Ring-Opening Reactions. 3.[1] Mechanistic Path vs. Ring Strain Control in Elimination and Substitution Reactions of 1,1-Dimethyl Cyclic Ammonium Ions and Their α,α'-Dimethyl-Substituted Derivatives

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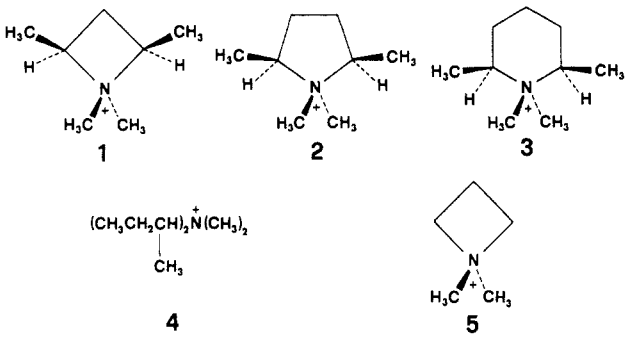
Received December 23, 1980

From the determination of product composition and overall second-order rate constants for the reactions of a number of cyclic quaternary ammonium ions with sodium methoxide in methanol and previous similar data, a complete set of partial rate coefficients for the ring-opening reactions (substitution and elimination) of 1,1-dimethyl cyclic ammonium ions and their α,α'-dimethyl-substituted derivatives for ring sizes 4–6 was made available. Such reactions are sensitive probes for steric strain and reaction mechanism requirements in the β-elimination reaction and for the different stereochemical requirements of elimination vs. substitution.

Ring opening of cyclic quaternary ammonium ions under the action of anionic reagents may occur by either substitution or elimination. In the preceding paper[1] we have reported that the ring-opening reactivity of such substrates appears to be affected by two major factors, i.e., the ring strain and the geometrical requirements of the reaction. The role of the latter factor was made apparent by the fact that the five-membered ring is more reactive in the ring-opening substitution reaction and less reactive in the ring-opening elimination reaction than expected from ring strain effects. If methyl groups are present at the α positions of the heterocyclic ring, a β-hydrogen is expected to be more easily eliminated from the side chain[2-4] than from the ring according to the Hofmann rule.[5] Since the C_α–CH_3 bond enjoys free rotation, the geometrical requirements of the elimination reaction from an α-methyl cyclic ammonium ion are significantly less severe than those of the corresponding α-unsubstituted compound. In such a case ring-opening reactivity should not suffer from any relevant restrictions imposed by the requirements of the reaction mechanism in connection with a change in size of the ring. Therefore, reactivity data are expected to essentially depend on ring strain relief.

To this end we have now investigated the reaction of sodium methoxide in methanol with a number of quaternary ammonium ions in order to have a complete comparison between the α-methyl-substituted series and α-unsubstituted series. Such ions include *cis*-1,1,2,4-tetramethylazetidinium (1), *cis*-1,1,2,5-tetramethylpyrrolidinium (2), and *cis*-1,1,2,6-tetramethylpiperidinium (3) and, also, di-*sec*-butyldimethylammonium (4) as an open chain analogue of the α-methyl-substituted ions and 1,1-dimetylazetidinium (5) as an additional member of the α-unsubstituted ions[1] (see Chart I). The ammonium salts were used as iodides with the five- and six-membered rings and the open-chain compound as usual and as perchlorates with the four-membered rings.

Chart I



Results and Discussion

The reactions were carried out in methanol solution, 0.1 M in methoxide ion and 0.05 M in substrate, and were followed to complete conversion in sealed ampules, apart from compound 5 (see Experimental Section). The overall reaction rates were measured by acid–base potentiometric microtitration of the total amine product formed. In order to allow a comparison with previous data, we chose the reaction temperature to be 130 °C. However, for the more reactive four-membered rings the reaction rates were determined at lower temperatures ranging from 70 to 90 °C

