

shall show in this article, the reversibility of step V \rightarrow VI can be discarded.

- (33) J. E. Dubois, M. Boussu, and C. Lion, *Tetrahedron Lett.*, 829 (1971).
 (34) D. Zook, W. E. Smith, and J. L. Greene, *J. Am. Chem. Soc.*, **79**, 4436 (1957).
 (35) Before use the organolithium compound was decanted under argon pressure

to eliminate excess lithium.

- (36) The accuracy of this method was verified from a standard solution containing the very same products as the reaction. For each product the average of the values found is $\pm 0.5\%$ of the theoretical value.
 (37) R. Kaiser, "Gas Chromatography", Vol. 1, Butterworths, London, 1963, p 182.

Metathetical Transposition of Bis-*tert*-alkyl Ketones. 2. Structural Effects on Alkyl Migration. Existence of Linear Relationship Networks

P. Bauer and J. E. Dubois*

Contribution from the Laboratoire de Chimie Organique Physique de l'Université de Paris VII, associé au C.N.R.S., 75005 Paris, France. Received July 1, 1975

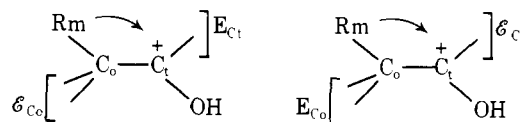
Abstract: Structure-migrating group interactions which are present during 1,2 migrations of alkyl groups Rm (Rm = Me or Et) have been studied as a function of the influence of a variable environment \mathcal{E}_{C_o} of the origin carbon C_o for a fixed environment \mathcal{E}_{C_t} of the terminal carbon C_t , and vice versa, on the partial rate constant (k_p^{Rm}) for migration in IV. The constants k_p^{Rm} were determined from a study, in 96% H_2SO_4 , of the metathetical transposition of 11 α, α' -bis-*tert*-alkyl ketones ($R_1R_2RmCCORt$ (I)) leading to 24 rearrangement pathways of the following type: $I \rightleftharpoons R_1R_2RmC_oC_t^+OHRt$ (IV) $\rightleftharpoons R_1R_2C^+COHRmRt$ (V) $\rightarrow R_1R_2RtCC^+OHRm$ (VI). In a first approximation values k_p^{Rm} were calculated while considering the return of step IV \rightleftharpoons V, during which group Rm migrates, as being negligible. This hypothesis was ultimately verified by measuring the return of this step by a study of the pinacol rearrangement of 16 glycols ($R_1R_2COHCOHRmRt$ (II) \rightarrow V \rightarrow IV + VI) chosen as constituting the structural limits for the studied environments \mathcal{E}_{C_o} and \mathcal{E}_{C_t} . Our results show that the return of step IV \rightleftharpoons V is too small to be the cause of the observed structural effects. The measured values of k_p^{Rm} cover a range of about three powers of ten. Linear relationships have been observed between $\log k_p^{Rm}$ and the number of carbon atoms, n_o and n_t , comprising the environments \mathcal{E}_{C_o} and \mathcal{E}_{C_t} ; $\log k_p^{Rm}(\mathcal{E}_{C_o}, \mathcal{E}_{C_t}) = \log k_{op}^{Rm} + an_o$, and $\log k_p^{Rm}(\mathcal{E}_{C_o}, \mathcal{E}_{C_t}) = \log k_{op}^{Rm} + bn_t$, in which $a = 0.017$ (Rm = Me) and 0.26 (Rm = Et) for $\mathcal{E}_{C_t} = t\text{-Bu}$; and $b = -0.63$ (Rm = Me) and -0.66 (Rm = Et) for $\mathcal{E}_{C_o} = \text{Me, Me}$. Thus, the environment \mathcal{E}_{C_t} opposes migration, whereas the environment \mathcal{E}_{C_o} assists it. Moreover, the effect of \mathcal{E}_{C_t} is more important than that of \mathcal{E}_{C_o} , but it is less sensitive to the nature of Rm. Among the structures studied two types of behavior are observed: a strict additivity of environmental effects as shown by the relationship $\log k_p^{Rm}(\mathcal{E}_{C_o}, \mathcal{E}_{C_t}) = \log k_{op}^{Rm} + an_o + bn_t + i$ (in which $i = 0$) and a partial additivity ($i \neq 0$). Each migrating group is characterized by a network of linear relationships. A comparison of the theoretical network ($i = 0$) with the experimental one shows that "i" is most often independent of the nature of Rm. It is likely that conformational effects and unbonded steric interactions will explain "i".

The migratory aptitude¹ of a group is a complex phenomenon which depends not only on the nature of the group, but also on the interactions between the group and the structure in which it migrates (group-structure interactions).² The lack of systematic information regarding these interactions is certainly one of the main reasons for the absence of quantitative data concerning the migratory aptitudes of alkyl groups.³

In the preceding article⁴ we have shown that the metathetical transposition of α, α' -bis-*tert*-alkyl ketones (Scheme I) was a reaction particularly suited to the obtainment of this kind of information. Reasoning that it is not possible to consider the notion of migratory aptitude without considering these interactions, we propose in this article to use this reaction for a systematic study of group-structure interactions in order to

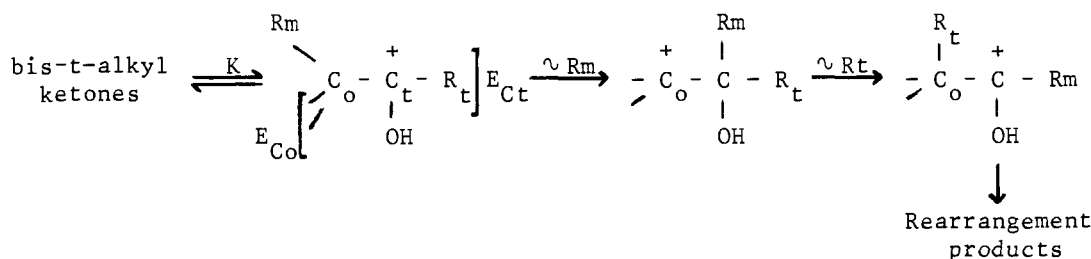
measure their importance and to attempt to specify the nature of the structural parameters responsible for this effect.

The complexity of this kind of interaction has led us to begin by separating arbitrarily the influence of the environments \mathcal{E}_{C_o} and \mathcal{E}_{C_t} of the origin and terminal carbons, C_o and C_t , of the migration.⁵ Thus, we have studied how the rate constant k_p^{Rm} varies as a function of \mathcal{E}_{C_o} when the environment of the ter-



minal carbon is held constant at \mathcal{E}_{C_t} and conversely, as a function of \mathcal{E}_{C_t} with \mathcal{E}_{C_o} constant. Every variable environment

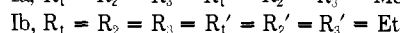
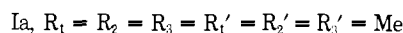
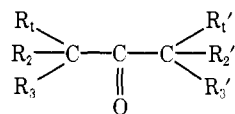
Scheme I



shall be expressed by \mathcal{E} and every constant environment by E.

Results

The study of the metathetical transposition of hexameth-



ylacetone (Ia) and hexaethylacetone (Ib) in 96% H_2SO_4 at 25 $^\circ\text{C}$ ⁴ indicates that the partial rate constant for migration (k_p^{Rm}) of a group R or R' may be calculated from

$$k_p^{\text{Rm}} = \frac{k_{\text{expt}}}{(1 - H(100/A))P} \frac{B}{100} = \frac{k_{\text{expt}}}{GP} \frac{B}{100} \quad (1)$$

in which k_p^{Rm} is the partial rate migration constant of a migrating group Rm; k_{expt} is the disappearance constant of ketones I in the medium; P is the statistical factor equal to the number of R or R' groups in I whose migration leads to the same product; B is the percentage of the different reaction pathways of the metathetical transposition of I; the term $G = 1 - H(100/A)$ takes into account the return of step IV \rightarrow V, during which the group Rm migrates (Scheme II), and is measurable by $H(100/A)$, in which H is the molar ratio of I in the sum of products I + III + X formed in 30 s by the pinacol rearrangement of glycols II; and A is the percentage of the pathway passing via ion V in the pinacol rearrangement of II leading to these same products. For a nil return $H(100/A) = 0$ and $G = 1$; $G < 1$ for a non-nil return.

In order to study the nature and importance of the interactions existing between a migrating group and the structure where the migration takes place, we present herein the constants k_p^{Rm} obtained from the metathetical transpositions of

eleven α, α' -bis-*tert*-alkyl ketones, ten of which are obtained by the progressive substitution of the methyl groups in Ia by ethyl groups, in such a fashion that Ia and Ib constitute, with the exception of Ik, the structural limits of the studied series.

