Structural and Mechanistic Effects on the Rates of Ring-Opening Reactions in the 5–16-Membered-Ring Region

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Partial rate coefficients have been determined for the reaction of cyclic dimethylammonium ions with sodium methoxide in the 7–16-membered-ring region. Three second-order parallel reactions take place and lead to exocyclic demethylation (A), ring-opening substitution (B), and ring-opening olefin-forming elimination (C). The results were compared with the behavior of the five- and six-membered rings. Reaction A shows negligible dependence on ring size. In contrast, reactions B and C are affected by ring size through ring strain and geometry of the transition state: the latter factor is held responsible for major differences in the reactivity profiles between such reactions.

The rate of ring-opening reactions involving bond cleavage of a given functional group incorporated in the ring can be affected by two major factors, i.e., (i) the presence of ring strain[1] in the ground state of the cyclic substrate and (ii) the ability of attainment of the configuration required in the transition state by the reaction mechanism. The importance of related conformational aspects has been stressed recently.[2] Since factors i and ii depend on the size of the ring to be cleaved, a kinetic investigation over a wide spectrum of selected ring sizes is expected to provide valuable information on the energetics of ring-opening reactions.

In a previous paper[3] we have shown that the reaction of *N*,*N*-dimethyl cyclic ammonium ions with sodium methoxide consists of three parallel transformations, i.e., an exocyclic demethylation (A), a ring-opening substitution (B), and a ring-opening olefin-forming elimination (C), as shown in Scheme I. Quantitative data were obtained for n = 5 and 6, dibutyldimethylammonium iodide being adopted as the reference open-chain system.

A kinetic investigation of this reaction, as extended to ring sizes other than five and six, allowed us to obtain data simultaneously for two ring-opening reactions distinctly different in their mechanistic features. The response of each individual reaction (B and C) to factor ii, as a function of ring size, is expected to be characteristic for reactions B and C. There is a definite need for studies of this kind in view of the paucity of quantitative data in this area as it appears from a recent review.[4]

Unlike the reverse ring-closure processes involving intramolecular reactions of bifunctional substrates,[5] entropy of activation is not expected to play a major role in ring-opening reactions B and C. In fact, provided the same bimolecular mechanism applies along a reaction series on changing ring size, $\Delta S^{\ddagger}$ values can be assumed to remain essentially unchanged.

In this paper we wish to report rate data for a number of ring sizes higher than six, including n = 7–9, 11, 13, and 16. Medium rings, n = 8–11, which are included in the group, are of special interest in view of the large strains associated with them.

Although reaction A does not lead to ring opening, nevertheless it is part of Scheme I. The related rate data are also reported and discussed in the present paper.

Scheme I

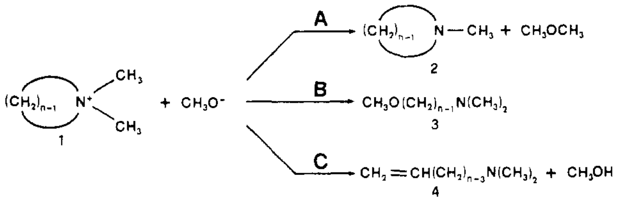

Table I. Product Analysis and Second-Order Overall Rate Constants (M^{-1} s^{-1}) for the Reaction of *N*,*N*-Dimethyl Cyclic Ammonium Ions with Sodium Methoxide in Methanol at 130 °C

	% reaction[c]			10^4k
n	A	B	C	(overall)[a]
5[b]	16.4 ± 0.5	82.5 ± 0.5	1.1 ± 0.1	3.80
6[b]	86.0 ± 0.6	3.6 ± 0.2	10.4 ± 0.2	0.702
7	22.1 ± 0.4	1.5 ± 0.1	76.4 ± 0.4	4.03
8	14.2 ± 0.4	2.4 ± 0.2	83.4 ± 0.2	6.83
9	14.1 ± 0.4	8.4 ± 0.1	77.5 ± 0.4	6.85
11	17.6 ± 0.1	7.8 ± 0.1	74.6 ± 0.1	5.23
13	53.9 ± 0.7	3.8 ± 0.1	42.3 ± 0.7	1.80
16	60.5 ± 0.2	2.6 ± 0.1	36.9 ± 0.3	1.77
open chain[b]	67.0 ± 0.2	2.1 ± 0.1	30.9 ± 0.2	1.40

[a] The precision in the overall rate constants was better than ±4%. [b] Data from ref 3. [c] A, demethylation; B, ring-opening substitution; C, ring-opening elimination.

Results

The reactions were carried out in methanolic solution, 0.1 M in methoxide ion and 0.05 M in the ammonium salt, and were followed to complete conversion at 130 °C in sealed ampules. The overall reaction rates were measured by the acid–base potentiometric microtitration of the total amine product formed. The product analyses were carried out by the gas chromatographic method on reaction mixtures obtained under the conditions of kinetic experiments. Product analyses and overall second-order rate constants are reported in Table I.

