27. *Liquid-phase Reactions at High Pressures. Part XIII.*[1] *Structural Effects in the Acceleration of Menschutkin Reactions by Pressure.*

By A. P. Harris and K. E. Weale.

The rates of a series of Menschutkin reactions have been measured at pressures up to several thousand atmospheres. The extent to which the reactions are accelerated by pressure depends on the molecular structure of the reactants and on the solvent. The theory that the structural variations arise directly from steric interference between non-bonded atoms and groups in the transition state is not supported by our results. The variations are attributed, instead, to differences in the degree and type of solvation of the transition states, which are imposed by the configurations of the reacting molecules.

The rates of reaction between tertiary amines and organic halides to form quaternary salts are substantially increased by pressures of a few thousand atmospheres. The effect has been studied several times but agreement has not been reached on the relative importance of the various factors. Variations in the structures of the reactants alter the amount of the acceleration considerably, but little systematic work has been available on this point. We have measured the effect of pressure on the rates of a series of Menschutkin reactions in order to examine in more detail the influence of structural changes and to obtain more information about the transition states of the reactions.

Experimental

Apparatus and Procedure.—The high-pressure equipment used was similar to that described in an earlier paper,[2] and the reactants were contained in a glass tube with a mercury seal. The same general procedure and method of analysis were used. Two 2 ml. portions were titrated after each run, and the determinations always agreed within 1%. The runs at 1 atm. were carried out in sealed ampoules of amber glass.

Materials.—*Methanol.* "AnalaR" methanol was purified by the Lund–Bjerrum method, as in previous work [2] (b. p. 64·7°).

Alkyl iodides. These were purified by the method previously used for methyl iodide and stored over triply distilled mercury in a desiccator in the dark. The b. p.s were methyl 42·8°, ethyl 72·2°, n-butyl 131°, isopropyl 89·5°.

Dimethylaniline. "AnalaR" dimethylaniline was refluxed with acetic anhydride for 24 hr. and fractionated. The middle fraction was dried (KOH), re-fractionated under reduced pressure (b. p. 95°/30 mm.) and stored under a vacuum.

NN-*Dimethylbenzylamine.* Purified as above, this had b. p. 181°.

Quinoline. Distilled (b. p. 238°), dried (KOH), and fractionated under reduced pressure (b. p. 110°/14 mm.).

Tri-n-propylamine. The "AnalaR" product, dried (KOH) and fractionated, had b. p. 156·5°.

Nitrobenzene. "AnalaR" nitrobenzene, distilled, dried (Na_2SO_4), and fractionated, had b. p. 210·8°.

Results.—Measurements were made on seven reactions in methanol as solvent and one in nitrobenzene. The reactions of s- and t-butyl iodide with dimethylaniline in methanol were also examined, but satisfactory rate constants could not be obtained because of olefin formation.

The initial concentration of each reactant was 0·1M except for the reactions of *NN*-dimethylbenzylamine and tri-n-propylamine with ethyl iodide in which they were 0·05M. In two cases the second-order rate constants increased as the reaction proceeded, a phenomenon reported by Laidler and Hinshelwood [3] and attributed to autocatalysis by the quaternary salt. In the reaction between dimethylaniline and n-butyl iodide the increase was about 20% at 50%

---

[1] Part XII, Kilroe and Weale, *J.*, 1960, 3849.

[2] Weale, *J.*, 1954, 2959.

[3] Laidler and Hinshelwood, *J.*, 1938, 858.

TABLE 1. *Second-order rate constants* (*k in l. mole*$^{-1}$ *sec.*$^{-1}$).

