Registry No.—1, 17206-75-6; 2, 17202-30-1; 1,2-cyclononadiene, 1123-11-1; 2,3-dibromocyclohexene, 17202-32-3.

New Synthesis of Some 1,5-Diazacyclooctanes

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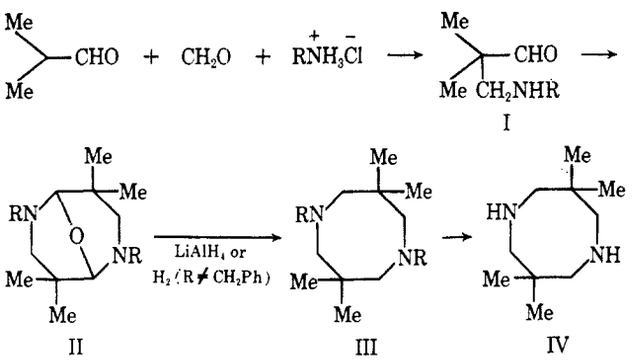
This is to report a new synthesis of 1,5-diazacyclooctanes substituted in the 3 and 7 positions (III). The sequence involves reductive cleavage of the oxygen bridge of a 9-oxa-2,6-diazabicyclo[3.3.1]nonane II, which is readily formed by condensation of the secondary β-amino aldehyde I obtained in the Mannich reaction of an α,α-disubstituted aldehyde, formaldehyde, and a primary amine hydrochloride. When R = benzyl, further hydrogenolysis of III leads to the disecondary amine IV.



The condensation of secondary β-amino aldehydes of type I was first observed by Mannich and Wieder,[1] who postulated structure II for these products on the basis of elemental analysis. This structure has now been verified by nmr spectroscopy. It has also been found that the rate of condensation is greatly increased by acid catalysis. Reduction of the 9-oxa-2,6-diazabicyclo[3.3.1]nonane II (R = Me) was effected in high yield (~80%) by lithium aluminum hydride or quantitatively by catalytic hydrogenolysis, using rhodium-on-alumina catalyst in acetic acid solvent. 3,3,7,7-Tetramethyl-1,5-diazacyclooctane (IV) was obtained by a two-stage reduction of II (R = CH_2Ph): lithium aluminum hydride reduction to III (R = CH_2Ph) in 78% yield, followed by quantitative catalytic reduction of III (R = CH_2Ph) using Pd–C in ethanol as solvent.[2]

The rate of the condensation reaction is dependent upon the nature of the substituent group R. Mannich and Wieder[1] reported that, when R = Me, a 40% yield of the 9-oxa-2,6-diazabicyclo[3.3.1]nonane accompanies the β-amino aldehyde (35%) during the distillation of the crude reaction product, and that condensation occurs rapidly upon allowing the β-amino aldehyde to stand at room temperature. When R = CH_2Ph, we found that little 9-oxa-2,6-diazabicyclo[3.3.1]nonane was formed during the distillation of the crude β-amino aldehyde, but it was obtainable readily upon heating to 50° in the presence of a catalytic amount of methanesulfonic acid. A 50% yield was obtained overnight.

(1) C. Mannich and H. Wieder, *Ber.*, **65**, 385 (1932).
(2) W. H. Harteung and R. Simonoff, *Org. Reactions*, **7**, 263 (1953).

Experimental Section

β-Methylamino-α,α-dimethylpropionaldehyde (I, R = Me) and 2,4,4,6,8,8-hexamethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (II, R = Me) were obtained, as described by Mannich and Wieder, as a colorless liquid, bp 45° (11 mm), in 30–35% yield, and a white crystalline solid, mp 68°, in 40% yield, respectively.

Nmr Data for 2,4,4,6,8,8-Hexamethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (II, R = Me).—Peaks were observed at δ 0.80 (s), 1.30 (s), 2.80 (s), 2.85 (q, J_{AB} = 14 cps), and 3.90 (s) in the ratio of 3:3:3:2:1; δ, in parts per million, refers to TMS (internal).

