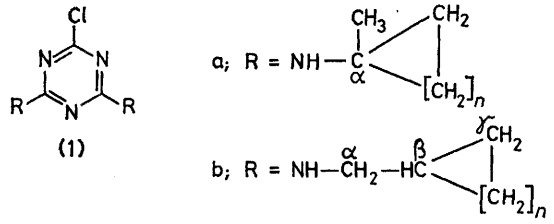
Thermal Dealkylation of 2,4-Bis(alkylamino)-6-chloro-*s*-triazines. Effect of Ring Size on Formation of Alicyclic Olefins. Part 3 [1,2]

By **Milan D. Muškatirović,* Bratislav Ž. Jovanović, Gordana A. Bončić-Caričić, and Živorad D. Tadić,** Department of Organic Chemistry, Faculty of Technology and Metallurgy, University of Beograd, Karnegieva 4, 11001 Beograd, Yugoslavia

The thermal dealkylation of 2,4-bis-(*N*-1-methylcycloalkylamino)-6-chloro-*s*-triazines and 2,4-bis-(*N*-cycloalkylmethylamino)-6-chloro-*s*-triazines containing five-, six-, and seven-membered rings gave mixtures of olefinic products in which endocyclic isomers predominated. In the case of 1-methylcycloalkyl derivatives this was attributed to the influence of thermodynamic and statistical as well as entropy effects. Steric effects were considered to be similar, since the transition states for both isomers could have planar arrangements, anticipating a boat conformation for the cyclohexyl derivative under the reaction conditions. The predominance of endocyclic isomers in the case of cycloalkylmethyl substrates as well as the presence of cycloalkylmethyl chloride in the products could not be explained by an E_i mechanism. Possible mechanisms for this dealkylation are discussed.

THE pyrolytic dealkylation of *NN'*-diprimary alkyl and *NN'*-disecondary alkyl derivatives of 2,4-diamino-6-chloro-*s*-triazines showed that the reaction most probably proceeds *via* an intramolecular six-membered cyclic transition state. It was found that the yield and direction of elimination reflect steric, thermodynamic, and statistical influences and that the contribution of these factors in the net effect varied from case to case.[1-3] Because of the pronounced steric interactions associated with alicyclic compounds we expected that interesting information concerning the structure of the transition state could be deduced from a study of the effect of ring size on the course of the dealkylation of cycloalkyl derivatives.

The olefins formed by thermal dealkylation of the three 1-methylcycloalkyl derivatives (1a; $n = 3$—5) were examined in order to determine the relative amounts of the two positional olefinic isomers (exo- and



endo-cyclic). In addition the thermal decomposition of the three cycloalkylmethyl derivatives (1b; $n = 3$—5) was also investigated. The olefinic products were analysed by g.l.c. and the results are given in Tables 1 and 2, respectively.

The data in Table 1 show that the three 1-methylcycloalkyl derivatives undergo thermal dealkylation to give a mixture of olefins in which the endocyclic isomer predominates. The olefin obtained by pyrolysis of the cyclopentyl derivative was composed of 97.7% 1-methylcyclopentene and 2.3% of methylenecyclopentane. As far as steric effects are concerned perfectly eclipsed structures are possible for both transition states. Elimination of the ring β-hydrogen atom suffers from steric restrictions since only two of the four β-hydrogen atoms can attain the preferred planar transition state. Consequently on statistical grounds predominance of exocyclic isomer formation was expected. Since this was not the case, the preference for endo- over exo-cyclic olefin formation can be attributed to the

TABLE 1

Yields * and composition of olefins formed by thermal dealkylation of 2,4-bis-(*N*-1-methylcycloalkylamino)-6-chloro-*s*-triazines (1a) at 250 °C

	Olefin (%)			Total amount
n	endo	exo	endo/exo	(%)
3	97.7	2.3	43	46.7
4	96.5	3.5	27	76.7
5	86.0	14.0	6	100.0

