

THE REACTIONS OF THE DISODIUM ADDUCT OF BENZOPHENONE ANIL¹

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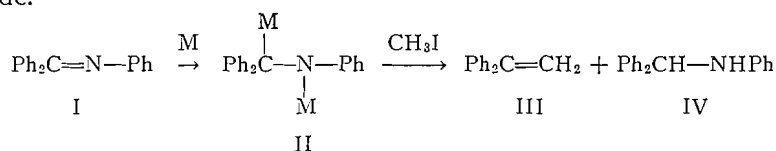
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ABSTRACT

The disodium adduct of benzophenone anil has been treated with a variety of reagents, and the products have been isolated and identified. With alkyl halides, ethylene oxide, and diethyl sulfate, alkylation occurs at the carbon atom. With tri- and tetra-methylene dibromide, nitrogen alkylation also occurs, thereby producing substituted pyrrolidine and piperidine derivatives. Benzaldehyde abstracts the alkali metal from the adduct whereas esters react to form the *N*-acyl derivatives.

INTRODUCTION

Solutions of benzophenone anil (I) in ether solvents react with alkali metals to form a complex (II) containing two atoms of alkali metal per mole of anil (1, 2). The chemical behavior of this adduct has been examined in the past (2-4), but conflicting results have been reported. In the original study by Schlenk and Bergmann (2), benzophenone anil was the only product formed when the adduct was treated with methyl iodide or with several other reagents. On the other hand, Mikhailov (3) reported the formation of 1,1-diphenylethylene (III) and *N*-benzhydrylaniline (IV) upon treatment of II with methyl iodide.



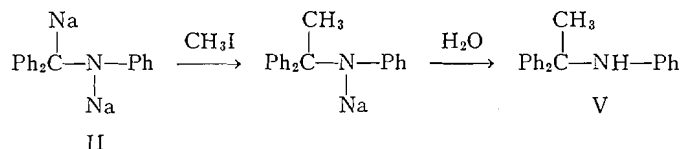
In our hands, the adduct II behaved in a manner quite different from that reported in these earlier studies. Generally speaking, the chemical behavior of the benzophenone anil adduct resembles that recently reported for the benzophenone ketyls (5-8).

Adduct Preparation

The reaction of benzophenone anil and sodium proceeds very rapidly in tetrahydrofuran. This is not surprising in view of the well-known efficacy of such solvents in the preparation of organometallic compounds. However, it is surprising that the adduct forms in diethyl ether with equal ease, especially since much longer reaction times have been employed elsewhere (2).

Reaction with Alkyl Halides

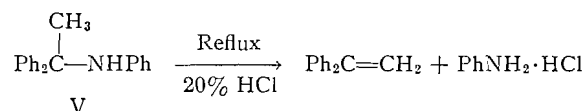
The disodium adduct II in tetrahydrofuran reacts smoothly with 1 equivalent of methyl iodide to produce the *C*-methyl derivative, *N*,1,1-triphenylethylamine (V). This behavior of the adduct was initially thought to be due to the use of tetrahydrofuran as solvent



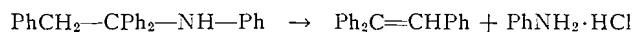
¹Contribution No. 142 from the Exploratory Research Laboratory.

rather than the diethyl ether used in the earlier investigations (2, 3). However, a repetition of the experiment with diethyl ether produced the same product accompanied by *N*-benzhydrylaniline, thus establishing that the same reaction is occurring but to a lesser extent.

The structure V of the reaction product is consistent with its nuclear magnetic resonance (n.m.r.) spectrum, and additional proof has been obtained by decomposition in 20% hydrochloric acid to 1,1-diphenylethylene and aniline.



A similar decomposition of *N*,1,1,2-tetraphenylethylamine to *N*,1,1-triphenylethylene has been reported (9).



This decomposition provides an explanation for Mikhailov's earlier observation (3) of the formation of 1,1-diphenylethylene from methyl halides and the alkali metal adducts of benzophenone anil. During his separation of the individual constituents of the crude reaction mixture, Mikhailov employed refluxing 20% hydrochloric acid. This undoubtedly resulted in decomposition of the initial reaction product to the observed unsaturated hydrocarbon. In the present experiments, the crude reaction product has also been examined by precipitating with hydrogen chloride the amines from the ether solution as their hydrochloride salts and examining the ether-soluble portion. Only small yields of 1,1-diphenylethylene have been observed.

The scope of this reaction has been investigated with a number of alkyl halides, and the results are summarized in Table I. Certain obvious trends are evident. The reaction is slow with bulky halides, such as *t*-butyl chloride, with a consequently reduced yield and the formation of *N*-benzhydrylaniline on hydrolysis. Inert halides, such as vinyl chloride, do not react whereas reactive halides, such as allyl or benzyl chloride, react rapidly, even at -60° .

The yield of product is lower with alkyl iodides than with alkyl bromides or chlorides. An investigation of the reaction products by thin-layer chromatography reveals the presence of unidentified by-products which increase in quantity when an alkyl iodide is used.

In the case of the simple alkyl halides, the products formed by nitrogen alkylation of the benzophenone anil adduct have not been isolated. However, with cyclopentyl halides, the amount of nitrogen alkylation is quite large and comparable to the carbon-alkylated product. The nitrogen-alkylated derivative VI may be isolated by decomposing the carbon-alkylated compound VII to cyclopentylidene diphenylmethane (VIII) with hydrochloric acid, leaving the nitrogen-alkylated product as the hydrochloride salt.

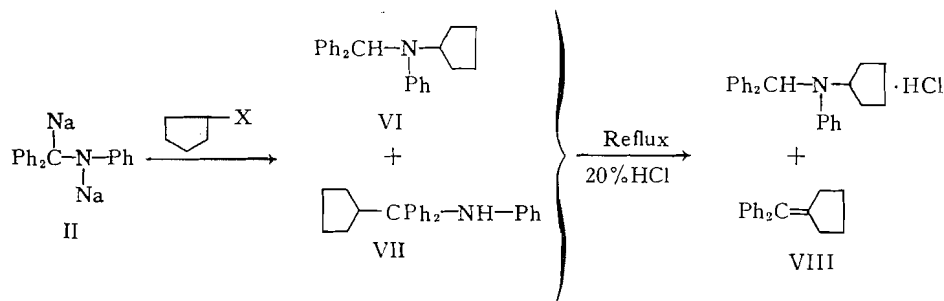


TABLE I
Reaction products with alkyl halides
$$\begin{array}{c} \text{Ph}_2\text{C}-\text{NH}-\text{Ph} \\ | \\ \text{R} \end{array}$$

