the water-insoluble product. Twenty grams of oily crystals was collected (fraction 1). A second component which remained in solution despite the addition of more water, was isolated in the form of oily crystals by saturating the solution with salt, and extracting the solution with chloroform. After displacing the chloroform with petroleum heptane and cooling, 13 g. of oily crystals was collected (crude 3,3-dimethylglutarimide). Fraction 1, after several recrystallizations from aqueous methanol and several subsequent recrystallizations from chloroform, was obtained in the form of asbestos-like fibers, m.p. 269°. This neutral compound contained bromine and gave the following results upon analysis.

Found: C, 28.2; H, 3.1; N, 4.3. Calcd. for $C_7H_9Br_2NO_2$: C, 28.1; H, 3.0; N, 4.7. Calcd. for $C_8H_{11}Br_2NO_4$: C, 27.8; H, 3.2; N, 4.1.

Since this compound failed to depress the melting point of camphor, a Rast molecular weight could not be determined. The identity of the compound was not established further.

LOS ANGELES 7, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Preparation of Geminally-substituted 4-Bromobutylamines. III. 4-Bromo-3,3-dimethylbutylamine[1]

BY RONALD F. BROWN AND NORMAN M. VAN GULICK

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The preparation and properties of 4-bromo-3,3-dimethylbutylamine hydrobromide are described. Several alternate synthetic routes were explored. The analogous hydroxy and methoxy amines were prepared also. The best sequence started with *asym*-dimethylsuccinic anhydride reduction to 2,2-dimethyl-1,4-butanediol and conversion to the dibromide, the more reactive bromine of which was replaced by an amino group by way of the Gabriel synthesis.

As part of a study on the effect of *gem*-substituents on the rate of ring closure of 4-bromobutylamines to pyrrolidines, the effect of position of substituents required the preparation of the hydrobromides of 4-bromobutylamine,[2] 4-bromo-1,1-dimethylbutylamine,[2] 4-bromo-2,2-dimethylbutylamine[3] and 4-bromo-3,3-dimethylbutylamine (I). A later paper will describe the rate studies. I was prepared by a method which depended upon the unreactivity of a neopentyl halide to displacement by intermolecular attack. The glycol, 2,2-dimethyl-1,4-butanediol, was converted to the dibromide, and the more reactive bromine replaced by an amino group *via* the Gabriel synthesis. The only unsatisfactory step was the conversion to dibromide, which despite repeated attempts with phosphorus tribromide and pyridine under various conditions gave consistent yields of around 10%. Reaction of the dibromide with potassium phthalimide gave N-(4-bromo-3,3-dimethylbutyl)-phthalimide in a yield of 80%. The Gabriel synthesis was carried out in dimethylformamide, an excellent solvent which allows the reaction to proceed at a low temperature in high yield.[4]

Compound I gave a positive nickel test for a primary amine and a slowly developing secondary amine test.[2,3] Cyclization was instantaneous in aqueous sodium hydroxide and treatment with benzenesulfonyl chloride gave 1-phenylsulfonyl-3,3-dimethylpyrrolidine identical to that derived from 4-bromo-2,2-dimethylbutylamine hydrobromide.[3] Thus the structures of I and its precursors were established unequivocally. That cyclization should occur rapidly in base is due to the fact that, although the neopentyl-type bromide is hindered with respect to intermolecular displacement, the structure is such that intramolecular displacement may occur readily. This point is nicely shown by examination of molecular models.

Another route to I from hydroxypivalaldehyde by condensation with nitromethane, dehydration, reduction and replacement of the hydroxy group by bromine was attempted. The addition of nitromethane to hydroxypivalaldehyde using diethylamine or sodium methoxide as a catalyst under a variety of conditions gave unreproducible yields of the nitro glycol. An attempt to avoid the difficult purification of the nitro glycol by substituting acetoxypivalaldehyde was not practical, since the corresponding product, from which the catalyst can be removed easily by washing with water, was obtained in very low yield. The reduction was straightforward.