P (atm.)	Temp.	10^5k	A (10^6 sec.$^{-1}$)	E (kcal. mole^{-1})
	Dimethylaniline + MeI			
1	25·0°	5·62	10·5	15·4
,,	30·0	8·40		
,,	35·0	12·6		
,,	40·0	19·1		
1500	52·5	154		
2875	17·5	20·5	87·1	15·5
,,	18·7	22·9		
,,	19·6	24·7		
,,	22·3	31·8		
,,	25·3	41·0		
	Dimethylaniline + EtI			
1	38·9	1·00	8·67	17·1
,,	42·5	1·37		
,,	47·3	2·07		
,,	52·5	3·18		
1500	52·5	12·0		
2875	33·8	5·57	98·2	17·2
,,	38·9	8·79		
,,	47·3	17·8		
,,	52·5	27·7		
4925	33·8	11·7	155	17·0
,,	38·9	18·6		
,,	47·3	37·5		
,,	52·5	57·6		
	Dimethylaniline + Bu^{n}I	(10^6k)		
1	47·1	4·66	10·8	18·1
,,	53·0	7·78		
,,	58·0	11·9		
,,	63·5	18·6		
1500	52·5	28·5		
2875	39·0	20·6	99·5	18·1
,,	43·0	29·5		
,,	47·5	43·8		
,,	57·6	106		
	Dimethylaniline + Pr^{i}I			
1	45·0	6·26	650	20·4
,,	50·0	10·3		
,,	55·0	16·7		
,,	57·8	21·7		
1500	52·5	72·7		
2875	45·0	90·4	7360	20·25
,,	50·0	147		
,,	55·0	240		
,,	58·5	330		
	Quinoline + EtI			
1	42·6°	4·88	940	20·6
,,	47·6	8·28		
,,	52·5	13·3		
,,	57·5	20·0		
1500	52·5	32·6		
2875	42·6	21·3	11,000	21·3
,,	47·6	35·6		
,,	52·5	58·1		
,,	57·5	91·2		
	Dimethylbenzylamine + EtI	(10^4k)		
1	42·5	1·33	182	17·5
,,	47·5	2·05		
,,	52·5	3·10		
,,	57·5	4·69		
1500	52·5	8·56		
2875	42·6	7·38	250	16·7
,,	47·6	11·3		
,,	52·3	16·6		
,,	57·5	24·0		
	Tri-n-propylamine + EtI	(10^5k)		
1	42·5	1·68	725	19·7
,,	47·7	2·88		
,,	52·5	4·47		
,,	57·5	6·96		
1500	42·8	5·02	2500	19·8
,,	47·5	8·55		
,,	52·5	14·0		
,,	57·5	20·5		
2875	42·5	11·4	1620	18·99
,,	47·5	18·8		
,	52·5	28·2		
,,	57·5	46·0		
	Dimethylaniline + EtI (in nitrobenzene)			
1	47·5	1·63	0·0128	13·05
	52·5	2·24		
	57·5	3·08		
1500	52·5	6·15		
2300	,,	9·51		
2600	,,	11·3		

conversion, and it was somewhat larger for the reaction between dimethylaniline and isopropyl iodide. In both cases the rate constant was found to be a linear function of the percent conversion, and satisfactory values were obtained by extrapolation to zero conversion.

The reaction in nitrobenzene reached equilibrium at about 60% conversion and this was taken into account in calculating the rate constants.

The rate constants were corrected for the compressibility of the solvent. The most accurate data available for methanol are Gibson's [4] which were determined at 25° and up to 1000 atm. Compressions at higher pressures and other temperatures were calculated by the procedure of Bett, Newitt, and Weale [5] with Larionov's sound-velocity data.[6] At 1 atm. and 25° the agreement between Gibson's measurements and Larionov's is within 0·01%. Gibson and Loeffler's

---

[4] Gibson, *J. Amer. Chem. Soc.*, 1935, **57**, 1551.

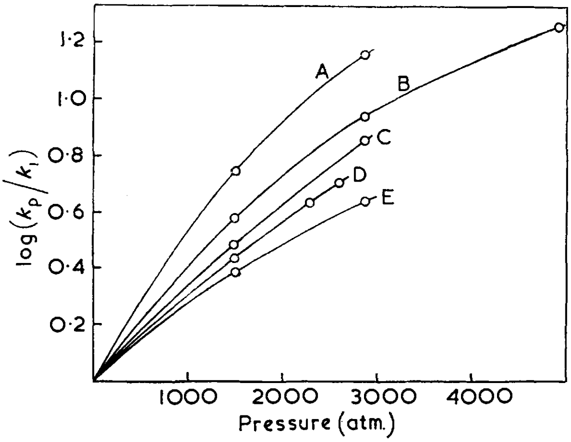
[5] Bett, Newitt, and Weale, *Brit. J. Appl. Phys.*, 1954, **5**, 243.