Alkyl halide	R	Yield (%)	Melting point (°C)	Analysis (%)					
				Theoretical			Found		
				C	H	N	C	H	N
CH ₃ I	CH ₃	46	53-54*	87.9	7.02	5.12	87.9	7.00	5.20
C ₂ H ₅ I	C ₂ H ₅	46	67-71†	87.8	7.38	4.87	87.5	7.50	4.97
C ₃ H ₇ Cl	C ₃ H ₇	66	81-84	87.6	7.70	4.65	87.6	7.44	4.63
C ₃ H ₇ Br	C ₃ H ₇	78							
C ₃ H ₇ I	C ₃ H ₇	40							
<i>i</i> -C ₃ H ₇ Cl	(CH ₃) ₂ CH	50	113-115	87.6	7.70	4.65	87.8	7.64	4.59
<i>t</i> -C ₄ H ₉ Cl	(CH ₃) ₃ C	22	116-117	87.5	8.00	4.44	87.6	7.89	4.29
CH ₂ =CH-CH ₂ Cl	CH ₂ =CH-CH ₂	81	75-77	88.2	7.08	4.68	88.5	7.02	4.70
C ₆ H ₅ CH ₂ Cl	C ₆ H ₅ CH ₂	67, 64§	144-147‡	89.4	6.65	4.01	89.8	6.58	4.07
CH ₂ =CH-Cl	CH ₂ =CH	0	—						

*Literature (3) m.p. 50-53°.

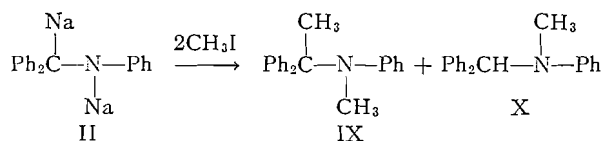
†Literature (11) m.p. 72-73°.

‡Literature (9) m.p. 143.5-144.5° and (19) 152-153°.

§Diethyl ether as reaction solvent.

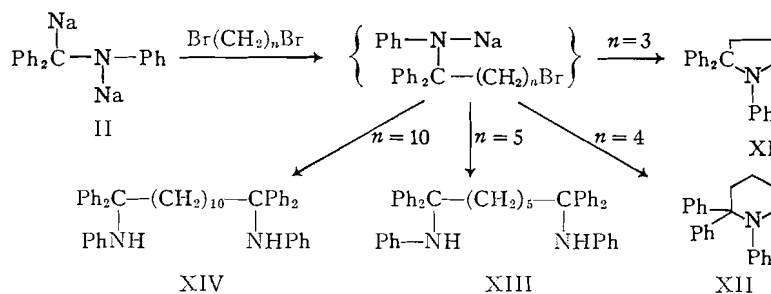
Attempts to synthesize an authentic sample of the tertiary amine VI from *N*-cyclopentylaniline and benzhydryl chloride were unsuccessful.

The reaction of the disodium adduct of benzophenone anil with 2 equivalents of methyl iodide produces a product whose n.m.r. spectrum is comparable with that expected for the dialkylated derivative, *N*-methyl-*N*,1,1-triphenylethylamine (IX). In addition to IX, a small amount of the nitrogen-alkylated derivative, *N*-methyl-*N*-benzhydrylaniline (X), can be isolated.

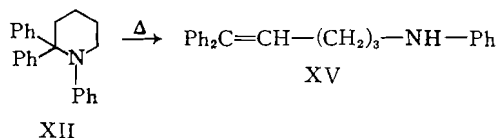


The dialkylated product IX is sufficiently stable that it can be distilled. However, attempts to purify it further by means of its hydrochloride, or by chromatography, result in it being decomposed to *N*-methylaniline and 1,1-diphenylethylene. Indeed, so facile is this decomposition that it can be effected by an equivalent amount of formic acid and the reaction followed by observation of the n.m.r. spectrum.

With polymethylene dibromides the sodium adduct of benzophenone anil reacts in two ways. Carbon alkylation presumably occurs first, and then, if the chain length of the pendant bromoalkyl group is of the proper length to bring the remaining bromo group into close proximity with the nitrogen atom, nitrogen alkylation occurs to form the heterocyclic derivative (XI or XII). However, if the chain length is too long, nitrogen alkylation is not favored and dimeric products result from the carbon alkylation of a second molecule of adduct to form the diamines (XIII or XIV).

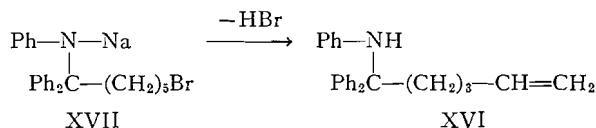


Distillation of 1,2,2-triphenylpiperidine (XII) effected its decomposition to an isomer which, on the basis of its n.m.r. spectrum, is believed to be *N*,1,1-triphenyl-5-aminopentene-1 (XV).

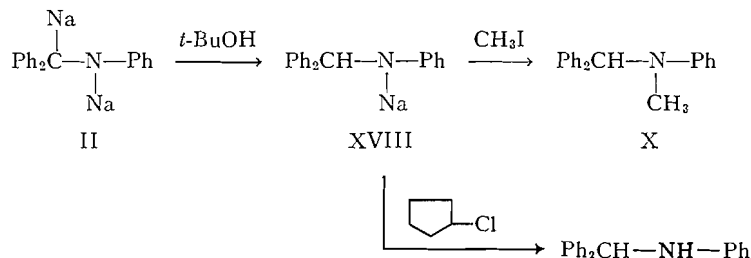


An additional product has also been isolated from the reaction leading to XIII. In this case, the material has been assigned the structure *N*,1,1-triphenyl-1-aminohexene-5

(XVI) on the basis of its n.m.r. spectrum. Its formation probably occurs by dehydrohalogenation of the intermediate XVII in a competitive side reaction.



A successful attempt has been made to take advantage of the selective reactivity of the two anionic sites in the disodium adduct of benzophenone anil by treating it first with 1 equivalent of an acid to form the amide ion XVIII, and then alkylating it with methyl iodide to produce *N*-methyl-*N*-benzhydrylaniline (X).

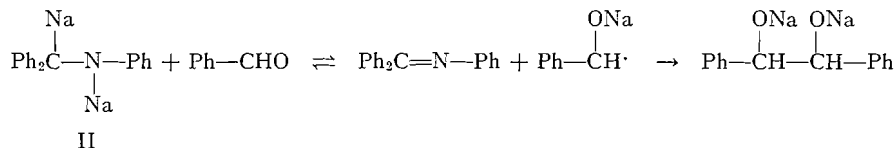


An attempt to apply this to the synthesis of *N*-cyclopentyl-*N*-benzhydrylaniline by treating XVIII with cyclopentyl chloride failed; only *N*-benzhydrylaniline was produced. It is not clear why the dianion of the disodium adduct of benzophenone anil is capable of nitrogen alkylation with cyclopentyl chloride whereas the monoanion XVIII is not.

