Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.75; H, 11.09; N, 6.56.

The alcohol **21** underwent 70% conversion to the formate (**22**) by prolonged (7 days) treatment with 75% (but not 90%) aqueous formic acid at 100°. The formate was reconverted to **21** by treatment with lithium aluminum hydride in ether. An analytical sample of **22** was prepared by vpc.

Anal. Calcd for $C_{14}H_{25}NO_2$: C, 70.85; H, 9.77; N, 5.90. Found: C, 71.21; H, 9.90; N, 5.88.

The acetate (**23**) was prepared by heating alcohol **21** and acetic anhydride for 16 hr at 100°. An analytical sample was prepared by vpc.

Anal. Calcd for $C_{15}H_{25}NO_2$: C, 71.67; H, 10.03; N, 5.57. Found: C, 71.79; H, 10.04; N, 5.41.

Analysis by vpc of the filtrate of the Clarke–Eschweiler product showed five major components constituting, in order of increasing retention times, 7.5%, 7%, 19%, 33%, and 22% of the total of 7.8 g. By retention times, the third proved to be the crystalline amino alcohol **21** and the fifth the formate thereof (**22**). Treatment of the entire sample with lithium aluminum hydride cleaved the formate, and on prolonged standing in concentrated ether solution most of alcohol **21** crystallized. Chromatography of the remaining liquid portion on Merck acid-washed alumina and elution first with ether, then with methanol, separated the two more volatile products from the major component (**27**). An analytical sample of **27** was prepared by vpc.

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.59; H, 11.07; N, 6.69. Found: C, 74.01; H, 11.06; N, 6.53.

The methiodide of **27**, recrystallized from isopropyl alcohol–THF, had mp 170–178°.

Anal. Calcd for $C_{14}H_{26}NOI$: C, 47.86; H, 7.46; N, 3.99. Found: C, 47.72; H, 7.60; N, 3.85.

On treatment with 65% formic acid for 90 hr at 100°, **27** was half converted to a mixture of the original two volatile products, **28** and **29**, the longer retained (**28**) predominating by 3:2. An analytical sample of **28**, prepared by vpc, had mp 28–32°.

Anal. Calcd for $C_{13}H_{21}N$: C, 81.61; H, 11.06; N, 7.82. Found: C, 81.00; H, 10.97; N, 7.38.

An analytical sample of **29** was prepared by vpc.

Anal. Calcd for $C_{13}H_{21}N$: C, 81.61; H, 11.06; N, 7.82. Found: C, 81.31; H, 10.93; N, 7.37.

Octahydro-2,6,6-trimethyl-7H-4a,7-methanoisoquinolin-5-one (**24**).—To 0.25 g of amino alcohol **21** in 4 ml of acetone was added dropwise with cooling 1 ml of Jones reagent, prepared by adding 12.5 g of chromic anhydride and 10.5 ml of concentrated sulfuric acid to 36 ml of water. The oxidation mixture was stirred for 1 hr, then made basic with sodium hydroxide, and extracted with ether. Evaporation of the extract left 0.25 g of colorless oil, by vpc a single material.

Anal. Calcd for $C_{13}H_{21}NO$: C, 75.31; H, 10.21; N, 6.76. Found: C, 75.22; H, 10.20; N, 6.54.

Mass Spectra.—Mass spectra were obtained routinely and were of major importance in confirming assigned structures; in particular, all cyclic Clarke-Eschweiler products gave strong molecular ion peaks. In Table I are listed the major peaks of higher mass for the cyclic products. We shall not speculate here on the nature of the fragmentation products, but it will be seen that the fragmentation patterns are consistent with the structures assigned.

TABLE I

Compd	Molecular ion	Other major peaks
trans-**2**	171	156, 138, 112
11	129	128, 114, 112, 111, 110, 96
trans-**7**	157	142, 124, 110, 98
14	143	142, 128, 126, 110, 84, 82
17	157	155, 142, 124, 112
21	209	208, 207, 206, 194, 190, 180, 179, 178, 148
22	237	236, 209, 194
23	251	250, 248, 208, 192, 190
27	209	194, 192, 191, 190, 176, 151, 150, 148
28	191	190, 176, 148, 134, 122
29	191	190, 176, 148, 123, 122

Acknowledgment.—We gratefully acknowledge the contribution of Dr. Elizabeth P. Burrows, who determined all of the mass spectra.