[6] Larionov, *Zhur. fiz. Khim.*, 1953, **27**, 1002.

compression data for nitrobenzene [7] can be accurately interpolated at different temperatures, and the correction for this solvent was calculated from the constants obtained by them for the Tait equation. The corrected rate constants are given in Table 1, together with rounded-off Arrhenius parameters. The rate constants for the reaction between dimethylaniline and methyl iodide at 1 atm. agree well with values determined by Evans, Watson, and Williams.[8] The constants for the reaction between dimethylaniline and ethyl iodide in methanol at 1 atm. are in reasonable agreement with those of Brown and Fried,[9] but the constant at 25° measured by Hamann and Teplitzky [10] appears slightly too high.

DISCUSSION

General.—All the reactions are substantially accelerated by pressure. At 52·5° the ratio k_{2875}/k_1 varies from 14·4 ($NPhMe_2 + Pr^nI$) to 4·4 (quinoline + EtI). The rate constants at 1 atm. vary with the nature of the reaction by a factor of about 50 and there appears to be no correlation between them and the pressure effect. In the reaction between dimethylaniline and the four iodides acceleration with pressure increases in the order Me < Et $\approx$ Bu < Pr^i, confirming Perrin and Williams's [11] observation that it is greater for the more complex reactants.



Effect of pressure on log k_p/k_1.
Reactions of dimethylaniline with (A) *isopropyl iodide,* (B) *ethyl iodide, and* (C) *methyl iodide, all in methanol, and* (D) *with ethyl iodide in nitrobenzene; also* (E) *of quinoline with ethyl iodide.*

Interpretations of the Pressure Effect.—The variation of rate constant with pressure is given by the equation

$$(\partial \ln k/\partial P)_T = -\Delta V^*/\boldsymbol{R}T$$

where ΔV^* is the molar volume change when the reactants are converted into the transition state. ΔV^* has negative values for reactions which are accelerated by pressure. The curvature of the plots of log k_p/k_1 against pressure obtained from our experimental results (see Figure) shows that the changes of volume become less and that the rate constants increase more and more slowly at higher pressures. Evans and Polanyi [12] pointed out that ΔV^* includes a term representing the different degrees of solvation of reactants and transition state. Eyring and his co-workers [13] neglected this term in calculating ΔV^* for two Menschutkin reactions, but evidence has accumulated [14] that in ion-producing

---

[7] Gibson and Loeffler, *J. Amer. Chem. Soc.*, 1939, **61**, 2515.
[8] Evans, Watson, and Williams, *J.*, 1939, 1345, 1348.
[9] Brown and Fried, *J. Amer. Chem. Soc.*, 1943, **65**, 1841.
[10] Hamann and Teplitzky, *Discuss. Faraday Soc.*, 1956, **22**, 114.
[11] Perrin and Williams, *Proc. Roy. Soc.*, 1937, *A*, **159**, 162.
[12] Evans and Polanyi, *Trans. Faraday Soc.*, 1935, **31**, 875; 1936, **32**, 1333.
[13] Glasstone, Laidler, and Eyring, " The Theory of Rate Processes," McGraw-Hill, New York, 1941, p. 472.
[14] Hamann, " Physico-Chemical Effects of Pressure," Butterworths, London, 1957.

reactions the greater part of ΔV^* is due to the volume changes accompanying increased solvation. It has frequently been assumed that in Menschutkin reactions the transition state is solvated to about the same extent as the product ions, but Gonikberg and Povkh [15] have advanced a different view, based on the effect of pressure on the reaction between ethyl iodide and pyridine in acetone. They estimated ΔV^* at 1 atm. and 30° to be -20 c.c./mole, whereas ΔV_s, the total volume change for the reaction in solution, is -54 c.c./mole in acetone.[16] They also measured the molar volume of the pure (unsolvated) liquid product and calculated the total volume change ΔV_0 in the absence of solvent to be $-20{\cdot}5$ c.c./mole at 30°. Their conclusion that the transition state is not solvated as completely as the product ions has been criticised by Hamann,[17] chiefly on the ground that ΔV^* at 1 atm. cannot be estimated accurately from a curve of the type shown in the Figure if there are no experimental points below 3000 atm. To meet this objection Gonikberg and Zhulin [18] measured the rate of the same reaction in acetone at 40° and at 1, 250, 500, 750, 1000, and 3000 atm. The new value obtained for ΔV^* at 1 atm. is -30 ± 1 c.c./mole, and ΔV_s at 20° was redetermined and found to vary between -58 and -54 c.c./mole as the reaction proceeded. The improved measurements still indicate that the transition state is less solvated than the quaternary salt and while it is possible that the graph of log k_p/k_1 against pressure shows increased curvature in the range 1—250 atm. it is probable that there is a significant difference between ΔV^* and ΔV_s. This is not surprising as the ionic charges in the transition state may not be fully developed and the ions have not separated sufficiently to permit formation of a complete solvent shell. Gonikberg and Zhulin's experimental points below 1000 atm. can be well predicted from a smooth curve of minimum curvature drawn through the points at 3000 and 1000 atm. and the origin. Therefore curves of this type have been drawn through the experimental points of the Figure and used to estimate the values of ΔV^* at 1 atm. in Table 2, which are discussed below. For the reaction between ethyl iodide and tri-n-propylamine ΔV^* is -24 c.c./mole and in this case we have determined ΔV_s at 19·6°, by a dilatometric method, to be $-56{\cdot}6$ c.c. mole, so that a similar difference between the two quantities occurs in methanol.