The rate constants for the individual reactions A–C are expressed by $k_A = k(a/100)$, $k_B = k(b/100)$, and $k_C = k(c/100)$, where k is the overall rate constant for any given ring compound in the series and a, b, and c are the percents of products 2, 3, and 4, respectively, for the reaction of that compound. Since the individual reactions involve the same substrate and reagent and are assumed to be all second-order, the related rate constants can be regarded as partial rate factors for each member of the series. All statistical

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(1) Sicher, J. *Prog. Stereochem.* **1962**, *3*, 202.

(2) Booth, H.; Bostock, A. H.; Franklin, N. C.; Griffiths, D. V.; Little, J. H. *J. Chem. Soc., Perkin Trans. 2* **1978**, 899.

(3) Illuminati, G.; Lillocci, C. *J. Org. Chem.* **1977**, *42*, 2201.

(4) Stirling, C. J. M. *Chem. Rev.* **1978**, *78*, 517.

(5) Galli, C.; Illuminati, G.; Mandolini, L.; Tamborra, P. *J. Am. Chem. Soc.* **1977**, *99*, 2591. Illuminati, G.; Mandolini, L.; Masci, B. *Ibid.* **1977**, *99*, 6308.

0022-3263/80/1945-3952$01.00/0

Table II. Second-Order Rate Constants for the Individual Reactions (Partial Rate Coefficients) of *N*,*N*-Dimethyl Cyclic Ammonium Ions with Sodium Methoxide in Methanol at 130 °C

n	10^4k^b		
	A	B	C
5^a	0.623	3.14	0.0418
6^a	0.604	0.0251	0.0729
7	0.891	0.0604	3.08
8	0.970	0.164	5.70
9	0.966	0.575	5.31
11	0.920	0.408	3.90
13	0.970	0.0684	0.761
16	1.07	0.0460	0.653
open chain^a	0.938	0.0294	0.433

[a] Data from ref 3. [b] A, demethylation; B, ring-opening substitution; C, ring-opening elimination.

factors reduce to unity since the three reactions have two equivalent sites in each case. The k_A, k_B, and k_C values are reported in Table II.

The identification of the reaction products and the determination of detector response corrections for VPC measurements of composition data required the preparation of the three series of products shown in Scheme I. Whenever possible, such compounds were obtained by an independent synthesis as described in the Experimental Section. This was the case for the *N*-methylazacycloalkanes (n = 7–9, 11, 13, and 16), ω-(dimethylamino)-1-alkyl methyl ethers (n = 7–9, 11, and 13), and ω-(dimethylamino)-1-alkenes (n = 7–9, 11, 13, and 16). A sample of the remaining compound, 15-(dimethylamino)-1-pentadecyl methyl ether, was obtained by the reaction under investigation as carried out on preparative-scale conditions, purified, and characterized. In some cases both procedures were applied.

Discussion

Demethylation Reaction. Reaction A is a bimolecular substitution at saturated carbon whereby the ring nitrogen in the starting substrate undergoes a drop in coordination number from 4 to 3 as it breaks away in the leaving group (eq 1). Although the ring is not opened in this reaction, the demethylation rate could be expected to depend on ring size.

$$\mathrm{MeO^- + Me{-}^+NR_3 \rightarrow [MeO^{\delta-}\cdots Me\cdots{}^{\delta+}NR_3] \rightarrow products} \quad (1)$$

$$\mathrm{R_3N + MeI \rightarrow [R_3N^{\delta+}\cdots Me\cdots{}^{\delta-}I] \rightarrow products} \quad (2)$$

This is indeed found in such reverse transformations as the quaternization of cyclic amines with methyl iodide[6] (eq 2) in methanol and acetonitrile. In both solvents the latter reaction displays a structured pattern (Figure 1a,b) and considerable dependence on ring size. This is particularly so in acetonitrile solution where the nucleophilicity of the amines is not appreciably modified by solvation. The observed behavior has been interpreted in terms of the accessibility of the nitrogen electrons as a function of the conformational structure of the ring. Accordingly, the quaternization of the strained cyclic amines in the medium-ring region displays a marked reactivity minimum.

Surprisingly, our data show (Table II and Figure 1c) that reactions 1 are nearly independent of ring size, the largest change in rate involving a factor of 1.8. In the medium-ring region, where ring strain should be lessened in going from the ammonium ion to the tricovalent amine, a rate enhancement would have been expected relative to the open-chain substrate.

