Mannich Reaction on Benzylmalonic Acid (34).—A mixture of 30 g (0.16 mol) of **34** (K & K Laboratories), 16.6 g (0.20 mol) of benzaldehyde, and 20 ml of 10% alcoholic NH_3 was heated for 1 hr on a steam bath and then 3 hr at 130° in an autoclave. The mixture was then added to 100 ml of 30% aqueous K_2CO_3 solution and the whole was extracted with three 70-ml portions of ether. The aqueous residue was slowly acidified with concentrated HCl and, on cooling, precipitated 7 g (19%) of **2-benzylcinnamic acid** (**35**), mp 159–160° (from ethanol–water) (lit.[32] mp 160°). The aqueous filtrate was extracted with three 50-ml portions of ether. The ether extracts were dried ($MgSO_4$) and evaporated to dryness and the residue was recrystallized from ethanol–ether to give 8 g (18%) of a 58:42 *erythro–threo* mixture of **13f** as determined by nmr spectroscopy: mp 226–227° dec; ir (KBr), 5.87 and 5.90 μ (C=O).

Registry No.—**8a**, 13086-19-6; **8b**, 16934-01-3; **8d**, 13088-65-8; **8e**, 13085-96-6; **8f**, 16934-04-6; **8h**, 13085-97-7; **9a**, 13085-98-8; **9b** (*cis*), 16933-57-6; **9b** (*trans*), 16933-58-7; **9d**, 13085-95-5; **9e**, 13085-99-9; **9f**, 16933-61-2; **9g**, 16933-62-3; **9h**, 13086-00-5; **10a**, 16933-64-5; **10b** (*cis*), 16933-65-6; **10b** (*trans*), 16933-66-7; **10c**, 16933-67-8; **10d**, 13088-60-3; **10e**, 16933-69-0; **11**, 16933-70-3; **12a**, 16933-71-4; **12b**, 16933-72-5; **12d**, 16933-73-6; **12e**, 16933-74-7; **12f**, 16933-75-8; **12g**, 16933-76-9; **12h**, 16933-77-0; **13a**, 16933-78-1; **13b**, 16933-79-2; **13d**, 16933-80-5; **13e**, 16933-81-6; **13f** (*threo*), 16933-82-7; **13f** (*erythro*), 16933-83-8; **13g** (*threo*), 16933-84-9; **13g** (*erythro*), 16933-85-0; **13i** (*meso*), 16933-86-1; **13i** (*dl*), 16933-87-2; **17a**, 16933-88-3; **17e**, 16933-89-4; **17f**, 16933-90-7; **17g** (*cis*), 16933-91-8; **17g** (*trans*), 16933-92-9; **17i** (*cis*), 16933-93-0; **17i** (*trans*), 16933-94-1; **18a**, 16933-95-2; **18b**, 16933-96-3; **18e**, 16933-97-4; **18f** (*cis*), 16933-98-5; **18f** (*trans*), 16933-99-6; **18g** (*cis*), 16934-12-6; **18g** (*trans*), 16934-13-7; **18i** (*cis*), 16934-14-8; **18i** (*trans*), 16934-15-9; **19a**, 16934-16-0; **19b**, 16934-17-1; **19i**, 16934-18-2; **22**, 16934-19-3; **23**, 16934-20-6; **24**, 16934-21-7; **25**, 16934-22-8; **27**, 16934-23-9; 1-carboxamido-2-methyl-1-cyclohexene-4,5-dicarboxylic anhydride, 16934-24-0; chlorosulfonyl isocyanate, 1189-71-5.

Acknowledgment.—We wish to thank Mr. Walter Meyer for the spin decoupling experiments and the New York State Science and Technology Foundation for a grant [SSF(7)-6] to the Department of Chemistry for the purchase of the A-60A nmr spectrometer.

(32) W. M. Radionov and E. A. Postovskaja, *J. Amer. Chem. Soc.*, **51**, 841 (1929).

Azetidines. IV. The Reaction of 1,1-Dimethyl-, 1-Benzyl-1-methyl-, and 1,1-Dibenzyl-3,3-dimethylazetidinium Salts with Alkali Metal Amides in Liquid Ammonia[1-3]

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Received February 8, 1968

Of several possibilities, only the Stevens rearrangement product arising from enlargement of the azetidine ring was obtained from the reaction of 1,1,3,3-tetramethylazetidinium iodide (**1**) with potassium amide in liquid ammonia. Similarly, 1-benzyl-1,3,3-trimethylazetidinium iodide (**8**) gave only the ring-enlarged Stevens product even though, in this case, a Sommelet product was also possible. In contrast, 1,1-dibenzyl-3,3-dimethylazetidinium bromide (**13**) gave a 98% yield of the Sommelet product plus a small amount of the Stevens product with the azetidine ring retained. Ion-pair mechanisms best account for these results.