Table I. Product Analyses and Overall Rate Constants for the Reaction of Some Cyclic Quaternary Ammonium Ions (Ring Size n = 4–6) and of the Open-Chain Analogue with Sodium Methoxide in Methanol at Various Temperatures[a]

compd	n	temp, °C	% reaction[b] A	B	C	$k_{overall}$, M^{-1} s^{-1}
1,1,α,α'-Tetramethyl Cyclic Ammonium Ion Series						
1	4	70.0		15.2	84.8	1.16×10^{-3}
1	4	80.0		13.5	86.5	4.82×10^{-3}
1	4	90.0		11.7	88.3	14.5×10^{-3}
1	4	130.0				1.19[c]
2	5	130.0	0.3		99.7	3.6×10^{-3}
3	6	130.0	1.8		98.2	2.1×10^{-3}
4	open chain	130.0	3.4		96.6	4.70×10^{-3}
1,1-Dimethyl Cyclic Ammonium Ion Series						
5	4	20.0		100		6.14×10^{-5}
5	4	29.3		100		2.61×10^{-4}
5	4	50.3		100		3.23×10^{-3}
5	4	60.0		100		1.26×10^{-2}
5	4	130.0				8.5[c]

[a] The precision in the product analysis was better than ±1%; that in the overall rate constants was better than ±5%. [b] A, demethylation; B, ring-opening substitution; C, ring-opening elimination. [c] Obtained by extrapolation.

(1) Part 2: Cerichelli, G.; Illuminati, G.; Lillocci, C. *J. Org. Chem.* **1980**, *45*, 3952.
(2) Stirling, C. J. M. *Chem. Rev.* **1978**, *78*, 531, 560.
(3) Cope, A. C.; Trumbull, E. R. *Org. React.* **1960**, *11*, 340–342.
(4) Booth, H.; Bostock, A. H.; Franklin, N. C.; Griffith, D. V.; Little, J. H. *J. Chem. Soc., Perkin Trans. 2* **1978**, 899.
(5) Saunders, W. H.; Cockerill, A. F. "Mechanisms of Elimination Reactions"; Wiley: New York, 1973; p 168.

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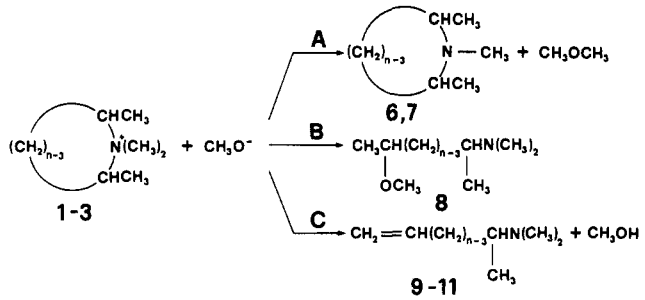
Scheme I



for compound 1 and from 20 to 60 °C for compound 5 and were extrapolated to 130 °C from the Arrhenius plots.

Product analyses were carried out by gas chromatography on the reaction mixtures under the conditions of the kinetic experiments. They are reported in Table I together with the overall rate constants.

Scheme I shows the three reactions observed in the present study for the α-methyl-substituted series (compounds 1–3). Only two of these were actually found in each case. The elimination reaction (reaction C) was exclusively of the Hofmann type and was the major process from all substrates. It provided 4-(dimethylamino)-1-pentene (9, n = 4), 5-(dimethylamino)-1-hexene (10, n = 5), 6-(dimethylamino)-1-heptene (11, n = 6), and a mixture of 1-butene, 2-butene (cis plus trans), and *sec*-butyldimethylamine from 1–4, respectively. The demethylation reaction (reaction A) was absent with the four-membered ring and yielded *cis*-1,2,5-trimethylpyrrolidine (6, n = 5), *cis*-1,2,6-trimethylpiperidine (7, n = 6), and di-*sec*-butylmethylamine from 2–4, respectively. The ring-opening substitution reaction (reaction B) yielded 4-(dimethylamino)-2-pentyl methyl ether (8, n = 4) from 1 and was absent with the other cyclic substrates and the open-chain compound.

Compound 5 showed only the ring-opening substitution reaction at all the investigated temperatures (reaction B, Scheme I in ref 1) and yielded 3-(dimethylamino)-1-propyl methyl ether.