1,3,3,5,7,7-Hexamethyl-1,5-diazacyclooctane (III, R = Me).—2,4,4,6,8,8-Hexamethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (106 g) was added in portions over a period of 15 min to a suspension of lithium aluminum hydride (35 g) in ether (600 ml). The mixture was refluxed for 1 hr and cooled; excess reagent was decomposed by addition of ethyl acetate (~200 ml), followed by water, until a pale gray precipitate was formed (~200 ml). The ether solution was decanted, dried over $MgSO_4$ and stripped. Distillation of the residue gave 78 g (79% yield) of product, bp 96° (25 mm). Nmr peaks were at δ 0.80 (s), 2.31 (s), and 2.40 (s) in the ratio of 6:3:4. *Anal.* Calcd for $C_{12}H_{26}N_2$: C, 72.6; H, 13.1. Found: C, 72.5; H, 13.1.

1,3,3,5,7,7-Hexamethyl-1,5-diazacyclooctane (III, R = Me).—Microhydrogenation of 2,4,4,6,8,8-hexamethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (II, R = Me) gave a hydrogen number 114 using $Rh-Al_2O_3$ catalyst in acetic acid as solvent (theoretical value for uptake of 2 mol of H_2 = 106). In another determination 1.95 mol of H_2 was taken up. ($Rh-Al_2O_3$ in ethanol caused no uptake.) 1,3,3,5,7,7-Hexamethyl-1,5-diazacyclooctane, identified by its nmr spectrum, was obtained.

β-Benzylamino-α,α-dimethylpropionaldehyde (I, R = CH_2Ph).—Isobutyraldehyde (81 g; 1.125 mol), paraformaldehyde (42 g; 1.40 mol), and benzylamine hydrochloride (150 g; 1.08 mol) were stirred vigorously and heated at 100° for 4 hr. After cooling, water (200 ml) was added and the mixture extracted with ether (200 ml). The aqueous solution was made alkaline with a solution of 100 g of KOH in 100 ml of water and extracted into three 200-ml portions of ether. The combined ether extracts of the alkaline solution were dried over $MgSO_4$ and stripped; 103 g (51% yield) of product, bp 93–100° (0.75 mm), was obtained by distillation. It was redistilled at 74° (0.25 mm), $n^{24}D$ 1.5113. *Anal.* Calcd for $C_{12}H_{17}NO$: C, 75.4; H, 8.9; N, 7.3. Found: C, 75.5; H, 8.9; N, 7.1.

2,6-Dibenzyl-4,4,8,8-tetramethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (II, R = CH_2Ph).—β-Benzylamino-α,α-dimethylpropionaldehyde (85 g) was heated to 50° overnight in the presence of a catalytic amount of methanesulfonic acid. Hexane (100 ml) was added, and the mixture was filtered. The solid was washed with hexane and dried to yield 40 g (50%). Recrystallization from ethyl acetate gave a product melting at 155–157.5°. Nmr peaks appeared at δ 0.85 (s), 1.30 (s), 3.08 (q, J_{AB} = 14.5 cps), 4.05 (s), 4.15 (s), 4.25 (s), and 7.30 (s) in the ratio of 3:3:2:1:1:1:5. *Anal.* Calcd for $C_{24}H_{32}N_2O$: C, 79.1; H, 8.8; N, 7.7. Found: C, 79.1; H, 8.7; N, 7.6.

1,5-Dibenzyl-3,3,7,7-tetramethyl-1,5-diazacyclooctane (III, R = CH_2Ph).—2,6-Dibenzyl-4,4,8,8-tetramethyl-9-oxa-2,6-diazabicyclo[3.3.1]nonane (36.1 g; 0.1 mol) was added portionwise over 5 min to a well-stirred suspension of lithium aluminum hydride (20 g; 0.6 mol) in ether (800 ml). The mixture was refluxed for 1 hr and then cooled. Excess reagent was decomposed using ethyl acetate followed by water. The ether solution was decanted, dried, and stripped, leaving a syrup which rapidly crystallized, 27.5 g (78% yield). Recrystallization from ethanol gave a product melting at 49–50°. Nmr peaks appeared at δ 0.70 (s), 2.50 (s), 3.75 (s), and 7.25 (s) in the ratio of 6:4:2:5. *Anal.* Calcd for $C_{24}H_{34}N_2$: C, 82.3; H, 9.7; N, 8.0. Found: C, 82.2; H, 9.8; N, 7.9.

