Iodination of Substituted Sodium Phenylpropiolates

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Rate constants were determined for the iodination by iodine of eleven substituted sodium phenylpropiolates $(XC_6H_4C=COO^-Na^+)$ in water at 30°. Reactions were conducted in the presence of iodide ion (0.1 M), and under these conditions the reaction is third order, first order in substrate, free iodine, and iodide ion. Hammett plots using σ or σ^+ are not linear. This is interpreted as indicating that the third-order reaction involves a termolecular transition state in which the extent of bond formation between the electrophilic iodine and the nucleophilic iodide ion and the substrate is not necessarily the same but depends on the nature of the substituent. The major products of the reactions are the substituted trans- α,β -diiodocinnamic acids. By-products in some of the reactions are substituted α,β,β -triiodostyrenes. Small amounts of ketonic products (<1%) were detected in all but one of the cases and arise from a small amount of solvent incorporation. Activation parameters were determined for the iodination of five of the sodium phenylpropiolates.

The kinetics of iodination of sodium phenylpropiolate in water is characterized by the three-term equation (eq 1)

$$k_{obsd} = k_t K[I^-]/(K + [I^-]) + k' K/(K + [I^-]) + k'' K/[I^-](K + [I^-])$$
(1)

where K is the dissociation constant of the triiodide ion. The experimental rate law is $-d[I_2]_T/dt = k_{obsd}[A][I_2]_T$, in which $[I_2]_T$ represents the total titratable iodine. The three terms have been interpreted to represent respectively an iodide ion catalyzed reaction by free iodine, $k_1[A][I_2][I^-]$, a reaction of free iodine, $k_2[A][I_2]$, and possibly a reaction by the hydrated iodine cation, $k_3[A][H_2OI^+]$, where A is the acetylenic substrate.²

The first, termolecular, term presumably involves an electrophilic attack because the anion of the acid reacts slightly faster than the acid itself. However, in the similar iodination of propiolic acid, the corresponding term could not be clearly designated as electrophilic or nucleophilic. It was assumed that in the reaction of propiolic acid, bond making to the nucleophile predominates somewhat over bonding to the electrophile in the rate-controlling step, and vice versa for the anion.³

In order to gain more insight into the nature of the termolecular term and to see what contributions the electrophile and nucleophile make to the transition state, it seemed of interest to study the effect of substitution on the iodination of substituted sodium phenylpropiolates $(XC_6H_4C=CCOO^-Na^+)$.

Results

Rates of iodination of 11 substituted sodium phenylpropiolates were determined at 30° in water, and the results are listed in Table I. The rate constants are averages of triplicate runs. The third runs were conducted after suitable time intervals with completely new solutions. The synthesis of the starting acids is described in the Experimental Section.

Effect of Iodide Ions. All reactions were conducted at a 0.1 M KI concentration. The contribution of the three terms in eq 1 depends on the iodide ion concentration. At high iodide ion concentration (0.02-0.10 M) the first term predominates and contributes over 90% to the total rate. At these concentrations of iodide ion the rate of the reaction is independent of the iodide ion concentrations.² Because we were only interested in the third-order term it was necessary first to establish that all the substituted acids follow the same rate law. The iodide ion dependence on the rate was therefore checked for a number of representative acids (Table II). The rate is indeed independent of the iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the high iodide ion concentration for these acids at the substituted acids follow the same rate law.

Table IRates of Iodination of Sodium Phenylpropiolates $([\mathbf{XC}_{0}\mathbf{H}_{4}\mathbf{C}\equiv\mathbf{CCOONa}] \simeq 0.040 \ M, \ [I_{2}] \simeq 0.02 \ M, \ [KI] = 0.100 \ M)$

