[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF PURDUE UNIVERSITY]

The Effect of Ring Size on the Rate of Solvolysis of the 1-Chloro-1-methylcycloalkanes[1,2]

BY HERBERT C. BROWN AND MITCHELL BORKOWSKI[3]

Cyclic compounds undergoing reaction at a ring atom exhibit striking changes in reactivity with variation in ring size. These differences in chemical behavior have been attributed to the changes in internal strain in the cyclic structures which accompany changes in the coördination number of the ring atom undergoing reaction (I-strain). To test the validity of the interpretation, the 1-chloro-1-methylcycloalkanes with rings of 4-, 5-, 6-, 7-, 8-, 9-, 10-, 11-, 13-, 15- and 17-carbon atoms were synthesized and the rates of solvolysis in 80% aqueous ethanol were determined. The rate of solvolysis for 1-chloro-1-methylcyclobutane is relatively slow ($k_1^{25°}$ 0.00224 hr.$^{-1}$), much slower than open-chain tertiary chlorides. 1-Chloro-1-methylcyclopentane and -heptane undergo solvolysis at a relatively fast rate ($k_1^{25°}$ 1.32 and 1.15 hr.$^{-1}$, respectively), whereas the corresponding cyclohexane derivative is quite slow ($k_1^{25°}$ 0.0106 hr.$^{-1}$). The rates reach a maximum with the eight-membered ring ($k_1^{25°}$ 3.03 hr.$^{-1}$) and then decrease to become essentially constant at 0.02–0.03 hr.$^{-1}$ with rings of thirteen members and greater. The results are in substantial agreement with the predictions based upon the I-strain concept. Methylcyclopropane was chlorinated photochemically at −20° in an attempt to synthesize 1-chloro-1-methylcyclopropane. The reaction product yielded essentially a single monochloride, C_4H_7Cl, which behaved in solvolysis studies as a typical tertiary halide ($k_1^{25°}$ 0.00067 hr.$^{-1}$). However, the product has been identified as the primary halide, cyclopropylcarbinyl chloride.

The reactivity of cyclic compounds is markedly influenced by variation in the size of the ring. For example, the bimolecular displacement reactions of cyclopropyl, cyclobutyl and cyclohexyl halides are very slow compared with the reactions of secondary halides and the corresponding derivatives of cyclopentane and cycloheptane.[4,5] On the other hand, to carbonyl group reagents cyclohexanone is quite reactive relative to open-chain ketones, whereas cyclopentanone and cycloheptanone are comparatively inert.[6,7]

It has been proposed that the effect of ring size on chemical reactivity can be accounted for in terms of I-strain—the increase in internal strain in a cyclic structure, resulting from alterations in bond angles and constellations, which accompanies a change in the coördination number of a ring atom in the course of reaction.[4] The available data are nicely correlated with the aid of this concept. However, these data are fragmentary and largely qualitative in nature. More complete, quantitative data are required to test satisfactorily the usefulness of the I-strain concept. To obtain such data we have undertaken rate studies in the cycloalkane series of one typical reaction of the (1) S_N1, (2) S_N2, (3) free radical and (4) carbonyl group types. The present paper reports a study of the rates of solvolysis of 1-chloro-1-methylcycloalkanes with 4- to 17-ring members.

Small Rings.—1-Chloro-1-methylcyclobutane, conveniently synthesized by the addition of hydrogen chloride to methylenecyclobutane at 0°, was solvolyzed in 80% aqueous ethanol at 25, 35 and 45°. The first-order rate constant at 25°, 0.00224 hr.$^{-1}$ is low compared to that for *t*-butyl chloride, 0.0321 hr.$^{-1}$, in the same solvent. The energy of activation was determined to be 24.2 kcal., as compared with 22.8 kcal. for *t*-butyl chloride.

The rate measurements were repeated in 80% ethanol which was 0.0847 *N* in sodium hydroxide. The observed rate constant at 25°, k_1 0.00206 hr.$^{-1}$, did not exhibit any increase in the rate of reaction which would indicate any tendency toward bimolecular displacement of halogen by hydroxyl ion.[8] The reaction is clearly of the type which Hughes and Ingold[9] have designated as S_N1.

The solvolysis does not appear to be accompanied by any rearrangement of the carbon skeleton. Solvolysis of the tertiary chloride at 100° in water, under neutral conditions, led to the isolation of 1-methylcyclobutanol in 54% yield. No attempt was made to recover olefin formed in the reaction, but the alcohol appeared to be homogeneous and free of other products. Demjanow and Dojarenko had previously shown that methylenecyclobutane can be converted without rearrangement into 1-methylcyclobutanol by treatment with 66% sulfuric acid.[10]

An attempt was made to synthesize 1-chloro-1-methylcyclopropane by the photochemical chlorination of methylcyclopropane at −20°. The product appeared to consist predominantly of a single monochloride, C_4H_7Cl, b.p. 85.5–85.7° at 736 mm., n^{20}_D 1.4349. A cooling curve for one of the center fractions indicated a purity of 94 mole per cent. with a calculated freezing point for the pure substance of −90.9°. The chloride underwent solvolysis in 80% ethanol as a typical tertiary halide, giving first order rate constants (hr.$^{-1}$) of 0.000666 at 25°, 0.00479 at 40°, 0.0279 at 55° and 0.162 at 70°. These data yield an energy of activation of 24.7 kcal. with a value of 14.92 for the logarithm of the frequency factor. The rate constant was not appreciably affected by the use of the solvent which

---

(1) Chemical Effects of Steric Strains. VI.

(2) Based upon a thesis submitted by Mitchell Borkowski in June, 1951, to the Graduate School of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Research Fellow at Purdue University, 1948–1951, under a contract with the Office of Naval Research for the study of "Steric Strains in Chemical Reactions."

(4) A summary of much of the available data concerning such reactions is contained in an earlier paper: H. C. Brown, R. S. Fletcher and R. B. Johannesen, THIS JOURNAL, **73**, 212 (1951).

(5) For more recent data on the reactivity of small ring compounds, see J. D. Roberts and V. C. Chambers, *ibid.*, **73**, 3176 (1951).

(6) F. P. Price and L. P. Hammett, *ibid.*, **63**, 2387 (1941).

(7) V. Prelog and M. Kobelt, *Helv. Chim. Acta*, **32**, 1187 (1949).

(8) The slight decrease in the rate constant observed in the presence of sodium hydroxide appears to be a general phenomenon. We have previously observed such a decrease in the solvolysis of *t*-butyl chloride, 1-chloro-1-methylcyclopentane and neopentyldimethylcarbinyl chloride. The decrease is attributed to strong solvation of the small hydroxyl ion by water molecules. Such solvation reduces the effective aqueous content of the solvent. See A. Zletz, M.S. Thesis, Wayne University, 1948.

(9) E. C. Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

(10) I. N. Demjanow and M. Dojarenko, *J. Russ. Phys. Chem. Soc.*, **45**, 176 (1913); *C. A.*, **7**, 2226 (1913); *Chem. Zentr.*, **84**, I, 2026 (1913).

was 0.0839 N in sodium hydroxide (k_1 0.00496 hr.$^{-1}$ at 40°).

In spite of this solvolytic behavior, characteristic of typical tertiary alkyl halides, the compound is apparently identical with the unusual primary chloride, cyclopropylcarbinyl chloride, recently studied by Roberts and Mazur.[11]

Common Rings.—1-Methylcyclopentanol, -hexanol and -heptanol were synthesized by the action of the methyl Grignard reagent on the cycloalkanones. The tertiary alcohols were readily converted into the tertiary chlorides by treatment with hydrogen chloride at 0°.