The Synthesis of Some Substituted 3-Nitro-1,5-pentanediamines[1]

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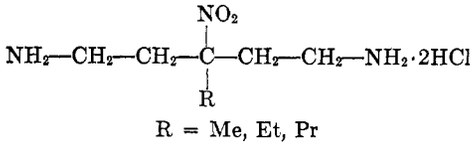
Alkyl-substituted 3-nitro-1,5-pentanediamines were synthesized from the corresponding substituted heptanediamides using the Hofmann reaction and from the substituted heptanedioic acids using the Curtius reaction. The expected piperidine was not obtained on pyrolysis of the dihydrochloride of 3-nitro-3-methyl-1,5-pentanediamine.

A limitation to the classical Ladenburg[3] synthesis of piperidine from the hydrochloride of pentanediamine is the availability of the starting diamines. In an attempt to extend this procedure to the synthesis of 4-substituted 4-nitropiperidines, we have synthesized a series of 3-nitro-3-alkylpentanediamines (I) and have examined



R = Me, Et, Pr

the behavior of one of these under pyrolytic conditions. The properties of these diamine dihydrochlorides and their precursors are summarized in Table I.

(1) Presented at the Southeast-Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec 1965.

(2) Abstracted in part from the M.S. Thesis of R. L. Johnson, University of Kentucky, 1962.

The diamines were obtained from the 4-nitro-4-alkylheptanediamides using the Hofmann reaction and from the 4-nitro-4-alkylheptanedioic acids using the Curtius reaction. The acid did not produce the diamine when Schmidt reaction conditions were used. The diacids and diamides in turn were obtained from reaction of an acrylic acid derivative with the appropriate nitroalkane.

The disubstituted heptanediamides reacted smoothly with alkaline sodium hypobromite to yield the 3-alkyl-3-nitro-1,5-pentanediamines (I) isolated as the dibenzoyl derivatives. Attempts to isolate the free amine directly from the reaction mixture failed.

The acid hydrolysis of the dibenzoyl derivatives of the 3-alkyl-3-nitro-1,5-pentanediamines (I) becomes increasingly difficult with increasing size of the alkyl group. Thus, the methyl compound is hydrolyzed with

(3) A. Ladenburg, *Ber.*, **17**, 388, 513 (1884).

TABLE I

PROPERTIES OF THE NITRO COMPOUNDS

R	Mp, °C	Recrystn solvent	Yield, %	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
				4-Nitro-4-alkylheptanediamides						
Me	134.5–135[a]	2-Propanol	39	$C_8H_{15}N_3O_4$	44.23	6.96	19.34	44.68	7.14	19.32
Et	91–92	Water	69	$C_9H_{17}N_3O_4$	46.79	7.43	18.18	46.58	7.38	17.92
Pr	123.5–124	Water	60	$C_{10}H_{19}N_3O_4$	48.98	7.75	17.14	49.01	7.78	17.00
				4-Nitro-4-alkylheptanedioic Acids						
Me	114–115[b]	Dichloroethane	29[c] (53)[d]	$C_8H_{13}NO_6$	43.85	5.97	6.39	44.18	6.08	6.00
Et	141–141.5	Water	60[c]	$C_9H_{15}NO_6$	46.35	6.48	6.01	46.77	6.48	5.92
Pr	138–139	Water	92[e]	$C_{10}H_{17}NO_6$	48.58	6.93	5.67	48.56	6.86	5.95
				N,N-Dibenzoyl-3-nitro-3-alkyl-1,5-pentanediamines						
Me	125–126	Chloroform–ether	53	$C_{20}H_{23}N_3O_4$	65.02	6.27	11.37	65.38	6.42	11.10
Et	190–191	Methanol	82	$C_{21}H_{25}N_3O_4$	65.78	6.53	10.98	65.65	6.37	11.03
Pr	175–176	Methanol	51	$C_{22}H_{27}N_3O_4$	66.49	6.85	10.58	66.06	7.04	10.35
				Dihydrochlorides of 3-Nitro-3-alkyl-1,5-pentanediamines						
Me	246–249 dec	Methanol	64 (38)[f]	$C_6H_{17}N_3O_2Cl_2$	30.80	7.33	17.65	30.72	7.42	18.11[g]
Et	234–235 dec	Methanol–ethyl acetate	44 (41)[f]	$C_7H_{19}N_3O_2Cl_2$	34.00	7.69	17.00	33.80	7.82	16.95[h]
Pr	235.5–237 dec	Methanol–ether	15 (45)[f]	$C_8H_{21}N_3O_2Cl_2$	36.78	8.04	16.09	36.50	8.25	15.97

