Anal. Calcd for $C_{19}H_{13}NO_2$: C, 79.44; H, 4.53; N, 4.88. Found: C, 79.65; H, 4.78; N, 4.75.

Decarboxylation of 3-Phenylpyrrolo[2,1-*a*]isoquinoline-1-carboxylic Acid. To 1.0 g of the acid of mp 218–219° was added 3 ml of quinoline freshly distilled from alumina, and 100 mg of copper chromite catalyst. The flask was placed in an oil bath and heated for 0.5 at 220°. The green mixture was poured into a slurry of ice and 10% hydrochloric acid. The mixture was extracted three times with 20 ml portions of methylene chloride. This solution was concentrated under an air stream, and the residual solid was dissolved in ether. The solution was extracted three times with 10-ml portions of 1 *N* sodium hydroxide solution. The ether solution was evaporated, and a few mg of 3-phenylpyrrolo[2,1-*a*]isoquinoline (**17**), mp 98.5–99°, was obtained. The same compound was also obtained in somewhat better yield by pyrolysis of the sodium salt of the acid. A mixture melting point of this material with a sample of authentic **17** prepared from β-(1-isoquinolyl)propiophenone[5,14] (**18**) by the method of Boekelheide and Godfrey[5] showed no depression. Also, the infrared spectra of the two samples were superimposable.

1-Formamido-3-phenylpyrrolo[2,1-*a*]isoquinoline. A mixture of 1.5 g (0.0052 mol) of 3-phenylpyrrolo[2,1-*a*]isoquinoline-1-carboxylic acid, mp 218–219°, and 5 ml of thionyl chloride was refluxed for 2 hr. The excess thionyl chloride was removed by distillation, and the residue was dissolved in methylene chloride. This solution of the acid chloride was added dropwise to 100 ml of ice cold ammonia, specific gravity 0.9, and stirred magnetically for 12 hr at ambient temperature. The resulting deep red amide was collected by suction filtration and recrystallized from ethanol, mp 204–205°. The yield was 1.1 g (73.3%) based on starting acid.

Anal. Calcd for $C_{19}H_{14}N_2O$: C, 79.72; H, 4.89; N, 9.79. Found: C, 79.58; H, 5.07; N, 9.59.

Since this was not identical with the sample of 2-formamido-3-phenylpyrrolo[2,1-*a*]isoquinoline, mp 168–169°, prepared by the method of Boekelheide and Godfrey,[5] this constituted evidence that the carboxyl group was located at the 1 position in the acid of mp 218–219°, as indicated above.

Reissert Salts. When 0.003 mol of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1**) was treated with 25 ml of cold 1 *N* sodium hydroxide solution, 2-benzoyl-1,2-dihydroisoquinaldonitrile, mp 125–126°, was recovered in greater than 90% yield.

2-*p*-Anisoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate, mp 210–212° dec, was prepared from 2-*p*-anisoyl-1,2-dihydroisoquinaldonitrile[15] in the same manner as described for the preparation of **1**.

Acknowledgment. This work was supported by a research grant (CA-06620) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

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Mechanism of 1,3-Dipolar Addition of Reissert Salts to Arylpropiolate Esters

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Contribution from the Department of Chemistry of the University of Massachusetts, Amherst, Massachusetts 01002. *Received October 19, 1970*

Abstract: The condensation reactions of 2-aroyl-1,2-dihydroisoquinaldonitrile hydrofluoroborates (**1**) with ethyl phenylpropiolate (**3a**) were carried out in dimethylformamide–ethanol solution. A kinetics investigation was undertaken under conditions which give rise only to the bridged intermediate **4**, and it was established that each reaction is a second- and first-order reversible one. The specific rate constants of these reactions were found to vary only slightly with changes in the substituent on the aroyl group of the Reissert salt. It is of particular significance that the rate of reaction of 2-*p*-anisoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1b**) with **3a** was found to be slower than that of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1a**) with **3a**. The activation parameters for the reaction of **1b** with **3a** were found to be $\Delta H^{\pm} = 16.3$ kcal/mol and $\Delta S^{\pm} = -25$ eu. The condensation reactions of **1a** with methyl *p*-methoxyphenylpropiolate (**3b**) and methyl *p*-nitrophenylpropiolate (**3c**) were carried out in ethanol–methylene chloride solution. These reactions were found to follow simple second-order kinetics and to give compounds of type **5** as the major products. In these reactions, also, there was a relatively small change in the rate of reaction with the change of substituent in the arylpropiolate ester. Furthermore, a substantial change in solvent polarity caused only a relatively small change in rate. In each of the reactions studied, only one of the two possible orientations of reagents leading to **4** and **5**, respectively, was found to be operative. The structures of all of the products were established in an unambiguous manner by spectral, degradative, and synthetic methods. On the basis of all of the criteria cited above, a concerted mechanism which entails essentially a synchronous formation of the two new covalent bonds is favored over a two-step, ionic mechanism for the 1,3-dipolar cycloaddition reactions under discussion.

