

THE JOURNAL OF Organic Chemistry[®]

VOLUME 31, NUMBER 7

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JULY 12, 1966

Metallation of N,N-Dimethylaniline^{1a}

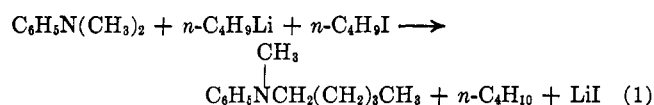
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Received March 10, 1966

N,N-Dimethylaniline was metallated by refluxing with *n*-butyl lithium. *o*-Dimethylaminophenyl-*t*-carbinols were obtained when the metallation mixture was treated with ketones. Ketones with α hydrogens gave carbinols which dehydrated under the reaction conditions producing the analogous conjugated olefins. The reaction of cyclohexene oxide with metallated dimethylaniline gave predominantly the olefin identical with 1-(*o*-dimethylaminophenyl)cyclohexene from dehydration of 1-(*o*-dimethylaminophenyl)-1-cyclohexanol. The *o*- and *m*-dimethylaminophenylbis(trifluoromethyl)carbinols were formed from hexafluoroacetone in 71 and 19% yield, respectively. These results parallel base-catalyzed hydrogen exchange data for dimethylaniline. The small amount, if any, of methyl group metallation seems to preclude participation of metallated dimethylaniline in α -alkylation reactions.

Interest in the mechanism of the α -alkylation reaction,² eq 1, led to the current investigation. Since one



possible route to the alkylation product may involve the initial α metallation of the amine, the reaction of *n*-butyllithium and N,N-dimethylaniline was studied.

This proton-abstraction process corresponds to the α metallation of ethers in ether cleavage with *n*-butyllithium³ or formation of the methyl metallated species in the reaction of methyl phenyl sulfide with *n*-butyllithium.⁴ With tertiary alkylarylamines, however, metallation has only been reported in the *ortho* positions.⁵ The *ortho*-metallation product of N,N-dimethylaniline was identified by reaction with benzophenone.⁶ However, the yield in this direct metallation using phenyllithium in ether at 100° was so poor (8%) that recent preparations of *o*-dimethylaminophenyllithium have used the action of lithium metal on *o*-bromo-N,N-dimethylaniline.⁷

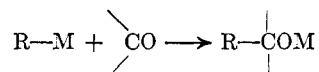
The predominance of *ortho* metallation in aromatic amines correlates well with the deuterium exchange rates of dimethylaniline with potassium amide in liquid ammonia.⁸ The relative rates of *ortho*:*meta*:*para*:

NCH₃ deuterium loss in dimethylaniline were 105:12:5.5:1.

Since we were interested in the possible products of reaction with dimethylaniline metallated by *n*-butyllithium in hexane, we have studied the reactions of ketones with metallated N,N-dimethylaniline.

Results and Discussion

Reaction of ketones with organometallics produces tertiary carbinols when the mixture is worked up by standard water quenching procedures. In order to



qualitatively and quantitatively determine the alcoholic products, we sought ketones giving products susceptible to gas chromatographic (gc) analysis. 2-Butanone and cyclohexanone reacted with metallated dimethylaniline giving products with the requisite volatility, Table I, but the complexity of the mixtures in gc prevented direct analyses even though the anticipated carbinols, 2-(*o*-dimethylaminophenyl)-2-butanol and 1-(*o*-dimethylaminophenyl)cyclohexanol, were isolated in 20 and 31% over-all yields, respectively, by vacuum distillation.

Products from incomplete reaction of *n*-butyllithium with dimethylaniline were discounted by the failure of the metallation mixture to give N-(*n*-pentyl)-N-methylaniline on addition of iodobenzene.² On this basis, metallation of dimethylaniline was complete after 12 hr of reflux.⁹

(9) After only 4 hr of reflux, metallation was incomplete as shown by the formation of a 5.5% yield of N-(*n*-pentyl)-N-methylaniline on addition of iodobenzene.²

(1) (a) This investigation was supported in part by Public Health Service Grant GM-09136, from the National Institute of General Medical Sciences; (b) to whom reprint requests should be sent: Department of Chemistry, Marshall University, Huntington, W. Va.

(2) A. R. Lepley and A. G. Giumanini, *Chem. Ind.* (London), 1035 (1965).

(3) K. Ziegler and H. G. Gellert, *Ann.*, **567**, 185 (1950).

(4) H. Gilman and F. J. Webb, *J. Am. Chem. Soc.*, **71**, 4062 (1949).

(5) H. Gilman and J. W. Morton, *Org. Reactions*, **3**, 258 (1954).

(6) G. Wittig and H. Merkle, *Chem. Ber.*, **75**, 1491 (1942).

(7) G. Wittig, G. Closs, and F. Mindermann, *Ann.*, **594**, 89 (1955).

(8) A. I. Shatenshtein and Y. I. Ranneva, *J. Gen. Chem. USSR*, **31**, 1317 (1961).

