Solid–Gas Reactions. Part I. Bromination

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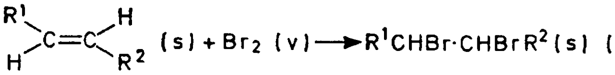
Solid αβ-unsaturated acids, amides, and ketones yield, on exposure to bromine vapour at room temperature, the '*trans*-adduct' in quantitative or near-quantitative yield even where addition of bromine in solution has been reported to be difficult. Polymorphic forms of several compounds differ in their rates of bromine uptake and addition. That crystal texture plays a role is suggested by the fixation of bromine in compounds which in the pure state add bromine slowly but which do so more rapidly in the presence of small amounts of impurities (*e.g.* photo-dimer or saturated derivatives).

PREVIOUS publications concerned with solid-state reactions have stressed the high degree of topochemical control in photochemical processes.[1] We now explore the range and limitation of the topochemical concept in these two-phase, two-component reactions. Schmitt [2] showed in 1863 that solid cinnamic acid reacts with bromine vapour to give cinnamic acid dibromide [reaction (1); $R^1 = Ph$, $R^2 = CO_2H$]. Many examples of this type of reaction have since appeared.[3,4] In view of the experimental simplicity of the reaction it was of interest to establish its general applicability; we also hoped to find examples suitable for more detailed analysis of the various processes involved in reaction (1), such as diffusion of bromine into the lattice, formation of charge-transfer complexes,[4] *etc.*



$$R^1HC{=}CHR^2\,(s) + Br_2\,(v) \longrightarrow R^1CHBr{\cdot}CHBrR^2\,(s)$$ (1)

EXPERIMENTAL

Materials.—The β- and γ-modifications of *m*-nitro-, *m*-chloro-, and *m*-bromo-*trans*-cinnamic acids were prepared according to published procedures.[5] *m*-Nitro-*cis*-cinnamic acid was prepared from the *trans*-acid [6] and purified by chromatography,[7] m.p. 153°.[6] α-Phenylcinnamic acid was prepared according to Stoermer and Voht.[8] *trans*-Stilbene was an Eastman Kodak product and 2,4-dinitrostilbene was prepared according to Thiele and Escales.[9] The two forms of fumaric acid [10] were checked by powder photography. Maleic acid, fumaramide,[11] and monomethyl fumarate were recrystallised from water. Monoethyl and dimethyl fumarate were obtained according to Schields [12] and Ing and Perkin.[13] Dimethylfumaric acid was prepared according to Lutz *et al.*[14] Citraconic and mesaconic acids were prepared by published procedures; [15] the latter was obtained in two crystalline modifications.[16]

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Methods.—Powder photographs were taken on a Guinnier or on a Debye–Scherrer camera with Cu-K_α radiation. N.m.r. spectra (δ/p.p.m.) were taken on a Varian A60 instrument for $(CD_3)_2SO$ solutions unless otherwise stated.

The quantitative experiments in which rates of bromine uptake were followed as a function of time were carried out on samples (average weight 20 mg) sieved to constant mesh size (350 mesh unless otherwise stated) and placed on a microscope coverslip. These samples were introduced into a modified washbottle containing a standard amount of liquid bromine, and immersed in a thermostat at 25 ± 0·2°. The samples were removed after measured intervals and introduced into a Cahn R.G. Electrobalance and weighed. The balance was attached to a water pump and the loss of weight during evacuation was displayed on a recorder.