The solvolysis of the three tertiary chlorides at 25° was studied previously.[4] The measurements were repeated and extended to other temperatures to permit calculation of the energies and entropies of activation.

At 25° the first-order rate constant for the 5-ring compound is 1.32 hr.$^{-1}$. It drops to 0.0106 for the cyclohexane derivative and rises to 1.15 for the 7-ring chloride. Similarly, the energy of activation rises from 20.8 kcal. for 1-chloro-1-methylcyclopentane to 24.9 for the 6-ring, and drops again to 21.2 for the 7-ring. The entropy of activation is somewhat greater for the cyclohexane derivative than for the 5- and 7-membered rings.

Thus, both the rate constant and the energy of activation show the 6-ring compound to be markedly different from the 5- and 7-ring derivatives. Moreover, the difference in reactivity between the cyclohexane derivative on the one hand, and the cyclopentane and -heptane derivatives on the other is primarily the result of a marked increase in the activation energy term.

The solvolysis of 1-chloro-1-methylcycloheptane proceeded smoothly and the rate data, on analysis, gave a single first-order constant. Previously, the solvolysis of this chloride had shown slight deviations which indicated the presence of a few per cent. of a less reactive tertiary halide.[4] In that case the cycloheptanone had been synthesized by the ring enlargement of cyclohexanone and it is probable that the ketone contained a small amount of a methylcyclohexanone, or some similar product, which reacted with the methyl Grignard reagent to give an isomeric tertiary alcohol, thereby complicating the rate data. The absence of the phenomenon in the present case, where the quantity of material permitted vigorous purification of the intermediates, demonstrates that 1-methylcycloheptanol does not undergo partial isomerization into a cyclohexane derivative upon treatment with hydrogen chloride as suggested previously.[4]

Medium Rings.—Our first attempts to prepare 1-methylcycloöctanol by reaction of methylmagnesium iodide with cycloöctanone, followed by distillation of the tertiary alcohol, failed. Dehydration occurred, even though the distillation was carried out at low pressures. The resulting olefin, 1-methylcycloöctene, was isolated in pure state and converted into the desired tertiary chloride by addition of hydrogen chloride at 0°. This material was fractionated under reduced pressure and utilized for the solvolysis experiments.

Godchot and Cauquil[12] had previously reported that they were unable to obtain 1-methylcycloöctanol in the pure state because of the great ease with which it undergoes dehydration to the olefin. It was of interest to look into the matter further. We found that crystallization from low boiling petroleum ether permitted isolation of samples of the tertiary alcohol of satisfactory purity.[13]

The ready dehydration of the 8-membered tertiary alcohol was paralleled by a marked tendency for the tertiary chloride to lose hydrogen chloride. Moreover, the tertiary chloride proved to be the most reactive of the 1-chloro-1-methylcycloalkanes studied. At 0, 25 and 35°, the rates of solvolysis are 0.115, 3.03 and 9.59 hr.$^{-1}$, respectively. The energy of activation is 21.1 kcal.

The tertiary alcohols containing rings of 9-, 10- and 11-members were synthesized from the cyclic ketones and methylmagnesium iodide. The tertiary alcohols are all solids and were conveniently purified by crystallization from petroleum ether. They were converted into the tertiary chlorides by treatment with hydrogen chloride. Because of the necessity for conserving material, only small quantities of the tertiary alcohols were prepared and no attempt was made to isolate and purify the tertiary chlorides. The crude products were used directly for the rate studies. This procedure is justified since the rates would not be significantly affected by appreciable quantities of such probable impurities as free hydrogen chloride, unreacted alcohol or olefin. The procedure was tested by taking a sample of 1-methylcycloheptanol, converting the alcohol to the chloride with hydrogen chloride, and utilizing the crude product directly for rate measurements. The first-order constant at 25° (1.15 hr.$^{-1}$) agreed perfectly with the value previously obtained for the tertiary chloride purified by fractionation.

The rate constants showed a steady decrease with increasing ring size, from 0.465 hr.$^{-1}$ for the 9-, to 0.188 for the 10-, to 0.127 for the 11-membered ring.

The conversion of the cyclic ketones to the tertiary alcohols in most cases proceeded smoothly with yields in the neighborhood of 60–95%. In the case of cyclodecanone, the yield was only 39% and it was noted that addition of the ketone to the solution of the methyl Grignard reagent was accompanied by the evolution of considerable quantities of a gas, presumably methane. If the gas is ascribed to enolization of the cyclodecanone, approximately one-third of the ketone reacted in this fashion. The amount of gas evolved is greatest with the 10-membered ring ketone and decreases in the order: $10 > 11 > 9 > 8$. The large rings (13, 15 and 17) do not liberate significant quantities of gas. Cope and Fenton[13] recently noted that they recovered

---

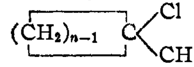
[11] J. D. Roberts and R. H. Mazur, THIS JOURNAL, **73**, 2509 (1951). For an interesting interpretation of the unusual reactivity of cyclopropylcarbinyl derivatives: C. G. Bergstrom and S. Siegel, Abstracts of Papers Presented to the Division of Organic Chemistry at the Meeting of the American Chemical Society, Boston, Mass., April 2-5, 1951, p. 33; J. D. Roberts and R. H. Mazur, *ibid.*, **73**, 3542 (1951).

[12] M. Godchot and G. Cauquil, *Compt. rend.*, **185**, 1202 (1927).

[13] A. C. Cope and S. W. Fenton, THIS JOURNAL, **73**, 1195 (1951), and L. E. Craig and C. E. Larrabee, *ibid.*, **73**, 1191 (1951), have recently noted that 1-ethyl-1-cycloöctanol behaves similarly and undergoes dehydration upon attempted distillation.

TABLE I

SUMMARY OF THE RATE DATA FOR THE SOLVOLYSIS OF THE 1-CHLORO-1-METHYLCYCLOALKANES IN 80% ETHANOL[a]

Tertiary chloride[b]  $(CH_2)_{n-1}C(Cl)CH_3$		Rate constant k_1 (hr.$^{-1}$)					
n	0°	25°	35°	45°	$E_{act.}$, kcal.	log A[c]	$S^‡ - S_0^‡$[d]
4		0.00224	0.00853	0.0293	24.2	15.09	−0.6
5	0.0513	1.32	4.06		20.8	15.36	+0.6
6		0.0106	0.0415	.149	24.9	16.28	+4.8
7	.0382	1.15	3.55	10.5	21.2	15.58	+1.6
8	.115	3.03	9.59		21.1	15.94	+3.3
9		0.465					
10		.188					
11		.127					
13		.0302	0.115	0.398	24.2	16.22	+4.6
15		.0192					
17		.0201					
Me_3CCl		.0302	.112	.363	22.8	15.22	0.0
Et_2MeCCl		.086					
n-Am_2MeCCl	.00115	.0480	.178	.568	23.8	16.12	+4.1

[a] d^{25}_4 0.8489. [b] Data for cyclopropylcarbinyl chloride are not included in this summary. [c] $k = Ae^{-E/RT}$. [d] Reference substance: *t*-butyl chloride.

considerable quantities of cycloöctanone from the reaction product of the ketone and ethylmagnesium iodide and also ascribed the result to ready enolization of the cyclic ketone. This phenomenon is being studied by more quantitative methods.

Large Rings.—The 1-chloro-1-methylcycloalkanes with 13-, 15- and 17-ring members were synthesized from the cycloalkanones by methods similar to those previously described. The first-order rate constant at 25° was 0.0302 hr.$^{-1}$ for 1-chloro-1-methylcyclotridecane, 0.0192 for 1-chloro-1-methylcyclopentadecane and 0.0201 for 1-chloro-1-methylcycloheptadecane.