The accompanying article[1] presents a description of the 1,3-dipolar addition reactions of certain types of munchnone imines (**2**), derived from the hydrofluoroborate salts of Reissert compounds, with ethyl phenylpropiolate (**3a**), ethyl tetrolate, and dimethyl acetylenedicarboxylate. The reaction of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1a**) with ethyl phenylpropiolate (**3a**) was of particular interest in that the initial, bridged intermediate, 2-carbethoxy-1,3-diphenyl-3-hydroxy-13-cyano-1,13-dihydrobenzpyrrocoline-3,13-lactim (**4a**), was isolable. This represented the first example of the isolation of such an intermediate among all of the known 1,3-dipolar addition reactions of the same general type involving munchnones, sydnones, and sydnone imines.[2]

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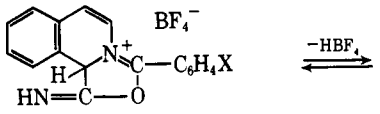
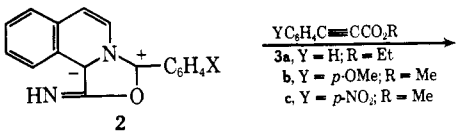
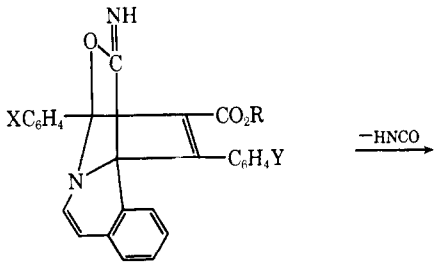
(2) (a) R. Huisgen, H. Gotthardt, and H. Bayer, *Angew. Chem., Int. Ed. Engl.*, 3, 135 (1964); (b) R. Huisgen, H. Gotthardt, H. O. Bayer, and F. C. Schaefer, *ibid.*, 3, 136 (1964); (c) F. H. Stewart, *Chem.*



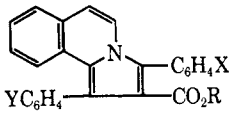
1a, X = H
b, X = p-OMe
c, X = m-Cl



2



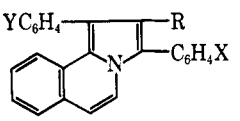
4a, X = Y = H; R = Et
b, X = p-OMe; Y = H; R = Et
c, X = m-Cl; Y = H; R = Et
d, X = H; Y = p-OMe; R = Me
e, X = H; Y = p-NO2; R = Me



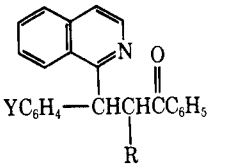
5a, X = p-OMe; Y = H; R = Et
b, X = m-Cl; Y = p-MeO; R = Et
c, X = H; Y = p-MeO; R = Me
d, X = H; Y = p-NO2; R = Me

The major objective of the present work was to study the detailed mechanism of the condensation reaction leading to the bridged intermediate **4**. The greatest emphasis has been placed on kinetics studies, inasmuch as conditions could be arranged under which there was no conversion of the intermediates **4a**, **4b**, and **4c**, respectively, to the corresponding fully aromatic heterocyclic compounds of type **5**. Thus, there was no ambiguity as to which step was being subjected to scrutiny in the kinetics investigations. However, the structures of all products were first established in a convincing manner so that there would be no question about the orientation being observed in the addition of the unsymmetrical 1,3-dipolar compounds to the likewise unsymmetrical 1,3-dipolarophiles. The same types of degradative procedures and independent syntheses were used as outlined in the accompanying article,[1] and therefore only the structural formulas of the key products and intermediates (**5**, **6**, **7**) are shown here. The details of these studies are given in the Experimental Section.

In all of these examples, there was no evidence for the formation of any isomer other than that of type **4** in the condensation of **1** with esters of type **3**. In most instances of 1,3-dipolar cycloaddition reactions, when two isomers are possible as a result of the use



6a, Y = H; X = p-OMe; R = H
b, Y = H; X = p-OMe; R = CONH2
c, Y = H; X = m-Cl; R = H
d, Y = H; X = m-Cl; R = CONH2
e, Y = p-OMe; X = H; R = H
f, Y = p-NO2; X = H; R = H



7a, Y = p-OMe; R = CO2Me
b, Y = p-OMe; R = H
c, Y = p-NO2; R = CO2Me
d, Y = p-NO2; R = H

of unsymmetrical reagents, one isomer usually predominates, often to the exclusion of the other isomer.[2e,3]