The reaction with sodium amide in liquid ammonia of tetraalkylammonium halides possessing a benzylic hydrogen was found by Kantor and Hauser[4] to be an excellent method for effecting the Sommelet rearrangement.[5] Subsequently Hauser and coworkers established, by two independent proofs,[6] that the mechanism for this reaction involved nucleophilic attack by an ylide carbon at the *ortho* position of the aromatic ring followed by tautomeric rearomatization.

The investigation of a number of quaternary salts of this type led to the implication that sodium amide in liquid ammonia was quite selective and gave exclusively either the Sommelet or the Stevens[7] (*e.g.*, with benzhydrylbenzyldimethylammonium ion[8]) rearrangement. More recent studies have shown that these early results were, at least in part, caused by a fortuitous choice of quaternary salts. Thus Jones, *et al.*,[9] Fery and Wilputte-Steinert,[10] Bumgardner,[11] and Jenny and Druey[12] have found examples in which the Stevens rearrangement accompanies the Sommelet rearrangement, and Klein and Hauser[13] have discovered that benzhydryltrimethylammonium ion, which had previously been reported to give only the Sommelet product, actually forms *ca.* 15% Stevens product.

The behavior of quaternary ammonium salts which do not possess a benzylic or similarly activated methylene group with alkali metal amides in liquid ammonia

(1) Part III: A. G. Anderson, Jr., and M. T. Wills, *J. Org. Chem.*, **33**, 2123 (1968).

(2) From the Ph.D. Thesis of M. T. Wills, University of Washington.

(3) Supported in part by State of Washington Initiative 171 Funds for Research in Biology and Medicine.

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

(5) (a) M. Sommelet, *Compt. Rend.*, **205**, 56 (1937); (b) H. E. Zimmerman, "Molecular Rearrangements," part I, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp 345–406; (c) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 223–229.

(6) F. N. Jones and C. R. Hauser, *J. Org. Chem.*, **26**, 2979 (1961); C. R. Hauser and D. N. van Eanam, *J. Amer. Chem. Soc.*, **79**, 5512, 6280 (1957); *J. Org. Chem.*, **23**, 865 (1958).

(7) T. S. Stevens, E. M. Creighton, A. B. Gordon, and M. MacNicol, *J. Chem. Soc.*, 3193 (1928); T. S. Stevens, *ibid.*, 2107 (1930). The mechanistic relationship of the Stevens and Sommelet rearrangements have been discussed by D. J. Cram[5c] and H. E. Zimmerman.[5b]

(8) C. R. Hauser, R. L. Manyik, W. R. Brasen, and P. L. Bayless, *J. Org. Chem.*, **30**, 1119 (1955).

(9) G. C. Jones, W. Q. Beard, and C. R. Hauser, *ibid.*, **28**, 199 (1963).

(10) L. P. A. Fery and L. Wilputte-Steinert, *Bull. Soc. Chim. Belges*, **73**, 154 (1964).

(11) C. L. Bumgardner, *J. Amer. Chem. Soc.*, **85**, 73 (1963).

(12) E. F. Jenny and J. Druey, *Angew. Chem.*, **74**, 152 (1962).

(13) K. P. Klein and C. R. Hauser, *J. Org. Chem.*, **31**, 4275 (1966).

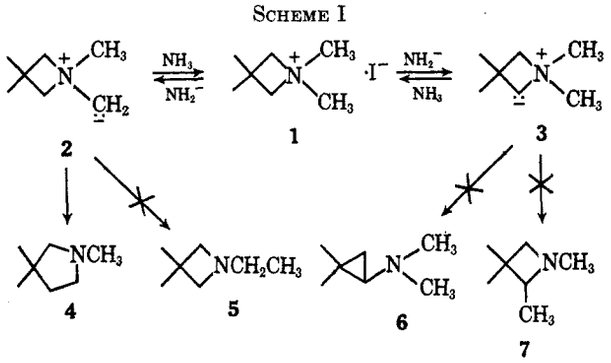
has been relatively little studied. Wittig and Burger[14] found that dimethylpyrrolidinium bromide gave Hofmann elimination products, dimethylpiperidinium bromide gave elimination and displacement products, and dimethylhexamethyleneammonium bromide gave a single elimination product. Thus no rearrangements were detected. The only rearrangement of such a system, to our knowledge, was found accidentally by Grovenstein and Rogers[15] to occur in the sodium–ammonia reduction of 2,2,2-triphenylethyltrimethylammonium iodide. A 93% yield of the Stevens product, 3,3,3-triphenylpropyldimethylamine, was obtained. The migration of the triphenylethyl (rather than a methyl) group was attributed to steric and electronic effects.

As a part of a study of tertiary and quaternary azetidines, we have examined the reactions of a series of methyl and benzyl quaternary azetidinium salts with alkali metal amides in liquid ammonia and have found that essentially exclusively Stevens or Sommelet rearrangements occur, depending on the structure of the quaternary ions.

