

281. Nucleophilic Reactions at Tertiary Carbon. Part 1. The 1,2-Dimethyl-1-Cyclohexyl Cation

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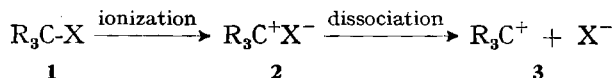
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Summary. Stereoisomeric ion pairs are implicated as intermediates in the solvolysis of *cis*- and *trans*-1-chloro-1,2-dimethylcyclohexane, *cis*-**4** and *trans*-**4**, respectively. This follows from the rates and products of these stereoisomeric tertiary chlorides in 80% ethanol and 50% acetone.

The composition of elimination and substitution products from *cis*-**4** and *trans*-**4** differs markedly and the differences are accentuated by silver ion. Furthermore, substitution products are formed with predominant inversion of configuration.

The equilibrium constant for isomerization of *cis*-**4** and *trans*-**4** shows the latter to be more stable by 0.7 kcal/mol. Since the solvolysis rates of the chlorides are equal, the transition state for *trans*-**4** is also more stable by 0.7 kcal. By inference the intermediates differ by a similar amount of energy which is ascribed to more efficient solvation of the *trans* ion pair **13**.

Evidence has accumulated in recent years that undissociated (contact or intimate) ion pairs **2** play an important role as intermediates in solvolytic reactions of tertiary halides and esters **1**. In certain solvents they form substitution and elimination products before dissociating to symmetrically solvated carbenium ions¹⁾ **3**.



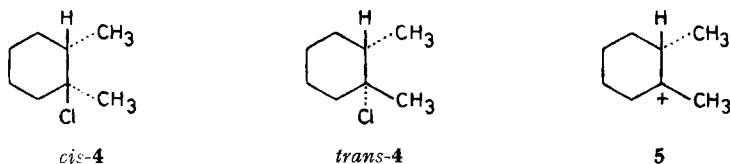
Thus in weakly dissociating solvents, such as 100% acetic acid and ethanol, the nucleofugal group X in tertiary systems **1** has a marked influence on the ratio of substitution and elimination products. This would not be the case if products were derived from free carbenium ions **3** [2]. The stereochemical course of solvolysis of optically active tertiary systems also implicates ion pairs. Thus, the tendency to form inverted rather than racemized substitution products increases with the nucleophilicity of the solvent and indicates an unsymmetrical intermediate [3].

In this and subsequent papers another way to determine the nature of the intermediate in the solvolysis of tertiary systems is described. This makes use of pairs of stereoisomers, both of which ionize to the same cation, such as the *cis*- and *trans*-isomer of 1-chloro-1,2-dimethylcyclohexane, *cis*-**4** and *trans*-**4**²⁾, respectively. Both of these tertiary chlorides should yield the 1,2-dimethylcyclohexyl cation (**5**) and, if this were free of the counterion Cl⁻, the same ratio of products should result from either one. On the other hand different products or ratios of products would be expected if the counter chloride ion remained in close proximity to the cation during the

¹⁾ The term 'carbenium ion' prevalent in the German literature rather than 'carbonium ion' has been advocated recently by Olah [1] and will be used in this and subsequent papers.

²⁾ *Cis* and *trans* with respect to the methyl substituents. IUPAC nomenclature [4] prescribes the names *r*-1-chloro-1,*trans*-2-dimethylcyclohexane for *cis*-**4** and *r*-1-chloro-1,*cis*-2-dimethylcyclohexane for *trans*-**4**, respectively.

product determining step. To the extent that the ion pairs retained the configuration of the original chloride they would represent stereoisomeric ion pairs.



The use of diastereoisomers instead of enantiomers offers several advantages. The need to resolve racemates and to establish configurational relationships between optically active reactants and products is eliminated. Furthermore, stereoisomeric tertiary chlorides, such as *cis*-4 and *trans*-4, are easily accessible and can be interconverted. From the equilibrium constant of isomerization the free energy difference ΔG of their ground states can be calculated. In combination with free energies of activation ΔG^\ddagger , which are available from the rate constants of the diastereoisomers, the ΔG values permit the calculation of the free energy differences of their transition states. Since intermediate carbenium ions resemble the transition states by which they are formed, as is generally assumed [5], the relative energies of the former can be deduced from those of the latter. A significant energy difference between the intermediates derived from the stereoisomeric chlorides *cis*-4 and *trans*-4 should reflect the influence of the counter chloride ion or any other factor, such as solvation or conformation.

