sodium-dried benzene for 0.5 hr. The solution was cooled and chloroacetanilide (4.25 g.; 0.025 mole) was added and the mixture heated under reflux for 1.25 hr. The mixture was then cooled and a solution of aniline (2.33 g., 0.025 mole) in benzene (10 ml.) was added. The mixture was refluxed for 1 hr. longer and then volatile solvents were removed at 50 mm. pressure; to the residue was added 50 ml. of additional benzene and evaporated once more to dryness at 50 mm. The dark residue was dissolved in cold absolute ethanol (75 ml.) and the solution cooled to 0°. Ice-cold 10% sodium hydroxide was added until the solution was strongly basic. The *amidine* could be induced to crystallize on scratching and then ice-cold water was added in small portions until all the amidine had precipitated (the final volume was then 225 ml.). The product was filtered and dried *in vacuo*. The *amidine* was purified by continuous extraction with petroleum ether (b.p. 30–60°). (Soxhlet apparatus). The yield was 2.37 g. (39%) m.p. 84–85°. Recrystallization from petroleum ether (b.p. 30–60°) and on cooling to −10° afforded the *amidine* as yellow plates, m.p. 86–88°.

Anal. Calcd. for $C_{14}H_{13}ClN_2$ (244.7): C, 68.71; H, 5.36; N, 11.44. Found: C, 68.63; H, 5.37; N, 11.48.

N,N′-Di(*p*-methoxyphenyl)chloroacetamidine, m.p. 78–80°, was synthesized in 43% yield from chloroaceto-*p*-anisidide by the above method.

Anal. Calcd. for $C_{16}H_{17}ClN_2O_2$ (304.8): C, 63.05; H, 5.62; N, 9.19. Found: C, 63.28; H, 5.59; N, 9.34.

N,N′-Di(*p*-ethoxyphenyl)chloroacetamidine was prepared from chloroacet-*p*-phenetidide as above in 48% yield. It melted at 81°, lit.,[14] m.p. 83°.

N,N′-Di(*p*-bromophenyl)chloroacetamidine was prepared in 10% yield, m.p. 131–133°.

Anal. Calcd. for $C_{14}H_{11}Br_2ClN_2$ (402.5): C, 41.77; H, 2.75; N, 6.96. Found: C, 41.87; H, 2.96; N, 7.06.

N,N′-Diphenyl-α-(acetylmercapto)acetamidine.—To suspension of sodium hydride (1.5 g.) in tetrahydrofuran (150 ml.) was added thiolacetic acid (2.28 g.; 0.03 mole). After the evolution of hydrogen had ceased, to mark the end of the formation of the sodium salt, a solution of N,N′-diphenylchloroacetamidine (7.35 g., 0.03 mole) in tetrahydrofuran (20 ml.) was added. The mixture was refluxed for 3 hr. and filtered while hot. The filtrate was evaporated *in vacuo* and the residue recrystallized from cyclohexane, filtered, and dried. It weighed 5.50 g. and represents a 73% yield, m.p. 115–117°. Recrystallization from cyclohexane raised the m.p. to 120–122°.

Anal. Calcd. for $C_{16}H_{16}N_2OS$ (284.4): C, 67.57; H, 5.67; N, 9.85; S, 11.28. Found: C, 67.57; H, 5.69; N, 10.00; S, 11.37.

Similarly, N,N′-Di(*p*-methoxyphenyl)chloroacetamidine formed the *thiol ester* in 75% yield, m.p. 138–139°.

Calcd. for $C_{18}H_{20}N_2O_3S$: C, 62.77; H, 5.85; N, 8.13; S, 9.31. Found: C, 62.79; H, 6.01; H, 8.25; S, 9.19.

N,N′-Di(*p*-ethoxyphenyl)chloroacetamidine was converted to the thiol ester in 54% yield, m.p. 112–114° and was crystallized from cyclohexane.

Anal. Calcd. for $C_{20}H_{24}N_2O_3S$ (372.5): C, 64.49; H, 6.50; N, 7.52. Found: C, 64.45; H, 6.49; N, 7.62.