Results and Discussion

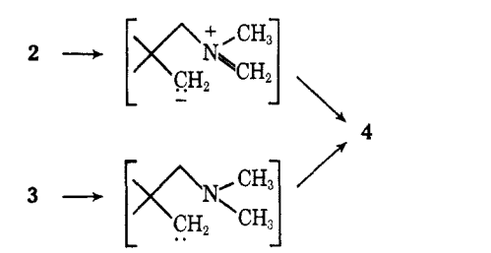
1,1,3,3-Tetramethylazetidinium Iodide (1).—The quaternary ion of this salt has two different types of α-hydrogens: those on the methyl and those on the ring methylene groups. The carbon–hydrogen bonds in the former would be sp^3 or nearly so, but the bonds in the latter would have relatively more S character and therefore would be more acidic.[16] The methylene hydrogens would be more sterically hindered, however, and thus the actual difference between the acidities of these and of the methyl hydrogens could be small. Qualitatively, therefore, both possible ylides (**2** and **3**) would be expected to be formed in appreciable amounts and four Stevens rearrangement products (**4**, **5**, **6**, and **7**) could result *via* the usual ionic mechanism (Scheme I).

SCHEME I



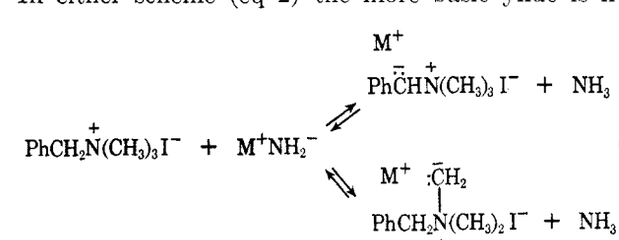
The reaction of **1** with potassium amide and liquid ammonia gave the Stevens product (**4**) in 70% yield. A small quantity (<1%) of higher molecular weight material of the same empirical formula was also obtained. The structure of **4** was indicated by the formation of a methiodide and a picrate, and by the nmr spectrum which consisted of a six-proton singlet at 1.03 ppm[17] (geminal methyls), two two-proton triplets (J = 3.5 cps) at 1.49 and 2.44 ppm (adjacent methylenes), a two-proton singlet at 2.14 ppm (isolated methylene), and a three-proton singlet at 2.17 ppm (N-methyl). None of the other three rearrangement products was found, nor were products derived from the nucleophilic attack on **1** by amide ion.

Thus the mechanism for this reaction must strongly favor the formation of **4** relative to the formation of **5**, **6**, or **7**. Concerted processes did not appear to do this. An ion-pair mechanism, however, would release the strain of the four-membered ring only in the transition of **2** to the ion-pair intermediate leading to **4** (eq 1). A further possibility was the rearrangement of ylide **3** to **4** by a carbene mechanism.[18] The addition of a 5 molar excess of cyclohexene to one run, however, did not produce a detectable amount of a norcarane product.



(1)

1-Benzyl-1,3,3-trimethylazetidinium Iodide (8).—This salt possesses three types of α hydrogens including a benzylic group. Thus three ylides are possible and, from these, seven Stevens and two Sommelet products are possible. Although the benzylic hydrogens are the most acidic and the corresponding ylide can undergo only a Stevens rearrangement, a number of examples are known[5,9–13] where the Sommelet rearrangement is dominant even though it involves a more basic ylide than the competing Stevens. Puterbaugh and Hauser[19] have obtained evidence for the conversion of the less basic into the more basic ylide in such a case, and have suggested that the second ylide is in *direct* equilibrium with the first *via* a cyclic 1,3-prototropic shift or similar process. Although quantitative data on the acidities of the species involved is not available, qualitative considerations[20] point to proton transfer by equilibria with the ammonia solvent as an alternative possibility. In either scheme (eq 2) the more basic ylide is irre-



(2)

(14) G. Wittig and T. F. Burger, *Ann.*, **632**, 85 (1960).

(15) E. Grovenstein and L. C. Rogers, *J. Amer. Chem. Soc.*, **86**, 854 (1964).

(16) C. Juan and H. S. Gutowsky, *J. Chem. Phys.*, **37**, 2198 (1962).

(17) Chemical-shift values are reported as δ values in parts per million relative to tetramethylsilane as an internal standard.

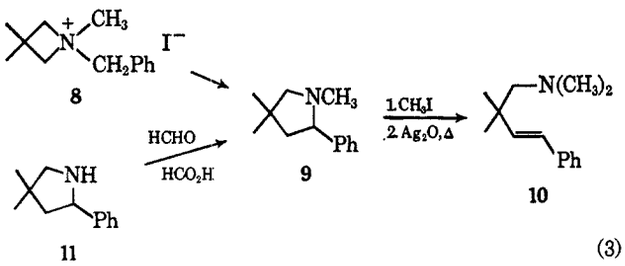
(18) G. Wittig and R. Polster, *Ann.*, **599**, 1 (1956); V. Franzen and G. Wittig, *Angew. Chem.*, **72**, 417 (1960); G. Wittig and D. Krause, *Ann.*, **679**, 34 (1964); F. Weygand, H. Daniel, and A. Schroll, *Ber.*, **97**, 1217 (1964).