4-Hydroxy-3,3-dimethylbutylamine differed from the isomer 4-hydroxy-1,1-dimethylbutylamine[2] in that the Hinsberg reaction gave only a base-soluble oil, which, upon treatment with benzenesulfonyl chloride and triethylamine, formed 1-phenylsulfonyl-3,3-dimethylpyrrolidine, identical with authentic material.[3] When 4-hydroxy-3,3-dimethylbutylamine was treated with thionyl bromide, a small quantity of gummy material was obtained which gave a trace of 1-phenylsulfonyl-3,3-dimethylpyrrolidine under Hinsberg conditions. This is not conclusive proof that I was formed, since the sulfonamide, only a trace of which was isolated, may have arisen from the hydroxy amine.

Acetoxypivalaldehyde decomposed extensively by several paths upon distillation at atmospheric pressure. The identified products were formaldehyde, isobutyl acetate and a colorless high boiling residue which may be the known dimer.[5] Even upon vacuum distillation decomposition occurred, but to a lesser extent. The distilled material effervesced for days, evolving an odorless gas, which was presumably carbon monoxide. Distillation of acetoxypivalaldehyde in the presence of a trace of toluenesulfonic acid gave rise to still

(1) Generously supported by the Office of Naval Research under Contract No. Nonr-723(00).

(2) R. F. Brown and N. M. van Gulick, THIS JOURNAL, **77**, 1079 (1955).

(3) R. F. Brown and N. M. van Gulick, *ibid.*, **77**, 1083 (1955).

(4) J. C. Sheehan and W. A. Bolhofer, *ibid.*, **72**, 2786 (1950).

(5) E. Späth and I. von Szilagyi, *Ber.*, **76**, 949 (1943).

another mode of decomposition, since an unsaturated gas, perhaps isobutylene, could be detected. This unusual behavior is in direct contrast to that of hydroxypivalaldehyde, which can be distilled with essentially no decomposition unless a trace of base is present, in which case formaldehyde and isobutyraldehyde are formed by a reverse aldol condensation.

Another attractive scheme for the synthesis of I started from *asym*-dimethylsuccinic anhydride; opening of the ring with ammonia, reduction and treatment with hydrobromic acid would lead to the product. The reduction with lithium aluminum hydride proceeded with difficulty because of poor solubility in boiling tetrahydrofuran and gave only a 16% yield of amino alcohol. Treatment of the amino alcohol with boiling hydrobromic acid gave 27% of a crystalline salt and a large quantity of intractable gum. The crystalline solid was shown to be 4-bromo-2,2-dimethylbutylamine hydrobromide instead of I by comparison of the melting point and X-ray powder diagram with those of authentic material and by formation of 1-phenylsulfonyl-3,3-dimethylpyrrolidine. That the 2,2-compound was produced in such quantity was unexpected, since it must have arisen from an abnormal opening of *asym*-dimethylsuccinic anhydride. This abnormal opening is not consonant with either steric or inductive effects. The isomeric *asym*-dimethylsuccinamic acids were isolated in the free state but losses were great due to facile cyclization giving *asym*-dimethylsuccinimide. Phenylhydrazine opened *asym*-dimethylsuccinic anhydride to give a homogeneous product, but treatment with lithium aluminum hydride failed to convert this product to 4-hydroxy-3,3-dimethylbutylamine in spite of the fact that this reagent is known to effect hydrogenolysis of N–N bonds.[6]

Based upon an observation by Hartung[7] that esters of cyanohydrins undergo facile hydrogenolysis at room temperature and under diminished pressure of hydrogen to give nitriles, the acetate of the cyanohydrin of hydroxypivalaldehyde was prepared. However, the ester[8] failed to take up hydrogen at one atmosphere. More drastic conditions were not attempted. Still another scheme, the replacement of the *p*-toluenesulfonate of 2,2-dimethylpropanediol by cyanide was tried. Although 1,3-dibromo-2,2-dimethylpropane does undergo displacement reactions, forcing is usually required.[9] It was found that 3-hydroxy-2,2-dimethylpropyl *p*-toluenesulfonate had not reacted with potassium cyanide after 14 hours in boiling ethanol. Forcing was not tried since dimethyltrimethylene oxide would have been formed under the basic conditions. To avoid this possibility, 3-methoxy-2,2-dimethylpropyl *p*-toluenesulfonate was prepared and successfully subjected to forcing conditions with potassium cyanide. Reduction of the nitrile afforded 4-methoxy-3,3-dimethylbutylamine, but boiling hydrobromic acid failed to cleave the ether. Further treatment with hydrogen bromide in acetic acid gave only rearranged products of an undetermined nature.