[a] Lit.[6] mp 129.5–131°. [b] Lit. mp 111–112°: V. I. Isagulyants and E. L. Markosyan, *Zh. Prikl. Khim.*, **37**, 1195 (1964). [c] Yield based upon nitroethane used in cyanoethylation followed by hydrolysis. [d] Yield based on nitroethane used in reaction with methyl acrylate, followed by hydrolysis. [e] Yield based on corresponding amide. [f] Over-all yields based on the substituted 4-nitroheptanedioic acid used in the Curtius reaction. [g] *Anal.* Calcd: Cl, 30.31. Found: Cl, 30.25. [h] *Anal.* Calcd: Cl, 28.34. Found: Cl, 28.90.

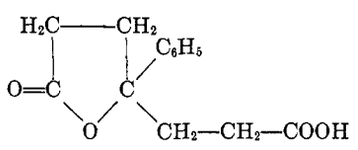
6 *N* hydrochloric acid in 60% yield while the propyl compound requires longer reaction times in an acetic acid–hydrochloric acid mixture to give a 15% yield.

The reaction of nitroethane, 1-nitropropane, and 1-nitrobutane with acrylamide (adapted from the procedure of Bruson[4]) to form the disubstituted heptanediamides occurred best when 40% aqueous potassium hydroxide was used as the catalyst. When Triton B was employed as catalyst, nitroethane and 1-nitropropane gave the disubstituted nitroalkanes while phenylnitromethane and 1-nitrobutane yielded only the monosubstituted nitro compound. Even with the potassium hydroxide catalyst, phenylnitromethane gave only 4-phenyl-4-nitrobutyramide. Although the cyanoethylation of phenylnitromethane has been reported to produce 4-nitro-4-phenylheptanedinitrile[5] this compound has not been isolated in our experiments using the same conditions. Application of the procedure of Wakamatsu and Shimo[6] in which a liquid ammonia solvent in a pressure vessel is used yielded the dinitrile. The elemental analysis and infrared and nmr spectra were consistent with the dinitrile structure. The melting point previously reported[5] for this compound showed considerable deviation from that observed in our laboratory.

Some difficulty was encountered in the formation of crystalline products during the isolation and purification of the heptanediamides since these compounds are strongly solvated.

The Curtius procedure was derived from a combination and modification of the procedures reported by Weinstock[7] and by Herzog, Gold, and Geckler.[8] The procedure generally produced better over-all yields of the diamine dihydrochlorides (38–45%) than the Hofmann procedure, and purification of intermediates was not required.

The precursor diacids were obtained by hydrolysis of the acrylic acid derivative adduct of the appropriate nitroalkane. The use of dilute hydrochloric acid and short reaction times provided good yields of the diacid. When 4-nitro-4-phenylheptanedinitrile was hydrolyzed under these conditions only the lactone II was obtained



II

in poor yield. A similar observation was reported by Westfahl[9] during the prolonged hydrolysis of 4-nitro-4-methylheptanedinitrile.

Because 3-nitro-3-methylpentanediamine is a substituted ptomaine, its acute oral toxicity was evaluated.[10] Surprisingly no effect was observed.

3-Nitro-3-methyl-1,5-pentanediamine was obtained from the dihydrochloride by treatment with sodium hydroxide. The compound appeared to be stable on distillation under nitrogen at 1 mm and on standing in a sealed ampoule for several months. Distillation of the substance at atmospheric pressure resulted in complete decomposition. Gas chromatographic analysis showed at least 13 components in the products, none of which was identified.

Pyrolysis of the dihydrochloride or the monohydrochloride of 3-nitro-3-methyl-1,5-pentanediamine produced considerable decomposition. A complex mixture of seven components along with some starting material was obtained.

Experimental Section

Melting points were taken on a Fisher-Johns melting point block and are uncorrected. Boiling points are uncorrected.

The following experiments are representative of those used to produce the compounds listed in Table I.