(19) W. H. Puterbaugh and C. R. Hauser, *J. Amer. Chem. Soc.*, **86**, 1105 (1964).

(20) Tetramethylammonium iodide is metalated by phenyllithium [G. Wittig and M. H. Wetterling, *Ann.*, **557**, 193 (1947)] but not by benzylsodium [W. Schlenk and J. Holtz, *Ber.*, **50**, 274 (1917)]. These findings would place the acidity of the compound between those of benzene and toluene, and give an estimated pK_A of 36 on the McEwen–Streitwieser–Applequist–Dessy scale.[5c] A benzylic methylene group adjacent to the positive nitrogen would be expected to be *ca.* 2 pK_a units more acidic. Since the pK_a of ammonia is estimated to be 35 (R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959) or 36 [N. S. Wooding and W. C. Higginson, *J. Chem. Soc.*, 774 (1952)], the acidities of the α hydrogens and of the ammonia are not greatly different.

versibly removed by conversion into the Sommelet product, and it is not unlikely that both are operative.

When **8** was treated with potassium amide and liquid ammonia the solution became blood red in color and a 79% yield of a Stevens rearrangement product (**9**) was obtained. No Sommelet or other Stevens products were found (eq 3). The conversion of **9** into the methiodide derivative and then Hofmann degradation (eq 3)

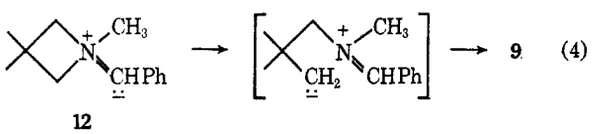


(3)

gave 4-dimethylamino-3,3-dimethyl-1-phenyl-1-butene (**10**), which was readily characterized by its nmr and ultraviolet spectra. The identification of **9** was confirmed by the Leuckart methylation of 2-phenyl-4,4-dimethylpyrrolidine (**11**).[21]

The reaction of **8** with sodium amide and liquid ammonia at a temperature (−50 to −45°) lower than that (−33°) used in the reaction with potassium amide resulted in the formation of a yellow-green color. There was obtained a 69% yield of **9** and a high boiling product which was not characterized.

As the benzylic hydrogens in **8** are probably about 100 times more acidic than the other α hydrogens,[5c] the benzylic ylide (**12**) would be formed the most readily. In addition, the rate of rearrangement of **12** must also be relatively fast since neither of the other possible rearrangement products from the methyl ylide (the Stevens as from **2** or the Sommelet as from **17**) was found. Again, no compounds which could have arisen from the ring carbanion ylide were detected and it is felt that an ion-pair mechanism as shown (eq 4) best accounts for the results.

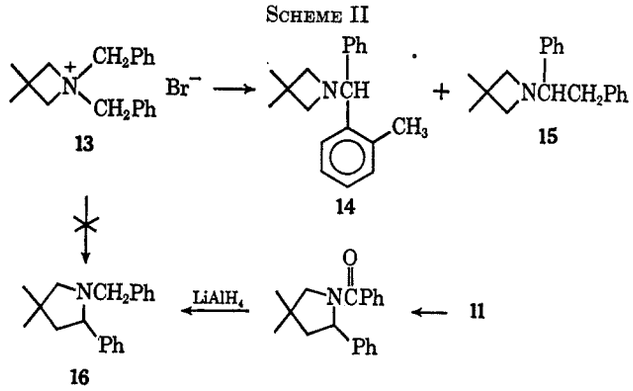


(4)

1,1-Dibenzyl-3,3-dimethylazetidinium Bromide (13).—From the reaction of **13** with either potassium amide or lithium amide in liquid ammonia were obtained a 98% yield of a Sommelet rearrangement product (**14**) and 2% yield of a Stevens rearrangement product (**15**) (see Scheme II). Potassium amide caused the reaction mixture to become red-brown in color whereas no color was produced with lithium amide. The expected ring-expanded Stevens product (**16**) was not found. To be certain that **16** was not present, it was synthesized by the lithium aluminum hydride reduction of the benzamide derivative of **11** and its gas chromatographic properties were determined and compared with those of **14** and **15**. The identity of the Sommelet product (**14**) was shown by its nmr spectrum and the comparison of the nmr spectrum of its methiodide derivative with that of the independently synthesized methobromide. The latter was prepared by the reaction

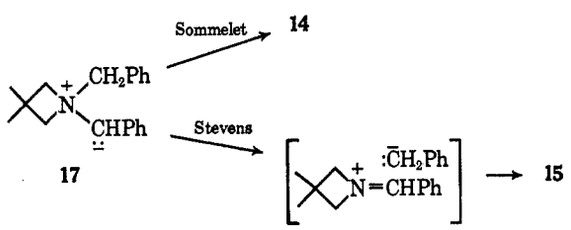
(21) A. G. Anderson, Jr., and M. T. Wills, *J. Org. Chem.*, **32**, 3241 (1967).