| Substituent | Registry no. | $k_{\rm obsd} 	imes 10^3$, l. (mol sec) ⁻¹ | ΔE_{a} , kcal/mol | log A | $\Delta S^*_{2^{98.2}}$, eu |
|----------------------|---------------------|---|------------------------------|-------|------------------------------|
| p-OCH ₃ | 53059-90-8 | 25.6 | | | |
| $p	ext{-}	ext{CH}_3$ | 53059 - 91-9 | 3.10 | 15.1 | 8.35 | -22.3 |
| m -CH $_3$ | 53059-92-0 | 1.75 | | | |
| H | 7063-23-2 | 1.30 | 15.0 | 7.93 | -24.2 |
| m -OCH $_3$ | 53059-93-1 | 1.15 | | | |
| p-Cl | 2532-21-0 | 1.11 | 15.0 | 7.86 | 24.6 |
| p-Br | 53059-94-2 | 0.979 | | | |
| m-Br | 53059-95-3 | 0.701 | 15.1 | 7.73 | -25.1 |
| m-Cl | 53059-96-4 | 0.685 | | | |
| m -NO $_2$ | 53059-97-5 | 0.385 | | | |
| p -NO $_2$ | 53059-98-6 | 0,310 | 15.7 | 7.79 | -24.9 |

 Table II

 Dependence of the Rate of Iodination on the Iodide

 Ion Concentration

| ([XC _β H ₄ C ≡ C COONa] | $\simeq 0.040$ | M , $[\mathbf{I}_2]$ | $\simeq 0.005$ | M) |
|--|----------------|------------------------|----------------|----|
| | | | | |

| [KI], M | $k_{\text{obsd}} \times 10^3$, l. (mol sec) ⁻¹ | [KI], <i>M</i> | $k_{ m obsd}$ $	imes$ 10 ³ , I. (mol sec) ⁻¹ |
|---------------|---|----------------------|---|
| Soc | dium | Sod | ium |
| p-methylphe | nylpropiolate | <i>m</i> -chloropher | nylpropiolate |
| 0.1200 | 2.82 | 0.1200 | 0.678 |
| 0.1000 | 2.79 | 0.0800 | 0.652 |
| 0.0800 | 2.78 | 0.0500 | 0,629 |
| 0.0500 | 2.81 | 0.0300 | 0.612 |
| 0.0300 | 3.04 | 0.0200 | 0.626 |
| 0,0200 | 3.50 | 0.0100 | 0.660 |
| 0.0100 | 5.12 | 0.0050^{a} | 0.606 |
| 0.0050^{a} | 5.59 | | |
| Soc | dium | \mathbf{So} | dium |
| m-bromoph | enylpropiolate | <i>m</i> -chloropher | hylpropiolate |
| 0.1200^{-1} | 0.695 | $(\mu = 2.00 M$ | $(\tilde{N}a\tilde{C}lO_4))$ |
| 0.0800 | 0.677 | 0.1200 | 1,17 |
| 0.0500 | 0.661 | 0.0800 | 1,17 |
| 0.0300 | 0.654 | 0.0500 | 1.20 |
| 0.0200 | 0.653 | 0.0100 | 1.39 |
| 0.0100 | 0.700 | 0.0050° | 1.22 |
| 0.0050^{a} | 0.675 | | |

^a $[I_2] \simeq 0.002 M.$

trations mentioned. The small decreases in rate as the iodide ion concentration is reduced from 0.12 M to approximately 0.02 \dot{M} are most likely due to an ionic strength effect because the reaction is highly sensitive to variations in the ionic strengths. When reaction is conducted at a constant ionic strength ($\mu = 2.0 M$), this effect disappears as shown in Table II for sodium *m*-chlorophenylpropiolate. When the second and third terms in eq 1 begin to gain im-

Table III Product Analysis

| | 11000 | co mary: | 51.5 | |
|-----------------------|---------------------|--------------------|--------------------------|-------------------------|
| Substituent | A , a mol $\%$ | $B,^b$ mol $\%$ | C, ^c mol % | D, ^d wt % |
| p-OCH ₃ | 0 | 0 | 62 | 0.67 |
| p -CH $_3$ | С | 29 | 19 | |
| m-CH ₃ | 62 | 16 | 9 | |
| H | 74 | | 0.5 | 0 |
| m -OCH $_3$ | 65 | 22 | 3.3 | 0.14 |
| p-Cl | 10 9 ° | | 5.5 | |
| p-Br | 104° | | 3.1 | 0.16 |
| m-Cl | $\tilde{2}$ | 99 | 0 | |
| $m	ext{-}\mathrm{Br}$ | 49 | 24 | 0 | |
| m-NO ₂ | 30 | 60 | 0 | |
| p -NO $_2$ | 118° | | 0 | 0.90 |

