412. *The Kinetics and Mechanisms of Carbonyl–Methylene Condensations. Part VIII.*[1] *The Reaction of Ethyl Cyanoacetate with Aromatic Aldehydes in Ethanol, in Water, and in Ethanol–Water Mixtures.*

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The reaction of ethyl cyanoacetate with five aromatic aldehydes in ethanol, in water, and in ethanol–water mixtures was studied. The effect of various acids, bases, and salts on the reaction was also determined. It is concluded from the kinetic results that the first step of the reaction is the dissociation of the active C–H bond of ethyl cyanoacetate, followed by a reaction between the carbanion so formed and the aldehyde. The mechanism of the reaction and its dependence on the various factors studied are discussed.

IN the two preceding papers we described the reaction of malononitrile with aromatic aldehydes. The kinetic results of these investigations were explained by a mechanism

TABLE 1. *First- and second-order initial rate coefficients of the reaction of ethyl cyanoacetate* (ECA) *with anisaldehyde* (AA), p-*tolualdehyde* (TA), *benzaldehyde* (BA), *and* m-*nitro-* (mNBA) *and* p-*nitro-benzaldehyde* (pNBA) *in* 95% *ethanol at* 40° (*unless otherwise stated*) (*concentrations in mole l.*$^{-1}$).

ECA	R·CHO	10^6k_1 (sec.$^{-1}$)	10^4k_2 (mole^{-1} l. sec.$^{-1}$)
0·002	0·005 AA	0·74	1·48
0·005	0·002 ,,	0·32	1·58
,,	0·005 ,,	0·80	1·61
,,	0·010 ,,	1·42	1·42
0·0045	0·020	2·74	1·37
0·005	0·05 ,,	3·75	0·75
0·01	0·01 ,,	0·98	0·98
0·01134 †	0·01 ,,	0·94	0·94
0·01134	0·02 ,,	2·38	1·19
,,	0·05 ,,	6·0	1·20
0·005 [a]	,, ,,	0·834	0·834
,, [a]	0·02 ,,	1·400	0·700
0·010 [a]	0·005 ,,	0·396	0·792
,, [a]	0·010 ,,	0·715	0·715
,, [a]	,, ,,	0·690	0·690
,, [a]	0·02 ,,	1·352	0·676
0·005	0·005 TA	3·74	7·48
0·01	,, ,,	4·02	8·04
,,	0·010 ,,	6·5	6·5
,,	0·02 ,,	12·2	6·10
0·02	0·005 ,,	2·99	5·98
,,	0·010 ,,	6·50	6·50
,,	0·02 ,,	13·0	6·50
0·03	0·01 ,,	5·36	5·36
0·05	0·005 ,,	2·74	5·48
,,	0·01 ,,	4·90	4·90
,,	0·02 ,,	11·0	5·50
0·10	0·01 ,,	4·49	4·49
0·01	0·01 BA	6·98	6·98
,,	0·02 ,,	10·41	5·20
,,	0·03 ,,	13·68	4·56
,,	0·05 ,,	18·32	3·66
0·02	0·01 ,,	5·24	5·24
0·2	0·02 BA	8·68	4·34
,,	0·05 ,,	14·84	2·93
0·03	0·01 ,,	4·63	4·63
0·04	0·04 ,,	8·06	2·01
0·05	0·01 ,,	1·4	1·4
,,	0·02 ,,	2·81	1·41
0·001	0·002 mNBA	75·5	378
,,	0·005 ,,	190·0	280
,,	0·01 ,,	348·0	348
0·005	0·001 ,,	36·4	365
,,	0·005 ,,	172·4	345
0·005	0·005 ,,	158·0	316
,,	0·010 ,,	350·0	350
0·01	0·005 ,,	175·0	350
0·0003	0·0003 pNBA	18·1	604
,,	0·001 ,,	58·7	587
0·0005 ‡	0·0005 ,,	27·0	540
,, ‡	,, ,,	29·2	584
,,	0·001 ,,	52·4	524
0·0007	0·0007 ,,	40·5	578
,,	0·001 ,,	56·9	569
0·001	0·0003 ,,	17·7	590
,,	0·0005 ,,	27·0	540
,,	0·0007 ,,	39·4	563
,,	0·001 ,,	58·8	588
0·002	0·001 ,,	48·2	482
,,	,, ,,	55·8	558
0·005	0·0002 ,,	10·4	519
0·0005 [a]	0·0005 ,,	24·0	480
0·001 [a]	0·001 ,,	46·8	468
0·002 [a]	,, ,,	46·3	463
,, [a]	0·002 ,,	81·8	409

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[1] Parts VI and VII, preceding papers.