As supporting evidence that the transition state in Menschutkin reactions is incompletely solvated the differences between entropies of activation ΔS^*, and the overall entropy change, ΔS, have been cited. Syrkin and Gubareva [19] give results which show that $-\Delta S$ is usually larger that $-\Delta S^*$ by 5 to 15 e.u., and the difference is greater if the entropy of activation is corrected for the " cratic " term (see p. 151). However, in the reaction between dimethyl-*o*-toluidine and methyl iodide in acetone [20] ΔS^* and ΔS at 44° are -40 (uncorrected) and $-32{\cdot}1$ respectively. This anomaly can be attributed to steric strain in the activated complex, and to hindered solvation of the charged nitrogen atom.

The only study of a reverse Menschutkin reaction at high pressure [21] yields ΔV^* $+3{\cdot}3$ c.c./mole, and this low value has been held to demonstrate close similarity between the quaternary salt and the transition state. However ΔV^* was calculated from the ratio k_{3000}/k_1, and the first-order rate constant depended on the initial concentration so that the significance of the result is doubtful.

ΔV^*, *the Volume of Activation.*—Values of ΔV^* at 1 atm. for the reactions of Table 1 are given in Table 2, together with those for other Menschutkin reactions for which rate constants at 1000 atm. or below are available. ΔV^* is obtainable from the curves, drawn in the way described, with an accuracy of 1—2 c.c./mole. The largest $-\Delta V^*$ is 47 c.c./mole

---

[15] Gonikberg and Povkh, *Zhur. fiz. Khim.*, 1949, **23**, 383.
[16] Perrin, *Trans. Faraday Soc.*, 1938, **34**, 150.
[17] Hamann, *Austral. J. Chem.*, 1956, **9**, 533.
[18] Gonikberg and Zhulin, *Austral. J. Chem.*, 1958, **11**, 285.
[19] Syrkin and Gubareva, *Acta Physicochim. U.R.S.S.*, 1938, **8**, 236.
[20] Weale, *Discuss. Faraday Soc.*, 1956, **22**, 122.
[21] Williams, Perrin, and Gibson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 684.

for the reaction between dimethylaniline and isopropyl iodide (Brower [22] has reported volume changes up to —64 c.c./mole for the reactions of bromonaphthalenes and bromoquinolines with an excess of piperidine at 150°). ΔV^* decreases with rising pressure and at 2500 atm. is usually only about half its initial value. The decrease is related to the increased initial density of the system, which brings the initial state closer in volume to the less compressible transition state, and it is significant that the variation of ΔV^* with the specific volume of the solvent is approximately linear in the experimental pressure range.

TABLE 2. *Volumes and entropies of activation at* 1 *atm.*

			$-\Delta V^*$ (c.c./mole)		$-\Delta S^*$
Reaction	Solvent	Temp.	exp.	G. & K.	(e.u.)
$NPhMe_2$ + MeI	MeOH	52·5°	26	15	30·4
$NPhMe_2$ + EtI	,,	,,	34	25	29·0
$NPhMe_2$ + EtI	$PhNO_2$	,,	20	25	41·9
$NPhMe_2$ + n-BuI	MeOH	,,	34	25	28·5
$NPhMe_2$ + i-PrI	,,	,,	47	40	20·4
Quinoline + EtI	,,	,,	20	13	19·7
$Ph·CH_2·NMe_2$ + EtI	,,	,,	27	13	22·9
NPr^n_3 + EtI	,,	,,	24	13	20·2
o-$C_6H_4Me·NMe_2$ + MeI (2)	,,	50·0	24	18	18·9
o-$C_6H_4Me·NMe_2$ + MeI (20)	$COMe_2$	,,	—	—	40·0
Pyridine + EtI (16, 18)	,,	40·0	30	10	35·3