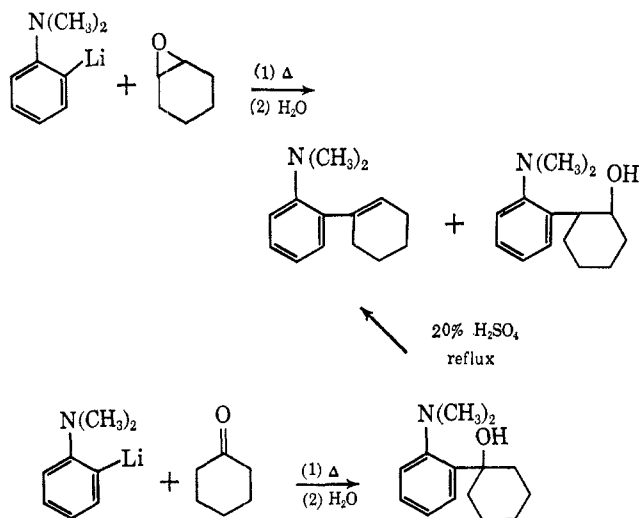
TABLE I
GAS CHROMATOGRAPHIC RETENTION RATIOS FOR
VOLATILE PRODUCTS FROM THE REACTIONS OF
METALLATED DIMETHYLANILINE

Compound	Retention ratio ^a
<i>m</i> -Dimethylaminophenylbis(trifluoromethyl)-carbinol	0.201
<i>o</i> -Dimethylaminophenylbis(trifluoromethyl)-carbinol	0.320
2-(<i>o</i> -Dimethylaminophenyl)-2-butanol	0.45
1-(<i>o</i> -Dimethylaminophenyl)cyclohexene	0.84
N-Benzhydryldimethylamine ^b	1.00
2-(<i>o</i> -Dimethylaminophenyl)cyclohexanol	1.38
1-(<i>o</i> -Dimethylaminophenyl)cyclohexanol	1.42

^a 0.25 in. \times 10 ft column of 20% GE-SF96 on 40-60 mesh Chromosorb W, 170 cc/min He flow, temperature 185°. ^b Retention time for standard, 14.6 \pm 0.7 min; peak width at half-height, 1.07 \pm 0.05 min.

Reaction of the metallated dimethylaniline with cyclohexene oxide gave information on one competing product. A low 20% sulfuric acid solubility of the first gc component in the less complex mixture from this reaction allowed separation of this product giving a 14% yield 1-(*o*-dimethylaminophenyl)cyclohexene, as identified by elemental analysis, and infrared and proton magnetic resonance (pmr) spectra. The absence of OH stretching vibrations and presence of an aromatic conjugated C=C stretching vibration at 6.22 μ in the infrared and the pmr single-proton olefinic CH multiplet centered at 5.70 ppm were used in this structure assignment. The structure (Scheme I) was confirmed by preparation of the same olefin on dehydration of 1-(*o*-dimethylaminophenyl)cyclohexanol with 20% sulfuric acid.

SCHEME I



2-(*o*-Dimethylaminophenyl)cyclohexanol (7% yield) was obtained as the minor component from this reaction of cyclohexene oxide with metallated dimethylaniline.

Acetophenone also gave an olefin under the conditions of reaction with the metallation mixture. The crude distilled products, 34% over-all yield, were not susceptible to gc analysis but acid extraction as in the previous case gave 1-(*o*-dimethylaminophenyl)-1-phenylethanol in 25% yield on distillation. The olefin in the reaction mixture was identical with α -(*o*-di-

methylaminophenyl)styrene obtained in 69% yield on sulfuric acid dehydration of the alcohol.

Base-catalyzed dehydration of alcohols occurs during the addition reaction, a tertiary carbinol with an α proton readily giving the conjugated olefin. This reaction is comparable with basic dehydration of a tertiary alcohol β to a carbonyl.¹⁰

Reaction of metallated dimethylaniline with ketones which do not contain α protons, benzophenone and *p,p'*-bis(dimethylamino)benzophenone, gave solid products. The crude carbinols from these reactions were obtained in 56 and 68%, respectively, but contained appreciable quantities of starting ketone and gave only 40 and 21%, respectively, over-all yields on recrystallization. The pure *o*-dimethylaminotritanol formation was greater than the crude yield of 8% previously reported.⁶ The *o,p',p''*-tris(dimethylamino)tritanol was a typical triphenylmethane indicator with a color change of colorless to blue in the pH range 1-3. These carbinols did not satisfy the gc criteria.