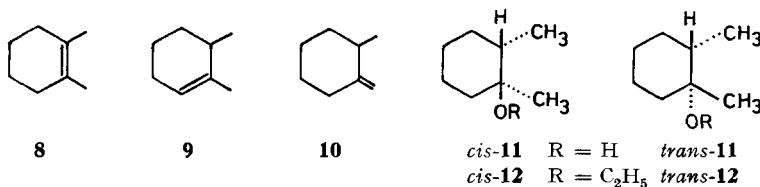
In this paper the preparation of the stereoisomeric chlorides *cis*-4 and *trans*-4, their equilibration and their solvolysis rates in 80% ethanol and 50% acetone are described. The mechanism is then discussed in the light of the results. Subsequent papers deal with the stereoisomers of 8-hydrindanyl chloride 6 and of 9-decalyl chloride 7 [6]. These compounds are derived from *cis*-4 and *trans*-4 by connecting the methyl substituents by one and two methylene groups, respectively, thereby introducing varying conformational constraint in the respective carbocations.



Results. – *Syntheses.* Chloro-1,2-dimethylcyclohexane (4) has been prepared by *Brown et al.* [7]. No attempt to separate stereoisomers was made, however, since a satisfactory first order rate constant in 80% ethanol was obtained. An improved procedure was found by *Fahey & Mc Pherson* [8] in the stereoselective addition of HCl to 1,2-dimethylcyclohexene (8) under controlled reaction conditions³⁾. Higher selectivity was achieved by the use of different solvents and temperatures. In ether at 0° 98% of *trans*-4 besides 2% *cis*-4 were obtained. Liquid HCl or HCl in methylene chloride at –98° furnished a mixture of 88% *cis*-4 and 12% *trans*-4. The oily and rather

³⁾ The authors obtained 93% *trans*-4 and 7% *cis*-4 in acetic acid containing tetramethylammonium chloride. In acetyl chloride 73% *cis*-4 and 27% *trans*-4 were obtained.

unstable chlorides were purified by gas liquid chromatography and identified by spectral data and by conversion to the olefins **8**, **9** and **10**⁴⁾. These olefins, the alcohols *cis*- and *trans*-**11** and the corresponding ethyl ethers *cis*- and *trans*-**12** were needed to identify the solvolysis products and were either known or were synthesized by conventional methods⁴⁾.



Solvolysis products. The products of *cis*- and *trans*-**4** in 50 vol. % acetone and 80 vol. % ethanol which were determined by gas liquid chromatography of the reaction solution are listed in Table 1. Product composition was unaltered when 1.2 molar equivalents of triethylamine were added. However, addition of 1.5 molar equivalents

Table 1. Yields (in %) of products from *cis*- and *trans*-**4** in 80 vol. % ethanol (70°) and 50 vol. % acetone (40°)

	olefins			alcohols 11		ethers 12	
	8	9	10	<i>cis</i>	<i>trans</i>	<i>cis</i>	<i>trans</i>
80% ethanol ^{a)}							
<i>cis</i> - 4	43	14	17	6	10	4	5.5
<i>trans</i> - 4	67	13.5	8.5	4.5	2	3.5	1
80% ethanol, AgNO ₃							
<i>cis</i> - 4	24	15	3.5	9	29	5	14.5
<i>trans</i> - 4	82	5.5	1	5.5	1.5	4	0.5
50% acetone ^{a)}							
<i>cis</i> - 4	30	8.5	7.5	23.5	30.5	–	–
<i>trans</i> - 4	60	10.5	4	17.5	8.5	–	–

^{a)} Containing 1.2 equiv. of triethylamine.

Table 2. Ratios of elimination to substitution products (*E/S*) and inversion to retention (*I/R*) for *cis*- and *trans*-**4**

	<i>E/S</i>	<i>I/R</i>
80% ethanol		
<i>cis</i> - 4	2.9	1.6
<i>trans</i> - 4	8.1	2.7
80% ethanol + AgNO ₃		
<i>cis</i> - 4	0.73	3.1
<i>trans</i> - 4	7.7	4.8
50% acetone		
<i>cis</i> - 4	0.85	1.3
<i>trans</i> - 4	2.8	2.0

⁴⁾ See experimental section.

of silver nitrate in 80% ethanol changed the yields considerably. Table 2 shows the ratios of elimination (olefins) to substitution products (alcohols, ethers) E/S and the ratio of inversion to retention products I/R for *cis*- and *trans*-4 under different conditions.