* Percentages throughout this paper were calculated on the basis of 2 moles of olefin per mole of substrate

TABLE 2

Yields and composition of olefins formed by thermal dealkylation of 2,4-bis-(*N*-cycloalkylmethylamino)-6-chloro-*s*-triazines (1b) at 280 °C

	Olefin (%)		endo/		Total amount
n	endo	exo	exo	$CH-[CH_2]_n-CHCH_2Cl$	(%)
3	48.0	4.3	11	47.6	7.5
4	53.5	5.2	10	41.2	19.4
5	73.2	18.7	4	10.8	21.3

thermodynamic control.[4] In addition, entropy considerations also favour elimination into the ring. This involves the minimal restriction of internal motion since only the orientation of one N–C bond is required since the necessary coplanarity of C_β–H and C_α–N bonds, due to the rigidity of a cyclopentyl ring, has already been attained. The transition state for the exocyclic isomer, which also necessitates the orientation of a CH_2–H bond, includes the loss of possible conformational rotation of the methyl group, thus disfavouring its formation.

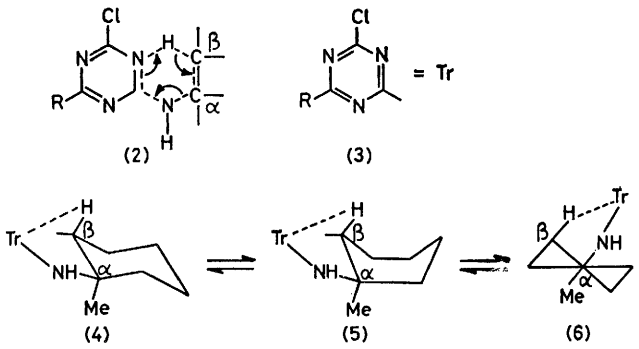
The ratio of the two positional olefinic isomers from the methylcyclohexyl derivative, 96.5% endo- and 3.5% exo-cyclic isomer, is higher than those reported for the

[1] Part 1, M. D. Muškatirović and Ž. D. Tadić, *J.C.S. Perkin II*, 1975, 1701.
[2] Part 2, Ž. D. Tadić, G. A. Bončić-Caričić, and M. D. Muškatirović, *J.C.S. Perkin I*, 1977, 1257.
[3] Ž. D. Tadić and S. K. Ries, *J. Agric. Food Chem.*, 1971, **19**, 46.
[4] R. B. Turner and R. H. Garner, *J. Amer. Chem. Soc.*, 1957, **79**, 253.

pyrolytic elimination of the corresponding esters, xanthates, and amine *N*-oxides.[5,6a-c] The product distribution is controlled by the factors already mentioned for the cyclopentyl substrate.

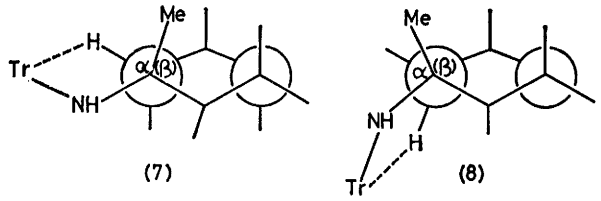
The stereorequirements for the transition state for formation of the endocyclic transition state are as follows.

(a) Sufficient flexibility of the six-membered cyclic transition state (2) allows elimination of the *s*-triazinyl (3) amino-group and the β-hydrogen atom in a synclinal orientation to each other so that the cyclohexyl group can exist in a chair (4), boat (5), and twist (6) conformation (Scheme 1).



