponding substituted piperidine, has been described by K. Miescher and H. Kaegi, U. S. Patents 2,486,792-2,486,796 (1949).



Under slightly different conditions, III gave 3,3-diphenyl-5-bromo-N,N-dimethylamylamine (VII) when treated with a large excess of 48% hydrobromic acid. The bromide (VII) in ethanolic ammonia yielded crude 4,4-diphenyl-1,1-dimethylpiperidinium bromide (VIII) and ammonium bromide. The analytical data for VIII indicated contamination with ammonium bromide, which has appreciable solubility in ethanol. The impure piperidinium bromide was sublimed *in vacuo* at 300° to give VI identical with that obtained through the intermediate IV.

The preparation of VI was also effected by the cyclization of 3,3-diphenyl-N,N,N′,N′-tetramethyl-1,5-pentanediamine (X),[11] which was prepared by the stepwise alkylation of diphenylmethane with β-dimethylaminoethyl chloride. Attempts to prepare X by the dialkylation of diphenylmethane with two moles of β-dimethylaminoethyl chloride resulted in the formation of mixtures and low yields of X. The pyrolysis of a mixture of X and its dihydrochloride gave impurity VI, the identity of the product being established by conversion to the methiodide. A mixture of this methiodide and that prepared from VI by the alternate routes showed no melting point depression.

In an attempt to prepare 1,5-dichloro-3,3-diphenylpentane, which could then be reacted with methylamine to give VI, II was alkylated with β-bromoethyl ethyl ether to yield XI. With hydrobromic acid in acetic acid, XI gave a 50% yield of a solid which analyzed for 4,4-diphenyltetrahydropyran (XII).[12] However, by heating XI with anhydrous hydrogen bromide in acetic acid, a 50% yield of the diacetate XIII was obtained. The latter was saponified to the glycol XIV, but several attempts to convert the glycol to the corresponding dichloride failed.



Experimental

3,3-Diphenyl-1-ethoxypropane (II).—To a stirred solution of potassium amide (30 g. of potassium) in 1100 ml. of liquid ammonia, there was added 126 g. (0.75 mole) of diphenylmethane.[9] Stirring was continued for one-half hour, followed by the slow addition of 114.7 g. (0.75 mole) of β-

(11) This reaction was based on the pyrolytic cyclization of bis-α-(β-dimethylaminoethyl)-phenylacetonitrile monohydrochloride to 4-phenyl-4-cyano-1-methylpiperidine hydrochloride; F. F. Blicke, J. A. Faust, J. Krapcho and E. Tsao, THIS JOURNAL, **74**, 1844 (1952).

(12) G. Wittig and O. Bub, *Ann.*, **566**, 113 (1950), have reported that refluxing a solution of 1,1-diphenylpentamethyleneglycol-1,5 in concentrated hydrochloric acid gave 2,2-diphenyltetrahydropyran. E. J. Greenhow, E. N. White and D. McNeil (*J. Chem. Soc.*, 2848 (1951)) have reported on the synthesis of fluorene-9-spiro-4′-tetrahydropyran by the reaction of 9-fluorenylsodium with 2,2′-dichlorodiethyl ether, followed by the cyclization of the resulting 2-chloroethyl-2,9′-fluorenylethyl ether with solid potassium hydroxide at 270°.

bromoethyl ethyl ether. The liquid ammonia was replaced with 800 ml. of anhydrous ether and the reaction mixture stirred at room temperature for five hours. The mixture was decomposed carefully with 500 ml. of water, the ether layer separated, dried over sodium sulfate, concentrated and the residue distilled *in vacuo;* yield 156 g. (87%), b.p. 128–131° (0.5 mm.).

Anal. Calcd. for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 84.74; H, 8.15.

5-Ethoxy-3,3-diphenyl-N,N-dimethylamylamine (III).—To a stirred solution of potassium amide (12.5 g. of potassium) in 800 ml. of liquid ammonia, there was added 72 g. (0.3 mole) of 3,3-diphenyl-1-ethoxypropane. The reaction mixture was stirred for one-half hour followed by the slow addition of 40 g. (0.37 mole) of freshly distilled β-dimethylaminoethyl chloride. When all of the ammonia had evaporated, the residue was decomposed with 500 ml. of water, the oil extracted with ether, the ether layer separated, dried and concentrated. The residual oil crystallized upon trituration with petroleum ether; yield 74.5 g. (80%), m.p. 104–105°.