Five- and Six-Membered Rings. Comparison of the partial rate coefficients in the two cyclic ammonium series (Table II) permits one to distinguish the two major factors involved in the ring-opening elimination at least in a qualitative way. The finding that elimination is the only existing ring-opening reaction with the five- and six-membered rings in the α-methyl-substituted series and that its rate is markedly higher than those for the corresponding rings in the α-unsubstituted series (by factors of 860 and 290) is in agreement with the view that the stereochemical requirements of the transition state are more easily met when the α-methyl group is present and enables the formation of the Hofmann product (ω-(dimethylamino)-1-alkene). The orientation effect is strong enough as to afford no Saytzeff product (ω-(dimethylamino)-2-alkene). By taking into account the limit of detection of the latter compound under the conditions of our experiments, we can calculate an upper limit for the rate of formation of the Saytzeff product, 1.8×10^{-5} and 1×10^{-5} M^{-1} s^{-1} for the five- and six-membered rings, respectively. The di-*sec*-butyldimethylammonium ion (α-methyl-substituted open-chain substrate) also undergoes elimination faster than the dibutyldimethylammonium ion (α-unsubstituted open-chain substrate) and displays Hofmann-type orientation (Table II). However, the Hofmann/Saytzeff ratio is only 5.7 for the α-methyl-substituted open-chain compound, which is markedly lower than that found for the five- and six-membered rings. By use of the above upper limit values, the orientation ratio for these ring compounds is greater than 200. This indicates that the geometry of such ring compounds is less favorable to the formation of the Saytzeff product than predicted by the orientation behavior in the α-methyl-substituted open-chain compound. The formation of the Saytzeff product from these rings apparently requires a considerably higher energy for the attainment of the optimum configuration of the system in the transition state. This interpretation is further confirmed by the fact that the Hofmann-type products are formed at nearly the same rate for the α-methyl-substituted open-chain compound and five- and six-membered rings.

Table II. Partial Rate Coefficients for the Ring-Opening Substitution and Elimination Reactions of Some Cyclic Ammonium Ions and of Their Open-Chain Analogues with Sodium Methoxide in Methanol at 130 °C

	α-Me-substituted[a]		α-unsubstituted[b]	
n	k_{subst}	k_{elim}	k_{subst}	k_{elim}
4	8.6×10^{-2} [c]	1.1 [c]	8.5 [c]	
5		3.6×10^{-3}	3.14×10^{-4} [d]	4.18×10^{-6} [d]
6		2.1×10^{-3}	2.51×10^{-6} [d]	7.29×10^{-6} [d]
open chain		3.9×10^{-3} [e]	2.94×10^{-6} [d]	4.33×10^{-5} [d]
		6.8×10^{-4} [f]		

[a] *cis*-1,1,α,α'-Tetramethyl cyclic ammonium ions and the open-chain analogue di-*sec*-butyldimethylammonium iodide. [b] 1,1-Dimethyl cyclic ammonium ions and the open-chain analogue dibutyldimethylammonium iodide. [c] Obtained by extrapolation. [d] Data from ref 1. [e] For 1-butene formation. [f] For 2-butenes (cis plus trans) formation.

Evidence for the fact that diversion of the β-hydrogen elimination from ring to α-methyl side-chain dramatically reduces the strains inherent to the β-elimination mechanism and uncovers the effects of ring strain relief on ring opening is shown by a clean-cut inversion in ring-opening reactivity order in going from the α-unsubstituted series (six-membered ring > five-membered ring) to the α-methyl-substituted series (five-membered ring > six-membered ring). The factors involved are not large, however; the six-/five-membered ring rate ratio in the former series and the reverse five-/six-membered ring ratio in the latter are both less than 2. This is not surprising since although cyclopentane is appreciably more strained than cyclohexane,[6] the free-energy difference in the transition state of the ring-opening reaction has been found to be only a small fraction of the strain energy difference known for cycloalkanes.[1]

Whereas the elimination reaction is facilitated by the presence of the α-methyl group, substitution is made more difficult. This is an expected effect for α branching in nucleophilic bimolecular substitution at saturated carbon.[7,8] The rate-depressing effect is sufficiently strong as to let the substitution product be undetectable.