S-[α-(Carboxamidino)ethyl]isothiourea Dihydrochloride, VII.—A suspension of thiourea (3.4 g., 0.05 mole) and α-chloropropionamidine hydrochloride (7.15 g., 0.05 mole) in tetrahydrofuran (50 ml.) was boiled under reflux for 48 hr. The solid was filtered off, m.p. 230–235° (with decomp.). Recrystallization from absolute methanol did not materially effect the m.p., 232–235° (with decomp.). The yield was almost quantitative.

Anal. Calcd. for $C_4H_{12}N_4Cl_2S$ (219.1): C, 21.92; H, 5.52; N, 25.57; S, 14.63. Found: C, 21.69; H, 5.45; N, 25.66; S, 14.71.

Acknowledgement.—The authors would like to thank Mr. Richard Egan for his fine technical assistance in this work, during the summers of 1961 and 1962.

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[14] H. P. Kaufmann, *et al.*, *Ber.*, **75**, 1585 (1942).

Ortho Substitution–Rearrangement of 2-(α-Hydroxybenzyl)benzyltrimethylammonium Ion and a Related Quaternary Ion–Alcohol by Excess Potassium Amide[1]

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In contrast to the 2-benzylbenzyltrimethylammonium ion which undergoes an elimination reaction to form polymeric hydrocarbon material, the 2-(α-hydroxybenzyl)benzyltrimethylammonium ion exhibits the *ortho* substitution–rearrangement with excess potassium amide in liquid ammonia. The success of this rearrangement appears to be dependent on deactivation of the benzylic hydrogen of the 2-α-hydroxybenzyl group by the negative charge on the adjacent oxygen atom in anion intermediates. The resulting 2-methyl-3-dimethylaminomethylbenzhydrol was obtained in yields of 60–79%. Besides this rearranged amino alcohol small amounts of the cleavage products, benzaldehyde and 2-methylbenzyldimethylamine, were isolated. Similarly the 2-(α-hydroxy-α-phenylbenzyl)benzyltrimethylammonium ion afforded 2-methyl-3-dimethylaminomethyltriphenylcarbinol in 75% yield.

It has previously been shown that the benzyltrimethylammonium ion[3] and a number of 2-, 3-, and 4-substituted benzyltrimethylammonium ions[4,5] undergo the *ortho* substitution–rearrangement with sodium amide or potassium amide in liquid ammonia. For example, the 2-ethyl quaternary ion I exhibits this type of rearrangement to form tertiary amine II in 90% yield.[4]

However, the 2- and 4-benzylbenzyltrimethylammonium ions, which have relatively active benzyl hydrogens in the 2- and 4-benzyl groups

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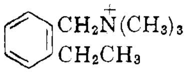
[1] Supported in part by the National Institutes of Health Grant No. CA-04-455-04.

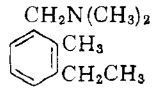
[2] National Science Foundation Fellow, 1961–1962.

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

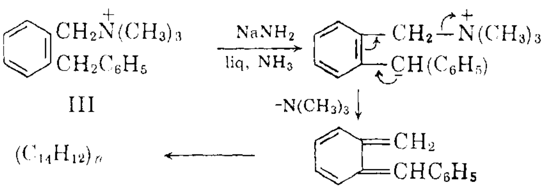
[4] C. R. Hauser and A. J. Weinheimer, *ibid.*, **76**, 1264 (1954).

[5] W. Q. Beard, Jr., and C. R. Hauser, *J. Org. Chem.*, **25**, 334 (1960).


I

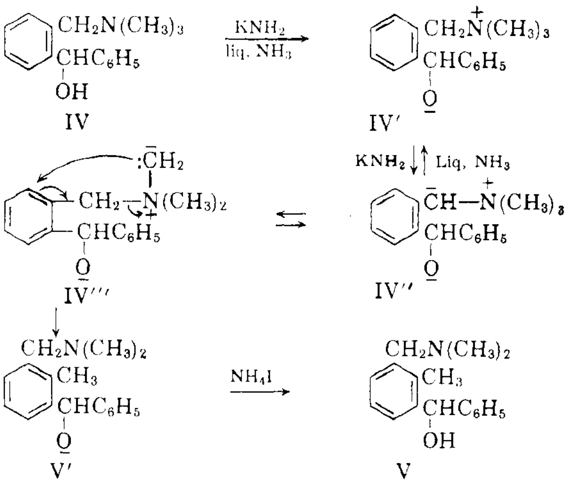

II

respectively, undergo exclusively an elimination reaction involving the aromatic ring to give polymeric hydrocarbon material.[6] The reaction of the former quaternary ion (III) is represented by Scheme A.