The migration constants k_p^{Rm} of the methyl and ethyl groups for ketones Ia and Ib, calculated starting from eq 1, were: $k_p^{\text{Me}} = 775 \times 10^{-8}$ and $k_p^{\text{Et}} = 8 \times 10^{-8} \text{ s}^{-1}$. The determined values of G were equal to 0.96 for Ia and 0.70 for Ib, i.e., approaching unity. Calculation of these two constants, from the following simplified equation

$$k_p^{\text{Rm}} = \frac{k_{\text{expt}}}{P} \frac{B}{100} \quad (2)$$

in which $G = 1$, respectively, yields $k_p^{\text{Me}}_{\text{Ia}} = 742 \times 10^{-8}$ and $k_p^{\text{Et}}_{\text{Ib}} = 5.5 \times 10^{-8} \text{ s}^{-1}$, thus showing that the deviation introduced by this approximation on the values of $\log k_p^{\text{Rm}}$ is 0.02 for Ia and 0.16 for Ib. This result shows that, insofar as these latter values constitute maximum deviations, the values of k_p^{Rm} can be calculated from eq 2 as a first approximation for the ketones included between Ia and Ib and for Ik structurally like Id. All values of k_p^{Rm} thus calculated are shown in Table I.

This approximation can, however, be questioned if, instead of comparing the structures related to ketones Ia, Ic, Id... Ib, one compares for each path of the metathetical transposition the nature of the migrating group, E_{Co} , and E_{Ct} . For Ia, Rm = Me, $E_{\text{Co}} = \text{Me, Me}$ and $E_{\text{Ct}} = t\text{-Bu}$; for Ib, Rm = Et, $E_{\text{Co}} = \text{Et, Et}$ and $E_{\text{Ct}} = \text{Et}_3\text{C}$; thus, for both compounds, the three structural parameters (Rm, E_{Co} , and E_{Ct}) are different. Under these conditions, nothing proves that the approximation of G in eq 2 can be extrapolated from the migration of a given group, Rm, migrating in variable \mathcal{E}_{Co} and \mathcal{E}_{Ct} environments. This leads us, so as to verify the validity of this approximation, to determine the values of G for the structures characterized by $\mathcal{E}_{\text{Co}} = \text{Me, Me}$ and Et, Et and by $\mathcal{E}_{\text{Ct}} = t\text{-Bu}$ and Et_3C which, for each migrating group, constitute the structural limits of

Scheme II

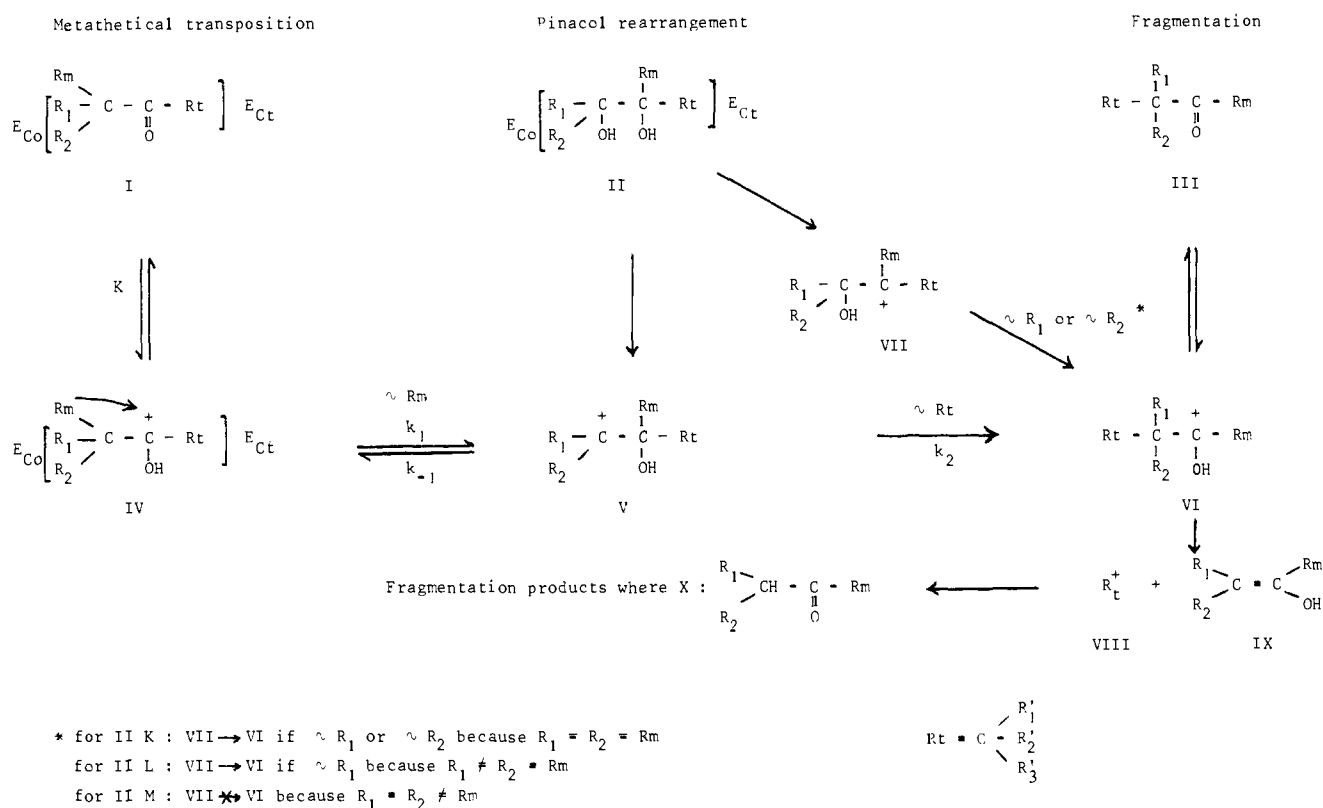


Table I. Experimental Rate Constants k_{expt} of Ketones I and Partial Constants k_p^{Rm} , Calculated by Equation 2, in Rearrangements of Bis-*tert*-alkyl Ketones, in 96 Weight % H_2SO_4 at 25 °C.

Ketones	R ₁	R ₂	R ₃	R' ₁	R' ₂	R' ₃	10 ⁸ - $k_{\text{expt}}^{\text{a}}$ s ⁻¹	R _m	ϵ_{Co}	ϵ_{Ct}	<i>Bb</i>	<i>Pf</i>	10 ⁸ - $k_p^{\text{Rm,c}}$ s ⁻¹	log k_p^{Rm} + 8	Paths
Ia	Me	Me	Me	Me	Me	Me	4450	R ₁	Me,Me	<i>t</i> -Bu	100	6	742	2.87	1
Ic	Me	Me	Me	Me	Me	Et	3080	R ₁	Me,Me	<i>t</i> -Am	17.5	3	180	2.25	4
								R' ₁	Me,Et	<i>t</i> -Bu	49	2	755	2.88	2
								R' ₃	Me,Me	<i>t</i> -Bu	33.5	1	1030	3.01	13
Id	Me	Me	Me	Me	Et	Et	4330	R ₁	Me,Me	<i>t</i> -Hex	2.8	3	40 ^d	1.60	7
								R' ₁	Et,Et	<i>t</i> -Bu	15.2	1	660	2.82	3
								R' ₂	Me,Et	<i>t</i> -Bu	82	2	1775	3.25	14
Ie	Me	Me	Me	Et	Et	Et	9000	R ₁	Me,Me	Et ₃ C	0.3	3	9 ^e	0.95	10
								R' ₁	Et,Et	<i>t</i> -Bu	99.7	3	2990	3.48	15
If	Me	Me	Et	Me	Me	Et	1180	R ₁	Me,Et	<i>t</i> -Am	62	4	183	2.26	5
								R ₃	Me,Me	<i>t</i> -Am	38	2	224	2.35	16
Ig	Me	Me	Et	Me	Et	Et	1400	R ₁	Me,Et	<i>t</i> -Hex	5	2	35 ^d	1.54	8
								R ₃	Me,Me	<i>t</i> -Hex	3.7	1	52 ^d	1.71	19
								R' ₁	Et,Et	<i>t</i> -Am	13	1	182	2.26	6
								R' ₂	Me,Et	<i>t</i> -Am	78.3	2	548	2.74	17
								R' ₃	Me,Me	Et ₃ C	0.4	1	11.1 ^e	1.04	22
Ih	Me	Me	Et	Et	Et	Et	2775	R ₁	Me,Et	Et ₃ C	0.3	2	4.2 ^e	0.62	11
								R' ₁	Et,Et	<i>t</i> -Am	99.3	3	918	2.96	18
								R' ₃	Me,Me	Et ₃ C	0.4	1	11.1 ^e	1.04	22
Ii	Me	Et	Et	Me	Et	Et	333	R ₁	Et,Et	<i>t</i> -Hex	16	2	26.6	1.42	9
								R ₂	Me,Et	<i>t</i> -Hex	84	4	70	1.84	20
Ij	Me	Et	Et	Et	Et	Et	277	R ₁	Et,Et	Et ₃ C	0.6	1	1.6 ^e	0.20	12
								R ₂	Me,Et	Et ₃ C	6	2	8 ^d	0.90	23
								R' ₁	Et,Et	<i>t</i> -Hex	93.4	3	86.5	1.94	21
Ib	Et	Et	Et	Et	Et	Et	33	R ₁	Et,Et	Et ₃ C	100	6	5.5	0.74	24
Ik	Me	Et	<i>n</i> -Pr	Me	Me	Me	5250	R ₁	Et, <i>n</i> -Pr	<i>t</i> -Bu	16	1	840	2.92	26
								R ₂	Me, <i>n</i> -Pr	<i>t</i> -Bu	54	1	2830	3.45	27
								R ₃	Me,Et	<i>t</i> -Bu	28	1	1470	3.17	28
								R' ₁	Me,Me	(Me,Et, <i>n</i> -Pr)C	2	3	35 ^d	1.54	25