Since fluoro alcohols were recently reported¹¹ as low boiling, we treated *n*-butyllithium with hexafluoroacetone. Comparison of the boiling point rise in 2-propanol (82°) and 2-methyl-2-hexanol (141°) or 2H-hexafluoro-2-propanol¹¹ (59°) and 1,1-bis(trifluoromethyl)-1-pentanol (115°) supported the feasibility of gc analysis for the reaction of hexafluoroacetone with metallated dimethylaniline. In addition, we determined the active lithium content¹² of the metallation mixture prior to ketone addition in order to get accurate yields in the ketone reaction. In duplicate reactions using 100 mmoles of active lithium from *n*-butyllithium, 89 \pm 2% of the activity was present after initial mixing with N,N-dimethylaniline and 54 \pm 4% remained after refluxing for 16 hr. Hexafluoroacetone gas was bubbled through this metallation mixture and aqueous quenching gave the carbinols. Two reaction products were observed and separated by preparative gc. Both of the compounds had the elementary analysis required for a dimethylaminophenylbis(trifluoromethyl)carbinol. Quantitative gc analysis based on the active lithium content after reflux gave yields of 19 and 71% for these carbinols. In the infrared spectrum, out-of-plane aromatic CH deformations occurred at higher wavelengths for the more abundant compound and the pmr aromatic multiplet (Table II) was split into two parts of two protons each. The pmr splitting disappeared in the hydrochloride of this compound. Since deshielding of ring protons occurs with electron withdrawing groups and the reverse is true for electron-donating substituents, splitting results when amino and bis(trifluoromethyl) carbinol group are *ortho* or *para*. The quaternization of nitrogen reversed the amino group affect condensing the two multiplets into a single complex band at 7.90 ppm. In *meta* substitution, the amino and carbinol groups interact with same ring protons and should give only a single multiplet. The wavelength of infrared, aromatic CH out-of-plane deformations increases in the order¹³ *para* < *meta* < *ortho*.

(10) K. Takeda, H. Minato, and M. Ishikawa, *Chem. Commun.*, 79 (1965).

(11) W. J. Middleton and R. V. Lindsey, Jr., *J. Am. Chem. Soc.*, **86**, 4948 (1964).

(12) H. Gilman and A. H. Haubein, *J. Am. Chem. Soc.*, **66**, 1515 (1944).

(13) L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1956, p 55.

TABLE II
 PROTON NUCLEAR MAGNETIC RESONANCE SPECTRA OF THE CARBINOLS FROM METALLATED DIMETHYLANILINE

Compound	Chemical shift ^a					
	C	CH ₂ COH	NAr	CH C,COH	Ar	H O
2-(<i>o</i> -Dimethylaminophenyl)-2-butanol	0.82 t (3)	1.46 s (3)	2.61 s (6)	1.76 q (2)	7.16 m (4)	8.6 s (1)
1-(<i>o</i> -Dimethylaminophenyl)cyclohexanol			2.60 s (6)	1.7 m (10) ^{b,c}	7.18 m (4)	8.5 s (1)
2-(<i>o</i> -Dimethylaminophenyl)cyclohexanol			2.65 s (6)	1.55 m (9) ^c	7.16 m (4)	3.30 m (2) ^d
1-(<i>o</i> -Dimethylaminophenyl)-1-phenylethanol		1.76 s (3)	2.19 s (6)		7.18 m (9)	8.12 s (1)
<i>o</i> -(Dimethylamino)tritanol			2.33 s (6)		7.07 s (14)	8.83 s (1)
<i>o,p',p''</i> -Tris(dimethylamino)tritanol			2.39 s (6)		6.70 m (6)	9.48 s (1)
			2.88 s (12)		7.14 m (6)	
<i>o</i> -Dimethylaminophenylbis(trifluoromethyl)-carbinol			2.90 s (6)		6.71 m (2)	3.61 s (1)
					7.46 m (2)	
<i>m</i> -Dimethylaminophenylbis(trifluoromethyl)-carbinol			2.73 s (6)		7.53 m (4)	13.40 s (1)

^a All peaks are relative to tetramethylsilane in parts per million; splitting: s = singlet, t = triplet, q = quartet, m = multiplet; all *J* values are 6.90 ± 0.1 cps; values in parentheses are relative integrated peak ratios in compound. ^b Multiplet with three broad peaks at 1.42, 1.64, and 1.75 ppm. ^c Includes methylenes bound only to other methylene or methyne groups. ^d CH multiplet and OH.

The physical properties of the more abundant compound were then those of *o*-dimethylaminophenylbis(trifluoromethyl)carbinol in agreement with predictions based on detection of only *ortho* products in the other ketone reactions. The structure of the isomeric *meta* compound was in accord with the carbinol formed in 19% yield.

Since metallation occurs in more than one ring position, the associative mechanism postulated for restriction to the *ortho* position^{5,14} is perhaps a predominant but not an exclusive route. The 5:1 ratio of *o*:*m*-carbinols is a reasonable approximation of the more detailed and exact order of dimethylaniline proton exchange ratios⁵ and is the same as the ratio observed on metallation of benzotrifluoride.¹⁴

Several conclusions are supported by these results. The relationship between isotope exchange rates and metallation suggest the presence of other isomeric products in many metallation reactions.⁵ In addition, our original question on the participation of a metallated species in the α -alkylation reaction is answered to the negative. The amount of methyl group metallation is <10% and probably at best 1 or 2%. This coupled with the slow metallation rate^{2,8} precludes the invocation of N-CH₂⁻ in the dimethylaniline α -alkylation reaction.

Experimental Section¹⁵

Chemicals.—Cyclohexene oxide and all ketones used in this study were commercially available. Commercial mono-free *N,N*-dimethylaniline was dried over sodium before use. *n*-Butyllithium (Foote Mineral, 15% in hexane) was analyzed by the double titration method for active lithium content¹² before use.

