Kinetics and Mechanism of Thermal Decomposition of Phenylmalonic Acids and Esters in Dimethyl Sulphoxide

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Rates of decarboxylation are reported for several phenylmalonic acids and esters in dimethyl sulphoxide at 55·4°. Only those compounds bearing at least one carboxylic proton are labile which establishes that intramolecular proton transfer is an integral part of the reaction mechanism.

THE thermal instability of malonic acids is well known and their decarboxylation is a valuable synthetic procedure.[1] Several aspects of the mechanism have been investigated, but the nature of the transition state is still disputed, mainly in regard to the timing of carbon–carbon bond fission[2] and the role of intramolecular proton transfer.[3]

The notion that intramolecular proton transfer is an integral part of the decarboxylation process comes mainly from repeated observations that only the molecular acid and half-neutralised acid decompose, whereas the dianionic salt is stable even in the molten state.[1,4] This argument is questionable in as much as the carbanion $^-CH_2CO_2^-$ formed by decomposition of the dianion must be an extremely high energy structure. Furthermore, the low primary isotope effect reported[5] for the decarboxylation of deuteriomalonic acid suggests that intramolecular proton transfer is not kinetically significant. To resolve this matter, we have investigated the thermal stability of several phenylmalonic acids

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[1] B. R. Brown, *Quart. Rev.*, 1951, **5**, 131.

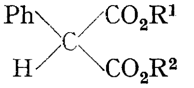
[2] P. E. Yankwich and M. Calvin, *J. Chem. Phys.*, 1949, **17**, 109.

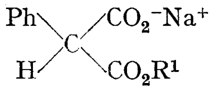
[3] K. R. Brower, B. Gay, and T. L. Konkol, *J. Amer. Chem. Soc.*, 1966, **88**, 1681.

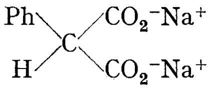
[4] G. A. Hall and E. S. Hanrahan, *J. Phys. Chem.*, 1965, **69**, 2402.

[5] A. T. Blades and M. G. H. Wallbridge, *J. Chem. Soc.*, 1965, 792.

and esters (I)—(VI) under aprotic conditions where ester hydrolysis is not significant. Dimethyl sulphoxide was chosen for its excellent solvent properties and phenylmalonic acid derivatives for their relatively high reactivity. Previous studies in aqueous dioxan have shown that both the molecular acid (I) and its half-neutralised salt (IV) readily lose carbon dioxide at *ca.* 55°.[4] Although Corey[6] has reported that ethyl potassium phenylmalonate decarboxylates at 110°, his experimental conditions would favour prior hydrolysis of the ester group.


(I) $R^1 = R^2 = H$
(II) $R^1 = H, R^2 = Et$
(III) $R^1 = R^2 = Et$


(IV) $R^1 = H$
(V) $R^1 = Et$


(VI)

EXPERIMENTAL

Materials.—Dimethyl sulphoxide (B.D.H.) was purified by fractional distillation from calcium hydride under nitrogen and stored over type A molecular sieve. Diethyl phenylmalonate (Aldrich) was fractionally distilled, taking only the middle cut. All the other substrates were obtained from this by hydrolysis under various conditions. Thus the parent acid (I) was prepared according to Basterfield and Hamilton[7] and purified by repeated recrystallization from diethyl ether–light petroleum, m.p. 152° (lit.,[8] 152—153°). The half-ester (II) was obtained by Corey's[6] method, and purified by repeated recrystallization from methylene chloride–light petroleum m.p. 76° (lit.,[6] 76—77°). The half-salt (IV) was prepared from phenylmalonic acid by partial neutralization,[9] m.p. 185° (decomp.) [lit.,[9] 184—185° (decomp.)] *Ethyl sodium phenylmalonate* (V) was obtained by neutralization of (II) with one equivalent of NaOH in ethanol at 0°. Any disodium salt precipitates from the reaction mixture and, after drying and removal of ethanol, the residue was washed with dry diethyl ether to remove unchanged ethyl hydrogen phenylmalonate. The product melted with decomposition at 115° (Found: C, 56·95; H, 4·55; Na, 9·75. $C_{11}H_{11}NaO_4$ requires C, 57·4; H, 4·8; Na 10·0%). The n.m.r. and i.r. spectra of all these compounds were consistent with the expected structures.

Kinetic Procedure.—The reactions were followed by measuring the volume of carbon dioxide evolved at timed intervals by means of a gas burette similar to that described by Frankel *et al.*[10] The reaction solution, contained in a round-bottomed flask (50 ml) immersed in a thermostatted bath, was stirred such that the rate of carbon dioxide evolution was independent of the stirring rate. The reaction flask was connected to the gas burette *via* a cooling condenser. The burette was maintained at 25° by circulating water through a concentric glass jacket.