Preparative brominations were carried out in desiccators in the dark on samples up to 100 g.

m-*Nitrocinnamic Acid.*—The change in weight, expressed as the molar ratio of acid : bromine, with time is shown in Figure 1(a). Both crystal modifications yielded quantitatively the same dibromide, m.p. 174°, δ 5·62 (2H, ABq, *J* 12 Hz). Figure 1(b) represents the bromination of the β-modification after being irradiated ($\lambda > 300$ nm) for 1 h under a Sunlamp in a rotating tube, all other conditions being the same. 90% Dibromide was obtained (indicating 10% of photo-dimer). Irradiation of the (light-stable) γ-form produced no effect on the rate of bromine uptake. The *cis*-isomer reacts with bromine vapour to give a compound, m.p. 119° [lit.,[6] 121° (from benzene)], δ 5·60 (2H, ABq, *J* 9 Hz), not identical with the bromination product of the *trans*-acid.

m-*Chloro*-trans-*cinnamic Acid.*—The rates of bromine uptake by the two crystal modifications of the chloro-derivative are shown in Figure 2. Both crystal forms yield the same dibromide, m.p. 178° (lit.,[17] 176°).

m-*Bromo*-trans-*cinnamic Acid.*—The two crystal forms of *m*-bromocinnamic acid added bromine to give 2,3-*dibromo*-3-m-*bromophenylpropionic acid*, m.p. 178° (from ethanol) (Found; C, 28·4; H, 1·85; Br, 61·2. $C_9H_7Br_3O_2$ requires C, 27·9; H, 1·8; Br, 62·0%).

α-*Phenylcinnamic Acid.*—The weight uptake of α-phenylcinnamic acid, m.p. 169—171°,[18] is shown in Figure 3. The product was the dibromide (m.p. of crude product 150—156°) as shown by i.r. and n.m.r. spectroscopy.

trans-*Cinnamide.*—The amide (0·91 g) gave, after 11 h, the dibromide, m.p. 215° (lit.,[19] 217°), δ 5·34 (2H, ABq, *J* 12 Hz), in quantitative yield.

trans-*Benzylideneacetophenone.*—The ketone (1·5 g) gave, after 3 h, a dibromide, δ 6·21 (2H, ABq, *J* 12 Hz), identical with that obtained from the similar reaction in solution.[20]

Stilbene.—*trans*-Stilbene (3·5 g) gave quantitatively in <4 h the *meso*-dibromide identified by m.p.[21] and i.r. spectrum.[22] *cis*-Stilbene, exposed to bromine vapour at 25° (l) and 0° (s), gave a product with m.p. and i.r. spectrum identical with those of the *meso*-dibromide. Solid *cis–trans* mixtures were also prepared from mixed melts of *cis*- and *trans*-isomers; the i.r. spectra of these mixtures (taken prior to bromination) indicated the presence of the *cis*-isomer in a proportion essentially unchanged by the melting procedure. Exposure to bromine vapour yielded pure *meso*-dibromide.

2,4-*Dinitrostilbene.*—*trans*-2,4-Dinitrostilbene (3·42 g) yielded after 5 h the dibromide (5·39 g), δ 6·24 (2H, ABq, *J* 12 Hz). The i.r. spectrum was identical with that of the dibromide prepared from the similar reaction in solution.[9]

Maleic and Fumaric Acids and Derivatives.—Maleic acid was brominated to DL-dibromosuccinic acid, m.p. 165° (lit.,[23] 164—170°), identified by i.r. spectroscopy.[24] The n.m.r. spectrum showed that the unrecrystallised product contains <5% of the *meso*-acid, since in a control experiment 5% of *meso*-dibromide added to the DL-isomer could clearly be detected. Fumaramide was resistant to bromine vapour. Monomethyl fumarate adds bromine very slowly [14·8 mg, after 69 h in bromine vapour, showed a small (1 : 0·16) irreversible weight uptake]. The bromination is shown in Figure 4, which also gives the weight uptake of the same compound after pre-irradiation for 1 h. The end-point (1 : 0·90) was reached in 24 h in this case. (The dimer of monomethyl fumarate does not absorb bromine under any conditions.) Dimethyl fumarate takes up bromine rapidly which then condenses on the solid phase; after degassing a material with molar ratio 1 : 1·0 is obtained, m.p. 57—58°; 250 g of dimethylfumarate can be brominated, at room temperature, in 36 h. The product is identical (powder photographs, m.p., and n.m.r. spectrum) with the dimethyl *meso*-dibromosuccinate.[13] Monoethyl fumarate, after 8 h bromination, had become pasty, with a molar ratio of 1 : 0·79 of acid to bromine. Further exposure for 14 h led to complete reaction, the degassed material spontaneously crystallising after a further 24 h. The dibromide [25] was identified by m.p. and n.m.r. spectrum.