(4) H. A. Bruson, U. S. Patent, 2,370,142 (Feb 27, 1945).
(5) G. S. Misra and R. S. Asthana, *Ann.*, **609**, 240 (1957).
(6) S. Wakamatsu and K. Shimo, *J. Org. Chem.*, **27**, 1069 (1962).
(7) J. Weinstock, *ibid.*, **26**, 3511 (1961).
(8) L. Herzog, M. Gold, and R. Geckler, *J. Am. Chem. Soc.*, **73**, 751 (1951).
(9) J. C. Westfahl, *ibid.*, **80**, 3428 (1958).
(10) Mead Johnson Research Center, Evansville, Ind.

4-Nitro-4-methylheptanediamide.—The procedure is that of Bruson.[4] To a stirred mixture of 80 g (1.12 moles) of acrylamide, 30 g (0.40 mole) of nitroethane, and 250 ml of dioxane, aqueous 40% potassium hydroxide was added until the pH was ~8.5. After the initial exothermic reaction subsided, heating was continued at 50° until the green color became orange (about 10 hr). After neutralization with dilute hydrochloric acid and evaporation to dryness, the product was recrystallized.

4-Nitro-4-phenylbutyramide.—When 100 ml of dioxane, 23 g (0.16 mole) of phenylnitromethane, 25 g (0.35 mole) of acrylamide, and about 5 ml of 4% aqueous potassium hydroxide were heated at 50° for 10 hr, the characteristic green color did not develop. On the usual work-up, 9.5 g of a white, crystalline product, mp 98–99°, was obtained. The material was base soluble and a green color was obtained on acidification of the basic solution.

Anal. Calcd for $C_{10}H_{12}N_2O_3$: C, 57.69; H, 5.77; N, 13.45. Found: C, 57.59; H, 5.91; N, 13.01.

Longer reaction periods or reaction of acrylamide with the 4-nitro-4-phenylbutyramide did not produce the substituted heptanediamide.

4-Nitro-4-methylheptanedioic Acid.—4-Nitro-4-methylheptanedinitrile was synthesized by the method of Wakamatsu and Shimo[6] from 75 g (1.0 mole) of nitroethane, 106 g (2.0 moles) of acrylonitrile, and 300 ml of liquid ammonia at −50°. After evaporation of the liquid ammonia the crude product was directly hydrolyzed with 250 ml of 18% hydrochloric acid (2-hr reflux period). The acid was decanted and the residue was refluxed with fresh acid for an additional 2-hr period. The acid solutions were removed by distillation *in vacuo* and the residue was recrystallized.

Methyl acrylate when used in place of acrylonitrile gave better yields.

The dinitrile could be produced in 60–70% yield by application of the procedure of Kanbe and Yasuda[11] in which a potassium fluoride catalyst in an ethanol solvent is used.

4-Nitro-4-phenylheptanedinitrile.—The procedure of Wakamatsu and Shimo[6] was adapted using a mixture of 15 g (0.091 mole) of phenylnitromethane, 19 g (0.18 mole) of acrylonitrile, and 100 ml of liquid ammonia in a pressure bottle at room temperature. After evaporation of the ammonia, the solid was removed by filtration and the filtrate was retreated with 3 g of acrylonitrile in liquid ammonia. After recrystallization from absolute methanol a total of 8.1 g (30%) of white crystals was obtained, mp 99–100°. Further recrystallization raised the melting point to 101–102° (lit.[5] mp 206–207°).

Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.33; H, 5.39; N, 17.21. Found: C, 64.39; H, 5.06; N, 17.49.

The infrared spectrum showed tertiary nitro absorption at 1545 cm^{-1} and the nmr spectrum showed a ratio of eight aliphatic protons to five aromatic protons. Benzylic protons were not observed.

Hydrolysis of 4-Nitro-4-phenylheptanedinitrile.—The nitrile (9.5 g) was heated at 80–90° with 140 ml of 18% hydrochloric acid for 4 hr, and the acid was evaporated on a rotary evaporator. The residue was extracted four times with 100 ml of chloroform and the extracts were dried over magnesium sulfate. The residue obtained after removal of drying agent and chloroform was recrystallized from water yielding 1.9 g (22%) of crystalline solid, mp 110–112°. Additional recrystallizations raised the melting point to 117–118°.

Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.65; H, 6.03. Found: C, 66.32; H, 5.72.