TABLE 1. (*Continued.*)

ECA	R·CHO	Added *	10^6k_1 (sec.$^{-1}$)	10^4k_2 (mole^{-1} l. sec.$^{-1}$)
0·01134 †	0·010 AA	0·00000484 Pip	3·88	3·88
,,	,, ,,	0·00000968 ,,	4·63	4·63
,,	,, ,,	0·000017 ,,	5·56	5·56
,,	,, ,,	0·0000242 ,,	7·02	7·02
0·01	0·01 BA	0·01 LiCl	11·53	11·53
,,	,, ,,	0·075 ,,	16·42	16·42
,,	,, ,,	0·100 ,,	17·24	17·24
,,	,, ,,	0·01 LiNO$_3$	11·53	11·53
,,	,, ,,	0·075 ,,	17·14	17·14
,,	,, ,,	0·00059 Me·CO$_2$PipH	14·11	14·11
,,	,, ,,	0·00059 HClO$_4$	0·0	0·0
,,	,, ,,	1% H$_2$O	10·35	10·35
,,	,, ,,	2% ,,	12·89	12·89
,,	,, ,,	3% ,,	16·80	16·80
,,	,, ,,	5% ,,	18·46	18·46
,,	,, ,,	10% ,,	19·88	19·88
,,	,, ,,	15% ,,	21·28	21·28
,,	,, ,,	20% ,,	23·35	23·35
,,	,, ,,	25% ,,	23·94	23·94
0·0005 ‡	0·0005 pNBA	0·00000484 Pip	34·0	680
,,	,, ,,	0·0000145 ,,	42·4	848
,,	,, ,,	0·0000242 ,,	50·5	1010
,,	,, ,,	0·0000484 ,,	56·5	1130
,,	,, ,,	0·0000965 ,,	69·0	1380
,,	,, ,,	0·00000488 HClO$_4$	29·2	584
,,	,, ,,	0·00000972 ,,	26·6	532
,,	,, ,,	0·0000195 ,,	25·6	512
,,	,, ,,	0·0000488 ,,	21·2	423
,,	,, ,,	0·000195 ,,	0·0	0·0
,,	,, ,,	(2%) H$_2$O	40·2	804
,,	,, ,,	(4%) ,,	46·8	937
,,	,, ,,	(20%) ,,	151·0	3020
,,	,, ,,	(30%) ,,	198·0	3960

* Pip = piperidine; PipH = piperidinium. [a] At 30°. † ‡ See text.

in which the governing (although not necessarily the rate-determining) step was the ionic dissociation of one of the C–H bonds of the active methylene group. The present paper describes the kinetics of the reaction of ethyl cyanoacetate with various aromatic aldehydes in ethanol, in water, and in their mixtures.

RESULTS

The kinetic results are summarised in Tables 1 and 2. As the reaction rate coefficients showed marked drifts in several cases, both first- and second-order initial rate coefficients have been calculated and are given.

In ethanol, with *p*-anisaldehyde, the variation in k_1 was about 20-fold over the concentration range studied, while the variation in k_2 was only about 2-fold. With *p*-tolualdehyde agreement with second-order kinetics was much better, the deviations being only about 20% of the average value. Benzaldehyde gave a rather poor fit for both k_1 and k_2 even though the concentration ranges covered were rather narrow. Both *m*- and *p*-nitrobenzaldehyde conformed quite well to second-order kinetics.

In water, the rate coefficients of the less reactive aldehydes, *i.e.*, *p*-anisaldehyde and *p*-tolualdehyde, fit neither the first- nor the second-order rate equation, although conforming somewhat better with the latter. With benzaldehyde, the first-order rate coefficients give a better fit than the second-order ones: they give a fairly good fit to the first-order rate equation with 0·002M of the methylene compound and 0·001—0·005M of benzaldehyde. When the methylene compound is in excess, the fit to the first-order equation is less good; with *p*-chlorobenzaldehyde, k_1 is reasonably constant. With *p*-bromobenzaldehyde only four runs were made, and these conform somewhat better to the first- than to the second-order rate equation. With *m*-nitrobenzaldehyde the order is intermediate, and *p*-nitrobenzaldehyde gave results which fit very well to the second-order rate equation.

TABLE 2. *First- and second-order initial rate coefficients of the reaction of ethyl cyanoacetate* (ECA) *with anisaldehyde* (AA), p-*tolualdehyde* (TA), *benzaldehyde* (BA), p-*chlorobenzaldehyde* (CA), p-*bromobenzaldehyde* (BRA), m-*nitrobenzaldehyde* (mNBA), *and* p-*nitrobenzaldehyde* (pNBA) *in water at* 32° (*unless otherwise stated*) (*concentrations in mole l.*$^{-1}$).