Mesaconic Acid.—Bromine uptake by either crystal modification at room temperature is very slow. Exposure of 10 mg at 50 ± 0·2° gave the results shown in Figure 5. Both forms eventually gave the same dibromide (1 : 1·0) identical (m.p., i.r., and n.m.r. spectra, and powder pattern) with the DL-*erythro*-αβ-dibromomethylsuccinic acid.[26]

Citraconic Acid.—Exposure of a sample for 50 min to bromine vapour led to the liquefaction of the entire sample, which could be degassed to leave the dibromide, m.p. 150—155°, identified by powder pattern and i.r. spectrum as DL-*threo*-αβ-dibromomethylsuccinic acid.[27]

Dimethylfumaric Acid.—The acid was exposed to bromine vapour at 15° (Figure 6). An uptake value of 1 : 0·90 was achieved after 68 h, m.p. (crude product) 185°. The i.r. spectrum shows the disappearance of the C=C bond; a small band at 1840 cm^{-1} absent from the starting compound appears in the product.

Crotonic Acid.—The acid (13·9 g) gave, after 28 h the dibromide, m.p. 84° (lit.,[27] 87°).

Crotonamide.—The amide (1·73 g) gave, in 80 min, the dibromide, m.p. 152°.

But-2-*ene*-1,4-*dicarbonitrile.*—Formation of *meso*-2,3-dibromo-1,4-dicyanobutane is rapid and quantitative; unless the concentration of bromine is kept low in the initial stages of the reaction undesirable side reactions occur.

But-2-*ene*-1,4-*dicarboxylic Acid.*—Addition of bromine to the solid is very rapid; reaction to the pure *meso*-dibromide

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can be carried out on a large scale. The *meso*-configuration has been confirmed by the three-dimensional structure analysis of the dimethyl ester.[28]

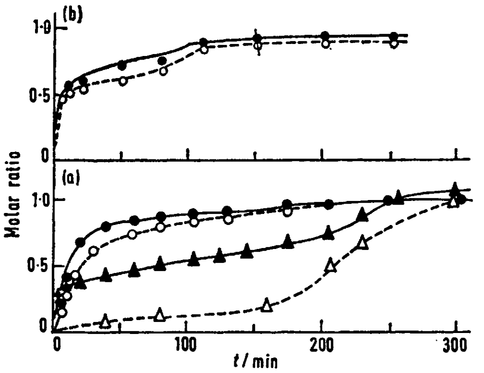

FIGURE 1 (a) Weight uptake of β-, and γ-forms of *m*-nitrocinnamic acid at 25°. ●, γ-form; ▲, β-form. Broken curves correspond to degassed values. (b) Weight uptake of the β-form of *m*-nitrocinnamic acid after irradiation. Broken curves correspond to degassed values

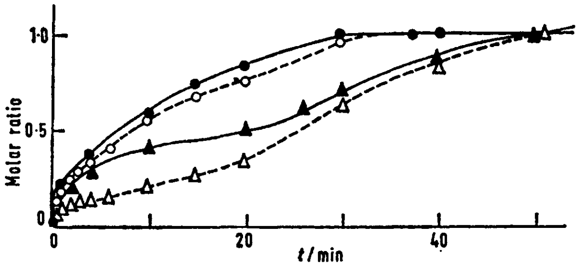

FIGURE 2 Weight uptake of β- and γ-forms of *m*-chlorocinnamic acid at 25°. ●, γ-form; ▲, β-form. Broken curves correspond to degassed values