3,3,7,7-Tetramethyl-1,5-diazacyclooctane (IV).—1,5-Dibenzyl-3,3,7,7-tetramethyl-1,5-diazacyclooctane (17.5 g; 0.05 mol), dissolved in ethanol (120 ml), was hydrogenated using 10% Pd–C (5 g) as a catalyst. Hydrogen uptake was completed in

30 min. The catalyst was filtered, and the solution was stripped, leaving a solid, 8.4 g (100% yield). Nmr peaks were present at δ 0.08 (s), 1.75 (s), and 2.60 (s) in the ratio of 6:1:4. A sharp-melting material (69–70°) was obtained by trituration of the diamine with warm water, followed by distillation from KOH, bp 110° (10 mm), and sublimation from barium oxide. *Anal.* Calcd for $C_{10}H_{22}N_2$: C, 70.6; H, 12.9; N, 16.5. Found: C, 70.4; H, 12.9; N, 16.6 (Dumas method).

Registry No.—I (R = CH_2Ph), 17288-10-7; II (R = Me), 17288-11-8; II (R = CH_2Ph), 17322-87-1; III (R = Me), 17288-12-9; III (R = CH_2Ph), 17288-13-0; IV, 17288-14-1.

Steric Effects in the Solvolysis of *cis*- and *trans*-1,1-Dichloro-2,3-dipropylcyclopropane[1]

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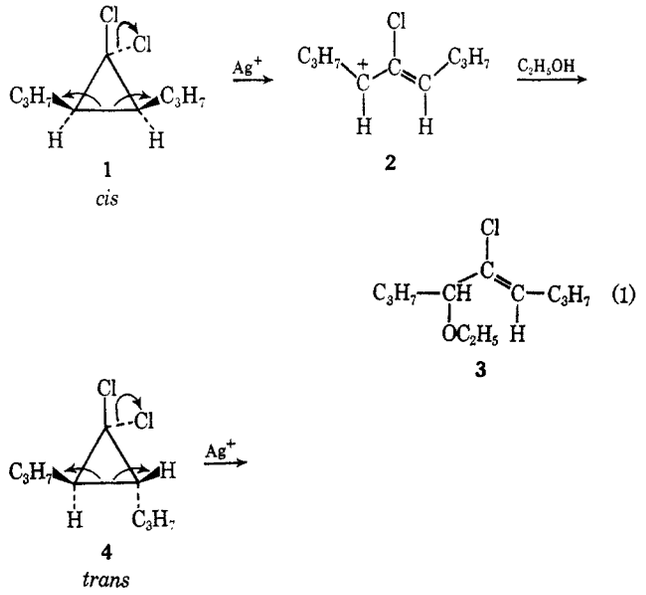
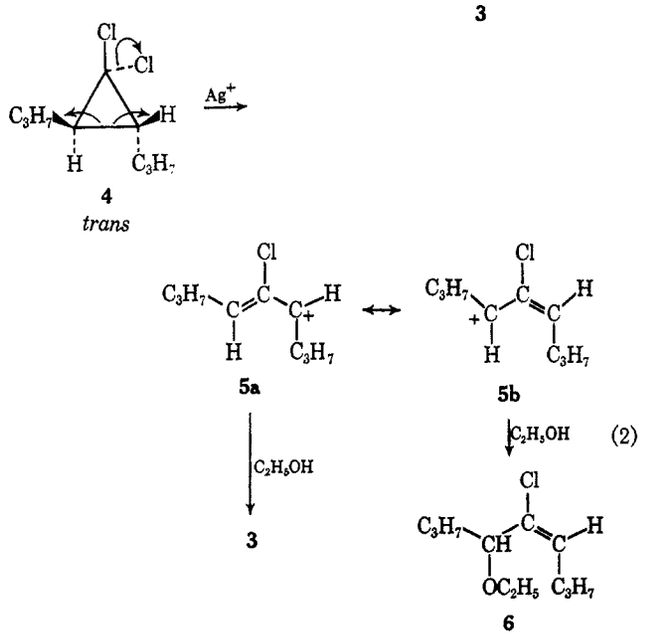
We have investigated the rates of solvolysis of the isomeric cyclopropanes **1** and **4** (eq 1 and 2), derived from *cis*- and *trans*-octene-4, at 80° in the presence of ethanolic silver nitrate. This method of ring opening of dihalocyclopropanes was first described by Skell and Sandler[2] and the scope of reaction has recently been extended by Sandler.[3] The observed difference in rates (k_{cis} = 1.29 × 10^{-5} sec^{-1}, k_{trans} = 5.33 × 10^{-7} sec^{-1}, k_{cis}/k_{trans} = 24.2) and the fact that both reactions gave only the *trans* chloro ether **3** are consistent with the combined data provided by (a) prior studies of mechanism of such ring-opening reactions,[2-5] (b) the work of DePuy[6] and coworkers concerning ring opening accompanying solvolysis of cyclopropyl tosylates, (c) the selection rules of Woodward and Hoffmann[6,7] for electrocyclic reactions, and (d) the relative rates of ring opening of the corresponding dichlorocyclopropanes derived from *cis*- and *trans*-propenyl ethyl ether[5] and from *cis*- and *trans*-cyclododecene.[8]

