72. *Nucleophilic Attacks on Carbon–Carbon Double Bonds. Part III.*[1] *Base-catalysed Hydrolysis of Activated Carbon–Carbon Double Bonds in* 95% *Ethanol.*

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The base-catalysed hydrolysis of compounds containing activated carbon–carbon double bonds of the type Ar·CH:CXY, where X and Y were cyano-, ethoxycarbonyl, or carbamoyl groups, has been investigated. The effect of varying both the β-substituents (X, Y) and the aryl group has been studied, and a mechanism is proposed for the reaction.

In the work recorded in the preceding paper, we studied the uncatalysed cleavage of arylmethylenemalononitriles in ethanol, as an example of the variation of β-substitution on the reactivity of the system Ar·CH:CXY. In continuation we have studied particularly the effect of various α-substituents (X and Y = cyano, ethoxycarbonyl, or carbamoyl) on the reactivity of *p*-MeO·C_6H_4·CH=CXY in the base-catalysed hydrolysis to *p*-MeO·C_6H_4·CHO and CH_2XY, and, more briefly, also the effect of varying the aryl group in the reaction of Ar·CH=C(CN)·CO_2Et.

Results

The hydrolysis of 4-methoxybenzylidenemalononitrile, *p*-nitro-, *p*-, and *o*-methoxy-, and unsubstituted ethyl α-cyano-β-phenylacrylate, α-cyano-β-*p*-methoxyphenylacrylamide, and 4-methoxybenzylidenemalonamide in 95% ethanol at several temperatures was followed spectrophotometrically. The rate measurements show that the reactions are all of the first order in the compounds studied and of the first order in the base (Table 1). Concentration ranges of 20- to 50-fold were studied for each compound.

The base concentration was altered usually only 4-fold, as with high base concentrations the reactions were too fast to be followed accurately. On the other hand, the extreme sensitivity of very low base concentrations (of the order of 10^{-4} mole $l.^{-1}$) to carbon dioxide, limited the working range and gave poor reproducibility even though care was taken to remove carbon dioxide by boiling the solvents before use.

The most active compound, ethyl α-cyano-β-*p*-nitrophenylacrylate was hydrolysed without a base, both alone and in the presence of various concentrations of salt. The rate coefficients of the hydrolysis of $5{\cdot}06 \times 10^{-5}$ mole $l.^{-1}$ of substrate at 40° were $4{\cdot}97 \times 10^{-5}$, $5{\cdot}65 \times 10^{-5}$, $5{\cdot}65 \times 10^{-5}$, and $5{\cdot}10 \times 10^{-5}$ in the presence of respectively 0, 0·2M-, 0·4M-, and 1·0M-lithium chloride. Owing to experimental difficulties, the accuracy of the results with 4-methoxybenzylidenemalonamide was less satisfactory than in the other cases. It was not feasible to calculate initial hydrolysis rates with this compound, and a different method had to be employed (see Experimental section).

As in the hydrolysis of arylmethylenemalononitriles, no hold-up of any intermediate hydroxy-compound could be detected in the reaction mixtures.

From the mean values of the rate coefficients at different temperatures the following activation energies were calculated: 11,700, 13,100, and 16,200 cal. mole^{-1} for 4-methoxybenzylidenemalononitrile, ethyl α-cyano-β-*p*-methoxyphenylacrylate, and α-cyano-*p*-β-methoxyphenylacrylamide, respectively.

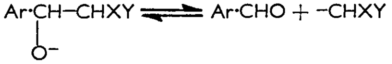
Discussion

The following mechanism is suggested for the base-catalysed hydrolysis:

$$(1)\qquad \underset{(I)}{\mathrm{Ar{\cdot}\overset{}{\underset{\beta}{C}H}{=}\underset{\alpha}{C}XY}} + \mathrm{OH^-} \rightleftharpoons \underset{(II)}{\mathrm{Ar{\cdot}CH(OH){-}C^-XY}}$$

$$(2)\qquad \mathrm{Ar{\cdot}CH(OH){-}C^-XY + H^+} \rightleftharpoons \underset{(III)}{\mathrm{Ar{\cdot}CH(OH){-}CHXY}} \rightleftharpoons \underset{(IV)}{\mathrm{Ar{\cdot}CH(O^-){-}CHXY}} + \mathrm{H^+}\ (\text{or } \mathbf{II} \rightleftharpoons \mathbf{IV})$$