Scheme A

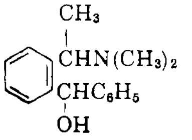
It has now been found that, in contrast to quaternary ion III, the related quaternary ion–alcohol IV exhibits the *ortho* substitution–rearrangement with two and three molecular equivalents of potassium amide in liquid ammonia to afford amino alcohol V in yields of 60 and 79%, respectively. Presumably monoanion IV′ and dianions IV″ and IV‴ are intermediates. Although dianion IV″ is probably formed initially, dianion IV‴ is regarded as the reactive intermediate (Scheme B).

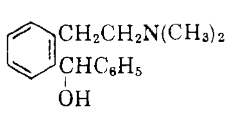


Scheme B

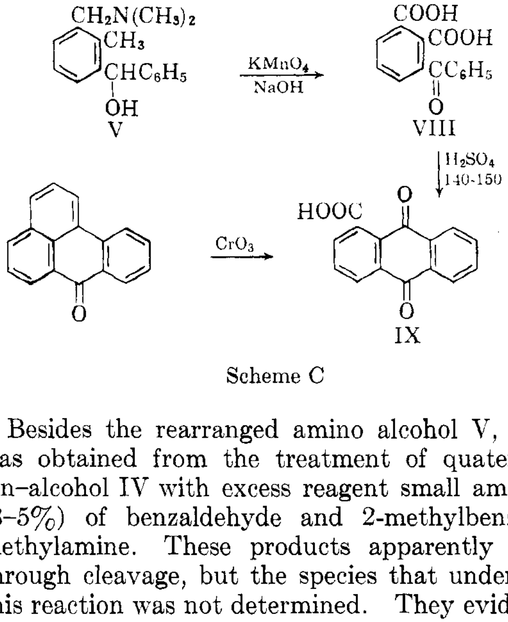
It was possible that, instead of V, an isomeric Stevens rearrangement product VI or VII might have been produced. These products would have arisen through a 1,2-shift of a methyl group within dianion IV″ or of the benzyl type group within dianion IV‴, respectively.

That the rearranged amino alcohol obtained was the *ortho* substitution product V, and not the Stevens product VI or VII, was supported by its infrared spectrum which showed bands at 850 cm.$^{-1}$ for the benzyldimethylamino group[5,7] and at 730 and 788 cm.$^{-1}$ for the three adjacent aromatic hydrogens.[8] The spectrum exhibited bands at 699 and 743 cm.$^{-1}$ for five adjacent aromatic hydrogens, but these hydrogens are present not only in V but also in VI and VII. The last two compounds also have four adjacent aromatic hydrogens, which should show a single band in the 770–735-cm.$^{-1}$ region.[8]


VI


VII

The structure of the product was confirmed as V by oxidation to form keto diacid VIII, which was cyclized by means of concentrated sulfuric acid[9] to give IX. The latter compound was independently synthesized by oxidation of benzanthrone[10] (Scheme C). No *o*-benzoylbenzoic acid, which would be expected from oxidation of either VI or VII, was found.



Scheme C

Besides the rearranged amino alcohol V, there was obtained from the treatment of quaternary ion–alcohol IV with excess reagent small amounts (3-5%) of benzaldehyde and 2-methylbenzyldimethylamine. These products apparently arose through cleavage, but the species that underwent this reaction was not determined. They evidently did not arise through cleavage of monoanion IV′ or V′, since these anions were found to be stable under similar conditions.

Incidentally none of cyclic ether X was found among the reaction products under any of the conditions employed. This ether has previously been

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(6) C. R. Hauser, W. Q. Beard, Jr., and F. N. Jones, *J. Org. Chem.*, **26**, 4790 (1961).