^a Pure substituted diiodocinnamic acid isolated. ^b Additional substituted diiodocinnamic acid calculated from iodine analysis of residue. See Experimental Section. ^c Substituted triiodostyrene isolated, based on the consumption of 1 mol of iodine per mole of styrene produced. ^d Ketonic material isolated. ^c See Experimental Section.

portance, the rate *increases* with a *decrease* in iodide ion concentration, and this is seen to begin when the iodide ion concentration is lowered to about $0.02 \ M$, although the turnover depends somewhat on the substituent. Since all acids tested show the same behavior, it is likely that all substituted acids behave like the unsubstituted one. At the iodide concentration here used it can safely be assumed that the first term in eq 1 greatly predominates, and that this is the reaction in which the substituent effect was studied.

Activation Parameters. These were determined for six of the acids from measurements of the rate constants at six different temperatures over a 25° range. Results are listed in Table I.

Product Isolation. Except a noted below, the major products of the addition reaction were the substituted α,β diiodocinnamic acids, which by analogy to the unsubstituted acid were considered to be the trans isomers. All showed loss of iodine on melting, characteristic of transbut not of cis-1,2-diiodoethylene.⁴ The acids were isolated from runs conducted on a large scale, but under conditions of the kinetic runs, and compared through melting points and ir spectra with authentic samples. Only one of the substituted iodinated products had previously been prepared. The others were synthesized as described in the Experimental Section. Because in all runs the concentration of the acetylenic acid was in excess of the iodine, the isolation of the products involved a separation of the two acids, which was difficult in some cases. In the first column in Table III are reported pure isolated acids, while in the second column are additional data obtained from an iodine analysis of the residual acid mixture. These figures are less certain than the former.

The second term in eq 1 is not completely eliminated, and from the reaction corresponding to this term a small amount of products derived from β -keto acids can be anticipated. These are formed by attack of water on a vinyl cationic intermediate followed by ketonization of the enol formed. Some ketonic products were formed from all acids except the unsubstituted acid and were characterized qualitatively by different retention times on tlc plates. In four of the isolation runs the presence of the keto acid was also established quantitatively by extraction with Girard's reagent and subsequent extraction with base (Table III). In the case of the *p*-bromo compound the product was identified more fully as *p*-bromobenzoylacetic acid (as the ethyl ester) by comparison of the nmr spectrum with that of unsubstituted benzoylacetic acid. In the same way, *p*-bromoacetophenone was also detected, which is formed by decarboxylation of the keto acid. Iodine-free material was isolated, since iodide ion, present in the reaction mixture, is known to remove halogen from halo- β -keto acids. It is assumed that all of the ketonic products are derivatives of benzoylacetic acid, because all displayed similar mobilities on tlc plates. The amounts of keto acid formed never exceeded 1% of the total products.

The other by-products are α,β,β -triiodostyrenes $(XC_6H_4CI=CI_2)$ which were identified by different retention times on the and elemental analysis in two cases. The amounts thus formed were small or absent when the substituents are electron withdrawing, but they increased as the substituent releases electrons, until the triiodostyrene became the major product in the case of sodium *p*-methoxyphenylpropiolate.

This was bothersome because in the formation of the styrene additional iodine is used up, and it was necessary to show that the rate constant for iodination of sodium *p*methoxyphenylpropiolate really represents the rate-determining iodination of the acetylenic acid to the diiodocinnamic acid.

