411. *The Kinetics and Mechanisms of Carbonyl–Methylene Condensations. Part VII.*[1] *The Reaction of Malononitrile with Aromatic Aldehydes in Ethanol.*

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The kinetics of the reaction of malononitrile with five aromatic aldehydes in ethanol have been investigated, a wide range of concentration of both reactants being used. The reaction was also studied in the presence of different acids, bases, and salts. The reaction follows second-order kinetics, but still shows the diagnostic features of an ionisation reaction. It is concluded that in the dissociation of the carbon–hydrogen bond of the active methylene group the concentration of the carbanion reaches equilibrium practically instantaneously on dissolution in ethanol. The subsequent steps of the reaction are discussed.

THE present paper describes the kinetics of the reaction of five aromatic aldehydes with malononitrile in 95% ethanol. These reactions follow strictly second-order kinetics and we show that the reaction takes place between the aldehyde and the anion $(CN)_2CH^-$ present in the solution in equilibrium concentration.

RESULTS

The kinetics of the reactions have been measured in ethanol at various concentrations and temperatures. The results (Table 1) show that the second-order rate expression holds over a wide range of concentrations of both reacting substances.

TABLE 1. *Second-order initial rate coefficients* (k_2 *in* mole^{-1} *l. sec.*$^{-1}$) *of the reaction of malononitrile* (MN) *with* p-*hydroxybenzaldehyde* (HA), p-*anisaldehyde* (AA), *benzaldehyde* (BA), p-*chlorobenzaldehyde* (CA), *and* p-*nitrobenzaldehyde* (pNBA), *at various concentrations and temperatures in* 95% *ethanol* (*concentrations in moles l.*$^{-1}$; k_2 *in mole*$^{-1}$ *l. sec.*$^{-1}$).

MN	Aldehyde	10^3k_2 at 40°	MN	Aldehyde	10^3k_2 at 40°	MN	Aldehyde	10^3k_2 at 40°
0·01	0·01 HA	0·885	0·001	0·01 AA	3·34	0·01	0·01 BA	32·8
0·02	,, ,,	0·892	0·002	,, ,,	3·49	0·002	0·002 CA	75·2
0·01	0·02 ,,	0·860	0·004	,, ,,	3·49	0·004	0·002 ,,	80·0
0·02	,, ,,	0·870	0·006	,, ,,	3·07	0·002	0·004 ,,	80·0
0·004	0·004 AA	3·04	0·01	,, ,,	3·25	0·004	0·004 ,,	80·0
0·006	0·006 ,,	3·30	0·02	,, ,,	3·08	0·006	0·006 ,,	72·0
0·008	0·008 ,,	3·01	0·03	,, ,,	3·20	0·008	0·008 ,,	71·1
0·01	0·01 ,,	3·25	0·04	,, ,,	2·97	0·01	0·01 ,,	75·2
,,	0·02 ,,	3·34	0·002	0·002 BA	33·3	0·001	0·001 pNBA	618
0·01	0·03 ,,	3·58	0·004	0·002 ,,	33·3	0·002	,, ,,	584
,,	0·04 ,,	3·34	0·002	0·004 ,,	33·3	0·001	0·002 ,,	616
,,	0·05 ,,	3·28	0·004	0·004 ,,	32·4	0·002	,, ,,	603
,,	0·06 ,,	3·08	0·008	0·008 ,,	31·6			

MN	Aldehyde	10^3k_2 at 30°	10^3k_2 at 35°	MN	Aldehyde	10^3k_2 at 30°	10^3k_2 at 35°
0·01	0·01 HA	0·584	0·718	0·002	0·002 CA	56·5	66·7
0·02	0·02 ,,	0·570	0·710	0·004	0·004 ,,	56·7	66·6
0·01	0·01 AA	2·19	2·70	0·001	0·001 pNBA	461	534
0·002	0·002 BA	23·3	28·0	0·001	0·002 ,,	470	525
0·004	0·004 ,,	23·0	27·1				

Effect of Various Added Substances on the Reaction Rates.—The effect of various added substances, both catalysts and inhibitors, on the reaction rates was also studied (see Table 2). It was found that weak bases (acetamide, pyridine, and aniline) had a very slight effect, whereas stronger bases, such as piperidine and piperidinium salts (acetate and benzoate), benzylamine, and ammonia catalysed the reaction strongly. The catalysed-reaction rates changed in a

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[1] Part VI, preceding paper.

roughly linear manner with the catalyst concentration. To test the relative effects of piperidine and piperidinium benzoate (see p. 2028), experiments were made with 0·002M-piperidine with the addition of various amounts of benzoic acid. This addition definitely inhibited the piperidine-catalysed rates.