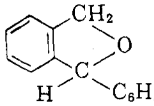
(7) We have observed that the infrared spectrum of α-methylbenzyldimethylamine, which is related to VI, shows a band at 825 cm.$^{-1}$. Benzyldimethylamine and various 2-, 3-, and 4-substituted benzyldimethylamines exhibit bands in the 837–850-cm.$^{-1}$ region (see ref. 5).

(8) See L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1958, p. 76–78.

(9) C. Graebe and M. Leonhardt, *Ann.*, **290**, 217 (1896).

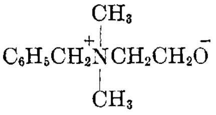
(10) A. G. Perkin, *J. Chem. Soc.*, **117**, 696 (1920).

obtained on heating the hydroxide of quaternary ion IV.[11]



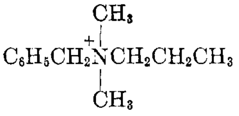
X

The success of the rearrangement of quaternary ion IV (Scheme B) appears to be dependent on the deactivation of the benzylic hydrogen of the 2-α-hydroxybenzyl group by the negative charge on the adjacent oxygen atom in intermediates IV′, IV″, and IV‴ (compare Scheme A). Indeed this was the basis for expecting at least some rearrangement of IV with excess reagent. A somewhat similar deactivation effect on the β-hydrogen of quaternary ion–alkoxide XI by the negatively charged oxygen atom has been observed recently.[12] Thus this quaternary ion–alkoxide underwent almost exclusively the *ortho* substitution–rearrangement with sodium amide in liquid ammonia, whereas quaternary ion XII, in which there is no such deactivation of the β-hydrogen, exhibited about as much elimination reaction as rearrangement with this reagent.[4]



$C_6H_5CH_2\overset{+}{N}(CH_3)_2CH_2CH_2\bar{O}$

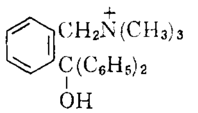
XI



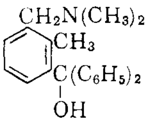
$C_6H_5CH_2\overset{+}{N}(CH_3)_2CH_2CH_2CH_3$

XII

Similarly quaternary ion–alcohol XIII underwent the *ortho* substitution–rearrangement with three molecular equivalents of potassium amide in liquid ammonia to form amino alcohol XIV in 75% yield. Presumably mono- and dianions corresponding to IV′, IV″, and IV‴ would be intermediates.

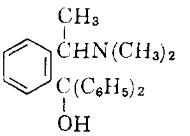


XIII

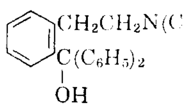


XIV

It was possible that, instead of XIV, the isomeric Stevens rearrangement product XV or XVI might have been produced. These products would have arisen through 1,2-shifts analogous to those mentioned above for the formations of VI and VII, respectively.



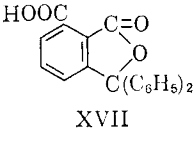
XV



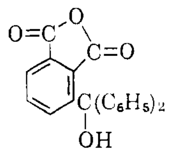
XVI

That the amino alcohol obtained had structure XIV, not XV or XVI, was supported by its infrared spectrum which showed bands at 847 cm.$^{-1}$ for the benzyldimethylamino group[5] and at 737 and 764 cm.$^{-1}$ apparently ascribable to the three adjacent aromatic hydrogens.[8]

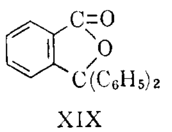
The structure of the amino alcohol was confirmed as XIV by oxidation to form a product, whose analysis fitted XVII or XVIII but not XIX, which might have been expected from either XV or XVI. Moreover, the oxidation product melted about 100° higher than XIX.[13]