(6) E. W. Schueler and C. Hanna, THIS JOURNAL, **73**, 4996 (1951); and J. A. Krynitsky, J. E. Johnson and H. W. Carhart, *ibid.*, **70**, 486 (1948).

(7) W. H. Hartung, *ibid.*, **50**, 3370 (1928).

(8) E. T. Stiller, S. A. Harris, J. Finkelstein, J. C. Keresztesy and K. Folkers, *ibid.*, **62**, 1787 (1940).

(9) M. D. Owen, G. R. Ramage and J. L. Simonsen, *J. Chem. Soc.*, 1211 (1938); A. Franke, N. Obermayer and F. Streng, *Monatsh. Chem.*, **34**, 1893 (1913).

Experimental[10]

2,2-Dimethyl-1,4-butanediol.—A solution of 64 g. of *asym*-dimethylsuccinic anhydride in 100 ml. of ether was added slowly to a refluxing slurry of 23.7 g. of lithium aluminum hydride in one liter of ether, and the mixture was heated under reflux for one hour. The mixture was cooled and decomposed with 191 ml. of 2-propanol. After adding 156 ml. of saturated salt solution, the mixture was filtered and the filter cake was washed with ether. The filtrate was distilled, giving 44.8 g. (76%) of glycol, b.p. 229–233°, lit. b.p. 123° (10 mm.).[11]

1,4-Dibromo-2,2-dimethylbutane was prepared by adding 70.3 g. of the glycol in 31.4 ml. of dry pyridine dropwise to 114 ml. of phosphorus tribromide at room temperature. After the addition, the mixture was stirred at 130° in an oil-bath for 2.5 hours. The reaction mixture was cooled, poured onto ice and extracted with chloroform. The chloroform solution was filtered to remove solid material and extracted with 1% sodium hydroxide until the aqueous layer remained basic. The chloroform solution was then extracted with concentrated sulfuric acid to remove unreacted glycol and bromohydrin, washed with water, and dried. Distillation afforded 20.5 g. of product (14.5%), b.p. 108–112° (22 mm.).

N-(4-Bromo-3,3-dimethylbutyl)-phthalimide was prepared by adding 10 g. of potassium phthalimide to a solution of 13.3 g. of the dibromide in 60 ml. of dimethylformamide. The solution was heated on the steam-bath for 1.5 hours; then 45 ml. of chloroform was added and the solution was poured into 100 ml. of water. The aqueous phase was separated and extracted with chloroform. The combined chloroform solutions were washed with dilute sodium hydroxide and water, and dried. The chloroform was removed on the steam-bath and the residue was distilled at the water-pump to remove 4.6 g. of an oil which passed over around 65°. This oil was unsaturated to bromine and to permanganate and, because of the boiling point, could be a bromohexene. The residue solidified upon cooling and was crystallized from petroleum hexane to give 9.0 g. (52.9%) of product, m.p. 60–61°.

Anal. Calcd. for $C_{14}H_{16}BrNO_2$: C, 54.20; H, 5.20; N, 4.52. Found: C, 54.41; H, 5.09; N, 4.35.

4-Bromo-3,3-dimethylbutylamine hydrobromide (I), was prepared by boiling a mixture of 9 g. of the phthalimide, 29 ml. of concentrated hydrobromic acid, and 29 ml. of acetic acid for 5 hours. The solution was chilled and the phthalic acid was collected and washed with a minimum quantity of acetic acid. The filtrate was evaporated to dryness *in vacuo* on the steam-bath and the residual traces of solvent were removed in a desiccator over potassium hydroxide. The product was crystallized from acetonitrile (12 ml. per g.) to give 4.5 g. (60%) of pure material, m.p. 245–246°dec.

Anal. Calcd. for $C_6H_{15}Br_2N$: C, 27.61; H, 5.79. Found: C, 27.54; H, 5.56.

Treatment with benzenesulfonyl chloride and aqueous sodium hydroxide gave 1-phenylsulfonyl-3,3-dimethylpyrrolidine, m.p. 49–50°. The mixed melting point with authentic material was undepressed.