Four-Membered Rings. The behavior of these rings in both series throws further light on the two major factors controlling the ring-opening reaction. In the α-unsubstituted compound the only observable reaction is substitution which occurs more than 25 000 times faster than with

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(7) Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: Ithaca, NY, 1969; p 436.
(8) Hine, J. "Physical Organic Chemistry"; McGraw-Hill: New York, 1962; p 176.

the α-unsubstituted five-membered ring (Table II). This large rate enhancement is very likely caused by the strongly increased ring strain in the small ring. In cycloalkanes the ring strain increases by 6 and 26 kcal/mol with cyclopentane and cyclobutane, respectively, with respect to cyclohexane.[6] Easy accessibility of the incoming reagent toward a ring position may be assumed to be an additional factor favoring ring-opening substitution in the small ring, as already noted for the five-membered ring in comparison with the six-membered ring and the open-chain compound.[1]

There is no detectable elimination with the α-unsubstituted ring. This further supports the view that β-elimination requires such a high energy for the transition state in order to acquire the appropriate geometry as to be unable to compete with substitution. The geometry is so unfavorable that the required energy more than offsets the strong strain relief which would accompany ring-opening also in this case. This energy barrier is circumvented in the α-methyl-substituted ring where the α-methyl group offers an alternative route to the reaction. Here the β-elimination reaction leads to the Hofmann product and is faster than substitution by a factor of ca. 13. Under conditions which reduce the energy barrier in elimination, the ring strain relief effect is expected to emerge again. Indeed, a marked rate enhancement, by a factor of 305, is observed in going from the five- to the four-membered ring in the α-methyl-substituted series.

In the case of five- and six-membered rings we have noted that the rate of substitution is presumably depressed in the α-methyl-substituted series by steric hindrance due to α branching of the polymethylene chain. With the four-membered rings this effect can be put in quantitative terms since both α-unsubstituted and α-methyl-substituted substrates provide measurable rates. The α-unsubstituted to α-methyl-substituted ratio is about 200. This effect can be interpreted in terms of the well-known α-methyl branching effect in S_N2 reactions.[7,8]

Concluding Remarks. The data reported in this work show that ring-opening of appropriate structures of common and small rings may be a sensitive probe for steric strain and transition-state conformational requirements in the β-elimination reaction and for the different stereochemical requirements of elimination vs. substitution.

Experimental Section

Proton magnetic resonance spectra were recorded on a JEOL JNM-C60HL spectrometer using Me_4Si as the internal standard. Mass spectra were obtained on a AEI MS12 spectrometer. Elemental analyses were performed by Alfred Bernhardt Microanalytisches Laboratorium. All melting and boiling points are uncorrected.

Gas Chromatography (GC). Quantitative GC was carried out on a Hewlett-Packard 5830A instrument using a 6 ft × 2 mm i.d. glass column packed with 10% Carbowax 20M–2% KOH on 80/100 Chromosorb W (Supelco). Preparative GC was carried out on a Fractovap B (C. Erba) instrument with columns of different lengths packed with 20% Carbowax 20M on firebrick (pretreated with sodium hydroxide). GC/MS experiments were performed on a 9 ft × $^1/_8$ in. o.d. column with the same packing as that used for quantitative GC. The analysis of butenes was performed at 0 °C on a 20 ft × $^1/_8$ in. o.d. column packed with 10% EDO-1 on 100/120 Chromosorb P AW (Supelco); 1-butene and *cis*- and *trans*-2-butenes for use as authentic samples were from Matheson.

Materials. A number of the following preparations were intended to be independent syntheses of authentic specimens for use in product analysis.

The assignment of the cis configuration in the following compounds was confirmed on the base of the NMR spectra of the final 1,1-dimethyl derivatives. In the cis molecules two singlets are expected for the two *N*-methyl groups. On the other hand, in the trans molecules the two *N*-methyl groups become equivalent, owing to symmetry, and only one singlet for six *N*-methyl protons can be observed.