While our work was in progress Gonikberg and Kitaigorodskii [23] published calculations of ΔV^* for some Menschutkin reactions which take account only of volume changes considered to occur as a result of the close approach of the reactant molecules, solvation effects being ignored. An N–C distance of 1·5 Å in the transition state is assumed and the volume decrease due to the approach of these two atoms is calculated as the volume of interpenetration of two spheres of radii 1·6 Å and 1·8 Å, which corresponds to 4·7 c.c./mole. The alkyl groups of the iodide are assumed to occupy a plane perpendicular to the N–C axis and the alkyl groups of the amine to be disposed pyramidally at angles of 108°. If the amine contains a phenyl group the N–phenyl bond is parallel to the plane of the alkyl groups, and if it contains a pyridine ring this is perpendicular to the plane. Some non-bonded atoms or groups are found to approach closer than the sum of their van der Waals radii and each of these " volumes of compression " is also calculated from the volume of interpenetration of the spheres. Gonikberg and Kitaigorodskii take ΔV^* to be the sum of the individual volumes of compression. In Table 2 we include values of ΔV^* calculated by this method (but with a correction of +4 c.c./mole to allow for partial separation of the iodine atom).

The " G. & K." volumes vary in the same way and to a similar extent as ΔV^* for most of the reactions in methanol but, if the calculations are even approximately correct, only a small part of ΔV^* arises from solvation, and the difference between the solvation of the transition state and the quaternary salt is considerably greater than that indicated by the difference between ΔV^* and ΔV_s. This seems an improbable conclusion, and the theory also does not account for the large difference in ΔV^* for the same reaction ($NPhMe_2$ + EtI) in methanol and in nitrobenzene. A further objection is that if the main effect of pressure is to overcome repulsions between non-bonded atoms arising in the transition state it should reduce the activation energy considerably (which is generally not observed) instead of changing principally the entropy of activation.

Steric repulsions between non-bonded atoms certainly occur in reactions involving the more complicated amines and iodides, and contribute, together with electron-displacement and solvation, to the differences in activation energies among Menschutkin reactions. In some cases steric hindrance is responsible for the absence of any appreciable reaction. We did not observe formation of a quaternary salt from *NN*-dimethyl-*o*-toluidine and

---

[22] Brower, *J. Amer. Chem. Soc.*, 1958, **80**, 2105.

[23] Gonikberg and Kitaigorodskii, *Proc. Acad. Sci. U.S.S.R., Chem. Section*, 1958, **122**, 665.

isopropyl iodide, and neither 2,5,*N*,*N*-tetramethyl- nor *o*-t-butyl-*NN*-dimethyl-aniline reacts with methyl iodide.[24] However, these non-bonded interactions are unlikely to give rise to the additive volume changes envisaged by Gonikberg and Kitaigorodskii. The variations of ΔV^* with molecular structure must be ascribed to other causes, and we consider that they reflect the influence of the structure and spatial distribution of substituent groups on the solvation of the transition state. This explanation is considered in greater detail in the following sections.

ΔS^*, *the Entropy of Activation.*—The entropies of activation for the reactions at 1 atm., calculated from the well-known equation:

$$k = (e\boldsymbol{k}T/\boldsymbol{h}) \exp (\Delta S^*/\boldsymbol{R}) \exp (-E/\boldsymbol{R}T)$$