Before kinetic measurements were taken, dry, cylinder CO_2 was used to saturate the solvent (usually 20 ml) and to flush out the apparatus. After thermal equilibrium had been achieved, the burette reading was adjusted to zero. The reaction was initiated either by breaking a previously added sealed glass ampoule containing an accurately weighed amount of substrate or by injecting a small volume of a solution of the substrate in dimethyl sulphoxide by means of a syringe through a 'Subaseal' stopper. Volume readings were taken at timed intervals at 25° and atmospheric pressure. They were adjusted to N.T.P. only if the barometric pressure fluctuated appreciably throughout the experiment.

RESULTS AND DISCUSSION

Decomposition of both (I) and (II) followed first-order kinetics [equation (1)] and infinity volumes were in excess of 95% of their expected values. To minimise error, however, rate coefficients were calculated, where

$$\text{Rate} = k_1[\text{Substrate}] \qquad (1)$$

feasible, by the Guggenheim[11] procedure. The error in determining k_1 values for (I) and (II) is estimated at ±8% and the constancy of k_1 over a fivefold variation in initial concentration of (II) listed in Table 1 is illustrative.

TABLE 1

Decarboxylation of ethyl hydrogen phenylmalonate (II) in dimethyl sulphoxide at 55·4°

10^2[(II)]/M	10^4k_1/s^{-1}
2·72	18·4
4·38	18·9
5·48	17·3
12·50	17·8

The decomposition kinetics of the monoanion (IV) were less straightforward in two ways. First, only *ca.* 85—95% of the expected CO_2 volume was evolved, even after 10 half-lives, and, secondly, satisfactory linear first-order kinetic plots could not be obtained for much more than 50% reaction. Thereafter, the k_1 coefficient either decreased or increased, depending on whether the theoretical or observed infinity volume was used. Further, neither the value of k_1 over the first 50% reaction was substantially altered, nor the fit of the data for subsequent reaction improved, by a least-squares iterative procedure that was independent of the actual infinity volume. Since similar deviation from first-order behaviour had been noted previously for the decomposition of (IV) in solvent dioxan,[4] it was desirable to establish the reason both for this effect and that of the lower than expected infinity volumes.

Addition of a small amount of HCl after 10 half-lives (when *ca.* 85—95% of the expected CO_2 had been released) resulted in further release of CO_2 until the expected volume was attained. This suggests that the phenylacetate ion produced by decomposition displaces the prototropic equilibrium of equation (2) to the right

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[6] E. J. Corey, *J. Amer. Chem. Soc.*, 1952, **74**, 5897.

[7] S. Basterfield and L. A. Hamilton, *Trans. Roy. Soc. Canada*, 1933, 125.

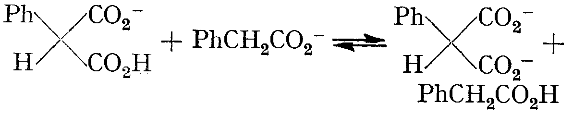
[8] 'Dictionary of Organic Compounds,' Eyre and Spottiswoode, London, 1965, vol. 4, p. 2702.

[9] S. Basterfield and J. W. Tomecks, *Canad. J. Res.*, 1933, **8**, 447.

[10] G. Frankel, R. L. Belford, and P. E. Yankwich, *J. Amer. Chem. Soc.*, 1954, **76**, 16.

[11] E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

to form unreactive disodium phenylmalonate (*vide infra*). The relevant pK_A values in solvent dimethyl sulphoxide are not known, but in aqueous solution they are closely similar {$pK_A(PhCH_2CO_2H)$ 4·32; pK_A-$[PhCHCO_2H(CO_2^-)]$ 5·03}.[12] This effect alone, however, would not entirely account for the deviation from first-order kinetics.


(2)

Values of k_1 computed from the initial 50% of reaction were found to increase slightly with the initial concentration of (IV), but to a much lesser degree than expected for a second-order process. Evidence in Table 2 shows that k_1 increases by only 40% for a nearly four-fold increase in the concentration of (IV), and these data lead to an apparent substrate order of 1·29. This result would be expected for decomposition by concurrent first- and second-order processes in which the first-order pathway is dominant, or for catalysis, or a salt effect, by the sodium phenylacetate product. Independent experiments also listed in Table 2 showed that added sodium phenylacetate did, indeed, mildly catalyse the decarboxylation reaction and the absence of a similar rate enhancement from added NaCl probably rules out a simple salt effect. Quinoline, and other nitrogen bases, are known to catalyse thermal decarboxylation to some extent [1] and it seems likely that the sodium phenylacetate acts similarly. Analyses of the kinetics to allow for catalysis by sodium phenylacetate produced by the reaction, assuming that this was both a concurrent or the only pathway to products, were no more satisfactory than the simple first-order plots. We therefore believe that (IV) undergoes decarboxylation predominantly by a unimolecular process, similar to that of the other phenylmalonic acid derivatives. The value of k_1 for the decarboxylation of (IV) given in Table 3 was obtained by the least-squares iterative procedure.