Kinetics. First order rate constants for *cis*- and *trans*-4 were determined conductometrically at three temperatures in the presence of ca. 1.2 equivalents of triethylamine. These were not affected by altering the concentration of base (Table 3). The rates of the chlorides were almost identical at 46°, *trans*-4 reacting slightly faster than *cis*-4 in 80% ethanol and slightly slower in 50% acetone. Both chlorides reacted within a factor of two as fast as *t*-butyl chloride and 1-methylcyclohexyl chloride (Table 4), two typical tertiary chlorides which react by the limiting [9] S_N1-E1 mechanism.

Table 3. First order rate constants for *cis*- and *trans*-4 ($c = 10^{-3} M^a$)

	Temp. (°)	k (s ⁻¹)	E [‡] (kcal)	S [‡] (cal/degree)
<i>cis</i> -4: 80% ethanol	60.05	2.94×10^{-4}		
„	69.07	7.57×10^{-4}		
„	78.08	1.83×10^{-3}		
„	46.00	$6.13 \times 10^{-5} b)$	23.6	– 6.0
50% acetone	34.75	2.95×10^{-4}		
„	44.86	8.51×10^{-4}		
„	54.64	2.39×10^{-3}		
„	46.00	$9.84 \times 10^{-4} b)$	21.1	– 8.3
<i>trans</i> -4: 80% ethanol	60.05	2.74×10^{-4}		
„	69.07	6.48×10^{-4}		
„	78.08	1.46×10^{-3}		
„	46.00	$6.50 \times 10^{-5} b)$	21.6	– 12.1
50% acetone	34.75	2.56×10^{-4}		
„	44.86	6.76×10^{-4}		
„	54.64	1.75×10^{-3}		
„	46.00	$7.73 \times 10^{-4} b)$	19.4	– 14.2

a) Containing 1.2 equiv. of triethylamine. b) Extrapolated.

Table 4. Relative first order rate constants in 80 vol. % ethanol (46°)

<i>cis</i> -4	<i>trans</i> -4	<i>t</i> -butyl chloride	1-methylcyclohexyl chloride
0.524	0.555	1.00 [10]	0.35 [7]

Isomerization. The chlorides *cis*- and *trans*-4 showed no tendency to isomerize in the solvents ether, tetrahydrofuran, chloroform, acetone and carbon tetrachloride at 46°, even in the presence of HCl. However, isomerization readily occurred in carbon tetrachloride saturated with HCl in the presence of ZnCl₂, in ether/HCl with 20% BF₃ and in 80% ethanol saturated with HCl. In the last case the chlorides *cis*- and *trans*-4 were only incompletely dissolved. The ratio of *trans*-4 to *cis*-4 at equilibrium at 46° was determined by gas liquid chromatography. Some of the measurements are listed

in Table 5 together with the corresponding free energy difference $\Delta G = RT \ln \textit{trans-4}/\textit{cis-4}$ ⁵⁾. The ratio determined by five different methods is approximately 3 and corresponds to a difference of ground state free energy ΔG of 0.7 kcal/mol.

Table 5. Ratio of *trans-4* and *cis-4* at equilibrium (46°)

	<i>trans-4/cis-4</i>	ΔG (kcal/mol)
HCl saturated CCl ₄ /ZnCl ₂	3.0	0.70
HCl saturated ether/20% BF ₃	3.0	0.70
HCl saturated 80% ethanol	2.8	0.66
HCl saturated 95% ethanol	3.0	0.70
1.3M HCl in CH ₃ COOH [8]	3.0	0.70

Discussion. – Table 1 shows that *cis*- and *trans-4* yield the same products, however in different amounts. In 50% acetone the ratio of elimination and substitution products is 0.85 for *cis-4* and 2.8 for *trans-4* (Table 2). In 80% ethanol the ratio is 2.9 for *cis-4* and 8.1 for *trans-4*. In the presence of silver ion this ratio is 7.7 for *trans-4* and drops to 0.73 for *cis-4*. Large differences are discernible in the yields of individual compounds (olefins, alcohols and ethers) from the stereoisomeric chlorides (Table 1).

It is noteworthy that substitution occurs with inversion and with retention of configuration. However, inversion predominates in all cases (Table 2). This trend is more pronounced for *trans-4* and is accentuated by silver ion. Product analysis therefore shows that the stereoisomeric chlorides **4** do not react by way of the same intermediate.