(3)



$$\mathrm{Ar{\cdot}\underset{\underset{O^-}{|}}{C}H{-}CHXY} \rightleftharpoons \mathrm{Ar{\cdot}CHO + {}^-CHXY}$$

$$(4)\qquad \mathrm{{}^-CHXY + H^+} \rightleftharpoons \mathrm{CH_2XY}$$

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[1] Part II, preceding paper.

TABLE 1.

First-order rate coefficients (k_1 in sec.$^{-1}$), and second-order rate coefficients ($k_2 = k_1/$[NaOH] in mole^{-1} l. sec.$^{-1}$) for base-catalysed hydrolysis of various compounds in 95% ethanol at different temperatures. (All concentrations in 10^{-5} mole l.$^{-1}$.)

4-*Methoxybenzylidenemalononitrile.* (i) At 31°.

Concn.	3·14	3·77	6·28	5·30
[NaOH]	9·37	9·37	9·37	16·8
10^4k_1	6·79	6·83	6·98	13·3
k_2	7·25	7·30	7·45	7·90

Mean 7·38 ± 0·20

(ii) At 40°.

Concn.	3·2	6·7	6·7
[NaOH]	9·4	7·5	3·7
10^4k_1	13·5	10·5	5·2
k_2	14·4	14·0	14·0

Mean 14·1 ± 0·3

(iii) At 48°.

Concn.	1·53	3·07	6·14	6·14
[NaOH]	7·5	7·5	7·5	15
10^4k_1	14·4	13·9	14·7	27·2
k_2	19·3	18·7	19·7	18·2

Mean 19·0 ± 0·5

*Et α-cyano-β-*p-*methoxyphenylacrylacetate.* (i) At 31°.

Concn.	1·02	2·54	5·08	5·08	5·08	5·08	5·08	5·08	7·62	25·4
[NaOH]	93·7	93·7	46·8	56·2	93·7	113	150	187	93·7	93·7
10^4k_1	8·85	8·97	4·7	5·35	8·33	10·6	13·3	16·6	8·27	8·55
k_2	0·95	0·96	1·00	0·95	0·89	0·94	0·89	0·89	0·88	0·91

Mean 0·93 ± 0·3

(ii) At 40°.

Concn.	1·38	2·77	5·53	5·61	5·61	5·61	5·61	28·1	56·1	56·1
[NaOH]	93·7	93·7	93·7	75·0	56·2	46·8	23·4	93·7	23·4	93·7
10^4k_1	14·9	17·8	16·2	11·8	9·1	8·3	3·78	17·3	3·95	16·4
k_2	1·58	1·90	1·73	1·58	1·62	1·77	1·62	1·85	1·69	1·75

Mean 1·71 ± 0·09

(iii) At 48°.

Concn.	2·35	4·7	4·7	7·05
[NaOH]	46·8	18·4	46·8	46·8
10^4k_1	13·5	4·95	13·0	13·3
k_2	2·88	2·64	2·77	2·85

Mean 2·78 ± 0·08

*α-Cyano-β-*p-*methoxyphenylacrylactamide.* (i) At 31°.

Concn.	1·81	3·61	7·32	7·32	7·32	73·2	73·2
[NaOH]	375	375	187	375	750	375	937
10^4k_1	7·65	7·80	3·45	6·80	13·3	6·49	15·75
k_2	0·204	0·208	0·184	0·181	0·178	0·174	0·164

Mean 0·185 ± 0·012

(ii) At 40°.

Concn.	1·43	2·87	2·87	5·73	5·73	28·7	57·3
[NaOH]	187	93·7	187	93·7	187	187	187
10^4k_1	6·60	3·33	6·53	3·32	6·37	6·36	6·33
k_2	0·352	0·355	0·349	0·354	0·340	0·340	0·337

Mean 0·349 ± 0·007

(iii) At 48°.