Elemental analysis indicated the absence of nitrogen. The infrared spectrum ($CHCl_3$) showed absorption at 1770 (γ-lactone carbonyl), 1708 (carboxylic acid carbonyl), 1170 (ester), and 1055 cm^{-1} (ester). Typical nitro absorption was not observed.

N,N′-Dibenzoyl-3-nitro-3-methyl-1,5-pentanediamine.—The procedure was adapted from the method of von Braun and Jostes.[12] A solution of sodium hypobromite was prepared at 0–5° by adding 155 g of bromine to a mixture of 215 g of sodium hydroxide, 425 ml of water, and 600 g of ice. To this solution, 100 g (0.46 mole) of 4-nitro-4-methylheptanediamide was added slowly so that the temperature did not exceed 10°. After an additional hour at 5–10°, the solution was heated to 50° and maintained at 50° for 5 hr. After cooling to room temperature, 280 g (2.0 moles) of benzoyl chloride was added portionwise with shaking. The solid which separated was removed, washed with water, and then dissolved in chloroform. The chloroform extract was washed with three 50-ml portions of 20% sodium hydroxide and then with dilute hydrochloric acid. Ether was added to the chloroform solution until the cloudpoint and then cooled to −25° overnight. The product was recrystallized from chloroform–ether.

N,N′-Dibenzoyl-3-nitro-3-ethyl-1,5-pentanediamine.—The procedure is similar to that used for the methyl compound except that the solid obtained was washed with water, dilute base, dilute acid, and ether, successively, followed by recrystallization from methanol.

3-Nitro-3-methyl-1,5-pentanediamine Dihydrochloride. A. Hydrolysis of the Dibenzoyl Derivative.—A mixture of 31.5 g (0.086 mole) of the dibenzoyl derivative and 300 ml of 6 *N* hydrochloric acid was refluxed for 16 hr. The solution was cooled, extracted with three 50-ml portions of ether, and evaporated to dryness under reduced pressure. The residue was recrystallized.

B. Curtius Reaction.—A mixture of 22 g (0.1 mole) of 4-nitro-4-methylheptanedioic acid and 40 ml of thionyl chloride was heated on a water bath until solution of the acid was complete and then heated for an additional 2 hr. The solution was cooled and filtered through a fritted-glass funnel, and the excess thionyl chloride was removed using a rotary evaporator. A solution of the acid chloride in 60 ml of acetone was added dropwise to a solution of 26 g (0.4 mole) of sodium azide in 60 ml of water at 0–5°. After the solution was stirred for 1 hr more, 100 ml of water was added and the red oil which separated was taken up in 100 ml of toluene. After the toluene extract was dried with magnesium sulfate, the solution was heated carefully until a gentle evolution of nitrogen resulted. (In one experiment the nitrogen evolution became violent.) When the nitrogen evolution subsided, the solution was heated overnight at 100°. The residue obtained upon evaporation of the toluene was treated with 60 ml of concentrated hydrochloric acid, heated carefully until the evolution of carbon dioxide subsided, and then refluxed overnight. The concentrated hydrochloric acid was removed by distillation under reduced pressure and the residue was dissolved in 3% hydrochloric acid and treated with decolorizing charcoal. After filtration through Celite and evaporation of the filtrate, the residue was triturated with 25 ml of absolute ethanol. The dibenzoyl derivative of the product was identical with the Hofmann reaction product. The melting point of a mixture of the product with an authentic sample was not depressed.

3-Nitro-3-methyl-1,5-pentanediamine.—A solution (100 g) of 40% aqueous sodium hydroxide was added to 17.4 g (0.075 mole) of 3-nitro-3-methyl-1,5-pentanediamine dihydrochloride. The amine was extracted with three 30-ml portions of chloroform and the extract was dried over magnesium sulfate. After removal of the drying agent and distillation of the chloroform, the residue was distilled under reduced pressure in a nitrogen atmosphere. The yield was 5.9 g (49%) of colorless liquid, bp 127.0–127.5° (1 mm), $n^{26}D$ 1.4858.

Anal. Calcd for $C_6H_{15}N_3O_4$: C, 44.72; H, 9.31; N, 26.08. Found: C, 44.64; H, 9.53; N, 26.27.