ECA	R·CHO	10^5k_1 (sec.$^{-1}$)	10^2k_2 (mole^{-1} l. sec.$^{-1}$)
0·001	0·001 AA	0·126	0·126
,,	0·002 ,,	0·286	0·143
0·002	0·001 ,,	0·141	0·141
,,	0·002 ,,	0·244	0·122
,,	0·005 ,,	0·444	0·089
0·003	0·003 ,,	0·389	0·130
0·004	0·004 ,,	0·325	0·081
0·005	0·002 ,,	0·197	0·098
,,	0·005 ,,	0·394	0·079
0·001 [a]	0·002 ,,	0·567	0·284
0·002 [a]	,, ,,	0·339	0·170
0·005 [a]	,, ,,	0·368	0·184
0·001	0·001 TA	0·58	0·58
,,	,, ,,	0·61	0·61
,,	0·002 ,,	1·38	0·69
,,	,, ,,	1·30	0·65
,,	0·005 ,,	3·90	0·78
0·002	0·001 ,,	0·45	0·45
,,	0·002 ,,	1·30	0·65
,,	0·005 ,,	2·54	0·51
0·005	,, ,,	1·70	0·34
0·001	0·001 BA	0·67	0·67
,,	0·002 ,,	0·92	0·46
,,	0·005 ,,	0·90	0·18
0·002	0·001 ,,	0·57	0·57
,,	0·002 ,,	0·67	0·34
,,	0·005 ,,	0·69	0·14
0·005	0·001 ,,	0·57	0·57
,,	0·002 ,,	1·22	0·61
,,	,, ,,	1·32	0·66
,,	0·005 ,,	1·81	0·36
,,	,, ,,	1·32	0·26
0·001 [a]	0·002 ,,	2·62	1·31
0·002 [a]	,, ,,	2·40	1·20
0·005 [a]	,, ,,	2·01	1·00
0·001	0·001 CA	2·23	2·23
,,	,,	1·91	1·91
0·001	0·002 CA	1·94	0·97
,,	0·005 ,,	2·40	0·48
0·002	0·001 ,,	1·80	1·80
,,	0·002 ,,	2·33	1·16
,,	0·005 ,,	2·11	0·42
0·005	,, ,,	1·93	0·39
0·001	0·001 BRA	2·48	2·48
,,	0·002 ,,	3·76	1·88
0·002	0·001 ,,	2·14	2·14
,,	0·002 ,,	2·92	1·46
0·00025	0·005 mNBA	2·88	5·76
0·0005	0·0005 ,,	2·56	5·12
,,	0·001 ,,	4·14	4·14
0·001	0·0005 ,,	2·07	4·14
0·001	0·001 ,,	5·2	5·2
,,	0·002 ,,	9·3	4·65
,,	,, ,,	8·9	4·45
0·002	0·001 ,,	5·27	5·27
,,	,,	5·98	5·98
,,	0·002 ,,	7·55	3·78
0·005	0·001 ,,	5·09	5·09
,,	,, ,,	5·31	5·31
,,	0·002 ,,	5·03	2·52
,,	,,	5·35	2·68
0·001 [a]	0·001 ,,	9·02	9·02
0·002 [a]	,, ,,	8·40	8·40
0·005 [a]	,, ,,	7·16	7·16
0·001	0·001 pNBA	29·8	29·8
,,	,, ,,	33·3	33·3
,,	0·002 ,,	58·3	29·2
,,	,, ,,	62·2	31·1
,,	0·005 ,,	120·0	24·0
0·002	0·001 ,,	28·2	28·2
,,	0·002 ,,	60·0	30·0
,,	0·005 ,,	13·90	27·8
0·005	0·005 ,,	137·5	27·5

ECA	R·CHO	Added $HClO_4$ (10^{-4} mole l.$^{-1}$)	10^5k_1 (sec.$^{-1}$)	10^2k_2 (mole^{-1} l. sec.$^{-1}$)
0·002	0·002 AA	0·24	0·152	0·076
,,	,,	0·96	0·048	0·024
,,	,, BA	0·48	0·40	0·20
,,	,,	0·96	0·24	0·12
,,	,, mNBA	0·48	4·02	2·01
,,	,,	0·96	2·26	1·13
,,	,, pNBA	1·0	10·5	5·25
,,	,,	5·0	1·7	0·85

[a] At 40°.

Effect of Added Acids, Bases, and Salts.—Addition of relatively small amounts of perchloric acid to the reaction mixture strongly depressed the reaction, and somewhat larger acid concentrations stopped it completely, both in water and in ethanol.

Addition of piperidine to the ethanolic reaction mixture increased the reaction rates, its effect being proportional to its concentration at very low concentrations. At somewhat higher base concentrations the effect was weaker. When the uncatalysed reaction was slow, *e.g.*, with *p*-anisaldehyde, the effect of the first, very small, amount of base (0·00000484M) was considerable (compare runs marked †), whereas the effect of the same amount of base was relatively small on a reaction, the non-catalysed rate of which was already comparatively fast (*e.g.*, with *p*-nitrobenzaldehyde, compare runs marked ‡). After this initial difference, the effect of small amounts of base on the rates was very similar. When 10^4k_2 for *p*-nitrobenzaldehyde and anisaldehyde is plotted against the piperidine concentration the two lines obtained run parallel to each other up to 0·0000242M of the base; thus, although the rates differ from each other with the two aldehydes by a factor of about 200, the absolute effect of the catalysts in both cases is the same.