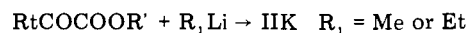
^a The standard deviation is $\pm 2\%$. ^b *B* is the percentage of the different reaction pathways of the metathetical transposition of I. Depending on the percentage corresponding to the paths and the GLC separation of the different compounds, the values are at ± 0.5 or ± 1 . For amounts below 2% the error may be as high as 25%. ^c The constants (calculated from eq 2) depend on the values found for k_{expt} and *B*. Values (except those with a further reference) are at $\pm 3\%$. ^d Values are at $\pm 10\%$. ^e Values are at $\pm 25\%$. ^f *P* is the statistical factor equal to the number of identical groups giving rise to the same product by migration.

these environments. Furthermore, verifications have been carried out on several intermediate structures.

Determining Parameter G. Depending on the structure of the glycol, the value of *G* can be directly deduced from the sum percentages of formed products, if each of the two pathways (via ion V and VII) of the pinacol rearrangement lead to different products (Scheme II). If both of these pathways lead to the same product, a tracer study with ¹³C, such as previously described,⁴ is required.

All of these glycols II fall into three populations: population IIK, in which $R_1 = R_2 = R_m$; population IIL, in which $R_1 \neq R_2 = R_m$; and population IIM, in which $R_1 = R_2 \neq R_m$, with $R_t = t\text{-Bu}, t\text{-Am}, t\text{-Hex}$, and Et_3C for each population.

The glycols IIK are synthesized by the method described in the previous article⁴



and the glycols IIL and IIM by successive condensations of methylolithium and ethyllithium or vice versa, with the α -ketoester.

When isotopic labeling is required, the α -ketoester is labeled on the carbonyl group with ¹³C and the products yielded by the pinacol rearrangement are analyzed as already mentioned⁴ by mass spectrometry. For glycols IIM the tracer studies are not necessary because the products, formed via V and VII, re different (Scheme II).

For structures characterized by a given migrating group ($R_m = \text{Me or Et}$), the limited environments ($\epsilon_{\text{Co}} = \text{Me, Me or Et, Et}$), and the environments $\epsilon_{\text{Ct}} = t\text{-Bu}, t\text{-Am}, t\text{-Hex}$, and

Et_3C , the values of *H*, *A*, and *G*, as well as those of $\log k_p^{\text{Rm}}$ deduced from eq 1 (compared to $\log k_p^{\text{Rm}}$ values obtained from eq 2), are given in Table II. These results show that the *G* values are never smaller than 0.68 and the deviation between the values of $\log k_p^{\text{Rm}}$, determined from eq 1 and 2, never goes beyond 0.17, i.e., it never exceeds the observed deviation for Ib by more than 0.01 (and this only once). Under these conditions the approximation on *G* appears to be acceptable; therefore, the values of $\log k_p^{\text{Rm}}$, calculated from eq 2, will serve as a basis for the following discussion.

Linear Relationships. To begin with, our results show that the partial rate constants k_p^{Rm} of a migrating group *Rm* can be considerably influenced by the structure in which the migration takes place.⁶ In effect, for methyl and ethyl groups, the range spans something approaching three powers of ten. This indicates clearly that in a determination of any quantitative scale of migratory aptitudes it is necessary to consider interactions between the overall structure and the migrating group.

Influence of Environments ϵ_{Co} and ϵ_{Ct} . For a given *Rm* group we see from Table I that each substitution of methyl groups by ethyl in ϵ_{Ct} produces a decrease in the migration rate of the group in question. Nevertheless, similar modifications in ϵ_{Co} have effects which appear less systematic, sometimes accelerating and sometimes retarding this rate.

Linear Relationships between $\log k_p^{\text{Rm}}$ and $f(n_o, n_t)$. The results in Table I lead to some interesting observations. Thus, for a given migrating group and a constant terminal environment ϵ_{Ct} , there exist linear relationships between $\log k_p^{\text{Rm}}$ and

Table II. Determination of G , Obtained by Pinacol Rearrangement of II: Influence of G on Constants k_p^{Rm}

\mathcal{E}_{C_0} Rm (R_1, R_2)	\mathcal{E}_{C_t} (Rt)	H^a	A^b	G^c	$\log k_p^{Rm} + 8^d$	Paths	$\log k_p^{Rm} + 8^e$	Paths	% of products passing via ion VII ^f	Δ hyperconjugation
Me Me,Me	<i>t</i> -Bu	0.04	100	0.96	2.89	1'	2.87	1	0	3
	<i>t</i> -Am	0.059	99.3	0.94	2.28	4'	2.25	4	0.7	3
	<i>t</i> -Hex	0.137	98.6	0.86	1.67 ^g	7'	1.60 ^g	7	1.4	3
	Et ₂ C	0.215	98	0.78	1.06 ^h	10'	0.95 ^h	10	2	3
Me Et,Et	<i>t</i> -Bu	0.085	100 ^f	0.90	2.87	3'	2.82	3	16	1
	<i>t</i> -Am	0.073	100	0.90	2.31	6'	2.26	6	26.5	1
	<i>t</i> -Hex	0.117	100	0.85	1.50	9'	1.42	9	22	1
	Et ₂ C	0.106	100	0.84	0.28 ^h	12'	0.20 ^h	12	32.5	1
Et Me,Me	<i>t</i> -Bu	0.26	96	0.73	3.08	13'	3.01	13	4	2
	<i>t</i> -Am	0.248	95	0.74	2.43	16'	2.35	16	5	2
	<i>t</i> -Hex	0.28	94	0.70	1.86 ^g	19'	1.71 ^g	19	6	2
	Et ₂ C	0.28	93	0.70	1.21 ^h	22'	1.04 ^h	22	7	2
Et Et,Et	<i>t</i> -Bu	0.15	100	0.85	3.61	15'	3.48	15	0	4
	<i>t</i> -Am	0.17	100	0.83	3.09	18'	2.96	18	0	4
	<i>t</i> -Hex	0.28	100	0.72	2.09	21'	1.94	21	0	4
	Et ₂ C	0.32	100	0.68	0.90	24'	0.74	24	0	4
Et Me,Et	<i>t</i> -Hex ^j	0.25	≥99	0.75	1.97 ^g	20'	1.84 ^g	20 ^g	≤1	3

^a The molar ratio between I and the sum of the products (I + III + X) formed in 30 s from the pinacol rearrangement of II. Values are at ± 0.005 . ^b A represents, in the pinacol rearrangement leading to products I, III, and X, the percentage of the pathway passing through ion V. Values which differ from 100 are at ± 0.5 . ^c Values are at ± 0.01 . ^d These values are calculated from eq 1, taking into account G . Values (except those with a further reference) are at ± 0.01 . ^e These values are calculated from eq 2, in which $G = 1$. Values (except those with a further reference) are at ± 0.01 . ^f When ion VII (Scheme II) gives only ketones other than III and X, A is equal to 100. ^g Values are at ± 0.04 . ^h Values are at ± 0.10 . ⁱ Values are at ± 0.5 . ^j This glycol belongs to population L.