Anal. Calcd. for $C_{21}H_{29}NO$: C, 80.99; H, 9.38; N, 4.49. Found: C, 80.94; H, 8.77; N, 4.37.

The hydrobromide salt melted at 150–151°, after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{21}H_{30}BrNO$: C, 64.29; H, 7.70. Found: C, 64.78; H, 7.36.

The methiodide melted at 193–194° after two recrystallizations from methanol–ether.

Anal. Calcd. for $C_{22}H_{32}INO$: C, 58.27; H, 7.11. Found: C, 58.40; H, 7.10.

5-Hydroxy-3,3-diphenyl-N,N-dimethylamylamine Hydrobromide (IV).—A solution of 50 g. (0.16 mole) of 5-ethoxy-3,3-diphenyl-N,N-dimethylamylamine in 275 ml. of 48% hydrobromic acid was refluxed for 22 hours. The solution was concentrated to dryness *in vacuo*, the residual oil dissolved in 200 ml. of absolute alcohol and diluted with ether. Upon cooling, 55.4 g. (95%) of the hydrobromide salt separated, m.p. 133–134°. After one recrystallization from ethanol, the white solid melted at 134–135°.

Anal. Calcd. for $C_{19}H_{26}BrNO$: C, 62.64; H, 7.19; N, 3.84; Br, 21.94. Found: C, 62.88; H, 7.64; N, 3.59; Br, 22.15.

The free base of IV was prepared by adding sodium carbonate to an aqueous solution of the hydrobromide salt (24 g.). The oil was extracted with ether, the ether dried, concentrated and the residue distilled; yield 15 g. (81%), b.p. 180–185° (1 mm.). The oil solidified and after recrystallization from petroleum ether melted at 93–95°.

Anal. Calcd. for $C_{19}H_{25}NO$: C, 80.52; H, 8.89. Found: C, 80.40; H, 8.56.

The methiodide melted at 213–214° after recrystallization from methanol–ether.

Anal. Calcd. for $C_{20}H_{28}INO$: C, 56.48; H, 6.63. Found: C, 56.12; H, 6.48.

4,4-Diphenyl-1,1-dimethylpiperidinium Chloride (V).—To a cooled solution of 13 g. (0.046 mole) of 5-hydroxy-3,3-diphenyl-N,N-dimethylamylamine in 100 ml. of dry pyridine, there was added slowly 15 g. of thionyl chloride. The reaction mixture was stirred for two hours at room temperature, poured on ice and made basic with dilute sodium hydroxide solution. Upon the addition of 200 ml. of ether to the reaction mixture, an insoluble brown oil separated between the ether and water layers. The brown oil was dissolved in ethanol, boiled with Darco and filtered. On cooling and dilution of the solution with ether, 6.5 g. (44.5%) of the quaternary hydrate was obtained, m.p. 81–82° (decomposed 115°) after several recrystallizations from ethanol–ether.

Anal. Calcd. for $C_{19}H_{24}ClN \cdot H_2O$: N, 4.38. Found: N, 4.36.

4,4-Diphenyl-1-methylpiperidine (VI).—Six grams of 4,4-diphenyl-1,1-dimethylpiperidinium chloride was heated for 30 minutes at 280–300° at 2 mm. in a vacuum sublimation apparatus. The white solid (4 g.) melted at 74–75° and the melting point of a mixture of the latter with 4,4-diphenyl-1-methylpiperidine prepared from VIII was not depressed (m.p. 73–75°).

4,4-Diphenyl-1-methylpiperidine Hydrochloride.—The hydrochloride was prepared by passing hydrogen chloride through an ethereal solution of VI, m.p. 234–235° after recrystallization from ethyl acetate.

Anal. Calcd. for $C_{18}H_{22}ClN$: C, 75.12; H, 7.70; N, 4.86. Found: C, 75.04; H, 7.96; N, 4.50.