Some experiments were made in ethanol with benzaldehyde, lithium chloride or nitrate being added to the reaction mixture. Their effect in similar concentrations was practically identical. Relatively the strongest accelerating effect was observed at the lowest concentration (0·01M) of the salt.

Addition of water to the ethanolic reaction mixture also accelerated the rates, although water, as one of the products of the reaction, must have also a retarding (mass-law) effect. To obtain more information on this point, the reaction rates of *p*-anisaldehyde, benzaldehyde, and *m*-nitrobenzaldehyde with ethyl cyanoacetate in various concentrations were measured at 32° and at 40° in different water–ethanol mixtures (Table 3). As with malononitrile [1] the rate–solvent composition graphs at 32° showed a maximum at 20—30% (w/w) of ethanol. From this maximum, the slope of the line leading towards pure water is generally steeper than that of the line leading towards pure ethanol. Moreover, the slope of the line tends to lessen as it approaches the highest ethanol concentrations, so the effect of added ethanol after about 60% is relatively less. At 40° fewer experiments were made, but these show that the general trend is the same, except that anisaldehyde and benzaldehyde give maximum rates in solvents which contain somewhat less ethanol, *i.e.*, only 15—20% w/w.

TABLE 3. *First-order rate coefficients* (10^5k_1 *sec.*$^{-1}$) *for the reaction of anisaldehyde* (AA), *benzaldehyde* (BA), *and* m-*nitrobenzaldehyde* (mNBA) *with ethyl cyanoacetate* (ECA) *in various water–ethanol mixtures at* 32° *and* 40°.

Solvent (w/w% EtOH)			0	7·77	15·69	23·61	32·74	42·06	56·31	73·47
ECA (mole l.$^{-1}$)	Aldehyde	Temp.								
0·001	0·002 AA	32°	0·286	0·430	0·529	0·524	0·427		0·209	0·130
0·002	,, ,,	,,	0·244	0·350	0·494	0·345	0·334		0·186	0·106
,,	0·005 ,,	,,	0·444	0·875	1·16	1·14	0·767		0·480	0·232
0·005	0·002 ,,	,,	0·197	0·282	0·334	0·456	0·279		0·199	0·102
,,	0·005 ,,	,,	0·394	0·736		1·06	0·679		0·476	0·204
0·001	0·002 ,,	40	0·567		0·635	0·650	0·496		0·450	
0·002	,, ,,	,,	0·339	0·540	0·645	0·535	0·460		0·262	
0·005	,, ,,	,,	0·368	0·370	0·600	0·494	0·414			
0·001	0·002 BA	32	0·92	1·02	1·91	2·84	2·18		1·69	0·57
,,	0·005 ,,	,,	0·90	0·94	1·48	1·31	2·51		1·79	
0·002	0·002 ,,	,,	0·67	1·14	2·32	1·99	2·10		1·68	0·52
,,	0·005 ,,	,,	0·69		1·29	1·35	2·05		1·76	0·54
0·005	0·002 ,,	,,	1·22		1·70	1·76	1·86		1·57	0·51
,,	0·005 ,,	,,	1·32		1·10	1·39	1·83		1·66	0·46
0·001	0·002 ,,	40	2·66		3·46	3·26	3·20			
0·002	,, ,,	,,	2·44		3·06	3·17	2·96			
0·005	,, ,,	,,	2·04		2·95	2·58	1·89			
0·00025	0·005 mNBA	32	2·88		5·04	5·68	7·00	5·96	5·80	3·76
0·0005	,, ,,	,,	2·56	3·46	4·66	6·08		5·80	5·40	3·84
0·001	,, ,,	,,	2·07	4·10	4·44	5·61	6·12		4·92	3·39
,,	0·001 ,,	,,	5·20	8·24	11·90	13·15	12·70	11·18	8·53	7·71
0·002	,, ,,	,,	5·27	7·92	10·67	11·68	12·60	10·50	9·18	6·79
0·005	,, ,,	,,	5·09	5·50	8·85	9·82	11·40	9·23	7·55	6·18
0·001	,, ,,	40	9·02	11·87	17·20	15·70		12·98		
0·002	,, ,,	,,	8·40	11·56	14·35	15·12	15·50	15·04		
0·005	,, ,,	,,	7·16	9·31	12·78	13·80	14·58			

Activation Energies.—The activation energies were calculated for *p*-methoxy- and *p*-nitrobenzaldehyde, from the mean of the values given in Table 1 at 30° and at 40°, being 9400 and 3800 cal./mole, respectively. Owing to large deviations from both k_1 and k_2 in Table 2, no activation energies were calculated for the reaction in water.

