The Alkyl Halide Catalysed Pseudomolecular Rearrangement of Imidates to Amides: an Explanation for the Ambident Nucleophilic Properties of Neutral Amides

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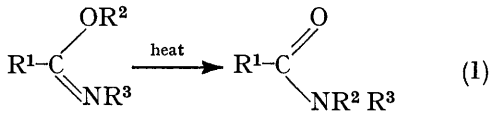
Kinetic studies are reported for the pseudomolecular rearrangement of *N*-methylbenzimidates to tertiary amides in nitrobenzene at 138°. The reaction is readily catalysed by alkyl halides (rate = k_2[*N*-methylbenzimidate][alkyl halide]) and is shown to proceed by a two-step mechanism involving a benzimidonium ion intermediate. Formation of this intermediate by an S_N2 reaction between substrate and alkyl halide is rate limiting. Quantitative yields of tertiary amide are usually obtained but, for the isopropyl halide catalysed conversion of isopropyl *N*-methylbenzimidates, a competitive *E*2 elimination gives *ca.* 40% propene and *N*-methylbenzamide. These results are discussed in relation to the ambident nucleophilic properties of neutral amides. They suggest that alkylation occurs more rapidly at the amide oxygen atom to give an imidate (kinetic product) which then rearranges in the presence of alkyl halide to the *N*-substituted amide (thermodynamic product). It is shown that silver salts inhibit the imidate–amide rearrangement by precipitating nucleophilic anions. This partly explains the preferential *O*-alkylation of amides in the presence of silver salts.

DESPITE its early discovery,[1] the rearrangement of imidates to substituted amides [equation (1)] has never been thoroughly examined. Information is most com-



(1)

plete for the thermal reaction with aryl imidates (Chapman rearrangement), which was shown by Wiberg and his colleagues [2] (and later confirmed by Wheeler *et al.*[3]) to proceed by an intramolecular mechanism. Likewise, there is good evidence [3,4] that allyl imidates rearrange readily *via* a [3,3] sigmatropic pathway similar to the Claisen reaction. The thermal rearrangement is less favourable for alkyl imidates, which usually require very high reaction temperatures (*ca.* 300°) yet give low yields of substituted amide.[5]

For compounds bearing branched chain R^2 substituents, Lander and Jewson [6] reported that dealkylation rather than rearrangement occurred on heating, and recent work [7] has confirmed this finding. It has also been known for a long time, however, that various alkylating agents [8] as well as BF_3 [9] and even H_2SO_4 [10] promote the rearrangement of alkyl imidates, although quantitative information is lacking. For example, Benson and Cairns [5b] found that conversion of methyl caprolactim to *N*-methylcaprolactam required temperatures of only 60° in the presence of dimethyl sulphate,

[1] W. Wislicenus and M. Goldschmidt, *Ber.*, 1900, **33**, 1470.
[2] K. B. Wiberg and B. I. Rowland, *J. Amer. Chem. Soc.*, 1955, **77**, 2205.
[3] O. H. Wheeler, F. Roman, and O. Rosado, *J. Org. Chem.*, 1969, **34**, 966.
[4] O. Mumm and F. Moller, *Ber.*, 1937, **70**, 2214.
[5] C. G. McCarty and L. A. Garner, 'The Chemistry of Amidines and Imidates,' ed. S. Patai, Wiley, London, 1975, p. 189.
[6] G. D. Lander and F. T. Jewson, *J. Chem. Soc.*, 1903, **83**, 766.
[7] N. Marullo, C. Smith, and J. Terapame, *Tetrahedron Letters*, 1966, 6279; J. W. Schulenberg and S. Archer, *Org. Reactions*, 1965, **14**, 1.
[8] (*a*) G. Lander, *J. Chem. Soc.*, 1903, **83**, 406, 419; (*b*) R. E. Benson and T. L. Cairns, *J. Amer. Chem. Soc.*, 1947, **70**, 2115; (*c*) A. E. Arbuzov and V. E. Shishkin, *Doklady Acad. Nauk S.S.S.R.*, 1961, **141**, 349; (*d*) A. E. Arbuzov and V. E. Shishkin, *J. Gen. Chem. U.S.S.R.*, 1964, **34**, 3628; (*e*) P. Beak, J. Bonham, and J. T. Lee, *J. Amer. Chem. Soc.*, 1968, **90**, 1569.
[9] F. Cramer and N. Hennrich, *Ber.*, 1961, **94**, 976.
[10] R. Roberts and P. Vogt, *J. Amer. Chem. Soc.*, 1956, **78**, 4778.