4,4-Diphenyl-1,1-dimethylpiperidinium Iodide.—This compound was prepared by refluxing a solution of VI in methyl iodide for one hour. After removal of the excess methyl iodide, the residue was recrystallized from methanol–ether; pale yellow solid, m.p. 302–303°.

Anal. Calcd. for $C_{19}H_{24}IN$: N, 3.56. Found: N, 3.28.

5-Bromo-3,3-diphenyl-N,N-dimethylamylamine Hydrobromide (VII).[13]—A solution of 8 g. (0.026 mole) of III and 150 ml. of 48% hydrobromic acid was refluxed for 22 hours. The solution was concentrated *in vacuo* and the residual oil which slowly solidified was crystallized from ethanol–ether; yield 7.8 g. (71%), m.p. 171–173°.

Anal. Calcd. for $C_{19}H_{25}Br_2N$: N, 3.28. Found: N, 2.99.

4,4-Diphenyl-1,1-dimethylpiperidinium Bromide (VIII).—Ammonia was bubbled through a solution of 2 g. of VII in 20 ml. of absolute ethanol for 10 minutes. The mixture was cooled, filtered, diluted with ether and a small amount of white solid obtained. The latter melted at 253.5–254.5° after two recrystallizations from ethanol–ether. Complete removal of the ammonium bromide could not be achieved.

Anal. Calcd. for $C_{19}H_{24}BrN$: C, 65.90; H, 6.98; N, 4.04; Br, 23.08. Found: C, 55.32; H, 6.00; N, 5.30; Br, 36.06.

4,4-Diphenyl-1-methylpiperidine (VI).—Two grams of impure VIII was heated at 280–320° at 2 mm. in a vacuum sublimation apparatus for one-half hour. The sublimed material was dissolved in ether, the ether layer washed wth water, dried and concentrated. The residual oil solidified upon standing and after recrystallization from ethanol–water melted at 73.8–74.8°.

Anal. Calcd. for $C_{18}H_{21}N$: C, 86.03; H, 8.42; N, 5.57. Found: C, 85.61; H, 7.96; N, 5.31.

3,3-Diphenyl-N,N-dimethylpropylamine (IX).—To a solution of potassium amide (12 g. of potassium) in one liter of liquid ammonia, there was added 51 g. (0.3 mole) of diphenylmethane. After stirring for 15 minutes, 35 g. (0.33 mole) of β-dimethylaminoethyl chloride was added to the deep-red reaction mixture. When all of the ammonia had evaporated, the residue was decomposed with water and the oily layer extracted with ether. The ether extracts were dried over sodium sulfate, the ether removed and the residue distilled *in vacuo;* yield 67 g. (92%), b.p. 121–126° (0.5 mm.), m.p. 42–44°.[14]

Anal. Calcd. for $C_{17}H_{21}N$: N, 5.85. Found: N, 6.03.

3,3-Diphenyl-N,N,N′,N′-tetramethyl-1,5-pentanediamine (X).—To a solution of potassium amide (6.5 g. of potassium) in 500 ml. of liquid ammonia, there was added 36 g. (0.15 mole) of 3,3-diphenyl-N,N-dimethylpropylamine. The reaction mixture was stirred for 30 minutes, followed by the addition of 30 g. (0.28 mole) of β-dimethylaminoethyl chloride. When all of the ammonia had evaporated, the mixture was decomposed with water, the oily layer extracted with ether, the ether extracts dried, concentrated and the residue distilled; yield 37 g. (80%), b.p. 148–154° (0.5 mm.).

Anal. Calcd. for $C_{21}H_{30}N_2$: N, 9.02. Found: N, 9.13.

The dihydrochloride was prepared by bubbling an excess of anhydrous hydrogen chloride through an ethereal solution of the free base. After one recrystallization from ethanol–ether, the white solid melted at 278–279°.