are given in Table 2. Although it has been suggested [25] that a " cratic " correction may be made to ΔS^* to allow for a change in the number of moles of solute species we prefer to use the experimental values for comparative purposes. In methanol these vary by a factor of about 1·6, and in the reactions between dimethylaniline and the four alkyl iodides ΔS^* varies inversely with ΔV^*, so that the largest volume decrease corresponds to the lowest entropy change. These differences, which determine the effect of pressure on the rate constants, are attributed to differences in the solvation of the transition state. A model of the *NNN*-trimethylanilinium iodide transition state show that there are four exposed segments of the nitrogen atom to which a methanol-oxygen atom can approach closely, *i.e.*, to within about 1 Å. The incipient positive ion of this transition state can therefore be solvated by four fairly tightly bound solvent molecules, and it is reasonable to suppose that this situation will correspond to a rather high entropy of activation and to a considerable, but not exceptionally large, volume of activation. In the *N*-ethyl-*NN*-dimethyl transition state only two of the segmental faces of the nitrogen atom are as accessible as before. Development of the positive charge may therefore demand the binding of a greater number of more distant methanol molecules. This difference is considered to result in an increased volume change, because of the greater volume of the solvation shell, but in a smaller entropy decrease. Finally, in the *N*-isopropyl-*NN*-dimethyl transition state only one segment of the nitrogen atom remains easily accessible to a methanol molecule. This is expected to result in weak binding of a still larger number of solvent molecules, and this instance corresponds to the greatest ΔV^* and the lowest ΔS^*. Laidler [26] has suggested that weaker binding will be associated with larger values of the temperature coefficient of ΔV^* which can be evaluated from the entropies of activation since $\delta \Delta V^*/\delta T = -\delta \Delta S^*/\delta P$. In the reaction of dimethylaniline with methyl iodide the entropy change, $-\Delta S^*$, decreases by 6 e.u. between 1 and 2875 atm., while for the reactions with ethyl and butyl iodide the change is about 11 e.u., which supports this interpretation. For reaction with isopropyl iodide the difference $\Delta S^*_{2875} - \Delta S^*_1$ is, however, 4·8 e.u. Probably the suggested correlation is inapplicable when there are large variations between the binding of different solvent molecules.

In the reactions of quinoline, benzyldimethylamine, and tri-n-propylamine with ethyl iodide fewer than four methanol molecules can approach closely the nitrogen atom of the transition state. The entropy of activation is less than for dimethylaniline but the values of ΔV^* are very similar. No detailed comparison is possible as there may be appreciable differences in the interaction between methanol and the unactivated amines in the initial state.

The Effect of the Solvent on ΔV^* *and* ΔS^*.—There is not much systematic information about the variation of the pressure effect for the same reaction in different solvents. The reaction between pyridine and ethyl iodide is accelerated by increase of pressure almost equally [27] in acetone and in hexane at 2980 atm., but the acceleration of the reaction

---

[24] Brown and Grayson, *J. Amer. Chem. Soc.*, 1953, **75**, 20; Brown and Nelson, *ibid.*, p. 24.

[25] Burris and Laidler, *Trans. Faraday Soc.*, 1955, **51**, 1497.

[26] Laidler, *Discuss. Faraday Soc.*, 1956, **22**, 88.

[27] Gibson, Fawcett, and Perrin, *Proc. Roy. Soc.*, 1935, *A*, **150**, 233.

between methyl iodide and *NN*-dimethyl-*o*-toluidine is about 30% greater in acetone than in methanol. An apparently general difference between acetone and methanol is that the effect of pressure on Menschutkin reactions in acetone is to increase both the A and the E factor, while in methanol parameter A is increased but E is usually little affected or is reduced.

There is a large difference between the pressure effect on the reaction of dimethylaniline and ethyl iodide in methanol and in nitrobenzene, which is one of the arguments against Gonikberg and Kitaigorodskii's hypothesis. ΔV^* is much smaller in nitrobenzene and its decrease with increasing pressure is less marked. The low value of ΔV^* is no doubt associated with the pronounced interaction between nitrobenzene and aromatic amines in solution,[28] and it is also probable that, because of their high polarity, fewer solvating molecules are required to reduce the free energy of activation. The smaller variation of ΔV^* may be attributable to the reduced compressibility of nitrobenzene compared with methanol.

The structures of methanol, acetone and nitrobenzene do not prevent close approach of the solvent-oxygen atom to the transition state nitrogen atom, but in other cases the solvent structure may increase the hindrance to solvation. This perhaps occurs to some extent in the reactions studied by Brower [22] with excess of piperidine as solvent. The bulkiness of transition-state and solvent configurations results in a larger, less strongly bound solvation shell, and a high volume of activation.

The authors are indebted to Mr. J. M. Stewart for data on the reaction in nitrobenzene, and one of them (A. P. H.) thanks the Edwards Trust and the C.S.I.R. of South Africa for financial assistance.

DEPARTMENT OF CHEMICAL ENGINEERING AND CHEMICAL TECHNOLOGY,
IMPERIAL COLLEGE, S. KENSINGTON,
LONDON, S.W.7.
[*Received, July* 18*th*, 1960.]

---

[28] Gibson and Loeffler, *J. Amer. Chem. Soc.*, 1940, **62**, 1324.