Reaction with Benzaldehyde

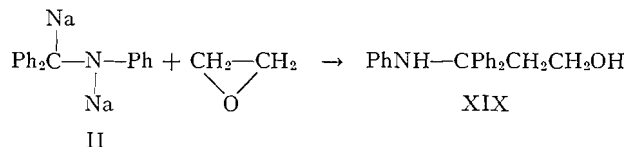
The reaction of the sodium adduct with aldehydes has been studied with benzaldehyde, an aldehyde free of enolizable (acidic) protons. The products which have been isolated are benzophenone anil and *dd, ll*-hydrobenzoin. In addition, the presence of *meso*-hydrobenzoin has been demonstrated spectroscopically.

Evidently, a transfer of the sodium from the benzophenone anil to the carbonyl group of the aldehyde occurs with regeneration of the starting material. Dimerization of the radical ion formed from the benzaldehyde produces the two diastereomeric hydrobenzoins. Similar transfers of alkali metal to carbonyl groups have been reported (6, 10).



Reactions with Ethylene Oxide

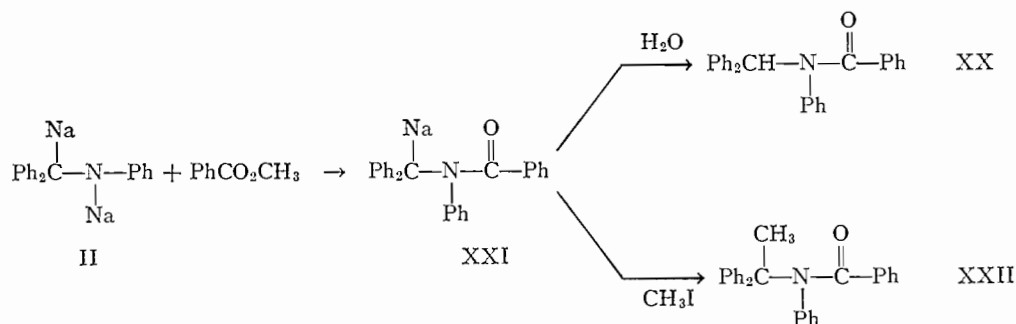
Treatment of the sodium adduct with 1 equivalent of ethylene oxide effected alkylation at the carbon atom to produce *N*,1,1-triphenyl-3-hydroxypropylamine (XIX).



Alkylation at the carbon atom is not surprising, since the anionic carbon should be more basic than the anionic nitrogen and should react faster.

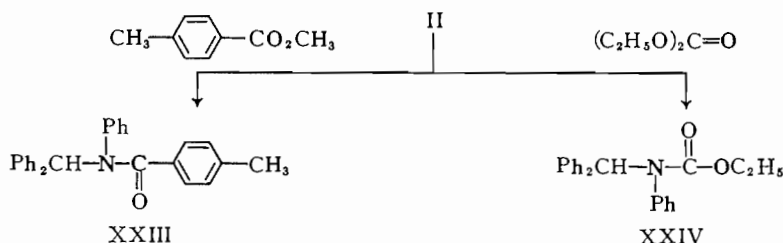
Reaction with Esters

Treatment of the disodium adduct of benzophenone anil with methyl benzoate produces *N*-benzhydrylbenzamide (XX) on hydrolysis of the initially formed reaction product XXI. That XXI is initially formed is shown by treating the intermediate with methyl iodide to produce *N*-phenyl-*N*-(1,1-diphenylethyl)benzamide (XXII).



The structure XX has been established by comparison with an authentic sample. In the infrared spectra, the amide carbonyl band appears at 1625 cm^{-1} for XX and at 1640 cm^{-1} for XXII. In the n.m.r. spectrum of XX, the benzylic proton is shifted downfield and becomes obscured by the aromatic proton band.

Similarly, methyl *p*-toluate and diethyl carbonate react with the disodium adduct II to produce the corresponding *N*-acyl derivatives XXIII and XXIV. In the latter case, the carbamate structure is indicated by the position of the carbonyl band in the infrared spectrum (1690 cm^{-1}) and by the presence of an ethyl group (from the diethyl carbonate) in the n.m.r. spectrum.



EXPERIMENTAL

Melting points are uncorrected and were determined in an open capillary with a Gallenkamp melting point apparatus. Infrared spectra were recorded on a Perkin-Elmer 221 with prism-grating interchange, using Nujol mulls of the compounds. Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer, using deuterated chloroform solutions, with tetramethylsilane as an internal reference. The chemical shifts reported are in parts per million downfield from the tetramethylsilane.

Benzophenone anil was prepared from benzophenone and aniline, with aniline hydrochloride as catalyst (12). The product, after two recrystallizations from 95% ethanol, melted at $113.5\text{--}115^\circ$. It was dried under vacuum at 45° and stored in a dry box. All operations connected with the preparation and reaction of the alkali metal complexes were performed in an atmosphere of purified and dried nitrogen.

Tetrahydrofuran and diethyl ether were purified by refluxing for at least 8 h over lithium aluminium hydride and distilling onto a fresh batch of hydride for storage. When needed, the solvent was refluxed for 2 h and the required amount permitted to distill into the reaction vessel, a modified Schlenk tube (13). The tube was transferred to a dry box, where the benzophenone anil and the sodium metal (freshly cut) were weighed and added. After the tube was sealed, it was removed from the dry box and agitated in a horizontal shaker until the reaction was complete.

To study the rate of adduct formation, aliquot samples of the deep reddish purple solution were withdrawn periodically and quenched in 1:1 ethanol-water, and the alkaline mixture was titrated with 0.1 *N* standard hydrochloric acid to determine the extent of reaction. Preparative conditions were standardized at 50 ± 5 g of solvent/0.01 mole of benzophenone anil, a 100% excess of sodium, and a reaction time of 4 h, which was sufficient to ensure completion of the reaction in both tetrahydrofuran and diethyl ether.

Thin-layer chromatography was carried out using silica gel G adsorbent 0.25 mm thick, with a 10 cm rise of the solvent front. Developing solvents varied and are specified in the experimental details. The detecting spray was a 1% solution of *p*-nitrobenzenediazonium tetrafluoroborate (14) in water.

