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SPRINGDALE, PA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

Consecutive Ortho Substitution Rearrangements Starting with 2- and 4-Substituted Benzyltrimethylammonium Ions[1]

WILLIAM Q. BEARD, JR.,[2] AND CHARLES R. HAUSER

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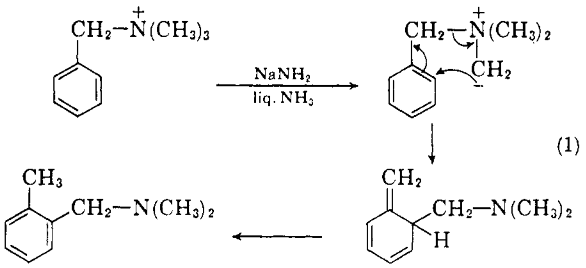
Ortho substitution rearrangements of 2-substituted benzyltrimethylammonium ions and of the methiodides of the products were found to take place not only when the substituent was methyl or ethyl as reported previously, but also when the substituent was methoxy or chlorine. Similar consecutive rearrangements were realized starting with 4-substituted benzyltrimethylammonium ions where the substituent was methyl, isopropyl, methoxy, or chlorine, but not when the substituent was cyano. The yields were generally good to excellent, but they were very low in the second rearrangement when the substituent was chlorine. The structures of the rearranged amines were established in several ways. These results extend considerably the usefulness of the ortho substitution rearrangement in synthesis. Infrared data for a number of benzyldimethylamines are presented.

It has previously been shown that the benzyltrimethylammonium ion undergoes the ortho substitution rearrangement with sodium amide in liquid ammonia to form 2-methylbenzyldimethylamine in 96% yield[3,4] The mechanism has been represented by Equation 1.[3] The methiodide of the product was further rearranged, and the process was repeated until the aromatic ring was completely substituted.[3]

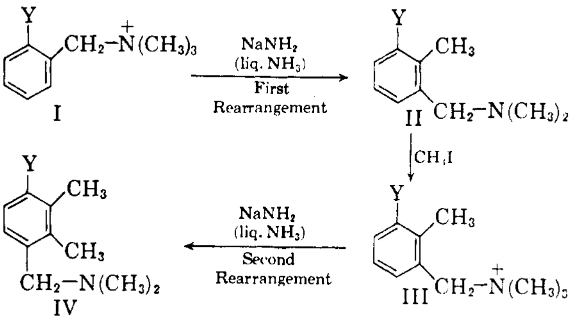


The α-methylbenzyltrimethylammonium ion also has been rearranged and the resulting 2-ethylbenzyldimethylamine rearranged through its methiodide.[5] This process was repeated once more.[5]

In the present investigation a study was made of the generality of this type of rearrangement starting with 2- and 4-substituted benzyltrimethylammonium ions.

Results with 2 - substituted benzyltrimethylammonium ions. The general reactions for two consecutive rearrangements starting with quaternary ammonium ions of this type may be represented by Scheme A.

Scheme A



Y = CH_3, C_2H_5, CH_3O, Cl

As indicated above, these two consecutive rearrangements have previously been observed when Y is methyl and ethyl. They have now been realized when Y is methoxy and chlorine. The yields, including those from the earlier examples for comparison, are summarized in Table I. The yields for the methylations of type II amines to form type III quaternary ions, which are not included in this table, were almost quantitative.

The structures of the two new amines IIc and IId from the first rearrangement in Scheme A were established by oxidations to known acids and anhydrides (Scheme B).

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(1) Supported in part by the National Science Foundation.

(2) Union Carbide Chemicals Co. Fellow, 1956–58.

(3) S. W. Kantor and C. R. Hauser, *J. Am. Chem. Soc.*, **73**, 4122 (1951).

(4) W. R. Brasen and C. R. Hauser, *Org. Syntheses*, 63–4, *Note 8 (1954)*.

(5) C. R. Hauser and A. J. Weinheimer, *J. Am. Chem. Soc.*, **76**, 1261 (1954).

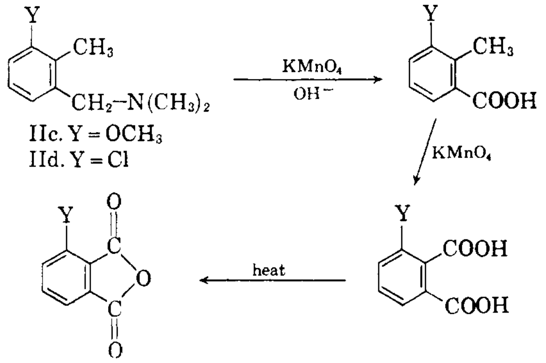
TABLE I

YIELDS OF REARRANGED AMINES II AND IV FROM QUATERNARY IONS I AND III WITH SODIUM AMIDE IN LIQUID AMMONIA

Quat. Ion	Y	Rearranged Amine No.	Rearranged Amine Yield, %	Quat. Ion	Rearranged Amine No.	Rearranged Amine Yield, %
Ia	CH_3	IIa	60–70[a]	IIIa	IVa	43[b]
Ib	C_2H_5	IIb	90[c]	IIIb	IVb	46[c]
Ic	OCH_3	IIc	84	IIIc	IVc	59
Id	Cl	IId	18(37)[d]	IIId	IVd	2

[a] Refs. 3 and 4. [b] Ref. 3. [c] Ref. 5. [d] Potassium amide was employed in ether at room temperature (25–30°).

Scheme B



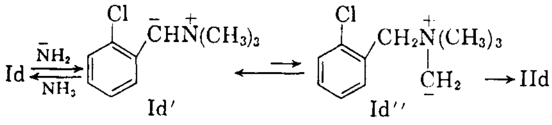
The structures of the two new amines IVc and IVd from the second rearrangement in Scheme A were supported by their infrared spectra, each of which showed a band in the 850–800 cm.$^{-1}$ region. These bands are attributed to the out-of-plane deformation frequency of the two adjacent hydrogens on the aromatic ring,[6] since the three vicinal hydrogens on the aromatic ring in amines IIc and IId absorbed in the 800–750 cm.$^{-1}$ region.[6] The structures of the amines IVc and IVd were further established by mild oxidations to the corresponding monocarboxylic acids, which gave satisfactory analyses.

It can be seen from Table I that the yields of the rearranged amines of type II from the first rearrangement in Scheme A were good to excellent not only when Y was methyl[3,4] or ethyl[5] but also when Y was methoxy (IIc, 84%). However, the yield of rearranged amine IId where Y was chlorine was only 18% in the usual medium, liquid ammonia, and 37% with potassium amide in ether at room temperature (25–30°).

Whereas the 2-ethyl and 2-methoxy quaternary ions (Ib and Ic) gave relatively little residual by-product, the 2-methyl quaternary ion Ia produced, besides the good yield of rearranged amine IIa, a considerable amount of neutral and basic dimeric and trimeric by-products, one of which was 2,2′-dimethylstilbene.[7]

The 2-chloro quaternary ion Id gave relatively little residual material with an equivalent of sodium amide in liquid ammonia even after 13 hours, which is much longer than the usual 1–2 hour reaction period. Yet the rearranged amine IId was obtained in only 18% yield, and 59% of the quaternary salt Id was recovered unchanged. When this quaternary ion was treated with two equivalents of sodium amide in liquid ammonia for 5 hours, essentially none of the rearranged amine IId was isolated. Instead, considerable amine residue was obtained, and 61% of the quaternary salt Id was recovered. Apparently this amine residue arose from further reaction of the rearranged amine IId with excess amide ion, since a similar amine residue was produced in a blank experiment with the amine IId and the reagent. The two samples of residue gave positive diazonium tests for primary aromatic amines and infrared bands at 3470 cm.$^{-1}$ and 3390 cm.$^{-1}$ for the N—H bond in primary amines.[8] Evidently these residues were formed by the benzyne type of reaction involving the chlorine atom of amine IId and the amide ion.[9] Incidentally, the quaternary ion Id did not appear to undergo appreciable benzyne reaction.[10]

These results indicate that the 2-chloro quaternary ion Id rearranged much more slowly than quaternary ions Ia–c. This might be due partly to a more unfavorable equilibrium than usual between the predominant benzyl carbanion Id′[11] and the methyl carbanion Id″, which presumably is the reactive intermediate in the rearrangement (Equation 2).[12]



(2)

It is possible that in the experiment in ether at a higher temperature (25–30°) the *ortho*- substitution rearrangement of quaternary ion Id was accompanied by some of the Stevens type of 1,2-

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[6] L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, 2nd. ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 78

[7] It was reported previously (ref. 3) and confirmed in the present work that yields of approximately 6–8% each of dimeric and trimeric neutral and basic by-products, totaling 25–30%, are produced.