The effect of lithium chloride and nitrate on the reaction rates was also investigated; the increase of the rates was roughly proportional to the concentrations of the salts. The salt effect is rather small, a concentration of 0·2M of either enhancing the rates by about 50%.

The inhibiting effect of added acid on the reaction rates was very large. In runs with the reactants at 0·01M-concentration, a concentration of even 0·0002M of perchloric acid had a measurable depressing effect, 0·0004M-perchloric acid reduced the rate to less than one-fifth of the original value, and 0·002M-perchloric acid gave a rate which was slower by a factor of 400,000 than that without the acid. Other acids, *i.e.*, hydrochloric, benzoic, and acetic acid, also inhibited the reaction. The inhibiting effect seems to be roughly proportional to the acid strength (see Table 2).

TABLE 2. *Second-order initial rate coefficients* (k_2 *in* $mole^{-1}$ *l.* $sec.^{-1}$) *of the reaction of* 0·01M-*anisaldehyde with* 0·01M-*malononitrile at* 40° *in ethanol in the presence of various added substances.*

Concn. of added substance *	10^2k_2
None	3·25
0·002M-$AcNH_2$	3·68
,, C_5H_5N	3·72
,, NH_2Ph	3·77
,, $Ph{\cdot}CO_2PipH$	6·20
,, $Me{\cdot}CO_2PipH$	6·43
,, NEt_3	10·50
,, $Ph{\cdot}CH_2{\cdot}NH_2$	11·50
,, Pip	28·40
,, Pip + 0·0002M-$Ph{\cdot}CO_2H$	17·20
,, Pip + 0·0004 ,,	14·80
,, Pip + 0·0008 ,,	10·00
,, Pip + 0·001 ,,	8·30
,, Pip + 0·002 ,,	6·20
0·00004M-Pip	4·00
0·00006 ,,	4·30
0·00008 ,,	4·43
0·00010 ,,	5·09
0·00020 ,,	6·12
0·00200 ,,	28·40
0·001M-$Me{\cdot}CO_2PipH$	5·50
0·002M ,,	6·42
0·003 ,,	7·50
0·006M-$Me{\cdot}CO_2PipH$	10·70
0·008 ,,	12·10
0·010 ,,	13·40
0·0002M-NEt_3	4·75
0·0004 ,,	5·60
0·0006 ,,	6·42
0·0010 ,,	7·75
0·0020 ,,	10·50
0·0100M-LiCl	3·60
0·0200 ,,	3·85
0·0400 ,,	4·01
0·2000 ,,	5·10
0·1000M-$LiNO_3$	5·00
0·1500 ,,	5·36
0·2000 ,,	5·66
None	3·25
0·00002M-$HClO_4$	3·10
0·00004 ,,	0·60
0·00200 ,,	0·000008
0·0004M-HCl	0·167
0·0010M-$Ph{\cdot}CO_2H$	2·30
0·0020M-$Ph{\cdot}CO_2H$	1·90
0·0010M-$Me{\cdot}CO_2H$	2·54

* Pip = piperidine; PipH = piperidinium.

TABLE 3. *Activation energies* (E_A) *for the reaction of different benzaldehydes,* p-$C_6H_4R{\cdot}CHO$, *with malononitrile in ethanol.*

R	OH	MeO	H	Cl	NO_2
E_A (cal./mole)	7800	7550	6400	6100	4800

TABLE 4. *Equilibrium constant* $K = [AMN][H_2O]/[AA][MN]$ *for forward and reverse reactions.*

Starting materials (mole/l.) (AA)	(MN)	H_2O	(AMN)	(AMN) at equilibrium (mole/l.)	K *
0·01	0·01	2·78	—	0·0081	6250
0·01	0·01	2·78	—	0·0081	6250
0·01	0·01	2·78	—	0·0082	7050
0·01	0·01	2·78	—	0·0080	5560
0·01	0·01	2·78	—	0·00815	6700
0·01	0·01	8·05	—	0·0071	6800
0·006	0·01	2·78	—	0·0055	6800
—	—	2·78	0·01	0·00805	5900
—	—	2·78	0·01	0·0082	7050

* The equilibrium constant *K* is very sensitive to small differences in the experimental determination, and a difference of 2% in the determination of the equilibrium concentration of anisylidene-malononitrile causes a difference of more than 20% in the value of the constant.