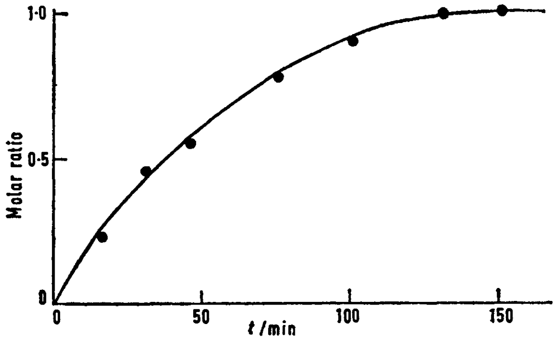

FIGURE 3 Weight uptake of α-phenylcinnamic acid at 20° (degassed values)

RESULTS AND DISCUSSION

Addition of bromine to solid αβ-unsaturated acids, amides, and ketones is rapid and quantitative in the majority of compounds studied. Compounds which are reportedly difficult to brominate under conventional solution conditions, *e.g.* maleic anhydride,[29] maleic acid[30] (catalysed by HBr), 2,4-dinitrostilbene[9] (100°), monoethyl fumarate[12] (sealed tube), α-phenylcinnamic acid (slowly in sunlight, plus other products[18]), and dimethylfumaric acid (isomerised by bromine in chloroform to yield a bromolactone in alkaline solution[31]) can be brominated by this technique. The reaction is also stereoselective; in the majority of compounds the products are *trans*-adducts: the n.m.r. spectrum of the solid-state bromination product of maleic acid showed that the maleic acid dibromide contains not more (and probably less) than 5% of the *meso*-isomer. We have found so far, as the only example of *cis–trans* isomerisation prior to or during bromine addition, the reaction of solid *cis*-stilbene (pure or incorporated into *trans*-stilbene) to give the *meso*-dibromide.

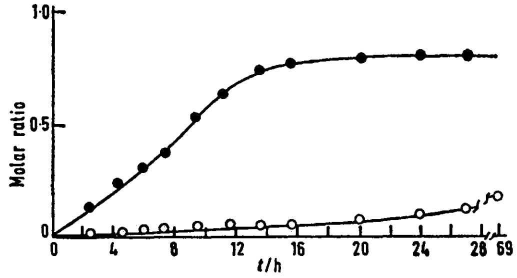

FIGURE 4 Weight uptake of monomethyl fumarate at 24°. ○, Monomethyl fumarate (degassed values); ●, monomethyl fumarate after irradiation (degassed values)

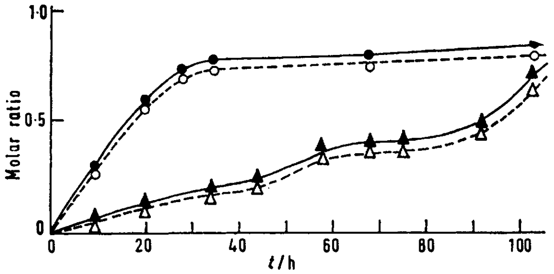

FIGURE 5 Weight uptake of mesaconic acid at 50°. ●, Form from water; △, form from ether. Broken curves correspond to degassed values

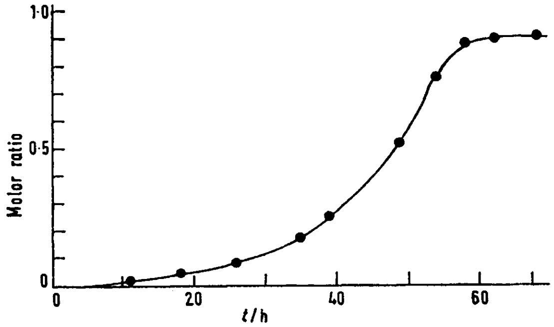

FIGURE 6 Weight uptake of dimethylfumaric acid at 15° (degassed values)

We note that, whilst the stereo-structure of the

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[30] K. Nozaki and R. A. Ogg, *J. Amer. Chem. Soc.*, 1942, **64**, 697.