SCHEME II



of 1,3,3-trimethylazetidine with bromophenyl-*o*-tolylmethane.

The exclusive Stevens rearrangement with ring expansion found for both **1** and **8** made the results with **13** somewhat unexpected. This was especially true with respect to formation of **15** rather than **16**. Thus both products obtained must arise from the benzyl carbanion ylide (**17**), and the ion pair shown is con-



sidered to be the most likely intermediate in the Stevens rearrangement. In a separate experiment the reaction of **13** with sodium ethoxide in ethanol appeared to give selective (96%) nucleophilic displacement at a ring methylene rather than at a benzylic or *ortho* carbon.

Experimental Section[22]

Reaction of 1,1,3,3-Tetramethylazetidinium Iodide (1)[1] with Potassium Amide in Liquid Ammonia.—A solution of 59 mmol of KNH_2 in 150 ml of liquid NH_3 was prepared in the manner described by Hauser and Harris[23] from 2.3 g (59 mg-atom) of K metal which had been washed free of mineral oil with isooctane. Commercial anhydrous NH_3 was dried by allowing it to vaporize through a tube filled with solid NaOH. Freshly distilled cyclohexene (10 ml)[24] and then 4.2 g (17.5 mmol) of pulverized **1** were added, the latter in portions over a period of 10 min with stirring. No color developed. Stirring was continued at the boiling point (−33°) for 10 hr. After the careful addition of 3 g (59 mmol) of solid NH_4Cl, 100 ml of ether was added slowly and the NH_3 was allowed to evaporate (overnight). The residual mixture was filtered, the solid salts were washed with ether, and the total filtrate was extracted with two 50-ml portions of 5% H_2SO_4. The acidic extract was washed with two 50-ml portions of ether, then cooled and made strongly basic with 50% NaOH solution.

(22) Melting points were taken on a Thomas–Hoover capillary melting point apparatus and are uncorrected. Ultraviolet spectra were recorded with a Cary Model 14 recording spectrophotometer. Infrared spectra were recorded with a Perkin-Elmer Model 21 infrared spectrophotometer. Mass spectra were recorded by Mr. R. Buddemeier on a Consolidated Engineering Corp. mass spectrometer, Type 21-103. Nuclear magnetic resonance spectra were recorded on a Varian Associates Model A-60 analytical nmr spectrometer and values are reported in parts per million (δ) relative to tetramethylsilane as an internal standard. Vapor phase chromatographic analyses were performed on an Aerograph Model 600 (Hy-Fi) apparatus using a 0.125-in. by 5-ft column of 20% cyanosilicone (XF-1150) on 60–80 mesh Chromosorb W unless otherwise indicated. Elemental analyses were performed by Dr. A. Bernhardt, Max Planck Institute, Mülheim (Ruhr), Germany.

(23) C. R. Hauser and T. M. Harris, *J. Amer. Chem. Soc.*, **80**, 6360 (1958).

(24) Other runs were identical except that no cyclohexene was added.

A solution of the organic layer in 70 ml of ether was dried ($CaSO_4$), concentrated by distillation through a 50-cm glass helices packed column, and the residue was transferred to a small one-piece distillation apparatus. 1,3,3-Trimethylpyrrolidine (**4**) was collected (0.95 g) as a colorless liquid: bp 110–111°; $n^{25}D$ 1.4192.[25] The ethereal forerun on treatment with picric acid gave 1 g of the picrate salt of **4**, corresponding to 0.31 g of the amine. The total yield was thus 1.26 g (70%). The methiodide derivative was obtained as granular crystals, mp 330–332°. A sample of **4** gave a single peak on vapor phase chromatography over silicone (20 ft), Ucon Polar, and polyester columns: nmr (CCl_4), δ 1.03 (s, 6), 2.14 (s, 2), 2.17 (s, 3), 1.49 (t, 2, J = 3.5 Hz), and 2.44 (t, 2, J = 3.5 Hz).

Anal. Calcd for $C_7H_{15}N$: mol wt, 113. Found (mass spectroscopy): mol wt, 113.

Recrystallization of the picrate twice from absolute ethanol afforded the analytical sample, mp 220–224° dec (lit.[25] mp 226–227°).

Anal. Calcd for $C_{13}H_{18}N_4O_7$: C, 45.61; H, 5.30; N, 16.35. Found: C, 45.63; H, 5.29; N, 16.32.

The residue from the distillation yielded 15 mg of colorless plates: mp 103–104°; nmr (CCl_4), δ 0.84 (s, 9 or 10), 1.99 (s, 2), and 2.44 (s, 4). A picrate, after recrystallization from ethanol, melted at 263–266° dec. The substance was not characterized further.

Anal. Calcd for $(C_{13}H_{18}N_4O_7)_n$: C, 45.61; H, 5.30; N, 16.35. Found: C, 45.79; H, 5.38; N, 16.36.