[8] Ref. 6, p. 249.

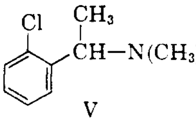
[9] J. D. Roberts, H. Simmons, Jr., L. Carlsmith, and C. Vaughan, *J. Am. Chem. Soc.*, **75**, 3290 (1953).

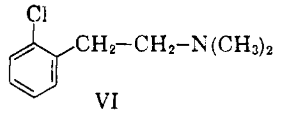
[10] The crude recovered salts gave an infrared spectrum identical with that of the pure starting quaternary salt, except for two additional bands from the ammonium chloride used in the neutralization of the reaction mixture.

[11] Because of the inductive effect of the *o*-chlorine atom the benzyl carbanion Id′ might be expected to be a considerably weaker base than the corresponding benzyl carbanions of quaternary ions Ia–c.

[12] Although some precipitate was present in the reaction mixture, it was no more noticeable than those observed with the quaternary ions that readily underwent the rearrangement.

shift, since the latter reaction is known to be favored at the expense of the former by an elevation of temperature.[13] The 1,2- shift of a methyl group within carbanion Id′ would form tertiary amine V and that of the 2-chlorobenzyl group within carbanion Id″, tertiary amine VI.

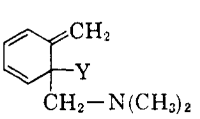

V

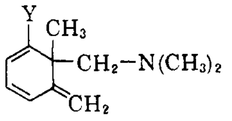

VI

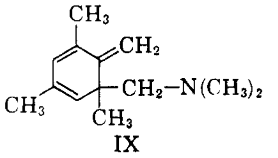
However, the amine isolated in 37% yield must have consisted at least largely of the *ortho*- substitution rearrangement product IId, since it produced on oxidation the acids and the anhydride shown in Scheme B. Apparently this oxidation process yielded no *o*-chlorobenzoic acid, which should have been formed had amines V or VI been present.

It can further be seen from Table I that the yields of amines of type IV from the second rearrangement in Scheme A were fairly good (43–59%) when Y was methyl, ethyl, or methoxy. However, the yield of amine IVd where Y was chlorine was only 2% even when quaternary ion IIId was treated with an equivalent of sodium amide in liquid ammonia employing the inverse addition procedure. Apparently the rearranged amine IVd was not formed in appreciably higher yield and then destroyed through the benzyne reaction, since most of the product consisted of amorphous neutral material.

It should be pointed out that the first and second rearrangements in Scheme A might have been accompanied by some reaction at the substituted *ortho*- position to form *exo*-methyleneamines of types VII and VIII, since the 2,4,6-trimethylbenzyltrimethylammonium ion rearranges to give the *exo*-methyleneamine IX in 70% yield.[14]


VII


VIII

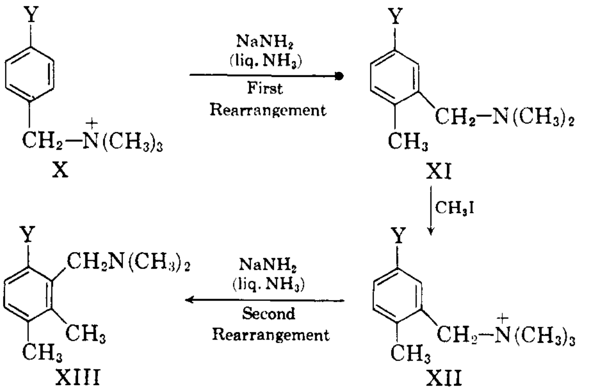

IX

Since *exo*-methyleneamine IX was shown to be decomposed readily by acid to form isodurene, the *exo*-methyleneamines VII and VIII presumably would have been converted to corresponding neutral compounds on acidification of the reaction mixtures.

Actually small amounts of compounds VII and VIII (Y = CH_3) must have been formed in the original relatively large scale experiments with quaternary ions Ia and IIIa, since *o*-xylene and hemillitene were isolated in yields of 1% and 3%, respectively. Small amounts of such products might have been produced in the present work, but they were not isolated.

Results with 4-substituted benzyltrimethylammonium ions. The general reactions for two consecutive rearrangements starting with quaternary ammonium ions of this type may be represented by Scheme C.

Scheme C



Y = CH_3, $(CH_3)_2CH$, CH_3O, Cl

These two consecutive rearrangements were realized when Y was methyl, isopropyl, methoxy, and chlorine, but not when Y was cyanide. The yields are summarized in Table II. The yields for the methylations of amines of type XI to form quaternary ions of type XII (Scheme C) were almost quantitative.

TABLE II

YIELDS OF REARRANGED AMINES VII AND IX FROM QUATERNARY IONS VI AND VIII WITH SODIUM AMIDE IN LIQUID AMMONIA

Quat. Ion	Y	Rearranged Amine No.	Rearranged Amine Yield, %	Quat. Ion	Rearranged Amine No.	Rearranged Amine Yield, %
Xa	CH_3	XIa	53–63	XIIa	XIIIa	84
Xb	$CH(CH_3)_2$	XIb	92	XIIb	XIIIb	68
Xc	OCH_3	XIc	93	XIIc	XIIIc	78
Xd	Cl	XId	54–60	XIId	XIIId	8
Xe	CN	XIe	0	—	—	—

The structures of the rearranged amines of type XI from the first rearrangement in Scheme C were established in several ways. That of amine XIa was determined by mild and vigorous oxidations to form the corresponding mono- and tricarboxylic acids, respectively. The latter acid was dehydrated to give the anhydride (Scheme D).

Rearranged amine XIb was independently synthesized from the Grignard reagent of 2-bromo-*p*-

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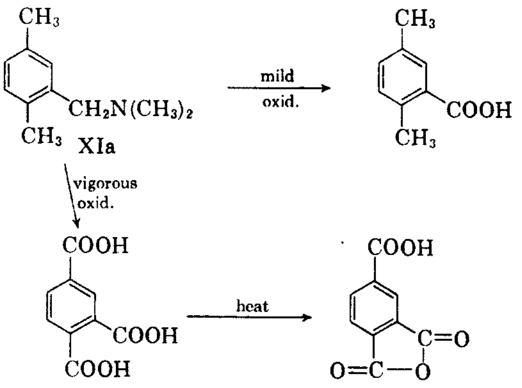
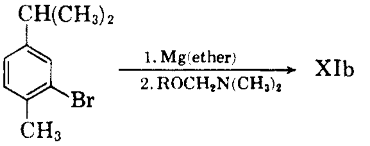
[13] C. R. Hauser, R. M. Manyik, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **20**, 1119 (1955); G. Wittig and H. Strieb, *Ann.*, **584**, 1 (1953).

[14] C. R. Hauser and D. N. Van Eenam, *J. Am. Chem. Soc.*, **76**, 1264 (1954).

Scheme D



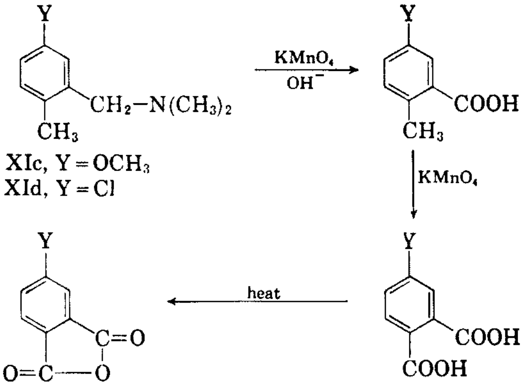
cymene and dimethylaminomethyl isobutyl ether (Equation 3, R = isobutyl).[15]



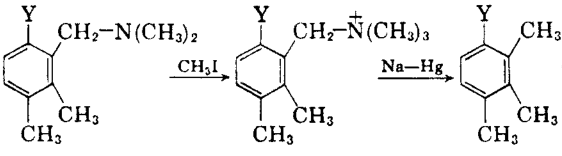
(3)

Rearranged amines XIc–d were oxidized to the corresponding monocarboyxlic acids and dicarboxylic acids, the latter compounds being dehydrated to form anhydrides (Scheme E).