Apart from the obvious synthetic value of 1,3-dipolar cycloaddition reactions, there has been considerable interest in the reaction mechanism.[3b,4] The principal question is whether the two new σ-bonds which are formed on fusion of the 1,3-dipolar compound with the dipolarophile are formed simultaneously or one after the other. In most cases, the evidence indicates that a concerted reaction occurs, and a symmetry-energy correlation diagram reveals that such a thermal cycloaddition reaction is allowed.[3b,4c,5] However, a competing two-step cycloaddition reaction may occur if the charges of the zwitterionic intermediate are adequately delocalized owing to the presence of suitable substituents.[6] Thus, the mechanism of any new example of a 1,3-dipolar addition reaction must be examined on the basis of its own individual characteristics.

Our first objectives with respect to the study of the mechanism of the reaction of **1a** with **3a** were (a) to find homogeneous reaction conditions leading only to the formation of **4a**, and then (b) to determine the order of reaction. Condition a was found to be satisfied by the use of dimethylformamide–95% ethanol (30:7, v/v) at temperatures in the range of 35–40°. Control experiments showed that **4a** only was produced under these conditions at times up to 16 hr; no ethyl 1,3-diphenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (**5**, X = Y = H; R = Et)[1] was produced. The same result was observed when **1b** or **1c** was used in place of **1a**. However, a mixture of compounds of types **4** and **5** was obtained when the reactions were allowed to proceed for many weeks.

The rate of disappearance of **3** could be followed by monitoring the triple bond absorption at 2218 cm^{-1} in the infrared spectrum. Two different types of plots were constructed to determine the order of the reaction. In the first, a conventional plot for an uncomplicated second-order reaction was prepared, as shown in Fig-

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(6) R. Huisgen and P. Otto, *J. Amer. Chem. Soc.*, **91**, 5922 (1969).

Table I. Specific Rate Constants for the Reactions of 2-Aroyl-1,2-dihydroisoquinaldonitrile Hydrofluoroborates (**1**) with Arylpropiolate Esters (**3**)

1	3	Temp, °C	Solvent pair (v/v)	System	$k \times 10^5$, l. mol^{-1} sec^{-1}
a	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	14.7
a	a	34.40 ± 0.05	DMF–EtOH (39:7)	Equilib	14.3
a	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	14.9
b	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	8.07
b	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	7.79
b	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	8.45
b	a	41.00 ± 0.05	DMF–EtOH (30:7)	Equilib	14.8
b	a	41.00 ± 0.05	DMF–EtOH (30:7)	Equilib	14.4
b	a	41.00 ± 0.05	DMF–EtOH (30:7)	Equilib	14.4
c	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	11.3
c	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	12.7
c	a	34.40 ± 0.05	DMF–EtOH (30:7)	Equilib	11.8
a	b	41.0 ± 0.1	EtOH–CH_2Cl_2 (3:1)	Nonequilib	180
a	c	41.0 ± 0.1	EtOH–CH_2Cl_2 (3:1)	Nonequilib	780
a	c	41.0 ± 0.1	EtOH–CH_2Cl_2 (1:1)	Nonequilib	140
a	c	41.0 ± 0.1	EtOH–CH_2Cl_2 (1:3)	Nonequilib	106

ure 1 for a typical experiment. This was found to be linear only for about 55–60% of the reaction when the initial concentrations of **1** and **3** were equal. However, when unequal concentrations of **1** and **3** were employed, and when a plot for a conventional, uncomplicated second-order reaction was made, a smooth curve rather than a straight line resulted. Thus, the reactions were shown not to be simple second-order ones.

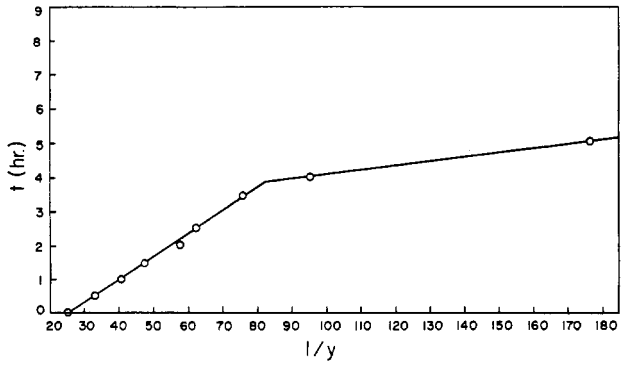
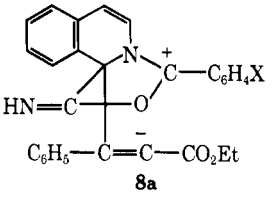


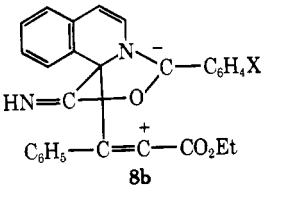
Figure 1. Plot of $1/y$ *vs.* time for reaction of 2-*p*-anisoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1b**) with ethyl phenylpropiolate (**3a**) at 41.00 ± 0.50°; concentration of **1b** = 0.0172 *M*, concentration of **3a** = 0.0172 *M*.