This conclusion is confirmed by a consideration of rate and equilibrium constants. Since the ground states of *trans*- and *cis-4* differ by 0.7 kcal (Table 5) and since their rates are practically the same (Table 3) their transition states must also differ by 0.7 kcal. Assuming that intermediates resemble the transition states of their formation [5] it follows that the first intermediates in the solvolysis of *cis*- and *trans-4* also differ in energy by approximately 0.7 kcal, as indicated in Fig. 1. Therefore, these are not identical. They could differ with respect to the location of the counter chloride ion as in the stereoisomeric ion pairs *cis*- and *trans-13*. In each case the 1,2-dimethylcyclohexyl cation should assume a conformation with an equatorial methyl group as has been shown to be the case for the related compound 2-methylcyclohexanone [11].

Attack of solvent at the back of the cationic centre in the ion pairs *cis*- and *trans-13* competes effectively with removal of the chloride ion to form the symmetrically solvated carbenium ion **14**. The alcohols and ethers are therefore formed with predominant inversion of configuration. However, solvent approach is less hindered on the quasi equatorial side, as in *trans-13*, than on the quasi axial side, as in *cis-13*, which explains the higher inversion to retention ratio in the case of the *trans*-chloride **4**. Furthermore, the solvent is favorably placed to abstract the C(2) hydrogen in the *trans* ion pair **13** and a hydrogen from the C(1)-methyl group in the *cis* ion pair **13**. This explains the relatively high yield of 1,2-dimethylcyclohexene **8** from *trans-4* and of 1-methyl-2-methylenecyclohexane **10** from *cis-4*.

⁵⁾ It is noteworthy that *Fahey & McPherson* [8] found the same ratio in acetic acid/HCl (Table 5).

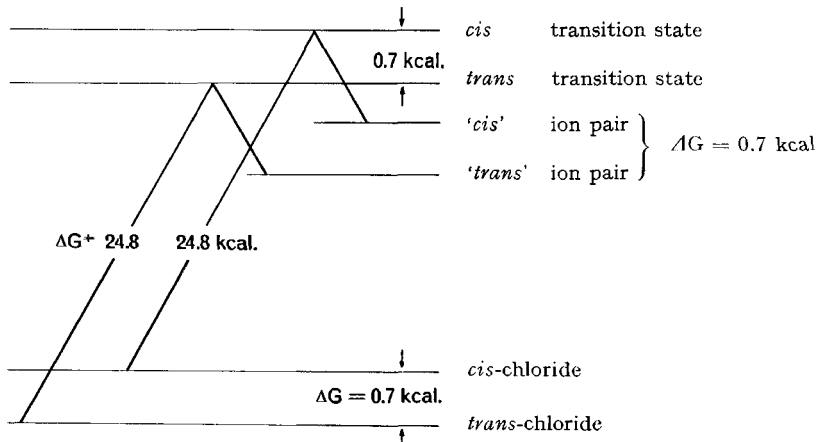
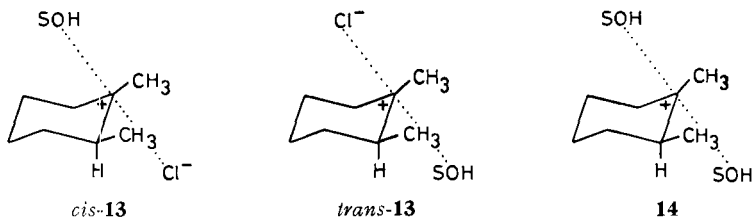
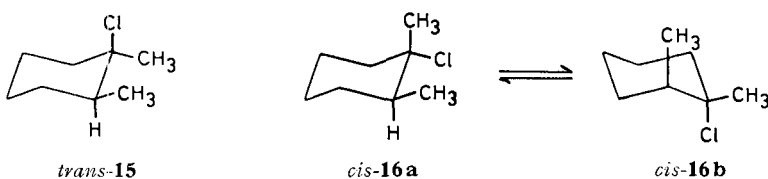


Fig. 1. Free energy diagram for *cis*- and *trans*-1,2-dimethylcyclohexyl chloride



More efficient cationic solvation of the *trans* ion pair **13** also accounts for the energy difference of ca. 0.7 kcal between the intermediate from *cis*- and *trans*-4. This easier and therefore tighter solvation is also reflected in the lower activation energies and the more negative activation entropies for the *trans*-chloride **4** in both solvents (Table 3).



