459. *Mechanism of Electrophilic Substitution at a Saturated Carbon Atom. Part VI.* The Pattern of Steric Effects among Alkyl Groups and Mechanisms in One-alkyl Mercury-exchange.*

By E. D. Hughes and H. C. Volger.

Steric retardations by alkyl groups in one-alkyl S_E2 mercury-exchanges are in the order: methyl < primary alkyl < secondary alkyl (so far as has yet been explored). Among primary alkyl groups, neopentyl is in no way special: it exerts only a slight steric retardation, closely similar to that of the ethyl group. In the example of neopentyl, steric retardations are in the mechanistic order, S_E2 < S_Ei-one-anion < S_Ei-two-anion. All these experimental findings can be plausibly understood having regard to the geometries of the relevant transition states.

It seems axiomatic that the pattern of steric effects over any range of structures, such as that of alkyl groups, must be very different in bimolecular substitutions that retain configuration from what it is in those that produce stereochemical inversion.

It is well established that bimolecular nucleophilic substitution produces inversion; and the pattern of steric effects among alkyl groups in such reactions is known. Probably the most widely discussed high-light of that pattern is the extreme resistance of neopentyl systems to substitution, a phenomenon discovered by Whitmore [1] and later explained by Dostrovsky and Hughes,[2] who showed that it was associated with, and confined to, S_N2 processes, which, according to the stereokinetic principle that had by that time been established, passed through a configuration-inverting transition state, the geometry of which accounted for the very low kinetic reactivities.

All the S_E2 substitutions [3] of mercury for mercury, which have been identified [4-6] in the foregoing Parts of this Series, proceed with retention of configuration. As is explained

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* Part V, *J.*, 1961, 1142.

[1] Whitmore and Fleming, *J. Amer. Chem. Soc.*, 1933, **55**, 4161; Whitmore, Wittle, and Popkin, *ibid.*, 1939, **61**, 1586; Whitmore, Popkin, Bernstein, and Wilkins, *ibid.*, 1941, **63**, 124.

[2] Hughes, *Trans. Faraday Soc.*, 1941, **37**, 603; Dostrovsky and Hughes, *J.*, 1946, 157 *et seq.* (7 papers).

[3] Charman, Hughes, and Ingold, *J.*, 1959, 2523.

[4] Charman, Hughes, and Ingold, *J.*, 1959, 2530.

[5] Charman, Hughes, Ingold, and Thorpe, *J.*, 1961, 1121.

[6] Hughes, Ingold, Thorpe, and Volger, *J.*, 1961, 1133.

below, we expect for them quite a different pattern of steric effects. Neopentyl substitutions should show no strong retardations, but should resemble other primary alkyl substitutions, as of ethyl compounds. Primary alkyl, including neopentyl, substitutions should be less sterically restricted than the simplest secondary alkyl substitutions, as of isopropyl or s-butyl compounds.

In order to check the body of theoretical predictions, here partly quoted, at its most sensitive point, we examined first the uncatalysed one-alkyl substitution, by mechanism S_E2, of mercuric bromide into neopentylmercuric bromide. This work took in also the same substitution under one-anion and two-anion catalysis by bromide ion,[7] where the mechanisms at work are of S_Ei character,[3] involving geometrical situations appreciably different from those belonging to the uncatalysed substitution S_E2.

A series of experiments was first made with neopentylmercuric bromide and radiomercuric bromide in ethanol at 100·3° without a catalyst. The rate-constants thus obtained were very rough, because, before the exchanges had gone far, decomposition set in with the production of a mercurous precipitate, which, even before there was enough of it to upset the stoicheiometry, disturbed the kinetics by inducing some kind of catalysis. Knowing that mercurous decompositions are usually less troublesome in fast mercury exchanges, we thought we should get better results by measuring the substitution under catalysis by lithium bromide, and deducing the uncatalysed rate by extrapolation to zero concentration of catalyst. This proved the better route to the uncatalysed rate, besides giving parallel information about the catalysed rates. The relevant data are in Table 1.

TABLE 1. *Second-order rate-constants of substitution ($k_2^{(1)}$ or $k_{2c}^{(1)}$ in mole^{-1} l. sec.$^{-1}$) of mercuric bromide (concentration a), in ethyl- or neopentyl-mercuric bromide (concentration b), either without catalysis, or in the presence of lithium bromide (concentration c), as followed by radiometric observation of mercury exchange in ethanol.*

(The radioactivity of mercury-203 was initially wholly in the inorganic mercuric salt. Reaction was followed through its progressive appearance in separated alkylmercuric salt. All concentrations and rate-constants are corrected for thermal volume changes of the solvent.)