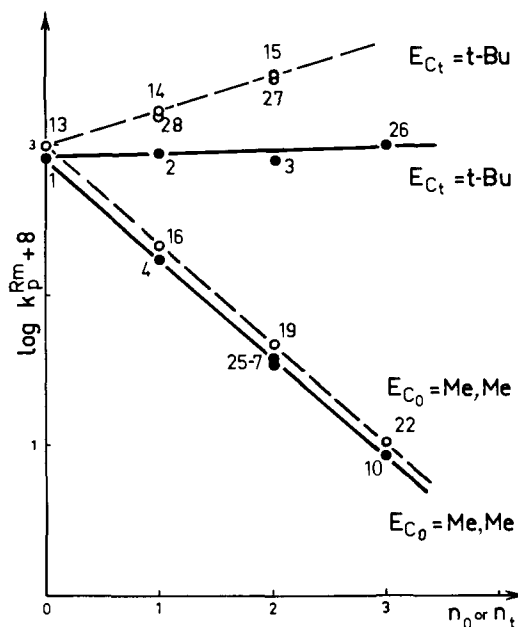


Figure 1. Influence of environments \mathcal{E}_{C_0} and \mathcal{E}_{C_t} on the migration of a group Rm. The continuous straight lines represent the relationships: $\log k_p^{Rm} = \log k_{op}^{Rm} + an_0$ ($\mathcal{E}_{C_t} = t\text{-Bu}$) and $\log k_p^{Rm} = \log k_{op}^{Rm} + bn_t$ ($\mathcal{E}_{C_0} = \text{Me,Me}$) for Rm = Me; the dotted straight lines are for Rm = Et. ($n_0 = 0$ for $\mathcal{E}_{C_0} = \text{Me,Me}$; $n_t = 0$ for $\mathcal{E}_{C_t} = t\text{-Bu}$). The numbers on the points in the diagram correspond to the paths in Table I.

the number n_0 of carbon atoms of \mathcal{E}_{C_0} (lines corresponding to $\mathcal{E}_{C_t} = t\text{-Bu}$, Figure 1). If $\log k_{op}^{Rm}$ corresponds to the logarithm of the constants of the group Rm in the reference structure for which $\mathcal{E}_{C_0} = \text{Me,Me}$ ($n_0 = 0$) and $\mathcal{E}_{C_t} = t\text{-Bu}$ ($n_t = 0$), then the equation representing these straight lines is

$$\log k_p^{Rm} = \log k_{op}^{Rm} + an_0 \quad (3)$$

These straight lines have a slope "a", which evidently depends on the nature of the migrating group. For Rm = Me, $\log k_{op}^{Rm} = 2.87$ (path 1) and $a_{\text{Me}} = 0.017$ (continuous straight line $\mathcal{E}_{C_t} = t\text{-Bu}$); for Rm = Et, $\log k_{op}^{Rm} = 3.01$ (path 13) and $a_{\text{Et}} = 0.26$ (dotted straight line $\mathcal{E}_{C_t} = t\text{-Bu}$) (Figure 1). The difference $a_{\text{Et}} - a_{\text{Me}} = 0.24$.

The same kind of linear relationships are observed between $\log k_p^{Rm}$ and the number n_t of carbon atoms of \mathcal{E}_{C_t} , as shown by the straight lines for $\mathcal{E}_{C_0} = \text{Me,Me}$. The equation for these straight lines is

$$\log k_p^{Rm} = \log k_{op}^{Rm} + bn_t \quad (4)$$

These straight lines have a slope "b", for which $b_{\text{Me}} = -0.63$ (continuous straight line Rm = Me, $\mathcal{E}_{C_0} = \text{Me,Me}$) and $b_{\text{Et}} = -0.66$ (dotted straight line Rm = Et, $\mathcal{E}_{C_0} = \text{Me,Me}$). In contrast to the "a" coefficients, these "b" coefficients are only slightly dependent on the nature of the migrating group, since $b_{\text{Et}} - b_{\text{Me}} = -0.03$. Furthermore, certain additional observations are suggested by the results obtained from ketone Ik (paths 25, 27, and 28).

Thus the coincidence of points 27 and 15 seems to indicate that the effect of a modification of n_0 is independent of the disposition of the carbons in \mathcal{E}_{C_0} . In fact, whether this environment is made up of two ethyl groups (point 15) or of a methyl and an *n*-propyl (point 27), the partial rate constants depend only on n_0 . The coincidence of points 25 and 7, which correspond, respectively, for migration of a methyl, to the environments $\mathcal{E}_{C_t} = \text{C}(n\text{-Pr,Et,Me})$ and $\text{C}(\text{Me,Et,Et})$ seems to indicate that, for \mathcal{E}_{C_0} of the same nature, the effect produced by a change of n_t becomes negligible beyond the position γ to the terminal carbon. Finally, when comparing points 28 and 14 (Table I), since the ethyl and *n*-propyl groups give practically the same values for k_p^{Rm} , this apparently indicates that a limit (the β position with respect to the origin carbon) seems also to exist for a migrating group when it is placed in identical \mathcal{E}_{C_0} and \mathcal{E}_{C_t} environments.

Additivity of Environmental Effects of \mathcal{E}_{C_0} and \mathcal{E}_{C_t} . The existence of the linear relationships in eq 3 and 4 poses the question of the additivity of such effects. According to this hypothesis, when the environments \mathcal{E}_{C_0} and \mathcal{E}_{C_t} vary simultaneously, the partial rate migration constant of a group should be calculable from

$$\log k_p^{Rm} = \log k_{op}^{Rm} + an_0 + bn_t + i \quad (5)$$

in which the term "i" is an interaction term considered, in a first approximation, as negligible.

Thus, $\log k_p^{\text{Me}}$ for a structure comprising $\mathcal{E}_{C_0} = \text{Et,Me}$ and $\mathcal{E}_{C_t} = t\text{-Am}$ ($n_0 = 1$, $n_t = 1$) yields a calculated value of log

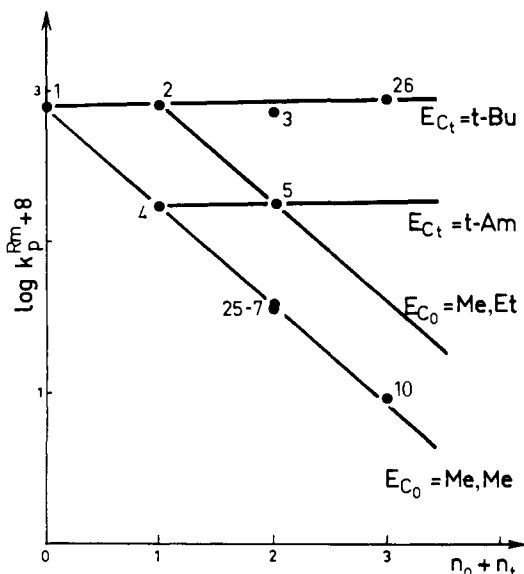


Figure 2. Additivity of environment effects. The position of point 5 shows, for $R_m = \text{Me}$, the parallelism of linear relationships when a strict additivity of environment effects is observed. This additivity is expressed in eq 5 when the term "i" is nil.

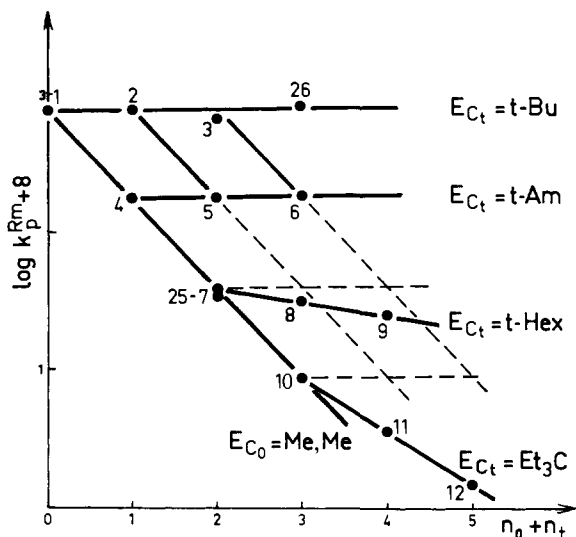


Figure 3. Methyl migration: a comparison of the theoretical and experimental networks. The theoretical network expresses the strict additivity of the environment effects ($i = 0$ in eq 5). The dotted lines represent the theoretical network when it differs from the experimental one. Large deviations for $t\text{-Hex}$ and Et_3C are observed and are identical with those in Figure 4 for Et migration.

$k_p^{\text{Me}} = 2.87 + 0.017 - 0.63 = 2.26$, in perfect agreement with the experimental value. This value (point 5, Figure 2) is thus located at the intersection of two straight lines which are respectively parallel to the straight lines $R_m = \text{Me}$, $E_{C_t} = t\text{-Bu}$ and $R_m = \text{Me}$, $E_{C_0} = \text{Me, Me}$.

Therefore, as long as the interaction term "i" in eq 5 can be considered negligible, the values of k_p^{Rm} obtained for variable environments of the origin and terminal carbons should be located at the nodes of a network of parallel straight lines which would be characteristic of the migrating group.⁷ We thereby obtain two networks: one for $R_m = \text{Me}$ (Figure 3), the other for $R_m = \text{Et}$ (Figure 4). The values thus calculated for the structures studied are given in Table III along with the experimental values.

Values of Interaction Terms. An examination of Figures 3 and 4 shows that, except for two points out of 24 (points 17 and

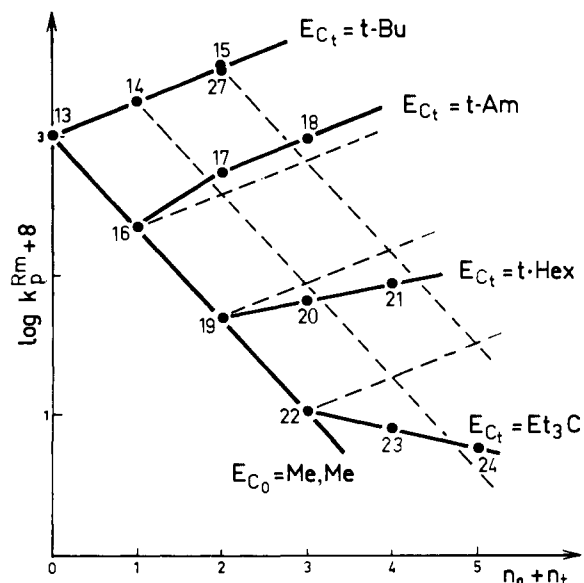


Figure 4. Ethyl migration: a comparison of the theoretical and experimental networks. The dotted lines represent the theoretical network when it differs from the experimental one. The straight line segment connecting point 17 and point 18 is parallel to the straight line $E_{C_t} = t\text{-Am}$ of the theoretical network.