In the second evaluation of the order of reaction and for determination of the specific rate constants, $\log [x_e(a^2 - xx_e)]/[a^2(x_e - x)]$ was plotted *vs.* t [x_e = equilibrium concentration of **3** (and **1**)] for the presumed reaction **1** + **3** ⇄ **4**, equal concentrations of **1** and **3** being used. This plot gave a straight line for the entire reaction in each case. A plot of $\log [(A - \lambda_1)]/[(A - \lambda_2)]$ *vs.* t was also found to be linear for the entire reaction (terms defined in the Appendix). This represents the type of plot which may be used for an equilibrium reaction when unequal concentrations of reagents are employed. Thus, it was shown that the reaction is a second- and first-order reversible one.

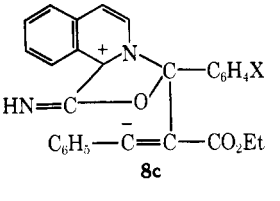
The order of the reaction having been established, the next step was to determine the relative rates of reaction of **1a**, **1b**, and **1c** with **3a**. Of the four possible structures for a zwitterionic intermediate, **8a** would be the most reasonable one from the point of view of the most efficient delocalization of charges. In addition, structures **8b** and **8d** can be criticized on the grounds that the alkyne, **3a**, is an electrophilic one and should therefore play the role of the Lewis acid in a two-step condensation reaction. Structure **8c** runs counter to the known chemistry of α,β-unsaturated esters; in all known conjugate addition reactions, the nucleophile adds to the β-carbon, not to the α-carbon atom. Thus, if a two-step mechanism for the 1,3-dipolar addition reaction under discussion is to be considered at all, it would have to be in terms of the formation of **8a** as an intermediate.



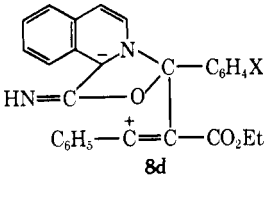
8a



8b



8c



8d

As shown in Table I, the rate of reaction of **1b** with **3a** is less than that of **1a** with **3a**. If the two-step, ionic pathway were followed, the presence of a *p*-methoxyl group in the acyl moiety would be expected to stabilize the zwitterionic intermediate **8a** (X = *p*-MeO), and the transition state leading to it, more than it would stabilize the mesoionic reagent **2** (X = *p*-MeO) and would cause an increase in rate relative to the unsubstituted case. The result actually obtained is clearly inconsistent with the intervention of **8a** as an intermediate and indicates that the mechanism involves the essentially synchronous formation of the two new covalent bonds.[7] Also, the fact that the relative rates

(7) The nature of the substituent, X, present on **1** would have some influence on the concentration of the mesoionic intermediate, **2**, which would, in turn, influence the rate of reaction leading to **4**. However, any base-strengthening effect of a *p*-methoxyl group on **1** would probably be proportional to σ_p-MeO and should be much less significant

of the three reactions, one influenced by the presence of a strong electron-donating group (*p*-MeO) and another by a fairly strong electron-withdrawing group (*m*-Cl), ranged only from 0.55 to 1.00 suggests the operation of a concerted mechanism.[8]

The rates of reaction of **1b** with **3a** were determined at different temperatures, and the activation parameters were found to be $\Delta H^{\pm} = 16.3$ kcal/mol and $\Delta S^{\pm} = -25$ eu. These values are of complex origin in that they are derived from the presumed equilibrium between **1b** and **2** (X = *p*-OMe) as well as from the rate-limiting condensation reaction of **2** (X = *p*-OMe) with **3a**. However, the same holds true for the $\Delta H^{\pm}$ (14.8–18.4 kcal/mol) and $\Delta S^{\pm}$ (−29 to −31 eu) values reported[8] for similar 1,3-dipolar cycloaddition reactions which are thought to be synchronous in nature. Thus, the close correspondence of the values suggest that the same type of mechanism is operative in both systems.