Scheme E



The structures of the rearranged amines of type XIII from the second rearrangement in Scheme C were established by reductions or oxidations. Amines XIIIa–b were converted to their methiodides, which were reduced by the Emde method (Equation 4).

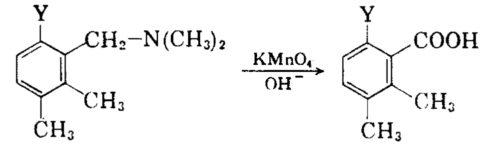


(4)

XIIIa, Y = CH_3
XIIIb, Y = $(CH_3)_2CH$

The prehnitene from amine XIIIa exhibited an infrared spectrum identical with that of an authentic sample of this hydrocarbon. The 4-isopropyl-1,2,3-trimethylbenzene from amine XIIIb gave, besides a satisfactory analysis, an infrared spectrum showing the same type of aromatic substitution as prehnitene.

Rearranged amines XIIIc–d were oxidized to the corresponding monocarboxylic acids, both of which gave satisfactory analyses (Equation 5).



(5)

XIIIc, Y = OCH_3
XIIId, Y = Cl

In further support for structures XIIIc–d, the infrared spectra of the amines lacked a band in the 900–860 cm.$^{-1}$ region which was present in the spectra of amines XIc–d. This band is attributed to an isolated hydrogen atom situated between two substituents on the aromatic ring.[16]

It can be seen from Table II that the yields of the rearranged amines of type XI from the first rearrangement in Scheme C were excellent (92–93%) when Y was isopropyl or methoxy, and good (53–63%) when Y was methyl or chlorine. The similarities and differences of these results compared to those from the 2-substituted quaternary ions are considered below.

Similar to the 2-methyl quaternary ion Ia, the 4-methyl quaternary ion Xa gave, besides the rearranged amine XIa, a considerable amount of neutral residual material from which the dimer 4,4′-dimethylstilbene was isolated in 8–10% yields. Also, a small amount of basic residue was obtained. However, this ratio of neutral to basic residual by-products was considerably higher than that obtained from quaternary ion Ia, with which the ratio was approximately 1:1.[3,7] Moreover, the yield of the rearranged amine appeared to be influenced by reaction conditions much less with quaternary ion Xa than with Ia.[17]

Like the 2-ethyl and 2-methoxy quaternary ions Ib and Ic, the 4-isopropyl and 4-methoxy quaternary ions Xb and Xc produced excellent yields of the rearranged amines with very little residual material. Incidently, the 93% yield of the rearranged amine XIc given in Table II was obtained with two equivalents of sodium amide in liquid ammonia on stopping the reaction after only 5 minutes. The yields listed for certain of the other

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(15) Similar reactions of Grignard reagents with dimethylaminomethyl alkyl ethers have been reported by G. M. Robinson and R. Robinson, *J. Chem. Soc.*, 532 (1923).

(16) Ref. 6, p. 79.

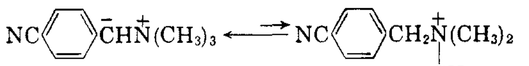
(17) Whereas the yields of 53–63% of amine XIa were obtained on varying the amount of ammonia used and the rate of addition of quaternary ammonium ion Xa, the 60–70% yield of amine IIa was lowered to 30% when quaternary ion Ia was added rapidly to the reagent in a relatively small amount of ammonia (ref. 3).

rearranged amines could probably also be obtained in much shorter time than the usual 1 to 2 hours allowed.

Whereas the 2-chloro quaternary ion Id produced only an 18% yield of the rearranged amine after 13 hours, the 4-chloro quaternary ion Xd gave 54–60% yields with an equivalent of sodium amide in liquid ammonia within 30 minutes to 1 hour. The inverse addition procedure was employed for the best yield, but the rapid addition of the quaternary salt Xd to the reagent gave almost as good yield.

Similar to the 2-chloro quaternary ion Id, the 4-chloro quaternary ion Xd gave considerable amine residue with two equivalents of the reagent, although some of the rearranged amine XId was isolated. This residue, the amount of which increased with the length of the reaction period, apparently arose from further reaction of the rearranged amine XId with excess reagent, since it gave a positive diazonium test and infrared bands for the N–H bond.

The failure of the 4-cyano quaternary ion Xe to rearrange with an equivalent of sodium amide liquid ammonia cannot be ascribed to side reactions, since 93% of the essentially pure quaternary salt was recovered after 3 hours. However, when two equivalents of the reagent were employed the recovered quaternary salt was quite impure.[18] Since color was produced, carbanions Xe′ and/or Xe″ were evidently produced. The failure of the latter to rearrange under the conditions employed might possibly be due to its relatively low concentration in equilibrium with the more weakly basic resonating carbanion Xe′ (Equation 6).



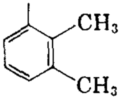
(6)

Xe′ Xe″

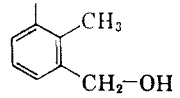
It can further be seen from Table II that the yields of tertiary amines of type XIII from the second rearrangement in Scheme C were good to excellent (68–84%) when Y was methyl, isopropyl, or methoxy. The larger size of the isopropyl group compared to the methyl group evidently had relatively little effect on the rearrangement. However, the yield was only 8% when Y was chlorine, and 57% of the quaternary salt XIIa was recovered.

The fact that the second rearrangement in Scheme C as well as that in Scheme A was realized in better yield when Y was alkyl or methoxy than when Y was chlorine was not anticipated on the basis of the current aromatic nucleophilic mechanism (see Equation 1). While this mechanism has been useful for correlating previous results, the present results suggest that it may need modification. A further study of the mechanism is now in progress.

Synthetic considerations. The ortho substitution rearrangements represented in Equation 1 and Scheme A ($Y = CH_3$) have previously been employed for the synthesis of not only the rearranged amines, but also of certain vicinal methyl derivatives. For examples, the methiodide of rearranged amine IIa has been converted by an Emde reduction to hemimellitene (XIV, $Y = CH_3$) in reproducible yields of 85–90%.[19] Also the ethobromide derivative of IIa has been converted by a displacement reaction with sodium acetate in acetic acid followed by saponification to 2,3-dimethylbenzyl alcohol (XV, $Y = OCH_3$) in reproducible over-all yields of 84–88%.[20]

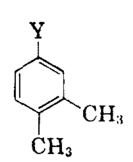


XIV

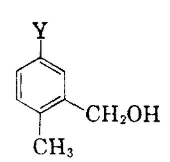


XV

The present results extend considerably the synthetic possibilities of the rearrangement. The reactions mentioned above should be applicable not only to other quaternary ions of Type II where Y is alkyl or methoxy. producing compounds of types XIV and XV, but also to those of rearranged amines of type IV (see Scheme A) or even to further rearranged amines, yielding higher substitution products. Moreover, such reactions should be feasible with quaternary ions of the rearranged amines of types XI and XIII (see Scheme C) to form compounds of types XVI and XVII and the corresponding higher substitution products in which Y is alkyl or methoxy.



XVI



XVII

Examples of the Emde reduction of the methiodides of type XIII rearranged amines are illustrated in Equation 4, in which the higher substitution products where Y is isopropyl or methyl are obtained in 66% and 75% yields, respectively.

Besides the types of compounds indicated above, certain carboxylic acids may be prepared conveniently through the *ortho*- substitution rearrangement. For example, the oxidation of rearranged amines IIc and XIc has produced 3-methoxy-2-methylbenzoic and 5-methoxy-2-methylbenzoic acids in yields of 80% and 83%, respectively.

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[18] Although the excess amide ion might be expected to attack the nitrile group to form an amidine, an infrared spectrum of the crude recovered quaternary salt failed to show bands for the N—H bond.

[19] W. R. Brasen and C. R. Hauser, *Org. Syntheses*, **34**, 56 (1954).

[20] W. R. Brasen and C. R. Hauser, *Org. Syntheses*, **34**, 58 (1954).

Infrared absorption spectra of benzyldimethylamines. All of the substituted benzyldimethylamines obtained in the present investigation and those others which were also examined exhibited a single moderate to strong band in their infrared spectra within the narrow range of 837–853 cm.$^{-1}$ This band appears to be specific for benzyldimethylamines and seems not to have been described previously. Table III summarizes the amines the spectra of which have been recorded and their characteristic absorption wave lengths in this region.