Concn.	1·24	2·48	4·94	4·94	4·94	7·41	49·4
[NaOH]	187	187	48·7	112·4	187	187	187
10^4k_1	15·0	14·6	3·6	8·6	12·8	12·5	12·7
k_2	0·80	0·78	0·74	0·72	0·68	0·66	0·68

Mean 0·72 ± 0·05

4-*Methoxybenzylidenemalonamide.* At 40°.

Concn.	18·4	46	184
[NaOH]	21,700	22,500	13,600
10^4k_1	0·560	0·563	0·370
k_2	0·000258	0·000250	0·000272

Mean 0·000260 ± 0·000008

*Et α-cyano-β-*o-*methoxyphenylacrylate.* At 40°.

Concn.	1·98	3·96	7·58	7·69	37·9	75·8
[NaOH]	32·2	32·2	16·1	32·2	19·3	32·2
10^4k_1	21	23	11	23	12·6	20
k_2	6·5	7·1	6·8	7·1	6·6	6·6

Mean 6·7 ± 0·3

*Et α-cyano-β-*o-2-*methoxyphenylacrylate.* At 40°.

Concn.	3·04	6·08	6·08	6·08	6·08	12·16	12·16	12·16
[NaOH]	16·5	16·5	33	66	82·5	16·5	33	66
10^4k_1	3·14	3·10	7·44	11·8	15·9	2·86	7·56	13·3
k_2	1·90	1·90	2·22	1·80	1·93	1·73	2·29	2·01

Mean 1·98 ± 0·14

The first and probably rate-determining step is the nucleophilic attack of the hydroxyl ion on the β-carbon atom of the double bond. The proportionality of the rate to the concentrations of both the compound and the base, the relatively large effects of substituents at the α- and β-positions of the double bond, and the fact that no hold-up of any intermediate could be detected support this view. The slow formation of the anion (II) is followed by its rapid protonation, to give compound (III) from which ionisation of the hydroxylic proton gives (IV). The latter ion is cleaved to the aldehyde and an anion which after rapid protonation by the medium gives the active methylene compound. The transformation (II) ⟶ (IV) may also take place in a single intramolecular proton transfer without affecting our scheme.

It has been shown in the preceding paper that reactive compounds are attacked in neutral solution by water molecules and that then only a negligible part of the reaction involves attack by hydroxyl ions in the medium. Also, it has been shown that the lower the reactivity (*i.e.*, the hydrolysis rate) of the compound studied, the more important becomes the incursion of the attack by hydroxyl ions, *e.g.*, in the reaction of 4-methoxybenzylidenemalononitrile (cf. Discussion in the preceding paper). The compounds studied here are all very much less reactive than 4-methoxybenzylidenemalononitrile and therefore we assume that practically all of the reaction involves attack by hydroxyl ions, even in the absence of added base. The fairly constant second-order (base-catalysed) rate coefficients (see Table 1) also suggest this explanation. In the absence of a base, the reactions studied (except for 4-methoxybenzylidenemalononitrile) were too slow to measure and, therefore, obviously no experiments could be made in the presence of added acid so as to give additional proof for the mechanism proposed.

The effect of substituents in the phenyl group of ethyl α-cyano-β-arylacrylates was in accord with the results obtained previously, with arylmethylenemalononitrile. Electron-attracting substituents increase the rate and ethyl α-cyano-β-*p*-nitrophenylacrylate, the most active compound in this series, could be hydrolysed without a catalyst. Its rate of hydrolysis is comparable with that of the arylmethylenemalononitriles and therefore we believe that the arguments of the previous paper (*i.e.*, attack by water) hold for it.

The rate of hydrolysis of ethyl α-cyano-β-*o*-methoxyphenylacrylate is greater than that of its *para*-isomer. We believe this to be due to a steric acceleration by the *o*-methoxy-group, which will assist the hydrolysis as a steric strain is released in the product. For chlorobenzylidenemalononitriles, the uncatalysed-hydrolysis rate of the *o*-chloro-isomer was approximately three times that of the *para*-isomer, which can be explained by the fact that in this case steric and inductive effects operate in the same direction.