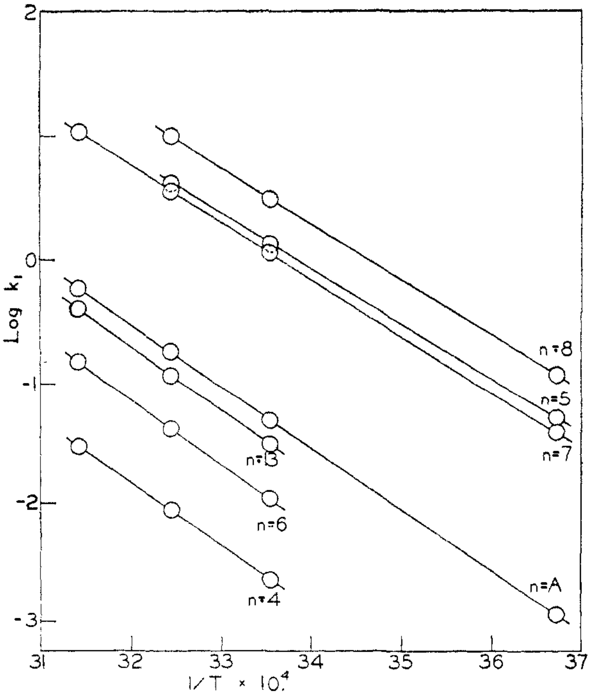


Fig. 1.—Activation energies for the solvolysis of the 1-chloro-1-methylcycloalkanes in 80% ethanol: n = number of ring atoms; A = n-Am_2MeCCl.

The rate constant for *t*-butyl chloride at 25° in the same solvent is 0.0321. It was surprising to find that the rate constants for the 15- and 17-membered ring compounds are smaller than that for *t*-butyl chloride itself. It was considered possible that the large hydrocarbon ring might affect the solvent in the neighborhood of the reactive group and modify its ionizing properties.

Previously the effect of chain-lengthening in the series RMe_2CCl (R = Et, *n*-Pr, *n*-Bu) had been studied.[14] No significant change in the rate constant had been observed with increase in length of the group R. However, the magnitude of the hydrocarbon radical in this series is far less than in the cyclic compounds under consideration here. Accordingly di-*n*-amylmethylcarbinyl chloride was synthesized and its rate of solvolysis studied. The observed rate constant, 0.0480 hr.$^{-1}$ at 25°, is definitely smaller than the value 0.086 previously observed for diethylmethylcarbinyl chloride.[14] Both the energies and entropies of activation appear to increase moderately in these large tertiary halides.

The experimental results are summarized in Table I and Fig. 1.

Discussion

Two major sources of internal strain may be recognized in the cycloalkanes and their derivatives: distortion of the bond angles from their preferred values and deviation of the carbon–hydrogen constellations from the preferred staggered arrangement.[15] Steric strain arising from compression of the van der Waals radii does not appear to be an important factor in the simple cycloalkanes and their derivatives,[16] although it should become an important factor with the introduction of bulky substituents.

In the 3- and 4-membered rings, the distortion of the bond angles appears to be the major source of

---

[14] H. C. Brown and R. S. Fletcher, THIS JOURNAL, **71**, 1845 (1949).

[15] K. S. Pitzer, *Science*, **101**, 2635 (1945); J. E. Kilpatrick, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2483 (1947).

[16] V. Prelog, *J. Chem. Soc.*, 420 (1950).

the strain present. The small angles increase the distance between the hydrogen atoms and presumably reduce the importance of the interactions which cause the staggered constellation to be favored. In rings of five members and more, the second factor (the constellation effect) is of major importance.[15] Thus, a planar cyclopentane molecule would require energetically unfavorable constellations and result in a large increase in energy. The strain is minimized by rotations of the carbon atoms and distortions of the bond angles. These changes result in a non-planar molecule and less unfavorable constellations.[15]

In 3- and 4-membered rings it is readily apparent that a change in the coördination number of a ring atom from four to three (reactions of the S_N1 and free radical types) and from four to five (reactions of the S_N2 type) should involve an increase in the internal strain and as a result such reactions should proceed relatively slowly.[4] On the other hand, reactions involving a change in the coördination number of a ring atom from three to four (reactions of the carbonyl group type) should involve a decrease in the internal strain and should proceed relatively rapidly.

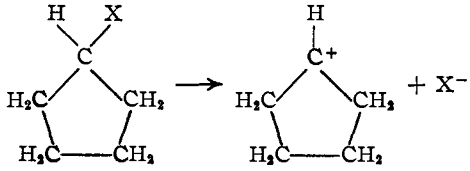
The slow solvolysis of 1-chloro-1-methylcyclobutane represents the first example involving a small ring of a reaction of the S_N1 type which does not proceed with rearrangement. The slow rate and the high activation energy supports the I-strain concept as applied to small rings.[17] It is of interest to point out that 1-methylcyclobutanol also appears to be unusually inert and does not undergo the iodine-catalyzed dehydration under conditions conducive to this reaction in other cases.[18,19]

In the common (5–7) and medium (8–12) rings, the constellation effect must be of far greater importance as a basis for internal strain than are the angle distortions. The effects are quite large. Accurate heat of combustion data show that cyclopentane and cycloheptane are 6–7 kcal. more strained than cyclohexane, which can exist in a relatively strain-free conformation with all carbon–hydrogen bonds nicely staggered.[20] Although good combustion data are not available for the larger rings, the maximum in density and minimum in molar refraction observed in rings with eight to twelve carbon atoms also point to the presence in these compounds of internal strains resulting from unstable conformations.[16]

The extension of the I-strain concept to these rings is not immediately apparent. An empirical approach has been adopted. The fragmentary data available[4] indicate that reactions involving a change in coördination number of 4 to 3 (reactions of the S_N1 and free radical types), and 4 to 5 (reactions of the S_N2 type) are strongly favored in the strained rings (5, 7; 8–12), but proceed more slowly in the case of the strain-free cyclohexane compounds. On the other hand, reactions involving a change in the coördination number from 3 to 4 in the rate-determining step (reactions of the carbonyl group type), proceed quite readily in the case of the cyclohexyl derivatives, but comparatively sluggishly in the derivatives of the strained rings.

It appears best to defer a detailed analysis of the changes in internal strain in these ring compounds with changes in the coördination number of a ring atom until the value of the proposed correlation has been fully tested by complete rate studies involving a representative reaction of each of the major types. Such studies are underway. However, it should be apparent that in solvolytic reactions of the type considered in the present paper, the formation of a carbonium ion from a cyclopentyl derivative should be accompanied by a marked decrease in the number and magnitude of the unfavorable constellations.

For example, if we consider the idealized case of a planar cyclopentyl derivative, there will be a total of ten bonds in the opposed position. Loss of a group to produce a carbonium ion will immediately reduce the number of opposed bonds to six. In this idealized case, the ionization would mean a decrease of approximately 4 kcal. in strain energy.

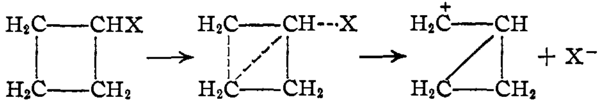


strained (10 bonds in opposition) less strained (6 bonds in opposition)

The difference in energy will probably be diminished somewhat in the actual molecule because of the necessity for accommodating a somewhat larger angle at the carbonium carbon and through reduction of the unfavorable constellations in both the parent compound and the ion by deviations from planarity.[15] However, there is little reason to doubt that the I-strain should be sufficiently large to furnish an important driving force in the cyclopentane derivatives. Similar relief of strain should accompany the loss of a bond in the cycloheptane compounds and in other rings which are strained as a result of constellation effects.