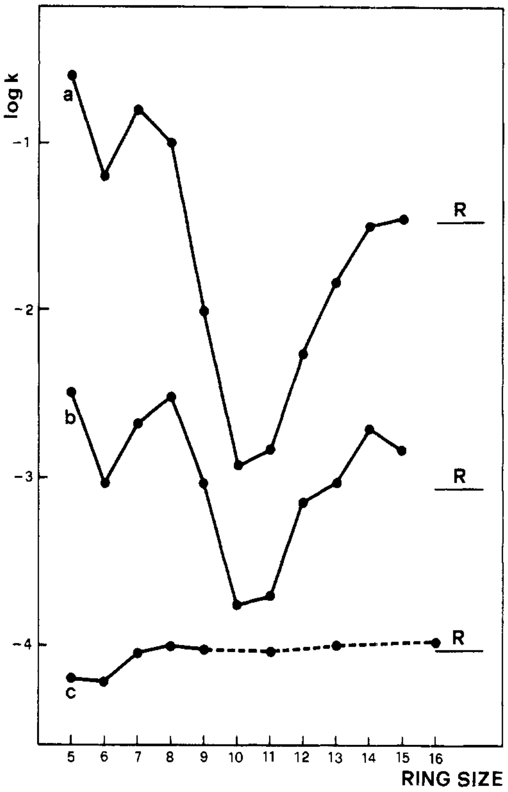

Figure 1. (a) Reactivities of the quaternization of *N*-methylazacycloalkanes with methyl iodide in acetonitrile at 25 °C vs. ring size.[6] (b) Reactivities of the quaternization of *N*-methylazacycloalkanes with methyl iodide in methanol at 25 °C vs. ring size.[6] (c) Reactivities of demethylation (reaction A) vs. ring size (this work). In each case, the reactivity level for the related reaction of the open-chain reference compound is shown (R).

Since transformations 1 and 2 are not strictly comparable to each other, an exact interpretation of this effect can hardly be offered. However, the strong ring dependence in reactions 2 can be explained by a relatively high degree of N–C bond making in a concerted process involving iodo as a good leaving group. In contrast, negligible ring dependence of reactions 1 presumably stands for a relatively low degree of C–N bond breaking in a concerted process involving quaternized nitrogen as a fairly poor leaving group. Although the methoxide ion is a more powerful nucleophile than amines, it is worth noting that reactions 1 are appreciably slower than reactions 2, thus showing the importance of the role of the leaving group in determining the reaction rate of these transformations.

Another reason calling for some caution in comparing the two reactions is the marked difference in the temperature used in the experiments, i.e., 130 °C for reaction 1 and 25 °C for reaction 2. While use of lower temperatures was not practicable for demethylation, the insensitiveness of this reaction to the structure of the substrate may also be contributed to by the fact that the relatively higher temperature used is possibly closer to its isokinetic temperature.

Ring-Opening Substitution. Reaction B is a bimolecular process involving attack of the nucleophile on an α ring carbon and an endocyclic C–N bond breaking and results in ring opening. The reaction displays a fairly marked dependence on ring size as shown by the data in Table II and the plot in Figure 2a. All the ring compounds examined except one (n = 6) react faster than the open-

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[6] Havel, M.; Krupička, J.; Svoboda, M.; Závada, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1429.

Table III. Free Energy of Activation Data[a] for the Ring-Opening Reactions of the *N,N*-Dimethyl Cyclic Ammonium Ions with Sodium Methoxyde and, for Comparison, Strain Energy Data[a] for Cycloalkanes[7]

	ring-opening subst		ring-opening elim			
n	$\Delta G^{\neq}$	$\delta\Delta G^{\neq\,b}$	$\Delta G^{\neq}$	$\delta\Delta G^{\neq\,b}$	strain energies[7]	δ(strain energy)[b]
5	30.3	−3.9	33.5	0.4	7.3	5.9
6	34.2	0	33.3	0	1.4	0
7	33.5	−0.7	30.3	−3.0	7.8	6.4
8	32.7	−1.5	29.8	−3.5	11.5	10.1
9	31.7	−2.5	29.9	−3.4	14.6	13.2
11	31.9	−2.3	30.1	−3.2	13.8	12.4
13	33.4	−0.8	31.4	−1.9	8.1	6.7
16	33.7	−0.5	31.5	−1.8	5.5	4.1

[a] Values expressed in kilocalories per mole. [b] Changes relative to the six-membered ring.

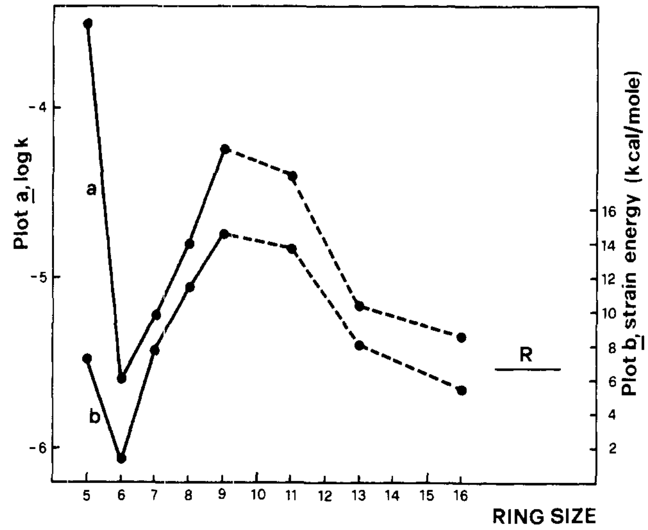

Figure 2. (a) Reactivities of ring-opening substitution (reaction B) vs. ring size and (R) reactivity level for the related reaction of the open-chain reference compound. (b) Strain energies of cycloalkanes[7] vs. ring size.

chain system by factors ranging from 1.6 (n = 16) to 20 (n = 9) to 107 (n = 5). The reaction rate of the six-membered ring is very close to that of the open-chain system and is slower by a depressing factor of 0.85.