Reaction with Alkyl Halides

The solution of the adduct was transferred from the excess sodium to an oven-dried, nitrogen-filled flask equipped with a Teflon-coated magnetic stirrer bar. The solution was then cooled with a dry ice and methanol mixture and stirred, and an equivalent amount of alkyl halide was introduced by a pipette or syringe. Stirring was continued for an hour at dry-ice temperatures and then the reaction was permitted to warm to room temperature spontaneously. The final solution, generally a deep reddish brown color, was treated with 15 ml of water to destroy any remaining adduct. Extraction with ether, followed by washing, drying, and evaporating the ether extract, served to isolate the crude reaction product as an oil or gummy solid.

From this point on, the procedures differed depending on the nature of the product or the information desired. The purification procedures and additional comments together with the analytical and n.m.r. data are given below. Unless otherwise specified, each experiment was carried out with the disodium adduct prepared from 0.01 mole of benzophenone anil.

Reaction with Methyl Iodide

The reaction with methyl iodide was repeated several times because of the conflicting literature reports on the nature of the products. The roughly quantitative evaluation of the reaction products that was employed resembled that used by Mikhailov (3) but under milder conditions. The crude reaction product was dissolved in 50 ml of diethyl ether and treated with hydrogen chloride. The amine salt which precipitated out was filtered off, dried, and weighed, and the ether filtrate was evaporated and the residue weighed (1,1-diphenylethylene). The amine salt was then suspended in a mixture of 25 ml of water and 25 ml of benzene. Any aniline hydrochloride that was present dissolved in the water layer, from which it was subsequently isolated by the addition of base and ether extraction. The hydrochloride of *N*,1,1-triphenylethylamine dissociated and the free amine dissolved in the benzene layer, from which it was isolated by evaporation. The yields so obtained were 2–13% aniline, 7–19% 1,1-diphenylethylene, and 71–90% *N*,1,1-triphenylethylamine.

The identity of the isolated 1,1-diphenylethylene was confirmed by distillation and by comparison of the infrared spectrum with that of an authentic sample. The identity of the aniline was confirmed by preparing the benzenesulfonamide derivative.

The crude *N*,1,1-triphenylethylamine was obtained as a gum, and the presence of *N*-benzhydrylaniline was suspected. Small amounts could be detected by thin-layer chromatography with cyclohexane containing 17% acetic acid as developing solvent: *N*-benzhydrylaniline, R_f 0.60; *N*,1,1-triphenylethylamine, R_f 0.43. However, the amount was too small to show a benzylic proton peak in the n.m.r. spectrum of the crude amine.

The crude reaction product was purified by recrystallization from methanol (10 ml/g). The hydrochloride decomposes above 170°, forming two layers in the melting point capillary. Nuclear magnetic resonance: CH_3 singlet at 2.0 (3.0 H), NH singlet at 4.2 (1.0 H), aromatic H's complex band at 6.2–7.6 (15.8 H).

A repetition of the above experiment with diethyl ether as the solvent for adduct formation and for reaction with methyl iodide led to the formation of substantial amounts of *N*-benzhydrylaniline. The crude reaction product, isolated as previously described, contained 32% of *N*-benzhydrylaniline,² as determined by the relative areas of the appropriate n.m.r. peaks: the benzyl proton at 5.4 caused by *N*-benzhydrylaniline and the methyl protons at 2.0 caused by *N*,1,1-triphenylethylamine.

Reaction with Ethyl Iodide

The crude reaction product was dissolved in 50 ml of diethyl ether and precipitated as the hydrochloride with hydrogen chloride. The dry salt (2.535 g, 81% yield) was neutralized with aqueous sodium hydroxide, extracted with ether, concentrated, and distilled, b.p. 165–172° at 2 mm, 1.745 g (61% yield). This material crystallized and was purified for analysis by recrystallization from methanol (6 ml/g). Nuclear magnetic resonance: CH_3 triplet at 0.74 (3.0 H), CH_2 quartet at 2.53 (1.9 H), NH singlet at 4.24 (1.0 H), aromatic H's complex band at 6.2–7.6 (14.7 H).

Reaction with Propyl Halides

The crude reaction product was purified by recrystallization from methanol (6 ml/g). Nuclear magnetic resonance: CH_3CH_2 broad band at 0.7–1.5 (4.9 H) with the methyl appearing as a distorted triplet at 0.8, CH_2 triplet at 2.51 (2.0 H), NH singlet at 4.4 (1.0 H), aromatic H's complex band at 6.2–7.8 (15.0 H).

²Reference 3 reports 25–33% *N*-benzhydrylaniline formed under similar reaction conditions.

Identical experiments were carried out with propyl chloride, propyl bromide, and propyl iodide. The yield was obtained by dissolving the crude product in 10 ml of hot methanol, cooling, seeding, and allowing to crystallize for 2 days (see Table I).

The crude reaction product was also examined by thin-layer chromatography with cyclohexane containing 17% acetic acid as developing solvent. Besides the spot caused by the product (R_f 0.59), two additional spots appeared: R_f 0.63 and 0.72. These were readily seen in the product derived from propyl iodide, but not in that derived from propyl chloride. The product from propyl bromide showed an intermediate amount.

Reaction with Isopropyl Chloride

The crude product was purified by recrystallization from methanol (10 ml/g). Nuclear magnetic resonance: CH_3 doublet at 0.82 (6.0 H), CH multiplet at 2.8 (1.0 H), NH singlet at 4.3 (0.8 H), aromatic H's complex band at 6.2–7.7 (14.4 H).

*Reaction with *t*-Butyl Chloride*

The crude reaction product was chromatographed on 70 g of Woelm grade I acidic alumina using, as eluting solvents, 350 ml of hexane and then four 150 ml portions of hexane containing methylene chloride in concentrations of 5%, 10%, 25%, and 50% (v/v), respectively. Fifty milliliters of eluent was collected per fraction, and the fractions were examined by thin-layer chromatography with cyclohexane containing 17% acetic acid as developing solvent. The first two fractions contained 0.111 g of unidentified material, the next three fractions contained 0.683 g (22%) of the product *N*,1,1-triphenyl-2,2-dimethylpropylamine (R_f 0.68), and the remaining fractions (total weight 1.58 g) were mixtures of benzophenone anil (R_f 0.42), *N*-benzhydrylaniline (R_f 0.57), and product.

The product was purified by recrystallization from methanol (40 ml/g). Nuclear magnetic resonance: CH_3 singlet at 1.0 (9.0 H), NH singlet at 4.8 (0.9 H), aromatic H's complex band at 5.9–7.9 (15.2 H).