It was of interest that a change of solvent caused a change in the order of the reaction of **1a** with **3a**. By the use of 95% ethanol–methylene chloride (3:1 v/v) at 41.0°, the order became a mixed one presumably corresponding to the situation

$$\mathbf{1a} + \mathbf{3a} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{4a} \xrightarrow{k_2} \mathbf{5a}$$

wherein the three specific rate constants are of the same order of magnitude. However, by use of **1a** with either **3b** or **3c**, the rate data were found to fit an uncomplicated second-order rate expression, indicating that k_2 is distinctly greater than k_1 or k_{-1} for these reactions. The values of the observed rate constants are given in Table I. Once again, the relatively small spread of the values (1.8–7.8 × 10^{-3} l. mol^{-1} sec^{-1}) is indicative of a concerted reaction.[9] Furthermore, variation of the solvent for the reaction of **1a** with **3c** from 1:3 to 3:1 (v/v) methylene chloride–95% ethanol (a change in the dielectric constant of about 10 units) brought about only a sevenfold decrease in rate (Table I). A similar change in the dielectric constant of the solvent system for the reaction of *C*-methyl-*N*-phenylsydnone with ethyl phenylpropiolate caused about a twofold change in rate.[10] Another, presumably concerted, 1,3-dipolar cycloaddition reaction, that of dimethylketene with *N*-isobutenylpyrrolidine, showed about a tenfold change in rate for a similar change of polarity of the solvent system.[6] Thus, the data for the reaction of **1a** with **3c** fall in between these other sets of relative rate data and suggest that all three systems follow the synchronous type of mechanism.

In summary, on the basis of several important criteria, *viz.*, selectivity in orientation, effects of substituents on rate and orientation, effect of change of solvent polarity on rate, and the magnitude of the activation parameters, a concerted 1,3-dipolar cycloaddition of **2** to **3** is favored over a two-step, ionic mechanism. These criteria include most of those listed by Gompper[11] for distinguishing between a single-step or a two-step process.

Experimental Section

Melting points were obtained by use of a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were taken on a Beckman Model IR-10 spectrometer. Nmr spectra were taken on a Varian Model A-60 spectrometer with tetramethylsilane as the internal reference standard. Chemical shifts are reported in parts per million (δ) with reference to tetramethylsilane, and coupling constants are reported in cycles per second (cps). Merck neutral aluminum oxide was used for column chromatography with benzene–chloroform mixture (1:1 v/v) as eluent unless otherwise specified. The solvents were suitably purified, dried, and stored over molecular sieves (Linde type 5A). Microanalyses were performed by the Microanalysis Laboratory, University of Massachusetts, Amherst, Mass. 01002.

2-Benzoyl-1,2-dihydroisoquinaldonitrile Hydrofluoroborate (1a). This salt, mp 196–198° dec, was prepared as described previously.[1]

2-*p*-Anisoyl-1,2-dihydroisoquinaldonitrile Hydrofluoroborate (1b). This salt, mp 210–212° dec, was prepared as described previously.[1] When 1.0 g of **1b** was treated with 25 ml of 1 *M* sodium hydroxide solution at room temperature, there was obtained 0.75 g (98%) of 2-*p*-anisoyl-1,2-dihydroisoquinaldonitrile, mp 173–174° after recrystallization from 95% ethanol.

2-*m*-Chlorobenzoyl-1,2-dihydroisoquinaldonitrile Hydrofluoroborate (1c). This salt, mp 197–199° dec, was obtained in 70% yield by reaction of 2-*m*-chlorobenzoyl-1,2-dihydroisoquinoaldonitrile[12] and hydrofluoroboric acid in acetic acid in the same manner as described previously[1] for the preparation of **1a**. Treatment of 1.0 g of **1c** with 25 ml of 1 *M* sodium hydroxide at room temperature gave 0.67 g (88%) of 2-*m*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile, mp 188–189° after recrystallization from 95% ethanol.

Preparation of Bridged Compounds (4). To a solution of 0.0172 mol of each salt **1** in 30.0 ml of purified dimethylformamide and 7.0 ml of 95% ethanol was added 0.0172 mol of ethyl phenylpropiolate, and the stirred solution was maintained at 35° for 16 hr. The solution was then added to 190 ml of saturated sodium bicarbonate solution, and the resulting mixture was extracted with ether. The ether solution was concentrated to dryness, and the residue was chromatographed on alumina. Each intermediate **4** was obtained by concentration of the appropriate eluent fractions to dryness and recrystallization of the residue from 95% ethanol. The position of equilibrium for each reaction system was different, but the mole fraction of unreacted **3a** at equilibrium at 35° varied about as follows: reaction with **1a**, 0.35; with **1b**, 0.43; with **1c**, 0.50. Although the yields were poorer, products that were easier to purify were obtained by the method described in the accompanying article.[1] The properties of the bridged compound **4a** have been described previously.[1] Compound **4b** was found to have mp 190–191° after recrystallization from 95% ethanol: ir ($CHCl_3$) 3440 (NH), 2840 (OCH_3), 1730 (C=O), and 1695 cm^{-1} (C=N); nmr ($CDCl_3$) δ 0.80 (t, 3 H, J = 7.5 cps), 3.9 (s and overlapping q, 5 H, J = 7.5 cps), 7.0–8.6 (m, 15 H), 8.95 (broad s, 1 H).