***cis*-2,4-Dimethylazetidine** was obtained in low yields from 3,5-dimethylisoxazole (Aldrich) according to the procedure described by Freeman,[9] apart from the conversion of 3,5-dimethylisoxazole to 4-amino-2-pentanol that was accomplished by using sodium in aqueous ether as described by Sicher.[10]

***cis*-1,1,2,4-Tetramethylazetidinium iodide** was obtained from *cis*-2,4-dimethylazetidine by reaction with CH_3I in the presence of sodium methoxide in methanol;[11] the crude product was recrystallized from absolute ethanol and dried under vacuum: yield 35%; ^1H NMR (CD_3CN) δ 4.2–4.7 (m, 2 H, 2 CHN^+ protons), 3.0 (s, 3 H, CH_3N^+ protons), 2.8 (s, 3 H, CH_3N^+ protons), 2.3–2.6 (m, 1 H, one of the methylene protons), 1.2–1.6 (d, 6 H, 2 CCH_3 groups). The second proton of the methylene group probably lies under the solvent signal. Anal. Calcd for $C_7H_{16}NI$: C, 34.87; H, 6.69; N, 5.81. Found: C, 34.48; H, 6.73; N, 5.55.

***cis*-1,1,2,4-Tetramethylazetidinium perchlorate (1)** was obtained in 65% yield from the corresponding iodide by treatment with $AgClO_4$ in methanol.[12] The product was purified as indicated for the iodide.

***cis*-1,2,5-Trimethylpyrrolidine (6, *n* = 5)** was obtained by the hydrogenation of 1,2,5-trimethylpyrrole (Schuchardt) in glacial acetic acid over rhodium on alumina according to the general procedure described by Augustine;[13] yield 60%.

***cis*-1,1,2,5-Tetramethylpyrrolidinium iodide (2)** was obtained by treatment of *cis*-1,2,5-trimethylpyrrolidine with CH_3I in benzene. The crude product was recrystallized from 2-propanol and dried under vacuum; yield 69%. The iodide ion content was checked by potentiometric titration and indicated a purity of 98%: ^1H NMR (CD_3OD) δ 3.6–4.1 (m, 2 H, 2 CHN^+ protons), 3.1 (s, 3 H, CH_3N^+), 2.7 (s, 3 H, CH_3N^+), 1.7–2.5 (m, 4 H, CH_2CH_2), 1.4 (d, 6 H, 2 CCH_3 groups).

***cis*-1,2,6-Trimethylpiperidine (7, *n* = 6)** was obtained from *cis*-2,6-dimethylpiperidine (Schuchardt) by the normal Eschweiler–Clarke procedure.[14]

***cis*-1,1,2,6-Tetramethylpiperidinium iodide (3)** was obtained from *cis*-2,6-dimethylpiperidine (Schuchardt) by treatment with CH_3I and sodium carbonate in water according to the procedure described in the literature.[15] The crude product was recrystallized from 2-propanol and dried under vacuum; yield 48%. The iodide ion content was checked by potentiometric titration and indicated a purity of 99%: ^1H NMR ($CDCl_3$) δ 3.9–4.4 (m, 2 H, 2 CHN^+ protons), 3.4 (s, 3 H, CH_3N^+), 2.9 (s, 3 H, CH_3N^+), 1.6–2.2 (m, 6 H, central methylene protons), 1.5 (d, 6 H, 2 CCH_3 groups).

5-(Dimethylamino)-1-hexene (10, *n* = 5) and 6-(dimethylamino)-1-heptene (11, *n* = 6) were obtained in 50% and 80% yields from the reactions of *cis*-1,1,2,5-tetramethylpyrrolidinium iodide (**2**) and *cis*-1,1,2,6-tetramethylpiperidinium iodide (**3**), respectively, with sodium methoxide in methanol at 130 °C as carried out on a preparative scale. The products were purified by preparative GC; bp 141 °C (lit.[16] 138–140 °C) and 165 °C [lit.[4] 142–148 °C (758 mmHg)], respectively. In the mass spectra the products showed molecular peaks at *m/e* 127 and 141, respectively, and a base peak at *m/e* 72, due to the fragment $^+CH(CH_3)N(CH_3)_2$. For both compounds: ^1H NMR ($CDCl_3$) δ 5.6–6.3 (br m, 1 H, CH=C), 4.8–5.3 (br m, 2 H, CH_2=C), 2.25 (s, 6 H, $N(CH_3)_2$), 0.95 (d, 3 H, CCH_3).