The greater stability of the *trans*-chloride **4** with respect to the *cis*-isomer is predictable from non-bonding steric interactions in the favoured conformations **15** and **16a–16b**, respectively, of these compounds⁶⁾. The free energy difference $\Delta G = 0.7$ kcal derived from equilibration measurements (Table 5) is somewhat smaller than that calculated from conformational energy increments [13], which is ca. 1.0 kcal. A similar analysis for the chair conformations **16a** and **16b** of *cis*-4 shows the former to be more stable by 0.2 kcal⁶⁾. It is noteworthy that ionization of the favoured conforma-

⁶⁾ Conformation **15** for *trans*-4 and a mixture of conformations **16a** and **16b** for *cis*-4 is also suggested by the IR. data (see experimental section).

tions *trans*-**15** and *cis*-**16a** [8] leads directly to the corresponding ion pairs *trans*-**13** and *cis*-**13**, respectively⁷⁾.

It is evident from Tables 1 and 2 that the composition of products from *cis*- and *trans*-**4** in 80% ethanol differs more when silver ion is added. The nature of the intermediates is therefore modified by coordination and neutralization of the chloride ion. Furthermore, a higher inversion to retention ratio results. It follows that silver chloride more effectively shields one side of the cation which must therefore be regarded as an encumbered carbenium ion [14].

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Experimental Part

Melting points (m.p.) were determined on a *Kofler* Block and are corrected. Boiling points (b.p.) are not corrected. IR. spectra were recorded on an *Beckmann* IR-8 spectrophotometer, NMR. spectra on a *Varian* A-60 or HA-100 D spectrometer. The chemical shift is given in ppm relative to TMS as an internal standard ($\delta = 0$). Gas liquid chromatography (GLC.) analyses were carried out on a *Perkin-Elmer* model F 11 with a flame ionization detector and glass columns, preparative GLC.-separations on an *Aerograph* Autoprep A 712.

Syntheses. *r*-1-Chloro-1,trans-2-dimethylcyclohexane (*cis*-1-chloro-1,2-dimethylcyclohexane (*cis*-**4**)). 10 ml methylene chloride were cooled to -98°) and saturated with dry HCl. 0.40 g 1,2-dimethylcyclohexene **8** were added dropwise with stirring and HCl was then bubbled into the solution for 30 min at -98° . 20 g ice were added to the solution, the latter was diluted with pentane and washed with cold saturated aqueous NaHCO_3 and ice water, dried over CaCl_2 and evaporated in a vacuum rotary evaporator. GLC. (10% Carbowax 20M on Chromosorb, 100 $^{\circ}$) showed quantitative conversion into a mixture of 88% *cis*-**4** and 12% *trans*-**4**. The chlorides underwent partial decomposition upon distillation, but preparative GLC. (10% Carbowax 20M at 110 $^{\circ}$) gave 122 mg (23%) pure *cis*-1-chloro-1,2-dimethylcyclohexane **4**.

IR. spectrum, film (cm^{-1}): 643, 750 (C—Cl expected [12] for *cis*-**4** 610–700). – NMR. spectrum in CS_2 (ppm): 1.05 (3H, *d*) CH_3 ; 1.46 (3H, *s*) CH_3 ; 1.0–2.1 (9H, *m*) CH_2 , CH.

$\text{C}_8\text{H}_{15}\text{Cl}$ (146.66) Calc. Cl 24.17% Found Cl 23.34%

The chlorides *cis*- and *trans*-**4** cannot be obtained analytically pure by GLC. due to contamination by Carbowax.

A mixture containing 88% *cis*-**4** and 12% *trans*-**4** was also obtained by dropwise addition of 1,2-dimethylcyclohexene **8** to condensed dry HCl without solvent at -98° .

r-1-Chloro-1,cis-2-dimethylcyclohexane (*trans*-1-chloro-1,2-dimethylcyclohexane) (*trans*-**4**)). 0.40 g 1,2-dimethylcyclohexene **8** were added at 0° to 30 ml ethyl ether saturated with dry HCl. HCl gas was bubbled through the solution for 20 min. After addition of 50 g ice, the ether solution was diluted with pentane, washed with cold saturated aqueous NaHCO_3 and ice water, dried over CaCl_2 and evaporated. GLC. showed quantitative conversion into a mixture of 95% *trans*-**4** and 5% *cis*-**4**. Preparative GLC. gave 175 mg (33%) of pure *trans*-1-chloro-1,2-dimethyl-cyclohexane.

IR. spectrum, film (cm^{-1}): 548, 570, 742 (C—Cl, expected [12] for *trans*-**4** 540–580). – NMR. spectrum in CS_2 (ppm): 1.01 (3H, *m*) CH_2CH ; 1.55 (3H, *s*) CH_3 ; 1.0–2.1 (9H, *m*) CH_2 , CH.