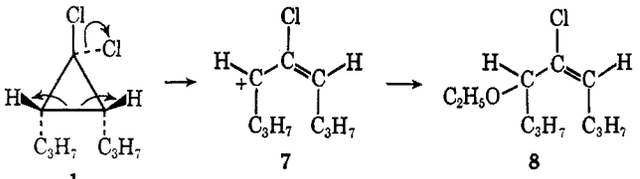


(1)



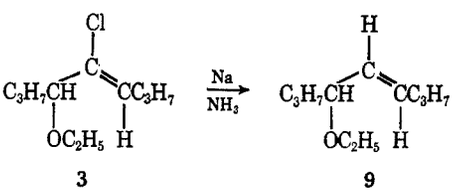
(2)

If these processes occur, as is now assumed,[6,7] by a process in which the groups *trans* to the leaving group rotate outward in a disrotatory manner, then it follows that the chlorine atom *cis* to hydrogen in **1** is lost preferentially. This is expected, since loss of the chlorine in **1** *cis* to alkyl, as shown in eq 3, would give a less favorable intermediate (or transition state) **7** in which



(3)

the two alkyl groups interact sterically. Such a process would lead to the *cis*-chloro ether **8** which is not observed. The more rapid rate of reaction of the *cis* isomer **1**, relative to the *trans* isomer **4**, is consistent with results previously described for the dihalocyclopropanes derived from *cis*- and *trans*-cyclododecene[8] and from *cis*- and *trans*-propenyl ethyl ether;[5] the results are those expected by considering steric demands of the intermediates (or transition states) comparable to **2** and **5**. The stereochemistry of the chloro ether **3** was determined by its reduction, with sodium in liquid ammonia, to *trans*-6-ethoxynonene-4 (**9**). The



infrared spectrum of **9** showed $\nu_{C=C}$ at 1662 cm^{-1} and strong absorption at 975 cm^{-1} indicative of *trans* hydrogen out of plane bending.[9] Since reduction of vinyl halides with sodium and liquid ammonia is known to be stereospecific,[10] with retention, it was concluded

(1) This work was supported by the National Science Foundation Grant GP-6169X.

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