Reaction with Allyl Chloride

The crude product, *N*,1,1-triphenyl-1-aminobutene-3, was purified by recrystallization from methanol (6 ml/g). Nuclear magnetic resonance: CH_2 doublet at 3.2 (2.0 H), $-\text{CH}=\text{CH}_2$ multiplet at 4.7–5.5 (3.2 H), NH singlet at 4.4 (0.8 H), aromatic H's complex band at 6.1–7.7 (15.3 H).

Reaction with Benzyl Chloride

The crude product, *N*,1,1,2-tetraphenylethylamine, was purified by recrystallization from *n*-butanol (5 ml/g). Nuclear magnetic resonance: CH_2 singlet at 3.75 (2.1 H), NH singlet at 4.48 (0.91 H), aromatic H's complex band at 6.1–7.6 (20.0 H).

Reaction with Vinyl Chloride

No color change of the sodium adduct was noted over an 18 h period. The crude product was a viscous oil whose infrared spectrum was identical with that of *N*-benzhydrylaniline.

Reaction with Cyclopentyl Chloride

The crude reaction product was examined by thin-layer chromatography with cyclohexane containing 17% acetic acid as developing solvent. Two products were detected: R_f 0.57–0.59 and 0.67–0.68.

The crude product (5.24 g) from 0.02 mole of adduct was boiled with 30 ml of 20% hydrochloric acid for 2 h. The final mixture was treated with 30 ml of ether and filtered. The insoluble solid, which amounted to 3.21 g (44% yield), was the hydrochloride of *N*-cyclopentyl-*N*-benzhydrylaniline, m.p. 180–184°. Purification was effected by dissolving in 15 ml of warm methanol and adding 70 ml of ether to precipitate the salt. Two such treatments raised the melting point to 190–193°. Nuclear magnetic resonance: cyclopentyl protons broad band at 1.65 (8.9 H), benzyl proton at 5.8 (0.87 H), aromatic H's complex band at 6.4–7.5 (15.0 H).

Anal. Calcd. for $\text{C}_{24}\text{H}_{26}\text{NCl}$: C, 79.2; H, 7.22; N, 3.85. Found: C, 78.7; H, 6.95; N, 3.78.

The ether layer in the filtrate from the amine hydrochloride was separated, washed, and evaporated, and the residue was distilled, b.p. 155–170° at 3 mm, to give 1.421 g of a partially crystalline liquid. A 0.50 g sample of this was recrystallized from 2 ml of methanol to give 0.20 g of cyclopentylidene diphenylmethane, m.p. 61–63°; the mixed melting point with an authentic sample was undepressed. The crude distillate was analyzed by vapor-phase chromatography, using a 7 ft long $\frac{1}{8}$ inch outside diameter column packed with 30% Apiezon on Chromosorb W heated at 248°, and using helium as carrier gas. The material was found to consist of 70% of cyclopentylidene diphenylmethane (representing a 21% yield) and 28% of an unknown material (relative retention time 1.53).

The authentic sample of cyclopentylidene diphenylmethane, m.p. 61–63°, was prepared from methyl cyclopentanecarboxylate and excess phenylmagnesium bromide followed by dehydration of the alcohol (without isolation) in refluxing acetic anhydride (15, 16). Nuclear magnetic resonance: CH_2 multiplet at 1.6 (4.0 H), CH_2 multiplet at 2.4 (4.0 H), aromatic H's singlet at 7.2 (9.8 H).

*Decomposition of *N*,1,1-Triphenylethylamine*

N,1,1-Triphenylethylamine (2.06 g, 0.076 mole) was refluxed with 10 ml of 20% hydrochloric acid for 1 h. The acid solution was extracted with 10 ml of benzene, washed twice with 5 ml of water, and dried over sodium sulfate. The dried solution was filtered and evaporated to give 1.075 g of a liquid residue. This was

distilled under vacuum, b.p. 76–82° at 2 mm, to yield 0.965 g (71%) of 1,1-diphenylethylene, whose infrared spectrum was identical with that of an authentic sample.

The aqueous acid phase and washings were combined, made alkaline, and extracted with ether. After the ether layer was washed, dried over sodium sulfate, and evaporated, a residue of 0.441 g of aniline (62%) was obtained. Its identity was established by preparing the benzenesulfonamide, m.p. 109–110°, undepressed on admixture with an authentic sample.

Reaction with 2 Equivalents of Methyl Iodide

The disodium adduct was treated with 0.02 mole of methyl iodide at –60°. Within 2 h the solution had decolorized, and thin-layer chromatography with 7:2:2 benzene – tetrahydrofuran – 98% formic acid as solvent showed the presence of four products: R_f 0.13, 0.26, 0.45, and 0.85. The first (R_f 0.13) and last (R_f 0.85), *N*-methylaniline and 1,1-diphenylethylene, respectively, were by far the largest; the other two were relatively small. One of these (R_f 0.39) is *N*-methyl-*N*-benzhydrylaniline (see below), and the other (R_f 0.26) is unknown.

The product was isolated by an ether extraction; after evaporation of the solvent, the residue (2.43 g) was distilled. Two fractions were collected: 0.746 g, b.p. 50–140° at 2 mm, and 1.225 g, b.p. 175–180° at 2 mm; 0.121 g was left as a residue. Thin-layer chromatography showed the first fraction to contain only *N*-methylaniline and 1,1-diphenylethylene, whereas the second contained these as the major components as well as the by-products, R_f 0.26 and 0.39.

The n.m.r. spectrum of this second fraction (CH_3 singlet at 1.79 (2.7 H), CH_2 singlet at 2.71 (3.0 H), aromatic H's complex band at 6.6–7.6 (16.8 H)) strongly indicated that the material was primarily *N*-methyl-*N*,1,1-triphenylethylamine. A small peak in the n.m.r. spectrum at 5.4 (equivalent to 0.2 H) was caused by an impurity, 1,1-diphenylethylene; this, in turn, affected the integration of the aromatic protons, giving too high a value. The addition of formic acid to the solution of the amine in the n.m.r. sample tube caused a marked change in the spectrum over a 24 h period. The peaks caused by the methyl groups decreased in intensity, the peak caused by the 1,1-diphenylethylene impurity grew larger, and a new peak appeared at 3.2 caused by *N*-methylaniline (in formic acid – deuterated chloroform).

N-Methyl-*N*,1,1-triphenylethylamine (0.547 g, 0.0019 mole) was dissolved in 25 ml of ether and treated with hydrogen chloride. A gum separated which crystallized when allowed to stand for 16 h. This was filtered off and weighed (0.275 g). The ether layer was evaporated to give 0.321 g (94% yield) of 1,1-diphenylethylene, whose identity was established by its infrared spectrum. The solid which was filtered off was treated with 5 ml of water containing 1 drop of concentrated hydrochloric acid and 5 ml of ether. The ether layer was separated, washed once with water, evaporated, and dried at 40° under vacuum.

