Anal. Calcd for $C_{23}H_{26}SO_2$: C, 75.37; H, 7.15. Found: C, 75.38; H, 7.17.

Registry No.—I, 13952-45-9; II, 13810-95-2; III, 13810-96-3; VII, 13810-97-4; VIII, 13810-98-5; IX, 13810-99-6; X, 13811-00-2; thiobenzophenone, 1450-31-3; α-phellandrene, 13811-01-3; tetraphenylethylene, 632-51-9; dibenzhydryl disulfide, 1726-02-9.

6-Azabicyclo[3.2.1]octanes

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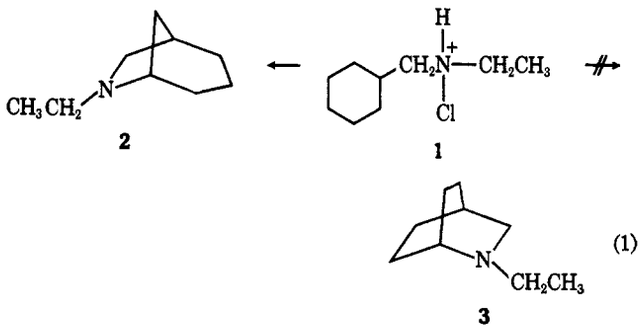
As part of our study of the rearrangements of azabicyclics *via* nitrenium ions,[2,3] we became interested in various synthetic routes to azabicycloalkanes. Prominent among the various synthetic methods for the preparation of azabicycloalkanes is the classical Hofmann–Löffler–Freytag reaction of monocyclic N-chloroamines.[4–7] It is generally accepted that this reaction involves homolytic cleavage of the N–Cl bond of the protonated N-chloroamine to yield an intermediate aminium radical which subsequently abstracts either a δ or ε hydrogen, producing, *via* a chain reaction, either a δ- or ε-chloroalkylamine acid salt. Basification and steam distillation then result in an intramolecular displacement of chloride ion to yield either a five- or six-membered heterocyclic ring.

It has been suggested[6,7] that the relative ease of δ- *vs.* ε-hydrogen abstraction is governed by the ability of the N–H–C angle to be close to 180° in the transition state, as well as by the tendency to minimize bond angle strain and steric repulsions in the transition state. However, when an apparent duality of reaction pathways exists, steric factors favoring one route, linearity of hydrogen transfer another, the relative importance of these two effects is difficult to predict *a priori*.[4,7] One such case which interested us owing to our involvement in azabicyclics was the reaction of N-chloro-N-ethylcyclohexanemethylamine (**1**).

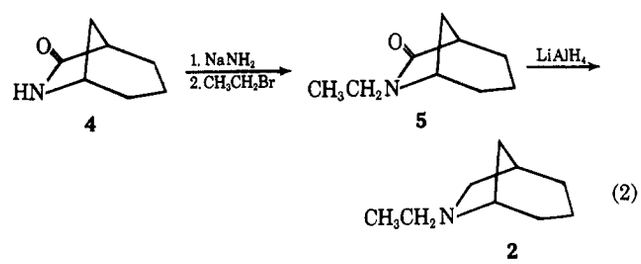
The synthesis of **1** was accomplished by reaction of the commercially available cyclohexanecarbonyl chloride with ethylamine and reduction of the resultant amide with lithium aluminum hydride to the corresponding amine, which was then converted into **1** *via* reaction with N-chlorosuccinimide (NCS).

The Hofmann–Löffler–Freytag reaction was carried out by irradiation of a solution of **1** in 85% sulfuric acid for 55 hr with a bank of ten 15-w Sylvania Blacklite fluorescent lamps. Subsequent basification, steam distillation, and Hinsberg separation gave a 10% yield of tertiary amines consisting of 95% of a major component, with two minor impurities constituting the remaining 5%. The major component was shown to



(1)

be 6-ethyl-6-azabicyclo[3.2.1]octane (**2**) (eq 1) by comparison with an authentic sample of **2** prepared as shown in eq 2 from the known[8] 6-azabicyclo[3.2.1]-octan-7-one (**4**). Comparison of vpc retention times



(2)

of the minor components of the Hofmann–Löffler–Freytag reaction products with that of an authentic sample[9] of 2-ethyl-2-azabicyclo[2.2.2]octane (**3**) demonstrated the complete absence of **3**.

Two rationalizations may be considered in accounting for the absence of **3** in the reaction mixture. If ε-hydrogen abstraction had occurred, subsequent stereospecific incorporation of chlorine might have proceeded to yield exclusively N-ethyl-*cis*-4-chlorocyclohexanemethylamine which would not be able to ring close *via* an intramolecular displacement. This rationale appears unsatisfactory since both *cis*- and *trans*-4-*t*-butylcyclohexyl halides are formed from various sources of 4-*t*-butylcyclohexyl radicals in the presence of halide-transfer agents.[10–12] A more logical explanation is that ε-hydrogen abstraction fails to occur owing to unfavorable nonbonded interactions which would destabilize the requisite transition state.