SCHEME 1

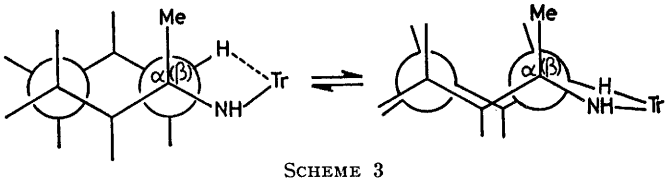
The same arguments have already been used to explain the different product distribution in the pyrolysis of esters compared with amine *N*-oxides, which, as is known, requires the complete eclipse of α- and β-linked leaving groups.[7] If this were the case, most probably the equatorial *s*-triazinylamino group participates with the axial β-hydrogen atom since the tendency to form a planar cyclic transition state for e,e-elimination (7) will cause increased steric interactions between the compressed axial α-methyl group and other axial hydrogen atoms, whereas such interactions are reduced in the transition state for an e,a-elimination (8) (Scheme 2).[8]



SCHEME 2

(b) The transition state demands a perfectly eclipsed arrangement of the *s*-triazinyl amino group and the β-hydrogen atom and therefore for endocyclic olefin formation the chair to boat inversion is required (Scheme 3).

We think that possibility (b) is more acceptable. This is based on the fact that a very strong eclipsing effect was demonstrated in the study of the dealkylation of *N*-acyclic-*s*-triazines which is expected only for the strictly



SCHEME 3

planar arrangement.[1] It must be also born in mind that at the temperatures of present experiments it can be expected that the chair–boat equilibrium is considerably displaced in favour of the less stable boat conformation.

The product distribution for the cycloheptyl derivative was expected to be close to that for the cyclopentyl substrate since the principal controlling factors are similar. The results of experiments (Table 1) show that the endo- : exo-cyclic olefin ratio is much smaller than for the cyclopentyl derivative. Examination of molecular models showed that the elimination into the ring is most probably less favoured in the case of the cycloheptyl derivative because of a nonbonded interaction in the transition state between the α-methyl group and the γ-hydrogen atom. For all three dealkylations the increase of total elimination is pronounced in going from the five- to the seven-membered cyclic derivative and it clearly reflects the ease of attainment of the stereorequirements.

The thermal decomposition of the cycloalkylmethyl substrates gives an interesting set of products (Table 2). The preferential formation of endocyclic olefin could be explained by a cyclic transition state which comprises simultaneous departure of the γ-hydrogen atom and the *s*-triazinylamino group accompanied by a βα-hydride shift and formation of a βγ-double bond. Without an investigation of the deuteriated analogues it is impossible to conclude where the hydrogen from the γ-carbon atom finishes up. Consideration of the possibilities shows that it could be on the ring nitrogen atom as was proposed for the normal E_i mechanism.[3] In this case the proposed mechanism would require the transition state to be a nonplanar seven-membered one, which is unexpected. The other possibility is an out-of-ring nitrogen atom which participates in the perfectly planar five-membered cyclic transition state. This is possible even for the cyclohexyl substrate given a boat conformation for the cyclohexyl group which can be expected for the reasons already mentioned. The third possible reaction path, similar to that proposed by Cope *et al.*, involves the normal (E_i) planar six-membered transition state (Scheme 1) and includes the removal of the β-hydrogen and the formation of a βγ double bond accompanied by a γα-hydride shift.[6b] A distinction among these three mechanisms is impossible at the time being.

The chloromethylcycloalkanes were identified among

[5] D. H. Froemsdorf, C. H. Collins, G. S. Hammond, and C. H. DePuy, *J. Amer. Chem. Soc.*, 1959, **81**, 643.

[6] (*a*) R. A. Benkeser and J. J. Hazdra, *J. Amer. Chem. Soc.*, 1959, **81**, 228; (*b*) A. C. Cope, C. L. Bumgardner, and E. E. Schweizer, *ibid.*, 1957, **79**, 4729; (*c*) W. J. Bailley and W. F. Hale, *ibid.*, 1959, **81**, 651.

[7] C. H. De Puy and R. W. King, *Chem. Rev.*, 1960, **60**, 431.