The mechanism of the side reaction which leads to the formation of substituted triiodostyrenes appears to be quite complex. It had been previously shown that α,β -diiodocinnamic acid does *not* react with iodine to form α,β,β -triiodostyrene, and it had therefore been assumed that the styrene was formed from a cationic intermediate as shown.²

$$C_{e}H_{5}\dot{C} = CCOO^{-} \text{ or } C_{e}H_{5}C = CCOO^{-} \rightarrow C_{e}H_{5}C \equiv CI + CO_{2} \xrightarrow{I_{2}} C_{e}H_{5}CI = CI_{2}$$

Because the third-order reaction does not proceed through a cationic intermediate, and because so much of the styrene was formed in the case of the *p*-methoxy compound, the possibility had to be considered that the sodium *p*-methoxy- α,β -diiodocinnamate first forms and then *does* react with iodine, as shown in eq 2. This proved to be the case. A

$$p-\mathrm{CH}_{3}\mathrm{OC}_{6}\mathrm{H}_{4}\mathrm{CI} = \mathrm{CICOO}^{-} + \mathrm{I}_{2} \longrightarrow$$
$$p-\mathrm{CH}_{3}\mathrm{OC}_{6}\mathrm{H}_{4}\mathrm{CI} = \mathrm{CI}_{2} + \mathrm{CO}_{2} + \mathrm{I}^{-} \quad (2)$$

solution of sodium p-methoxy- α,β -diiodocinnamate reacts with iodine in the presence of iodide ion to form p-methoxytriiodostyrene. Subsequently, the observation was made that sodium p-methoxy- α,β -diiodocinnamate even reacts to form the styrene in the absence of iodine but in the *presence* of iodide ion, which must therefore furnish the additional iodine.⁵ Finally, sodium p-methoxy- α , β -diiodocinnamate decarboxylated on standing overnight in water in the absence of iodine or iodide ion, to form what is possibly a mono- or diiodostyrene.⁶ There are, therefore, several routes by which the styrene can be formed in this case, which do not necessarily involve the original iodine. The rate of iodination of sodium *p*-methoxyphenylpropiolate is very fast, but the kinetics of the reaction did not behave abnormally. The average extent of reaction in the kinetic runs was 88%, and good second-order rate constants were always obtained. In the isolation runs the reaction was allowed to stand for 2 weeks, and the diiodocinnamic acid formed initially had ample time to react further to form the styrene.

It is therefore assumed that the iodination of *p*-methoxyphenylpropiolate leads in the rate-determining step to the α,β -diiodo acid, which in a series of steps reacts further to form the styrene. This view is strengthened by the observation that, if in the preparative iodination of the methoxy acid at 0 to 5° the product was isolated immediately, Iodination of Substituted Sodium Phenylpropiolates

81% of p-methoxy- α,β -diiodocinnamic acid is obtained, but if the reaction was carried out at room temperature for 1 day, almost all of the product was the styrene. It is therefore also assumed that the rate constant reported in Table I is the real rate constant for iodination to the diiodo acid, but some doubt about the reliability of this rate constant cannot be erased. This is also true for the p-methyl compound, which shows a relatively large amount of styrene formation.

Discussion

The rate constants in Table I indicate that the termolecular term involves essentially an electrophilic attack because the *p*-methoxy compound reacts the fastest and the *p*-nitro acid the slowest. The overall differences in rates are not large, and consequently the activation energies are not very revealing and are all of the same order of magnitude, although the reaction of the *p*-nitro compound has the highest activation energy. The activation entropies have uniformly large negative values as had been observed earlier for the unsubstituted acid.² Rate constants and activation parameters for the unsubstituted acid agree well with those previously reported.

Although the general trend of the rate constants is that expected of an electrophilic attack, a Hammett plot of the data against either σ or σ^+ is nonlinear. A break in the straight line, as observed in Figure 1, is often taken as a change in mechanism, but the two straight lines have been drawn rather arbitrarily, and the data can equally well be represented by a smooth least-squares parabola.¹

The most convincing explanation is similar to one that has been advanced for the bromide ion catalyzed bromination of substituted phenylmethylacetylenes, which behaves very similarly.⁷ The third-order terms in iodination,^{2,3} in some brominations,^{7,8} as well as in hydrochlorination,⁹ have generally been considered to involve termolecular reactions of transition states of the type shown in 1 for io-



dination (Ad_3E) . Although the reactions are termolecular, the transition states are assumed to be slightly different for each compound, depending on the substituent. The relative extent of bond formation between the substrate and the electrophilic iodine and the nucleophilic iodide ion has proceeded to a different degree for each of the compounds. When the substituent is strongly electron donating, bonding of the substrate to the electrophile predominates over that to the nucleophile and the transition state will have a considerable amount of carbonium ion character, which is aided by the substituent. When the substituent is electron attracting, the bonding of the nucleophile to the triple bond will have progressed further than bonding to the electrophile, and this is aided by the nitro group. The various transition states will have varying extents of electrophilic and nucleophilic bond formation, although kinetically all are third order.