Metallated Dimethylaniline Solution.—In general, *n*-butyllithium solution was added to an excess of dimethylaniline and the solution was heated under reflux overnight.⁹ The solution of metallated dimethylaniline was used directly in reactions and over-all yields based on initial *n*-butyllithium are given. Active lithium content was determined after initial mixing and after 16 hr of reflux for the conditions used in the hexafluoroacetone reactions. When 12.2 ml (100 mmoles) of dimethylaniline was

mixed with 65 ml of 1.6 *N* (100 mmoles) *n*-butyllithium solution, immediate analysis indicated 89 ± 2 mmoles of active lithium while after the reflux period only 54 ± 4 mmoles of active lithium remained.

2-(*o*-Dimethylaminophenyl)-2-butanol.—Dry-distilled 2-butanone, 5.8 g, in 12 ml of anhydrous pentane was added during 15 min to the metallated solution above, formed from 15 ml of dimethylaniline and 65 ml of 1.6 *N* butyllithium in hexane. After refluxing overnight, 25 ml of water were added to the cooled solution. Separation of the organic phase, drying with sodium sulfate, and distillation gave 3.0 g (20% over-all yield) of the product: bp 163 (33 mm); refractive indices of *n*^{20D} 1.5089, *n*^{25D} 1.5072, and *n*^{30D} 1.5050.

Anal. Calcd for C₁₂H₁₉NO: C, 74.65, H, 9.91; N, 7.25. Found: C, 74.40; H, 10.04; N, 7.24.

The infrared spectrum had bands at 2.9–3.1 w, 3.26 m, 3.34 s*, 3.46 s, 3.56 m, 6.24 w, 6.34 w, 6.72 s, 6.83 m, 7.77 m, 8.45 m, 8.95 w, 9.18 w, 9.60 s, 10.04 m, 10.64 s, 12.9 m, and 13.2 s μ .

1-(*o*-Dimethylaminophenyl)cyclohexanol.—Freshly distilled cyclohexanone, 10 ml, in 25 ml of dry pentane was added during 30 min to the metallated solution above, formed from 15 ml of dimethylaniline and 65 ml of 1.6 *N* butyllithium in hexane. After an additional 3.5 hr of reflux, ice was added to the cooled solution. The organic layer which separated was combined with two 25-ml ether extracts and dried over sodium sulfate. Distillation gave 6.8 g (31% over-all yield) of the product boiling at 97° (0.07 mm): refractive indices of *n*^{20D} 1.5332, *n*^{25D} 1.5313, and *n*^{30D} 1.5292.

Anal. Calcd for C₁₄H₂₁NO: C, 76.66; H, 9.65; N, 6.39. Found: C, 76.51; H, 9.73; N, 6.55.

The infrared spectrum had bands at 3.0–3.2 w, 3.27 m, 3.40 s*, 3.50 s, 3.59 m, 6.38 w, 6.75–6.93 s, 7.43 w, 7.78 m, 8.46 w, 8.71 w, 9.08 w, 9.63 m, 9.83 w, 10.13 m, 10.67 s, 10.98 w, 11.7 w, 11.97 w, 12.9 m, 13.26 s, and 14.4 w μ .

2-(*o*-Dimethylaminophenyl)cyclohexanol and 1-(*o*-Dimethylaminophenyl)cyclohexene.—Cyclohexene oxide (8.7 ml, 80 mmoles) was gradually added during 6 hr to a refluxing metallated solution previously formed from 18 hr of reflux of 12.2 ml (100 mmoles) of dimethylaniline and 50 ml of 1.6 *N* (80 mmoles) *n*-butyllithium solution. Reflux was continued for another 18 hr and the reaction mixture was cooled and quenched with ice. Gas chromatography of the organic layer indicated the presence of two components with peak area ratios of 2:1. Most of the unreacted dimethylaniline was removed by distillation and the residue was dissolved in ether. The ether solution was washed repeatedly with 10% sulfuric acid. The combined acid layers were just neutralized with concentrated ammonia and extracted thoroughly with ether. This ether solution was washed with water and dried over anhydrous sodium sulfate; the solvent was distilled off. Gc on the residue still indicated two products. Separation of products was effected by their difference in 20% sulfuric acid solubility. The product corresponding to the second gc peak was much more soluble in this solvent. The first few extractions with 20% sulfuric acid contained most of the second product and a trace of the first gc component. Continued extraction gave exclusively the first compound. Pure samples for infrared and pmr spectra and elemental analysis were collected from the gc.

(14) J. D. Roberts and D. Y. Curtin, *J. Am. Chem. Soc.*, **68**, 1658 (1946).

(15) Physical properties (infrared and pmr spectra and refractive indices) were measured in the standardized manner previously described: A. R. Lepley and R. H. Becker, *Tetrahedron*, **21**, 2365 (1965). Gas chromatography was carried out at 185° on an F and M Model 500 with the columns and conditions of A. R. Lepley and W. A. Khan, *J. Org. Chem.*, **31**, 2064 (1966). Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Melting and boiling points are uncorrected.