Anal. Calcd for $C_{29}H_{24}N_2O_4$: C, 74.98; H, 5.21; N, 6.03. Found: C, 75.00; H, 5.07; N, 5.85.

Compound **4c** was found to have mp 185–186° after recrystallization from 95% ethanol: ir ($CHCl_3$) 3440 (NH), 1730 (C=O), and 1700 cm^{-1} (C=N); nmr ($CDCl_3$) δ 0.8 (t, 3 H, J = 7.5 cps), 4.0 (q, 2 H, J = 7.5 cps), 7.2–8.6 (m, 15 H), and 8.9 (broad s, 1 H).

Anal. Calcd for $C_{28}H_{21}N_2O_3Cl$: C, 71.72; H, 4.48; N, 5.98. Found: C, 71.70; H, 4.83; N, 5.98.

Pyrolysis of 3-*p*-Anisyl-2-carbethoxy-1-phenyl-3-hydroxy-13-cyano-3,13-dihydrobenzpyrrocoline-3,13-lactim (4b). A 150-mg (3.15 × 10^{-4} mol) sample of **4b** was placed in a microsublimator

than the effect of the substituent on the stability of the transition state leading to **8a** (X = *p*-OMe), which would probably be proportional to σ_p^+-OMe. The fact that **1c** undergoes reaction with **3a** at a slightly faster rate than **1b**, however, might be attributable to the relative influences of the substituents on the presumed equilibrium between **1** and **2**.

(8) The reactions of *N*-arylsydnones with ethyl phenylpropiolate in cumene at 140° are considered to be synchronous 1,3-dipolar cycloadditions. The relative rates have been found to vary with change of substituents on the *N*-aryl group as follows: phenyl, 1.00; *p*-anisyl, 0.72; *p*-chlorophenyl, 1.82; *p*-tolyl, 0.92. R. Huisgen and H. Gotthardt, *Chem. Ber.*, **101**, 1059 (1968).

(9) The Diels–Alder reaction (the prototype of concerted cycloaddition) of methyl arylpropiolates with tetracyclone in phenylcyclohexane at 175.5° has been subjected to a kinetic study. The specific rate constants varied from 1.19 × 10^{-3} l. mol^{-1} sec^{-1} for the *p*-methoxyphenylpropiolate to 7.75 × 10^{-3} l. mol^{-1} sec^{-1} for the *p*-nitrophenylpropiolate ester: I. Benghiat and E. I. Becker, *J. Org. Chem.*, **23**, 885 (1958).

(10) R. R. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **8**, 602 (1969).

(11) R. Gompper, *ibid.*, **8**, 312 (1969).

(12) F. D. Popp and A. Soto, *J. Chem. Soc.*, 1760 (1963).

and heated in an oil bath. The temperature of the bath was kept at about 200° for 30 min. During this time, a white porcelain-like substance sublimed and accumulated on the cold finger. This substance was collected and washed with ether, chloroform, and water, respectively. After it had been dried, it was found to be insoluble in both organic solvents, and in dilute acid and base. It melted above 300° and is presumed to be a polymer of isocyanic acid $(HNCO)_n$.[1]

The reaction mixture was extracted with ether, the ether solution evaporated to dryness, and the residue subjected to column chromatography. The compound from the first yellow band, after recrystallization from 95% ethanol, gave 45 mg (34% yield) of ethyl 3-*p*-anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (**5a**): mp 121–122°; ir ($CHCl_3$) 1840 (CH_3O), 1700 (C=O), and 1200–1250 cm^{-1} (pyrrolo ring); nmr ($CDCl_3$) δ 0.78 (t, J = 7.5 cps), 3.80–3.95 (overlapping s and q), and 6.5–7.6 (m).

Saponification of Ethyl 3-*p*-Anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (5a). A solution of 2.5 g of **5a** and 0.2 g of potassium hydroxide in 50 ml of 95% ethanol was refluxed for 24 hr, cooled, and acidified with 5% hydrochloric acid. The mixture was extracted with benzene, the benzene extract dried over anhydrous magnesium sulfate and filtered, and the benzene evaporated. The residue was crystallized from 95% ethanol to give 0.8 g (34%) of colorless 3-*p*-anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic acid, mp 240–241° dec.

Anal. Calcd for $C_{26}H_{19}NO_3$: C, 79.37; H, 4.87; N, 3.56. Found: C, 79.25; H, 4.91; N, 3.65.