TABLE III

Amine	Infrared Absorption Frequency,[a] Cm.$^{-1}$
Benzyldimethylamine	849
2,3-Dimethylbenzyldimethylamine	847
2,5-Dimethylbenzyldimethylamine	848
3-Methoxy-2-methylbenzyldimethylamine	844
5-Methoxy-2-methylbenzyldimethylamine	837
3-Chloro-2-methylbenzyldimethylamine	847
5-Chloro-2-methylbenzyldimethylamine	838
5-Isopropyl-2-methylbenzyldimethylamine	842
2,3-Dimethyl-4-methoxybenzyldimethylamine	850
2,3-Dimethyl-6-methoxybenzyldimethylamine	850[b]
2,3-Dimethyl-6-isopropylbenzyldimethylamine	847
6-Chloro-2,3-dimethylbenzyldimethylamine	849[b]
4-Chloro-2,3-dimethylbenzyldimethylamine	853
2,3,6-Trimethylbenzyldimethylamine	849[b]

[a] All spectra run on a Perkin-Elmer Model 21 Infrared Spectrophotometer unless otherwise designated. [b] Spectra run on Perkin-Elmer Infracord.

It is interesting to note that the methiodides of these amines do not absorb in this region. The dimethylaminomethyl group alone is probably not responsible for the absorption, since several substituted β-phenylethyldimethylamines were found to show no absorption within this range. The band is also weak or absent in many α-substituted benzyldimethylamines which have been prepared in this laboratory.

EXPERIMENTAL[21]

2-Methoxybenzyltrimethylammonium bromide (Ic). 2-Methoxybenzoic acid (76 g., 0.5 mole) was reduced with 25 g. (0.6 mole) of 95% lithium aluminum hydride in 1000 ml. of anhydrous ether by the method used for the reduction of 3,5-dimethoxybenzoic acid[22] to give 59.5 g. (86%) of 2-methoxybenzyl alcohol, b.p. 125–127° at 13 mm., lit.,[23] b.p. 125–127° at 13 mm.

This alcohol (59.5 g., 0.43 mole) was treated with 58.0 g. (0.215 mole) of phosphorus tribromide in 750 ml. of ether and allowed to stand overnight. The excess phosphorus tribromide was hydrolyzed with ice and the layers separated. The ether layer was washed with water and sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Distillation yielded 73.0 g. (85%) of 2-methoxybenzyl bromide, b.p. 114.5–116° at 10 mm., lit.,[24] b.p. 115° at 10 mm. This bromide polymerized unless used within a few hours.

A solution of the freshly prepared bromide (73 g., 0.36 mole) in 350 ml. of acetonitrile cooled in an ice bath was treated with an excess (29 g., 43 ml., 0.5 mole) of liquid trimethylamine. After 1 hr., 1500 ml. of ether was added gradually with stirring to precipitate the 2-methoxybenzyltrimethylammonium bromide (Ic), which was collected on a suction funnel, washed with ether, and dried in a vacuum desiccator. Yield, 89 g. (94%), m.p. 188.5–189.5°. Since it was somewhat hygroscopic, its picrate was prepared for analysis. After three recrystallizations from 95% ethanol it melted at 152.5–153°.

Anal. Calcd. for $C_{17}H_{20}N_4O_8$: C, 50.00; H, 4.94; N, 13.72. Found: C, 49.96; H, 5.15; N, 13.71.

Rearrangement of quaternary salt Ic to form amine IIc. To a stirred suspension of 0.20 mole of sodium amide in 300 ml. of liquid ammonia[25] was added during 10 min. 26.0 g. (0.1 mole) of 2-methoxybenzyltrimethylammonium bromide (Ic). The color of the reaction mixture was reddish purple, which soon faded to gray. After 1 hr. 10.7 g. (0.2 mole) of solid ammonium chloride was added, and the liquid ammonia was evaporated as an approximately equal volume of ether was added. The resulting ethereal suspension was filtered (to remove the salts) and extracted with three 100-ml. portions of 2*N* hydrochloric acid.[26] The ether solution was dried over magnesium sulfate and evaporated, leaving no appreciable residue. The combined acid extract was carefully made strongly basic with solid sodium hydroxide, cooled with ice, and extracted with two 100-ml. portions of ether. This ethereal solution of the amine was dried over magnesium sulfate and distilled, yielding 15.10 g. (84%) of 3-methoxy-2-methylbenzyldimethylamine (IIc), b.p. 111–113° at 9.5 mm., n_D^{25} 1.5176, and leaving 0.90 g. of acid-soluble pot residue.

Anal. Calcd. for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.91. Found: C, 73.86; H, 9.74; N, 7.97.

The picrate, recrystallized twice from 95% ethanol, melted at 125–125.5°.

Anal. Calcd. for $C_{17}H_{20}N_4O_8$: C, 50.00; H, 4.94; N, 13.72. Found: C, 50.03; H, 4.84; N, 13.74.

Oxidation of a 2.0 g. sample of amine IIc was effected at room temperature with 6.0 g. of potassium permanganate in 100 ml. of 0.5*N* sodium hydroxide solution. A 3.0-g. portion of the potassium permanganate was added at first, and three 1.0-g. portions were each added after the color of the preceding portion had disappeared. After filtration through a Supercel mat the filtrate was acidified and the product collected. After one recrystallization from aqueous ethanol the yield was 1.48 g. (80%) of 3-methoxy-2-methylbenzoic acid, m.p. 145–146°, lit.,[27] m.p. 145–146°.

Further oxidation of the above monoacid was effected by heating a 0.5-g. sample with 0.95 g. of potassium permanganate in 100 ml. of 0.05*N* sodium hydroxide solution until the purple color had disappeared (about 15 min.). The manganese dioxide was removed by filtration through a Supercel mat, and the filtrate was acidified and filtered again to remove a small amount of the starting monoacid. The solution was saturated with sodium sulfate and extracted with ether, which was then dried over magnesium

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[21] Analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Melting points were determined on a Fisher melting point block and are corrected. Infrared spectra were produced on either a Perkin-Elmer Model 21 spectrophotometer or a Perkin-Elmer Infracord.

[22] R. Adams, M. Harfienst, and S. Leowe,. *J. Am. Chem. Soc.*, **71**, 1624 (1949).

[23] M. G. Vavon, *Compt. rend.*, **154**, 359 (1912).

[24] E. Späth, *Monatsh.*, **34**, 1996 (1913).

[25] See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, 122 (1954).

[26] The acid extraction was omitted in subsequent experiments, since no neutral material was obtained.

[27] L. F. Fieser and W. C. Lothrop, *J. Am. Chem. Soc.*, **58**, 749 (1936).

sulfate and evaporated to give 0.17 g. of 3-methoxyphthalic acid. After two recrystallizations from ethanol and hexane the product melted at 169.5–170.5° dec., lit.,[28] m.p. 173–174° dec.

A small sample of this dicarboxylic acid was boiled in a test tube to give 3-methoxyphthalic anhydride, m.p. 158–158.5°, lit.,[28] m.p. 160–161°.[28]

3-Methoxy-2-methylbenzyltrimethylammonium iodide (IIIc). To a stirred, cooled solution of 28.64 g. (0.16 mole) of 3-methoxy-2-methylbenzyldimethylamine (IIc) in 150 ml. of acetonitrile was added 43.0 g. (0.30 mole) of methyl iodide. Crystallization began within a few minutes. After 1 hr. the precipitation was completed by the addition of 500 ml. of dry ether while the mixture was stirred vigorously. The salt was collected on a suction filter, washed with dry ether, and dried in a vacuum desiccator. The yield was 50.9 g. (97%) of 3-methoxy-2-methylbenzyltrimethylammonium iodide (IIIc), m.p. 225° dec. A sample recrystallized from a mixture of ethanol and acetonitrile melted at 227° dec.

Anal. Calcd. for $C_{12}H_{20}INO$: C, 44.73; H, 6.25; N, 4.35. Found C, 44.88; H, 6.34; N, 4.34.

Rearrangement of IIIc *to 2,3-dimethyl-4-methoxybenzyldimethylamine* (IVc). This reaction was carried out with 30.1 g. (0.094 mole) of 3-methoxy-2-methylbenzyltrimethylammonium iodide (IIIc) and 0.112 mole of sodium amide in 300 ml. of liquid ammonia as described for Ic. The color, which was blue-black during the addition, became a light purple shortly after the addition was complete.

From the neutral fraction 1.67 g. of light brown amorphous material was obtained. Distillation of the basic fraction yielded 0.58 g. of forerun, b.p. 120–126° at 9 mm., n_D^{25} 1.5195, and 10.72 g. (59%) of 2,3-dimethyl-4-methoxybenzyldimethylamine (IVc), b.p. 126–127.5° at 9 mm., n_D^{25} 1.5204, and 1.96 g. of pot residue.