The first gc component, 1-(*o*-dimethylaminophenyl)cyclohexene, had a retention ratio of 0.84, yield of 14% (gc), and infrared absorption bands at 3.45 s*, 3.55 s, 3.61 m, 6.22 m, 6.70 s, 6.90 s, 6.97 m, 7.55 m, 7.85 w, 8.10 w, 8.34 m, 8.60 m, 8.78 m, 9.02 m, 9.49 m, 9.95 w, 10.50 s, 10.88 m, 11.60 w, 11.80 w, 12.45 w, 13.11 m, and 13.45 s μ .

Anal. Calcd for C₁₈H₁₉N: C, 83.53; H, 9.51. Found: C, 83.62; H, 9.56.

The pmr spectrum had an aliphatic CH multiplet centered at 2.00 ppm, a methyl on nitrogen singlet at 2.65 ppm, an olefinic CH multiplet centered at 5.70 ppm, and an aromatic multiplet centered at 6.90 ppm. These peaks had the respective integrated peak area ratio of 8:6:1:4.

The second gc component, 2-(*o*-dimethylaminophenyl)cyclohexanol, had a retention ratio of 1.38, yield of 7.4% (gc), and infrared absorption bands at 2.90 m, 3.23 w, 3.39 s*, 3.48 s, 3.58 m, 5.89 w, 6.28 w, 6.71 s, 6.91 s, 7.70 m, 7.80 m, 8.15 w, 8.45 m, 8.69 m, 8.92 w, 9.14 w, 9.40 m, 9.59 m, 10.20 w, 10.38 w, 10.60 m, 11.45 w, 11.80 w, 12.19 w, 13.32 s, and 14.40 w μ .

Anal. Calcd for C₁₃H₂₁NO: C, 76.71; H, 9.58; N, 6.39. Found: C, 76.94; H, 9.75; N, 6.11.

Dehydration of 1-(*o*-Dimethylaminophenyl)cyclohexanol.—The carbinol, 0.67 g, was refluxed for 2 hr with 20 ml of 20% H₂SO₄. The mixture was cooled in ice and made basic with cold aqueous NaOH. The solution was extracted with ether, the ether layer was dried over anhydrous Na₂SO₄, decanted, and the solvent was evaporated. Gc analysis of this product using benzhydryldimethylamine as a standard gave a retention ratio of 0.86 and indicated the formation of 0.28 g (69% yield) of 1-(*o*-dimethylaminophenyl)cyclohexene and the recovery of 0.11 g of unreacted 1-(*o*-dimethylaminophenyl)cyclohexanol. Infrared analysis of the gc-purified olefin was identical with that of the olefin from the cyclohexene oxide reaction.

1-(*o*-Dimethylaminophenyl)-1-phenylethanol.—Dry acetophenone, 29 g, in 20 ml of anhydrous pentane was added during 45 min to the metallated solution above, formed from 47 ml of dimethylaniline and 20 ml of 1.6 *N* butyllithium in hexane. After 10 hr of reflux the solution was cooled and 30 ml of water was cautiously added. After drying over magnesium sulfate, distillation of the organic phase gave 18.5 g (34% over-all crude yield) of a very viscous yellow oil boiling at 125–130° (0.4 mm). Although the product redistilled sharply, pmr and C, H, N analyses indicated appreciable impurities. Therefore the compound was dissolved in diethyl ether and extracted with three 30-ml portions of 10% sulfuric acid. The combined acid solutions were extracted twice with ether. The remaining acid solution was treated with 50 ml of 30% ammonia while cooling. Extraction with three 25-ml portions of ether, drying the combined ether layers over sodium sulfate, and distillation gave 15 g (25% over-all yield) of viscous liquid boiling at 117.5° (0.2 mm): refractive indices of *n*_D²⁰ 1.5708, *n*_D²⁵ 1.5687, and *n*_D³⁰ 1.5667. On prolonged standing the material crystallized: mp 50.5–53°.

Anal. Calcd for C₁₆H₁₉NO: C, 79.63; H, 7.99; N, 5.81. Found: C, 79.40; H, 8.12; N, 6.01.

The infrared spectrum had bands at 3.15–3.3 w, 3.32 m, 3.42 s, 3.48 m, 3.58 m, 3.60 m, 3.65 m, 6.28 w, 6.38 w, 6.78 s, 6.89 s, 6.97 s, 7.16–7.4 w, 7.82 w, 8.25 w, 8.50 m, 8.72 w, 8.95–9.1 w, 9.36 w, 9.6 s, 10.7 s, 11.92 w, 13.0 s, 13.2 s, 13.35 s, 14.23 s*, and 14.6 w μ .

α -(*o*-Dimethylaminophenyl)styrene.—1-(*o*-Dimethylaminophenyl)-1-phenylethanol, 1.4 g, was refluxed for 1.5 hr with 20 ml of 20% sulfuric acid. The mixture was cooled in ice and poured into an ice-cold solution of 4.3 g of sodium hydroxide in 20 ml of water. The organic layer was removed by extracting twice using 15-ml portions of ether. The ether layers were combined, dried over sodium sulfate, decanted, and distilled. A colorless oil was obtained, 0.9 g (69% yield), boiling at 94–97° (0.05 mm): refractive indices of *n*_D²⁰ 1.6028, *n*_D²⁵ 1.6008, and *n*_D³⁰ 1.5988.