Table III. Comparison of $\log k_p^{\text{Rm}}$ Experimental and $\log k_p^{\text{Rm}}$ Calculated from the Linear Relationship (eq 5)

Paths	$R_m = \text{Me}$				$R_m = \text{Et}$			
	n_o^a	n_t^a	Calcd ^b	Expt ^c	n_o^a	n_t^a	Calcd ^b	Expt ^c
1	0	0		2.87	13	0	0	3.01
2	1	0	2.89	2.88	14	1	0	3.25
3	2	0	2.90	2.82	15	2	0	3.49
4	0	1	2.24	2.25	16	0	1	2.35
5	1	1	2.26	2.26	17	1	1	2.59
6	2	1	2.27	2.26	18	2	1	2.83
7	0	2	1.61	1.60 ^d	19	0	2	1.69
8	1	2	1.63	1.54 ^d	20	1	2	1.93
9	2	2	1.64	1.42	21	2	2	2.17
10	0	3	0.98	0.95 ^e	22	0	3	1.03
11	1	3	1.00	0.62 ^e	23	1	3	1.27
12	2	3	1.01	0.20 ^e	24	2	3	1.51
25	0	3	0.98	1.54 ^d	27	2	0	3.49
26	3	0	2.92	2.92				

^a For $E_{C_0} = \text{Me, Me}$, $n_o = 0$; for $E_{C_t} = t\text{-Bu}$, $n_t = 0$. ^b These values are calculated from eq 5, in which the term "i" = 0. ^c The experimental logarithms are obtained from the values of k_p^{Rm} (Table I). Values (except those with a further reference) are at ± 0.01 . ^d Values are at ± 0.04 . ^e Values are at ± 0.10 .

18), the experimental values fall on the straight lines which correspond to constant environments E_{C_t} .

In addition, a decrease in slope "a" of lines $E_{C_t} = t\text{-Hex}$ and Et_3C in the lower part of the networks is observed. This decrease, Δa , is the same for a given terminal environment regardless of the nature of the migrating group. For $E_{C_t} = t\text{-Hex}$, $\Delta a = 0.11$; for $E_{C_t} = \text{Et}_3\text{C}$, $\Delta a = 0.4$.

Finally, the straight-line segment joining points 17 and 18 (Figure 4) is parallel to the straight line corresponding to $E_{C_t} = t\text{-Am}$, showing that a structural effect increases the reactivity in the same proportion for these two structures.

Discussion

A study of Table II shows first that for each pinacol rearrangement the percentages of pathways passing via VII increase as the C-H hyperconjugation difference between ions V and VII decreases. This result implies that the relative sta-

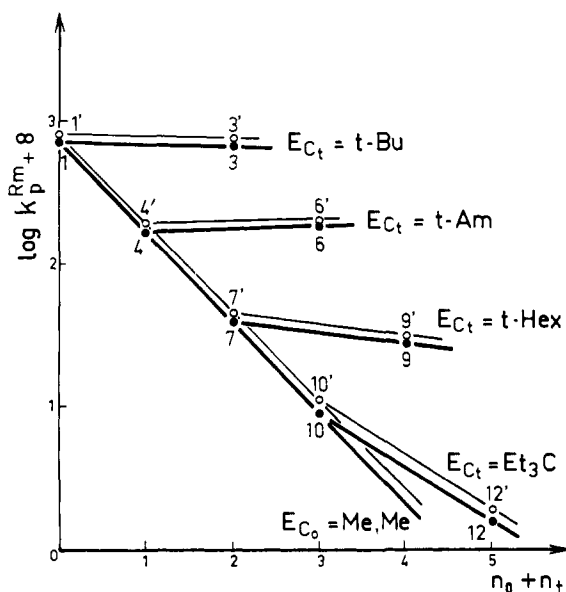


Figure 5. Influence of G in morphology of the methyl network. The heavy lines link the values of $\log k_p^{Rm}$ calculated from simplified eq 2. The light lines link the values of $\log k_p^{Rm}$ calculated from eq 1.

bilities of both of these ions are decisive. This tends to confirm the hypothesis advanced in the previous article concerning the multistep character of the pinacol rearrangement mechanism in 96% H_2SO_4 .

In Table II the determined values of G are all smaller than 1, thus proving that the return of step $IV \rightarrow V$ exists in each and every case. This return is comparatively more important when $Rm = Et$ than when $Rm = Me$.

However, the approximation on G is not at the root of the structural effects observed in the networks shown in Figures 3 and 4. Indeed, as shown in Figures 5 and 6, the morphology of the networks from eq 2 are compared to those obtained from eq 1. In particular, angular coefficients "a" of straight lines $E_{C_t} = t-Bu$, $t-Am$, $t-Hex$, and Et_3C remain unchanged. Thus, other factors must explain these structural effects.

In the case of the paths whose experimental values of $\log k_p^{Rm}$ agree with the calculated values (Table III, Figures 3 and 4) one is tempted to interpret the observed reactivities in terms of electronic effects measured, for example, by the Taft σ^* for which the additivity principle has frequently been observed. Although the structural variations observed do not allow the use of a sufficiently large σ scale to obtain significant linear free-energy relationships, one can however make the following observations.

If the electronic effects play a major part in determining the energy of the transition state, then: either the structure of the transition state of step $IV \rightarrow V$ is very much like that of ion IV and, since the substituents making up environments E_{C_o} and E_{C_t} are equidistant from the carbonium center of ion IV, any replacement of a Me by an Et in the E_{C_o} environment should, therefore, have an influence comparable to an equivalent replacement in the E_{C_t} environment; or the structure of the transition state is very much like that of ion V, in which case any replacement of a Me by an Et in the E_{C_o} environment should have a much greater influence than any equivalent replacement in the E_{C_t} environment, since the substituents making up E_{C_o} are directly fixed onto the carbonium center in V.

However, we observed that every substitution of a Me by an Et in E_{C_o} leads to a variation of $\log k_p^{Rm}$ which is much smaller than one which would result from an analogous substitution in E_{C_t} . For example, this is verified for the substitution of a Me

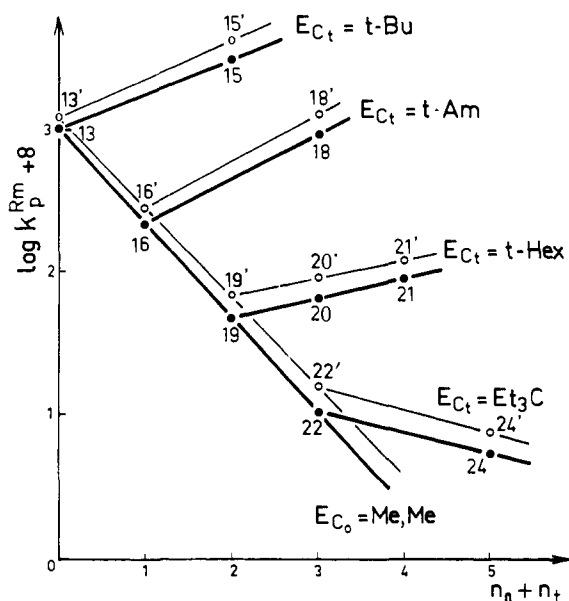
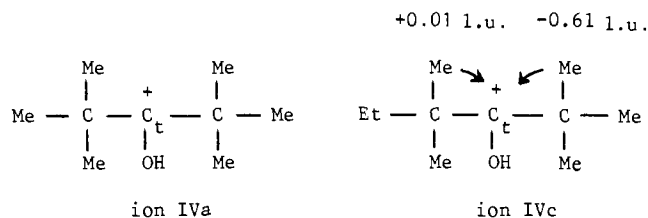


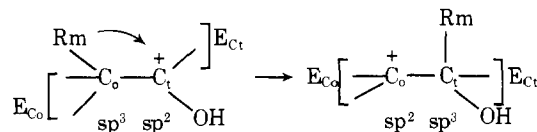
Figure 6. Influence of G in morphology of the ethyl network. The heavy lines link the values of $\log k_p^{Rm}$ calculated from simplified eq 2. The light lines link the values of $\log k_p^{Rm}$ calculated from eq 1. The position of point 20' which is found on the straight line $E_{C_t} = t-Hex$ tends to show that the approximation on G is without influence on the linear relationship (eq 5).

Scheme III



by an Et in ketone Ia. A comparison of the values of $\log k_p^{Me}$ of the methyls of ion IVa to those of the methyls of ion IVc (Scheme III) shows an increase in $\log k_p^{Me}$ of 0.01, for a change in E_{C_o} (paths 2 and 1), and a decrease of -0.6 for a change in E_{C_t} (paths 1 and 4) (Table III). Thus, it appears that electronic effects do not seem to cause the observed reactivity variations.