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.76; H, 9.71; N, 7.24.

The methiodide of a 2.0 g. sample of amine IVc was prepared with excess methyl iodide in 15 ml. of acetonitrile. After the mixture had stood for 30 min., it was heated to boiling and the methiodide slowly precipitated by the careful addition of anhydrous ether. A yield of 3.15 g. (91%), m.p. 232–233°, was obtained. The melting point was not raised by further recrystallization.

Anal. Calcd. for $C_{13}H_{22}INO$: C, 46.58; H, 6.62; N, 4.18. Found: C, 46.34; H, 6.55; N, 4.07.

Oxidation of 2.0 g. of amine IVc with 5.2 g. of potassium permanganate as described for amine IIc yielded after one recrystallization from aqueous ethanol 0.80 g. (42%) of 2,3-dimethyl-4-methoxybenzoic acid, m.p. 204–205°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.36: H, 6.71.

2-Chlorobenzyltrimethylammonium chloride (Id). This quaternary salt was prepared in 96% yield from 161 g. (1 mole) of 2-chlorobenzyl chloride and 118 g. (2 moles) of liquid trimethylamine as described for Ic. Its melting point was 208–209°.

The picrate, after one recrystallization from 95% ethanol, melted at 166.5–167.5°.

Anal. Calcd. for $C_{16}H_{17}N_4ClO_7$: C, 45.00; H, 4.02; N, 13.12. Found: C, 45.17; H, 4.16; N, 13.23.

Rearrangement of quaternary salt Id *to amine* IId. (A) *In liquid ammonia.* To a suspension of 0.15 mole of sodium amide in 500 ml. of liquid ammonia was added through Gooch tubing as rapidly as possible 33.0 g. (0.15 mole) of 2-chlorobenzyltrimethylammonium chloride (Id). The mixture was allowed to stir under a Dry Ice reflux condenser for 13 hr. The initial bright green color gradually changed to yellow and then to tan. Ammonium chloride 8.02 g., 0.15 mole was added for neutralization, and the ammonia was replaced by ether as it was evaporated. The salts were removed by filtration and the ether evaporated from the filtrate. Distillation of the residue yielded 4.59 g. (18%) of 3-chloro-2-methylbenzyldimethylamine (IId), b.p. 103–106.5° at 9.5 mm., n_D^{25} 1.5248, and 1.68 g. of acid-soluble pot residue.

The ether-insoluble salts mentioned above were triturated with 250 ml. of hot acetonitrile and filtered. Dilution of the filtrate with ether precipitated 19.5 g. (59%) of recovered 2-chlorobenzyltrimethylammonium chloride (Id), m.p. 204–206°, mixed m.p. 205–207°.

Recovery of 92–93% of the starting material was observed with 1–2 equivalents of amide ion within 45 min.

(B) *With potassium amide in ether.* To a solution of 0.20 mole of potassium amide in liquid ammonia[29] was added rapidly 55 g. (0.2 mole) of 2-chlorobenzyltrimethylammonium chloride (Id). After 10 min., 400 ml. of dry ether was added, the ammonia being allowed to evaporate while the mixture was stirred for 22 hr. Hydrolysis was carried out carefully with 100 ml. of water, then 250 ml. of 2*N* hydrochloric acid. The layers were separated, and the aqueous phase was carefully made strongly basic by the addition of solid sodium hydroxide. Ice was added and the mixture extracted with three 100-ml. portions of ether. The ether solution was dried over magnesium sulfate and the solvent evaporated. The residue was distilled to give 14.82 g. of a fraction boiling at 105–109° at 10.1 mm. and 5.04 g. of undistillable tar. Redistillation of the distillable fraction yielded 13.36 g. (37%) of 3-chloro-2-methylbenzyldimethylamine (IId), b.p. 105.5–108° at 10 mm., n_D^{25} 1.5246.

Anal. Calcd. for $C_{10}H_{14}ClN$: C, 65.40; H, 7.68; N, 7.63. Found: C, 65.52; H, 7.63· N, 7.66.

The picrate, recrystallized three times from 95% ethanol, melted at 140–140.5°.

Anal. Calcd. for $C_{16}H_{17}ClN_4O_7$: C, 46.56; H, 4.14; N, 13.56. Found: C, 46.49; H, 4.04; N, 13.57.

Almost the same yield (33%) of amine IId was obtained when quaternary ion Id was treated with two equivalents of potassium amide in ether for 24 hr. However, more basic tar was obtained.

Mild oxidation of 2.0 g. of amine IId as described for IIc gave 1.0 g. (53%) of 3-chloro-2-methylbenzoic acid, m.p., 157.5–158.5°, lit.,[30] m.p. 159°.

Further oxidation of a 0.2 g. sample of the above monoacid was effected with 0.39 g. of potassium permanganate to give 0.20 g. of 3-chlorophthalic acid, m.p. 182–184°, lit.,[31] m.p. 186°.

A small sample of the acid was boiled in a test tube, yielding 3-chlorophthalic anhydride, m.p. 120–121.5°, lit.,[31] m.p. 122°.

3-Chloro-2-methylbenzyltrimethylammonium iodide (IIId). This quaternary salt was prepared from 17.8 g. (0.097 mole) of 3-chloro-2-methylbenzyldimethylamine (IId) and 28.4 g. (0.200 mole) of methyl iodide. Yield, 31.3 g. (99%), m.p. 223.5–225.5° dec. After two recrystallizations from a mixture of acetone and ethanol the yield was 25.4 g. (84%), melting at a constant 238–238.5° dec.

Anal. Calcd. for $C_{11}H_{17}ClIN$: C, 40.57; H, 5.27; N, 4.31. Found: C, 40.76; H, 5.01; N, 4.30.

Rearrangement of quaternary salt IIId *to amine* IVd. To 26.4 g. (0.081 mole) of 3-chloro-2-methylbenzyltrimethylammonium iodide (IIId) in 300 ml. of liquid ammonia was added over a 10-min. period a suspension of 0.085 mole of sodium amide in 200 ml. of liquid ammonia (inverse addition). After 2.5 hr. the reaction mixture was neutralized with 4.56 g. (0.085 mole) of solid ammonium chloride and the ammonia replaced by ether. The product was worked up by the usual procedure, employing acid extraction.

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(28) W. Bentley, R. Robinson, and C. Weizmann, *J. Chem. Soc.*, 91, 110 (1907).

(29) See C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, 81, 1160, (1959).

(30) E. Noelting, *Ber.*, **37**, 1025 (1904).

(31) M. T. Bogert and L. Boroschek, *J. Am. Chem. Soc.*, **23**, 751 (1901).

The neutral fraction consisted of 5.0 g. of a light yellow amorphous solid.

The viscous amine fraction (1.5 g.) was distilled to give 0.32 g. (2%) of 4-chloro-2,3-dimethylbenzyldimethylamine (IVd), b.p. 126–127° at 10 mm., n_D^{25} 1.5309.

Anal. Calcd. for $C_{11}H_{16}ClN$: C, 66.82; H, 8.16; N, 7.09. Found: C, 67.04; H, 8.27; N, 7.25.

The methiodide, prepared in acetonitrile from a few drops of the amine and excess methyl iodide, melted at 235–235.5° after one recrystallization from a mixture of ethanol and hexane.

Anal. Calcd. for $C_{12}H_{19}ClIN$: C, 42.44; H, 5.63; N, 4.13. Found: C, 42.24; H, 5.47; N, 3.97.

The crude ether-insoluble salts were triturated in 150 ml. of water, and the insoluble portion was collected on a filter. After one recrystallization from ethanol 3.5 g. (14%) of the starting quaternary iodide IIId was recovered, m.p. 233–234°, mixed m.p. 238–238.5°.

Oxidation of 0.18 g. of amine IVd was effected with 0.49 g. of potassium permanganate added in four portions to the amine in 20 ml. of 0.5*N* sodium hydroxide solution. After filtration the solution was acidified, and the product was collected and recrystallized once from aqueous ethanol. A yield of 0.08 g. (49%) was obtained of 4-methoxy-2,3-dimethylbenzoic acid, m.p. 180–182°. Another recrystallization from ethanol and hexane raised the melting point to 183°.

Anal. Calcd. for $C_9H_9ClO_2$: C, 58.56; H, 4.82. Found: C, 58.73; H, 5.03.