Activation Energies.—From the results in Table 1, the activation energies were calculated (see Table 3) for the reaction of malononitrile with the five aromatic aldehydes studied.

Reversibility and Equilibria.—The reaction is reversible, and practically identical equilibria were reached under identical conditions, whether starting from *p*-anisaldehyde (AA) and malononitrile (MN) or from the condensation product (AMN) (see Table 4). Addition of water to the " forward " reaction mixture, although enhancing the initial rates, displaced the equilibrium position towards the starting materials. In all cases the equilibrium constant, K, calculated from the equation $K = [AMN][H_2O]/[AA][MN]$, gave reasonably constant values for different reactions both in the " forward " and the " reverse " direction. If anisylidenemalononitrile was dissolved in a 0·001M-solution of perchloric acid in ethanol, no measurable reverse reaction took place during 48 hr.

Discussion

The foregoing results show that in changing the solvent from water [1] to 95% ethanol, the kinetics of the reaction change from first to second order. The rate coefficients with different *para*-substituted benzaldehydes give the following series: $NO_2 > Cl > H > MeO > OH$. This is the order which is to be expected in view of the influence of the different *para*-substituents on the development of a positive charge on the carbonyl-carbon atom, and it is the same order as is found for bimolecular nucleophilic substitution in aromatic compounds.[2] Obviously, the common factor in aromatic S_N2 reactions and the present case is the presence of a positively charged reaction site.

The results in Table 1 show that the reaction is of first order in each of the reacting substances. Nevertheless, the runs in the presence of acids (Table 2) show the characteristic and diagnostic feature of a unimolecular reaction, *i.e.*, depression of the rate by common ions. We believe, therefore, that the mechanism of the reaction is the following:

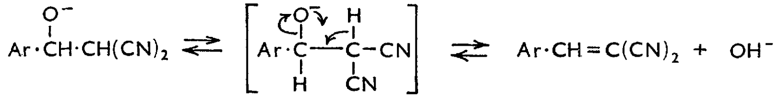
$$CH_2(CN)_2 \underset{\text{Fast}}{\overset{\text{Fast}}{\rightleftharpoons}} {}^-CH(CN)_2 + H^+ \qquad (1)$$

$$Ar{\cdot}CHO + {}^-CH(CN)_2 \xrightarrow[\text{Slow}]{} {}^-O{\cdot}CHAr{\cdot}CH(CN)_2 \qquad (2)$$

$${}^-O{\cdot}CHAr{\cdot}CH(CN)_2 \xrightarrow[H^+]{\text{Fast}} HO{\cdot}CHAr{\cdot}CH(CN)_2 \xrightarrow{\text{Fast}} Ar{\cdot}CH{=}C(CN)_2 \qquad (3)$$

According to this scheme the equilibrium (1) is immediately established on dissolution of malononitrile in ethanol. The overall reaction rates will then be of first order in each of the reactants, the amount of malononitrile anions being proportional to the total amount of the malononitrile present. The rate depression caused by added acids can be explained by the mass-law effect of added hydrogen ions on the equilibrium.

As no difference was found between reaction rates, whether measured by the disappearance of the aldehyde or, as usual, by the appearance of the product, we conclude that no intermediate is accumulating in the reaction mixture, at least not in measurable quantities. Therefore, we assume that the steps following step (2) are fast. We believe that the formation of the double bond in the product may take place through a four centre transition step, in which the protonation of the intermediate (3) is not necessary:



Such a mechanism, in which a hydroxyl ion is eliminated in the final, product-forming step, would help to explain the fact that protonic acids inhibit both the forward and the reverse reactions. This inhibition would then be the result of a common-ion effect in the rate-determining forward step (1), and an inhibition of the reverse reaction by the reduction of the concentration of hydroxyl ions in the solvent.

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[2] Bunnett and Zahler, *Chem. Rev.*, 1951, **49**, 273.