and, following Lander,[5a] Arbuzov and Shishkin [5c,d] demonstrated alkyl halide catalysed ' rearrangement ' of alkyl benzimidates. The Russian workers [5c,d] suggested that alkylimidonium ion intermediates were involved, and these entities have been isolated.[5d,e]

Our interest in the kinetics and mechanism of the imidate–amide rearrangement stems from its relevance to recent explanations [11] for the nucleophilic properties of the amide function, as discussed below. Some of the results have been reported as a communication.[12]

EXPERIMENTAL

Substrates and Reagents.—Alkyl *N*-methylbenzimidates were prepared from *N*-methylbenzimidoyl chloride [13] and the appropriate alcohol. A solution of the alcohol (0.06 mol) in very dry ether (10 ml) was added dropwise with stirring to *N*-methylbenzimidoyl chloride (0.06 mol) also in very dry ether (25 ml) at 0 °C. After stirring for a further 2 h the solution was kept overnight at 0° by which time colourless crystals of the alkyl *N*-methylbenzimidonium hydrochloride salt had precipitated from solution. These were filtered off by vacuum in a dry box (very hygroscopic) and washed well with dry ether. The neutral alkyl *N*-methylbenzimidate was obtained by treating a dilute solution of the hydrochloride salt in very dry ether at 0° with an equimolar amount of Et_3N also in dry ether. After stirring at 0° for 2 h the solvent was removed as rapidly as possible at 0° under vacuum. The residue was vacuum distilled and the middle cut taken. Methyl *N*-methylbenzimidate had b.p. 71° at 5 Torr (lit.,[14] 91—94° at 13 Torr), ethyl ester b.p. 56° at 0.6 Torr (lit.,[14] 105—108° at 15 Torr), n-propyl ester b.p. 60° at 0.6 Torr, isopropyl ester b.p. 58° at 0.75 Torr (lit.,[8c] 162—163° at 10 Torr). These compounds were also characterised by $\nu_{max.}$ 1 670, 1 280, 1 110, and 714 cm^{-1}, n.m.r. spectra (Table 1), and microanalyses. The principal isomer present (>98%) in all cases appeared to bear *E*-antiperiplanar stereochemistry in line with other observations.[15]

Methyl and ethyl iodide (Koch–Light puriss) were used without further purification: the other alkyl halides were purified by vacuum distillation and stored over $CaSO_4$. AnalaR nitrobenzene was dried over calcium hydride and vacuum distilled.

Kinetics.—In most cases the reaction was followed by n.m.r. assay using a Varian T60 instrument. The reaction solution was prepared by weight directly in the clean n.m.r. tube, which was then sealed after the contents had been frozen. Reaction was initiated by immersing the tube in a thermostatted tank at 138°. At timed intervals, the tube was withdrawn from the bath, cooled quickly in running water, and then allowed to equilibrate thermally in the n.m.r. instrument at 35° (*ca.* 10 min) before its spectrum was recorded and integrated. Independent checks showed that insignificant reaction occurred during the n.m.r. assay. Timing was restarted on re-immersing the tube in the bath at 138°.