Relief of ring strain is expected to be a major factor in causing rate enhancement in the ring-opening process. The reactivity profile (Figure 2a) typically shows a maximum in the medium-ring region (n = 8–11) where ring strain is known to be strong.[1] Unfortunately, strain-energy data for cyclic dimethylammonium ions are not available. However, since the ammonium ions consist of saturated rings whose members are all tetrahedral it seemed justified to compare the reactivity profile with the strain-energy[7] profile for cycloalkanes (see also Table III). The latter is reported as plot b in Figure 2.

Use of convenient arbitrary scales of the two quantities shows that they depend on ring size in a closely similar way despite the peculiar position of the five-membered ammonium ion which will be discussed later. We may wonder to what extent ring strain contributes to the free energy of activation. On plotting ΔG^{*} changes for the cyclic ammonium ion reaction relative to the least strained member (n = 6) as a function of the corresponding strain energy changes for the cycloalkanes (Figure 3 and Table III), the $\delta\Delta G^{*}$ values are found to decrease regularly as the δ(strain energy) values increased. The pattern is that of a mildly curved line which corresponds to an average drop in ΔG^{*} of 0.2 kcal/mol per 1 kcal/mol of δ(strain energy) increase.

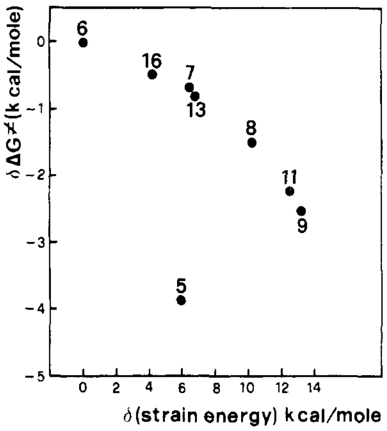

Figure 3. ΔG^{*} changes for the ring-opening substitution vs. strain energy changes of the cycloalkanes[7] (changes are relative to the six-membered ring).

This means that only 20% of the strain is transmitted through the transition state. Although cycloalkanes appear to provide a reasonably good qualitative model for ring strains of the cyclic ammonium ions under examination, the failure to observe a strictly linear correlation in the plot of Figure 3 may stand for an imperfect fit of the model. Therefore, a further speculation on the shape of this line does not seem to be worth pursuing at present.

The high reactivity of the five-membered ring relative to the six-membered ring has already been discussed.[3] The present data provide a deeper insight on the behavior of this ring. Such a reactivity is appreciably higher than that of the medium-ring compounds. Therefore, it does not seem to be totally accounted for by the strain energy of the five-membered ring which is markedly lower than that of the nine-membered ring and other medium rings, as clearly indicated by the cycloalkanes (Table III).

Another important factor is the steric requirement of the approaching nucleophile. This may contribute to the reactivity pattern in two different ways. In the five-membered ring the nucleophile lies in a plane staggered with respect to the C–H bonds of the adjacent methylene group and should follow an especially unhindered path along the reaction coordinate.[3,8] On the other hand, in the medium-ring compounds the reaction path is likely to be more hindered than in the reference open-chain system, and this may partly offset the rate-enhancing effect of the high strain. The six-membered-ring compound is characterized by a small strain energy, and since it reacts at a rate only slightly below that of the open-chain system, it should not suffer from an especially strong conformational retarding effect.

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(7) Greenberg, A.; Liebman, J. F. In "Strained Organic Molecules"; Academic Press: New York, 1978; p 66.

(8) Eliel, E. L.; Hutchins, R. O.; Mebane, R.; Willer, R. L. *J. Org. Chem.* **1976**, *41*, 1052.

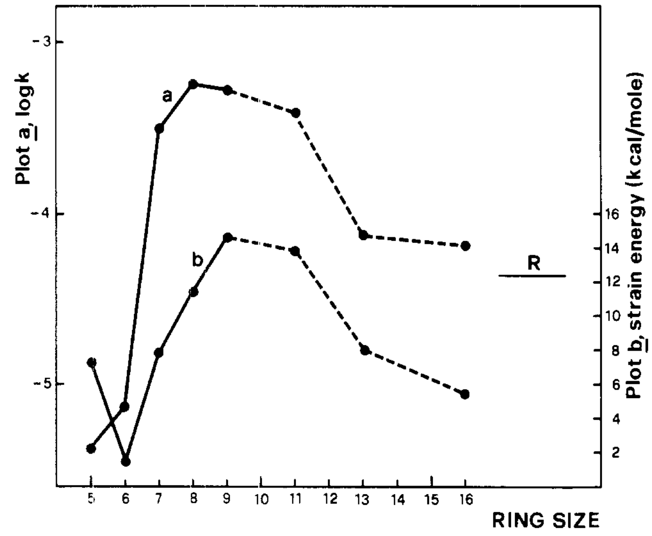


Figure 4. (a) Reactivities of ring-opening elimination (reaction C) vs. ring size and (R) reactivity level for the related reaction of the open-chain reference compound. (b) Strain energies of cycloalkanes[7] vs. ring size.