The fact that in pure water the dissociation of the malononitrile is the main rate-determining step, while in ethanol a pre-equilibrium is established instantaneously, shows that, at least for the purpose of the present case, *i.e.*, for assisting the dissociation of the carbon–hydrogen bond of malononitrile, ethanol is a stronger base than water (see discussion in preceding and following papers). For the explanation of our results it is necessary to assume that co-operation of several phenomena, *e.g.*, nucleophilicity, solvation of both ions formed, etc., establishes an equilibrium faster in ethanol than in water.

The influence of various bases on the reaction rates has been investigated in some detail. It has been claimed by Cope [3] that ammonium salts and salts of organic amines with organic acids are better catalysts for Knoevenagel-type condensations than are the free bases. This was explained in terms of Brønsted's theory of acid–base catalysis.[4] Cope's results are based on yields of product (from the reaction of ketones with cyanoacetic esters) recovered after a standard reaction period in the presence of the various catalysts. Now, yields do not always reflect reaction rates, and this may well be the cause of the discrepancy between Cope's results and ours. In a similar reaction (*i.e.*, the Perkin condensation of aromatic aldehydes with acetic anhydride in the presence of potassium acetate) it was found [5] that the yield of the product falls considerably with time after reaching a maximum value. On the other hand, it has also been observed that added acetic acid has a retarding effect on the Perkin condensation.[6]

According to our reaction scheme the reaction rates will be proportional to the amount of the carbanions formed from the active methylene compound. Therefore, any substance in the reaction mixture, which is able to supply protons, will depress the reaction rates by depressing the ionisation of the active methylene group. Accordingly, we have to expect that piperidinium acetate or benzoate must be a weaker catalyst than piperidine alone, owing to equilibria of the type:

$$C_5H_{10}NH_2{\cdot}OAc \rightleftharpoons C_5H_{10}NH + {}^-OAc + H^+$$

Even though the absolute amount of protons supplied by the salts is small, it is probably still large in comparison with the dissociation of the active methylene group. This is demonstrated in the series of experiments where to a standard reaction mixture of anisaldehyde, malononitrile, and piperidine in ethanol, varying amounts of benzoic acid were added (see Table 2). The retarding effect of the acid is especially large on the addition of small amounts of benzoic acid, *e.g.*, the rate with 0·02M-piperidine is about twice as high as the rate with the same concentration of base in the presence of 0·004M-benzoic acid.

The effect of different bases, in identical concentrations, is, as expected, in about the same order as their basic strengths. With different concentrations of the same base, the rates are roughly proportional to its concentration in the reaction mixture. Both these facts can be explained by the effect of basic strength and the concentration of the catalyst on the dissociation equilibrium of the malononitrile.

The effect of salts added to the reaction mixture was rather small. Lithium chloride and nitrate had about the same influence, the effect of the latter being slightly larger.

The magnitudes of the activation energies of the reactions of malononitrile with the different aldehydes are in the order expected from the effect of the *para*-substituents, *i.e.*, $OH > MeO > H > Cl > NO_2$. The values obtained are rather low (5—8 kcal./mole).

The Hammett Equation.—We plotted the logarithms of the rate coefficients for the reactions of the five aldehydes against the corresponding Hammett substituent constants. With the values given by Jaffe [7] the correlation was rather poor. On the other hand, with

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[3] Cope, *J. Amer. Chem. Soc.*, 1937, **59**, 2327.

[4] Brønsted, *Chem. Rev.*, 1928, **5**, 231.

[5] Chapell, Thesis, Cornell University, 1933, quoted in " Organic Reactions," Vol. I, p. 238.

[6] Kalnin, *Helv. Chim. Acta*, 1928, **11**, 977.

[7] Jaffe, *Chem. Rev.*, 1953, **53**, 191.

Brown's σ values,[8] all points except that for *p*-hydroxybenzaldehyde fell on a straight line. From the slope of this line the reaction constant ρ was calculated to be +1·45. The deviation of the value for *p*-hydroxybenzaldehyde is easily explained by the fact that this aldehyde contains a strongly acidic phenolic group. The acid dissociation of this group retards the reaction owing to its common-ion effect on the dissociation of the active methylene group. Indeed, the value of *p*-hydroxybenzaldehyde lies below the line connecting the other points, *i.e.*, the rate is slower than would be expected from the Hammett relation.

EXPERIMENTAL

Materials.—These were purified as described in the preceding paper.