The Hammett plots for the two linear approximations are better when σ^+ rather than σ values are used (Figure 1). The superiority of σ^+ values is understandable if one realizes that only for the most electron-donating substituents are the substituent constants significantly different. It is for compounds with these substituents that a considerable partial positive charge would be generated on the benzylic



Figure 1. A Hammett plot of rates of iodination against σ^+ .

carbon atom. Because this charge can be effectively delocalized into the ring and the substituent, the correlation of their rates ought to be better with σ^+ constants. A truly synchronous transition state, in which no charge at all is developed, might be expected to be better correlated with σ values.

An approximate measure of the degree of electron delocalization and positive charge development can be obtained from the ρ values of the correlations. When plotted against σ^+ , ρ is -1.66 ± 0.10 for the three fastest and -0.774 ± 0.01 for the remaining compounds. These are much lower than ρ in those addition reactions to olefins and acetylenes where carbonium ion intermediates are thought to be involved. In those cases ρ is usually around $-4.^{10}$ The low ρ values obtained here are, however, in accord with a transition state in which the effects of the electrophile and nucleophile are more nearly balanced. They are compatible with the approximate value of -1.9 reported for the slower compounds in the bromide ion catalyzed bromination of phenylacetylenes.⁷

The behavior of the substituted acids in iodination also strengthens the argument that the third-order term represents, in fact, a termolecular, although not completely synchronous, reaction. The various alternatives that can be considered for this term, such as bimolecular reaction by triiodide ion, or a series of bimolecular reactions, involving iodine and iodide ion and an ionic intermediate, would less well account for the observed behavior, although all are kinetically equivalent.³ Fast reversible complexing of the acetylene with iodine, followed by attack of iodide ion, would also account for the kinetics and would avoid postulating a termolecular reaction,¹¹ but it would not be as compatible with the near absence of solvent-incorporated products.

| | | | | | /sis, % |
|--------------------------|--------------|-----------------|---|-------------------------|-----------------------------|
| Substituent | Registry no. | Mp, deg | Calcd for | Calcd | Found |
| $p	ext{-OCH}_3$ | 53178-57-7 | 117.7-118.1 dec | $C_{10}H_8I_2O_3$ | C, 27.93 | C, 28.18 |
| $p	extsf{-}	extsf{CH}_3$ | 53059-99-7 | 158.6–159.4 dec | $\mathbf{C}_{10}\mathbf{H}_{8}\mathbf{I}_{2}\mathbf{O}_{2}$ | C, 29.01 | C, 28.82 |
| m -CH $_3$ | 53060-00-7 | 134.1-134.9 dec | $\mathbf{C_{10}H_8I_2O_2}$ | H, 1.95 C, 29.01 | C, 28.83 |
| p-Cl | 53060-01-8 | 159.0-159.8 dec | $C_9H_5CH_2O_2$ | H, 1.95 C, 24.88 | H, 1.97 C, 24.76 |
| m-Cl | 53060-02-9 | 143.1–143.9 dec | $C_9H_5ClI_2O_2$ | H, 1.16 C, 24.88 | H, 1.19 C, 24.67 |
| <i>p</i> -Br | 53060-03-0 | 158.2-159.0 dec | $C_9H_5BrI_2O_2$ | H, 1.16 C, 22.57 | H, 1.10 C, 22.39 |
| m-Br | 53060-04-1 | 163.4–164.2 dec | $C_9H_5BrI_2O_2$ | H, 1.05 C, 22.57 | H, 1.08 C, 22.45 |
| p-NO ₂ | 53060-05-2 | 174.0-174.8 dec | $C_{9}H_{5}I_{2}NO_{4}$ | H, 1.05 C, 24.29 | H, 1.03 C, 24.26 |
| m-NO. | 53060-06-3 | 148 2-149 0 dec | C.H.I.NO. | H, 1.13 C 24.29 | \dot{H} , 1.10 C 24.41 |
| 110-1102 | 00000-00-0 | 140.2 140.0 ucc | 09110121104 | H, $1,13$ | H, 1.14 |