Hydroxypivalaldehyde was prepared from formaldehyde, isobutyraldehyde and potassium carbonate using the procedure of Kapp.[12]

2,2-Dimethyl-4-nitro-3-butenyl Acetate.—Various procedures for condensing hydroxypivalaldehyde with nitromethane were tried, using sodium hydroxide and methoxide and diethylamine as condensing agents. The best procedure is given. The aldehyde (48.3 g.), 25.4 ml. of redistilled nitromethane and 48.7 ml. of dry diethylamine were allowed to stand for 5 hours at room temperature. The mixture was acidified with acetic acid and partitioned between ethyl acetate and saturated salt solution. Distillation af-

(10) All m.p.'s and b.p.'s are uncorrected. Analyses by Mr. W. J. Schenck of this department.

(11) L. Bouveault and G. Blanc, *Compt. rend.*, **137**, 328 (1903).

(12) R. Kapp, F. D. Pickel and L. T. Rosenberg, U. S. Patent 2,434,246 [*C. A.*, **42**, 2271 (1948)]; also see ref. 8.

forded 51 g. (66%) of nitro glycol, b.p. 80–180° (2 mm.). Dehydration was accomplished by heating 12.4 g. with 16.2 ml. of acetic anhydride to a temperature of 120°, whereupon an exothermic reaction set in, raising the temperature to 151°. In 5 minutes the solution had cooled to 120°. This temperature was maintained by external heating for an additional 10 minutes. The mixture was taken up in ether and extracted with water. Distillation gave 10.4 g. (73%) of product, b.p. 103–115° (2 mm.).

3,3-Dimethyl-4-hydroxybutylamine.—A solution of 10.3 g. of the nitro ester in 25 ml. of tetrahydrofuran was added to a slurry of 6.3 g. of lithium aluminum hydride in 100 ml. of tetrahydrofuran over a 15-minute period with cooling in a water-bath. After an 0.5-hour reflux period the reaction was worked up in the usual manner to give 4.1 g. (64%) of product, b.p. 122–127° (24 mm.). This material formed an oxalate, m.p. 214° dec.

Thionyl bromide was prepared by the procedure of Elderfield.[13] A solution of 0.2 g. of the amino alcohol in 5 ml. of dry benzene was treated with an equivalent of thionyl bromide in 5 ml. of dry benzene over a 3-hour period. The mixture was stirred for an additional 3 hours. The solution was evaporated *in vacuo*, giving a gummy dark-colored solid. This was treated with sodium hydroxide and benzenesulfonyl chloride, giving a trace of 1-phenylsulfonyl-3,3-dimethylpyrrolidine (m.p. and mixed m.p.).

Acetoxypivalaldehyde was prepared on a 4-mole scale by adding toluene to the methylene chloride solution of hydroxypivalaldehyde, as obtained in the previously used procedure, and codistilling the water. Acetic anhydride (410 ml.) was added over a period of 30 minutes to the boiling solution. The heating was continued for an additional hour and the excess anhydride was decomposed by the addition of alcohol. The solution was extracted with water and dilute base. Distillation gave 305 g. (53%) of product, b.p. 85–105° (18 mm.), and a considerable amount of effervescing residue. The material was redistilled twice at atmospheric pressure to give 120 g. (21%), b.p. 180–188° (lit. b.p. 182°),[14] a considerable low boiling forerun and residue. The low boiling material was fractionated to give isobutyl acetate, b.p. 111–114°, since basic hydrolysis gave isobutyl alcohol, b.p. 105–108°, which with phenyl isocyanate gave the phenylurethan, m.p. 86°.

The attempted condensation of acetoxypivalaldehyde with nitromethane was conducted by adding 0.22 mole of nitromethane to a solution of 0.2 atom of sodium in 150 ml. of absolute methanol, followed by the addition of 0.2 mole of the aldehyde in 50 ml. of absolute methanol over a period of 15 minutes, keeping the temperature around 10° by cooling. The white salt of nitromethane soon went into solution giving a golden color. The solution was cooled to 0° and 0.5 mole of acetic acid was added dropwise. The solution was allowed to stand overnight and then partitioned between water and chloroform. At 18 mm., material distilled continuously up to 110°. At 1 mm. the residue distilled continuously from 95 to 140° giving only 16 g. of a mixture.