Since the linearity of hydrogen transfer is a major factor in determining which hydrogen is abstracted, a detailed examination was made of models of the appropriate transition states for δ- and ε-hydrogen abstraction. The transition state for ε-hydrogen abstraction would provide for a C–H· · ·N angle of about 180°, but this transition state would require the boat conformation of cyclohexane. By comparison, the transition state for δ-hydrogen abstraction would have a C–H· · ·N angle of approximately 145°; however, this transfer would proceed through the preferred cyclohexane chair conformation. Apparently, for the cyclohexane–methylaminium radical, nonbonded interactions are more important than linearity of hydrogen transfer in determining whether a δ or ε hydrogen is transferred. This can be compared with the cyclo-

(1) American Cyanamid Fellow, 1964–1965; Goodyear Foundation Fellow, 1965–1966.
(2) P. G. Gassman and B. L. Fox, *Chem. Commun.*, 153 (1966).
(3) P. G. Gassman and B. L. Fox, *J. Am. Chem. Soc.*, **89**, 338 (1967).
(4) For a recent review, see M. Wolff, *Chem. Rev.*, **63**, 55 (1963).
(5) S. Wawzonek and T. P. Culbertson, *J. Am. Chem. Soc.*, **81**, 3367 (1959).
(6) E. J. Corey and W. R. Hertler, *ibid.*, **82**, 1657 (1960).
(7) P. G. Gassman and D. Heckert, *Tetrahedron*, **21**, 2725 (1965).
(8) F. R. Hewgill and P. R. Jeffries, *J. Chem. Soc.*, 2767 (1955).
(9) W. Schneider and R. Dillmann, *Chem. Ber.*, **96**, 2377 (1963).
(10) F. D. Greene, C. C. Chu, and J. Walia, *J. Am. Chem. Soc.*, **84**, 2463 (1962).
(11) E. Eliel and R. V. Acharya, *J. Org. Chem.*, **24**, 151 (1959).
(12) H. H. Lau and H. Hart, *J. Am. Chem. Soc.*, **81**, 4897 (1959).

pentaneethylaminium radical where the linearity of hydrogen transfer is the dominant factor.[7]

Experimental Section

N-Ethylcyclohexanecarboxamide.—To a cold solution of 5.0 g (0.034 mole) of cyclohexanecarbonyl chloride[13] in 20 ml of dry benzene was added with cooling a cold solution of 3.52 g (0.080 mole) of ethylamine in 20 ml of dry benzene. After standing for 12 hr at ice-bath temperature, the reaction mixture was washed with 1 *N* sodium hydroxide, water, and then with dilute hydrochloric acid. The aqueous washings were made basic, combined, and extracted with benzene. The benzene solutions were combined and dried; the solvent was removed to yield 5.18 g (98%) of the desired amide as white crystals, mp 98.0–99.5° (lit.[14,15] mp 95, 92°).

N-Ethylcyclohexanemethylamine.—A solution of 5.0 g (0.032 mole) of N-ethylcyclohexanecarboxamide in 100 ml of anhydrous ether was added dropwise to a stirred slurry of 5.0 g (0.132 mole) of lithium aluminum hydride in 25 ml of anhydrous ether. The reaction mixture was stirred for 8 hr and 20 ml of water was added dropwise with cooling. The reaction mixture was stirred for 0.5 hr and the inorganic salts were removed by filtration and washed thoroughly with ether. The ethereal solution was dried over anhydrous magnesium sulfate and the drying agent was removed by filtration. Removal of the solvent and fractional distillation of the residue gave 3.38 g (74%) of N-ethylcyclohexanemethylamine: bp 69–70° (13 mm), $n^{31}D$ 1.4480.

6-Ethyl-6-azabicyclo[3.2.1]octane (2) *via* the Hofmann–Löffler–Freytag Reaction of N-Chloro-N-ethylcyclohexanemethylamine.—A solution of 26 g (0.185 mole) of N-ethylcyclohexanemethylamine and 26 g (0.196 mole) of N-chlorosuccinimide in 500 ml of ether was stirred for 3 hr. The succinimide which formed was precipitated by the addition of 500 ml of petroleum ether (bp 30–60°). The succinimide was removed by filtration and the filtrate concentrated on a rotary evaporator.

The residue was dissolved with cooling in 200 ml of cold 85% sulfuric acid contained in a quartz vessel. The reaction mixture was flushed with nitrogen, stoppered, and irradiated with a bank of ten 15-w Sylvania Blacklite fluorescent tubes for 55 hr at 10°. The reaction mixture was made basic with cold 40% sodium hydroxide (external cooling required) and the resultant basic solution was steam distilled until the distillate was no longer basic to pH paper. The receiver from the steam distillation contained enough dilute hydrochloric acid to neutralize the distilling amine. This acid solution was concentrated to *ca.* 300 ml on a rotary evaporator, made basic, and continuously extracted with ether for 72 hr. The ether extract was dried over anhydrous magnesium sulfate, the drying agent removed by filtration, and the solvent distilled off to leave an amber liquid containing a mixture of secondary and tertiary amines.