---

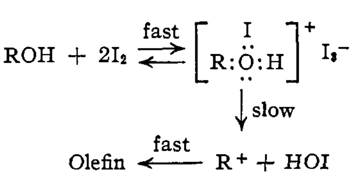
[17] The solvolysis of cyclobutyl chloride and cyclobutyl tosylate has recently been described. J. D. Roberts, Twelfth National Organic Symposium of the American Chemical Society, June 12-15, 1951, Denver, Colorado, pp. 44-46. In these cases the reactions proceed with rearrangement and the ionization step may be facilitated by participation of a ring atom.



Such participation by ring atoms in the norbornyl series has been demonstrated by S. Winstein and co-workers: S. Winstein and D. S. Trifan, THIS JOURNAL, **71**, 2953 (1949).

[18] W. Shand, V. Schomaker and J. R. Fischer, *ibid.*, **66**, 636 (1944).

[19] The iodine catalyzed dehydration of a tertiary alcohol presumably involves the rate-determining ionization of an oxonium derivative

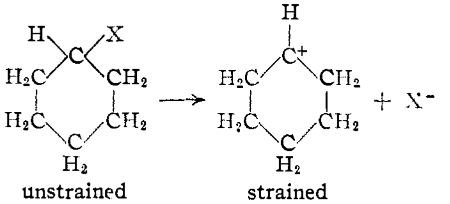


$$\mathrm{ROH} + 2\mathrm{I_2} \underset{}{\overset{\text{fast}}{\rightleftarrows}} \left[\mathrm{R{:}\overset{\displaystyle I}{\ddot{\underset{..}{O}}}{:}H}\right]^+ \mathrm{I_3^-} \xrightarrow{\text{slow}} \mathrm{R^+ + HOI} \xrightarrow{\text{fast}} \text{Olefin}$$

M. L. Dhar, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Maw and L. I. Woolf, *J. Chem. Soc.*, 2113 (1948).

[20] R. Spitzer and H. M. Huffman, THIS JOURNAL, **69**, 211 (1947); C. W. Beckett, K. S. Pitzer and R. Spitzer, *ibid.*, **69**, 2488 (1947).

On the other hand, the constellations in cyclohexane are already highly favorable. Removal of an ion from a cyclohexyl derivative should not improve the situation in the same way. Indeed, consideration of the molecular model suggests that the introduction of an atom with a preferred value of 120° would be expected to have a deleterious effect on the symmetry and stability of the cyclohexyl system and reactions of this kind may be expected to proceed somewhat less readily than in open-chain compounds.



Conversely, reactions involving a change in coördination number of a ring atom from 3 to 4 (reactions of the carbonyl group type) should be strongly favored in the cyclohexyl derivative and should proceed sluggishly in the strained rings (5, 7, 8–12).

The results of the present study strongly support this interpretation. The rates of hydrolysis of 1-chloro-1-methylcyclopentane and -heptane are both very fast, proceeding roughly 100-fold faster than the corresponding cyclohexane derivative. It is also of interest that the effect shows up primarily in the energy of activation term. There is a difference of approximately 4 kcal. in the activation energies for the solvolysis of the two strained-ring derivatives (5, 7) and the strain-free compound (6).[21]

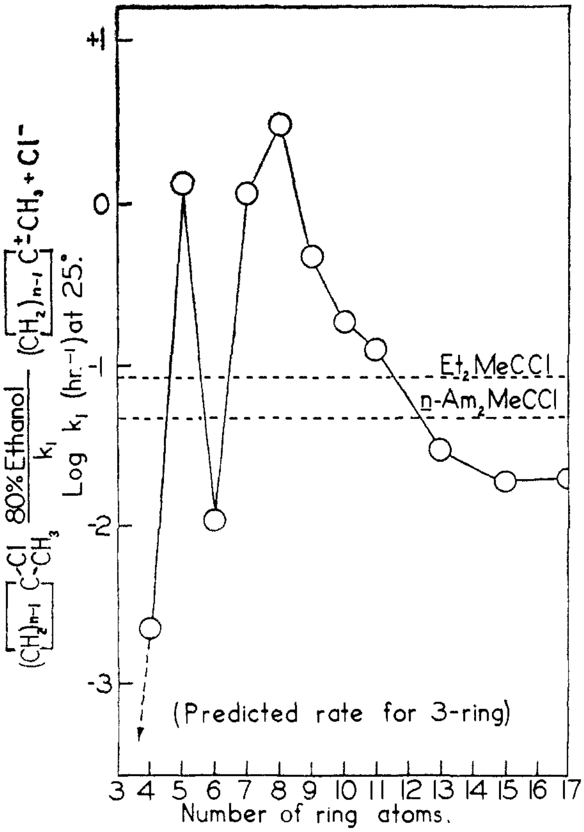
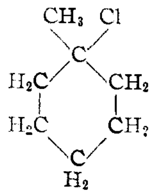
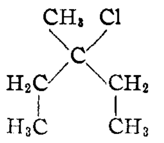


Fig. 2.—Effect of ring size on solvolysis rate.

1-Chloro-1-methylcyclohexane solvolyzes at a rate approximately one-eighth that of diethylmethylcarbinyl chloride. This decrease in rate suggests that the introduction of an atom with a preferred angle of 120° into the stable cyclohexane system must be a destabilizing factor. In other words, the increase in rate of the 5- and 7-membered rings over related open-chain compounds is considered to be primarily the result of strain in the parent compound, strain which is partially relieved in the carbonium ion. The decrease in rate of the 6-membered ring over related open-chain compounds is attributed primarily to strain in the carbonium ion with the original compound being relatively strain-free.





The high rates of solvolysis of the medium ring compounds (8- to 11-) may be interpreted similarly. The strain present in the parent compounds, strain due primarily to constellation effects, is reduced in the carbonium ion. The carbonium ions are thereby stabilized relative to the initial halide and consequently are formed with greater ease in the solvolysis than are related open-chain derivatives.

As the ring size is increased, these strain effects disappear and the reactivities approach those of the open-chain compounds.

The change in the solvolysis rates with ring size is illustrated in Fig. 2. The effect of ring size in this reaction is quite similar to that previously noted by Prelog and his co-workers in the dissociation of the cyclic cyanohydrins[22] (Fig. 3A) and in the polarographic reduction of the Girard-T derivatives of cyclic ketones[23] (Fig. 3B).

In the solvolysis reaction reported in the present paper the maximum in rate is observed in the medium ring compounds at the 8-membered derivative. In the dissociation of the cyanohydrins the maximum in instability is observed in the 10-membered derivative, whereas in the polarographic reduction, the maximum is observed with the 8-membered compound. We cannot at this time offer any explanation for the observed shift in the precise position of the maximum. However, it should be recalled that I-strain is only one of the factors which will determine the relative rates of reaction of ring compounds. Such items as entropy effects, F-strain, solvation, neighboring groups, etc., may well play a part, and in some cases may even become predominant. In view of the complexity of the problem, it is somewhat

---

[21] The solvolysis of cyclopentyl tosylate in anhydrous acetic acid also proceeds much faster than cyclohexyl tosylate with a difference of 3.3 kcal. in the energy of activation and 5.3 e.u. in the entropy of activation for the two compounds (private communication from Professor S. Winstein).

[22] V. Prelog and M. Kobelt, *Helv. Chim. Acta*, **32**, 1187 (1949).

[23] V. Prelog and O. Häfliger, *ibid.*, **32**, 2088 (1949).

surprising that the available evidence on the relative reactivities of simple ring compounds is in such good agreement with the predictions of the I-strain concept. This suggests that in these compounds I-strain must be much more important than the other factors mentioned.