$\text{C}_8\text{H}_{15}\text{Cl}$ (146.66) Calc. C 24.17% Found Cl 23.16%

⁷⁾ Conformation **15** of *trans*-**4** has the antiplanar orientation of the chlorine and the C(2)-hydrogen atom which is conducive to anchimeric hydrogen participation and would lead to a bridged transition state or intermediate. However, neither the relative rate (Table 4) nor the stereochemical course (predominant inversion) of the solvolysis of *trans*-**4** calls for such participation in the rate or product determining step. The same conclusion was reached by *Nevitt & Hammond* [15] in the case of *trans*-bromo-1,2-dimethylcyclohexane.

⁸⁾ The cooling bath was prepared from methanol and liquid nitrogen, see [16].

The chemical shifts in the NMR.-spectra of *cis*- and *trans*-**4** corresponded to those of the alcohols *cis*- and *trans*-**11** and their ethyl ethers **12**. Furthermore, all *trans*-1,2-dimethylcyclohexyl compounds had shorter retention times on GLC. than the corresponding *cis*-compounds. The following results of bimolecular elimination of HCl with ethanolic potassium hydroxide support these assignments [17].

Elimination of HCl from cis- and trans-4. 20 mg (0.13 mmol) of the chloride were heated with 0.5 ml 5M ethanolic potassium hydroxide at 80° for 15 h. The mixture was diluted with 20 ml water and extracted continuously in a *Kutscher-Steudel* extractor with pentane. The pentane solution was analyzed by GLC. (2.5% SE 52, 60°). All experiments were repeated at least once and gave the same results within the limit of error. It was shown that the olefins were stable under the conditions of the reaction. *Cis-4* yielded 66.5% 2,3-dimethylcyclohexene **9**, 30.5% 1-methyl-2-methylenecyclohexane **10** and 3% 1,2-dimethylcyclohexene **8**. *Trans-4* gave 83.5% 1,2-dimethylcyclohexene **8**, 13.5% 2,3-dimethylcyclohexene **9** and 3% 1-methyl-2-methylenecyclohexane **10**. The olefins were identified by comparison with authentic samples (*vide infra*).

1, trans-2-Dimethylcyclohexan-r-ol and 1, cis-2-dimethylcyclohexan-r-ol (cis- and trans-1,2-dimethylcyclohexanol) (cis-11 and trans-11). 2-Methylcyclohexanone was treated with methyl magnesium iodide according to a procedure of *Pasto & Klein* [18]. Distillation gave 77% of a mixture of 79% *trans*-1,2-dimethylcyclohexanol and 21% *cis*-1,2-dimethylcyclohexanol (by GLC.), b.p. 67–70°/17 Torr. The isomeric alcohols were separated by preparative GLC. (10% Carbowax 20M, 155°).

cis-1,2-Dimethylcyclohexanol 11. IR. spectrum, film (cm⁻¹): 3480 (broad, OH), 1115, 991, 913. – NMR. spectrum in CCl₄ (ppm): 0.89 (3H, *d*) CH₃; 1.02 (3H, *s*) CH₃; 1.53 (1H, *s*) OH; 1.0–1.8 (9H, *m*) CH₂, CH.

trans-1,2-Dimethylcyclohexanol 11. IR. spectrum, film (cm⁻¹): 3470 (broad, OH), 1170, 1009, 937. – NMR. spectrum in CCl₄ (ppm): 0.88 (3H, *m*) CH₃–CH; 1.13 (3H, *s*) CH₃; 1.53 (1H, *s*) OH; 1.1–1.8 (9H, *m*) CH₂, CH.

1,2-Dimethylcyclohexene 8 and 2,3-dimethylcyclohexene 9. 22.5 g (0.176 mol) of a 79:21 mixture of 1,2-dimethylcyclohexanols *trans*-**11** and *cis*-**11** were heated with 2.4 g 85% phosphoric acid. The olefins were distilled off azeotropically and dried over MgSO₄. Redistillation at 134–137° (Lit. [20] b.p. 129–131°) gave 14.3 g (74%) of a mixture of 77% 1,2-dimethylcyclohexene **8**, 22% 2,3-dimethylcyclohexene **9** and 1% 1-methyl-2-methylenecyclohexane **10** (by GLC.). The two major olefins were separated by preparative GLC. (10% Carbowax 20M, 70°) or chromatography on a column filled with 10% silver nitrate on silica gel (elution with petrol ether b.p. 40–65°).