The mixture of amines was reacted with 200 ml of 20% sodium hydroxide and excess benzenesulfonyl chloride. After stirring for 12 hr, the solids which formed were removed by filtration and the filtrate was continuously extracted with ether for 72 hr. The extract was dried over anhydrous magnesium sulfate. Removal of the drying agent and solvent followed by distillation of the residue gave 2.53 g (10%) of **2** which was shown to be 95% pure by vpc on 15% Ucon 50-HB5100 on 42–60 firebrick. Preparative vpc provided analytically pure material.

Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.75; H, 12.23; N, 10.08.

6-Azabicyclo[3.2.1]octan-7-one (4).—*m*-Aminobenzoic acid was converted into **4** in a two-step process consisting of catalytic hydrogenation and thermal cyclization according to the procedure of Hewgill and Jeffries.[8] Substitution of 5% ruthenium on carbon for the Adams catalyst used by these earlier workers raised the yield in the catalytic hydrogenation from 21 to 85% of *cis*-3-aminocyclohexanecarboxylic acid. Thermal cyclization afforded **4** in 70% yield.

6-Ethyl-6-azabicyclo[3.2.1]octan-7-one (5).—A mixture of 0.39 g (0.01 mole) of sodium amide and 0.759 g (6.06 mmoles) of **4** in 10 ml of toluene was refluxed for 4 hr, cooled, and excess ethyl bromide was added. The reaction mixture was refluxed for 13 hr, cooled; the precipitated salts were removed by filtration. The solvent was removed *via* fractional distillation and the residue was vacuum distilled to give 0.42 g (45%) of **5**, bp 76° (0.45 mm). Preparative vpc on 5% SE 30 on 60–80 Chromosorb W gave an analytical sample, $n^{25}D$ 1.4855.

Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.31; H, 9.81; N, 9.28.

6-Ethyl-6-azabicyclo[3.2.1]octane (2).—Following the procedure outlined above, 2.24 g of **4** was ethylated and immediately reduced with lithium aluminum hydride (2.0 g) in 200 ml of anhydrous ether over a 10-hr period. Water (8.0 g) was added dropwise to the cooled reaction mixture and the precipitated inorganic salts were removed by filtration. The filtrate was dried over anhydrous magnesium sulfate and filtered; the solvent was distilled off. The residue was fractionally distilled to yield 1.05 g of **2** (42% yield from **4**), bp 75–76° (29 mm). The infrared and nuclear magnetic resonance spectra were identical with those of the product obtained from the Hofmann–Löffler–Freytag reaction of **1**.

Registry No.—**2**, 14002-06-3; **5**, 14002-07-4; N-ethylcyclohexanemethylamine, 14002-08-5.

Acknowledgment.—The authors are indebted to the National Cancer Institute for Public Health Service Grant CA-07110 which supported this investigation.

(13) Purchased from Aldrich Chemical Co. and used without further purification.

(14) J. v. Braun, F. Jostes, and W. Munch, *Ann.*, **453**, 113 (1927).

(15) E. K. Harvill, R. M. Herbst, E. C. Schreiner, and C. W. Roberts, *J. Org. Chem.*, **15**, 662 (1950).

Liquid Phase Oxidations of Cyclic Alkenes. II[1]

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A previous paper of the same title[2a] described the effect of ring size on the competition between the addition and hydrogen abstraction mechanisms in oxidations of cyclic alkenes. This note presents some additional results obtained with norbornene and cyclododecatriene which were not appropriate for inclusion in our more recent papers[2b,c] on oxidations of acylic alkenes.

Oxidation of Norbornene[2.2.1]bicycloheptene.—The oxidation of this hydrocarbon (from Aldrich Chemical Co.) is of interest because the allylic hydrogen atoms are at bridgehead positions and the double bond is "strained"; that is, the C_1–C_2–C_3 angle is less than the 120° preferred by normal olefins.[3]

Details are given in Table I. The initial rate of oxygen absorption, 0.0253 mole/l. hr, was followed by moderate autocatalysis, and gives a calculated $k_p/(2k_t)^{1/2}$ value of 0.268 (l./mole hr)$^{1/2}$. Thus the reactivity of norbornene in oxidation is nearly equal to that of cyclohexene (0.31).

A titration of the reaction mixture showed that only 5% of the absorbed oxygen appeared as hydroperoxide. The oxidate was analyzed by the usual proce-

(1) Research sponsored by AFOSR (SRC)-OAR, U.S.A.F. Contract No. AF49(638)-1102.

(2) (a) D. E. Van Sickle, F. R. Mayo, and R. M. Arluck, *J. Am. Chem. Soc.*, **87**, 4824 (1965); (b) D. E. Van Sickle, F. R. Mayo, R. M. Arluck, and M. G. Syz, *ibid.*, **89**, 967 (1967); (c) D. E. Van Sickle, F. R. Mayo, E. S. Gould, and R. M. Arluck, *ibid.*, **89**, 977 (1967).

(3) The heat of hydrogenation is 25.7 kcal/mole for cyclopentene and 33.1 kcal/mole for norbornene; R. B. Turner, W. R. Meadow, and R. E. Winkler, *ibid.*, **79**, 4116, 4133 (1957).