Run	Temp.	Followed %	a (M)	b (M)	c (M)	$10^5k_{2c}^{(1)}$
Neopentylmercuric Bromide (bromide-catalysed)						
144	100·3°	14	0·091	0·092	0·0202	10·1
146	,,	16	0·091	0·092	0·0314	13·5
142	,,	10	0·091	0·092	0·0438	17·4
145	,,	29	0·094	0·093	0·063	23·0
143	,,	29	0·091	0·092	0·098	31·1
159	,,	25	0·093	0·092	0·127	34·5
158	,,	44	0·091	0·092	0·160	39·3
149	,,	40	0·091	0·092	0·188	41·8
Ethylmercuric Bromide (uncatalysed)						$10^5k_2^{(1)}$
153	72·9°	3	0·098	0·0262	—	0·76
152	100·2	5	0·155	0·0500	—	4·9
151	100·3	4	0·114	0·0407	—	5·8

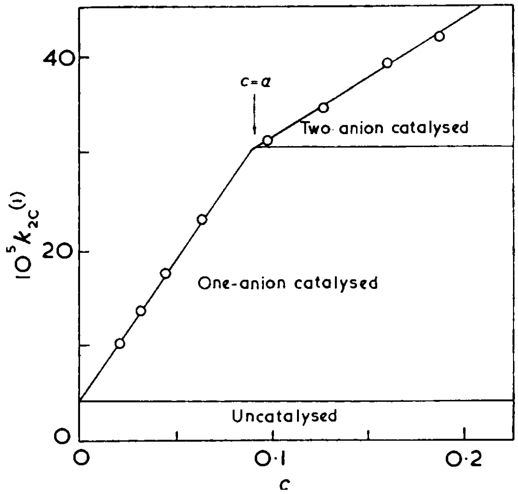
A plot of the rate-constants for the neopentyl exchange reaction is shown in the Figure, which it is interesting to compare with the analogous plot for the methyl exchange reaction, as given in Fig. 1 of Part V.[7] Both plots refer to calculated second-order rate-constants of substitution, $k_{2c}^{(1)}$, derived from the experimental rate-constants of label-transfer, κ_1, and the rates of exchange, k_0, by the relations[5] $k_{2c}^{(1)} = \kappa_1/(a + b) = k_0/ab$; and they show these substitution rate-constants as functions of the concentration c of the lithium bromide catalyst, in a series of experiments in which the concentrations, a, of mercuric bromide, and b, of the alkylmercuric bromide, were kept constant. Both curves consist of two straight lines, meeting with a break of gradient about the point at which the concentration of lithium bromide equals that of the mercuric bromide ($c = a$). However, there are differences.

[7] Charman, Hughes, Ingold, and Volger, *J.*, 1961, 1142.

One difference relates to the intercept. In the methyl exchange, the catalysis by bromide ion is so strong that, on the scale on which the plot of rates has to be made, the curve appears to pass through the origin, the intercept representing the uncatalysed rate-constant being unreadably small—though, fortunately, that rate-constant can be measured independently and directly. In the neopentyl exchange, on the other hand, the catalysis is so far weakened that, when the rate-plot is made, the uncatalysed rate-constant appears as an easily readable intercept. We think that the value thus found, $k_2^{(1)} = 4{\cdot}2 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$, is good to about 10%.

The other notable difference relates to the change of gradient at the break. In the plot of methyl exchange, the gradient increases at that point; in the plot for neopentyl, it decreases. In Part V,[7] where the theory of one-anion and two-anion catalysis was developed, it was noted that an increase of gradient, the only form of break that had been observed up to that time, was not required by the theory, which would allow a decrease of gradient to appear, such as that which has now been found. The difference implies that, whilst, on passing from the methyl to the neopentyl mercury-exchange, anion catalysis is generally weakened, as we have seen, yet two-anion catalysis suffers a substantially greater weakening than does one-anion catalysis.

Dependence of the second-order rate-constant of one-alkyl substitution, $k_{2c}^{(1)}$, by mercuric bromide in neopentylmercuric bromide in ethanol at 100·3°, *on the concentration, c, of added lithium bromide, the concentrations of the mercury-exchanging substances being a* = *b* = 0·92M. The curve is that of the equation on p. 2362, with $k_2^{(1)} = 4{\cdot}2 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$, $\kappa_1 = 26{\cdot}4 \times 10^{-5}$ mole^{-1} l. sec.$^{-1}$, and $\kappa_2 = 122 \times 10^{-5}$ mole^{-2} l.^{2} sec.$^{-1}$.