2-Phenyl-1,4,4-trimethylpyrrolidine (**9**).—A mixture of 0.7 g (4 mmol) of 4,4-dimethyl-2-phenylpyrrolidine,[21] 1 g (20 mmol) of formic acid, and 0.5 ml (6 mmol) of aqueous 37% formaldehyde was heated to 95° and maintained at this temperature for 8 hr. The mixture was cooled, 3 ml of 4 N aqueous HCl was added, and the whole was then evaporated to dryness under reduced pressure. The brown, crystalline residue was dissolved in water and the basified (NaOH) solution was extracted with ether. The ethereal extract was dried (Na_2SO_4), concentrated, and distilled, giving 0.6 g (80%) of **9** as a colorless oil: bp 100–101° (6 mm), bp 43–44° (0.2 mm); $n^{25}D$ 1.5030. Vapor phase chromatography at 120° of a sample gave a single peak with a retention time of 3 min. After recrystallization from ethanol, the picrate melted at 111–113° and the methiodide, obtained as tiny, tan needles, melted at 201–202°. The infrared and nmr spectra were recorded.

Anal. Calcd for $C_{13}H_{19}N$: C, 82.47; H, 10.12; N, 7.40. Found: C, 82.54; H, 10.00; N, 7.47.

4-Dimethylamino-3,3-dimethyl-1-phenyl-1-butene (**10**).—A solution of 0.58 g (3.07 mmol) of 2-phenyl-1,4,4-trimethylpyrrolidine (**9**) in 3 ml of acetonitrile was treated with excess CH_3I and then stirred for 2 hr. After evaporation of the solvent and excess CH_3I, 2 ml of H_2O and 0.46 g (6 mmol) of Ag_2O were added and the mixture was stirred for 3 hr. After filtration and evaporation of the filtrate to dryness under reduced pressure, the residue (presumed to be the quaternary ammonium hydroxide) was heated at 100–150° (0.5–0.1 mm). There was obtained 0.2 g (33%) of **10** as a colorless oil, bp 89–90° (1 mm). Vapor phase chromatography on a Craig polyester column at 175° gave a single peak with a retention time of 10 min; ir (CCl_4), 6.22 μ (weak, conjugated double bond); uv max (95% EtOH) mμ (log ϵ) at 250 (4.04), 284 (2.98), and 292 (2.79); nmr (CCl_4), δ 1.07 (s, 6), 2.16 (s, 2), 2.20 (s, 6), 6.16 (s, 2), and 7.13 (m, 5).

The methiodide, after three recrystallizations from ethanol, melted at 185–186°.

Anal. Calcd for $C_{15}H_{24}NI$: C, 52.15; H, 7.01; N, 4.06. Found: C, 52.08; H, 7.14; N, 3.93.

Reaction of 1-Benzyl-1,3,3-trimethylazetidinium Iodide (8) with Alkali Amide and Liquid Ammonia. A. With Potassium Amide.—To a solution of 60 mmol of KNH_2[23] in 150 ml of liquid NH_3 was added 6.4 g (20 mmol) of **8** in portions over a period of 1 hr and the mixture was then stirred at −33° for 2 hr. During the addition the solution became deep red in color. The addition of 4 g of solid NH_4Cl discharged the color. Ether (65 ml) was added and then the NH_3 was evaporated. Filtration and evaporation of the ether gave 3.2 g of reddish oil. Distillation of 2.7 g of this product afforded 2.5 g (corresponding to 79%) of 2-phenyl-1,4,4-trimethylpyrrolidine (**9**) as a colorless oil, bp 105–106° (10 mm). Vapor phase chromatography of the product showed only one component and the substance was identical (infrared and nmr spectra, vpc retention time, and mixture melting point of picrate) with an authentic sample.

Treatment of **9** with excess CH_3I, then with Ag_2O, and, finally, heating under reduced pressure as described for the preparation of **10** gave a product which was identical (ultraviolet, infrared, and nmr spectra) with an authentic sample of **10**.

B. With Sodium Amide.—To a cooled (−50°), stirred suspension of 5.85 g (0.15 mol) of $NaNH_2$ in 300 ml of liquid NH_3 was added 15.9 g (0.05 mol) of **8** in portions over a period of 1.5 hr and then stirring was continued at −50 to −45° for 1 hr. The color of the reaction mixture was yellow-green. After the addition of 7.4 g of solid NH_4Cl the mixture was worked up as described in part A and there was obtained 6.52 g (69%) of **9**, bp 43–44° (0.2 mm), plus some higher boiling material which was not identified.

1-(Phenyl-*o*-tolylmethyl)-1,3,3-trimethylazetidinium Bromide.—An equimolar (6 mmol) mixture of phenyl-*o*-tolylmethyl bromide [bp 141–145° (0.8 mm), lit.[26] bp 136–138° (0.3 mm); $n^{25}D$ 1.6154], prepared from the treatment of the corresponding carbinol[27] with HBr,[28] and 1,3,3-trimethylazetidine[1] in CH_3CN (5 ml) was stirred at room temperature for 4 hr and then diluted with ether. The precipitated bromide salt was recrystallized from ethanol–ether, mp 124–130°. The nmr spectrum was identical with that of the corresponding iodide obtained from **14**.