[31] D. S. Tarbell and P. D. Bartlett, *J. Amer. Chem. Soc.*, 1937, **59**, 407.

product (' *trans*-adduct ') is independent of the crystal structure of the organic component, significant differences in the rates of bromine uptake are shown by the crystal modifications of dimorphic compounds (*m*-substituted *trans*-cinnamic acids, mesaconic acid) and by chemically related compounds (*e.g.* monomethyl and monoethyl fumarates) crystallising in different packing arrangements.

The three (*m*-NO_2-, -Cl-, and -Br-cinnamic) acids were exposed in their two pure crystal modifications to bromine vapour at constant temperature (25°). The γ-modification of the three acids takes up bromine continuously, whereas the β-form reaches a plateau corresponding to between 30 and 40 mol % of bromine, after which uptake of bromine continues at a faster rate (Figures 1 and 2). In a second series of experiments the samples were removed from the bromine atmosphere and degassed (*ca.* 25 mmHg), when the amount of fixed bromine was determined as weight increase. Since the brominated γ-modification showed essentially no loss of bromine the addition of all absorbed bromine to the double bond had evidently taken place in the interval between exposure and application of the vacuum. On the other hand, the major portion of the bromine absorbed by the β-modification could be rapidly removed at *ca.* 25 mmHg. There was no visual evidence (microscope) of a liquid phase on the crystals even with the large amount of ' absorbed ' bromine. The β-phase of the cinnamic acids was recovered unchanged from the degassing procedure (except for small amounts of the dibromide); conversion into the thermodynamically stable γ-modification had not taken place.

Two further as yet qualitative observations are relevant. First, the behaviour of the β-form at higher temperatures steadily approaches the pattern shown by the γ-type at room temperature; the plateau increasingly shortens and eventually disappears at *ca.* 50°. Secondly, the amount of bromine that can be degassed at 25° decreases with increasing time between removal from the bromination vessel and the application of the vacuum. We conclude that the 30—40 mol % of bromine taken up by the β-form has diffused into the solid phase, and that bromine has reached sites in these crystal structures from which transfer to the double bond is a relatively slow step at this particular temperature, slower at any rate than in the γ-form.

The two forms of mesaconic acid gave the uptake–time curves in Figure 5. While there is no evidence for diffusion of bromine into non-reactive sites (the amount of removable bromine at each stage of the reaction being negligible), the rates of diffusion and reaction in the two crystal structures are clearly different.

We note the very slow bromination of monomethyl fumarate (Figure 4) as against the rapid addition to the monoethyl ester. Even though in the later stages of bromine addition the lower-melting ester turns pasty (presumably because of the lowered m.p. of the mixture of two low-melting substances or possibly because of condensation of bromine on the dibromide) the reaction of both esters can be classified as a true solid-state reaction.

Since the chemical effects of the two alkyl groups cannot be very different, this difference in rates may reasonably be ascribed chiefly to the change in packing arrangement. The rates of bromine addition to both esters in solution ($CHCl_3$ or AcOH) have been found to be negligibly low at room temperature; hence this is another example of a reaction which is slow in solution but fast in the solid state.