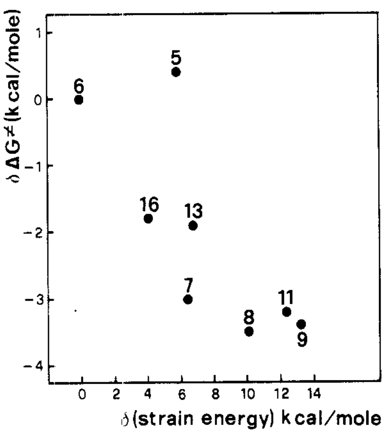
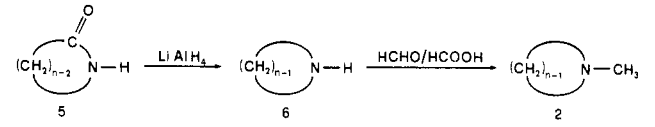


Figure 5. $\Delta G^{\ddagger}$ changes for the ring-opening elimination vs. the strain-energy changes of the cycloalkanes[7] (changes are relative to the six-membered ring).

Ring-Opening Elimination. The reaction pattern for the bimolecular elimination reaction (reaction C) is also fairly highly structured and ring-size dependent (Table II). The largest reactivity change is observed between the eight- and five-membered rings and involves a factor of 136. Except for the five- and six-membered rings, all the other compounds are more reactive than the open-chain system.

On application of the same treatment of the data as for the substitution reaction, the plots reported in Figures 4a and 5 are obtained. Although there is still a general analogy between the observed pattern for the elimination reaction and that for the ring strain of cycloalkanes as a function of ring size, the analogy is significantly less stringent than that observed for the substitution reaction (Figure 2a), and the $\delta\Delta G^{\ddagger}$ vs. δ(strain energy) correlation displays a considerable scattering within a general trend of decrease in $\delta\Delta G^{\ddagger}$ as δ(strain energy) increases. A decidedly strong deviation is observed for the five-membered-ring reactivity also in this case. It would have been of interest to compare the reactivity behavior with the strain energy of cycloalkenes since the transition state for the ring-opening elimination is expected to acquire a cycloalkene structure to some extent. The lack of strain energy data for most of the ring sizes has, however, prevented a comparison of this kind. We interpret the observed behavior by assuming that the reactivity of the ring-opening elimination reaction besides being a function of the strain energy of the ring depends on the specific conformational requirements of the transition state of each individual member of the series. A higher sensitivity of the elimination reaction (relative to substitution) to ring size is likely to derive from a deep involvement of the structural changes in the transition state over a large portion of the ring structure according to the peculiar geometry of the transition state for this reaction. This is dramatically shown by the five-membered ring (Figure 4a) for which the strain relief is more than offset by the severe geometry requirements of the transition state.

Scheme II

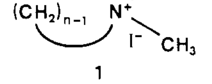


Experimental Section

Proton magnetic resonance spectra were recorded on a JEOL JNM-C60HL spectrometer using Me$_4$Si as the internal standard. Mass spectra were obtained on a AEI MS12 spectrometer. VPC analyses were performed on a GI Fractovap (C. Erba) using two glass columns: a 2-m column packed with 10% Carbowax 20M–2% KOH on 80/100 Chromosorb W (Supelco) and a 2-m column packed with 10% Apiezon L–2% KOH on 80/100 Chromosorb W (Supelco). Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium. All melting and boiling points are uncorrected.

N-Methylazacycloalkanes. N-Methylazacycloalkanes (Scheme II, compounds **2**, n = 7–9, 11, 13, and 16) were obtained in 49–90% yield by the N-methylation of the corresponding azacycloalkanes **6** by the Clarke–Eschweiler method.[9] Azacycloalkanes **6**, n = 7–9, were commercial samples (C. Erba, Fluka, and Aldrich, respectively); azacycloalkanes **6**, n = 11, 13, and 16, were obtained from the corresponding lactams **1** by reduction with LiAlH$_4$ in ether,[10] the yields being 78, 75, and 93%, respectively. Compounds **5**, n = 11 and 13, were commercial samples (Fluka). Compound **5**, n = 16, was prepared in 44% yield from the cyclopentadecanone (Fluka) according to the procedure described by Ruzicka:[10,11] cyclopentadecanone → cyclopentadecanone oxime → lactam. The crude products **2** were distilled under vacuum. The purified compounds were found to be better than 99% pure by VPC. Structure assignments for compounds **2** were made on the basis of ^{1}H NMR spectroscopy: ^{1}H NMR (CDCl$_3$) δ 2.1–2.5 (complex multiplet with a sharp peak at 2.2, 7 H, CH$_2$N(CH$_3$)CH$_2$), 1.1–1.7 (complex multiplet with a strong peak centered at 1.4, "central methylene protons"). The melting points of the picrates of the synthesized amines are in agreement with the literature values. Yields and physical constants are reported in Table IV.

***N*,*N*-Dimethylazoniacycloalkane Iodides.** *N*,*N*-Dimethylazoniacycloalkane iodides (compounds **1**, n = 7–9, 11, 13, and 16) were obtained in 55–89% yield from the corresponding compounds **2** by treatment with CH$_3$I in benzene at room temperature for 12–24 h. The crude products were recrystallized and dried under vacuum in an Abderhalden apparatus. Compound **1**, n = 11, was recrystallized from methanol. The other



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[9] Icke, R. N.; Wisegarver, B. B. In "Organic Syntheses"; Wiley: New York, 1955; Collect. Vol. 3, p 723.