Opening of *asym*-Dimethylsuccinic Anhydride with Amines.—A solution of 12.8 g. of *asym*-dimethylsuccinic anhydride in 50 ml. of ether was added to 5 g. of liquid ammonia in 50 ml. of ether with Dry Ice cooling. The precipitate (16.0 g., 99%) was collected, powdered and slowly added as a suspension in 100 ml. of tetrahydrofuran to a refluxing slurry of 12 g. of lithium aluminum hydride in 200 ml. of tetrahydrofuran. Violent evolution of ammonia occurred. After 11 hours of heating, 250 ml. more of tetrahydrofuran was added, but the voluminous solid failed to dissolve. After a total reflux time of 24 hours, the reaction was worked up by adding 2-propanol and a minimum amount of water. The slush was centrifuged and the supernatant liquid was distilled giving 1.85 g. (16%) of amino alcohol, b.p. 117–121° (21 mm.). The nickel tests were positive for a primary amine and negative for a secondary amine.[2,3] The Hinsberg reaction gave 1-phenylsulfonyl-3,3-dimethylpyrrolidine (m.p. and mixed m.p. with authentic material) and a trace of a base-soluble sulfonamide, m.p. 93–94°.

The amino alcohol (0.5 g.) was added to 10 ml. of concentrated hydrobromic acid and the solution was distilled from an oil-bath at 150° until 7 ml. of distillate had been collected. The remaining liquid was removed *in vacuo* and the residue was extracted with ethylene chloride, leaving a gum. The ethylene chloride solution was chilled and the crystalline product was recrystallized from acetone several times, decreasing the initial m.p. from 186–187° dec. to 182–184° dec. This substance gave no m.p. depression when mixed with authentic 4-bromo-2,2-dimethylbutylamine hydrobromide, m.p. 188–189° dec., in varying proportions. That these compounds were identical was proved both by the fact that both gave the same Hinsberg product, and also by the Debye–Scherrer powder technique. Thus, 6.8-hour exposures to an X-ray source operating at 30 kv. and 15 ma. with a copper target and nickel filter gave powder diagrams which were completely superimposable.

A preliminary run in which both succinamic acids were obtained (subsequent runs failed to afford any more than one isomer) was carried out by adding a solution of 6.4 g. of the anhydride in 25 ml. of ether to 3 g. of liquid ammonia in 25 ml. of tetrahydrofuran in a Dry Ice-bath. After removal of excess ammonia by boiling on the steam-bath for a short while, water and 4.2 ml. of concentrated hydrochloric acid were added. The three-phase system (solid plus 2 liquid phases) was filtered to remove the low melting solid, and the organic layer was separated and evaporated to dryness to give crude higher melting solid. Both materials were found to be insoluble in all solvents except water and alcohols, in which they are quite soluble. Both were recrystallized from 2-propanol (a, m.p. 124–125°; b, m.p. 136–137°). Both of these compounds are cyclized to the known succinimide, m.p. 106–108°, by brief heating. Both acids depressed each other's melting point as well as the m.p. of the succinic acid (m.p. 136–138°). The major product was the low melting isomer. Other runs were made in which the ammonium succinimate was treated with methanolic sodium hydroxide to give the sodium salt, which was recrystallized several times from methanol. The free acid was liberated by treatment with the theoretical quantity of sulfuric acid in 2-propanol. Yields were low, perhaps because of acid-catalyzed cyclization. Recrystallization losses were also great.

Phenylhydrazine in benzene at room temperature converts the anhydride to a homogeneous hydrazide-acid, m.p. 185–186° dec., in 95% yield. Heat converts it to the cyclic hydrazide, m.p. 132–133°, lit.[15] m.p. 131–132°.

The hydrazide-acid (23.6 g.) suspended in 100 ml. of tetrahydrofuran was added slowly to a stirred refluxing slurry of 17.1 g. of lithium aluminum hydride and 400 ml. of tetrahydrofuran. All organic matter remained in solution. After the addition, the mixture was heated under reflux for 1 hour, and then decomposed with 2-propanol and a minimum of water. After separation, distillation gave material, b.p. 116–128° (27 mm.). The material was taken up in acetone and oxalic acid was added. Only a very small quantity of material, m.p. 185°, precipitated. This was slightly soluble in acetone, in contradistinction to the oxalates of aniline and phenylhydrazine, and reduced Benedict solution, as does phenylhydrazine.