The residue from the evaporation was dissolved in 5 ml of ether and treated with hydrogen chloride. A gummy solid (0.037 g) separated out and was dissolved in 1 ml of methanol; the solution was treated with 10 ml of ether, and a solid (0.020 g, m.p. 150–152.5°) precipitated out. The mixed melting point of the solid with *N*-methyl-*N*-benzhydrylaniline hydrochloride was 153–155° and its infrared spectrum was identical with that of an authentic sample.

The aqueous acid layer was made basic, extracted with ether, and evaporated to give 0.156 g (88% yield) of *N*-methylaniline, identified by comparison of its infrared spectrum with that of an authentic sample.

Reaction with 1,4-Dibromobutane

The adduct from 0.02 mole of benzophenone anil was treated with 2.38 ml (0.02 mole) of 1,4-dibromobutane at –60°. The crude orange product, isolated as previously described, amounted to 6.25 g. This was dissolved in 40 ml of *n*-hexane, and chromatographed on 60 g of Woelm grade I basic alumina packed in a 16 × 430 mm column, with 100 ml of *n*-hexane and then 100 ml of hexane – 10% benzene as eluting solvent. The color remained on the column and was not further investigated, and 5.22 g of a semisolid was recovered. This was dissolved in 60 ml of hot methanol and cooled to approximately 30 °C, and the warm solution was decanted from the gums which separated. Cooling the decantate to 10° overnight gave 2.77 g (44% yield), m.p. 74.5–77°, of 1,2,2-triphenylpiperidine.

The gum (1.35 g) crystallized when allowed to stand, and melted at 74–76.5°; the mixed melting point with the above product was 74–76.5°. The combined yield was 65%. Nuclear magnetic resonance: CH_2 broad band at 1.6 (3.95 H), CH_2 complex triplet at 2.5 (1.9 H), CH_2 complex triplet at 3.75 (1.9 H), aromatic H's complex band at 6.5–7.6 (15.0 H). The spectrum was unchanged after the solution was shaken with D_2O , indicating the absence of an amine proton.

Anal. Calcd. for $\text{C}_{23}\text{H}_{23}\text{N}$: C, 88.1; H, 7.41; N, 4.47. Found: C, 88.1; H, 7.16; N, 4.52.

At one point, an attempt was made to purify the crude product by vacuum distillation. The main fraction, b.p. 210–220° at 1 mm, was a yellow mobile liquid (the original crude material was a gum) and had an R_f (1:1 cyclohexane–chloroform) of 0.45, whereas the original material had an R_f of 0.70. Evidently some change had occurred, perhaps caused by trace amounts of acid remaining in the crude product.

This material (1.501 g) was dissolved in 25 ml of diethyl ether and treated with hydrogen chloride. The solid which precipitated (1.326 g, m.p. 175–180°) was dissolved in 10 ml of methanol; 35 ml of diethyl ether was added to give 1.115 g, m.p. 180–183°. An analytical sample was recrystallized from methanol, m.p. 182–184°. Nuclear magnetic resonance of the free amine: CH_2 quartet at 1.65, CH_2 quintet at 2.06 (combined

areas 4.0 H), CH₂ triplet at 2.96 (1.95 H), NH singlet at 3.34 (1.0 H), CH triplet at 6.00 (0.85 H), aromatic H's complex band at 6.4–7.4 (15.5 H).

Anal. Calcd. for C₂₃H₂₄ClN: C, 78.9; H, 6.92; N, 4.00. Found: C, 78.8; H, 6.71; N, 3.96.

The structure appears to be *N*,1,1-triphenyl-5-aminopentene-1.

Reaction with 1,3-Dibromopropane

The reaction of the sodium adduct and 1,3-dibromopropane was quite rapid at –60 °C. The crude product (3.265 g) was crystalline and was readily purified by recrystallization from methanol (20 ml) to give 2.24 g (75% yield) of 1,2,2-triphenylpyrrolidine, m.p. 112–114°. The analytical sample, after two additional crystallizations, had m.p. 115–116.5°. Nuclear magnetic resonance: CH₂ quintet at 1.74 (1.8 H), CH₂ triplet at 2.60 (1.85 H), CH₂ triplet at 3.70 (1.85 H), aromatic H's complex band at 6.0–7.6 (15.0 H).

Anal. Calcd. for C₂₂H₂₁N: C, 88.2; H, 7.08; N, 4.68. Found: C, 88.6; H, 7.06; N, 4.66.

Reaction with 1,5-Dibromopentane

The crude reaction product (3.35 g) was dissolved in 15 ml of hot *n*-propanol and allowed to stand for 24 h at room temperature. The product, *N,N'*,1,1,7,7-hexaphenylheptanediamine-1,7, separated slowly, 1.513 g (51% yield), m.p. 141–145°. Two recrystallizations from *n*-propanol gave an analytical sample, m.p. 154–156°. Nuclear magnetic resonance: CH₂ broad band at 1.1 (6.0 H), CH₂ broad band at 2.4 (3.8 H), NH very broad band at 4.2 (1.7 H), aromatic H's complex band at 6.2–7.7 (30.0 H).

Anal. Calcd. for C₄₃H₄₂N₂: C, 88.0; H, 7.23; N, 4.78; mol. wt. 589. Found: C, 88.3; H, 6.95; N, 4.87; mol. wt. 590.

The filtrate from the crude product was concentrated under vacuum, and the residue (1.53 g) was dissolved in 20 ml of hexane and placed on a 16 × 430 mm column of Woelm grade I basic alumina. Elution was carried out with 150 ml of hexane, 100 ml of hexane – 10% benzene, 100 ml of hexane – 25% benzene, 100 ml of hexane – 50% benzene, and finally 100 ml of benzene – 50% methylene chloride. The eluate was collected in 50 ml fractions. Fractions 1, 2, and 3 contained no material, and the remaining fractions contained 1.24 g. Examination of these by thin-layer chromatography with benzene – tetrahydrofuran – 98% formic acid (70:15:15) as developing solvent showed that fractions 4–7 (1.01 g) contained an unknown material and that fraction 9 (0.131 g) was the hexaphenylheptanediamine. The unknown material was combined and recrystallized from 25 ml of methanol, with cooling to 10°, to give 0.637 g of a solid, m.p. 55–58°. This was recrystallized again for an analytical sample, m.p. 58–59°.

Anal. Calcd. for C₂₄H₂₅N: C, 88.0; H, 7.71; N, 4.28. Found: C, 87.8; H, 7.72; N, 4.41.