The experimental data permits the conclusion that there are some crystal structures in which the rates of diffusion are larger than the reaction to the dibromide (β-modification of *m*-substituted *trans*-cinnamic acids), whilst in others the rates of these two processes are roughly comparable or reversed. Furthermore, in the latter category there are evident differences between rates of addition to the double bond which in polymorphic forms (mesaconic acid) or in closely related compounds (monomethyl and monoethyl fumarate) are unlikely to be due to different rates of reaction of the molecular species, and which should therefore be ascribed to differences in rates of diffusion into the crystal lattice. Two observations confirm this. First, the differences in bromination rate of the two fumarates follow the differences in density (Me, 1·47; Et, 1·32 g cm^{-3}) reflecting differences in molecular packing (Me, $a = 14{\cdot}14$, $b = 3{\cdot}99$, $c = 5{\cdot}60$ Å; $\alpha = 72° 6'$, $\beta = 98° 8'$, $\gamma = 83° 8'$; space group $P\bar{1}$: Et, $a = 11{\cdot}15$, $b = 5{\cdot}21$, $c = 5{\cdot}89$ Å; $\alpha = 89° 47'$, $\beta = 92° 55'$, $\gamma = 97° 59'$; space group $P\bar{1}$). Secondly, since diffusion into the crystal lattice is a function of texture as well as of structure small defects, whether produced by impurities or by chemical reaction (thermal or radiation) particularly close to surface, could influence the rate of diffusion and of addition. It has been shown [5] that the γ-modification of *m*-nitro-*trans*-cinnamic acid is stable to u.v. radiation whereas the β-form gives a photodimer: irradiation ($\lambda > 300$ nm) prior to bromination leaves the uptake and addition patterns of the γ-form unaffected; the β-form on the other hand now shows the uptake and degassing curves of Figure 1(b). Similarly, pre-irradiation of monomethyl fumarate (known to give a photodimer [32]) significantly increases the rate of bromination (Figure 4). The effect of melting (with minor damage to the material) is to increase the rate of bromine uptake, which in turn is very significantly raised by the admixture of 5% of methyl succinate *via* the melt to the crystalline phase. The most pronounced effect on the rate of bromine uptake is shown by pre-irradiation with γ-radiation. In all cases the same *trans*-dibromide is formed. These experiments together with the variation in bromine uptake and fixation constitute conclusive proof that the state of the solid, as regards crystal structure as well as texture, is an operative factor in the bromination from the gas phase.

Recent work on bromine addition to single crystals of

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[32] T. Sadeh and G. M. J. Schmidt, *J. Amer. Chem. Soc.*, 1962, **84**, 3970.

trans-substituted olefins of the type $R^1CH{:}CHR^2$ crystallising in a chiral space group, has shown[33] that formation of the *erythro*-dibromide is accompanied by optical induction to the extent of 6% for $R^1 = p$-tolyl and $R^2 = p$-toluoyl. According to the crystal-structure analysis[34] of this olefin (*p,p'*-dimethylchalcone) in space group $P2_12_12_1$ the molecule has a strongly twisted and hence chiral conformation; since the crystal structure is devoid of centres of inversion or mirror elements of symmetry, all molecules of one single crystal (barring twinning or disorder phenomena) have identical handedness. Since formation of the dibromide is subject to optical induction addition takes place to a molecule subject to conformational constraint, that is in or on the crystal.

We cannot therefore accept as generally valid the statement made by Buckles *et al.*[3] that reactions of solids with bromine take place in an adsorbed phase on the surface of the crystals or in a film of solution formed by the aromatic compound dissolved in liquid bromine. Formation of a liquid phase is indeed observed when dibromides are left in bromine vapour; consequently, exposure of the unsaturated component for longer periods of time than required for completion of bromination, or exposure of samples in thick layers, unless frequently stirred, may lead to a liquid phase. In none of the compounds having m.p.s >70° and exposed in sufficiently thin layers has formation of a liquid phase or condensation of liquid bromine been observed before completion of the reaction.

We do not wish to comment at this stage on the mechanism of bromine addition in the solid-phase reaction; the formation of the *trans*-adduct, as in the majority of solution reactions, is in our opinion neither evidence for a common mechanism in the two phases nor proof for the formation of a dissolved phase on the crystal surface. We conclude at this stage that our qualitative data indicate the role of crystal structure in the combined processes of diffusion and reaction.

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