2,2-Dimethylpropanediol.—The procedure of Meyersburg[16] was modified slightly. To a solution of 5 moles of isobutyraldehyde and 850 ml. of 35% formaldehyde was added slowly with cooling a solution of 213 g. of potassium hydroxide in 1700 ml. of 95% ethanol. After standing for 16 hours, the alcohol was distilled, the residue was saturated with sodium chloride and extracted with 1-butanol. The extract was distilled and the fraction of b.p. 120–193° was collected and treated with a mixture of carbon tetrachloride and chloroform. The crystals were collected and recrystallized twice from carbon tetrachloride and chloroform to give 243 g. (47%) of m.p. 129–131°, lit.[16] m.p. 130°. The low yield probably was due to the use of old formalin.

3-Hydroxy-2,2-dimethylpropyl *p*-Toluenesulfonate.—*p*-Toluenesulfonyl chloride was purified by dissolving 200 g. in 250 ml. of benzene. The solution was decanted from insoluble solids into a separatory funnel and washed with 50 ml. of dilute sodium hydroxide, followed by 50 ml. of saturated sodium chloride. The solution was dried with potassium carbonate and decolorized with a small quantity of charcoal. The solution was evaporated to a small volume. Petroleum hexane was added and the solution was chilled, giving 170 g. (80%) of colorless needles.

The procedure of Sekera and Marvel[17] was used. A solu-

(13) R. C. Elderfield and collaborators, THIS JOURNAL, **68**, 1579 (1946).

(14) L. Wessely, *Monatsh. Chem.*, **21**, 216 (1900).

(15) S. Levy and P. Englander, *Ann.*, **242**, 189, 203 (1887).

(16) P. Meyersburg, *Monatsh. Chem.*, **26**, 41 (1905).

(17) V. C. Sekera and C. S. Marvel, THIS JOURNAL, **55**, 345 (1933).

tion of 10.4 g. of the glycol in 32.2 ml. of dry pyridine was cooled to 20° while a solution of 19 g. of *p*-toluenesulfonyl chloride in 50 ml. of dry ether was added over a period of 0.5 hr. After the mixture had been stirred for 3 hours at room temperature, the pyridine was removed by neutralizing with 30 ml. of concentrated hydrochloric acid and washing the ether solution with water. The ether was displaced with methanol on the steam-bath and water was added to the point of cloudiness. Chilling deposited 5.4 g. of oily crystals of the di-*p*-toluenesulfonate (unaffected by acetic anhydride) which was recrystallized from aqueous acetone, m.p. 116–120°. Addition of more water to the mother liquor gave the mono-*p*-toluenesulfonate as an oil which was used directly in the next step.

The oil was dissolved in 65 ml. of 95% ethanol and a solution of 7.9 g. of potassium cyanide in 21 ml. of water was added. After a 14-hour reflux period, the mixture was extracted with benzene and the solution was distilled at the aspirator. No volatile material passed over at the expected temperature of 100°, and at a bath temperature of 200°, pyrolysis of the unchanged *p*-toluenesulfonate commenced.

2,2-Dimethyl-3-methoxypropanol.—Sodium (11.5 g.) was dissolved in a solution of 57.3 g. of 2,2-dimethylpropanediol in 300 ml. of absolute *t*-amyl alcohol. The solution was cooled and 46 ml. of methyl iodide was added and the mixture was stirred for 3 hours at room temperature. Water was added and the organic layer was separated and dried. Distillation gave 30.3 g. (73% conv.) of product, b.p. 150–160°, and 14.2 g. of unreacted glycol.

4-Methoxy-3,3-dimethylbutyronitrile.—A solution of 49 g. of *p*-toluenesulfonyl chloride was added to a solution of 30.3 g. of the methoxy alcohol in 129 ml. of pyridine and after 1 hour on the steam-bath, the mixture was treated with water and 75 ml. of concentrated hydrochloric acid and extracted with petroleum hexane. The solvent was removed on the steam-bath and the 32 g. of residue was taken up in 200 ml. of ethylene glycol. After the addition of 11.8 g. of potassium cyanide, the solution was distilled until the distillate was no longer cloudy. The 2-phase distillate was partitioned between water and petroleum pentane. The organic solution was separated and distilled, giving 3.1 g. (10%) of oil, b.p. 165–175°.