[10] Ruzicka, L.; Kobelt, M.; Häfliger, O.; Prelog, V. *Helv. Chim. Acta* **1949**, *32*, 544.

[11] Ruzicka, L.; Goldberg, M. W.; Hürbin, M.; Boekenoogen, H. A. *Helv. Chim. Acta* **1933**, 16, 1323.

Table IV. Yields and Physical Constants of *N*-Methylazacycloalkanes 2

n	yield,[a] %	bp, °C (pressure, mm)	lit. bp, °C (pressure, mm)	picrate mp, °C	lit. picrate mp, °C
7	64	137	138-139[b]	220-221	220.5-221.5[c]
8	67	159-160	157-160[c]	205-207	206-208[c]
9	53	97-98 (60)	62-63(16)[d]	201-202	199-201[c]
11	70	108-109 (25)	78-80(10)[e]	188-189	185-186[e]
13	56	130 (18)	127(17)[e]	152-153	152.3-153[e]
16	20	117 (0.2)	93-95(0.05)[d]	93-93.5	93-94[d]

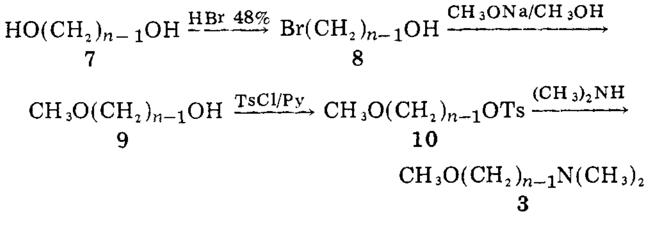
[a] Yields reported are overall yields. [b] Rentsch, C.; Lüssi, H. *Macromol. Chem.* **1972**, *153*, 269. [c] Leonard, N. J.; Musker, W. K. *J. Am. Chem. Soc.* **1959**, *81*, 5631. [d] Ruzicka, L.; Salomon, G.; Meyer, K. E. *Helv. Chim. Acta* **1937**, *20*, 109. [e] Lukeš, R.; Havlíčková, L. *Collect. Czech, Chem. Commun.* **1961**, *26*, 2245.

Table V. Yields, Physical Constants, and Analytical Data for the Preparation of ω-(Dimethylamino)-1-alkyl Methyl Ethers 3 [$CH_3O(CH_2)_{n-1}N(CH_3)_2$]

			calcd, %			found, %		
n	yield,[a] %	bp, °C (pressure, mm)	C	H	N	C	H	N
7	57	81-82 (18)[b]	67.87	13.29	8.79	67.88	13.07	8.81
8	46	98-99 (19)	69.31	13.38	8.08	69.25	13.18	8.13
9	46	112-113 (18)	70.53	13.45	7.48	70.76	13.43	7.66
11	19	145-146 (20)	72.50	13.57	6.50	72.67	13.37	6.60
13	50	167-168 (17)	74.01	13.66	5.76	74.03	13.55	5.97

[a] Yields reported are overall yields. [b] Lit. (Drake, N. L. *J. Am. Chem. Soc.* **1946**, *68*, 1542) bp 78 °C (11 mm).

Scheme III



$$\underset{7}{HO(CH_2)_{n-1}OH} \xrightarrow{HBr\ 48\%} \underset{8}{Br(CH_2)_{n-1}OH} \xrightarrow{CH_3ONa/CH_3OH}$$

$$\underset{9}{CH_3O(CH_2)_{n-1}OH} \xrightarrow{TsCl/Py} \underset{10}{CH_3O(CH_2)_{n-1}OTs} \xrightarrow{(CH_3)_2NH} \underset{3}{CH_3O(CH_2)_{n-1}N(CH_3)_2}$$

salts were recrystallized from absolute ethanol. The iodide ion content was checked by potentiometric titration and indicated a purity of 98-99%.