In the solvolysis of the 1-chloro-1-methylcycloalkanes there is apparently no very important difference in the entropy of activation terms of individual ring compounds, nor between the ring compounds as a class and simple open-chain tertiary chlorides (Table I). In other reactions, however, differences in the entropies of activation between ring compounds and open-chain derivatives may be quite important.[6] In such cases the relative reactivity of open-chain derivatives and ring compounds may be modified somewhat from that predicted from a consideration of I-strain alone. To unravel the relative importance of I-strain and other factors in determining reactivities of ring *versus* open chain compounds, it is important to obtain rate data at several temperatures to permit a comparison of the effects of structure on both the energies and the entropies of activation.

Experimental Part

Kinetic Measurements.—The solvent used in the hydrolysis measurements was an ethanol–water mixture containing approximately 80% ethanol by volume d^{25}_4 0.8489. The procedure used for the determination of the rate constants is essentially that described in a previous paper.[14] At the higher temperatures the rate measurements were made utilizing thin-walled glass capsules.

To illustrate the precision attained in the measurements a typical set of rate data is reported in Table II.

TABLE II

RATE DATA FOR THE HYDROLYSIS OF 1-CHLORO-1-METHYLCYCLOUNDECANE IN 80% ETHANOL AT 25°

t, hr.	*x*, ml.	*a* − *x*, ml.	k_1, hr.$^{-1}$
0	0.035 (x_0) 2.197 (a)	 2.162 ($a - x_0$)	
1	0.295	1.902	0.128
2	.530	1.667	.130
3	.715	1.482	.126
4	.905	1.292	.129
5	1.055	1.142	.126
6	1.180	1.017	.126
9	1.505	0.692	.127
11	1.655	.542	.126
12	1.725	.472	.127

Mean k_1 = 0.127 hr.$^{-1}$

A. **The Small Rings. 1-Chloro-1-methylcyclobutane.**—Pentaerythrityl bromide[24] was purified by exhaustive extraction with acetone.[25] Reduction with zinc[18] gave an 85–94% yield of the hydrocarbon mixture. The product was fractionated in a steel helix packed column rated at 70 theoretical plates (column A). Forty-one grams of methylenecyclobutane (b.p. 42.0° at 744 mm., n^{20}_{D} 1.4209), was treated at 0° with hydrogen chloride until no more gas was absorbed. The crude product was distilled through a 20-inch glass spiral column (column B). An 89% yield of 1-chloro-1-methylcyclobutane (b.p. 89.5–91.4 at 742 mm., n^{20}_{D} 1.4310) was obtained.

1-Methylcyclobutanol.—1-Chloro-1-methylcyclobutane, 9.2 g., and 75 ml. of water were heated under reflux. Several drops of phenolphthalein indicator were added and the reaction mixture was maintained neutral by continuous addition of 0.1 *N* sodium hydroxide. After the theoretical quantity of base had been added, the solution was extracted with ether and the product distilled. No attempt was made to recover olefin. The product, 4.1 g., distilled constantly at 116–118° at 742 mm. with n^{25}_{D} 1.4333; the yield was 54%.[26] We were intrigued by the report that the alcohol is stable toward dehydration of iodine[18] and subjected it to the Lucas test for tertiary alcohols. The mixture immediately became cloudy.

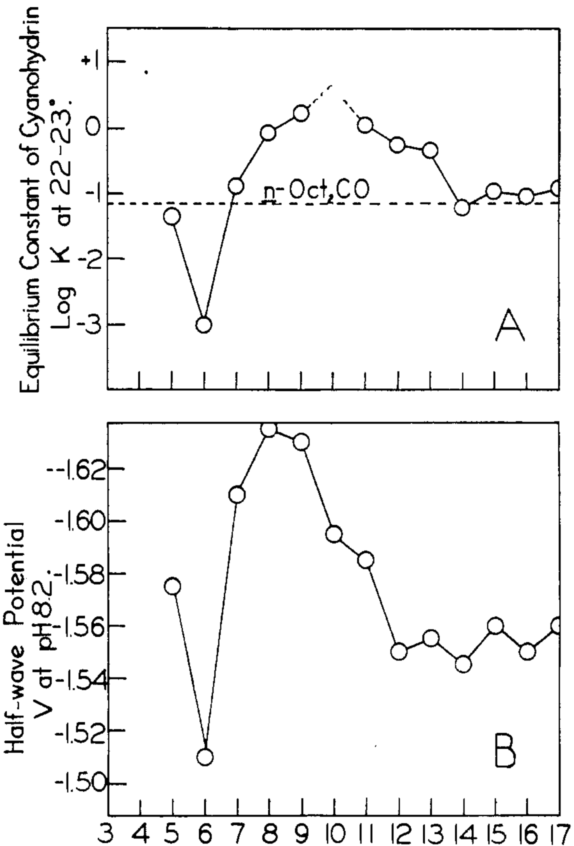


Fig. 3.—Effect of ring size on the dissociation of cyanohydrins (A) and the polarographic reduction of the Girard-T hydrazones (B).

Chlorination of Methylcyclopropane.—The action of hydrogen bromide on 1,3-butanediol at 100° resulted in a 67% yield of 1,3-dibromobutane (b.p. 87–92° at 50 mm., n^{20}_{D} 1.5080–1.5089). The dibromide was obtained in 77% yield by the action of phosphorus tribromide on the diol, using equimolar quantities of the phosphorus halide and the alcohol, rather than the large excess of halide utilized by Fargher and Perkin.[27] The debromination of 1,3-dibromobutane with zinc in aqueous ethanol[28] produced methylcyclopropane in yields of 70–88%.

Approximately 75 g. of methylcyclopropane was placed in a 500-ml. three-necked flask fitted with a thermometer well and cooled to −20°. The three necks of the flask were fitted with a precision bore stirrer, a low temperature (−80°) condenser and an inlet tube with a sintered glass dispersion disc to introduce the chlorine below the surface of the hydrocarbon. A measured amount of chlorine was introduced slowly through a flowmeter as the flask was subjected to strong illumination. A ratio of 4 to 6 moles of hydrocarbon per mole of chlorine was used. After the reaction was com-

---

[24] H. B. Schurink, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 476.

[25] M. J. Murray and E. H. Stevenson, THIS JOURNAL, **66**, 812 (1944).

[26] Shand, Schomaker and Fischer (Ref. 22) report b.p. 115–118° at 747 mm., n^{24}_{D} 1.4333.

[27] R. G. Fargher and W. H. Perkin, *J. Chem. Soc.*, **105**, 1353 (1914).

[28] N. Demjanow, *Ber.*, **28**, 21 (1895); W. A. Lott and W. G. Christiansen, *J. Am. Pharm. Assoc.*, **27**, 125 (1938); **20**, 207 (1931); **19**, 341 (1930).

plete, the excess hydrocarbon was evaporated slowly through the condenser maintained at 5° and collected. The product was removed, the recovered hydrocarbon returned to the flask along with additional material, and the chlorination repeated. In this way a total of 342 g. of chlorinated product was obtained.

A portion of the product, 207 g., was distilled through a jacketed glass spiral column, 50 cm. in length. Of 121 g. collected in the range 48–90°, 115 g. or 95% of this material came over at 80–90°. There was 87 g. of residue which appeared to be much higher boiling and was not further investigated.

A portion of the material in fractions which distilled at 80–87°, comprising 78% of the material collected below 90°, was put through a micro concentric tube column tested at 65 theoretical plates. A total of 91% of this material was collected at 85.5–85.7° at 736 mm. with constant refractive index, n^{20}_D 1.4349, and d^{25}_4 0.981.

Anal. Calcd. for C_4H_7Cl: C, 53.05; H, 7.79; Cl, 39.16. Found: C, 53.05; H, 7.64; Cl, 39.0, 39.4.