Examination of Table 1 indicates that the extent of reaction can be ascertained from either the decrease in n.m.r. absorption of the α-proton of the *O*-alkyl substituent in the reactant imidate or (with the exception of the conversion of methyl *N*-methylbenzimidate into *NN*-dimethylbenzamide) from the increase in the *N*-methyl absorption of the product. Usually both changes were monitored and used to calculate rate coefficients from which a mean value was derived. To minimise errors arising from fluctuation of signal strength, these time-dependent absorptions were normalised by reference to a readily resolvable invariant portion of the n.m.r. spectrum, usually the total *N*-methyl absorption in both reactant and product. Pseudo-first-order rate coefficients (rate = k_0 [substrate]) were calculated from equation (2) where $[substrate]_t/[substrate]_0 = (O{-}CH_n{-})_t/(O{-}CH_n{-})_0$ or $(=NCH_3)_t/(=NCH_3)_0$. Values of k_0 were constant to *ca.* 80% reactions when

$$k_0 = \frac{2.303(\log[substrate]_{t_2}/[substrate]_0 - \log[substrate]_{t_1}/[substrate]_0)}{t_2 - t_1} \quad (2)$$

the insensitivity of the n.m.r. procedure (∓5%) introduced significant error in the measurement of small band integrals. The average value of k_0 is accurate to ∓15%. Results for a typical experiment (isopropyl iodide catalysed rearrangement of isopropyl *N*-methylbenzimidate) are given in Table 2.

In a few cases, rate coefficients were also measured by a titrimetric technique involving rapid acid hydrolysis of unchanged alkyl *N*-methylbenzimidate to give $MeNH_3^+ Cl^-$ (and *N*-methylbenzamide) which was titrated potentiometrically (Radiometer auto-titrator). Details of the procedure have been given elsewhere.[16] Rate coefficients obtained by the n.m.r. and titrimetric methods agreed with ∓15%.

Product Analysis.—Products could be identified from n.m.r. spectra of the reaction solutions and assignments were confirmed by spiking with authentic materials. For representative experiments, products were isolated on completion of the reaction and identified by t.l.c., i.r., and

TABLE 1

Chemical shifts (δ) relative to TMS for reactants and products in nitrobenzene

Compound	Chemical shift (δ) and multiplicity	
	OCH_n	NCH_3
PhC(OMe)NMe	3.84(s)	3.11(s)
PhC(OEt)NMe	4.30(q)	3.11(s)
PhC(OPr^n)NMe	4.19(d)	3.12(s) [a]
PhC(OPr^n)NMe	5.33(m)	3.12(s) [a]
	CH_nI	
MeI	2.08(s)	
EtI	3.43(q)	
Pr^{n}I	3.16(t)	
Pr^{i}I	4.31(septet)	
	NCH_n	NCH_3
$PhCONMe_2$	3.07(s)	3.07(s)
PhCONMeEt	3.3(m)	3.03(s)
PhCONMePr^n	3.4(m)	3.00(s)
PhCONMePr^i	4.3(m)	2.92(s)
PhCONHMe		3.13(d)

[a] Minor peak (*ca.* 2%) also present at δ 3.28, probably due to *Z* antiperiplanar isomer (see ref. 15).

[11] B. C. Challis and J. A. Challis, ' Chemistry of Amides ', ed. J. Zabicky, Wiley, London, 1970, p. 731.

[12] B. C. Challis and A. D. Frenkel, *J.C.S. Chem. Comm.*, 1972, 303.

[13] W. R. Vaughan and R. D. Carlson, *J. Amer. Chem. Soc.*, 1962, **84**, 773.

[14] H. Paul, A. Weise, and R. Dettner, *Chem. Ber.*, 1965, **98**, 1450.

[15] G. Fodor and B. A. Phillips, ref. 5, p. 132.