Anal. Calcd for C₁₆H₁₇N: C, 86.05; H, 7.67; N, 6.27. Found: C, 86.00; H, 7.96; N, 6.09.

The infrared spectrum had bands at 3.28 m, 3.39 m, 3.51 m, 3.59 m, 6.28 s, 6.71 s*, 6.91 s, 7.01 m, 7.56 m, 7.92 w, 8.4 w, 8.62 m, 8.80 w, 9.11 w, 9.58 m, 9.74 w, 10.51 s, 11.1 s, 12.80 s, 13.08 s, 13.22 s, 14.12 s, and 14.35 m μ . The pmr indicated a methyl on nitrogen singlet at 2.46 ppm, a conjugated asymmetric olefinic methylene quartet at 5.41 ppm (*J* = 11.7 and 1.6 cps), and an aromatic multiplet centered at 7.12 ppm. These resonances had integrated areas in the ratio of 6:2:9, respectively.

***o*-(*N,N*-Dimethylamino)tritanol.**—Benzophenone, 4.5 g, was added in small portions to the metallated solution above, formed

from 6 ml of dimethylaniline and 12 ml of 1.6 *N* butyllithium in hexane. Reflux was continued for 1 hr. Water, 15 ml, was added to the cooled solution and the organic layer was retained. On standing, 3.1 g (56% over-all yield) of a yellow crystalline product separated: mp 159.5–160.5°. Recrystallization of the crude product from ethanol gave a slight increase in the melting point to 160.5–161.5° (lit.⁶ mp 158–160°). The infrared spectrum had bands at 3.0–3.2 w, 3.3 m, 3.4 m, 3.5 m, 3.58 m, 6.34 w, 7.82 m, 6.74 s, 6.87 s, 6.93 s, 7.2 m, 8.3 w, 8.49 m, 9.10 m, 9.63 s, 9.77 s, 9.98 w, 10.61 m, 10.72 m, 11.0 w, 11.12 m, 12.8–13.1 s, and 14.21 s* μ .

***o,p',p''*-Tris(*N,N*-dimethylamino)tritanol.**¹⁶—Michler's ketone, 6.7 g, in 25 ml of anhydrous pentane was added to the metallated solution above, formed from 6 ml of dimethylaniline and 12 ml of butyllithium in hexane. Reflux was continued for 3 hr. Water, 30 ml, was added and the solution was refluxed with stirring for 1 hr. The solid was filtered and washed with water giving 6.6 g (68% over-all yield) of crude material, mp 145–187°. Recrystallization from 95% ethanol gave 2.1 g (21% over-all yield) of a light yellow solid, mp 213°.

The infrared spectrum had bands at 3.1–3.3 w, 3.4 m, 3.5 m, 3.6 m, 6.21 s, 6.31 w, 6.60 s*, 6.78 m, 6.93 m, 7.40 s, 7.81 w, 8.17 m, 8.41 m, 8.60 m, 8.9 w, 9.12 w, 9.4–9.5 w, 9.63 m, 10.57 m, 10.66 m, 11.08 m, 12.19 s, 12.8 w, and 12.99 m μ .

The pmr of this compound was measured in deuteriochloroform.

1,1-Bis(trifluoromethyl)-1-pentanol.—Hexafluoroacetone gas was bubbled through 65 ml of 1.6 *N* *n*-butyllithium for 1.5 hr while stirring at room temperature. The mixture was then heated to reflux and hexafluoroacetone addition was continued until cessation of gas absorption. Gas flow was stopped and the mixture was refluxed for 1.5 hr. The mixture was cooled, quenched with ice-water, and acidified with HCl. Gc analysis at 75° using the column and flow rate previously described¹⁵ gave a retention ratio for the product of 0.815 with respect to *n*-pentanol. The weight to peak area ratio correction factor determined from weighed samples of the purified product and standard was 1.69:1. The yield of product was 49% (gc). The product was purified by extraction of the hexane solution twice with 50 ml of 20% NaOH aqueous. The combined alkaline layers were washed with hexane, cooled on ice, and slowly acidified by addition of 6 *N* HCl. A red oil separated which was extracted with hexane and distilled giving a colorless liquid: bp 53–55° (60 mm), 115° (760 mm); refractive indices of *n*_D²⁰ 1.3448, *n*_D²⁵ 1.3429, *n*_D³⁰ 1.3416. The product had infrared bands at 2.90 m, 3.39 m, 3.49 m, 5.90 w, 6.85 m, 7.26 m, 7.45 m, 7.80 s, 8.28 s*, 8.65 s, 8.95 s, 9.42 m, 9.71 m, 10.18 m, 10.50 m, 10.92 w, 11.20 w, 13.10 w, 13.35 w, 13.61 w, 13.95 m and 14.40 w μ . The pmr spectrum had a hydroxyl group singlet at 3.97 ppm and a complex CH multiplet centered at 1.45 ppm with the integrated relative intensity ratios of 1:9, respectively.