XVII



XVIII



XIX

Since the oxidation product was recrystallized from ethanol–water, it seems more likely to be the acid lactone XVII than the anhydride carbinol XVIII. Structure XVII was supported by the infrared spectrum, which showed bands at 1752 cm.$^{-1}$ for a lactone carbonyl[14] and at 1710 cm.$^{-1}$ for a carboxyl carbonyl.[15] The spectrum also exhibited broad bands over the range 2500–3000 cm.$^{-1}$ with the main band near 3000 cm.$^{-1}$ and a smaller band at 2660 cm.$^{-1}$. These peaks may be ascribed to the OH of the carboxyl group.[16] No absorption was observed in the 1820–1870-cm.$^{-1}$ region; a band in this region should have been present had the product contained a cyclic anhydride group as in XVIII.[17] Neither did the spectrum (determined in benzene) show a band in the 3200–3650-cm.$^{-1}$ region; a band in this region should have been present had the product contained a carbinol hydroxyl group as in XIX. The spectrum of triphenylcarbinol, when run in carbon tetrachloride, exhibits a strong band at 3615 cm.$^{-1}$ for this group.[18]

Experimental[19]

2-(Dimethylaminomethyl)benzhydrol.—This compound was prepared by the method developed recently in this laboratory[20] involving the ring-metalation of benzyldimethylamine with butyllithium in ether, followed by condensation of the resulting lithio derivative with benzalde-

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[11] H. W. Bersch, R. Meyer, A. v. Mletzko, and K. H. Fischer, *Arch. Pharm.*, **291**, 82 (1958).

[12] C. C. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 806 (1962).

[13] See F. N. Jones and C. R. Hauser, *ibid.*, **27**, 4020 (1962).

[14] See ref. 8, p. 186.

[15] See ref. 8, p. 168.

[16] See ref. 8, p. 162.

[17] See ref. 8, p. 127.

[18] R. E. Richards and H. W. Thompson, *J. Chem. Soc.*, 1260 (1947).

[19] Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tenn. All melting points and boiling points are uncorrected. Infrared spectra were produced on a Perkin–Elmer Model 21 spectrophotometer in potassium bromide pellets. A 2-ft. silicon gum rubber column was used for the production of vapor phase chromatograms.

[20] F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 701 (1962). The details indicated in this communication will be published soon.

hyde. The product, m.p. 72.5–73.5°, was obtained in 54% yield.

2-(α-Hydroxybenzyl)benzyltrimethylammonium Iodide (IV).—To a stirred solution of 53.3 g. (0.22 mole) of 2-(dimethylaminomethyl)benzhydrol in 250 ml. of acetonitrile was added, during 30 min., a solution of 35.3 g. (0.25 mole) of methyl iodide in 100 ml. of acetonitrile. After refluxing for 30 min. and stirring for 6 hr. longer, more (35.3 g., 0.25 mole) of methyl iodide was added, and the mixture was refluxed for 4 hr., and stirred overnight. After cooling, dry ether was added to precipitate 81.8 g. (98%) of salt IV, m.p. 189–192°, lit.,[11] m.p. 174°.

Anal. Calcd. for $C_{17}H_{22}INO$: C, 53.27; H, 5.79; N, 3.66. Found: C, 53.00; H, 5.93; N, 3.77.

Rearrangement of Salt IV to Form Amino Alcohol V.—To a stirred solution of 0.15 mole of potassium amide in 300 ml. of commercial, anhydrous liquid ammonia[21] (Dry Ice-acetone condenser) was added, during 10 min., 19.2 g. (0.05 mole) of salt IV. The resulting red-colored reaction mixture was stirred for 1 hr., then neutralized with 21.8 g. (0.15 mole) of ammonium iodide. The liquid ammonia was evaporated as 250 ml. of anhydrous ether was added. The resulting ethereal suspension was filtered, and the filtrate extracted with 3 *N* hydrochloric acid. The combined acid extract was made basic with cold 6 *N* sodium hydroxide. The mixture was extracted with ether, and the extract dried over anhydrous magnesium sulfate. The solvent was removed to leave 10.1 g. (79%) of 2-methyl-3-dimethylaminomethylbenzhydrol (V), m.p. 83–88° and at 93–94° after two recrystallizations from hexane.

Anal. Calcd. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 79.89; H, 8.21; N, 5.49.

The original ethereal filtrate (after the acid extraction) was dried and evaporated to leave a few drops of benzaldehyde isolated as its 2,4-dinitrophenylhydrazone, m.p. and mixed m.p. 243–245°.