ω-(Dimethylamino)-1-alkyl Methyl Ethers. These compounds (**3**, n = 7-9, 11, and 13) were prepared by following a four-step synthetic procedure (Scheme III). Compounds **3** (n = 8, 9, 11, and 13) are new compounds. All intermediates and final products were characterized by ^1H NMR spectroscopy. The bromohydrins **8** were obtained by the reaction of HBr with the appropriate α,ω-alkanediol **7** [n = 8, 9, and 11 (Fluka); n = 13 (Merck)] according to a modified Degering and Boatright's procedure,[12] with toluene (for the diol with n = 8) and *n*-heptane (for the diols with n = 9, 11, and 13) as the extracting solvents. The compounds were purified by chromatography on silica gel, with benzene containing increasing amounts of methanol (1-6%) as eluent: compound **8** (n = 8), 70% yield, $n^{19}{}_D$ 1.4816 (lit.[13] $n^{23}{}_D$ 1.4808); compound **8** (n = 9), 65% yield, $n^{19}{}_D$ 1.4791; compound **8** (n = 11), 69% yield, $n^{19}{}_D$ 1.4801 (lit.[14] $n^{25}{}_D$ 1.4817); compound **8** (n = 13), 74% yield, mp 28-30 °C (lit.[15] mp 28.6 °C). All compounds were TLC pure. Treatment of such compounds with CH_3ONa in CH_3OH gave nearly quantitative yields of the methoxy alcohols **9**. Compound **9**, n = 7, was obtained from commercial $Cl(CH_2)_6OH$ (Fluka). The crude methoxy alcohols were converted to the corresponding tosylates **10** by treatment with *p*-toluenesulfonyl chloride in pyridine. The yields for compounds **10** were 76% (n = 7), 83% (n = 8), 82% (n = 9), 51% (n = 11), and 79% (n = 13). Treatment of the crude tosylates **10** with 4 equiv of dimethylamine in methanol at 120 °C for 12-14 h in a steel pressure bomb gave **3** (n = 7-9, 11, and 13) in 75, 86, 88, 56, and 98% yields, respectively. For analytical purposes the products were purified by chromatography on alumina, with petroleum ether containing increasing amounts of ether (1-20%) as eluent, and distilled under vacuum. The purified compounds were found to be better than 98% pure by VPC. Structure assignments were carried out by ^1H NMR spectroscopy, mass spectroscopy, and elemental analysis data: ^1H NMR ($CDCl_3$) δ 3.2-3.5 (m, 5 H, CH_2OCH_3), 2.1-2.4 (m, 8 H, $CH_2N(CH_3)_2$), 1.2-1.8 (complex multiplet with a strong peak centered at 1.3, "central methylene protons"). In the mass spectrum compounds **3** showed the expected molecular peaks. A base peak at m/e 58 was found in all cases, probably due to the fragment $(CH_3)_2N^+{=}CH_2$. Yields, physical constants, and analytical data of the synthesized compounds are listed in Table V. Compound **3**, n = 16, namely, $CH_3O(CH_2)_{15}N(CH_3)_2$, was obtained in very low yield by the reaction of the cyclic quaternary ammonium iodide (compound **1**, n = 16) with sodium methoxide in methanol as carried out on a preparative scale and carefully purified by column chromatography, as previously reported.[3] The product thus obtained was 99% pure by VPC and showed NMR and mass spectra consistent with the given structure. The derived picrate (yellow plates from ethanol) had a melting point of 75-76 °C. Anal. Calcd for $C_{24}H_{42}N_4O_8$: C, 56.01; H, 8.23; N, 10.89. Found: C, 56.27; H, 8.39; N, 11.07.

ω-(Dimethylamino)-1-alkenes. These compounds, $CH_2{=}CH(CH_2)_{n-3}N(CH_3)_2$ (**4**, n = 7-9, 11, 13, and 16), were prepared according to two different procedures. Compounds **4**, n = 7-9, and 13, were obtained in low yields by the reaction of the cyclic quaternary ammonium iodides (compound **1**, n = 7-9 and 13) with sodium methoxide in methanol as carried out on a preparative scale, purified carefully by column chromatography, and isolated by preparative VPC, as previously reported.[3] Compounds **4**, n = 11 and 16, were obtained from the cyclic quaternary ammonium iodides (**1**, n = 11 and 16) after conversion into the corresponding hydroxides and pyrolysis under vacuum.[16] Compound **4**, n = 11, was obtained in 48% yield; bp 124 °C (34 mm) [lit.[17] bp 94-94.5 °C (11 mm)]. Compound **4**, n = 16, after distillation was not pure enough for analytical purposes and was further purified by chromatography on alumina with petroleum ether containing increasing amounts of ether (2-20%) as eluent. It was finally distilled under vacuum: bp 120 °C (0.05 mm); overall yield 5%. The recovery was not quantitative, since several fractions from both chromatography and distillation containing the product in

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a less pure form were discarded.

All synthesized amines were found to be better than 99% pure by VPC. Structure assignments were carried out by ^1H NMR spectroscopy, mass spectroscopy, and elemental analysis data: ^1H NMR ($CDCl_3$) δ 5.4–6.1 (br m, 1 H, CH=C), 4.7–5.2 (br m, 2 H, CH_2=C), 1.8–2.5 (br m, with a prominent peak standing at 2.2, 10 H, $CH_2N(CH_3)_2$ and CH_2CH=), 1.0–1.8 (br m, "central methylene protons").

In the mass spectrum such compounds showed the expected molecular peaks: $n = 7$, m/e 127; $n = 8$, m/e 141; $n = 9$, m/e 155; $n = 11$, m/e 183; $n = 13$, m/e 211; $n = 16$, m/e 253. A base peak at m/e 58 was found in all cases and was probably due to the fragment $(CH_3)_2N^+{=}CH_2$.

Product Analysis. The identification of the components of the reaction mixture was accomplished by VPC comparison between the actual reaction mixtures and authentic samples of the products of the three competing reactions. For the comparison, two different types of column were used with identical results.

The product composition was determined under kinetic conditions by VPC measurements, according to a previously described procedure.[3] A Carbowax column and an Apiezon column were used for ring sizes with $n = 8$, 9, and 16 and for ring sizes with $n = 7$, 11, and 13, respectively.