In spite of the importance and the great number of examples of nucleophilic attack on activated carbon–carbon double bonds (see Part I of this series) and the great number of qualitative comparative studies, based usually on relative yields of products, we found no recorded quantitative kinetic work on the effect of different α-substituents studied by us on the electrophilic reactivity of the β-carbon atom. Walker and Young[2] studied the hydrolysis of mononitrochalcones with the nitro-group in the *o*-, *m*-, and *p*-positions of the aroyl group. Notwithstanding the similarity of the substituents and their remoteness from the reaction site, they found considerable differences in the hydrolysis rates (*o* : *m* : *p*, 1 : 3 : 5).

We compared the effect of α-substituents by studying the hydrolysis rates of the 4-methoxybenzylidene derivatives of malononitrile, ethyl cyanoacetate, cyanoacetamide, and malonamide. As in previous cases, when the uncatalysed reaction rates were comparatively very slow, with these compounds the attack was by hydroxyl ions only, without incursion of attack by water molecules.

Resonance structures of the main types (V)—(VII) (X = CN, CO_2Et, $CO{\cdot}NH_2$)

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[2] Walker and Young, *J.*, 1957, 2045.

contribute to the electrophilic character of the β-carbon atom. The relative rates at 40° are: $C(CN)_2$ 1; $C(CN){\cdot}CO_2Et$ 0·1; $C(CN){\cdot}CO{\cdot}NH_2$ 0·025; $C(CO{\cdot}NH_2)_2$ 0·00002. The effect of the cyano-groups is thus much greater than that of the other α-substituents: replacement of one cyano-group by a carbamoyl group lowers the rate by a factor of 40, while the second similar replacement lowers it again by a factor of 1250.

$^{+}CHAr{\cdot}CX{:}C{:}N^{-}$ (V) $^{+}CHAr{\cdot}CX{:}C(O^{-}){\cdot}OEt$ (VI) $^{+}CHAr{\cdot}CX{:}C(O^{-}){\cdot}NH_2$ (VII)

A qualitative relation exists between the reactivity of the four 4-methoxybenzylidene derivatives and the *K* bands in their ultraviolet absorption spectra. There is a comparatively small decrease in the molar extinction coefficients when going from the dicyano-compound ($\lambda_{max.}$ 348 mμ, ε 29,800) through the cyano-ethoxycarbonyl compound ($\lambda_{max.}$ 344 mμ, ε 28,500) to the cyano-carbamoyl compound ($\lambda_{max.}$ 337 mμ, ε 27,600), followed by a large decrease in the dicarbamoyl compound ($\lambda_{max.}$ 274 mμ, ε 12,000). At the same time $\lambda_{max.}$ is displaced from longer to shorter wavelengths. We believe that excited structures such as (V) largely determine both the reactivity of these compounds and their absorption characteristics.

It is of interest to compare the present results with those on the condensation of active methylene compounds with aromatic aldehydes. The qualitative order of reactivity of various active methylene compounds towards aldehydes,[3] namely, $CH_2(CN)_2 > CH_2(CN){\cdot}CO_2Et > CH_2(CN){\cdot}CO{\cdot}NH_2$, is preserved in the hydrolysis of the corresponding arylmethylene compounds.

EXPERIMENTAL

Materials.—Ethyl *trans*-α-cyano-β-*p*-nitro-[4] (m. p. 170°), -*p*-methoxy-[4] (m. p. 84°), -*o*-methoxy-phenylacylate[5] (m. p. 77°) and the unsubstituted ester[4] (m. p. 50°), 4-methoxybenzylidenemalononitrile[4] (m. p. 116°), α-cyano-β-*p*-methoxyphenylacrylamide[4] (m. p. 213°), and 4-methoxybenzylidenemalonamide[4] (m. p. 206°) were prepared by condensing the appropriate aldehyde (0·1 mol.) in ethanol (50 ml.) with an equivalent amount of the active methylene compound with ethanolic 0·1N-sodium hydroxide (1 drop) as catalyst. The compounds were crystallised from propan-1-ol to constant m. p. and constant spectra.