Anal. Calcd for C₇H₁₀F₆O: C, 37.51; H, 4.50. Found: C, 37.54; H, 4.65.

***o*- and *m*-Dimethylaminophenylbis(trifluoromethyl)carbinol.**—The metallation of 12.2 ml (100 mmoles) of dimethylaniline with 65 ml of 1.6 *N* (100 mmoles) of *n*-butyllithium solution was carried out as described above. The mixture, analyzed for 54 \pm 5 mmoles of active lithium compound, was cooled to room temperature and gaseous hexafluoroacetone was passed through the metallation mixture until absorption ceased, ca. 4 hr. The completion of reaction was confirmed by a negative color test I,¹⁷ i.e., yellow rather than blue solution. At this point, the reaction mixture was brown with a lower layer of tarry material. The reaction mixture was gently refluxed for 1 hr and cooled, 25 ml of ice-water was added, and the mixture was refrigerated overnight. Gc of the organic layer indicated two reaction products. The reaction mixture was extracted repeatedly with ether. The combined ether extracts were washed with water and dried over anhydrous sodium sulfate. This solution (1 ml) was used for determination of retention ratios and yields of the two products. 2-(*o*-Dimethylaminophenyl)-2-butanol, the standard for quantitative analysis, was weighed into this solution and 50- μ l samples were injected into the gc operating at 150° with a flow rate of 170 cc/min. A calibration correction of 1.2 was established for the peak area of product/standard by using weighed samples of pure isolated product. The retention ratios at 150° were 0.466

(16) A. G. Giumanini, A. B. Giumanini, and A. R. Lepley, *Boll. Chim. Farm.*, **104**, 290 (1965).

(17) H. Gilman and F. Schulze, *J. Am. Chem. Soc.*, **47**, 2002 (1925).

and 0.771 and their respective yields were 19.0 and 71.0% based on active lithium content after reflux.

The ether solution was repeatedly extracted with 2 *N* HCl which removed the second gc component. During the first hydrochloric acid extraction a crystalline solid, mp 183–186° dec, separated. It was filtered and dried and had infrared peaks at 2.95 m, 3.18 m, 3.48 m, 3.80 s, 3.90 s, 4.00 m, 4.09 m, 6.21 w, 6.61 m, 6.78 m, 6.85 m, 7.10 w, 7.40 w, 7.58 w, 7.70 m, 7.90 s*, 8.21 s*, 8.50–8.60 s, 8.70 s, 9.00 s, 9.79 w, 10.06 w, 10.21 s, 10.46 m, 10.68 s, 11.10 w, 10.85 s, 13.40 m, and 14.12 s μ . The pmr of the salt was run in deuterium oxide using the water singlet at 4.81 ppm (relative to TMS) as a conversion standard to δ_{TMS} . A 15% solution of the salt had methyl on nitrogen singlet resonance at 3.33 ppm and an aromatic multiplet centered at 7.90 ppm. The relative peak areas by integration were 6:4, respectively.

Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{ClF}_6\text{NO}$: C, 40.09; H, 3.71; Cl, 10.98; F, 35.38; N, 4.34. Found: C, 39.83; H, 3.99; Cl, 10.42; F, 35.02; N, 4.49.

The salt gave only the second gc component on treatment with dilute sodium hydroxide solution.

The ether solution from above and the hydrochloric acid extracts were worked up separately.

The ether solution was washed well with water, dried over anhydrous sodium sulfate, and distilled, bp 70° (0.3 mm), giving a pale yellow oil. This compound corresponds to the first gc component, has a characteristic pleasant smell, crystallized on

standing to a bright pale yellow solid, mp 46–48°, and had infrared bands at 2.9–3.0 m, 3.4 m, 5.45 m, 5.58 m, 6.22 m, 6.50 s, 6.72 m, 6.88 m, 6.98 m, 7.05 m, 7.70 s, 7.95 s*, 8.2 s, 8.40–8.45 s, 8.71–8.80 m, 8.90 s, 9.05 m, 9.65 m, 10.30 s, 10.42 m, 10.62 m, 10.81 s, 11.30 w, 12.74 w, 12.91 w, 13.10 m, 13.50 w, and 14.08 s μ .

Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{F}_6\text{NO}$: C, 46.10; H, 3.84; N, 4.88; F, 39.79. Found: C, 45.73; H, 3.82; N, 4.93; F, 39.27.

On the basis of the elemental analysis, infrared spectrum and pmr spectrum (Table II), this compound was assigned the structure *m*-dimethylaminophenylbis(trifluoromethyl)carbinol.