TABLE 2

Effect of substrate concentration and added salts on the rate of decarboxylation of hydrogen sodium phenylmalonate (IV) in dimethyl sulphoxide at 55·4°

$10^2[(IV)]/M$	[Salt]/M	$10^4k_1/s^{-1}$
3·20		48·0
4·13		50·0
6·05		57·6
8·26		58·0
9·90		63·0
11·72		70·0
2·75	0·108 NaCl	52·4
3·27	0·062 $PhCH_2CO_2^-Na^+$	65·6
2·98	0·109 $PhCH_2CO_2^-Na^+$	77·0
2·93	0·114 $PhCH_2CO_2^-Na^+$	85·6

Rates of Decarboxylation.—First-order rate coefficients [equation (1)] for the decarboxylation of compounds (I)—(VI) in dimethyl sulphoxide at 55·4° are listed in Table 3. Dimethyl sulphoxide is known [13] to enhance the decarboxylation of malonic acid by a factor of 25 relative to solvent H_2O, and the rate coefficient for (I) reported in Table 3 is 26 times that obtained by Hall and Hanrahan [4] in H_2O at 55°. Thus the catalytic effect of dimethyl sulphoxide is similar for both malonic acids.

TABLE 3

First-order rate coefficients for the decarboxylation of phenylmalonic acids and esters in dimethyl sulphoxide at 55·4°

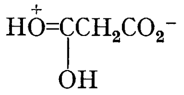
Substrate	$10^4k_1/s^{-1}$
(I)	2·6
(II)	18
(III)	No reaction
(IV)	48—70 *
(V)	No reaction
(VI)	No reaction

* From initial 50% reaction (see text).

Hall and Hanrahan [4] also reported that the monoanion (IV) decomposes faster than (I) in dioxan–water (by a factor of 10 in 80% dioxan) and a similar difference is apparent from first-order rate coefficients taken over the initial 50% reaction (*vide supra*).

The monoester (II) decomposes more readily than (I) by a factor of *ca.* 7, reflecting, perhaps, the inductive effect of the ethyl group. The most significant result, however, is the stability of the corresponding sodium salt (V): apart from a trace of CO_2 (<10%) evolved during the first hour, probably the result of hydrolysis by adventitious water to the labile acid (II), species (V) was completely stable at 55·4°. An interesting point is that on addition of one equiv. of concentrated HCl to (V), which was unchanged after 20 h at 55·4°, rapid evolution of CO_2 ensued and the total volume after 40 min was that expected for complete decarboxylation of the substrate. Since the relative rates for (I), (II), and (IV) suggest that (V) would be the most labile species if charge were the only consideration, the stability of (V) establishes unequivocally that decarboxylation of malonic acids requires an intramolecular proton transfer. This is confirmed by the thermal stability of both the dianion (VI) and the diester (III).

The question of the low deuterium isotope effect for the decarboxylation of malonic acid [5] remains. Two explanations come to mind. One is that proton transfer occurs in a rapid, pre-equilibrium step to give the zwitterion (VII), which then slowly eliminates CO_2.


$$H\overset{+}{O}=\underset{\displaystyle OH}{\underset{|}{C}}CH_2CO_2^-$$
(VII)

Only small, secondary deuterium isotope effects would then be expected. The other is that proton transfer, although synchronous, is rapid relative to C–C bond fission, and the primary isotope effect is reduced because

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[12] See G. Kortum, W. Vogel, and K. Andrussow, 'Dissociation Constants of Organic Acids in Aqueous Solutions,' Butterworths, London, 1961.

[13] S. H. Kerr, M.Sc. Thesis, University of St. Andrews, 1966.

vibration about an equilibrium position restores zero-point energy to the O–H bond in the transition state. Such an argument has been advanced to account for the low primary deuterium isotope effects associated with base-catalysed cyclisation of chlorohydrins.[14] Deuterium isotope effect measurements for the decarboxylation of sodium hydrogen malonates would distinguish between these explanations.

We thank the S.R.C. for studentships to S. H. K. and I. A. M., and H. S. Rzepa for assistance with the computations.

[1/108 *Received, 2nd February*, 1971]

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[14] C. G. Swain, D. A. Kuhn, and R. L. Schowen, *J. Amer. Chem. Soc.*, 1965, **87**, 1553.