4-Methoxy-3,3-dimethylbutylamine.—The total quantity of nitrile, plus forerun and residue in 20 ml. of 2-butanol was added to a stirred slurry of 4 g. of molten sodium in 20 ml. of toluene. After decomposition with ethanol, water and 20 ml. of concentrated hydrochloric acid were added and the solvent was distilled. After treatment with charcoal, the solution was made basic and the amine extracted with benzene. The benzene solution was extracted with dilute hydrobromic acid and the extract was evaporated *in vacuo*, giving about 5 g. (60%) of very hygroscopic crystals of the hydrobromide. The nickel tests were positive for a primary amine and negative for a secondary amine.[2] The Hinsberg test gave a base-soluble oil, which resisted crystallization. Concentrated hydrobromic acid was distilled from the salt to give a hygroscopic solid resembling the original salt. A small portion was treated with the nickel reagent after prior neutralization with sodium bicarbonate and gave a strong test for a primary amine. Therefore, not much I was formed, if any. The methoxyamine salt was boiled with anhydrous hydrogen bromide in acetic acid for 16 hours and, after removal of the solvent *in vacuo*, the dark residue was treated with benzenesulfonyl chloride and aqueous base to give a black oil insoluble in base. (Acidification of the reaction mixture precipitated nothing, so no primary amine had survived the hydrolysis.) The black oil was chromatographed on alumina from 3:7 carbon tetrachloride and petroleum hexane to give a crude yellowish solid, which was fractionally oiled from carbon tetrachloride and petroleum hexane to give a colorless but still impure solid, m.p. 52–64°. This material liquefied when mixed with authentic 1-phenylsulfonyl-3,3-dimethylpyrrolidine.

LOS ANGELES 7, CALIFORNIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Formation of 3,3,5-Trimethyl-2-pyrrolidone by the Cleavage of 5-Ethoxy-2,2-dimethylvalerophenone with Sodamide[1]

BY RONALD F. BROWN AND NORMAN M. VAN GULICK

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In an attempt to prepare 5-ethoxy-2,2-dimethylvaleramide, the cleavage with sodamide of 5-ethoxy-2,2-dimethylvalerophenone was tried, but the unexpected product proved to be the lactam of 4-amino-2,2-dimethylvaleric acid. Presumably, the reaction proceeds by elimination of ethanol as well as benzene to give 2,2-dimethyl-4-pentenamide which then cyclizes in the basic media. The sensitivity of the ether to cleavage may be due to the nascent phenyl anion which is very close to the hydrogen which is beta to the ethoxy group, leading to a concerted cleavage and E_2 type elimination.

In the course of attempts to prepare the hydrobromide of 4-bromo-1,1-dimethylbutylamine,[2] an attractive route appeared to be the cleavage with sodamide of 5-ethoxy-2,2-dimethylvalerophenone (I) to give 5-ethoxy-2,2-dimethylvaleramide, which, by the Hofmann rearrangement, should yield 4-ethoxy-1,1-dimethylbutylamine, the precursor of the desired product.

$$EtOCH_2CH_2CH_2CMe_2COC_6H_5 \xrightarrow{NaNH_2}$$

$$EtOCH_2CH_2CH_2CMe_2CONH_2 \xrightarrow{Br_2 + NaOH}$$

$$EtOCH_2CH_2CH_2CMe_2NH_2 \xrightarrow{HBr}$$

$$BrCH_2CH_2CH_2CMe_2NH_2 \cdot HBr$$

Compound I was prepared readily by the alkylation of isobutyrophenone with 3-ethoxypropyl bromide, but subsequent cleavage with sodamide gave a partially crystalline product which was subjected to conditions for rearrangement. To our surprise, only a trace of crude amine was formed, primary as determined by the Duke test[3] and this could not be the required amine which does not give a positive primary amine test.[2] The main product was recovered starting material, which proved to be 3,3,5-trimethyl-2-pyrrolidone (II), the properties of which were identical with those reported by Haller and Bauer[4] for authentic material from the cleavage of allyldimethylacetophenone with sodamide and from an independent synthesis. These workers proposed, but did not prove, that their cleavage proceeded normally to give 2,2-dimethyl-4-pentenamide (III), which then cyclized under the basic conditions.

(1) Generously supported in part by the Office of Naval Research under Contract No. Nonr-723(00).

(2) R. F. Brown and N. M. van Gulick, THIS JOURNAL, **77**, 1079 (1955).

(3) F. R. Duke, *Ind. Eng. Chem., Anal. Ed.*, **17**, 196 (1945).

(4) A. Haller and E. Bauer, *Compt. rend.*, **158**, 1086 (1914).