[8] D. V. Banthorpe, 'Elimination Reactions,' Elsevier, Amsterdam–London–New York, 1963, p. 167.

the products in all three cases. The amounts ranged from 47.6 to 10.8%. Since these chloro derivatives could be formed by addition of hydrogen chloride (also identified in the gaseous products) to one of the isomeric olefins, thereby changing the product ratio, an investigation of effect of hydrogen chloride on the pure exocyclic olefin was carried out (see Experimental section). The concentration of hydrogen chloride used corresponded to the amount formed under the conditions of dealkylation. Chloroalkanes were not detected showing that these compounds cannot arise from an addition reaction. Their formation most probably can be attributed to attack of the nucleophilic chloride ion on the α-carbon atom which in the transition state for the E_i mechanism can exhibit partially developed carbonium ion character (Scheme 1). This explanation is supported by kinetic studies on *para*-substituted 2,4-bis-(α-phenylethylamino)-6-chloro-*s*-triazine pyrolysis. It was shown that in the transition state corresponding to that for exocyclic olefin formation in the dealkylation of cycloalkylmethyl substrates, the α-carbon atom is electron deficient (reaction constant ρ *ca.* −3.0).[9] This has also been demonstrated for α-phenyl-substituted acetate pyrolysis.[10]

The data in Table 2 point to a decrease in the yield of chloro derivatives with increasing ring size. This can be explained by increasing interaction between the incoming chloride ion and the cycloalkyl group forming the activated complex of an S_N2 reaction. It is interesting to note that not even traces of chloroalkanes were observed in experiments with 1-methylcycloalkyl substrates (Table 1), suggesting that in this case the E_i reaction predominates. This, together with the decrease of chloro derivatives and increase of exocyclic olefin with ring size (Table 2), can be cited in support of the proposed mechanism for chloromethylcycloalkane formation.

The possibility of exo- to endo-cyclic olefin inversion due to the presence of gaseous hydrogen chloride was also checked. The observed conversion was <10% which means that it does not invalidate the endo : exo ratio as a characteristic of pyrolytic dealkylation.

Thermal dealkylation of cycloalkylmethyl derivatives is the only reaction among pyrolytic eliminations of related compounds in which the formation of endocyclic olefin predominates.[5,6b,c] Furthermore, it is the only case where thermal decay of *s*-triazine derivatives gives rise to chloroalkane formation. This product distribution indicates that the mechanism of dealkylation is most probably heterogeneous.

EXPERIMENTAL

Preparation of Olefins, Amines, and s-*Triazine Derivatives.*—1-Methylcycloalkylamines with five-, six-, and seven-membered rings were synthesised by the Ritter–Kalish procedure.[11] The related 1-methylcycloalkenes were obtained in the normal way.[5,6c,12] The three cycloalkylmethylamines were prepared from the corresponding cycloalkylacetamides by reduction with lithium aluminium hydride.[13] The reaction of cyanuric chloride (Fluka) and the synthesised amines gave the new 2,4-bis-(*N*-1-methylcycloalkylamino)- and 2,4-bis-(*N*-cycloalkylmethylamino)-6-chloro-*s*-triazines (Tables 3 and 4).[14] All *s*-triazine derivatives were checked by t.l.c. and elemental analyses for purity. I.r. spectra were recorded with a Perkin–Elmer 457 spectrophotometer and mass spectra with a Varian Mat CH-5 spectrophotometer.

Investigation of the Effect of Gaseous Hydrogen Chloride on Products.—The experiment was conducted as follows. The gaseous products formed by thermal dealkylation were absorbed in 0.1N sodium hydroxide. The excess of the base was titrated with 0.1N-sulphuric acid. The amount of hydrogen chloride exceeded *ca.* 30%. The same amount of hydrogen chloride was introduced into the dealkylation apparatus and together with the appropriate amount of pure exocyclic olefin exposed to the usual experimental conditions. The products were analysed for olefin content.