Stock solutions of ethanolic sodium hydroxide were standardised against potassium hydrogen phthalate and stored in Polythene bottles. The titre did not change during a week, after which new solutions were prepared. These were diluted with ethanol to give the required base concentration, immediately before use.

Ethanol.—Ethanol was purified as described in the preceding paper.

Spectral Data.—The spectra were determined with a Beckman DU spectrophotometer and photomultiplier. The spectra of ethyl α-cyano-β-*p*-nitro- and unsubstituted -phenylacrylate are in agreement with those in the literature.[6] For ethyl *trans*-α-cyano-β-*o*-methoxyphenylacrylate $\lambda_{max.} = 360$ mμ ($\varepsilon = 11{,}200$). All the compounds obeyed the Beer–Lambert law in the concentration ranges used.

Product Analysis.—Each compound (200 mg.) was boiled for 1 hr. with 0·02N-sodium hydroxide in 95% ethanol and treated with an acid solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazones of the aldehydes were identified by m. p. and mixed m. p.

Kinetic Runs.—The hydrolysis of ethyl α-cyano-β-*p*-nitrophenyacrylate was studied by using a stock solution of the compound in benzene, as described in the preceding paper.[1] Stock solutions of all the other compounds were prepared in ethanol. New stock solutions were prepared each three days, and no hydrolysis was detected during this time. To a measuring flask containing the required catalyst solution and pure ethanol (which was boiled immediately before use to expel dissolved carbon dioxide) there was added the substrate from the stock solution. The absorbance was measured in a spectrophotometer chamber (thermostat), as described in procedure (*b*) of the preceding paper, at the wavelength of maximum

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[3] Patai, Zabicky, and Israeli, *J.*, 1960, 2038.

[4] Zabicky, *J.*, 1961, 683.

[5] Baker and Howes, *J.*, 1953, 119.

[6] Patai and Zabicky, *J.*, 1960, 2030.

absorption of the starting materials being used (except for ethyl 4-methoxybenzylidenemalonamide). As the products had only very small absorption at these wavelengths, no correction was necessary for the calculation of initial rate coefficients.

Treatment of Data.—By plotting the optical densities at various intervals of time, initial rate coefficients (k_1) were calculated as described in the preceding paper. The values obtained by this method were divided by the base concentration to obtain k_2 values of Table 1.

Difficulties in the kinetic work occurred with 4-methoxybenzylidenemalonamide. First, the extinction coefficient of *p*-methoxybenzaldehyde was slightly greater than that of the compound at the maximum wavelength of the latter. Secondly, owing to the low absorption of the compound, more concentrated solutions had to be used, and therefore the rate coefficients tended to fall, as equilibrium was approached at comparatively lower reaction percentages; and moreover the required high base concentrations may have catalysed the hydrolysis of the amide group. Measurements were conducted at 282 mμ (the wavelength of maximum absorption of the aldehyde), where the extinction coefficient of the starting material was 10,600, and that of the aldehyde 17,600. The values of the optical densities for 5%, 10%, 15%, and 20% reaction were calculated for each initial concentration, and the corresponding times were taken from the optical density–time graphs. The mean values of the k's obtained in this way are given in Table 1.

The results of typical run are given in the annexed Table.

Hydrolysis of $5{\cdot}73 \times 10^{-5}$ mole l.$^{-1}$ of α-cyano-β-*p*-methoxyphenylacrylamide in the presence of $18{\cdot}74 \times 10^{-4}$ mole l.$^{-1}$ of NaOH at 40° in 95% ethanol.

Time (sec.)	0	60	90	120	150	180	210	240	270
$10^3 \log (I_0/I)$	1498	1470	1442	1410	1380	1350	1321	1292	1265

$k_1 = k_2/[\text{NaOH}] = (D_0 - D)/D_0t = (1527 - 1292)/(1527 \times 240) = 6{\cdot}39 \times 10^{-4}$ sec.$^{-1}$. $k_2 = 3{\cdot}41 \times 10^{-1}$ mole^{-1} l. sec.$^{-1}$.

A control experiment with ethyl α-cyano-β-*p*-methoxyphenylacrylate was conducted by the method described previously.[1] No hold-up of any intermediate was detected.

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