4-Methylbenzyltrimethylammonium bromide (Xa). This salt was prepared from 55.5 g. (0.3 mole) of α-bromo-*p*-xylene (b.p. 105–106° at 20 mm.) as described for salt Ic. The yield was 74 g. (99%), m.p. 196–197°, reported m.p. 194°.[32]

Rearrangement of Xa *to form amine* XIa. This reaction was carried out with 24.4 g. (0.1 mole) of 4-methylbenzyltrimethylammonium bromide (Xa) and 0.2 mole of sodium amide in 300 ml. of liquid ammonia essentially as described for Ic. The addition period was 45 min., and the reaction was allowed to run for an additional 45 min. The initial deep red-violet color persisted throughout the reaction period.

The neutral fraction, 4.0 g. of yellow fluorescent solid, was recrystallized from 95% ethanol, yielding 1.0 g. (10%) of 4,4′-dimethylstilbene, m.p. 171–173°, lit.,[33] m.p. 178°. An additional recrystallization from 95% ethanol raised its melting point to 174–175°. It was oxidized with 3N nitric acid (18 hr. refluxing) to *p*-toluic acid, m.p. 174–175°, reported m.p. 177°.[34] Admixture with an authentic sample gave a melting point of 176–176.5°.

Distillation of the basic products yielded 10.25 g. (63%) of 2,5-dimethylbenzyldimethylamine (XIa), b.p. 89.5–90.7° at 11 mm., n_D^{25} 1.5044, and less than 1 g. of residue.

Anal. Calcd. for $C_{11}H_{17}N$: C, 80.92; H, 10.50; N, 8.58. Found: C, 80.89; H, 10.35; N, 8.57.

A picrate, after three recrystallizations from 95% ethanol, melted at 121.5–122°.

Anal. Calcd. for $C_{17}H_{20}N_4O_7$: C, 52.00; H, 5.14; N, 14.30. Found: C, 52.10; H, 4.94; N, 14.33.

Slightly lower yields of XIa (down to 53%) were obtained using a smaller volume of liquid ammonia.

Oxidation of a 2.0 g. sample of amine XIa was effected with 6.0 g. of potassium permanganate in 100 ml. of 0.5*N* sodium hydroxide solution. After recrystallization of the product once from aqueous ethanol a yield of 1.0 g. (54%) of 2,5-dimethylbenzoic acid was obtained, m.p. 129–130°, lit.,[35] m.p. 132°. Admixture with an authentic sample gave a melting point of 131.5–132°.

Vigorous oxidation of amine XIa *to trimellitic acid and conversion to its anhydride.* A 2.0 g. sample of amine XIa and 20 g. of potassium permanganate were added to 100 ml. of 0.1*N* sodium hydroxide solution and the mixture was refluxed for 17 hr. The manganese dioxide was removed by filtration through a mat of Hyflo Supercel. The resulting clear filtrate was made strongly acidic with hydrochloric acid and saturated with sodium sulfate. The product was extracted with three 100-ml. portions of ether, which were combined, dried, and evaporated. A yield of 1.9 g. (74%) of crude trimellitic acid, m.p. 217–218°, was obtained. One recrystallization from a mixture of benzene and methanol raised the melting point to 228°, lit.,[36] m.p. 224–225°.

A small portion of the product was boiled in a test tube, producing trimellitic anhydride, m.p. 159–160°, lit.,[37,38] m.p. 162.5–163.5°, 157–158°.

2,5-Dimethylbenzyltrimethylammonium iodide (XIIa). This salt was obtained in 99% yield from 26.08 g. (0.16 mole) of 2,5-dimethylbenzyldimethylamine (XIa) and 43 g. (0.30 mole) of methyl iodide as described for IIIc. The melting point was 250° (darkened at 245°) and was not changed by recrystallization from acetonitrile.

Anal. Calcd. for $C_{12}H_{20}IN$: C, 47.25; H, 6.56; N, 4.59. Found: C, 47.28; H, 6.74; N, 4.79.

Rearrangement of XIIa *to form amine* XIIIa. This rearrangement was carried out with 45.75 g. (0.15 mole) of 2,5-dimethylbenzyltrimethylammonium iodide (XIIa) and 0.30 mole of sodium amide in 750 ml. of liquid ammonia essentially as described for Ic. The addition period was 45 min., and the reaction was allowed to proceed for an additional 1.75 hr. Distillation of the crude products[26] yielded 22.17 g. (84%) of 2,3,6-trimethylbenzyldimethylamine (XIIIa), b.p. 108–110.5° at 10 mm., n_D^{25} 1.5160, and 1.22 g. of amine residue.

Anal. Calcd. for $C_{12}H_{19}N$: C, 81.30; H, 10.80; N, 7.90. Found: C, 81.50; H, 10.94; N, 7.90.

2,3,6-Trimethylbenzyltrimethylammonium iodide. This salt was obtained in 93% yield from 10.62 g. (0.06 mole) of 2,3,6-trimethylbenzyldimethylamine (XIIIa) and 14.2 g. (0.10 mole) of methyl iodide as described for IIIc. The melting point was 194° dec.

Anal. Calcd. for $C_{13}H_{22}IN$: C, 48.91; H, 6.95; N, 4.39. Found: C, 48.78; H, 6.98; N, 4.40.

Emde reduction to form prehnitene. The *Org. Syntheses* procedure used for the preparation of hemimellitene[19] was employed, using 15.95 g. (0.05 mole) of 2,3,6-trimethylbenzyltrimethylammonium iodide and 210 g. of 5% sodium amalgam. The product was isolated in this case by steam distillation and extraction of the steam distillate with ether. Distillation of the dried ether extracts yielded 5.02 g. (75%) of prehnitene, b.p. 95–97° at 25 mm., n_D^{25} 1.5185, reported b.p. 97–98° at 25 mm., n_D^{25} 1.5183.[39] The infrared spectrum was identical with that of an authentic sample.

4-Isopropylbenzyltrimethylammonium bromide (Xb). 4-Isopropylbenzyl alcohol (60 g., 0.4 mole) was treated with 54.2 g. (0.2 mole) of phosphorus tribromide essentially as described in the preparation of Ic. The reaction period was only 1 hr. Distillation of the product yielded 71.2 g. (84%) of *p*-isopropylbenzyl bromide, b.p. 118–120° at 14 mm., lit.,[40] b.p. 108–109° at 14 mm.

This bromide (71.0 g., 0.33 mole) was treated with 40 g. (60 ml., 0.67 mole) of liquid trimethylamine as described for Ic. The salt was difficult to crystallize upon addition of the ether, presumably because of its extremely hygroscopic character. It was handled in a dry box. A yield of 81.4 g.

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(32) J. von Braun and H. Engel, *Ann.*, **436**, 299 (1924).

(33) E. Spath, *Monatsh.*, **35**, 470 (1914).

(34) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 279.

(35) R. L. Shriner, R. C. Fuson, and D. T. Curtin, *The Systematic Identification of Organic Compounds*, 4th ed., John Wiley and Sons, Inc., New York, N. Y., 1956.

(36) A. Baeyer and V. Villiger, *Ber.*, **32**, 2445 (1899).

(37) W. Schultze, *Ann.*, **359**, 143 (1908).

(38) A. Baeyer, *Ann.*, **166**, 341 (1873).

(39) C. R. Hauser and D. N. Van Eenam, *J. Org. Chem.*, **23**, 865 (1958).

(40) J. W. Baker and W. S. Nathan, *J. Chem. Soc.*, **1935**, 1844.

(90%) of 4-isopropylbenzyltrimethylammonium bromide (Xb) was thus obtained, m.p. 139–140° (softening at 125°).

Anal. Calcd. for $C_{13}H_{22}BrN$: C, 57.35; H, 8.15; N, 5.15. Found: C, 57.53; H, 8.35; N, 5.16.

Rearrangement of Xb *to form amine* XIb. The rearrangement was effected during 1.5 hr. with 27.2 g. (0.1 mole) of 4-isopropylbenzyltrimethylammonium bromide (Xb) and 0.2 mole of sodium amide in 300 ml. of liquid ammonia essentially as described for Ic.[26] Distillation yielded 17.46 g. (92%) of 5-isopropyl-2-methylbenzyldimethylamine (XIb), b.p. 108–111.5° at 10 mm., $n_{\rm D}^{25}$ 1.4989.

Anal. Calcd. for $C_{13}H_{21}N$: C, 81.61; H, 11.06; N, 7.32. Found: C, 81.82; H, 11.03; N, 7.23.