In another experiment, 38.3 g. (0.10 mole) of salt IV was added to 0.20 mole of potassium amide in 300 ml. of liquid ammonia. After 2 hr., 0.2 mole of ammonium iodide was added, and the liquid ammonia replaced by 250 ml. of ether. The ethereal suspension was filtered. The filtrate was dried, and 200 ml. of the solvent evaporated. A vapor phase chromatogram on the supernatant liquid showed two peaks, which were identified by retention times as benzaldehyde and 2-methylbenzyldimethylamine. Rearranged amino alcohol V appeared to decompose at the high temperature necessary for elution. Ether (200 ml.) was added, and the resulting solution extracted with 3 *N* hydrochloric acid. Evaporation of the ether layer left 0.5 g. (3%) of benzaldehyde isolated as its 2,4-dinitrophenylhydrazone. The acid extract was made basic with sodium hydroxide, and the mixture extracted with ether. After drying, the solvent was removed. The residue (15.3 g.) was recrystallized from hexane to give amino alcohol V (60%), m.p. 89–91°. Evaporation of the hexane mother liquor left an oil, which was distilled to give 0.8 g. (5%) of 2-methylbenzyldimethylamine, b.p. 63–65° at 2.5 mm.; m.p. and mixed m.p. of picrate 110–113°.

Oxidation of a 4-g. sample of the rearranged amino alcohol was effected in 200 ml. of refluxing 1 *N* sodium hydroxide with potassium permanganate, 4-g. portions of the latter reagent being added at 5-min. intervals until the purple color persisted. After refluxing overnight, the excess permanganate was destroyed with 10 ml. of ethanol, and the manganese dioxide was removed by suction filtration. The colorless basic filtrate was acidified with concentrated hydrochloric acid to give 1.9 g. (44%) of keto diacid VIII (dried in vacuum desiccator), m.p. 119–127°, lit.,[22] m.p. 121–125–146°. Neut. equiv. calcd. for monohydrate: 144.1. Found: 147.9.

The melting point of this product was depressed to 95–112° on admixture with an authentic sample of *o*-benzoylbenzoic acid (m.p. 126–128°).

Cyclization of a 0.5-g. sample of keto diacid VIII was effected in concentrated sulfuric acid solution (5 ml.) by heating at 140–150° for 15 min. The resulting amber liquid was poured onto ice to give anthraquinone-1-carboxylic acid (IX), which was obtained as yellow needles, m.p. 290–294°, after recrystallization from nitric acid.[9] This melting point was not depressed on admixture with an authentic sample of IX (m.p. 293–296°) prepared by oxidation of benzanthrone.[10] Moreover, the infrared spectra of the two samples were identical.

Stability of Monoanion IV′.—To a stirred suspension of 38.3 g. (0.10 mole) of quaternary iodide IV in 250 ml. of liquid ammonia was added, through a stopcock attached to the bottom of a flask, a solution of 0.10 mole of potassium amide in 250 ml. of liquid ammonia (inverse addition procedure). After 5 hr., the resulting gray suspension was treated with 0.10 mole of ammonium iodide, and the liquid ammonia was replaced by 250 ml. of ether. The resulting ethereal suspension was filtered. No isolable amount of amine or benzaldehyde was obtained on working up the ethereal filtrate. After drying, the solid salt material on the funnel weighed 53.9 g., which is only slightly lower than the combined amount (54.6 g.) of quaternary iodide IV and potassium iodide. That at least most of the starting iodide IV was recovered was shown by treatment of this mixture with three equivalents of potassium amide in liquid ammonia to give rearranged amino alcohol V in 65% yield. Also a trace of benzaldehyde was isolated as its 2,4-dinitrophenylhydrazone.