On the basis of its n.m.r. spectrum, the structure was considered to be *N*,1,1-triphenyl-1-aminoheptene-5. The spectra showed a broad CH₂ band at 1.3 (2.0 H), a CH₂ quartet at 1.9 (2.2 H), a complex triplet at 2.5 (2.0 H), an NH band at 4.35 (0.85 H), two major peaks with complex fine structure at 4.7 and 4.9 caused by the vinyl group, a complex multiplet at 5.5 (total area 2.8 H), and a complex series of peaks at 6.1–7.4 (15.5 H) caused by the aromatic protons.

Reaction with 1,10-Dibromodecane

The crude reaction product from 0.01 mole of the sodium adduct in tetrahydrofuran and 1.5 g (0.005 mole) of 1,10-dibromodecane (3.751 g) was recrystallized from 25 ml of methanol and 13 ml of benzene. The recrystallized product amounted to 3.114 g (94% yield), m.p. 152–155°, of *N,N'*,1,1,12,12-hexaphenyldodecanediamine-1,12 having an orange color. Attempts to remove this color by recrystallization from *n*-butanol in the presence of Norit failed. Purification was finally effected by placing a solution of 1.65 g of the product in 30 ml of 1:1 hexane–benzene on a 16 × 450 mm column of 60 g of Woelm grade I basic alumina. Elution with 300 ml of the solvent removed 1.47 g of an almost colorless material, m.p. 147–152°; the color remained on the column. Two recrystallizations from *n*-butanol (20 ml/g) raised the melting point to 155–156.5°. Nuclear magnetic resonance: CH₂ broad band at 1.07 (8.0 H), CH₂ broad band at 2.48 (1.9 H), NH broad band at 4.26 (0.8 H), aromatic H's complex band at 6.2–7.7 (15.0 H).

Anal. Calcd. for C₄₈H₅₂N₂: C, 87.7; H, 7.99; N, 4.26; mol. wt. 657. Found: C, 88.0; H, 8.09; N, 4.15; mol. wt. 660.

Reaction with Benzaldehyde

The crude reaction product (3.41 g) was recrystallized from 20 ml of ethanol to give 0.987 g of benzophenone anil, m.p. 107–110°. A recrystallized sample of this, m.p. 110–113°, showed no depression on admixture with an authentic sample.

The filtrate from the recovered benzophenone anil was evaporated and the residue chromatographed on 70 g of Woelm grade I basic alumina packed into a 16 × 430 mm column. Elution with 250 ml of 1:1 benzene–hexane removed 1.36 g of a solid which, on recrystallization from 10 ml of hexane, gave 0.967 g, m.p. 77–80°. Investigation of this material by thin-layer chromatography with benzene as developer showed that it consisted of benzophenone anil (*R*_f 0.60) and *N*-benzhydrylaniline (*R*_f 0.73); n.m.r. analysis established that it was a mixture of 1 part of the former and 2 parts of the latter.

It was necessary to use methylene chloride plus 5% methanol and finally acetone plus 5% methanol to remove anything more from the alumina column. These eluents gave 0.701 g of a solid which, on recrystallization from 10 ml of benzene, gave 0.395 g of *dd, ll*-hydrobenzoin, m.p. 113–120°, undepressed on admixture

with an authentic sample. Comparison of the infrared spectrum of the isolated material with that of an authentic sample confirmed its identity.

The solvent in the benzene filtrate from the recrystallization was evaporated and the residue was recrystallized from water to give 0.176 g of a solid, m.p. 80–85°. An examination of the infrared spectrum of this material showed it to be a mixture of *dd, ll*-hydrobenzoin and *meso*-hydrobenzoin.

The authentic sample of *meso*-hydrobenzoin was prepared by sodium borohydride reduction of benzoin in 80% dioxane. It was recrystallized from water and had m.p. 134–136.5°.

dd, ll-Hydrobenzoin was prepared by acetolysis of α -stilbene dibromide by the procedure of Breuer and Zincke (17). Two recrystallizations from 80% water – 20% ethanol gave material having m.p. 117–120°.

The total yields of isolated compounds were 50% benzophenone anil and 25% *N*-benzhydrylaniline (based on the original benzophenone anil), and 65% of the diastereomeric hydrobenzoin (based on the benzaldehyde used).

Reaction with Ethylene Oxide

The crude reaction product from 0.01 mole of adduct and 0.01 mole of ethylene oxide amounted to 3.12 g. This was crystallized from 15 ml of petroleum ether (b.p. 30–60°) to give 2.17 g (72% yield) of an orange solid, m.p. 118–122°. Recrystallization from 25 ml of hexane and 10 ml of benzene with 2 g Norit and a hot filtration sufficed to remove the color and give an analytical sample, m.p. 122–125°. Nuclear magnetic resonance: CH₂ triplet at 2.67 (1.85 H), CH₂ triplet at 3.51 (2.0 H) superimposed on a broad NHOH band at 3.3–3.7, aromatic H's complex band at 6.2–7.6 (14.5 H). The peak areas were determined after the NHOH band was eliminated with D₂O. The difference between the peak areas of the 3.5 triplet plus the NHOH band before and after D₂O treatment established that the broad NHOH band corresponded to 1.9 H.

Anal. Calcd. for C₂₁H₂₁NO: C, 83.1; H, 6.99; N, 4.62. Found: C, 83.6; H, 6.96; N, 4.57.

Reaction with Methyl Benzoate

The crude reaction product from 0.01 mole of sodium adduct and 0.01 mole of methyl benzoate was recrystallized from 10 ml of methanol to give 2.50 g (69% yield) of *N*-benzhydrylbenzanilide, m.p. 108–110°; the mixed melting point with an authentic sample was undepressed, and the infrared spectra of the material and of an authentic sample were identical.

The authentic sample was prepared by refluxing *N*-benzhydrylaniline and an equivalent amount of benzoyl chloride in pyridine for 16 h. The crude product was crystallized from hexane, and recrystallized once from hexane and once from methanol, m.p. 108–109°. Nuclear magnetic resonance: aromatic H's only in a complex band at 6.5–7.5 (the benzylic proton is shifted into the aromatic region).

Anal. Calcd. for C₂₆H₂₁NO: C, 85.9; H, 5.83; N, 3.85. Found: C, 85.7; H, 5.70; N, 3.80.

Reaction with Methyl *p*-Toluate

The crude product was purified by one crystallization from methanol and two recrystallizations from hexane to give 1.562 g of *N*-phenyl-*N*-benzhydryl-*p*-toluamide, m.p. 112.5–114° (41% yield). Nuclear magnetic resonance: CH₃ singlet at 2.15 (3.0 H), aromatic H's complex band at 6.5–7.5 (20.0 H), indicating that the 19 aromatic protons and the 1 benzyl proton are in the same region.