Let us next consider more particularly the results applying to the uncatalysed one-alkyl substitution, S_E2. As we already have[6] a good value for the methyl rate, our determination of the neopentyl rate completes the comparison of main interest. However, a little filling-in is possible. We have made some approximate measurements of the ethyl rate by the direct method, which is feasible in that case. These results also are included in Table 1.* We did not attempt similar measurements of the isopropyl rate, because of

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* Sintova's rates for the corresponding n-propyl exchange[8] are about twice as large as ours for ethyl, though we would have expected the rate for the higher homologue to be slightly the smaller (for entropic reasons: the activation energies should be identical). This comparison might, however, be affected by the unknown experimental cause which makes Nefedov, Sintova, and Frolov's rates, for the methyl example,[9] about 2½ times as large as the rates we recorded in Part IV[6] for that reaction in like conditions.

[8] Sintova, *Zhur. neorg. Khim.*, 1957, **2**, 1205.

[9] Nefedov, Sintova, and Frolov, *Zhur. fiz. Khim.*, 1956, **30**, 2356.

past troubles with the mercurous decomposition in the similar s-butyl case, and because we had already obtained a good comparison of methyl and s-butyl S_E2 rates in one-alkyl substitution, by going over from bromides to the faster-reacting acetates,[6] thus evading the mercurous disturbance. The figures which seem worth comparing are put together in Table 2.

TABLE 2. *Effect of alkyl structure on second-order rate-constants of substitution* ($k_2^{(1)}$ *in* mole^{-1} l. sec.$^{-1}$) *and on relative rate in uncatalysed one-alkyl mercury-exchange*

$$\mathrm{RHgX} + \mathrm{HgX_2} \rightleftharpoons \mathrm{RHgX} + \mathrm{HgX_2}$$

where X *is bromide or acetate, in ethanol at* 60° *or* 100°.

R	$10^5k_2^{(1)}$ Bromides at 100°	$10^5k_2^{(1)}$ Acetates at 60°	Relative rates
Methyl	12·8	500	100
Ethyl	5·4	—	42
Neopentyl	4·2	—	33
s-Butyl	—	30·9	6

We can further compare the methyl and neopentyl groups with regard to the rates of the two bromide-catalysed mercury-exchanges that proceed by mechanisms of S_Ei type. For both alkyl groups, we have experimental relations of the form,[7]

$$k_{2c}^{(1)} = k_2^{(1)} + \begin{cases} \kappa_{1(c/a)} & (c < a) \\ \kappa_1 + \kappa_{2(c-a)} & (c > a) \end{cases}$$

where the catalytic constants κ_1 and κ_2 are as entered in Table 3. The one-anion constant κ_1 has the dimensions of a second-order rate-constant. Hence the convenient measure of the strength of one-anion catalysis is the value of the dimensionless ratio $\kappa_1/k_2^{(1)}$. The two-anion constant κ_2 has the dimensions of a third-order rate-constant. Thus the most convenient measure of the strength of two-anion catalysis is the dimensionless ratio $a\kappa_2/k_2^{(1)}$. Two-anion catalysis becomes just equally strong with one-anion when $a\kappa_2 = \kappa_1$. Hence the dimensionless ratio $a\kappa_2/\kappa_1$, which is simply the ratio of the slopes of the two branches of such a curve as is in the Figure, is the best measure of the relative strengths of two- and one-anion catalysis. All these dimensionless ratios are given in Table 3.

TABLE 3. *Values and ratios for methyl and neopentyl groups of* (a) *the rate-constants,* $k_2^{(1)}$ *of the uncatalysed mercury exchanges of the alkylmercuric bromide with mercuric bromide in ethanol,* (b) *the catalytic constants,* κ_1 *and* κ_2 *of the one- and two-anion catalyses of these exchanges by bromide ion,* (c) *the dimensionless measures,* $\kappa_1/k_2^{(1)}$ *and* $a\kappa_2/k_2^{(1)}$, *of the strengths of the one- and two-anion catalyses, and* (d) *the dimensionless measure,* $a\kappa_2/\kappa_1$, *of the relative strengths of the two catalyses.*

[For methyl at 100°, a had various values; for methyl at 60°, a = 0·095; for neopentyl at 100°, a = 0·092M. Units: $k_2^{(1)}$ and κ_1 in mole^{-1} l. sec.$^{-1}$ and κ_2 in mole^{-2} l.^{2} sec.$^{-1}$.]