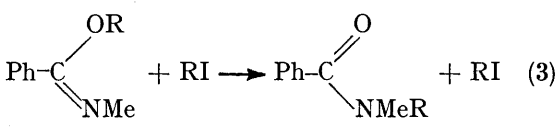
[16] A. D. Frenkel, Ph.D. Thesis, London, 1973.

mixed m.p. with authentic materials. Particular attention was paid to the presence of *N*-methylbenzamide whose formation would be indicative of either hydrolysis or dealkylation of the substrate. None was found except for the isopropyl halide catalysed conversion of isopropyl *N*-methylbenzimidate as discussed further below. Here, the formation of propene was evident from the n.m.r. spectra and confirmed by showing that gaseous reaction products decolourised bromine water. The quantitative product analysis (% *N*-isopropyl *N*-methylbenzamide *versus* % *NN*-dimethylbenzamide) required to analyse the kinetic data was obtained from the n.m.r. spectrum on completion of each reaction (Table 1). The error in measuring these concentrations is *ca.* ∓ 5%.

RESULTS AND DISCUSSION

In the absence of added alkyl halides, the substrates were stable on heating in most solvents (including nitrobenzene) at 180° for several days. This confirms the absence of a significant thermal reaction under the conditions employed for kinetic studies. Rearrangement occurred much more readily in the presence of alkyl halides, but the rate depended on solvent, decreasing in the order nitrobenzene > [$^2H_6$]acetone > $CDCl_3$ > [$^2H_6$]benzene > CCl_4 > cyclohexane. With $CDCl_3$ significant amounts of alkyl chloride formed and with [$^2H_6$]dimethyl sulphoxide a relatively rapid reaction (which was not examined further) occurred even at 53° to give other than rearrangement products. The dependence on solvent polarity implied above suggests that rearrangement involves ionic intermediates and is therefore pseudomolecular.

The most suitable solvent from practical considerations was nitrobenzene, in which most experiments were carried out at 138°. Rearrangement was clean (to give the corresponding tertiary amide quantitatively) with methyl, ethyl, and n-propyl *N*-methylbenzimidates [equation (3)], but a second product (see below) was



(3)

R = Me, Et, or Pr^n

obtained from the reaction of isopropyl *N*-methylbenzimidate with isopropyl halides. Generally, pseudo-first-order rate coefficients (rate = k_o[substrate]) were reproducible to at least 80% reaction and they showed a first-order dependence on the concentration of added alkyl halide. It follows that the pseudomolecular rearrangement rate is given by equation (4). Values of k_2 obtained in nitrobenzene at 138° are summarised in Table 3.

$$\text{rate} = k_2[\text{substrate}][\text{RHal}] \quad (4)$$

As mentioned above, complications arose for the reaction of isopropyl *N*-methylbenzimidate with isopropyl halides in that moderate amounts of *N*-methylbenzamide were formed at the expense of the expected *N*-isopropyl-*N*-methylbenzamide.*

TABLE 2

Calculation of k_o for Pr^{i}I catalysed pseudomolecular rearrangement of PhC(OPr^i)NMe in nitrobenzene at 138°. Initial [PhC(OPr^i)NMe] = 0.778M, [Pr^{i}I] = 0.483M

t/min	ΣNCH_3 integral	NCH_3(Pr^i) integral	% Reaction	10^5 k_o/ s^{-1}	OCH integral	% Reaction [a]	10^5 k_o/ s^{-1}
0	86	0	0		28	0	
38	84	10	19	9.4	20	27	13.7
102	83.5	23.5	46	10.0	14	49	11.0
164	84.5	32	61	9.7	12.5	55	8.0
220	83.5	35.5	69	9.7	8.5	69	8.8
275	86	44	83	10.5	5.0	82	10.4
∞	81	50	100			100	

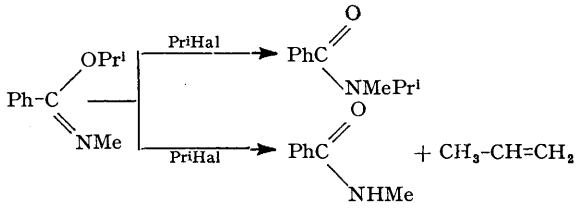
[a] Calculated from OCH integral after correction for variations in amplifier gain.