Rate Measurements. The overall rates were measured by acid–base potentiometric microtitration of the total amine product formed according to a previously described procedure.[3]

Registry No. **1** ($n = 7$), 20422-15-5; **1** ($n = 8$), 27397-03-1; **1** ($n = 9$), 74366-38-4; **1** ($n = 11$), 74366-39-5; **1** ($n = 13$), 36735-08-7; **1** ($n = 16$), 74366-40-8; **2** ($n = 7$), 1192-95-6; **2** ($n = 8$), 19719-81-4; **2** ($n = 9$), 4802-48-6; **2** ($n = 11$), 19719-82-5; **2** ($n = 13$), 19719-84-7; **2** ($n = 16$), 74366-41-9; **3** ($n = 7$), 58390-19-5; **3** ($n = 8$), 74366-42-0; **3** ($n = 9$), 58390-20-8; **3** ($n = 11$), 74366-43-1; **3** ($n = 13$), 74366-44-2; **3** ($n = 16$), 74366-45-3; **3** ($n = 16$) picrate, 74366-46-4; **4** ($n = 7$), 52254-56-5; **4** ($n = 8$), 27397-04-2; **4** ($n = 9$), 16083-54-8; **4** ($n = 11$), 27397-10-0; **4** ($n = 13$), 21951-17-7; **4** ($n = 16$), 74366-47-5; **5** ($n = 16$), 50768-64-4; **6** ($n = 7$), 111-49-9; **6** ($n = 8$), 1121-92-2; **6** ($n = 9$), 5661-71-2; **6** ($n = 11$), 294-42-8; **6** ($n = 13$), 295-03-4; **6** ($n = 16$), 295-66-9; **7** ($n = 8$), 629-30-1; **7** ($n = 9$), 629-41-4; **7** ($n = 11$), 112-47-0; **7** ($n = 13$), 5675-51-4; **8** ($n = 8$), 10160-24-4; **8** ($n = 9$), 50816-19-8; **8** ($n = 11$), 53463-68-6; **8** ($n = 13$), 3344-77-2; **10** ($n = 7$), 74366-48-6; **10** ($n = 8$), 74366-49-7; **10** ($n = 9$), 74366-50-0; **10** ($n = 11$), 74366-51-1; **10** ($n = 13$), 74366-52-2.

Iron Carbonyl Promoted Additions of Perhalomethanes to Carbon–Carbon Double Bonds[1]

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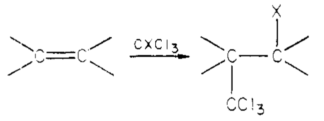
The addition of CCl_4 and $CBrCl_3$ to carbon–carbon double bonds, catalyzed by $Fe_2(CO)_9$ and $Me_3NFe(CO)_4$, is reported. In the case of CCl_4, these reactions afford $\alpha,\alpha,\alpha,\gamma$-tetrachloro-substituted derivatives with simple alkenes, whereas with norbornadiene and with the bicyclobutane bridged enone **1** and diene **2** rearranged products are obtained. The addition of CCl_4 to alkyl-substituted conjugated dienes leads to products that contain the iron carbonyl moiety. IR spectroscopic measurements revealed that the initial step of the catalyzed processes involves a reaction of the iron carbonyl with the perhalomethane to provide transient species of the type FeL_mX (L = CO, Me_3N; X = Cl, Br) and a trichloromethyl radical. A redox chain mechanism is proposed for the catalyzed process, implying addition of the (possibly complexed) trichloromethyl radical to the carbon–carbon double bond and subsequently abstraction of a halogen atom (X) by the (possibly complexed) substrate radical from FeL_mX to yield the $\alpha,\alpha,\alpha,\gamma$-tetrahalo derivative. The addition of CCl_4 to alkyl-substituted conjugated dienes supplies evidence for the possible intermediacy of σ complexes between substrate radical and species FeL_mX, trapped as stable diene iron tricarbonyl complexes in this particular case; the mode of addition was found to be consistent with the proposed mechanism for catalyzed additions by using deuterium-labeled 2,3-dimethylbutadiene.

The addition of CCl_4 and $CBrCl_3$ to alkenes has received considerable interest as a method to form new carbon–carbon single bonds. This reaction which involves a scission of a C–Cl bond in the case of CCl_4 and of a weaker C–Br bond in the case of $CBrCl_3$ usually gives rise to the formation of α,α,α-trichloro-γ-halo (chloro or bromo) derivatives (eq 1). Various methods are available for the conversion of the trichloromethyl moiety into other functionalities, for instance, into a carboxyl group by hydrolysis,[2,3] into a dichloromethylene group by dehydrohalogenation,[4–6] and into a (hydroxy)methyl group by reduction.[4,5,7]



X = Cl, Br

The addition of CCl_4 to alkenes has been accomplished either by a free-radical reaction initiated by peroxides or by UV irradiation[8,9] or by the application of transition-metal systems.[10] However, the former reaction is often inconvenient in the case of simple alkenes because of a competing telomerization;[8] therefore, the addition of

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