DISCUSSION

The reaction of aromatic aldehydes with ethyl cyanoacetate, like their reaction with malononitrile,[1] shows the diagnostic features of a dissociation-governed reaction, *i.e.*, the inhibition by added common (hydrogen) ions and a considerable positive salt effect. Nevertheless, the overall rates follow very nearly second-order kinetics in ethanol and varying orders with different aldehydes in water. We believe that the reaction scheme proposed for the condensations with malononitrile can be applied to the present case too. The marked effect of added protonic acids can be reasonably explained by the mass-law effect of the common hydrogen ions on the dissociation (1). This effect will retard, or even completely inhibit the reaction in all cases, whether step (1) is rate-determining or not. The observed overall rates will be determined by the relative magnitudes of the rate coefficients k_1, k_2, and k_3. In the case of the reaction in ethanol, rates are approximately of second order, and we believe that this means that step (1) is practically instantaneous (in both directions), and the reaction of the carbanion with the aldehyde becomes the rate-determining step. The possibility of a slow, rate-determining reaction between the aldehyde and the undissociated ethyl cyanoacetate molecule is excluded by the inhibiting effect of added acid. Deviations from the second-order rate law were largest when the aldehyde was in a large (5- or 10-fold) excess over the ethyl cyanoacetate, giving lower second-order rate coefficients. This may have been caused, at least partly, by traces of acid impurities in the aldehyde used, and also by the inherent tendency of a reactant in excess to " weigh " less than its actual molar concentration. Even so, the maximum deviation from the mean of 12 runs with anisaldehyde at 40° (1·17 mole^{-1} sec.$^{-1}$) is only about $\pm 40\%$, although these runs cover a concentration range of aldehyde from 0·002M to 0·011M. With *p*-tolualdehyde, covering a 10-fold concentration range in the ethyl cyanoacetate and a 4-fold concentration range in the aldehyde, the maximum deviation from the mean second-order rate coefficient of 12 runs is about $\pm 20\%$. With both *m*- and *p*-nitrobenzaldehyde the second-order rate law is obeyed satisfactorily in the concentration range studied.

$$\mathrm{CH_2(CN)\cdot CO_2Et} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} {}^{-}\mathrm{CH(CN)\cdot CO_2Et} + \mathrm{H^+} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

$$\mathrm{X\cdot C_6H_4\cdot CHO} + {}^{-}\mathrm{CH(CN)\cdot CO_2Et} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} {}^{-}\mathrm{O\cdot CH(C_6H_4X)\cdot CH(CN)\cdot CO_2Et} \quad . \; . \; . \quad (2)$$

$${}^{-}\mathrm{O\cdot CH(C_6H_4X)\cdot CH(CN)\cdot CO_2Et} \xrightarrow[\text{(several steps)}]{k_3} \mathrm{X\cdot C_6H_4\cdot CH{=}C(CN)\cdot CO_2Et} \quad . \; . \; . \; . \; . \quad (3)$$

The least satisfactory results were obtained with benzaldehyde. According to our reaction scheme, with the same active methylene compound, the more reactive aldehydes should have a tendency to approach first-order kinetics, and the less reactive to approach second-order kinetics. Now, in the present case the fastest aldehydes give good second-order kinetics, and so the much slower benzaldehyde would also be expected to obey the second-order rate law accurately. Nevertheless, in runs covering a concentration range of only 5-fold in both aldehyde and ethyl cyanoacetate, the second-order rate coefficients vary from 1·4 to 6·98 mole^{-1} sec.$^{-1}$. Benzaldehyde is the most difficult aldehyde to work with; it oxidises very easily and its solutions in ethanol are less stable than those of other aromatic aldehydes. It may well be, therefore, that the results with benzaldehyde are poor owing to experimental difficulties.

On the other hand, a slow rate-determining dissociation followed by much faster subsequent steps should result in overall first-order kinetics, independently of the nature and concentration of the aldehyde. Although this condition is never fully satisfied, the observed reaction rates in water indicate that, at least with some aldehydes, the reaction approaches such a mechanism.

In water, anisaldehyde and *p*-tolualdehyde give nearly second-order kinetics; benzaldehyde gives an intermediate order, but the rates conform better to the first- than to the second-order rate equation; *p*-chlorobenzaldehyde gives a fairly good fit to the first-order rate equation, whereas *p*-bromo- and *p*-nitro-benzaldehyde approach second-order kinetics. Our results can be summarised thus:

Substituent	*p*-MeO	*p*-CH_3	H	*p*-Cl	*p*-Br	*m*-NO_2	*p*-NO_2
Overall rate	Slow	⟶	⟶	⟶	⟶	⟶	Fast
Reaction order ...	2nd	⟶	⟶	1st	⟶	⟶	2nd

The first part of this sequence is easily understandable in terms of our hypothesis regarding the mechanism of the reaction, but we cannot suggest a satisfactory explanation for the change in reaction order in the second part of the series.