Attempted distillation at atmospheric pressure under a nitrogen atmosphere produced a colorless distillate. Gas chromatographic analysis of the distillate using a 4-ft SE-30 column at 250° showed the distillate to be a mixture consisting of 13 components, none of which was starting material.

Pyrolysis of 3-Nitro-3-methyl-1,5-pentanediamine Monohydrochloride.—Freshly prepared silver oxide (0.025 mole) was added to an aqueous solution containing 11.5 g (0.05 mole) of 3-nitro-3-methyl-1,5-pentanediamine dihydrochloride. The insoluble material was removed by filtration and the filtrate was evaporated to dryness *in vacuo*. The dry residue was heated to its decomposition point (185–190°) under nitrogen, and the temperature was gradually raised to 250° and maintained at this temperature for 45 min. After cooling, the residue was extracted with chloroform and dissolved in water, and the aqueous solution was made strongly alkaline. Extraction of the solution with chloroform, followed by drying of the extract and removal of the chloroform, produced a dark brown oil. Analysis of the oil by gas chromatography using a 4-ft SE-30 column at 250° showed seven components in the oil, one of which was identical with the free amine. Further identification or separation of the components was not achieved.

(11) S. Kanbe and H. Yasuda, *Sci. Papers Inst. Phys. Chem. Res.* (Tokyo), **58**, 148 (1965).

(12) J. V. von Braun and F. Jostes, *Ber.*, **59**, 1091 (1926).

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Cyclization of 4-Acetyl-1-dialkylamino-1-cyclohexenes to 4-(Dialkylamino)bicyclo[2.2.2]octan-2-ones[1]

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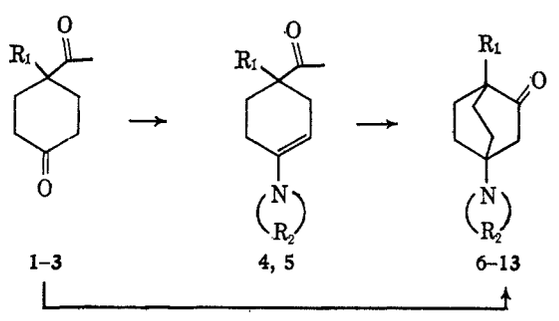
An acid-catalyzed cyclization of 4-acetyl-1-dialkylamino-1-cyclohexenes leading to 4-(dialkylamino)bicyclo-[2.2.2]octan-2-ones has been reported.

In a previous publication,[2] we reported an acid-catalyzed cyclization of 4-acetyl-1-methoxy-1-cyclohexene leading to 4-methoxybicyclo[2.2.2]octan-2-one. We would now like to describe a novel cyclization[3] of 4-acetyl-1-dialkylamino-1-cyclohexenes leading to 4-(dialkylamino)bicyclo[2.2.2]octan-2-ones.

Reaction of 4-acetyl-4-methyl-1-cyclohexanone (**2**) with morpholine in boiling benzene afforded 4-acetyl-4-methyl-1-morpholino-1-cyclohexene (**5**).[5] Treatment of **5** with a catalytic amount of acetic acid at 180–205° for 7.5 hr gave 1-methyl-4-morpholinobicyclo-[2.2.2]octan-2-one (**9**) in 70% yield. The transformation could be carried out without isolating enamine **5**. Thus, a reaction of a toluene solution of 4-acetyl-4-methyl-1-cyclohexanone (**2**) with morpholine in the presence of *p*-toluenesulfonic acid furnished **9** in 71% yield.

An analogous cyclization was carried out with other secondary amines. Reaction of 4-acetyl-4-methyl-1-cyclohexanone (**2**) with piperidine in the presence of an acid catalyst furnished 1-methyl-4-piperidinobicyclo[2.2.2]octan-2-one (**10**), and with pyrrolidine 1-methyl-4-pyrrolidinobicyclo[2.2.2]octan-2-one (**11**). Variations in substituents in the 4 position of the 4-acetyl-1-cyclohexanone structure had little influence on the reaction. Reaction of 4-acetyl-1-cyclohexanone (**1**) and 4-acetyl-4-phenyl-1-cyclohexanone (**3**) each with secondary amines such as morpholine, pyrrolidine, or piperidine gave the 4-(dialkylamino)bicyclo[2.2.2]-octan-2-ones, respectively. Table I summarizes the physical constants of the 4-(dialkylamino)bicyclo-[2.2.2]octan-2-ones (**6–13**).