R	$10^5k_2^{(1)}$ 100°	$10^5k_2^{(1)}$ 60°	$10^5\kappa_1$ 100°	$10^5\kappa_1$ 60°	$10^5\kappa_2$ 100°	$10^5\kappa_2$ 60°	$\frac{\kappa_1}{k_2^{(1)}}$	$\frac{a\kappa_2}{k_2^{(1)}}$	$\frac{a\kappa_2}{\kappa_1}$
Methyl	12·8	0·49	—	35	—	500	71	97	1·26
Neopentyl	4·2	—	26·4	—	122	—	6·3	2·7	0·425
$\frac{\text{Neopentyl}}{\text{Methyl}}$	0·33	—	—	—	—	—	0·089	0·028	0·31

When, having these data for different alkyl groups, we put the alkyl groups under comparison, whilst it is important that rate constants and catalytic constants should be compared only at common temperatures, it is not so important that the dimensionless ratios should, because they do not contain the time dimension. In Table 3 we compare the methyl and neopentyl groups with respect to their uncatalysed rate-constants at a common temperature for one-alkyl mercury-exchange, and also with respect to the strengths, and relative strengths, of the one-anion and two-anion catalysis of this exchange by bromide ion.

Proceeding now to a discussion of Tables 2 and 3, we can summarise Table 2: the uncatalysed S_E2 rate of one-alkyl mercury-exchange for methyl as the alkyl group, is cut down by factors between 2 and 3 for the ethyl and neopentyl groups, and by a factor of 17 for the s-butyl group. Thus, primary alkyl groups, including neopentyl, can exert only a slight steric effect, whilst the secondary group seems to exert a moderate one.

That this is the kind of pattern of steric effects to be expected from our picture of the configuration-retaining transition state in S_E2 substitutions is shown by the following figures, though they cannot be given more than an illustrative significance, because of the imperfections in our knowledge of the parameters involved.

We first define a " reaction plane," through C_α and the two mercury atoms, and a " median line " on it, through C_α and symmetrically between the mercury atoms. Next we define a " symmetry plane," cutting the reaction plane perpendicularly along the median line. Then the most sterically favourable position for the ethyl group will put C_β on the symmetry plane. The most favourable conformation for the neopentyl group will also put its C_β there, and will place one C_γ in that position, of the possible two in that plane, which is nearer the mercury atoms. The most favourable conformation for the isopropyl group will be such that its secondary hydrogen atom lies in the reaction plane. The s-butyl group can be assumed to have the positions of its C_β atoms similarly determined, its C_γ being then arranged remotely from the mercury atoms. We take the C_α–Hg distance as 2·3 Å (*i.e.*, rather longer than the normal bond length) and the Hg–Hg separation as 3·0 Å (*i.e.*, rather greater than of nearest neighbours in mercury metal). We assume normal dimensions in the alkyl groups. Then it can be computed that, in the ethyl transition-state, the only non-bonding compressions are two equal ones between the β-Me group and the two mercury atoms, each C_β–Hg distance being 3·08 Å. Similarly, in the neopentyl transition state, the only compressions are two equal ones between the symmetrically placed γ-Me group and the two mercury atoms, each C_γ–Hg distance being 3·05 Å. Again, in the isopropyl transition state the only compressions will be two equal ones between the two β-Me groups and one of the mercury atoms, each C_β–Hg distance being 2·70 Å. We suppose that very similar compressions will apply to the β-Me and β-CH_2 groups in the s-butyl transition state.

It is difficult to arrive at a good figure for the methyl–mercury touching distance. But bearing in mind that the only two 6-quantum electrons of mercury are in the bonds, so that it is the core-size that most matters, we have taken the centre-to-centre distance as 3·35 Å. The calculated transition-state compressions are then as follows:

ethyl	2 of 0·27 Å
neopentyl	2 ,, 0·30 Å
isopropyl (s-butyl probably similar)	2 ,, 0·66 Å

Though it is convenient to treat the methyl groups as a whole, the compressions are really with hydrogen atoms, and experience of calculating compression energies between hydrogen and heavy atoms allows us to say at once that the energy resulting from such a calculated compression as 0·3 Å would be of the order of 0·1 kcal./mole, whilst for one of 0·7 Å it would be of the order of 1 kcal./mole. Whilst allowances for entropic effects have to be made, these are clearly the sort of energy figures that could be regarded as consistent with the rate pattern disclosed in Table 2.