1,2-Dimethylcyclohexene 8. IR. spectrum, film (cm⁻¹): 1640 (broad, C=C), 1272, 1226, 1140, 1009, 922, 868. – NMR. spectrum in CCl₄ (ppm): 1.88 (4H, *m*) CH₂; 1.55 (10H, broad *s*) CH₃ and CH₂.
C₈H₁₄ (110.20) Calc. C 87.19 H 12.81% Found C 86.91 H 12.99%

2,3-Dimethylcyclohexene 9. IR. spectrum, film (cm⁻¹): 3025 (C=C–H), 1640 (broad, C=C), 1152, 1109, 1034, 1015, 973, 872, 799. – NMR. spectrum in CCl₄ (ppm): 5.30 (1H, *s*) =CH; 1.9 (3H, *m*) CH₂ and CH; 1.6 (7H, *m*) CH₃ and CH₂; 1.00 (3H, *d*) CH₃.

1-Methyl-2-methylenecyclohexane 10. 4.08 g (36 mmol) of 2-methylcyclohexanone were added dropwise under nitrogen to a solution of 35 mmol triphenylphosphoromethylene in 40 ml dimethylsulfoxide, prepared *in situ* from 12.1 g triphenylmethylphosphonium bromide and sodium hydride according to *Greenwald et al.* [19]. The reaction mixture was heated to 50° for 1 h and the olefin isolated by flash distillation at 20–60°/12 Torr, washed with water, dried over MgSO₄ and redistilled at 125–126° (Lit. [20] b.p. 124.5–124.8°) to give 2.40 g (66%) 1-methyl-2-methylenecyclohexane (**10**). IR. spectrum, film (cm⁻¹): 3080 (=CH₂), 1640, 1238, 1090, 886. – NMR. spectrum in CCl₄ (ppm): 4.50 (2H, broad *s*) =CH₂; 1.00 (3H, *d*) CH₃; 0.9–2.3 (9H, *m*) CH₂, CH.

r-1-Ethoxy-1, trans-2-dimethylcyclohexane (cis-1-ethoxy-1,2-dimethylcyclohexane) (cis-12). 740 mg (5.78 mmol) *cis*-1,2-dimethylcyclohexanol (**11**) were dissolved in 7 ml hexane, treated with 1.3 equiv. of butyllithium in hexane and refluxed for 1 h under nitrogen. The solvent was distilled off and replaced by 5 ml hexamethylphosphortriamide. 5 g (30 mmol) ethyl iodide were added and the solution stirred at room temperature for 20 min. The reaction mixture was diluted with water and extracted with pentane. The pentane solution was washed with water, dried over

MgSO₄ and evaporated through a short *Vigreux* column. Separation of the crude product by chromatography over silicagel (elution with petrol ether) gave 121 mg (13%) of the ether *cis*-**12**.

IR. spectrum in CCl₄ (cm⁻¹): 1254, 1128, 1075 (C—O), 867. - NMR. spectrum in CCl₄ (ppm): 3.33 (2H, *q*) OCH₂; 1.7 (1H, *m*) CH; 1.6–1.1 (8H, *m*) CH₂; 1.10 (3H, *t*) CH₃; 1.00 (3H, *s*) CH₃; 0,85 (3H, *d*) CH₃.

r-1-Ethoxy-1, *cis*-2-dimethylcyclohexane (*trans*-1-ethoxy-1,2-dimethylcyclohexane) (*trans*-**12**). 403 mg (3.14 mmol) *trans*-1,2-dimethylcyclohexanol (**11**) were treated with butyllithium in hexane followed by ethyl iodide in hexamethylphosphortriamide as above. Chromatography gave 63 mg (13%) ethyl ether *trans*-**12**. IR. spectrum in CCl₄ (cm⁻¹): 1392, 1254, 1160, 1114, 1074 (C—O), 868. - NMR. spectrum in CCl₄ (ppm): 3.26 (2H, *q*) OCH₂; 1.75 (1H, *m*) CH; 1.3 (8H, broad *m*) CH₂; 1.11 (3H, *t*) CH₃; 1.08 (3H, *s*) CH₃; 0.86 (3H, *m*) CH₃—CH.

Preparative Solvolyses. All runs were repeated twice.