The approach to second-order kinetics in water with the " fast " aldehydes could be, at least in part, due to a complex-formation between these aldehydes and the active methylene compound. If the formation of such a complex would give a geometrically favourable configuration for the subsequent reaction, then the complex-formation could be the rate-determining step, but the reaction would be still inhibited by added acids, as the ionisation of the C–H bond of the active methylene compound incorporated in the complex could still be a necessary step for the subsequent reaction. The fact that substituents in the aldehyde which activate the carbonyl group are those which also may be expected to favour complex-formation may be significant in this connection. Such a complex may be held together by interaction between the $\overset{\delta+}{C}=\overset{\delta-}{O}$ dipole of the aldehyde and the $\overset{\delta-}{C}-\overset{\delta+}{H}$ dipole of the active methylene compound. Owing to the fast reaction between the reactants, we could devise no experiment to prove or disprove this hypothesis by, *e.g.*, measuring differences in the absorption spectra of the two reactants alone or mixed together.

An additional complicating factor may be the low solubility of the aromatic aldehyde in water. Even if a solution does not precipitate the solute after long standing, it is by no means certain that a solute such as *p*-nitrobenzaldehyde in a solvent such as water is in true molecular solution, for it may be present as small or large aggregates. If so, then in these cases the stoicheiometric concentrations are meaningless for kinetic purposes, as the terms in the conventional rate equations will not reflect the actual concentrations of particles per unit volume. For instance, in a unimolecular reaction where $A \xrightarrow{v_1} B$ and $B + C \xrightarrow{v_2}$ Product, and $v_1 < v_2$, v_1 will be rate-determining only if the concentration of C is comparable with that of A, and the overall rate will tend to conform to second-order kinetics if $[C] \ll [A]$.[2] In these equations it is assumed that the stoicheiometric concentrations of A and C are identical with or proportional to the actual number of reactant particles per unit volume. If, however, the reactant is present in solution in the form of larger aggregates, the reaction velocity will be determined, not by the stoicheiometric concentration term, but by the actual number of such aggregates per unit volume, and such a condition would then be manifested by the observation of second-order kinetics in a basically unimolecular reaction. Further, the presence of aggregates may cause heterogeneous catalysis of the reaction.

Influence of Solvent Constitution on the Reaction Rates.—It is a moot point whether water or ethanol is the stronger base. On the one hand, the autoprotolysis constant of ethanol ($pK = 19{\cdot}1$ at 25°) is higher than that of water ($pK = 14{\cdot}0$ at 25°),[3] but, on the other hand, Braude and Stern [4] explain the fact that the basicity of water was found to be greater than that of ethanol (as deduced from measurement of acidity function values,

[2] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons, London, 1953, p. 314.

[3] Hammett, " Physical Organic Chemistry," McGraw-Hill, New York, 1940, p. 250.

[4] Braude and Stern, *J.*, 1948, 1975.

and the change of these values in different water–ethanol mixtures) by changes in the structure of the solvent. According to them, ". . . pure water will have a smaller proton affinity than a mixture of 90% of water with 10% of ethanol, as in pure water the proton affinity of individual molecules is partly satisfied by hydrogen bonding with neighbouring molecules. On addition of organic solvent the tetrahedral structure will be gradually broken down . . ." Our results then could be explained by this hypothesis, but we could reach similar conclusions also by assuming that ethanol, in the present case at least, behaves as a stronger base than water. It has been stated by Ingold [5] that the strengths of acids and bases do not have to stand in the same order in different solvents. One could indeed argue that, if that is so, then the "basicity" of different solvents does not have to stand necessarily in the same order for different reactions. So, if for our case ethanol is a stronger base than water, we could also explain the data in Table 3 (as well as the results in Table 4 of Part VI of this series) as follows: addition of ethanol to water enhances the reaction rates owing to the catalytic effect of the more basic ethanol. Starting from pure ethanol, the addition of water, owing to its greater solvating power and higher dielectric constant, stabilises the carbanions formed, effectively depressing their recombination rate with protons. The result of the sum of the various effects is that in a certain water–ethanol mixture the rate coefficient–solvent constitution curve has a maximum. This maximum is found to be very nearly at the same position (20—30% of ethanol) in the reaction of ethyl cyanoacetate with all the three aldehydes studied.