(13) An attempt to prepare the free base of VII by the alkylation of 3,3-diphenyl-N,N-dimethylpropylamine with ethylene dibromide and potassium amide, according to the procedure of K. Miescher and H. Kaegi, U. S. Patent 2,486,792 (ref. 10), yielded 3,3-diphenyl-N,N-dimethyl-N-(β-bromoethyl)-propylammonium bromide, m.p. 195–196°. *Anal.* Calcd. for $C_{19}H_{25}Br_2N$: C, 53.42; H, 5.90; N, 3.28. Found: C, 53.46; H, 5.37; N, 2.93. This compound gave no depression in melting point when admixed with an authentic sample (m.p. 194–195°) prepared by heating 3,3-diphenyl-N,N-dimethylpropylamine and ethylene dibromide.

(14) D. W. Adamson, *J. Chem. Soc.*, S. 144 (1949), prepared this compound by an alternate procedure, m.p. 44–45°. O. Eisleb, *Ber.*, **74**, 1433 (1941), described the preparation of 3,3-diphenyl-N,N-diethylpropylamine by the alkylation of diphenylmethane with sodamide and β-diethylaminoethyl chloride in toluene in a yield of 14%.

Anal. Calcd. for $C_{21}H_{32}Cl_2N_2$: N, 7.30. Found: N, 6.91.

4,4-Diphenyl-1-methylpiperidine (VI).—A mixture of 11 g. of 3,3-diphenyl-N,N,N′,N′-tetramethyl-1,5-pentanediamine dihydrochloride and 6 g. of 3,3-diphenyl-N,N,N′,N′-tetramethyl-1,5-pentanediamine was heated at 290–310° for 20 minutes. When the evolution of trimethylamine had ceased, the glassy solid was dissolved in water, the aqueous solution made basic with dilute sodium hydroxide solution and the oil extracted with ether. The ether extracts were dried, concentrated and the residue distilled; yield 6.3 g., b.p. 168–174° (2 mm.). After one recrystallization from petroleum ether, the solid melted over a range of 63–70°. The methiodide melted at 302–303° after one recrystallization from methanol–ether and did not depress the melting point of a sample of 4,4-diphenyl-1,1-dimethylpiperidinium iodide (m.p. 302–303°) prepared from IV.

1,5-Diethoxy-3,3-diphenylpentane (XI).—To a solution of potassium amide (10 g. of potassium) in 500 ml. of liquid ammonia, there was added 55.8 g. (0.23 mole) of II. After the reaction mixture had been stirred for 0.5 hour, 37 g. (0.24 mole) of β-bromoethyl ethyl ether was added and the mixture was stirred at room temperature until all of the ammonia had evaporated. The residue was decomposed with water, the oil extracted with ether and the ether extracts concentrated. The residue was dissolved in ethanol and upon dilution with water, a white solid crystallized; yield 53 g. (74.5%), m.p. 58–59°.

Anal. Calcd. for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.88; H, 8.50.

1,5-Diacetoxy-3,3-diphenylpentane (XIII).—A solution of 30 g. (0.096 mole) of XI and 250 ml. of glacial acetic acid containing 100 g. of anhydrous hydrogen bromide was refluxed for 48 hours. The acetic acid was removed *in vacuo*, the residual oil dissolved in ether and the ether layer washed with a cold 5% sodium bicarbonate solution. The ether extracts were dried over sodium sulfate, filtered, concentrated and the residue distilled; yield 17.7 g. (54%), b.p. 180–197° (1 mm.). The viscous oil solidified and after three recrystallizations from petroleum ether melted at 73–74°.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.11; H, 6.68.

1,5-Dihydroxy-3,3-diphenylpentane (XIV).—A solution of 21 g. (0.062 mole) of XIII, 100 ml. of 50% sodium hydroxide and 150 ml. of 95% ethanol was refluxed for 20 hours. The ethanol was distilled off, the reaction mixture poured on ice and the solid filtered. After several recrystallizations from benzene–petroleum ether the white solid (12 g., 76%) melted at 108–109°.

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.67; H, 7.86. Found: C, 79.28; H, 8.19.