Reaction of 1,1-Dibenzyl-3,3-dimethylazetidinium Bromide (13) with Alkali Amide in Liquid Ammonia. A. Potassium Amide.—To 60 mmol of KNH_2[23] in 150 ml of liquid NH_3 was added 7 g (20 mmoles) of **13** in portions over a period of 1 hr and the mixture was stirred at −33° for 2.5 hr. The red-brown color which developed was discharged when 4 g of solid NH_4Cl was added. After the addition of 75 ml of ether, the NH_3 was allowed to evaporate. Filtration and then evaporation of the ether left 5.6 g of a viscous yellow oil which solidified on standing. Distillation gave 5.2 g (98%) of a colorless oil [bp 108–110° (0.15 mm), $n^{25}D$ 1.5519] which solidified on standing, mp 48–51°. The nmr spectrum corresponded to that expected for 3,3-dimethyl-1-(phenyl-*o*-tolylmethyl)azetidine (**14**).

Anal. Calcd for $C_{19}H_{23}N$: C, 85.99; H, 8.73; N, 5.28. Found: C, 85.96; H, 8.71; N, 5.38.

The picrate after one recrystallization from ethanol melted at 233–234°. The structure of **14** was confirmed by the identity of the nmr spectrum of its methiodide, mp 150–156° dec (after recrystallization from ethanol), with that of a synthetic sample of the corresponding methobromide.

Anal. Calcd for $C_{20}H_{26}NI$: C, 58.97; H, 6.43; N, 3.44. Found: C, 59.10; H, 6.48; N, 3.56.

Vapor phase chromatography of the product at 190° indicated it to consist of 98% **14** and 2% a substance which was identified by its retention time as 3,3-dimethyl-1-(1,2-diphenylethyl)-azetidine (**15**).[21] No evidence for the presence of **16** was found.

B. With Lithium Amide.—To the $LiNH_2$ formed from 0.105 g (15 mg-atoms) of Li wire and 50 ml of dry liquid NH_3 as given in the literature[29] was added with stirring 1.73 g (5 mmol) of **13** over a 20-min period and stirring was continued at −33° for 4 hr. No color developed. The mixture was worked up as described under part A and afforded 1.28 g (97%) of product as a yellow oil which was identical (picrate, mp 233–234°; vapor phase chromatographic analysis showed 98% **14** and 2% **15**) with that obtained in A. No **16** was found.

1-Benzyl-4,4-dimethyl-2-phenylpyrrolidine (**16**).—Benzoyl chloride (1.4 g, 10 mmol) was slowly added to 0.85 g (5 mmol) of 4,4-dimethyl-2-phenylpyrrolidone,[21] with stirring, followed by 4 ml of 10% NaOH. Stirring was continued for 30 min and the mixture was then extracted with 50 ml of ether. The ethereal extract, after being washed with dilute sodium hydroxide and then water, was evaporated to dryness. Recrystallization of the residue from aqueous ethanol and then from absolute methanol gave 1.3 g (61%) of a product presumed to be the benzoyl derivative, mp 104–106°.

A solution of the derivative in 30 ml of dry ether was added over a 5-min period to 30 ml of ether containing 0.5 g of $LiAlH_4$.

(25) N. J. Leonard and V. W. Gash, *J. Amer. Chem. Soc.*, **76**, 2781 (1954). These authors reported bp 77–79° and $n^{20}D$ 1.3842 for **4**. The discrepancy between these values and those of the present work led to the further characterization of our product.

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The mixture was refluxed for 4 hr, treated with 2 ml of saturated Na_2CO_3, filtered, and finally extracted with 30 ml of 5% aqueous HCl. The acidic extract was extracted with ether and then basified with excess 50% NaOH. The organic layer which formed was taken up in ether and the dried (Na_2SO_4) ether solution was evaporated to dryness. Distillation of the residue under reduced pressure gave 0.72 g (55%) of **16** as a colorless oil [bp 119–120° (0.2 mm), $n^{24}D$ 1.5467] which solidified on standing, mp 48.5–49.5°. The nmr spectrum was consistent with the structure assigned.

Anal. Calcd for $C_{19}H_{23}N$: C, 85.99; H, 8.73; N, 5.28. Found: C, 86.14; H, 8.84; N, 5.36.

The picrate melted at 125–127° after recrystallization from ethanol.