The Hammett Equation.—From the results in Table 1, when σ^+ values [6,7] are plotted against log k_2, the points fall on a straight line (the value for benzaldehyde is neglected). The ρ value calculated from the slope of the log k_2–σ line in ethanol was 1·65, somewhat higher than the ρ value found for the reaction of malononitrile in ethanol ($\rho = 1{\cdot}45$). When the values of ln k_1 for reaction mixtures containing 0·001M of each of the reactants in water were plotted against the σ^+ values, a line was obtained from the slope of which the reaction constant ρ was calculated to be 1·5.

Jaffe [8] calculated the ρ value as 0·226 for the reaction of aromatic aldehydes with diethyl malonate in the presence of piperidine and hexanoic acid, in ethanol, from the data given by Pratt and Werble.[9] For data [10] for the reaction of aromatic aldehydes with malonic acid we calculated the value of ρ as $0{\cdot}57 \pm 0{\cdot}18$. As expected, in all cases studied the value of ρ is positive, as the reaction is facilitated by a low electron density at the reaction site, *i.e.*, at the carbonyl carbon atom,[11] and therefore electron-attracting substituents (*e.g.*, nitro-groups) enhance the rates, while electron-donating substituents (*e.g.*, methoxy-groups) lower them. We believe that low ρ values for carbonyl–methylene condensations also show that the main rate-determining step of the reaction is the ionic dissociation of the C–H bond of the active methylene group, whereas higher ρ values show a more important contribution of the polarisation of the carbonyl group of the aldehyde to the transition stage of the rate-determining step.

EXPERIMENTAL

Materials.—*Alcohol.* Commercial ethanol was distilled, and a 15 l. fraction of constant-boiling solvent was treated with 150 g. of zinc powder and 150 g. of potassium hydroxide pellets,[12] refluxed for 5 hr., and distilled with a Vigreux column, then passed through a Dowex-50-packed column, distilled again, and stored in a stoppered bottle in the dark. The purified ethanol was boiled for 15 min. before use, to expel dissolved carbon dioxide.

Ethanol–water mixtures. These were prepared before use and kept in a delivery flask,

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[5] Ingold, ref. 2, p. 726.

[6] Okamoto and Brown, *J. Org. Chem.*, 1957, **32**, 485.

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

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

[9] Pratt and Werble, *J. Amer. Chem. Soc.*, 1950, **72**, 4638.

[10] Patai and Goldmann-Rager, *Bull. Res. Council Israel*, 1958, **7**, *A*, 59.

[11] Jaffe, ref. 8, p. 217.

[12] Bladon, Henbest, and Wood, *Chem. and Ind.*, 1951, 866.

protected from carbon dioxide. The determinations of specific gravity were made with a pycnometer at 20° and the corresponding compositions were taken from the literature.[13]

Water. Redistilled water was boiled for 20 min. before use to expel carbon dioxide.

Commercial ethyl cyanoacetate ("AnalaR ") was redistilled and a cut of b. p. 204°/700 mm. was used.

Aldehydes. Benzaldehyde (B.D.H.) was purified by the method suggested in ref. 14 and, immediately before use, distilled with a Vigreux fractionating column, the fraction boiling at 174° being used. *p*-Tolualdehyde (Light & Co.) was steam-distilled, dried over " Drierite," and distilled with a Vigreux column, the fraction of b. p. 199—200° being redistilled before use. *p*-Anisaldehyde (B.D.H.) was distilled with a Vigreux column at 244°, and then at 113—114°/9 mm. *m*-Nitrobenzaldehyde was prepared by nitration of benzaldehyde [15] and purified by repeated crystallisations: it was dissolved in ethanol–water (2 : 1) at 50°, and the solution filtered and cooled slowly with constant stirring in order to avoid precipitation of uncrystallised oily drops. Purification was carried on until white needles, m. p. 56°, were obtained. *p*-Nitrobenzaldehyde was prepared by nitration of benzylidene diacetate [16] and purified by recrystallisations from boiling ethanol–water (2 : 1) until a white product, m. p. 106°, was obtained. *p*-Chlorobenzaldehyde (Light & Co.), recrystallised twice from ethanol–water (3 : 1) and dried, had m. p. 47°.[17] *p*-Bromobenzaldehyde was prepared from *p*-bromotoluene [18] and recrystallised until m. p. 58° was obtained.

TABLE 4. *Absorption spectra.*[a]