TABLE 3

Rates of pseudomolecular rearrangement (k_2) and elimination (k_2') for the reaction of alkyl *N*-methylbenzimidates with alkyl halides in nitrobenzene at 138 °C. Initial [substrate] *ca.* 0.9M, [alkyl halide] 0.04—1.3M

Substrate	Alkyl halide	% Rearrangement	10^5 k_2/l mol s^{-1}	10^5 k_2'/l mol s^{-1}
PhC(OMe)NMe	MeI	100	1320	
PhC(OEt)NMe	EtI	100	154	
PhC(OPr^n)NMe	Pr^{n}I	100	50	
PhC(OPr^i)NMe	Pr^{i}I	60	12.9	8.6
PhC(OPr^i)NMe	Pr^{i}Br	65	0.91	0.49
PhC(OPr^i)NMe	Pr^{i}Cl	70	0.004 5	0.002
PhC(OPr^i)NMe	MeI	100	3680	

Evidence that dealkylation occurred *via* an elimination reaction was found in the identification of propene as a co-product. Since both isopropyl *N*-methylbenzimidate



SCHEME 1 Concurrent elimination and pseudomolecular rearrangement of isopropyl *N*-methylbenzimidate in the presence of isopropyl halides

and *N*-isopropyl-*N*-methylbenzamide (the normal 'rearrangement' product) were stable indefinitely under the reaction conditions it follows that pseudomolecular rearrangement and elimination are concurrent (Scheme

* This factor was not taken into account previously.[12] Accordingly, rate coefficients are lower than reported in ref. 12.

1). Further evidence to this effect comes from the kinetic studies.

Overall pseudo-first-order coefficients (k_o) measured from either the loss of substrate or the formation of *N*-isopropyl-*N*-methylbenzamide agreed satisfactorily (Table 2), which implies a common rate equation (rate = k_o [substrate]) for both elimination and rearrangement. Further, k_o showed an approximate first-order dependence on added isopropyl iodide with a constant proportion (*ca.* 40% with isopropyl iodide) of elimination throughout (Table 4). The ratio k_o: [Pr^i I] decreases slightly with increasing isopropyl halide concentration, which may arise from changes in solvent

TABLE 4

Rate coefficients and % rearrangement for the Pr^{i}I catalysed rearrangement of isopropyl *N*-methylbenzimidate in nitrobenzene at 138°. Initial [PhC(OPr^i)NMe] *ca.* 0.9M

[Pr^{i}I]/M	10^5 k_o/s^{-1}	10^4 k_o[Pr^{i}I]$^{-1}$/ l mol^{-1} s^{-1}	Rearrangement %
0.246	5.4	2.18	60
0.483	9.9	2.04	62
0.622	13.4	2.16	60
0.783	12.0	1.53	60
1.04	18.3(18.2) [a]	1.76(1.74)	60(60)

[a] Figures in parentheses for duplicate experiments.

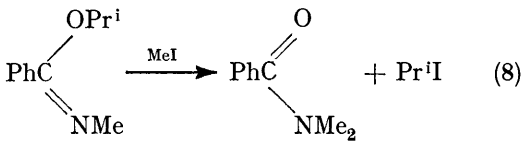
polarity (see above). Nonetheless, the kinetics are well represented by equation (5) (that expected for the concurrent pathways described by Scheme 1), where k_2 = pseudomolecular rearrangement rate coefficient and k_2' is the rate coefficient of *N*-methylbenzamide formation. The k_2 and k_2' coefficients were evaluated from k_o and the product ratio in the usual way [equations (6) and (7)] and these data for reaction with Pr^{i}Cl, Pr^{i}Br,

$$\text{rate} = (k_2 + k_2')([\text{substrate}][\text{Pr}^i\text{I}]) \quad (5)$$

$$k_2 = k_o \,\%\, [N\text{-isopropyl-}N\text{-methylbenzamide}]/100\,[\text{Pr}^i\text{Hal}] \quad (6)$$