Attempted Preparation of 1,5-Dichloro-3,3-diphenylpentane.—To a cold (0°) stirred solution of 10 g. (0.039 mole) of XIV in 150 ml. of dry pyridine, there was added slowly 15 g. of thionyl chloride. A precipitate formed and the mixture was stirred for two hours in an ice-bath and for an additional two hours at room temperature. The reaction mixture was poured on ice, acidified and a gum was obtained. The latter slowly crystallized and consisted chiefly of unreacted XIV (m.p. 105–109°). The experiment was repeated using dimethylaniline instead of pyridine, but only a tarry residue was obtained.

4,4-Diphenyltetrahydropyran (XII).—A solution of 15.5 g. (0.05 mole) of 1,5-diethoxy-3,3-diphenylpentane, 150 ml. of 48% hydrobromic acid and 75 ml. of glacial acetic acid was refluxed for 22 hours. The reaction mixture was cooled, poured on ice, the oil extracted with benzene, and the benzene extracts concentrated. The residual solid was crystallized from ethanol; yield 6 g. (51%), m.p. 85–86°.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.69; H, 7.61. Found: C, 85.55; H, 7.36.

N,N-Bis-(3,3-diphenylpropyl)-benzylamine.—To a solution of potassium amide (13.1 g. of potassium) in 800 ml. of liquid ammonia, there was added slowly 28 g. (0.168 mole) of diphenylmethane. The deep-red reaction mixture was stirred for one hour, followed by the addition of 39 g. (0.168 mole) of N,N-bis-(β-chloroethyl)-benzylamine.[6] After the addition of 500 ml. of anhydrous ether, the reaction mixture was allowed to stir overnight and was then decomposed with water. The ether layer was separated, dried, concentrated and distillation of the oil resulted in decomposition. The residue, when triturated with petroleum ether, gave 24 g. (58%) of a tan solid which melted at 102–103°, after three recrystallizations from ethanol.

Anal. Calcd. for $C_{37}H_{37}N$: N, 2.82. Found: N, 2.99.

Acknowledgment.—The authors wish to express their appreciation to Mr. Edwin Conner and his staff for the microanalyses reported in this paper.

BLOOMFIELD, NEW JERSEY

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, UNIVERSITY OF CALIFORNIA]

The Hydrolysis of Some Cyanocinnamic Acids

BY HENRY RAPOPORT, ARTHUR R. WILLIAMS, ORVILLE G. LOWE AND WILLIAM W. SPOONCER

RECEIVED OCTOBER 16, 1952

The hydrolysis of 2-(2′-cyanophenyl)-cinnamic acid (I) has been shown to proceed through β-amino-β-[2-(2′-carboxyphenyl)]-phenylpropionic acid (IV) as the major path. The very slow elimination of ammonia from the latter compound is responsible for the slow ammonia evolution during the hydrolysis of I to 2-(2′-carboxyphenyl)-cinnamic acid (V).

During the course of work on the synthesis of dibenzocycloheptadiene,[1] conversion of 2-(2′-cyanophenyl)-cinnamic acid (I) to 2-(2′-carboxyphenyl)-cinnamic acid (V) was a projected step. It was finally accomplished by hydrolysis with potassium hydroxide in ethylene glycol at 200° for 48 hours. However, when boiling aqueous potassium hydroxide was used, conditions which had been eminently successful in hydrolyzing other nitriles in the synthetic sequence, only 50% of the theoretical quantity of ammonia had been evolved by the end of a two-week period. This unexpected result has been investigated, and the reaction path and intermediates have been found to provide a reasonable explanation for the extremely slow ammonia evolution.

A comparison of the rate of ammonia evolution from 2-(2′-cyanophenyl)-cinnamic acid (I) and a number of model compounds was sought first in order to indicate possibly the cause of this very slow hydrolysis of I. The compounds prepared and subjected to hydrolysis were *p*-cyanobenzoic acid and 2-(2′-cyanophenyl)-benzoic acid, to explore possible steric and electronic effects, and *p*-cyanocinnamic acid, to test the rather remote chance that ammonia, as liberated, was adding to the α,β-unsaturated acid portion. The hydrolyses were all carried out with boiling 1 *N* aqueous potassium

(1) H. Rapoport and A. R. Williams, THIS JOURNAL, **71**, 1774 (1949).