The short summary of Table 3 is that, whilst, on changing from methyl to neopentyl as the alkyl group, the S_E2 rate of exchange is cut down by a factor of 3, the S_Ei rates under one-anion and two-anion catalysis are reduced by the respective factors 3 × 11 and 3 × 36, *i.e.*, by extra factors of 11 and 36. Evidently the change of mechanism has brought in extra steric retardation, and more of it into two-anion than into one-anion catalysis.

Qualitatively, these effects should be expected. For whereas in the open S_E2 transition state, all bromine atoms lie in the reaction plane, and hence well out of the way of primary alkyl groups, including the neopentyl group, in the cyclic S_Ei transition states *gem*-Br_2-pairs occur, which are out-of-plane, one such pair in the one-anion transition state, and two in the two-anion (cf. formulæ I and II of Part V [7]); and one bromine atom of each such pair must lie on that side of the reaction plane which contains the bulk of all primary alkyl groups, and in particular, the γ-Me of the neopentyl group. We must obviously expect steric compression between this γ-Me and the nearer bromine atom of each *gem*-Br_2-pair in the S_Ei transition states.

If, for illustration, we take the normal $HgBr_2$ and $HgBr_3^-$ bond-lengths as 2·4 and 2·7 Å, respectively, adopting the latter length for the *gem*-Br_2-pairs, and supposing that the bonds of quadrico-ordinate mercury in the bridged transition states are tetrahedrally arranged, an assumption consistent with reasonable bridge-lengths, then we can calculate that the shortest C_γ–Br distances in the neopentyl one-anion and two-anion transition states are equal to 3·20 Å. There will be one such distance in the one-anion and two in the two-anion transition states. Though the resulting extra compressions in these S_Ei transition states will be between hydrogen and bromine, we may again treat the Me-group as a whole, taking the centre-to-centre CH_3–Br touching distance as 3·95 Å. The extra compressions then become

S_Ei (one-anion catalysis)	1 of 0·75 Å
S_Ei (two-anion catalysis)	2 ,, 0·75 Å

These compressions imply energies in the neighbourhood of 1—2 kcal./mole, which is consistent in order of magnitude with the extra retardations suffered by the S_Ei mechanisms, as compared with the S_E2 mechanism, according to the results in Table 3.

We leave untouched the matter of polar effects of alkyl groups in these reactions. We started by expecting them to be small, because the retention of configuration in all S_E2 mercury exchanges shows that the carbon–metal bond does not become much more ionic in the transition state than it is in the initial state; [3] *i.e.*, there would be little or no polar demand on the alkyl group from the reaction centre. It does seem that polar effects are indeed small enough to be very difficult to distinguish at all in the present results.

EXPERIMENTAL

Materials.—Ethylmercuric bromide was prepared in the usual way from ethylmagnesium bromide and mercuric bromide. Crystallised from ethanol it formed leaflets, m. p. 188—190° (uncorr.) [lit., 198° (corr.)]. Neopentyl chloride, a kind gift from Dr. E. S. Swinbourne, was converted by way of its Grignard derivative in 70% yield, into *neopentylmercuric bromide,*

TABLE 4. *Run* 149: $[HgBr_2] = 0{\cdot}0910$, $[neo\text{-}C_5H_{11}HgBr] = 0{\cdot}0919$, $[LiBr] = 0{\cdot}188$M. Initially the ^{203}Hg was wholly in the $HgBr_2$. It was measured in timed samples of separated $C_5H_{11}HgBr$. Concentrations and rate-constants are corrected for the thermal volume-change undergone by the solvent, ethanol, on being taken to the reaction temperature, 100·3°.

t (min.)	Count $C_5H_{11}HgBr$ [min.$^{-1}$ (corr.)]	% Reaction $= 100\,(1 - f)$	$10^5k_{2c}{}^{(1)}$ (corr.)
0	28·2	3·9	—
20	65·8	12·4	43·0
40	76·8	20·6	44·1
70	152·9	30·0	38·5
105	169·5	40·3	41·4
			41·8

which crystallised from ethanol in needles, m. p. 95—96° (Found: C, 17·1; H, 3·5; Br, 23·4. $C_5H_{11}BrHg$ requires C, 17·1; H, 3·2; Br, 22·7%).

Kinetics.—The methods of starting and stopping runs, of separating products from timed samples for radiometric examination, and the method of examination, were all as described in Part IV [6] for the exchange reaction of methylmercuric bromide with mercuric bromide. The conditions of the runs, and the rate-constants obtained, were as noted in Table 1. A specimen run is recorded in Table 4.

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