Anal. Calcd. for C₂₇H₂₃NO: C, 85.9; H, 6.15; N, 3.71. Found: C, 85.6; H, 5.98; N, 3.58.

Reaction with Diethyl Carbonate

Diethyl carbonate (0.01 mole) produced 3.15 g of a crude product which was chromatographed on 60 g of Woelm basic alumina grade I. Fifty milliliter fractions were collected and the solvents used were 100 ml of hexane, 100 ml of hexane – 10% benzene, 50 ml of hexane – 25% benzene, and 100 ml of hexane – 50% benzene.

This treatment removed 1.82 g of material from the column. Additional eluting solvent containing methyl-ene chloride removed the remaining material, but no products could be isolated from it.

The 1.82 g was covered with petroleum ether (b.p. 30–60°). After the mixture had stood overnight at 10°, the solution was decanted from the ethyl *N*-benzhydrylphenylcarbamate, which amounted to 1.53 g (46% yield), m.p. 54–58°. Two recrystallizations from 20 ml of petroleum ether (b.p. 30–60°), with cooling to 10°, gave 1.03 g of the carbamate, m.p. 60–62°. Nuclear magnetic resonance: CH₃ triplet at 1.1 (3.3 H), CH₂ quartet at 4.1 (2.0 H), CH singlet at 6.7 (1.0 H), aromatic H's complex band at 6.8–7.4 (15.0 H):

Anal. Calcd. for C₂₂H₂₁NO₂: C, 79.7; H, 6.35; N, 4.23. Found: C, 80.0; H, 6.01; N, 4.24.

Reaction with Diethyl Sulfate

The crude product obtained when the sodium adduct was treated with 0.01 mole of freshly distilled diethyl sulfate amounted to 2.98 g. One recrystallization from 10 ml of petroleum ether (b.p. 30–60°) gave 1.78 g (62% yield) of *N*,1,1-triphenylpropylamine, m.p. 67–70.5°.

Stepwise Reaction with Methyl Benzoate and Methyl Iodide

The sodium adduct (0.01 mole) was allowed to react with 0.01 mole of methyl benzoate for 1 h at –60° and for 4 h at room temperature. The solution was then cooled again to –60° and 0.01 mole of methyl iodide added; after the solution had warmed to room temperature, it was allowed to stand overnight.

The crude product, isolated by ether extraction, amounted to 3.47 g and was crystallized from 30 ml of *n*-hexane to give 2.39 g (63% yield) of the benzamide of *N*,1,1-triphenylethylamine, m.p. 142–144°. One recrystallization from *n*-butanol and one from isopropanol raised the melting point to 146.5–149°. Nuclear magnetic resonance: CH₃ singlet at 2.0 (2.9 H), aromatic H's complex band at 6.7–7.6 (20.0 H), very similar in structure to that of *N*-benzhydrylbenzanilide.

Anal. Calcd. for C₂₇H₂₃NO: C, 85.9; H, 6.15; N, 3.71. Found: C, 85.9; H, 6.13; N, 3.70.

Preparation of N-Methyl-N-benzhydrylaniline³

A solution of 15.0 g (0.074 mole) of benzhydryl chloride and 17.4 g (0.162 mole) of *N*-methylaniline in 50 ml of benzene was stirred at room temperature for 16 h, during which time a precipitate formed. The solution was examined by thin-layer chromatography with 7:2:2 benzene – tetrahydrofuran – 98% formic acid as solvent to follow the progress of the reaction: *N*-methylaniline, *R*_f 0.12; product, *R*_f 0.59; by-products of unknown constitution, *R*_f 0.30, 0.42, and 0.74.

The solution was washed with 10% potassium hydroxide, the benzene stripped off, and the residue distilled, collecting the main fraction, b.p. 185–205° at 4 mm, 8.50 g. This was dissolved in 100 ml of diethyl ether, and hydrogen chloride was passed briefly through the solution. The resulting precipitate amounted to 2.4 g, m.p. 152–203° (decomp.).

The filtrate from this first salt was again treated with hydrogen chloride to give 4.63 g of a second crop, m.p. 159–160°. This was dissolved in 15 ml of chloroform, the solution was filtered to remove a small amount of insoluble material, and 25 ml of ether was added. The product amounted to 4.40 g, m.p. 160–161°. Nuclear magnetic resonance: CH₃ singlet at 3.33 (2.90 H), CH singlet at 6.44 (1.02 H), aromatic H's in two broad bands at 6.9–8.7 (15.0 H); for the free amine: CH₃ singlet at 2.73 (2.95 H), CH singlet at 6.15 (0.92 H), aromatic H's complex band at 6.5–7.5 (15.0 H).

Anal. Calcd. for C₂₀H₂₀NCl: C, 77.5; H, 6.52; N, 4.52. Found: C, 77.1; H, 6.59; N, 4.35.

*Stepwise Reaction with *t*-Butyl Alcohol and Methyl Iodide*

The disodium adduct was treated at –60° with 0.94 ml (0.01 mole) of *t*-butyl alcohol. After the dark-green solution was allowed to warm to room temperature for 2 h, the solution was recooled and 0.62 ml (0.01 mole) of methyl iodide added. When warmed to room temperature, the solution changed from a dark-green color through a royal blue to a clear pale yellow. After 16 h, the solution was treated with water, and the reaction product isolated by ether extraction.

The gummy residue remaining after evaporation of the ether was dissolved in 50 ml of diethyl ether, and hydrogen chloride was bubbled through to precipitate the hydrochloride of *N*-methyl-*N*-benzhydrylaniline, 2.80 g, m.p. 146–149°. This salt was dissolved in 10 ml of methanol and the solution treated with 25 ml of ether. The solid which precipitated amounted to 2.0 g (65% yield), m.p. 160–161°, undepressed on admixture with an authentic sample. Its infrared spectrum was identical with that of the authentic sample.

*Stepwise Reaction with *t*-Butyl Alcohol and Cyclopentyl Chloride*

The above experiment was repeated with 0.01 mole of cyclopentyl chloride instead of the methyl iodide. The crude reaction product gave 2.77 g (92% yield) of the hydrochloride of *N*-benzhydrylaniline, m.p. 196–198°. Dissolution in 40 ml of methanol followed by crystallization from 60 ml of ether gave 2.17 g (72% yield) of the salt, m.p. 198–200°, undepressed on admixture with an authentic sample. Its infrared spectrum was identical with that of the authentic sample.

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³This procedure follows that used by Cromwell and Fitzgibbon (18) for similar compounds.

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