Table IV

Experimental Section

Melting points were taken with a Hershberg melting point apparatus and are corrected. Infrared spectra were taken on a Perkin-Elmer infracord and nmr spectra on a Varian A-56/60 nmr spectrophotometer in $CDCl_3$ or acetone which contained TMS. All pH measurements were made on a Beckman Model G pH meter. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

Materials. Phenylpropiolic acid (Aldrich Chemical Co.) was recrystallized four times from CCl_4 and had a mp of $137.6-138.4^{\circ}$ (lit.¹² 136.9-137.5°).

The synthesis of the substituted phenylpropiolic acids started with commerciapavailable substituted benzaldehydes, which were convejzto substituted cinnamic acids by a Doebner reaction. The cinnamic acids were brominated, and the resulting substituted α,β -dibromohydrocinnamic acids were dehydrobrominated with KOH to the substituted phenylpropiolic acids according to individual literature procedures. Yields ranged from 30 $(m - NO_2)$ to 75% (p-CH₃). The recrystallized acids had the following mp (literature mp in parentheses): p-CH₃O 144.8-145.4° (144.0-144.4°);¹² p-CH₃ 147.0-147.8° (149–150°);¹³ m-CH₃O 109.5-110.5° (109°);¹⁴ m-CH₃ 135.6-136.4° (135–136°);¹⁵ p-Cl 192.9-194.2° (192–193°);¹² m-Cl 146.0-146.8° (144.3-145.1°);¹² m-NO₂ 144.4-145.1° (143.7-144.4°).¹² Two of the acids were analyzed be cause their mp differed from literature values. p-Bromophenylpropiolic acid, mp 186.7–187.3° (201°).¹⁶ Anal. Calcd for $C_9H_5BrO_2$: C, 48.03; H, 2.24. Found: C, 48.19; H, 2.35. *m*-Bromophenylpropiolic acid, mp 163.6-164.4° (135-136°).17 Anal. Calcd for C₉H₅BrO₂: C, 48.03; H, 2.24. Found: C, 47.99; H, 2.24. The pnitro compound was prepared by direct nitration of phenylpropiolic acid in 25% yield and had mp 201.3-202.0° dec (204-205° dec).¹² Another 24% consisted of the ortho isomer, mp 158.8– 160.8° (160.5– 161.0°).¹² Four methyl esters were prepared and had (106°);¹⁶ p-NO₂ 111.5–113.5° (112–113°);¹⁵ p-Br 106.4–107.0° (51–52°).¹⁵ m-NO₂ 49.5–51.5° (51–52°).¹⁵ the following mp: p-Cl 91.1-92.1° (92-94°);¹⁵ p-Br 106.4-107.0°

The sodium salts of the acids were prepared in absolute ethanol and ether with sodium ethoxide as previously described.²

All of the substituted α,β -diiodocinnamic acids were made by iodination of the corresponding propiolic acid in aqueous solution containing K₂CO₃, I₂, and KI, according to the procedure reported for the synthesis of the *m*-methoxy acid, mp 140.8–141.6° dec (lit. 142°).¹⁴ The main variation was the reaction time which varied from 20 min at 5° for the *p*-methoxy compound to 15 days at room temperature for the *p*- nitro acid. The yields of substituted trans - α,β -diiodocinnamic acid (XC₆H₄CI=CICOOH) averaged 63% after one or two crystallizations from CHCl₃-petroleum ether. All decompose at the mp with release of iodine. Mp and analyses appear in Table IV.

Two of the substituted styrenes (XC₆H₄CI=CI₂) were isolated in sufficient amounts and were analyzed after crystallization from ethanol-water. *p*-Methoxy- α , β , β -triiodostyrene, mp 102.2-102.9° dec. Anal. Calcd for C₉H₇I₃O: C, 21.12; H, 1.38. Found: C, 21.21; H, 1.38. *p*-Methyl- α , β , β -triiodostyrene, mp 73.5-74.3° dec. Anal. Calcd for C₉H₇I₃: C, 21.80; H, 1.42. Found: C, 22.02; H, 1.54.