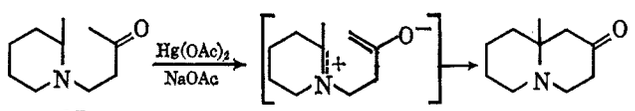


1, R_1 = H
2, R_1 = CH_3
3, R_1 = C_6H_5
4, R_1 = H; R_2 = $(CH_2)_2O(CH_2)_2$
5, R_1 = CH_3; R_2 = $(CH_2)_2O(CH_2)_2$
6, R_1 = H; R_2 = $(CH_2)_2O(CH_2)_2$
7, R_1 = H; R_2 = $CH_2(CH_2)_3CH_2$
8, R_1 = H; R_2 = $CH_2(CH_2)_2CH_2$
9, R_1 = CH_3; R_2 = $(CH_2)_2O(CH_2)_2$
10, R_1 = CH_3; R_2 = $CH_2(CH_2)_3CH_2$
11, R_1 = CH_3; R_2 = $CH_2(CH_2)_2CH_2$
12, R_1 = C_6H_5; R_2 = $(CH_2)_2O(CH_2)_2$
13, R_1 = C_6H_5; R_2 = $CH_2(CH_2)_3CH_2$

Assignments of structures for cyclization products are based on the nmr and infrared spectra (*cf.* Table I). The nmr spectra of cyclization products confirmed the presence of an isolated methylene group α to the carbonyl group, τ 7.50–7.80; a bridgehead hydrogen for compounds **6**, **7**, and **8**, τ 7.75–7.90; a tertiary methyl group for compounds **9**, **10**, and **11**, τ 9.06–9.14; a phenyl group for compounds **12** and **13**, τ 2.74–2.75. Infrared spectra of cyclization products confirmed the presence of a carbonyl group (*cf.* Table I).

It appears that cyclization[6] of 4-acetyl-1-dialkylamino-1-cyclohexenes proceeds *via* iminium ions in a way that is formally analogous to the cyclization[2] of 4-acetyl-1-methoxy-1-cyclohexene (**14**) leading to 4-methoxybicyclo[2.2.2]octan-2-one (**15**). The mechanism involves reaction of an iminium ion and an enolate anion[8] (*cf.* **16**). Reaction of iminium ions are known to undergo rapid attack by a wide variety of nucleophilic agents.[10]

(6) The cyclization may be compared with that[7] of a Mannich base (**17**) leading to compound **18** in the presence of mercuric acetate and sodium acetate.



(1) Bridged Ring Compounds. VI. Paper V: K. Morita and Z. Suzuki, *J. Org. Chem.*, **31**, 233 (1966).

(2) K. Morita and T. Kobayashi, *ibid.*, **31**, 229 (1966).

(3) An acid-catalyzed condensation of an enamine with aldehydes has been reported to furnish α,β-unsaturated aldehydes.[4]

(4) N. V. Volkova and A. A. Yasnikov, *Dokl. Acad. Nauk SSSR*, **149**, 94 (1963).

(5) K. Morita, M. Nishimura, and H. Hirose, *J. Org. Chem.*, **30**, 3011 (1965).

(7) F. Bohlman and O. Schmidt, *Chem. Ber.*, **97**, 1354 (1964).

(8) The mechanism of Mannich reaction presumably involves reaction of an iminium ion derived by a condensation of a carboxyl compound with an amine and an active methylene group.[9]

(9) T. S. Cummings and J. R. Shelton, *J. Org. Chem.*, **25**, 419 (1960). Also see, H. Böhme and H. Ellenberg, *Chem. Ber.*, **92**, 2976 (1959).

(10) The reaction of iminium ion with Grignard reagents, lithium alkyls, and potassium cyanide [N. J. Leonard and A. S. Hay, *J. Am. Chem. Soc.*, **78**, 1984 (1956); R. M. Scribner, *J. Org. Chem.*, **30**, 3203 (1965)], and with 3-bromopropylamine leading to a synthesis of tetrahydropyridine nuclei [R .F. Parcell, *J. Am. Chem. Soc.*, **81**, 2596 (1959); R. D. Parcell and F. P. Hauck, *J. Org. Chem.*, **28**, 3468 (1963)] has been reported.