The chloroalkanes produced by thermal dealkylation were characterised by mass spectrometry and by g.l.c. by comparison of their retention times with those of authentic

TABLE 3

2,4-Bis-(*N*-1-methylcycloalkylamino)-6-chloro-*s*-triazines (1a)

				C (%)		H (%)		N (%)	
n	Yield (%)	M.p. (°C)	Formula	Reqd.	Found	Reqd.	Found	Reqd.	Found
3	90	173—175	$C_{15}H_{24}ClN_5$	58.15	57.7	7.8	7.85	22.6	22.45
4	90	158—160	$C_{17}H_{28}ClN_5$	60.45	60.35	8.35	8.4	20.7	19.8
5	95	121—122	$C_{19}H_{32}ClN_5$	62.35	61.9	8.8	8.75	19.15	18.75

TABLE 4

2,4-Bis-(*N*-cycloalkylmethylamino)-6-chloro-*s*-triazines (1b)

				C (%)		H (%)		N (%)	
n	Yield (%)	M.p. (°C)	Formula	Reqd.	Found	Reqd.	Found	Reqd.	Found
3	100	228—230	$C_{15}H_{24}ClN_5$	58.15	57.95	7.8	8.0	22.6	22.2
4	100	235	$C_{17}H_{28}ClN_5$	60.45	60.45	8.35	8.35	20.7	20.75
5	100	222—224	$C_{19}H_{32}ClN_5$	62.35	62.5	8.8	8.8	19.1	18.7

[9] M. D. Muškatirović and B. Ž. Jovanović, unpublished data.
[10] R. Taylor, G. G. Smith, and W. H. Wetzel, *J. Amer. Chem. Soc.*, 1962, **84**, 4817.
[11] J. J. Ritter and J. Kalish, *J. Amer. Chem. Soc.*, 1948, **70**, 4048.
[12] E. R. Alexander and A. Mudrak, *J. Amer. Chem. Soc.*, 1959, **72**, 1810.
[13] V. M. Mićović and M. V. Mihailović, *J. Org. Chem.*, 1953, **18**, 1190.
[14] J. T. Thurston, J. R. Dudley, D. W. Kaiser, J. Hechenbleikner, F. C. Schaefer, and D. Holm-Hansen, *J. Amer. Chem. Soc.*, 1951, **73**, 2983.

samples prepared by independent syntheses from the corresponding alcohols.[15]

Thermal Dealkylation of 1-Methylcycloalkylamino and Cycloalkylmethylamino Derivatives.—Thermal decompositions were conducted by heating the substrate (1 mol) at 250 or 280° in a thermostatted oil-bath (±1 °C) for 1 h in an apparatus previously described.[3] The gaseous products were transferred by nitrogen to a thermostatted burette (80 °C) from which samples were taken and analysed by g.l.c. Authentic samples of the olefins were used as standards. Except for methylenecyclohexane which was commercially available (Fluka) the olefins were prepared in the normal way. Methylene-cyclopentane and -cycloheptane were synthesised by the Chugaev reaction from the corresponding 1-methylcycloalkylmethanols.[6a,12] The endocyclic olefins were obtained by the usual procedure.[5,6c]

Estimation of Olefins by G.l.c.—A Varian Aerograph 1400 gas chromatograph was used, with nitrogen as carrier gas. The column (2 m × 0.003 m) was packed with diethylene glycol–silver nitrate (30%) on Chromosorb R (60—80 mesh). The column temperature was maintained at 50 °C, the injection temperature was varied from 80 to 90 °C, and the flame ionization detector temperature was 130 °C. Satisfactory separations of isomeric 1-methylcycloalkenes and methylenecycloalkanes as well as the corresponding cycloalkylmethyl chlorides were obtained in all cases. Product proportions were calculated by triangulation (estimated accuracy ±2%).

This work was supported by the Republican Association of Science, SR Serbia, Yugoslavia. We thank Professor D. Jeremić, Faculty of Science, Beograd, and Institute of Chemistry, Technology and Metallurgy, Beograd, for the interpretation of the mass spectra.

[7/1306 *Received*, 21*st July*, 1977]

[15] N. Turkiewicz, *Ber.*, 1939, **72**, 1052.