The hydrochloric acid solution was washed once with ether, cooled in ice, made alkaline with sodium hydroxide solution, and extracted with ether. The ether extracts were washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. A pale brown crystalline solid with a pleasant odor was obtained. This material corresponds to the second gc component, was soluble in concentrated sodium hydroxide solutions but extractable with ether, recrystallized from ligroin, mp 73–75°, and had infrared bands at 3.1–3.2 m, 3.45 m, 6.21 m, 6.60 m, 6.80 m, 6.85 m, 6.95 w, 7.18 m, 7.82 s, 8.15 s, 8.26 s, 8.40 s*, 8.60 m, 8.78 s, 9.00 s, 9.55 w, 9.86 w, 10.37 m, 10.55 m, 10.70 s, 12.01 m, 12.15 m, 13.02 w, 13.55 w, and 14.18 m μ .

Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{F}_6\text{NO}$: C, 46.10; H, 3.84; N, 4.88; F, 39.79. Found: C, 46.16; H, 3.79; N, 5.17; F, 39.75.

On the basis of the elemental analysis, infrared spectrum, and pmr spectrum (Table II), this compound was assigned the structure of *o*-dimethylaminophenylbis(trifluoromethyl)carbinol.

Benzene Addition to Dialkylanilines^{1a,b}

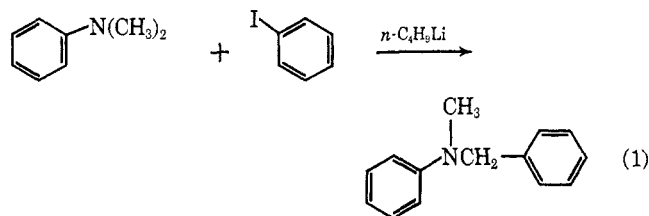
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Received March 10, 1966

Benzene generated by the action of *n*-butyllithium on fluoro- and chlorobenzene has been treated with dialkylanilines. Reaction with dimethylaniline gave *N*-methyl-diphenylamine, *N*-ethyl-diphenylamine, and *o*-(dimethylamino)biphenyl. The analogous compounds, *N*-(2-butyl)diphenylamine and *o*-(diethylamino)biphenyl, were identified in benzene reaction with diethylaniline. The *o*-(dialkylamino)biphenyls were formed by reaction of benzene with the *ortho*-metallation product of the dialkylanilines. Slow benzene generation or elevated temperatures favor formation of this product. The diphenylamines were rearrangement or elimination products from an intermediate betaine formed by benzene addition of the unshared nitrogen electrons. The formation of *N*-benzyl-*N*-methylaniline by α substitution was not observed.

The recent use of iodobenzene in the α substitution of dimethylaniline,² eq 1, suggests as alternative possibili-



ties that (a) a benzyne intermediate may participate in the α -substitution reaction, or (b) the α -substitution reaction may furnish a method of differentiating between benzyne and nonbenzyne intermediates in aromatic dehydrohalogenation reactions. The iodo group which participates in α alkylation was found to be the least effective halide in biphenyl formation from phenyllithium and halobenzenes,³ a reaction later shown to follow a benzyne mechanism.^{4,5} Iodobenzene was also

the least reactive halobenzene in the reactions with lithium piperidide to give *N*-phenylpiperidine.⁶

Both of these reactions are hypothetically additions of an organo metallic or carbanion to the benzyne intermediate. A more sensitive method of differentiating between benzyne and alternative mechanisms, such as double displacement, would be to use a less reactive benzyne trap. The benzyne addition of tertiary amines might be such a reaction.

Several products were observed in the benzyne reaction with triethylamine. Wittig and Benz⁷ identified the major product as *N,N*-diethylaniline and a minor component as *N*-(2-butyl)-*N*-ethylaniline.⁸ The mechanism in this reaction, as in other tertiary amine reactions with benzyne,^{9,10} proceeds *via* addition of the nonbonding electrons on nitrogen to the active benzyne site. Only one of the unoccupied aromatic positions is

(4) R. Huisgen, "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Corp., New York, N. Y., 1960, p 75.

(5) H. Heaney, *Chem. Rev.*, **62**, 81 (1962).

(6) R. Huisgen and J. Sauer, *Chem. Ber.*, **93**, 192 (1959).

(7) G. Wittig and E. Benz, *ibid.*, **92**, 1999 (1959).

(8) This compound was earlier erroneously identified as *o*-*N,N*-triethylaniline: G. Wittig and W. Merkle, *ibid.*, **76**, 109 (1943). The correction in identification was overlooked in a recent review.⁵

(9) H. Hellman and W. Unsel, *Ann.*, **631**, 82, 95 (1960); H. Hellmann and G. W. Scheytt, *ibid.*, **642**, 22 (1961).

(10) H. Hellman and W. Unsel, *ibid.*, **631**, 85 (1960).

(1) (a) Presented in part before the Division of Organic Chemistry, 148th National Meeting of the American Chemical Society Chicago, Ill., Sept. 1964, Abstracts, 92S; (b) this investigation was supported by Public Health Service Grant GM-09136, from the National Institute of General Medical Sciences; (c) to whom reprint requests should be sent: Department of Chemistry, Marshall University, Huntington, W. Va.

(2) A. R. Lepley and A. G. Giumanini, *Chem. Ind.* (London), 1035 (1965).

(3) G. Wittig and W. Merkle, *Chem. Ber.*, **75**, 1491 (1942).