	Substituted benzaldehydes			Substituted ethyl benzylidenecyanoacetates		
Substituent	λ (mμ)	$10^{-4}\,\varepsilon$	Note	λ (mμ)	$10^{-4}\,\varepsilon$	Note
None	245 (max.)	1·250	*b*	223 (max.)	0·900	*c*
	280 (max.)	0·152	*b*	228 (max.)	0·940	
	299	0·032	*d*	299 (max.)	1·910	*d*
p-Methoxy	282 (max.)	1·760		240 (max.)	1·150	
	360	0·000	*d*	344 (max.)	2·960	
				360	2·157	*d, e*
p-Methyl	255 (max.)	1·360		230 (max.)	1·020	
	335	0·006	*d*	235 (max.)	1·020	
				320 (max.)	2·580	
				335	1·717	*d, e*
p-Chloro	256 (max.)	1·680		229 (max.)	0·790	
	312	0·000	*d*	233 (max.)	0·755	
				312 (max.)	2·180	*d*
p-Bromo	260 (max.)	1·740		230 (max.)	1·000	
	315	0·000	*d*	235 (max.)	0·890	
				315 (max.)	2·740	*d*
m-Nitro	231 (max.)	1·250	*f*	268 (max.)	1·800	
	300	0·130	*d*	300	1·480	*d, e*
p-Nitro	265 (max.)	1·160		304 (max.)	1·830	*d*
	304	0·200	*d*	345	0·236	*d, e*
	345	0·026	*d*			

(*a*) The molar absorbance coefficients of ethyl cyanoacetate, piperidine, perchloric acid, lithium chloride, and lithium nitrate were found to be negligible in the range studied. (*b*) Cf. Braude, *Ann. Reports*, 1945, **42**, 105. (*c*) There was practically no difference in the spectrum of this substance in ethanol or in water. All other condensation products were precipitated during attempts to prepare their aqueous solutions. (*d*) Kinetic measurements were made at these wavelengths. (*e*) It was not possible to work at the $\lambda_{\text{max.}}$ of the condensate, owing to the high absorption of the aldehyde at that wavelength. (*f*) Cf. Walker and Young, *J.*, 1957, 2041. Data in this paper are erroneous for *m*-nitrobenzaldehyde (personal communication by Dr. Y. R. Young).

Piperidine (B.D.H.) was distilled with a Vigreux column, the fraction of b. p. 104—105°/700 mm. being used. Perchloric acid (Baker's "Analysed ") (12N) was diluted as needed. Lithium chloride and nitrate (Baker's "Analysed ") were dried in an oven at 110° to constant weight.

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[13] " Handbook of Chemistry and Physics," Chemical Rubber Publishing Co., Cleveland, Ohio, 39th Edn., 1957.

[14] Vogel, " A Textbook of Practical Organic Chemistry," Longman, Green & Co., London, 1948, p. 173.

[15] Icke, Redeman, Wisegarver, and Alles, *Org. Synth.*, Coll. Vol. III, 1955, p. 644.

[16] Lieberman and Connor, *Org. Synth.*, Coll. Vol. II, 1943, p. 441.

[17] Jackson and White, *Ber.*, 1878, **11**, 1043.

[18] Coleman and Honeywell, *Org. Synth.*, Coll. Vol. II, 1943, p. 89.

Condensation products, Ar·CH=C(CN)·CO_2Et. These were prepared by refluxing for 1—4 hr. 20 g. of ethyl cyanoacetate with an equimolecular weight of the corresponding aldehyde, 50 ml. of ethanol and a few drops of piperidine. They were purified by recrystallisation from ethanol, until m. p.s identical with the literature values were obtained.

Ethyl p-*bromobenzylidenecyanoacetate. p*-Bromobenzaldehyde (0·002 mole), ethyl cyanoacetate (0·025 mole), piperidine (0·2 ml.), and ethanol (10 ml.) were refluxed for 1 hr. and allowed to cool; the product was filtered off and washed with two portions of ethanol; ethyl *p*-bromobenzylidenecyanoacetate (0·012 mole), m. p. 96°, was obtained; after several recrystallisations it had m. p. 97·5° (Found: C, 51·6; H, 3·5; Br, 28·1; N, 4·9; OEt, 15·4. Calc. for $C_{12}H_{10}O_2NBr$: C, 51·5; H, 3·6; Br, 28·5; N, 5·0; OEt, 16·1%).

Absorption Spectra.—These were determined for all the aldehydes and condensation products in purified ethanol. A Beckman DU-spectrophotometer with photomultiplier was used. All the observed products obeyed the Lambert–Beer law in the concentration ranges used. Data for the aldehydes and condensation products used are summarised in Table 4.

Kinetic Measurements.—Standard solutions of freshly purified reactants (other than aldehydes) were prepared and kept for no more than 3 days; aldehyde solutions were prepared on the day of use. Kinetic runs were made by pipetting the appropriate volumes of standard solutions of the two reactants into a measuring flask partially filled with the solvent, then rapidly filling it to the mark with more solvent and shaking it; standard solutions, solvent, and pipettes were all kept at the experimental temperature. Measurements were made in two ways: by taking samples at various time intervals and quenching the reaction by diluting it with enough ethanol to make absorbance measurements feasible, or by placing a sample of the reaction mixture in a ground-glass stoppered silica absorption cell placed in the spectrophotometer chamber at the experimental temperature, using a Beckman Dual Thermospacer Set, and measuring *in situ* the changes in the absorbance of the reaction mixture.

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