The compound solvolyzes in 80% ethanol giving a first-order constant which is not affected by sodium hydroxide (Table III).

TABLE III

RATE DATA FOR THE SOLVOLYSIS OF CYCLOPROPYLMETHYL CHLORIDE AT 40°

t, hr.	*x*, ml.	*a* − *x*, ml.	k_1, hr.$^{-1}$
	Aqueous ethanol, 80%		
0	0.045 (x_0)		
∞	7.345 (*a*)	7.289 ($a - x_0$)	
6	0.264	7.081	0.00483
19	.690	6.455	.00479
27	.934	6.411	.00475
45	1.464	5.881	.00477
51	1.620	5.725	.00474
66	2.034	5.311	.00480
92	2.616	4.729	.00470
			Mean k_1 = 0.00477 hr.$^{-1}$
	Aqueous ethanol, 80%, 0.0836 *N* sodium hydroxide		
0	7.640 (x_0)		
∞	0.235 (*x*)	7.405 ($x_0 - x$)	
5	7.460	7.225	0.00492
19	6.960	6.725	.00507
24	6.795	6.560	.00505
41	6.255	6.020	.00505
68	5.500	5.265	.00502
95	4.850	5.615	.00498
117	4.390	4.155	.00494
137	4.045	3.810	.00485
161	3.635	3.400	.00484
			Mean k_1 = 0.00497 hr.$^{-1}$

In an attempt to establish the identity of the chloride, it was treated with magnesium and the resulting Grignard reagent was carbonated to yield the acid (b.p. 90–100° at 20 mm., n^{20}_D 1.4350–1.4358). A portion of the acid was converted to the amide by treatment first with thionyl chloride and then ammonia. Recrystallization from benzene gave crystals, m.p. 103–104°.

Anal. Calcd. for C_5H_9NO: C, 60.58; H, 9.15; N, 14.13. Found: C, 60.40; H, 9.10; N, 14.09.

The *p*-bromophenacyl ester, recrystallized from 90% ethanol, melted at 59.5–60.5°. A mixture with an authentic sample of the *p*-bromophenacyl ester of 1-methylcyclopropanecarboxylic acid (m.p. 59–60)[29] melted at 40–47°.

Anal. Calcd. for $C_{13}H_{13}O_3Br$: C, 52.52; H, 4.41. Found: C, 52.83; H, 4.96.

It has recently been reported that the halide obtained from cyclopropylcarbinol and phosphorus tribromide (presumably cyclopropylcarbinyl bromide[11]) forms a Grignard reagent which reacts to give derivatives of allylacetic acid.[30] Moreover, the *p*-bromophenacyl ester of the acid obtained in this way melted at 57–58° and did not depress the melting point of an authentic sample of the corresponding ester of allylacetic acid.[30] The chloride obtained in the present study is therefore considered to be cyclopropylcarbinyl chloride.

B. **The Common Rings. 1-Chloro-1-methylcyclopentane.**—Cyclopentanone was prepared from adipic acid[31] and converted with methylmagnesium bromide into 1-methylcyclopentanol (b.p. 133–136° at 745 mm., m.p. 32–34°) which was in turn converted into the tertiary chloride (b.p. 66° at 121 mm., n^{20}_D 1.4467).

1-Chloro-1-methylcyclohexane.—Cyclohexanone (Eastman Kodak Co.) was converted into the tertiary alcohol (b.p. 72–73.5° at 29 mm., n^{20}_D 1.4609) and then into the chloride (b.p. 83–84° at 100 mm., n^{20}_D 1.4578).

1-Chloro-1-methylcycloheptane.—The action of methylmagnesium iodide on cycloheptanone (Geigy) (b.p. 172–174° at 747 mm., n^{20}_D 1.4613) produced 1-methyl-1-cycloheptanol (b.p. 82–83.5° at 20 mm., n^{20}_D 1.4690). Passage of hydrogen chloride into the cooled alcohol furnished an 83% yield of the tertiary chloride boiling in the range 77–77.5° at 20.5 mm., n^{20}_D 1.4710.

Anal. Calcd. for $C_8H_{15}Cl$: C, 65.49; H, 10.31; Cl, 24.17. Found: C, 65.74; H, 10.38; Cl, 23.82.

C. **The Medium Rings. 1-Methylcyclooöctanol.**—1-Methylcyclooöctanol has not been previously prepared. The alcohol undergoes dehydration with extreme ease[12,13] and attempts to purify it by distillation led only to 1-methylcyclooöctene. The alcohol was finally isolated through the following procedure.

A solution of 4.06 g. (0.032 mole) of cyclooöctanone[32] (m.p. 38°) in 50 ml. of anhydrous ether was added to methylmagnesium iodide, prepared from 14.2 g. (0.1 mole) of methyl iodide in 30 ml. of ether and 2.43 g. (0.1 g. atom) of magnesium turnings in 15 ml. of ether, over a period of 45 minutes, followed by further refluxing for four hours. (A total of 35 ml. of gas, measured at S.T.P., was evolved.) The mixture was titrated with a saturated solution of ammonium chloride.[33] The ether solution of the alcohol was washed with sodium carbonate solution and dried over potassium carbonate. The ether was removed under vacuum, leaving a white crystalline residue behind. After two recrystallizations of the crude product from petroleum ether (35–37°), approximately 2 g. of tertiary alcohol (m.p. 34–36°) was obtained. A third recrystallization did not alter the melting point.

Anal. Calcd. for $C_9H_{18}O$: C, 76.02; H, 12.76. Found: C, 75.83; H, 12.72.

1-Methylcyclooöctene.—The olefin (b.p. 159–164° at 741 mm., n^{20}_D 1.4710), obtained in early attempts to purify 1-methylcyclooöctanol by distillation, was converted into the tertiary chloride (b.p. 64–65° at 4 mm., n^{20}_D 1.4796) with hydrogen chloride at 0°.

Anal. Calcd. for $C_9H_{17}Cl$: C, 67.27; H, 10.67; Cl, 22.07. Found: C, 69.15; H, 10.71; Cl, 20.45.

The tertiary chloride is much less stable than the other compounds prepared in this study. On standing in a sealed glass capsule, the originally colorless sample developed a brown coloration and free hydrogen chloride. After longer periods, fine droplets of heavier liquid were observed. Since our samples were sent away for analysis and several days intervened before the analysis could be performed, we believe that the low value for chlorine is primarily the result of such decomposition subsequent to preparation of the sample.

Cyclononanone.—Dimethyl azelate was prepared by the esterification of technical azelaic acid. The product (b.p. 142–150° at 10 mm., n^{20}_D 1.4350–1.4363) was utilized in the acyloin condensation, following the procedure described by Prelog and Stoll and their co-workers.[34] The crude

---

[29] S. Siegel and C. G. Bergstrom, THIS JOURNAL, **72**, 3815 (1950).

[30] L. I. Smith and S. McKenzie, Jr., *J. Org. Chem.*, **15**, 74 (1950). See also I. M. Demjanow and M. Dojarenko, *J. Russ. Phys. Chem. Soc.*, **43**, 835 (1911); *C. A.*, **6**, 479 (1912).

[31] J. F. Thorpe and G. A. R. Kon, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 192.

[32] Kindly furnished by Professor V. Prelog.

[33] L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., New York, N. Y., 1941, pp. 409–410.

[34] (a) V. Prelog, L. Frenkiel, M. Kobelt and P. Barman, *Helv. Chim. Acta*, **30**, 1741 (1947); (b) M. Stoll and J. Hulstkamp, *ibid.*, **30**, 1815 (1947); M. Stoll and A. Rouvé, *ibid.*, **30**, 1822 (1947).