Product Isolation. These were carried out essentially as described before.² The isolation runs were 0.04 M in substituted so-

dium phenylpropiolates, 0.025 M in I₂, and 0.10 M in KI. The volume of solution was 200 or 250 ml. The extent of reaction was determined periodically by titrating 1-ml aliquots and varied from 65 to 100%, with an average of 75%. The solutions were filtered to remove any precipitated triiodostyrene, and the flask was rinsed with chloroform to remove any adhering material. The acidified filtrate afforded the acids. These were filtered and the filtrate was extracted several times with chloroform. The two chloroform extracts were combined.

The acid mixture, which contained starting material and diiodo acid, was crystallized from chloroform-petroleum ether $(30-40^{\circ})$ until a diiodo acid of constant mp was obtained. In some cases a second crop of less pure material was also isolated, which may account partly for yields of over 100% reported in Table III. For instance, a 91% yield of pure *p*-bromo- α , β -diiodocinnamic acid was isolated, and subsequently 13% of slightly less pure material was obtained, bringing the total to 104%.

When the acid mixture could not be further separated, it was analyzed for iodine. These figures are only approximate, because the iodine analysis was not completely consistent with a carbonhydrogen analysis carried out on two of the mixtures. However, though many of the phenylpropiolic and diiodocinnamic acids have similar mp and solubilities, the diiodocinnamic acids all melt with decomposition. The melting point range and extent of decomposition can be used as a rough measure of the iodinated product present. The results in Table III are consistent with these observations. Also, data obtained from iodine analysis constitute usually a minor fraction of the pure isolated product, and only in two cases $(m-Cl and m-NO_2)$ do they constitute the major part.

All combined residues were further analyzed by tlc. The solvent systems were chloroform saturated with formic acid for acidic substances and 90% petroleum ether (30-40°)-10% ether for nonacidic.¹⁸ $R_{\rm f}$ values of the acids were compared with those of authentic samples. In addition to the two acids, and, in most cases, the styrene, a fourth substance was found in all but one case, which was more mobile than the two acids in the chloroform-formic acid system. Because it was expected to be ketonic, the residues of four of the isolation runs were treated with Girard's Reagent T, essentially according to the procedure of Fieser.¹⁹ The work-up of this reaction afforded four fractions, an acidic ketonic and nonketonic, and a nonacidic ketonic and nonketonic one. The ketonic acidic product from the reaction of sodium p-bromophenylpropiolate was identified by nmr. It had been converted to the ethyl ester during the reaction with Girard's reagent, which contained ethanol and acetic acid. The nmr spectrum of ethyl p-bromobenzoylacetate $(p-BrC_6H_4COCH_2COOC_2H_5)$ showed a three-proton triplet at τ 8.72 and a two-proton quartet at au 5.83 for the ethyl protons, a two-proton singlet at τ 5.92 for the methylene group, a two-proton multiplet at τ 1.95 for the ortho protons, and a two-proton multiplet at τ 2.48 for the meta protons. The nmr spectrum of unsubstituted ethyl benzovlacetate showed corresponding resonances at τ 8.79, 5.80, 5.87, 1.82, and a three-proton multiplet at τ 2.39 for the remaining aromatic protons. From the ketonic nonacidic fraction, p-bromoacetophenone was obtained and similarly identified. The reactions of the p-CH₃O, m-CH₃O, and p-NO₂ compounds did not yield amounts of ketonic material sufficient for further identification but were assumed to have yielded similar products.