Di-*sec*-butylmethylamine and *sec*-butyldimethylamine were obtained from di-*sec*-butylamine (Merck) and *sec*-butylamine (Fluka), respectively, by the Eschweiler–Clarke procedure.[14]

(9) Freeman, J. P.; Pucci, D. G.; Binsch, G. *J. Org. Chem.* **1972**, *37*, 1894.
(10) Sicher, J.; Pankova, M.; Jones, J.; Svoboda, M. *Collect. Czech. Chem. Commun.* **1959**, *24*, 2727.
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(15) Goerdeler, J. In "Methoden der Organischen Chemie (Houben-Weyl)"; George Thieme Verlag: Stuttgart, 1958; Vol. 11, Part 2, p 613.
(16) Merling, G. *Justus Liebigs Ann. Chem.* **1891**, *264*, 310.

Di-*sec*-butyldimethylammonium iodide (4) was obtained from di-*sec*-butylmethylamine by treatment with CH_3I in anhydrous benzene. The crude product was recrystallized from anhydrous ethanol–ethyl acetate to give white crystals: 38% yield; mp 145.5–146 °C. Anal. Calcd for $C_{10}H_{24}NI$: C, 42.11; H, 8.48; N, 4.91. Found: C, 41.94; H, 8.47; N, 4.93.

***sec*-Butyl methyl ether** was obtained from sodium *sec*-butoxide and CH_3I.[17]

1,1-Dimethylazetidinium iodide was prepared in 59% yield from azetidine (Fluka), CH_3I, and sodium methoxide in methanol.[11] The iodide ion content of a sample recrystallized from absolute ethanol was equal to 99% of the calculated value (potentiometric titration).

1,1-Dimethylazetidinium perchlorate (5) was obtained in 39% yield by the reaction of the corresponding iodide with $AgClO_4$ in methanol.[12] The product was recrystallized from absolute ethanol and dried: ^1H NMR (CD_3CN) δ 4.25 (t, 4 H, 2 CH_2N^+ groups), 3.2 (s, 6 H, $^+N(CH_3)_2$), 2.2–2.8 (m, 2 H, β-methylene group). Anal. Calcd for $C_5H_{12}ClNO_4$: C, 32.35; H, 6.52; N, 7.55. Found: C, 32.90; H, 6.64; N, 7.43.

3-(Dimethylamino)-1-propyl methyl ether was obtained in 68% yield from 3-(dimethylamino)-1-chloropropane (Fluka) and sodium methoxide in refluxing methanol: bp 126–127 °C (lit.[18] 129–130 °C); ^1H NMR (CCl_4) δ 3.2–3.4 (m, 5 H, CH_2OCH_3), 1.8–2.4 (m, 8 H, $CH_2N(CH_3)_2$), 1.4–1.8 (m, 2 H, β-methylene group).

Allyldimethylamine was obtained in 36% yield from the reaction of allyl bromide and dimethylamine in benzene: bp 61–65 °C [lit.[19] 61 °C (726 mmHg)]; ^1H NMR (CCl_4) δ 5.4–6.1 (m, 1 H, CH=C), 4.7–5.2 (m, 2 H, CH_2=C), 2.8 (d, 2 H, CH_2), 2.1 (m, 6 H, $N(CH_3)_2$).

***cis*-1,2,4-Trimethylazetidine and 1-methylazetidine** were obtained from *cis*-2,4-dimethylazetidine and azetidine (Fluka), respectively, by the Eschweiler–Clarke procedure.[14] In both cases the reaction yielded mixtures of amines that were analyzed by GC/MS. The above compounds were unequivocally identified by their mass spectra: molecular peaks at m/e 99 and 71, base peaks at m/e 84 and 42, respectively, as expected for cyclic amines of this type.[20]

Product Analysis. The product composition was determined under kinetic conditions. Four ampules from each set of rate measurements were kept at the reaction temperature for a time interval corresponding to at least 80% reaction. The content of the ampules (5 mL) was transferred into a 10-mL flask, acidified with 6 N HCl, and evaporated to dryness on a rotatory evaporator at 30 °C. The solid residue was treated with 9 N NaOH (3 mL), and the oganic bases were extracted with ether. The ether extracts were analyzed by GC.

In the case of compound 1 the identification of the components of the reaction mixture was accomplished by GC/MS. In the other cases the identification was performed by GC comparison between the actual reaction mixtures and authentic samples of the products of the three competing reactions. In some cases both procedures were applied. In the GC experiments the results did not change on using different types of columns at varying temperatures.