Stability of Monoanion V′.—To a stirred solution of 0.05 mole of potassium amide in 250 ml. of liquid ammonia was added 12.8 g. (0.05 mole) of rearranged amino alcohol V. This compound appeared to be converted to its potassium salt, which precipitated, soon coagulating and darkening. After 3 hr., 0.05 mole of ammonium iodide was added, the ammonia replaced by 250 ml. of ether, and the resulting ethereal suspension filtered. The filtrate was dried over anhydrous magnesium sulfate, and approximately 200 ml. of the solvent was removed, some white crystals precipitating. A vapor phase chromatogram on the supernatant liquid showed no peaks when the temperature of the column was maintained at 100°, and at 290° the starting amino alcohol V decomposed affording a broad peak. No bands corresponding to benzaldehyde and 2-methylbenzyldimethylamine were observed. The volume of the ethereal solution was restored to 250 ml. to dissolve the crystals, and the solution was extracted with 3 *N* hydrochloric acid. No isolable amount of benzaldehyde was obtained on evaporating the dried ethereal solution. The combined acid extract was made basic, and the mixture extracted four times with ether. The combined ethereal extract was dried, and the solvent removed to give 12.0 g. (94%) of recovered amino alcohol V, m.p. 90–91° after recrystallization from hexane.

2-(Dimethylaminomethyl)triphenylcarbinol.—This compound (m.p. 153.5–154°) was prepared in 80% yield by the metalation of benzyldimethylamine with butyllithium in ether, followed by condensation of the resulting lithio derivative with benzophenone.[20]

2-(α-Hydroxy-α-phenylbenzyl)benzyltrimethylammonium Iodide (XIII). To a stirred, hot solution of 8.7 g. (0.027 mole) of 2-(dimethylaminomethyl)triphenylcarbinol in 70 ml. of acetonitrile was added slowly 8.7 g. (0.06 mole) of methyl iodide in 50 ml. of acetonitrile. After refluxing for 8 hr., the reaction mixture was cooled, and 350 ml. of anhydrous ether was added to precipitate 11.7 g. (92%) of salt XIII, m.p. 175–177° dec., 176–178° dec., and 179–181° dec., depending on rate of heating. Recrystallization from ethanol–hexane failed to raise the melting point. The analytical sample was evidently the monohydrate.

Anal. Calcd. for $C_{23}H_{26}INO \cdot H_2O$: C, 57.86; H, 5.91; N, 2.93. Found: C, 58.00; H, 5.92; N, 3.10.

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[21] See C. R. Hauser and T. M. Harris, *J. Am. Chem. Soc.*, **80**, 6360 (1958).

[22] M. Hayashi, S. Turnoka, I. Morikawa, and H. Namikawa, *Bull. Chem. Soc. Japan*, **11**, 184 (1936).

Rearrangement of Salt XIII to Form Amino Alcohol XIV.—To a stirred solution of 0.06 mole of potassium amide in 300 ml. of liquid ammonia was added, during 10 min., 10.0 g. (0.021 mole) of salt XIII. After 6 hr., 10.2 g. (0.07 mole) of ammonium iodide was added, and the ammonia replaced by 250 ml. of ether. The ethereal suspension was filtered, and 20 ml. of 3 *N* hydrochloric acid was added dropwise to the filtrate. The resulting white precipitate was collected, and added to 150 ml. of 4 *N* sodium hydroxide. Ether (200 ml.) was added and the mixture stirred until all precipitate had dissolved. The ethereal solution was separated from the aqueous layer and the latter washed with 200 ml. of ether. The combined ether portions were dried over anhydrous magnesium sulfate and the solvent removed to give 5.2 g. (75%) of 2-methyl-3-dimethylaminomethyltriphenylcarbinol (XIV), m.p. 96–103°. A sample was recrystallized from hexane to a constant melting point of 102–104°.

Anal. Calcd. for $C_{23}H_{25}NO$: C, 83.34; H, 7.60; N, 4.23. Found: C, 83.27; H, 7.45; N, 4.09.

Oxidation of a 2-g. sample of the product was effected in 100 ml. of 1 *N* sodium hydroxide (refluxing) by adding potassium permanganate in 3-g. portions at 5-min. intervals until the purple color persisted. After refluxing overnight, the excess permanganate was destroyed with ethanol, and the manganese dioxide removed by filtration. The filtrate was acidified to precipitate 0.9 g. of crystalline product (XVII or XVIII), m.p. 190–203° and at 210–212° after recrystallization from ethanol–water.

Anal. Calcd. for $C_{21}H_{14}O_4$: C, 76.35; H, 4.27. Found: C, 76.17; H, 3.94.