Reaction of 1,1-Dibenzyl-3,3-dimethylazetidinium Bromide (13) with Sodium Ethoxide.—Compound **13** (5 mmol, 1.73 g) was added to 50 ml of ethanol containing 20 mmol (1.36 g) of sodium ethoxide and the homogeneous solution was refluxed for 10 hr. Water (25 ml) was then added and the ethanol was removed by distillation. An ethereal extract of the residue was dried over Na_2SO_4 and the solvent was then evaporated. The yellow oil (1.5 g, 96%) which remained, $n^{25}D$ 1.5268, was indicated to be 3-dibenzylamino-2,2-dimethyl-1-ethoxypropane by its relatively long (10.5 min) retention time on vapor phase chromatography at 195°, by its infrared spectrum, and by its nmr spectrum (CCl_4): δ 0.75 (s, 6), 2.42 (s, 2), 3.02 (s, 2), 3.54 (s, 4), 1.05 (t, 3, J = 3.5 Hz), 3.26 (q, 2, J = 3.5 Hz), and 7.20 (m, 10).

Registry No.—**4**, 16911-20-9; **4** methiodide, 16959-96-9; **9**, 16911-21-0; **9** picrate, 16911-22-1; **9** methiodide, 16957-22-5; **10**, 16911-23-2; **10** methiodide, 16911-24-3; **14**, 16911-25-4; **14** methiodide, 16911-26-5; **14** picrate, 16911-27-6; **16**, 16911-28-7; **16** picrate, 16911-29-8; 3-dibenzylamino-2,2-dimethyl-1-ethoxypropane, 16911-30-1; ammonia, 7664-41-7.

Pyrrolo[1,2-*a*]indole Chemistry. Reactions of a Tridentate Carbanion[1]

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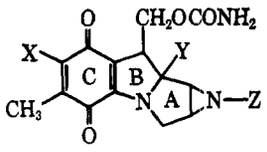
The pyrrolo[1,2-*a*]indole anion **8** has been acylated by a group of electrophiles, including ethyl carbonate, ethyl chloroformate, dimethyl oxalate, phenyl isocyanate, and carbon dioxide. Its tridentate character has been demonstrated by the isolation of products arising from attack at the 1, 3, and 9 positions. One product, the ester **11**, is the first simple example of the 3H-pyrrolo[1,2-*a*]indole system. The chemistry of ester **11** was studied, to no avail, as a possible route to the mitomycin structural array **1** or **2**.

The tetracyclic array of the mitomycins **1** and the stereochemically simpler aziridinomitosenes **2** is a



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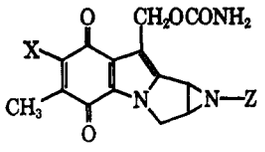

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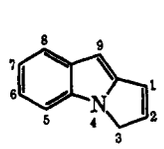
unique heterocyclic system with potent biological activity.[2] Substantial progress has been made by a Lederle group[3] in the elaboration of synthetic pathways to various tricyclic derivatives in the pyrrolo[1,2-*a*]indole series. However, the final attainment of a tetracyclic product by attaching an aziridine moiety to the tricyclics using a variety of cyclization methods was not achieved.

Our paper approach to the synthetic problem of aziridine annelation was to obtain a tricyclic compound **3** with unsaturation in the position appropriate for ring addition *via* the elegant method of dipolar addition of azide[4] followed by subsequent photochemical decomposition of the resultant triazoline.[5] The major drawback to our scheme was that the simple 3H-pyrrolo-[1,2-*a*]indole structure **3** was not known. The early report of a dehydrative acetylation of N-phenacylanthranilic acid to afford 9-hydroxy-3-keto-1-phenyl-3H-pyrrolo[1,2-*a*]indole (**4**) is not correct.[6,7] The enamine **5**, not completely characterized, may be an example of the desired system.[3b] An authentic, but more complex, 3 H derivative, the 3-methylenecarboxylate **6**, has



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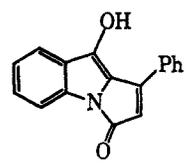

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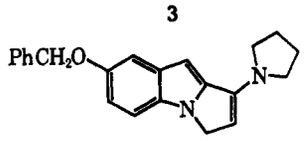

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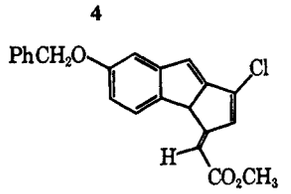

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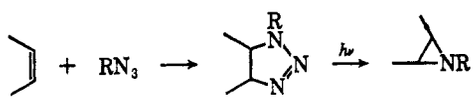
been characterized as well.[8] Two independent syntheses directed toward the preparation of the simple heterocycle **3** both afforded the isomeric 9H-pyrrolo-[1,2-*a*]indole (**7**). The Hofmann elimination route (Scheme I, path 1)[3b] and the elegant and general heterocyclic synthesis *via* a vinylphosphonium salt (Scheme I, path 2)[9] are usually unambiguous, position-specific



(1) (a) Presented at the Third Middle Atlantic Meeting of the American Chemical Society, Philadelphia, Pa., Feb 2, 1968, Abstracts, p H74. (b) Taken from the Ph.D. Thesis of K. F. B., Fordham University, 1968. (c) This research was supported by a grant from the Public Health Service, NIH GM 12758, for which we are most grateful.

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