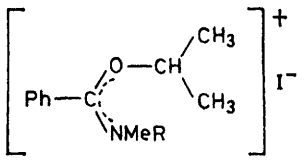
$$k'_2 = k_o \,\%\, [N\text{-methylbenzamide}]/100\,[\text{Pr}^i\text{Hal}] \quad (7)$$

Pr^{i}I, and MeI are also summarised in Table 3. The absence of significant dealkylation (*i.e.* quantitative formation of *NN*-dimethylbenzamide) with MeI requires further explanation. These reactions were made with excess (1.2—1.5 equiv.) of methyl iodide, a more reactive reagent than isopropyl iodide by a factor of *ca.* 280 (Table 3). Thus the one equivalent of isopropyl iodide released (and observed by n.m.r.) on forming *NN*-dimethylbenzamide [equation (8)] has an insignificant effect (the calculated amount of *N*-isopropyl-*N*-methylbenzamide



(8)

formed is only *ca.* 0.3%). The lack of *N*-methylbenzamide formation is mechanistically more interesting, as it shows that the concurrent elimination noted above cannot proceed *via* an imidonium ion intermediate (I),



(I)

because the extent of this reaction would then be largely independent of the *N*-alkyl substituents, and, *inter alia*, of the structure of the alkyl halide reagent (RI). In turn, this implies that the concurrent pseudomolecular rearrangement and elimination reactions observed with isopropyl halide reagents proceed by independent pathways not involving a common reactive intermediate.

Mechanism of the Pseudo-molecular Rearrangement Reaction.—The observation of second-order kinetics [equation (4)] implies a bimolecular mechanism along the lines suggested by both Lander [8a] and Arbuzov and Shishkin [8c,d] (Scheme 2). The rate-limiting step must be S_N2 to explain both the sharp reduction in rate along the series Pr^{i}I > Pr^{i}Br > Pr^{i}Cl for the rearrangement of isopropyl *N*-methylbenzimidate and the decrease in rate with increased branching of the catalyst (MeI > EtI > Pr^{i}I). Either formation (step k_a) or decomposition (step k_b) of the intermediate (II) meets this criterion, but the rapid reaction of isopropyl *N*-methylbenzimidate with MeI (k_2 = 0.037 l mol^{-1} s^{-1}) shows that steric hindrance at the *O*-alkyl substituent is not kinetically important and that step k_a must therefore be rate limiting. The slower MeI catalysed pseudomolecular rearrangement rate for methyl *N*-methylbenzimidate (k_2 0.013 l mol^{-1} s^{-1}) reflects expected inductive effects for the *O*-alkyl substituents on the reactivity of the imidate nitrogen atom.

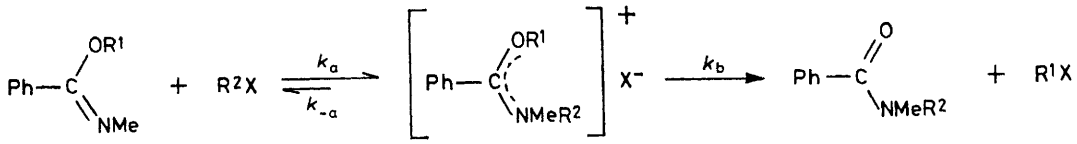
Mechanism of the Elimination Reaction.—This, too, must be bimolecular, and we have already excluded decomposition of the imidonium ion intermediate (I). It follows that propene must arise from normal *E*2 elimination of isopropyl halide with the benzimidate (pK_a 5.7 [17]) acting as base catalyst. The reaction could be stepwise (as in Scheme 3) or concerted *via* an eight-membered cyclic transition state. Tentative confirmation for a base catalysed pathway came from brief examination of the reaction between 2-phenylpyridine [which has both similar basicity (pK_a 4.5 [18]) and steric properties to the benzimidate] and isopropyl iodide in nitrobenzene at 138°. Here, *ca.* 60% of the *N*-isopropyl-2-phenylpyridinium salt was obtained at a rate *ca.* five times slower than the rearrangement of isopropyl *N*-methylbenzimidate together with substantial amounts of propene.