A second hypothesis is that the observed reactivity variations are related to steric compression and decompression, which take place at carbons C_o and C_t in the migration step. The reactivity increase related to an increase in n_o , when n_t is constant, may be explained by a relief in the steric strain caused by a change in the hybridization of the C_o ; $sp^3 \rightarrow sp^2$. Conversely, a reactivity decrease related to an increase in n_t , when n_o is constant, may be explained by an increase in the steric strain caused by a change in the hybridization of the C_t ; $sp^2 \rightarrow sp^3$.



A correlation of the following type

$$\log k_p^{Rm}/k_{op}^{Rm} = \delta(E_s(E_{C_t}) - E_s(E_{C_o}))$$

can be envisaged in order to check this out; however, the Taft E_s are not proportional to the number of carbon atoms, but are rather influenced by topology.⁸

Partial correlations with, on the one hand, the E_s of E_{C_o} :

$$\log k_p^{Rm}/k_{op}^{Rm} = \delta E_s(E_{C_o}, E_{C_t})$$

and, on the other hand, the E_s of \mathcal{E}_{C_1} :

$$\log k_p^{Rm}/k_{op}^{Rm} = \delta E_s(\mathcal{E}_{C_1}, \mathcal{E}_{C_0})$$

bring other difficulties into play. In the first case, this treatment is not possible, since the values of the E_s of groups Me and Et are virtually identical (0.00 and 0.07). In the second case, certain parameters of the tertiary groups (notably E_{st-Hex}) are not clearly determined. Furthermore, each correlation would only bear on a very limited number of values.

Finally, because of the high degree of steric hindrance of the studied ketones and the great difference between the transition states of step IV \rightarrow V and the hydrolysis of the esters, the faulty correlation with the Taft parameters would not necessarily mean that the steric effects play a secondary role in this case.

Thus, it is apparent that simple correlations with Taft's steric or polar parameters are still inadequate for interpreting these data and that a treatment taking into account the conformational requirements for the migration of Rm is called for. This is all the truer since when one compares the Δa decrease of angular coefficient "a" in the lower part of the two networks (Figures 3 and 4), one observes the existence of an opposition effect to the migration, which seems to be independent of the nature of the migratory group. Such an effect can result from the appearance of considerable interactions in these heavily hindered structures between environments \mathcal{E}_{C_0} and \mathcal{E}_{C_1} , thereby destabilizing, on the level of ions IV, the conformers favoring migration of the Rm group. X-ray, ir spectroscopic, and theoretical (CNDO-2) studies of type I ketones are presently underway for the purpose of determining the nature of the privileged conformers. A quantitative interpretation of these global results will be attempted in a forthcoming article.

Conclusion

The metathetical transposition of α, α' -bis-*tert*-alkyl ketones allows us to measure the partial rate migration constants k_p^{Rm} and systematically study interactions between environments \mathcal{E}_{C_0} and \mathcal{E}_{C_1} and the migrating group, Rm.

The results are surprising on two counts: the magnitude of the phenomenon observed, since for a given migrating group the reactivity spans nearly three powers of ten, and behavior as shown by linear relationships between $\log k_p^{Rm}$ and n_o and $\log k_p^{Rm}$ and n_t for $E_{C_0} = \text{Me, Me}$, accompanied by a partially observed additivity law. The linear relationships thus obtained are incorporated into a network whose morphology apparently characterizes the behavior of the migrating group relative to the structure hosting the migration.

The observed effects, most likely of steric and conformational origin, show that the notion of migrating tendencies (MT), equal to $k_p^{Rm}/k_p^{R'm}$ (partial rate constant ratio of two different groups migrating within comparable E_{C_0} and E_{C_1} environments),⁹ is not sufficient for establishing a scale of migratory aptitudes. Indeed, there will be as many values of MT as there are different environments. On the other hand, insofar as each migrating group can be characterized by a network like those described herein, one can envisage the possibility of classifying the groups from a broader notion, bringing into play a parameter, derived from these networks, which would express the sensitivity of these groups to changes in environments E_{C_0} and E_{C_1} . Thus, for example, the more a migrating group is sensitive to variations in \mathcal{E}_{C_0} and \mathcal{E}_{C_1} , the greater the angle of its network, measured by the sum of absolute values of the angular coefficients "a" + "b", will be, and vice versa.

Studies are presently under way in order to specify the validity of this notion, as well as the steric and conformational nature of "structure-migrating group" interactions.

Experimental Section

General. Gas chromatographic analyses were run on a Varian Aerograph Model 1200 equipped with a flame ionization detector and an electronic integrator; Varian Model 475.

Preparative separations were carried out on a Varian Aerograph Model 1440 equipped for micropreparative work.

Ir spectra were measured on a Perkin-Elmer 225 spectrophotometer; NMR spectra were measured on a Jeol C-60 HL spectrometer; mass spectra were taken on a Thomson 208 HL mass spectrometer equipped with a line molecular injector accessory.

Synthesis of α, α' -Bis-*tert*-alkyl Ketones (Ia to Ik). All α, α' -bis-*tert*-alkyl ketones were prepared according to the general procedure previously described for Ia¹⁰ by condensation of an organomagnesium compound with an acid chloride, in the presence of a catalyst (cuprous chloride), in dried ether at low temperature (-5°C).

The acid chlorides were obtained from corresponding acids. Except for pivalic acid (Aldrich), the other acids were prepared by carboxylation of the corresponding Grignard reagents.

The *tert*-butylmagnesium and *tert*-amylmagnesium chloride were prepared under refluxing ether at 0.8 M; the 1-ethyl-1-methylpropylmagnesium and 1,1-diethylpropylmagnesium chloride were prepared at 0.4 M.

2,2,4,4-Tetramethyl-3-pentanone (Ia) was prepared by condensation of *tert*-butylmagnesium chloride and pivaloyl chloride. The yield of pure product was 80%: bp 69.5°C (48 mm); n_D^{25} 1.4170; ir 1686.5 cm^{-1} (C=O), (lit. bp 152°C (760 mm); n_D^{25} 1.4171).

3,3,5,5-Tetraethyl-4-heptanone (Ib) was prepared by condensation of 1,1-diethylpropylmagnesium chloride and 2,2-diethylbutanoyl chloride. The yield of pure product was 30%: bp 115°C (3 mm); mp $44-45^\circ\text{C}$; ir 1678 cm^{-1} (C=O).

2,2,4,4-Tetramethyl-3-hexanone (Ic) was prepared by condensation of *tert*-amylmagnesium chloride and pivaloyl chloride. The yield of pure product was 50%: bp 62°C (13 mm); n_D^{25} 1.4268; ir 1684.5 cm^{-1} (C=O).

2-Ethyl-2,4,4-trimethyl-3-hexanone (Id) was prepared by condensation of 1-ethyl-1-methylpropylmagnesium chloride and pivaloyl chloride. The yield of pure product was 55%: bp 75°C (11 mm); n_D^{25} 1.4360; ir 1682.5 cm^{-1} (C=O).

4,4-Diethyl-2,2-dimethyl-3-hexanone (Ie) was prepared by condensation of 1,1-diethylpropylmagnesium chloride and pivaloyl chloride. The yield of pure product was 30%: bp 40°C (1 mm); n_D^{25} 1.4450; ir 1681.5 cm^{-1} (C=O).

3,3,5,5-Tetramethyl-4-heptanone (If) as prepared by condensation of *tert*-amylmagnesium chloride and 2,2-dimethylbutanoyl chloride. The yield of pure product was 50%: bp 80°C (14 mm); n_D^{25} 1.4354; ir 1682.5 cm^{-1} (C=O).

3-Ethyl-3,5,5-trimethyl-4-heptanone (Ig) was prepared by condensation of 1-ethyl-1-methylpropylmagnesium chloride and 2,2-dimethylbutanoyl chloride. The yield of pure product was 50%: bp 75°C (2.5 mm); n_D^{25} 1.4447; ir 1680 cm^{-1} (C=O).

3,3-Diethyl-5,5-dimethyl-4-heptanone (Ih) was prepared by condensation of 1,1-diethylpropylmagnesium chloride and 2,2-dimethylbutanoyl chloride. The yield of pure product was 30%: bp 84°C (2.5 mm); n_D^{25} 1.4533; ir 1679 cm^{-1} (C=O).

3,5-Diethyl-3,5-dimethyl-4-heptanone (Ii) was prepared by condensation of 1-ethyl-1-methylpropylmagnesium chloride and 2-ethyl-2-methylbutanoyl chloride. The yield of pure product was 36%: bp 90°C (3 mm); n_D^{25} 1.4569; ir 1679 cm^{-1} (C=O).

3,3,5-Triethyl-5-methyl-4-heptanone (Ij) was prepared by condensation of 1,1-diethylpropylmagnesium chloride and 2-ethyl-2-methylbutanoyl chloride. The yield of pure product was 33%: bp 98°C (2 mm); n_D^{25} 1.4596; ir 1678 cm^{-1} (C=O).