Independent synthesis of amine XIb. (A) *Dimethylaminomethyl isobutyl ether.* This compound was prepared in 25% yield by the directions of Robinson and Robinson.[15] Its boiling point was 129.5–131.5°, reported b.p. 124–126°.

(B) *Reaction with 2-p-cymyl magnesium bromide.* The reaction was carried out with 25.6 g. (0.12 mole) of 2-bromo-*p*-cymene, 3.49 g. (0.16 g. atom) of magnesium turnings, and 10.5 g. (0.08 mole) of the above dimethylaminomethyl isobutyl ether according to the general procedure of Stewart and Hauser[41] for the addition of Grignard reagents to α-amino ethers. A yield of 9.74 g. (64%) of 5-isopropyl-2-methylbenzyldimethylamine b.p. 108–111° at 10 mm., $n_{\rm D}^{25}$ 1.4975, was obtained. Redistillation of the product yielded 7.70 g. (50%), b.p. 108–109.5° at 9.8 mm., $n_{\rm D}^{25}$ 1.4978. An infrared spectrum was identical with that of amine XIb.

A methiodide, prepared from the above amine and methyl iodide, melted at 190–191° dec. Admixture with a sample of methiodide XIIb produced no depression of the melting point.

5-Isopropyl-2-methylbenzyltrimethylammonium iodide (XIIb). This quaternary salt was obtained in 98% yield from 21.01 g. (0.11 mole) of 5-isopropyl-2-methylbenzyldimethylamine (XIb) and 22.72 g. (0.16 mole) of methyl iodide as described for IIIa. The melting point was 190–191° dec.

Anal. Calcd. for $C_{14}H_{24}IN$: C, 50.45; H, 7.25; N, 4.20. Found: C, 50.51; H, 7.25; N, 4.38.

Rearrangement of XIIb *to form amine* XIIIb. This reaction was effected with 33.3 g. (0.1 mole) of 5-isopropyl-2-methylbenzyltrimethylammonium iodide (XIIb) and 0.2 mole of sodium amide in 300 ml. of liquid ammonia essentially as described for Ia. The initial deep blue color changed rapidly to violet, which persisted.

The neutral fraction, 1.9 g. of dark liquid, yielded no distillable material.

The basic products were distilled in two fractions: 12.90 g., b.p. 121–124° at 9 mm., $n_{\rm D}^{25}$ 1.5090; 0.90 g., b.p. 124–126° at 9 mm., $n_{\rm D}^{25}$ 1.5098; 1.73 g. of residue left in the pot. The two distillable fractions were combined as 2,3-dimethyl-6-isopropylbenzyldimethylamine (XIIIb), 13.80 g. (68%); the analytical sample was taken from the first fraction.

Anal. Calcd. for $C_{14}H_{23}N$: C, 80.76; H, 11.99; N, 7.25. Found: C, 81.02; H, 11.79; N, 7.07.

The picrate, after two recrystallizations from 95% ethanol, melted at 152.0–152.5°.

Anal. Calcd. for $C_{20}H_{26}N_4O_7$: C, 55.29; H, 6.03; N, 12.90. Found: C, 55.40; H, 6.26; N, 13.10.

2,3-Dimethyl-6-isopropylbenzyltrimethylammonium iodide. This salt was prepared in 99% yield from 6.30 g. (0.0307 mole) of 2,3-dimethyl-6-isopropylbenzyldimethylamine (XIIIb) and 8.52 g. (0.06 mole) of methyl iodide as described for IIIc. Its melting point was 169–169.5° dec.

Anal. Calcd. for $C_{15}H_{26}IN$: C, 51.84; H, 7.55; N, 4.03. Found: C, 51.60; H, 7.78; N, 4.13.

Emde reduction to form 2,3,4-trimethylisopropylbenzene. This reduction was carried out with 10.00 g. (0.0288 mole) of 2,3-dimethyl-6-isopropylbenzyltrimethylammonium iodide and 120 g. of 5% sodium amalgam essentially in accordance with the *Org. Syntheses* procedure for the preparation of hemimellitene.[19] The product was steam distilled from the reaction mixture and extracted with ether from the steam distillate. The dried ether extractions were distilled yielding 3.08 g. (66%) of 2,3,4-trimethylisopropylbenzene, b.p. 95–98° at 8.3–8.6 mm., $n_{\rm D}^{25}$ 1.5127. Its infrared spectrum was very similar to that of 1,2,3,4-tetramethylbenzene (prehnitene).

Anal. Calcd. for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 88.63; H, 11.16.

4-Methoxybenzyltrimethylammonium bromide (Xc). Anisyl alcohol (69.0 g., 0.5 mole) was treated with 68 g. (0.25 mole) of phosphorus tribromide as described for Ia. The reaction period was 1 hr. A yield of 87.3 g. (87%) of 4-methoxybenzyl bromide, b.p. 124–126° at 12 mm., lit.,[24] b.p. 126° at 12 mm., was obtained.

The halide (89 g., 0.44 mole) was treated with excess trimethylamine in acetonitrile as described for Ic. A yield of 110 g. (96%) of 4-methoxybenzyltrimethylammonium bromide (Xc), m.p. 148.5–149°, reported m.p. 146°,[42] was obtained.

Rearrangement of Xc *to form amine* XIc. To a suspension of 0.20 mole of sodium amide in 250 ml. of liquid ammonia was added over a 30-sec. period a solution of 26.0 g. (0.10 mole) of 4-methoxybenzyltrimethylammonium bromide (Xc) in 150 ml. of liquid ammonia. No color change was observed. At the end of 5.0 min. a solution of 10.7 g. (0.20 mole) of ammonium chloride in liquid ammonia was added rapidly. The ammonia was replaced by ether and the inorganic salts removed by filtration. Distillation yielded 16.53 g. (93%) of 5-methoxy-2-methylbenzyldimethylamine (XIc), b.p. 106–108.5° at 7.3 mm., $n_{\rm D}^{25}$ 1.5133.

Anal. Calcd. for $C_{11}H_{17}NO$: C, 73.74; H, 9.49; N, 7.83. Found: C, 73.58; H, 9.43; N, 7.90.

The picrate, after two recrystallizations from ethanol, melted at 129–129.5°.

Anal. Calcd. for $C_{17}H_{22}N_4O_8$: C, 50.00; H, 4.94; N, 13.72. Found: C, 50.28; H, 5.14; N, 13.49.

Oxidation of a 1.0 g. sample of XIc with 3.0 g. of potassium permanganate in 50 ml. of 0.5*N* sodium hydroxide solution yielded, after one recrystallization from aqueous ethanol, 0.77 g. (83%) of 5-methoxy-2-methylbenzoic acid, m.p. m.p. 146°, lit.,[43] m.p. 146°.

Further oxidation of a 0.2 g. sample of the above monoacid was accomplished with 0.38 g. of potassium permanganate in the usual manner. There was obtained 0.14 g. of 4-methoxyphthalic acid, m.p. 168.5–169.5°. One recrystallization from a mixture of ethanol and hexane raised the melting point to 169–170°, lit.,[44] m.p. 170°.

A small sample of the above diacid was boiled in a test tube, producing 4-methoxyphthalic anhydride, m.p. 93.5–94°, lit.,[45] m.p. 93°.

5-Methoxy-2-methylbenzyltrimethylammonium iodide (XIIc). This salt was prepared in 99% yield from 15.43 g. (0.086 mole) of 5-methoxy-2-methylbenzyldimethylamine (XIc) and excess methyl iodide as described for IIIc. The melting point was 166–167°.

Anal. Calcd. for $C_{12}H_{20}INO$: C, 44.73; H, 6.25; N, 4.35. Found: C, 44.50; H, 6.34; N, 4.34.

Rearrangement of XIIc *to form amine* XIIIc. The reaction was effected with 27.0 g. (0.0844 mole) of 5-methoxy-2-methylbenzyldimethylamine (XIIc) and 0.10 mole of sodium amide in 300 ml. of liquid ammonia essentially as described for Ia. The initial maroon color did not fade.

Only 0.1 g. of neutral material was obtained.

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[41] A. T. Stewart, Jr., and C. R. Hauser, *J. Am. Chem. Soc.*, **77**, 1098 (1955).

[42] J. von Braun, W. May, and R. Michaelis, *Ann.*, **490**, 189 (1931).

[43] O. Jacobsen, *Ber.*, **16**, 1964 (1883).