Ambident Nucleophilic Properties of Amides.—The

[17] J. T. Edward and S. C. R. Meacock, *J. Chem. Soc.*, 1957, 2009.

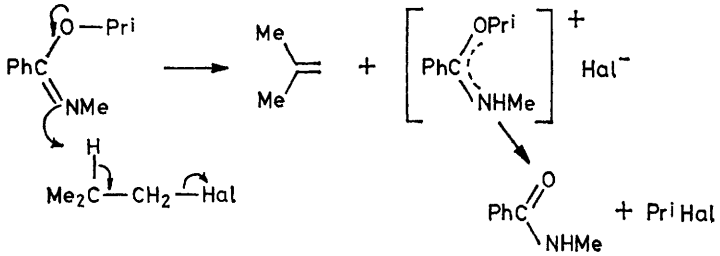
[18] D. D. Perrin 'Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965, p. 171.

findings for the rearrangement process sustain a recent explanation for the apparent nucleophilic reactivity of amide oxygen and nitrogen atoms.[11] Briefly, there is evidence (summarised in ref. 11) for predominant *N*-alkylation under acidic or basic conditions, but mixed



(II)

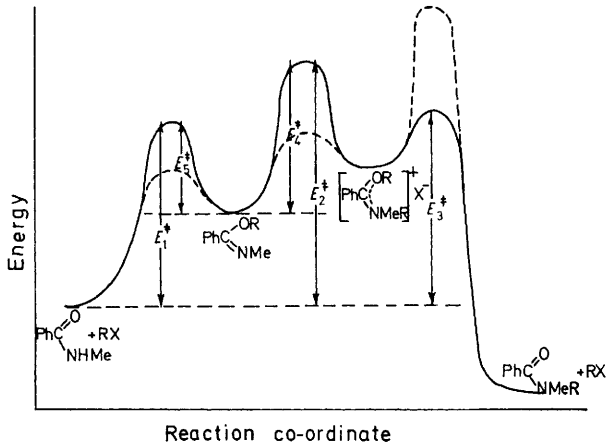
SCHEME 2 Mechanism for the alkyl halide catalysed pseudomolecular rearrangement of alkyl *N*-methylbenzimidates



SCHEME 3 Mechanism of propene formation from isopropyl halide and isopropyl *N*-methylbenzimidate

N- and *O*-alkylation under neutral conditions. Further, *O*-alkylation is favoured under mild neutral conditions by reactive reagents (*e.g.* triethyloxonium fluoroborate,[19] dimethyl sulphate [8b,20]) and in the presence of Ag^+.[21] Although amides can be regarded as potential 1,3-ambident nucleophiles, explanations based on either Kornblum's [22] theory, or more recent perturbation treatments,[23] are unsatisfactory. For example, Gompper and Christmann [24] found that tertiary alkyl halides halides gave both faster rates ($Bu^tCl > Bu^sCl > Bu^nCl$) and higher yields of *N*-substituted products for the alkylation of formamides above 110°. Despite the authors conclusions,[24] the kinetic and product findings are mutually incompatible within the context of either Kornblum's or the perturbation explanation as both predict that *O*-alkylation should increase with increasing S_N1 character (charge control) of the alkylation reaction.

An alternative explanation, suggested by tentative evidence (see ref. 11) that reaction temperature influences product orientation, is that alkylation of neutral amides normally proceeds at the oxygen atom, with *N*-substitution arising from subsequent rearrangement.[11] Thus alkyl imidates are the kinetic products and *N*-alkylamides the thermodynamically stable ones. Strong support for this explanation comes from our observation that alkyl imidates rearrange under catalysis by alkyl halides and by other electrophilic entities.[12] The potential energy diagram for this mechanism (Figure) can be deduced from our results and leads to some interesting conclusions. The inequality $E_1^{\ddagger} < E_2^{\ddagger}$ stems directly from the assumption of kinetic and thermodynamic product control and $E_3^{\ddagger} < E_2^{\ddagger}$ from deductions that step k_a (Scheme 2) is rate-limiting for the rearrangement of alkylimidates. Less obvious is the requirement that $E_4^{\ddagger} < E_1^{\ddagger}$ stemming from the isolation of *N*-methylbenzamide in the rearrangement of isopropyl *N*-methylbenzamide: clearly, isopropyl halides