4-Ethyl-2,2,4-trimethyl-3-heptanone (Ik) was prepared by condensation of 1-ethyl-1-methylbutylmagnesium chloride and pivaloyl chloride. The yield of pure product was 30%: bp 85°C (25 mm); n_D^{25} 1.4377; ir 1683 cm^{-1} (C=O).

All the ketones, which were obtained either directly by distillation or by purifying the distillate by GLC, were $\geq 99\%$ pure and were identified by their ir and NMR spectra. As far as we know, ketones Ib-Ik are not described in literature.

Synthesis of Glycols. The glycols were prepared by reaction of MeLi or EtLi with the corresponding methyl ketoester (RtCOCOOME), itself obtained from ketone RtCOMe (where Rt = *t*-Bu, *t*-Am, *t*-Hex, or Et₃C).

¹³C-labeled diols were prepared from sodium acetate·3H₂O, labeled

on the carbonyl with 56–57% ^{13}C , which was dehydrated by heating in a nickel crucible, then transformed into acetyl chloride by reaction with thionyl chloride. The following manipulations were the same as for unlabeled glycols.

(1) Ketones: RtCOMe. The ketones were prepared according to the general procedure used for the above α,α' -bis-*tert*-alkyl ketones by condensation of RtMgCl with acetyl chloride in dried ether at -10°C in the presence of cuprous chloride. Thus for 3,3-dimethyl-2-butanone (ebullioscopic constant (eb) 40°C (78 mm); ir 1710.4 cm^{-1} ($\text{C}=\text{O}$)), 3,3-dimethyl-2-pentanone (eb 54.5°C (51 mm); ir 1709.6 cm^{-1} ($\text{C}=\text{O}$)), 3-ethyl-3-methyl-2-pentanone (eb 76°C (55 mm); ir 1706 cm^{-1} ($\text{C}=\text{O}$)), and 3,3-diethyl-2-pentanone (eb 88.5°C (45 mm); ir 1705 cm^{-1} ($\text{C}=\text{O}$)) the yield was $\approx 60\%$.

(2) Ketoester: RtCOCOme. Ketones RtCOMe were oxidized by potassium permanganate in aqueous NaOH. Ketone (0.1 mol) was rapidly added to 0.2 mol of KMnO_4 in 750 ml of water containing 10 g of NaOH at room temperature. The mixture was stirred for 5 h, then filtered on a Büchner funnel (eliminating MnO_2) and concentrated until one-fifth of the initial volume remained. Concentrated HCl (38 ml) were slowly added in small amounts. The floating oily liquid was decanted and the aqueous layer was salted out with sodium chloride and extracted twice with ether. The combined extracts were dried (Na_2SO_4) and concentrated.

The obtained ketoacid (RtCOCO OH) was stirred with 15 g of methanol (Merck) and 7.5 g of concentrated H_2SO_4 . The mixture was heated under reflux for 2 h (oil bath at 90°C). After cooling, the mixture was decanted, extracted three times with pentane, and the organic layer was neutralized with NaHCO_3 and dried over $\text{Na}_2\text{SO}_4\text{-CaCl}_2$. The solvents (pentane and methanol) were evaporated under reduced pressure (50 mm) and the ketoester was distilled, except when GLC purity $>95\%$. For methyl 3,3-dimethyl-2-oxobutanoate (eb 60°C (19 mm); n^{25}_D 1.4130), methyl 3,3-dimethyl-2-oxopentanoate (n^{25}_D 1.4250), methyl 3-ethyl-3-methyl-2-oxopentanoate (n^{25}_D 1.4309), and methyl 3,3-diethyl-2-oxopentanoate (eb 92°C (10 mm); n^{25}_D 1.4350) the yield was $\approx 70\%$. They were characterized by their ir and NMR spectra.

(3) Synthesis of Population K Glycols Where $\text{R}_1 = \text{R}_2 = \text{R}_m = \text{Me}$. The structure of these glycols required ^{13}C labeling. They were synthesized under the same conditions as previously described for 2,3,4,4-tetramethyl-2,3-pentanediol¹⁰ by condensation of the corresponding labeled ketoester into an excess solution of methyl lithium in dried ether at room temperature.

The following four glycols were all purified by preparative GLC (10 ft \times 0.250 in. column with 10% SE-30) at 150, 160, 160, and 170°C , respectively.

2,3,4,4-Tetramethyl-2,3-pentanediol-3- ^{13}C was obtained from the methyl 3,3-dimethyl-2-oxobutanoate-2- ^{13}C (70% yield; n^{25}_D 1.4542).

2,3,4,4-Tetramethyl-2,3-hexanediol-3- ^{13}C was obtained from the methyl 3,3-dimethyl-2-oxopentanoate-2- ^{13}C (70% yield; n^{25}_D 1.4650).

4-Ethyl-2,3,4-trimethyl-2,3-hexanediol-3- ^{13}C was obtained from methyl 3-ethyl-3-methyl-2-oxopentanoate-2- ^{13}C (70% yield; n^{25}_D 1.4727).

4,4-Diethyl-2,3-dimethyl-2,3-hexanediol-3- ^{13}C was obtained from methyl 3,3-diethyl-2-oxopentanoate-2- ^{13}C (60% yield; n^{25}_D 1.4800).

(4) Synthesis of Population K Glycols Where $\text{R}_1 = \text{R}_2 = \text{R}_m = \text{Et}$. The structure of these glycols also required labeling with ^{13}C . They were synthesized under the same conditions as previously reported for 3,4,5,5-tetraethyl-3,4-heptanediol¹⁰ by condensation of the corresponding labeled ketoester into an excess solution of ethyllithium in dried pentane at room temperature.

The following four glycols were all purified by preparative GLC (10 ft \times 0.250 in. column with 10% SE-30) at 160, 170, 180, and 195°C , respectively.

3,4-Diethyl-5,5-dimethyl-3,4-hexanediol-4- ^{13}C was obtained from methyl 3,3-dimethyl-2-oxobutanoate-2- ^{13}C (25% yield; n^{25}_D 1.4709).

3,4-Diethyl-5,5-dimethyl-3,4-heptanediol-4- ^{13}C was obtained from methyl 3,3-dimethyl-2-oxopentanoate-2- ^{13}C (18% yield; mp 39°).

3,4,5-Triethyl-5-methyl-3,4-heptanediol-4- ^{13}C was obtained from methyl 3-ethyl-3-methyl-2-oxopentanoate-2- ^{13}C (16% yield; n^{25}_D 1.4817).

3,4,5,5-Tetraethyl-3,4-heptanediol-4- ^{13}C was obtained from methyl 3,3-diethyl-2-oxopentanoate-2- ^{13}C (10% yield; mp 66.5°C).

(5) Synthesis of Population M Glycols. Six of the glycols were synthesized by action of 1 M methyl lithium added slowly under argon pressure on a corresponding ketoester (2:1) diluted in five volumes of dried ether, then the mixture was poured off under the same conditions into an excess of 1.5 M ethyllithium¹¹ in dried ether at room temperature. After hydrolysis, the mixture was extracted with ether. The extract was washed with water and dried over MgSO_4 , and the solvent was evaporated. Thus, the following glycols, all purified by preparative GLC, were obtained.

3-Ethyl-4,5,5-trimethyl-3,4-hexanediol was synthesized from methyl 3,3-dimethyl-2-oxobutanoate (20 ft \times 0.250 in. column with 10% SE-30 at 155°C ; 27% yield; mp 50.5°C).

3-Ethyl-2,4,4-trimethyl-2,3-hexanediol and 3-ethyl-4,5,5-trimethyl-3,4-heptanediol were obtained in the same manipulation from methyl 3,3-dimethyl-2-oxopentanoate (10 ft \times 0.250 in. column with 10% SE-30 at 152°C ; 17% yield for each; n^{25}_D 1.4670 and 1.4772, respectively).

3,4-Diethyl-2,4-dimethyl-2,3-hexanediol and 3,5-diethyl-4,5-dimethyl-3,4-heptanediol were both obtained in the same manipulation from methyl 3-ethyl-3-methyl-2-oxopentanoate (10 ft \times 0.250 in. column with 10% SE-30 at 162°C ; 36% yield, n^{25}_D 1.4743 for the first; 14% yield, mp 52.5°C for the second).

3,4,4-Triethyl-2-methyl-2,3-hexanediol was synthesized from methyl 3,3-diethyl-2-oxopentanoate (20 ft \times 0.250 in. column with 10% SE-30 at 200°C ; 55% yield; mp 40°C).

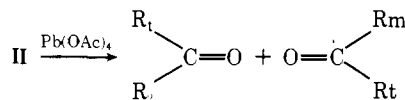
Contrary to these glycols, two other population M glycols were obtained by first adding ethyllithium; however, they were also purified by preparative GLC.