Spectral Data.—As several of our absorption data are different from previously published values, both are given in Table 5. Numbers in parentheses are values found in the literature.

Analysis of Products.—The substituted benzylidenemalononitriles obtained in the reaction had the same m. p.s as described in the literature.[9]

Kinetic Runs.—Stock solutions of the reactants in ethanol were kept in the dark, as malononitrile tended to decompose in the light. These solutions were unchanged, as checked frequently by their spectra, for 3—4 days. The runs were carried out in stoppered bottles in a thermostat bath; samples were taken at intervals of 3—5 min. at the beginning and at greater intervals later, and quenched by strong dilution with ethanol (25—100-fold), and the absorption of the product at its $\lambda_{max.}$ was measured immediately. At that wavelength, the absorption of the other compounds present in the mixture could be neglected, except that with *p*-nitrobenzylidenemalononitrile the absorption had to be corrected for the *p*-nitrobenzaldehyde present.

TABLE 5. *Spectral data.*

	Aldehydes (p-X·C_6H_4·CHO)		Benzylidenemalononitriles [p-X·C_6H_4·CH=C(CN)$_2$]			Aldehydes (p-X·C_6H_4·CHO)		Benzylidenemalononitriles [p-X·C_6H_4·CH=C(CN)$_2$]	
X	$\lambda_{max.}$ (mμ)	10^{-2} ε	$\lambda_{max.}$ (mμ)	10^{-2} ε	X	$\lambda_{max.}$ (mμ)	10^{-2} ε	$\lambda_{max.}$ (mμ)	10^{-2} ε
H	246	126	308	220	HO ...	285	146	433	433
	(244)	(130) [a]	(307)	(216) [b]		(281·5)	(140) [a]		
MeO ...	281	163	351	303	Cl ...	257	165	319	240
	(276·5)	(155) [a]	(348)	(312) [b]	NO_2 ...	265	114	306	200
						(265)	(114)	(303)	(157) [d]
						306	18		

[a] Burawoy and Chamberlain, *J.*, 1952, 2312. [b] Jansen, Engelhardt, and Middleton, *J. Amer. Chem. Soc.*, 1958, **80**, 2815. [c] Walter and Young, *J.*, 1957, 2041. [d] Kertel and Hoffmann, *Z. phys. Chem.*, 1941, *B*, **50**, 390.

Calculations.—The initial second-order rate coefficients were calculated from the integrated form of the equation $dx/dt = k(a - x)(b - x)$, where a and b are the concentrations of the aldehyde and of the malononitrile respectively, and x is the amount which had reacted at time t. The value of k_2t was plotted against t, and k_2 calculated from the slope. Data for a typical run were as tabulated.

Reaction of 0·05M-*anisaldehyde with* 0·01M-*malononitrile at* 40° *in ethanol. Samples diluted* 100-*fold.*

Time (sec.)	60	300	600	840	1140	1380	1680	1860	2400
D	0·024	0·156	0·290	0·40	0·502	0·61	0·70	0·78	0·96
Product formed (10^4M)	0·8	5·2	9·7	13·2	16·8	20·4	23·4	26·0	32·0
k_2t	0·161	1·03	2·06	2·86	3·72	4·65	5·42	6·20	7·95
10^3k_2	2·69	3·44	3·44	3·42	3·29	3·36	3·25	3·32	3·32

k_2 from graph: $3·28 \times 10^{-3}$ mole^{-1} l. sec.$^{-1}$.

Control Experiments.—Some runs were made with *p*-anisaldehyde and malononitrile in which the absorption of the samples was measured both at 351 mμ ($\lambda_{max.}$ for the product) and at 282 mμ ($\lambda_{max.}$ for the aldehyde). The values calculated from the disappearance of the carbonyl absorption followed roughly the same line as those calculated from the absorption of the product. As found previously,[1] the reproducibility of the carbonyl absorption values

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[8] Brown and Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4980.

[9] Corson and Stoughton, *J. Amer. Chem. Soc.*, 1928, **50**, 2825; Hertel and Hoffmann, *Z. phys. Chem.*, 1941, *B*, **50**, 382.

was lower and the deviations were generally greater. Nevertheless, the results proved that no appreciable hold-up of intermediate product occurred.

Equilibrium Measurement.—These runs were left at 40° for several days, until the absorpton measurements showed no more change.

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