Decarboxylation of 3-*p*-Anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic Acid. The procedure used was similar to that reported by Buckles and Wheeler.[13] A mixture of 0.25 g of the acid of mp 240–241° dec, 3 ml of quinoline, and 20 mg of copper chromite catalyst (K & K Lab. Chem.) was heated for 1 hr at 250°. The dark mixture was then poured into a slurry of ice and sufficient 10% hydrochloric acid to neutralize the quinoline. The desired product was extracted into ether, the ether solution dried over magnesium sulfate and filtered, and the solvent removed under reduced pressure. The residue was then subjected to column chromatography. The product from the first band, upon recrystallization from 95% ethanol, gave 140 mg (64%) of 3-*p*-anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline (**6a**); mp 94–95°; ir ($CHCl_3$) 2840 (OCH_3), 1610 (conjugated C=C), and 1200–1250 cm^{-1} (pyrrolo ring); nmr ($CDCl_3$) δ 3.75 (s), 6.6–7.9 (m).

Anal. Calcd for $C_{25}H_{19}NO$: C, 85.93; H., 5.48; N, 4.01. Found: C, 85.85; H, 5.49; N, 3.80.

3-*p*-Anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxamide (6b). This compound, mp 164–165°, was prepared from the lithium salt of 2-*p*-anisoyl-1,2-dihydroisoquinaldonitrile and cinnamonitrile in essentially the same manner as described for the preparation of 1,3-diphenylpyrrolo[2,1-*a*]isoquinoline-2-carboxamide in the accompanying article.[1]

Anal. Calcd for $C_{26}H_{20}N_2O_2$: C, 79.57; H, 5.14; N, 7.14. Found: C, 79.40; H, 5.38; N, 7.14.

3-*p*-Anisyl-1-phenylpyrrolo[2,1-*a*]isoquinoline (6a). Reaction of 2.0 g of **6b** with 40 ml of 85% phosphoric acid at 180° for 2 hr, with subsequent neutralization and extraction with benzene, gave 0.45 g (51%) of **6a**, mp 93.5–95.0° after crystallization from absolute ethanol–chloroform (95:5 v/v). A mixture melting point with the product of decarboxylation of 3-*p*-anisyl-1-phenylpyrrolo[2,1-*a*]-isoquinoline-2-carboxylic acid showed no depression, and the ir spectra of the two samples taken in chloroform solution were superimposable.

Pyrolysis of 2-Carbethoxy-3-*m*-chlorophenyl-1-phenyl-3-hydroxy-13-cyano-3,13-dihydrobenzpyrrocoline-3,13-lactim (4c). A 2.0-g (0.00427 mol) sample of **4c** was placed in a sublimator and heated in an oil bath at 200° for 30 min. The pyrolysate was extracted with ether, the ether solution evaporated, and the residue chromatographed. The compound from the first band was recrystallized from aqueous ethanol and amounted to 0.80 g (44%) of ethyl 3-*m*-chlorophenyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (**5b**): mp 107–108°; ir ($CHCl_3$) 1700 (C=O) and 1200–1250 cm^{-1} (pyrrolo ring); nmr ($CDCl_3$) δ 0.78 (t, J = 8 cps), 3.95 (q, J = 8 cps), and 6.5–7.8 (m).

Anal. Calcd for $C_{27}H_{20}NO_2Cl$: C, 76.15; H, 4.70; N, 3.29. Found: C, 75.99; H, 4.74; N, 3.29.

Proof of Structure of 5b. Since most of the steps in the proof of structure of **5b** parallel those described for **5a** and for similar compounds described in the accompanying article,[1] only the compounds and their properties will be listed, except where a change of procedure was required. Saponification of **5b** afforded 3-*m*-chlorophenyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic acid: mp 153–154° dec after crystallization from ethanol–water; yield 51%. Decarboxylation of the acid gave 3-*m*-chlorophenyl-1-phenylpyrrolo[2,1-*a*]isoquinoline (**6c**) as an oil; its infrared spectrum was taken in chloroform solution. The lithium salt of 2-*m*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile was treated with cinnamonitrile to give 3-*m*-chlorophenyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxamide (**6d**), mp 228–229° after crystallization from 95% ethanol, in 53% yield.

Anal. Calcd for $C_{25}H_{17}N_2OCl$: C, 75.66; H, 4.30; N, 7.06; Cl, 8.70. Found: C, 75.55; H, 4.39; N, 7.05; Cl, 8.92.