In 80% ethanol: 0.004M solutions of 11 mg of the chlorides *cis*- or *trans*-**4** and 10 mg (1.2 equivalents) triethylamine in 20 ml 80 vol. % ethanol were heated at 70° for 5 h. The solutions were diluted with water and extracted continuously with pentane in a *Kutscher-Steudel* extractor. The extracts were directly analyzed by GLC. (4% SE 30, 60–85°) and the products identified by comparison with authentic samples. Solvolyses in the absence of triethylamine gave the same product composition within the experimental error of GLC. analysis ($\pm 2\%$). The experiments were repeated in the presence of 16 mg (1.2 equivalents) silver nitrate at 70°, stirred for 2 h and analyzed as above.

In 50% acetone: 0.004M solutions of 11 mg *cis*- or *trans*-**4** in 20 ml 50 vol. % acetone were stirred at 40° for 5 h and analyzed as above.

Kinetic Measurements. 80 vol. % ethanol ($d_{20}^{20} = 0.8525$) was prepared by mixing 1146.0 g abs. ethanol and 363.9 g bidistilled water. 50 vol. % acetone ($d_{20}^{20} = 0.9344$) was obtained by mixing 394.5 g acetone and 498 g bidistilled water.

The rates of reaction were measured by conductometric methods described earlier [21]. The conductivity cell was filled with 20 ml of a 10⁻³M solution in 80 vol. % ethanol containing 1.2 equivalents of triethylamine and immersed in a water thermostat with a temperature deviation of $\pm 0.05^\circ$. The reactions were followed for approx. three half lives.

The reaction rate constants were calculated with the aid of a computer using the least square method. Based on the equation for first order reactions

$$\ln(c_\infty - c_i) = -kt_i + \ln(c_\infty - c_0)$$

where c_i = concentration at the time t_i and

k = reaction rate constant,

a linear regression is calculated with given c_∞ and variable c_0 from 30–40 time/concentration readings measured as conductivity in arbitrary units. c_∞ can be determined experimentally, but has too much statistical weight and is therefore determined by iteration of the linear regression. The iteration starts with a c_∞ 1% higher than the highest experimental c_i . c_∞ is increased by 2% until the sum of the squares of the deviations between calculated and experimental concentration c_i is a minimum. c_∞ is then varied by $(1/5) \times 2\%$, $(1/5)^2 \times 2\%$, and so on. The iteration is terminated when two subsequent calculations of k differ by less than $10/100$ and the sums of the squares of the deviations between the last and last but one minimum differ by less than $10/100$. The calculated curve and the experimental data are plotted so that any deviation from ideal first order behaviour can easily be seen.

The correlation coefficient was usually 0.9999, and always better than 0.9985. Solvolyses are therefore cleanly first order in chloride. All measurements were repeated at least twice, and reaction rate constants were reproducible within $\pm 1\%$. Added base (triethylamine) showed a slight acceleration due to a normal salt effect.

Equilibrations. General procedure. Solutions of pure chlorides *cis*- and *trans*-**4** and their mixtures were sealed in ampoules. Equilibration was reached by shaking in a water thermostat at 46.0° for 7 to 25 days. The ampoules were opened, the reaction mixture poured onto ice and extracted with pentane. The extracts were washed with ice-cold aqueous NaHCO₃ and ice water, dried over CaCl₂ and analyzed by GLC. (10% Carbowax 20M on Chromosorb DMCS, 100°). All measurements were carried out 6 to 10 times and gave reproducible isomer ratios within $\pm 1\%$ (Table 5).

HCl/ZnCl₂ in carbon tetrachloride. 20 mg chloride were dissolved in 1 ml carbon tetrachloride saturated with dry HCl. A trace of powdered dry zinc chloride was added. The isomeric chlorides were accompanied by approx. 10% olefins and unknown impurities.

HCl/BF₃ in ethyl ether. 20 mg chloride were dissolved in 1 ml ethyl ether saturated with dry HCl. 0.25 ml freshly distilled boron trifluoride ethyl etherate were added. The equilibrated mixture contained less than 5% impurities.

HCl/80% ethanol. When 20 mg chloride were treated with 1.5 ml 80% aqueous ethanol saturated with HCl the chlorides did not dissolve completely. The equilibrated mixtures contained 6% olefins and traces of ethyl ethers.

HCl/95% ethanol. 20 mg chloride were dissolved in 1.5 ml 95% aqueous ethanol saturated with HCl. The equilibrated mixtures contained less than 1% impurities, but considerable amounts of ethyl chloride.

Elemental analyses were carried out by Mr. E. Thommen. The NMR. spectra were recorded by Mr. K. Aegerter.

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