Potential energy diagram for the alkylation of *N*-methylbenzamide by alkyl halides

do not readily alkylate *N*-methylbenzamide under our conditions in agreement with the high temperature (>150°) usually employed for these reactions. It is also clear from the Figure that addition of halogen acids to alkyl *N*-methylbenzimidates must lead to the formation

[19] H. Meerwein, W. Florian, N. Schon, and G. Stopp, *Annalen*, 1961, **641**, 1; H. Meerwein, P. Borner, O. Fuchs, M. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber*, 1956, **89**, 2060; L. Weintraub, S. R. Oles, and N. Kalish, *J. Org. Chem.*, 1968, **33**, 1679.

[20] H. Bredereck, F. Effenberger, and E. Henseleit, *Chem. Ber.*, 1965, **98**, 2754; H. Bredereck, G. Simchem, and W. Kantlehner, *ibid.*, 1971, **104**, 924.

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[22] N. Kornblum, R. A. Smiley, R. K. Blackwood, and C. Iffland, *J. Amer. Chem. Soc.*, 1955, **77**, 6269.

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[24] R. Gompper and O. Christmann, *Chem. Ber.*, 1959, **92**, 1935.

of *N*-methylbenzamide ($E_5^{\ddagger} < E_4^{\ddagger}$) and this effect has been realised with HBr.[12] The corresponding energy diagram for reactive alkylating agents such as triethyloxonium fluoroborate which give predominantly alkyl imidate is shown as the dotted line in the Figure. A reduction of both $E_1^{\ddagger}$ and $E_2^{\ddagger}$ is anticipated, but the inhibition of rearrangement to *NN*-dialkylamides must result from an increase in $E_3^{\ddagger}$ occasioned by the absence of strongly nucleophilic anions. A similar explanation may also account for the effect of Ag^+ on alkylation by alkyl halides.

Inhibition of Alkylimidate Rearrangements by Silver Ion.—The last hypothesis was tested by examining the influence of added $AgNO_3$ on the methyl iodide catalysed rearrangement of methyl *N*-methylbenzimidate in both [$^2H_6$] acetone and nitrobenzene at 138°. Precipitation of AgI from the reaction solutions was apparent, but *NN*-dimethylbenzamide was isolated in 91% yield on completion. Good pseudo-first-order plots (rate = k_o[methyl *N*-methylbenzimidate]) were obtained and evidence in Table 5 shows that a slight excess of $AgNO_3$ over methyl iodide reduces k_o by a factor of *ca.* 33 in both solvents. Thus silver salts promote the *O*-alkylation of amides by inhibiting the pseudomolecular rearrangement. The observation of *any* rearrangement in the presence of $AgNO_3$ may, however, seem surprising. Significantly, the n.m.r. spectra of the reaction solutions showed a new singlet at δ 4.13 after addition of $AgNO_3$,

TABLE 5

Effect of $AgNO_3$ on the rate of MeI catalysed pseudomolecular rearrangement of methyl *N*-methylbenzimidate at 138°

Solvent	[$AgNO_3$]/M	[MeI]/M	$10^5 k_o/s^{-1}$
Nitrobenzene		0.27	355
Nitrobenzene	0.32	0.27	10.8
[$^2H_6$]Acetone		0.443	258
[$^2H_6$]Acetone	0.448	0.443	7.7

whose integral corresponded to that expected for the added methyl iodide. This suggests that methyl nitrate forms, which acts as a less effective catalyst than methyl iodide. Methyl nitrate should be a better alkylating agent than methyl iodide, but NO_3^- is a poorer nucleophile than I^-.

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