Reactions of Benzaldehyde with Ethyl Cyanoacetate

Kinetic Determinations. Iodine and all salts were reagent grade chemicals. The salts were dried at 120-140° overnight before use. The temperature of the kinetic runs was $30.00 \pm 0.05^{\circ}$, except for those used to determine the activation parameters, which varied from 15.0 to 50.0°. Complete stock solutions were made up at the appropriate temperatures. The procedure for the kinetic runs was that used before.² All rate constants were determined by leastsquares analysis, and the probable errors in individual rate constants averaged 0.5%. Duplicate runs were carried out for each set of conditions, except for runs used for the Hammett plot, for which triplicate determinations were made. Rate constants of the duplicate or triplicate runs usually agreed within 2%. Additional determinations were made if the error was greater. All reported rate constants are the observed rate constants. The true third-order rate constants, k_t (eq 1), can be obtained by dividing the observed rate constants by K (1.55 × 10⁻³ at 30°).²⁰ Activation energies had least-squares errors of 0.1-0.2 kcal and activation entropies of 0.1-0.4 eu.

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Registry No .--- m- Bromophenylpropiolic acid, 29835-28-7; pmethoxy- α,β,β -triiodostyrene, 53060-07-4; p-methyl- α,β,β -triiodostyrene, 53060-08-5; p-bromophenylpropiolic acid, 25294-65-9.

References and Notes

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- (5) From the filtrate of the styrene, there was obtained, after acidification, not only the expected unreacted p-methoxy- α,β -diiodocinnamic acid but also some *p*-methoxyphenylpropiolic acid, which indicates some reversibility of the iodination under these conditions. This nonacidic material melted at $49-52^{\circ}$ after one recrystallization from ethanol-water and contained halogen (Beilstein test). The amount
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Reactions of Benzaldehyde and Analogs with Ethyl Cyanoacetate in Ethanolic Ammonia¹

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Reactions of benzaldehyde and analogs with ethyl cyanoacetate in ethanolic ammonia produce α -cyanohydrocinnamamides, 2,6-dihydroxy-3,5-dicyano-4-phenylpyridines, and dimeric products. Similar reactions in aqueous ammonia or Cope-Knoevenagel condensations also produce some of these products. Those facts suggest that the reaction mechanisms are the same. The report elucidates the structures of dimeric products such as 3,5-dicyano-4,6-diphenyl-5-ethoxycarbonyl- α -piperidones.

LeMoal, et al.² and Nagai, et al.³ have reported the Cope-Knoevenagel condensation of para-substituted berizaldehydes with excess ethyl cyanoacetate to produce ethyl α -cyano-para-substituted cinnamates 1, but have not yet reported that the reaction products were always accompanied by trace amounts of high melting by-products. In the case of p-nitrobenzaldehyde, the above reaction gave a noticeable amount of a dimeric product (4d), which was assigned a cyclobutane structure (6) by LeMoal, $et \ al.^2$ From benzaldehyde and ethyl cyanoacetate, a similar dimeric product (4) was obtained by Carrick⁴ with sodium ethoxide in ethanol or by Issoglio⁵ and Guareschi⁶ with aqueous ammonia; however, these authors did not elucidate the structure of that product.

Table I shows the results of the reactions of para-substituted benzaldehydes with ethyl cyanoacetate in ethanolic ammonia at 0°. The formula for 3, the ammonium salt of 2,6-dihydroxy-3,5-dicyano-4-(para-substituted phenyl)pyridines,^{5,6} has been assigned on the basis of spectral data.

Table I Product Yield (mol %) for the Reactions of Para-Substituted Benzaldehydes and Ethyl Cyanoacetate in Saturated-Ethanolic Ammonia at 0°

| | | Product ^a | |
|-----------------|------|----------------------|------|
| Х | 2 | 3 ^b | 4 |
| н | | 6.7 | 38.4 |
| MeO | 10.1 | 9.6^{c} | 15.5 |
| C1 | 23.2 | 38.7° | |
| \mathbf{NO}_2 | 21.2 | 34.6° | |

^a At the similar reactions in concentrated aqueous ammonia, $X = H^6$ and $X = NO_2$,⁵ respectively, produced 2, 3, and 4. Ir data of 2a (Nujol) 3380 and 3195 cm⁻¹ (NH₂), 2250 cm⁻¹ (CN), 1660 and 1620 cm⁻¹ (amide C=O). ^b Yields of 3 of Cope-Knoevenagel condensation: X = H, 0.002%; X = MeO, 0.001%; X = Cl, 0.72%, $X = NO_2$, 1.18%. These compounds are not dehydrated. ^c Monohydrated.