In the case of the open-chain compound, a further analysis was carried out to find out the composition of the butenes mixture: one ampule was shaken and broken into a glass bottle provided with a silicone rubber septum; a gas sample was withdrawn with a gas syringe and analyzed gas chromatographically for the content in butenes; the identification was accomplished by comparison with authentic samples of 1-butene and of *cis*- and *trans*-2-butene.

Reaction of *cis*-1,1,2,4-tetramethylazetidinium perchlorate (1) with sodium methoxide in methanol at 90 °C gave 4-(dimethylamino)-1-pentene [**9**, n = 4: 88.3%; mass spectrum, m/e 113 (molecular peak), 72 (base peak, $CH^+(CH_3)N(CH_3)_2$)] and 4-(dimethylamino)-2-pentyl methyl ether [**8**, n = 4: 11.7%; mass spectrum, m/e 145 (molecular peak), 72 (base peak)]. The absence of the demethylation product was confirmed by GC comparison with an authentic specimen of *cis*-1,2,4-trimethylazetidine.

Reaction of *cis*-1,1,2,5-tetramethylpyrrolidinium iodide (2) at 130 °C gave *cis*-1,2,5-trimethylpyrrolidine (**6**, n = 5; 0.3%) and 5-(dimethylamino)-1-hexene (**10**, n = 5; 99.7%).

Reaction of *cis*-1,1,2,6-tetramethylpiperidinium iodide (3) at 130 °C gave *cis*-1,2,6-trimethylpiperidine (**7**, n = 6; 1.8%) and 6-(dimethylamino)-1-heptene (**11**, n = 6; 98.2%).

Reaction of di-*sec*-butyldimethylammonium iodide (4) at 130 °C gave di-*sec*-butylmethylamine (3.4%) and *sec*-butyldimethylamine (96.6%). The relative composition of the butene mixture was 1-butene (85.0%), *trans*-2-butene (5.7%), and *cis*-2-butene (9.3%). The percentages of the elimination reactions leading to 1-butene and 2-butene (cis plus trans) are 82.1% and 14.5%. The corresponding rate constants are shown in Table II. A portion of the content (1 μL) of the ampules was directly injected into the gas chromatograph in order to check for any presence of *sec*-butyl methyl ether, i.e., the product of reaction B (Scheme I) that, in fact, could not be detected.

Reaction of 1,1-dimethylazetidinium perchlorate (5) in the temperature range 20–60 °C gave 3-(dimethylamino)-1-propyl methyl ether. The absence of both demethylation and elimination products was confirmed by GC comparison with an authentic specimen of 1-methylazetidine and of allyldimethylamine, respectively.

Runs were carried out on the ammonium salts in the absence of sodium methoxide, in order to check the occurrence of solvolyses and of any substitution by the iodide ion. All such reactions were negligibly slow as compared to the reaction with methoxide (GC analysis).

The (dimethylamino)alkenes were subjected to the actual conditions of reaction and were shown by GC not to give isomerization.

Rate Measurements. The reactions were carried out in sealed ampules, except for compound 5. For the latter the reactions were carried out at 20, 30, and 50 °C in a volumetric flask immersed into a thermostating bath; at 60 °C kinetics were measured by a batchwise procedure using a vessel provided with a thermostating jacket.[21] The overall rates were measured by acid–base potentiometric microtitration of the total amine product formed according to a previously described procedure.[22] The rate constants at 130 °C for the reactions of the four-membered rings 1 and 5 were calculated from the partial rate coefficients obtained at lower temperatures from the Arrhenius plots (r = 0.998).

Registry No. 1, 77415-42-0; 2, 77429-50-6; 3, 16561-11-8; 4, 77429-51-7; 5, 77415-44-2; *cis*-1,1,2,4-tetramethylazetidinium iodide, 77415-45-3; *cis*-2,4-dimethylazetidine, 34414-35-2; *cis*-2,6-dimethylpiperidine, 766-17-6; di-*sec*-butylmethylamine, 26819-66-9; 1,1-dimethylazetidinium iodide, 77415-46-4.

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