"acyloin fraction" (b.p. 110–124° at 12 mm.) was obtained in yields up to 26%. It was reduced to cyclononanone by the zinc–hydrochloric acid method.[34a] The method is apparently highly dependent upon the nature of the zinc. In order to accomplish the conversion, the procedure described[34a] required modification.

Professor Prelog[35] informed us that it is of great importance that the zinc and hydrochloric acid used for the reduction be very pure; the reduction is completely inhibited by small amounts of iron, nickel or platinum salts, and the yield is reduced by copper salts, while the presence of mercury salts leads to hydrocarbons. However, we were unable to obtain reduction with high purity zinc, while the use of Mallinckrodt technical zinc metal dust yielded predominantly either the ketone or the hydrocarbon, depending upon conditions. The following procedure was developed and utilized for the synthesis of cyclononanone and the higher cyclic ketones.

A mixture of 23 g. of crude "acyloin fraction," 58 g. of glacial acetic acid and 58 g. of zinc metal dust (Mallinckrodt) was placed in a 500-ml. round-bottomed flask provided with a reflux condenser. Concentrated C.P. hydrochloric acid, 33 ml., was added and the flask heated at 100°. Additional 33-ml. portions of hydrochloric acid were introduced at the end of 0.5 and 1.0 hour. After a total of 1.5 hours, the mixture was allowed to cool, 100 ml. of water added and extracted with ether. The ether extract was washed with dilute sodium carbonate solution followed by water, and then dried over anhydrous sodium sulfate. The ether was removed and the residue was distilled from a small Claisen flask under reduced pressure. The weight of "ketone fraction" (b.p. 90–110° at 16 mm.) was 12.65 g.; yield 61%. The "ketone fractions" from several such reductions were combined and rectified under reduced pressure (Column B). The cyclononanone (b.p. 92–96° at 12 mm., n^{40}_{D} 1.4682–1.4696) was utilized for the preparation of the tertiary alcohol.

1-Methylcyclononanol.—The methyl Grignard, 0.21 mole, was reacted with 9.8 g. (0.07 mole) of cyclononanone. The addition required an hour and the mixture was refluxed for a further six hours. (Approximately 170 ml. of gas was evolved.) After hydrolysis with saturated ammonium chloride solution,[33] the ether solution was tinged yellow. The solution was dried, the ether was removed, and the crystalline residue was recrystallized from petroleum ether (35–37°) with the addition of Norite. The yield was 6.42 g. (59%) of white crystalline tertiary alcohol, m.p. 45–49°. A second recrystallization raised it to 51–52°.

Anal. Calcd. for $C_{10}H_{20}O$: C, 76.84; H, 12.90. Found: C, 76.83; H, 12.92.

1-Chloro-1-methylcyclononane.—Hydrogen chloride was conducted into 0.72 g. of the tertiary alcohol for two hours at room temperature. The alcohol began to liquify immediately. The small aqueous layer was removed with a capillary and the colorless organic layer was dried over a granule of calcium chloride, after which the dissolved hydrogen chloride was removed by pumping. The crude chloride contained 85% hydrolyzable chloride and was utilized directly for the rate measurements.

1-Methylcyclodecanol.—The "sebacoin fraction" (b.p. 75–85° at 0.1 mm.) was obtained in yields up to 40%. A small portion of the crude product was recrystallized from 50% ethyl ether–petroleum mixture. The product was colorless, m.p. 36–37.5°, n^{55}_{D} 1.4788.

The reduction was carried out as described for the preparation of cyclononanone. A 73% yield of "ketone fraction" (b.p. 95–112° at 12 mm.) was obtained. The "ketone fractions" from several reductions were combined and distilled through column B. The material, b.p. 106–109° at 12 mm., was cooled with ice-water and allowed to crystallize. The mother liquor (approximately one-third of the original material) was separated and the product (m.p. 22–24°, n^{30}_{D} 1.4784) utilized for the synthesis of the tertiary alcohol.

The 1-methylcyclodecanol was obtained in yield of 39% of material, m.p. 43–49°. Further recrystallization raised the melting point to 52.5–53.1°. (A reaction mixture of 0.18 mole of methylmagnesium iodide and 0.055 mole of cyclodecanone evolved approximately 400 ml. of gas.)

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.57; H, 13.02. Found: C, 77.83; H, 12.91.

1-Methylcycloundecanol.—Dimethyl undecanedioate (Edcan Laboratories, b.p. 139–150° at 3 mm., n^{20}_{D} 1.4379–1.4391) yielded "acyloin fraction" (b.p. 88–93° at 0.08 mm., n^{55}_{D} 1.4803) in 61% yield. The crude acyloin melted at 26–29° and this was raised to 29–32° after recrystallization from petroleum ether.

Reduction of the "acyloin fraction" yielded 55% of "ketone fraction" (b.p. 110–120° at 12 mm., n^{20}_{D} 1.4806). The semicarbazone prepared from a portion of the "ketone fractions" had m.p. 200–201° after one recrystallization from ethanol. Combined "ketone fractions" from several reductions were refractionated and the center fractions (b.p. 114–120° at 12 mm.), n^{20}_{D} 1.4811, were utilized for the synthesis of the tertiary alcohol.

The ketone was converted to the tertiary alcohol by a procedure similar to that described for 1-methylcyclononanol. (The reaction mixture, 0.05 mole cycloundecanone and 0.15 mole of methylmagnesium iodide, evolved 275 ml. of gas.) The ether was pumped off from the dry ether solution and the crude residue was taken up in methanol. On cooling, 0.60 g. of white crystalline product was separated on a filter. After recrystallization from petroleum ether, the product was obtained in the form of fine needles, m.p. 128.5–129.5°; C, 78.43, 78.66; H, 12.20, 11.98. Nothing further was done to identify this by-product. The remaining material could not be recrystallized from methanol. However, recrystallization from petroleum ether yielded 5.92 g. (64% yield) of material, m.p. 32–38°. Further recrystallization raised the melting point to 40–42°.

Anal. Calcd. for $C_{12}H_{24}O$: C, 78.19; H, 13.13. Found: C, 77.92, 78.15; H, 13 .02, 12.91.

D. The Large Rings. **1-Methylcyclotridecanol.**—Cyclotridecanone (m.p. 30°),[36] 0.028 mole, was treated with 0.09 mole of methylmagnesium iodide. (Approximately 23 ml. of gas was collected.) The product was recrystallized from methanol, discarding a small quantity of white insoluble material. A 92% yield of product, m.p. 75.5–76.5° was obtained.

Anal. Calcd. for $C_{14}H_{28}O$: C, 79.14; H, 13.29. Found: C, 79.23; H, 13.42.

1-Methylcyclopentadecanol.—From 0.027 mole of cyclopentadecanone[36] (m.p. 61.5–64.5°) and 0.09 mole of methyl Grignard there was obtained 5.20 g. (80% yield) of the tertiary alcohol, m.p. 83–85°. (Approximately 9 ml. of gas was evolved from the Grignard reaction mixture.) A second recrystallization raised the melting point to 83.5–85°.

Anal. Calcd. for $C_{16}H_{32}O$: C, 79.95; H, 13.42. Found: C, 80.09; H, 13.40.

1-Methylcycloheptadecanol.—The alcohol was prepared from 0.023 mole of cycloheptadecanone[36] (m.p. 58–60°) and 0.07 mole of methylmagnesium iodide. (Approximately 16 ml. of gas was evolved.) The crude product was recrystallized from methanol. A 92% yield of material melting at 77.5–78.5° was obtained.

Anal. Calcd. for $C_{18}H_{36}O$: C, 80.52; H, 13.52. Found: C, 80.71; H, 13.68.