3-Ethyl-2,4,4-trimethyl-2,3-pentanediol was synthesized by action of 0.25 M ethyllithium added slowly under argon pressure on methyl 3,3-dimethyl-2-oxobutanoate (1:1); the mixture was then poured off under the same conditions into an excess of 1 M methyl lithium in dried ether (glycol yield 18%; n^{25}_D 1.4613; 30 ft \times 0.250 in. column with 15% Carbowax at 190°C).

3,5,5-Triethyl-4-methyl-3,4-heptanediol was synthesized by action of 0.5 M ethyllithium added slowly under argon pressure on methyl 3,3-diethyl-2-oxopentanoate (2:1), then poured off under the same conditions into an excess of 1 M methyl lithium in dried ether (diol yield 11%; mp 44.5°C ; 10 ft \times 0.250 in. column with 10% SE-30 at 180°C).

(6) Synthesis of 4,5-Diethyl-3,5-dimethyl-3,4-heptanediol (population L glycol). This glycol was obtained from 6 g (0.035 mol) of methyl 3-ethyl-3-methyl-2-oxopentanoate in 50 ml of dried ether added slowly to 0.15 mol of 1 M ethyllithium in dried ether¹¹ at room temperature under argon. The mixture was half concentrated, then poured off under argon pressure into 0.15 mol of 1.5 M methyl lithium and refluxed for 1 h. After hydrolysis, extraction, and drying, the glycol was purified by preparative GLC (10 ft \times 0.250 in. column with 10% SE-30 at 170°C ; 5% yield; n^{25}_D 1.4804).

Identification of Glycols. The glycols of populations K, L, or M were identified by their ir and NMR spectra and their structures were determined by oxidation with lead tetraacetate by identification of the resulting ketones. Glycol (3×10^{-4} mol) and 35×10^{-5} mol of lead



tetraacetate (humidified with about 10–15% acetic acid) were placed in 250 μl of dried benzene in a quickfit flask with stirring. The mixture was refluxed for a 1-h period, with an $85\text{--}90^\circ\text{C}$ bath. After cooling the solution was decanted and neutralized with K_2CO_3 . The two resulting ketones were identified by GLC with two columns (10 ft \times 0.125 in.) with 10% SE-30 and 15% Carbowax 20M by comparison of their retention times with those from authentic samples.

Except for IIa, as far as we know, the above glycols are not described in the literature.

^{13}C Analysis of Population K Labeled Glycols. In a little flask 2 ml of H_2SO_4 (96 wt %) and 2×10^{-3} mol of glycol were rapidly mixed (about 1 min) and poured onto ice. After extraction with chloroform and neutralization with K_2CO_3 , ketone III or X (Scheme II)¹² was separated by GLC (10 ft \times 0.250 in. 10% SE-30 column at 55, 120, or 130°C , according to boiling points of ketones).

2,3,4,4-Tetramethyl-2,3-pentanediol-3- ^{13}C yielded III, whose isotopic analysis by high resolution mass spectra has been previously reported.⁴ 2,3,4,4-Tetramethyl-2,3-hexanediol-3- ^{13}C (which also

yielded III), 4-ethyl-2,3,4-trimethyl-2,3-hexanediol-3-¹³C, and 4,4-diethyl-2,3-dimethyl-2,3-hexanediol-3-¹³C (which yielded X) were studied in a similar manner, since the interesting peaks from III or X are the same (*m/e* 43.045 for -COCH₃; 43.089 for -CH(CH₃)₂; 44.048 for -¹³COCH₃; and 44.092 for -¹³CH(CH₃)₂).

The isotopic study of 3,4-diethyl-5,5-dimethyl-3,4-hexanediol-4-¹³C, 3,4-diethyl-5,5-dimethyl-3,4-heptanediol-4-¹³C, and 3,4,5-triethyl-5-methyl-3,4-heptanediol-4-¹³C were carried out in the same conditions as for 3,4,5-tetraethyl-3,4-heptanediol-4-¹³C previously described.⁴ These four glycols yielded the same fragmented ketone X, whose interesting peaks are *m/e* 57 for -COC₂H₅; 71 for -CH(C₂H₅)₂; 58 for -¹³COC₂H₅; and 72 for -¹³CH(C₂H₅)₂.¹³

Kinetic Procedure for α,α' -Bis-*tert*-alkyl Ketones. In a hemolysis tube, 0.6 ml of H₂SO₄ (96 wt %) and 6×10^{-4} mol of ketone were mixed and placed in a thermostat at 25 °C. After a suitable delay, the mixture was poured onto ice. THF (10–12 drops) and two drops of heliantin were added. The solution was cooled in an ice bath and neutralized by 20% NaOH. This solution was salted out with sodium chloride at room temperature and extracted twice with THF. The combined extracts were dried over Na₂SO₄. Eight to ten samples were taken for each ketone. The percentages of different components were determined by GLC (10 ft \times 0.125 in. column with 15% DEGS; programming temperature 4 °C/min; limit temperature according to boiling points of ketones composing the fraction¹⁴) using specific calibration factors for peak area measurement.¹⁵ The percentage B of the different reaction pathways of the metathetical transposition is the average of the percentage obtained for each assay.

The GLC retention times and the ir and NMR spectra obtained for each of the fragmented ketones (separated by preparative GLC) were identical with those of authentic samples.

Kinetic Procedure for Glycols. In a hemolysis tube, 0.3 ml of H₂SO₄ (96 wt %) and 3×10^{-4} mol of glycol were rapidly mixed (time <30 s) and immediately poured onto ice. The extractions by THF, the identification, and the determination of the percentages of different components were made in the same conditions as described above for the kinetic procedure of the ketones. Two to three assays were taken for each glycol.

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References and Notes

- (1) The term migratory aptitude is used in a broad sense: the ability of a group to migrate.
- (2) M. J. McCall, J. M. Townsend, and W. A. Bonner, *J. Am. Chem. Soc.*, **97**, 2743 (1975).
- (3) The migratory aptitude of ethyl with respect to methyl varies in literature from 35 to 1: D. J. Cram and J. D. Knight, *J. Am. Chem. Soc.*, **74**, 5839 (1952); R. L. Heidke and W. A. Saunders, *J. Am. Chem. Soc.*, **88**, 5816 (1966).
- (4) Cf. accompanying article: J. E. Dubois and P. Bauer, *J. Am. Chem. Soc.*, preceding paper in this issue.
- (5) In a first approximation the interactions between these environments are considered negligible.
- (6) The structure in which the migration takes place means the whole of the molecule or the ion excluding the migrating group.
- (7) This network is termed theoretical when "r" in eq 5 is set equal to zero.
- (8) J. E. Dubois, A. Panaye and J. MacPhee, *C. R. Acad. Sci. Ser. C*, **280**, 411 (1975).
- (9) R. L. Heidke and W. H. Saunders, *J. Am. Chem. Soc.*, **88**, 5816 (1966).
- (10) Cf. experimental section of the accompanying article.
- (11) The ethyllithium was prepared according to the usual procedure in dried ether at -20 °C, then brought progressively to room temperature and decanted to another flask under argon pressure to eliminate excess lithium.
- (12) According to the fragmentation rate of ketone III, either ketone III or fragmented ketone X is found in the medium.
- (13) The use of high resolution was not required, since the fragments have distinctly different masses.
- (14) Gas chromatographic analyses were run on a Varian Aerograph Model 1200 equipped with a flame ionization detector with an electronic integrator Varian Model 475. The precision of this method was verified from a standard solution containing the very same products as the reaction. For each product the average of the values found is $\pm 0.5\%$ of the theoretical value.
- (15) R. Kaiser, "Gas Chromatography", Vol. 1, Butterworths, London, 1963, p 182.

Conformational Preferences of Hexahydropyridazine Derivatives

G. R. Weisman and S. F. Nelsen*

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. Received February 6, 1976

Abstract: The conformations of some hexahydropyridazine derivatives were determined by ¹³C NMR. 1,2,3,3,6,6-Hexamethylhexahydropyridazine is an approximately 95:5 mixture of the axial-equatorial *N*-methyl (*ae*): *ee* conformations at -130 °C. 1-Ethyl-2-methylhexahydropyridazine is about a 91:9 mixture of *ae*:*ee* conformations at ca. -90 °C, although 1,2-dimethylhexahydropyridazine is about a 65:35 *ee*:*ae* mixture at -70 °C. Only *ee* conformations of 1,6-diazabicyclo[4.3.0]nonane and 1,6-diazabicyclo[4.4.0]decane were detected.

Introduction

We have recently established by use of variable-temperature ¹³C NMR¹ that for 1,2-dimethylhexahydropyridazine (**1**), the diequatorial *lee* conformation is about 0.3 kcal/mol lower in enthalpy than *lae*, but that *laa* is not detectably populated at

low temperature. In contrast, the 3,6-dimethylated analogues **2** and **3** exist so predominantly in *ae* conformations that peaks or even broadening caused by the presence of *ee* conformations were not observed. Activation parameters for conversion of *lee* to the [*lae* \rightleftharpoons *lea*] mixture (involving the "nonpassing" ring reversal which does not force lone pairs to pass each other in