[44] M. Freund and E. Gobel, *Ber.*, **30**, 1392 (1897).

[45] C. Schall, *Ber.*, **12**, 829 (1879).

Distillation of the amine fraction yielded 12.63 g. (78%) of 2,3-dimethyl-6-methoxybenzyldimethylamine (XIIIc), b.p. 121–123° at 9.5 mm., n_D^{25} 1.5178.

Anal. Calcd. for $C_{12}H_{19}NO$: C, 74.57; H, 9.91; N, 7.25. Found: C, 74.93; H, 9.89; N, 7.56.

The methiodide was prepared from 2.0 g. of amine XIIIc and excess methyl iodide in acetonitrile. When the product was precipitated gradually by the slow addition of anhydrous ether to the hot solution, a yield of 3.38 g. (98%) of 2,3-dimethyl-6-methoxybenzyltrimethylammonium iodide, m.p. 167.5–168°, was obtained.

Anal. Calcd. for $C_{13}H_{22}INO$: C, 46.58; H, 6.62; N, 4.18. Found: C, 46.82; H, 6.48; N, 4.04.

Mild oxidation of a 2.0 g. sample of amine XIIIc was effected with 5.5 g. of potassium permanganate by the usual procedure. After one recrystallization from aqueous ethanol, 0.48 g. (25%) of 2,3-dimethyl-6-methoxybenzoic acid, m.p. 154.5–156°, was obtained. A second recrystallization from ethanol and hexane raised the melting point to 156.5–158°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.77; H, 6.79.

4-Chlorobenzyltrimethylammonium iodide (Xd). 4-Chlorobenzyl chloride (48.3 g., 0.3 mole) was treated with excess trimethylamine as described for Ic. A yield of 63 g. (96%) of 4-chlorobenzyltrimethylammonium chloride, m.p. 195–197°, was obtained. One recrystallization from acetonitrile and ether raised the melting point to 201.5–202°. This salt was extremely hygroscopic, so it was converted to its iodide.

The above chloride (17.5 g., 0.0795 mole) was dissolved in a minimum amount of hot acetonitrile. A solution of 11.9 g. (0.0795 mole) of sodium iodide in 300 ml. of hot acetonitrile was added gradually with stirring. The mixture was heated to boiling and filtered while hot. Anhydrous ether (1000 ml.) was added to the cooled filtrate, and the quaternary iodide was collected on a filter. A yield of 19.3 g. (78%) of 4-chlorobenzyltrimethylammonium iodide (Xd), m.p. 249.5–250°, was obtained.

Anal. Calcd. for $C_{10}H_{15}ClIN$: C, 38.54; H, 4.84; N, 4.49. Found: C, 38.61; H, 4.85; N, 4.51.

Rearrangement of Xd *to form amine* XId. This reaction was effected with 21.8 g. (0.070 mole) of 4-chlorobenzyltrimethylammonium iodide (Xd) and 0.074 mole of sodium amide as described for IIId (inverse addition). The yield was 7.65 g. (60%) of 5-chloro-2-methylbenzyldimethylamine (XId), b.p. 102–105° at 9.7 mm., n_D^{25} 1.5219. Most of the product (7.45 g., 58%) boiled at 104–105° at 9.7 mm.

Anal. Calcd. for $C_{10}H_{14}ClN$: C, 65.39; H, 7.68; N, 7.63; Cl, 19.30. Found: C, 65.61; H, 7.74; N, 7.60; Cl, 19.48.

Oxidation of a 2.0 g. sample of amine XId was accomplished by the usual procedure with 6.0 g. of potassium permanganate. After one recrystallization from aqueous ethanol a yield of 1.25 g. (67%) of 5-chloro-2-methylbenzoic acid, m.p. 165.5–166.5°, lit.,[46] m.p. 168.5–169.5°, was obtained.

Further oxidation of a 0.2 g. sample of the above monoacid was effected in the usual manner with 0.39 g. of potassium permanganate. A yield of 0.18 g. of residue was left from the ether extractions. After a washing with benzene the 4-chlorophthalic acid melted at 152–153°, lit.,[47] m.p. 150.0–150.5°.

A small sample of the above diacid was boiled in a test tube, producing 4-chlorophthalic anhydride, m.p. 94.5–95.5°, lit.,[44] m.p. 98.5°.

5-Chloro-2-methylbenzyltrimethylammonium iodide (XIId). This salt was prepared in 99% yield from 18.39 g. (0.10 mole) of 5-chloro-2-methylbenzyldimethylamine (XId) and 28.4 g. (0.2 mole) of methyl iodide essentially as described for IIIc. The melting point was 226° dec.

Anal. Calcd. for $C_{11}H_{17}ClIN$: C, 40.57; H, 5.27; N, 4.31. Found: C, 40.64; H, 5.54; N, 4.55.

Rearrangement of XIId *to form amine* XIIId. This rearrangement was carried out with 32 g. (0.0985 mole) of 5-chloro-2-methylbenzyltrimethylammonia iodide (XIId) and 0.105 mole of sodium amide as described for the rearrangement of IIId. The reaction period was 6 hr., the green color of the anion persisting throughout.

The neutral fraction contained 4.0 g. of light yellow amorphous material.

The amine fraction yielded 1.51 g. (8%) of 6-chloro-2,3-dimethyl benzyldimethylamine (XIIId), b.p. 119–121° at 11 mm., n_D^{25} 1.5290.

Anal. Calcd. for $C_{11}H_{16}ClN$: C, 66.82; H, 8.16; N, 7.09. Found: C, 66.92; H, 8.30; N, 7.29.

A picrate, recrystallized once from 95% ethanol, melted at 176–177°.

Anal. Calcd. for $C_{17}H_{19}ClN_4O_7$: C, 47.81; H, 4.49; N, 13.12. Found: C, 47.92; H, 4.70; N, 13.07.

The ether-insoluble salts exhibited an infrared spectrum identical with that of the starting quaternary salt with two additional bands characteristic of the ammonium chloride known to be present. When this mixture was triturated with acetonitrile, filtered, and treated with excess ether, a precipitate of 18.3 g. (57%) of recovered 5-chloro-2-methylbenzyltrimethylammonium iodide (XIId), m.p. 216–218° dec., was obtained. Admixture with an authentic sample produced no depression of the melting point.

Mild oxidation of a 1.0 g. sample of amine XIIId with 2.5 g. of potassium permanganate by the usual procedure yielded after one recrystallization from aqueous ethanol 0.15 g. (16%) of 6-chloro-2,3-dimethylbenzoic acid, m.p. 144.5–145°.

Anal. Calcd. for $C_9H_9ClO_2$: C, 58.56; H, 4.82. Found: C, 58.43; H, 4.82.

4-Cyanobenzyltrimethylammonium bromide (Xe). 4-Cyanobenzyl bromide[48] (49 g., 0.25 mole) was treated with excess liquid trimethylamine as described for Ia. The yield was 62.0 g. (97%) of 4-cyanobenzyltrimethylammonium bromide (Xe), m.p. 235–235.5°.

Anal. Calcd. for $C_{11}H_{15}BrN_2$: C, 51.77; H, 5.92; N, 10.98. Found: C, 51.76; H, 5.91; N, 10.89.

Treatment of Xe *with sodium amide in liquid ammonia.* 4-Cyanobenzyltrimethylammonium bromide (Xe) (30.2 g., 0.10 mole) was added quickly to a suspension of 0.102 mole of sodium amide in 300 ml. of liquid ammonia. Throughout the 3-hr. reaction period the color remained a bright pea-green. After neutralization with 5.4 g. (0.102 mole) of ammonium chloride, the ammonia was replaced by ether. The mixture was filtered. No residue remained upon evaporation of the filtrate.

The ether-insoluble material was extracted with acetonitrile in a Soxhlet extractor. Upon treatment of the extract with a large excess of ether, 28 g. (93%) of recovered 4-cyanobenzyltrimethylammonium bromide (Xe), m.p. 229–231°, was obtained. Admixture with an authentic sample produced no depression of the melting point.

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(46) K. von Auwers and L. Harres, *Z. physik. Chem.*, [A], **143,** 16 (1929).

(47) W. Miersch, *Ber.*, **25,** 2116 (1892).

(48) Fa-Ki Tcheou, Yu-Tsun Shih, and Kwan-Liang Lee, *J. Chinese Chem. Soc.*, **17,** 150 (1950); *Chem. Abstr.*, **47,** 3254^g (1953).