The Higher 1-Chloro-1-methylcycloalkanes.—Two procedures were utilized for the conversion of the tertiary alcohols into the tertiary chlorides. In the first, the solid alcohols were dissolved in petroleum ether (60–70°) and hydrogen chloride was passed into the solution during several hours as the flask was cooled with ice-water. The solution was dried, the ether removed under vacuum and the crude tertiary chloride was utilized for the rate measurement. The reaction of the tertiary alcohol with hydrogen chloride under these conditions proved sluggish. It proved more satisfactory to pass the hydrogen chloride directly over the solid alcohol. Reaction was rapid—within a few minutes the material liquefied and could be readily saturated with the acid. No difficulty was encountered in separating the liquid tertiary chlorides from the droplet of water which was formed in the reaction. There was some evidence that some of the tertiary chlorides are solids in the pure state and might have been obtained in crystalline form. However, since the rate data were not affected by the impurities present and the quantity of material was so small, it was decided to proceed with the crude material.

In practically all cases the crude chlorides analyzed for 80–90% tertiary chloride. In the case of the 10-membered

---

[35] Private communication.

[36] Kindly furnished by Dr. M. Stoll.

ring the reaction of the tertiary alcohol with hydrogen chloride was anomalous. The hydrogen chloride was passed into 2.65 g. of 1-methylcyclodecanol at room temperature for three hours. The alcohol liquefied, turned pink in color, and a small aqueous layer separated. After separation, drying over a granule of calcium chloride, and pumping to remove dissolved hydrogen chloride, it was noted that the product was pink in color and less viscous than the other tertiary chlorides. The product was low in chlorine, so a crystal of ferric chloride was added and the liquid was again treated with hydrogen chloride. However, even after this treatment the product contained only 35% hydrolyzable chloride. Nevertheless, the crude product underwent solvolysis smoothly, giving good first-order constants. Time did not permit a more detailed study of the phenomenon.

Di-*n*-amylmethylcarbinyl Chloride.—The action of *n*-amylmagnesium chloride on ethyl acetate yielded the tertiary alcohol (b.p. 84.5-86.5° at 2 mm., $n^{20}\mathrm{D}$ 1.4401). The alcohol was converted to the chloride with hydrogen chloride. The crude product contained 95% of the theoretical hydrolyzable chloride and was utilized directly for the rate measurements.

Acknowledgment.—We are indebted to the Office of Naval Research for the financial support which made this study possible, to Mrs. E. Kapper for synthesizing di-*n*-amylmethylcarbinyl chloride, to Dr. S. Siegel for a sample of the *p*-bromophenacyl ester of 1-methylcyclopropanecarboxylic acid, and to Drs. V. Prelog and M. Stoll for samples of several of the cycloalkanones.

LAFAYETTE, INDIANA RECEIVED AUGUST 13, 1951

[CONTRIBUTION FROM THE DIVISION OF DAIRY PRODUCTS RESEARCH LABORATORIES, UNITED STATES DEPARTMENT OF AGRICULTURE]

Chromatography of Methyl Stearate, Methyl Oleate, Methyl Linoleate and Methyl Linolenate: A Concept of Amplified Chromatographic Separations[1]

BY FLOYD E. KURTZ

More effective separations than previously reported of C_{18} esters, judged on the basis of completeness and time involved, have been obtained. A study of distribution coefficients of both single and mixed solutes and of certain column operating conditions has led to a concept of chromatography which predicts more effective separations than otherwise obtainable by the proper use of solutes of intermediate adsorption affinities. This prediction was verified experimentally. The similarities and differences between amplified chromatographic separations and those obtained by carrier displacement chromatography are briefly discussed.

The most effective chromatographic separations of the C_{18}-fat acids seem to be those of Riemenschneider, *et al.*,[2] who used silicic acid as adsorbent, petroleum ether for developing and took precautions to exclude air during the operation of the column. Pure methyl linoleate, first appearing in the eluate after 17 hours development, was isolated from the esters of the associated C_{18}-acids of tobacco seed oil in 27% yield. Similarly, from linseed oil, 98% methyl linolenate, first appearing in the eluate after 45 hours development, was isolated in 32% yield. Pure methyl linolenate was obtained by a repetition of this process on the best fractions. These separations were made for the purpose of obtaining samples of pure esters from natural products and did not reflect any extensive attempt to find optimum conditions.

Without differentiating between its components, Taylor has reported that air is held more tenaciously by silica gel than is water.[3] This indicates the difficulty that may be encountered in attempting to provide completely air-free conditions on a column. The extension of chromatography to the isolation of minor constituent unsaturated fat acids from mixtures would, therefore, appear to be favored by conditions affording maximum yields with a minimum time of development. The chromatographic process has been examined with this application in mind.

Materials. Solvents. Petroleum Ether.—Skellysolve F was distilled and the fraction of b.p. 35–50° collected. **Benzene.** A.C.S. thiophene-free grade benzene was washed repeatedly with water, dried over anhydrous potassium carbonate, filtered, distilled, and the fraction, b.p. 80°, collected. **Methanol.** A.C.S. 99.5% methanol was used as purchased.

Solutes. Stearic Acid.—Eastman Kodak Co. "Eastman" grade acid was crystallized three times from acetone; m.p. 68.5°, neut. equiv. 284.0 (calcd. 284.3). **Methyl stearate** was prepared from the purified stearic acid; m.p. 38.0°, acidity 0.2% (calcd. as stearic acid). **Methyl caproate** was prepared from Eastman grade caproic acid; b.p. 149.0–149.5°, $n^{20}\mathrm{D}$ 1.4048. **Methyl myristate** was prepared from Eastman grade myristic acid and a portion of uniform boiling point chromatographed on silica gel. A sample was selected for further work from the middle of a series with a uniform $n^{20}\mathrm{D}$ value of 1.4369. **Methyl oleate,** iodine value 85.6 (calcd. 85.7), $n^{20}\mathrm{D}$ 1.4522, which was prepared by the method of Wheeler and Riemenschneider[4] was used in obtaining the data of Fig. 1a and Tables I–III. That used in the remainder of the experiments was purchased from the Hormel Foundation, Austin, Minn.; iodine value 85.4, $n^{20}\mathrm{D}$ 1.4522. **Methyl linoleate,** iodine value 172.6 (calcd. 172.4), $n^{20}\mathrm{D}$ 1.4616 and **methyl linolenate,** iodine value 260.0 (calcd. 260.4), $n^{20}\mathrm{D}$ 1.4711, were purchased from the Hormel Foundation.

All melting points recorded above are corrected; boiling points are uncorrected. Each of the unsaturated esters was chromatographed and the refractive indices of the middle fractions, representing the major portion of each sample, were found to be identical with the values for the unchromatographed esters.

Adsorbents.—All adsorbents in Table I were used as purchased. **Silica gel.**—Standard silica gel, the type normally obtained from commercial sources, which was purchased from the Davison Chemical Corp., Baltimore, Md., was used throughout the investigation except as otherwise noted in Table I. For the data of Table I and of Fig. 1a the gel was used as purchased. Otherwise it was purified by extracting with acetone until no more soluble matter was obtained, drying with a current of air, washing with distilled water and activating at 175° for 18 hours. From this material the partially deactivated gels were prepared by contact with the vapors of the deactivating

---

(1) Taken in part from a thesis submitted to the Faculty of the Graduate School of the University of Maryland in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1951.

(2) R. W. Riemenschneider, S. F. Herb and P. L. Nichols, Jr., *J. Am. Oil Chemists' Soc.*, **26**, 371 (1949).

(3) R. K. Taylor, *Ind. Eng. Chem.*, **37**, 649 (1945).

(4) D. H. Wheeler and R. W. Riemenschneider, *Oil & Soap*, **16**, 207 (1939).