Halogen–Metal Interchange of 2-, 3-, and 4-Bromobenzyldimethylamines with *n*-Butyllithium. Grignard Reagent of 2-Bromobenzyldimethylamine[1,2]

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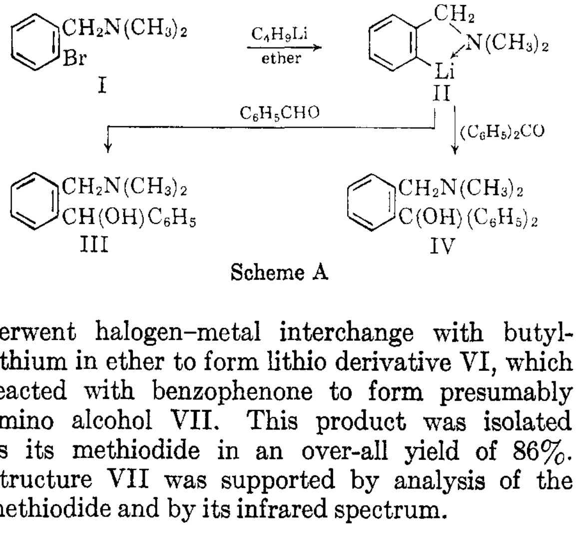
2-Bromobenzyldimethylamine underwent rapid halogen–metal interchange with *n*-butyllithium to form 2-lithiobenzyldimethylamine, which reacted with benzaldehyde and benzophenone to give the corresponding amino alcohols. 4-Bromobenzyldimethylamine also interchanged with butyllithium to give 4-lithiobenzyldimethylamine, which reacted with benzophenone to produce the amino alcohol. However, treatment of 3-bromobenzyldimethylamine with butyllithium gave a mixture of products. 2-Bromobenzyldimethylamine formed a Grignard reagent, but the other two isomers did not.

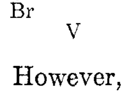
Although numerous aryl halides have been shown to undergo halogen–metal interchanges with *n*-butyllithium in ether,[3] reactions of 2-, 3-, and 4-bromobenzyldimethylamines appear not to have been studied previously with this reagent. We have found that the 2-bromo isomer I readily undergoes such an interchange with this reagent at room temperature to form II and presumably *n*-butyl bromide. This reaction was demonstrated by condensation of II with benzaldehyde and benzophenone to give amino alcohols III and IV in over-all yields of 68 and 80%, respectively (Scheme A).

The melting point of amino alcohol III agreed with that reported for this compound by Bersch and Meyer,[4] who prepared it from 2-dimethylaminomethylbenzaldehyde and phenylmagnesium bromide. This structure was further supported by reduction of III with sodium and ethanol in liquid ammonia to form 2-benzylbenzyldimethylamine.[5] The structures of amino alcohols III and IV were confirmed by synthesis through the Grignard reagent of I (see next section). The infrared spectra of III and IV were consistent with the assigned structures.

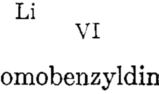


Scheme A

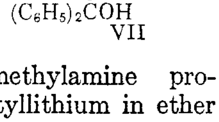
Similarly, 4-bromobenzyldimethylamine (V) underwent halogen–metal interchange with butyllithium in ether to form lithio derivative VI, which reacted with benzophenone to form presumably amino alcohol VII. This product was isolated as its methiodide in an over-all yield of 86%. Structure VII was supported by analysis of the methiodide and by its infrared spectrum.



V



VI



VII

However, 3-bromobenzyldimethylamine produced a dark solution with butyllithium in ether (four hours), and addition of benzaldehyde or benzophenone afforded a complex mixture from which no crystalline product was isolated. This halogen–metal interchange might have been complicated by metalation at the position between the dimethylaminomethyl group and bromine atom,

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[1] Supported by the Army Research Office (Durham).

[2] For a Communication see F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **27**, 701 (1962).

[3] See R. G. Jones and H. Gilman, *Org. Reactions*, **VI**, 339 (1951).

[4] H.-W. Bersch and R. Meyer, *Arch. Pharm.*, **287**, 613 (1954).

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