A mixture of 2.0 g (0.00508 mol) of **6d** and 40 ml of 85% phosphonic acid was stirred and heated at 240° for 2 hr. The cooled mixture was poured onto cracked ice, neutralized with 10% sodium hydroxide solution, and extracted with benzene. The benzene extract was dried over anhydrous magnesium sulfate and filtered, and the benzene evaporated. The residue was subjected to column chromatography. Evaporation of the eluent of the first band gave **6c**, an oil, the infrared spectrum of which, taken in chloroform solution, was superimposable on that of the product of decarboxylation of the compound identified above as 3-*m*-chlorophenyl-1-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic acid, mp 153–154° dec. The compound obtained by evaporation of the eluent of the second band amounted to 0.1 g and was proved to be (see below) *m*-chlorophenyl β-phenyl-β-(1-isoquinolyl)ethyl ketone, mp 111–112°.

Anal. Calcd for $C_{24}H_{18}NOCl$: C, 77.52; H, 4.85; N, 3.74. Found: C, 77.13; H, 4.88; N, 3.56.

Ethyl α-*m*-chlorobenzoyl-β-phenyl-β-(1-isoquinolyl)propionate was prepared by the reaction of the lithium salt of 2-*m*-chlorobenzoyl-1,2-dihydroisoquinaldonitrile with ethyl cinnamate in a manner similar to that used previously for the preparation of α-carbethoxy-β-(1-isoquinolyl)-β-phenylpropiophenone.[1] The product, mp 120–121° after recrystallization from 95% ethanol, was obtained in 52% yield.

Anal. Calcd for $C_{27}H_{22}NO_3Cl$: C, 73.05; H, 4.96; N, 3.15. Found: C, 72.89; H, 5.14; N, 2.84.

Hydrolysis and decarboxylation of ethyl α-*m*-chlorobenzoyl-β-phenyl-β-(1-isoquinolyl)propionate by the action of 85% phosphoric acid at 150° for 10 min gave *m*-chlorophenyl β-phenyl-β-(1-isoquinolyl)ethyl ketone, mp 111–112°, in 84% yield. A mixture melting point of the two samples of the ketone showed no depression, and their infrared spectra were superimposable. Cyclization of the ketone by the action of concentrated sulfuric acid on the steam bath with subsequent treatment with ice and extraction with ether gave **6c**, an oil, the infrared spectrum of which was superimposable on those of the two samples of the same compound described previously.

Reaction of 1a with Methyl *p*-Methoxyphenylpropiolate (3b). A mixture of 2.0 g (0.0057 mol) of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1a**), 2.0 g (0.011 mol) of methyl *p*-methoxyphenylpropiolate (**3b**),[9] 20 ml of methylene chloride, and 30 ml of 95% ethanol was stirred and warmed to effect solution. The methylene chloride was allowed to evaporate over a period of 3 hr. The residual solution was concentrated to dryness and the residue suspended in water and extracted with benzene. The benzene solution was dried, concentrated, and chromatographed on alumina, a 1:1 mixture of benzene and chloroform being used as the eluent. The first compound to pass through the column was methyl 1-*p*-anisyl-3-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (**5c**), 1.2 g. Recrystallization of this product from ethanol gave colorless needles: mp 135–136°; ir ($CHCl_3$) 1705 (C=O), 2840 (CH_3O), and 1200–1250 cm^{-1} (pyrrolo ring); nmr ($CDCl_3$) δ 3.42 (s, 3 H), 3.88 (s, 3 H), 6.55–7.60 (m, 15 H).

Anal. Calcd for $C_{27}H_{21}NO_3$: C, 79.59; H, 5.20; N, 3.44. Found: C, 79.49; H, 5.08; N, 3.41.

The second material to pass through the column consisted of a mixture of **5c** and another compound. However, attempted crystallization of this mixture from 95% ethanol gave only an insoluble product which had the properties[1] of the polymer of HNCO; **5c** was obtained from the ethanol filtrate. Thus, the second component was probably **4d**, which decomposes more readily than the other compounds of type **4** described earlier.

Proof of Structure of 5c. Saponification of 1.0 g of **5c** gave 0.7 g of 1-*p*-anisyl-3-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic acid, mp 226–227° dec. Decarboxylation of 0.1 g of the acid afforded 0.05 g of 1-*p*-anisyl-3-phenylpyrrolo[2,1-*a*]isoquinoline (**6e**), mp 116–118°.

(13) R. E. Buckles and N. G. Wheeler, *Org. Syn.*, 33, 88 (1953).

Anal. Calcd for $C_{25}H_{19}NO$: C, 85.93; H, 5.48; N, 4.01. Found: C, 85.71; H, 5.54; N, 3.95.

The condensation of the lithium salt of 2-benzoyl-1,2-dihydroisoquinaldonitrile with methyl *p*-methoxycinnamate gave α-carbomethoxy-β-(1-isoquinolyl)-β-*p*-anisylpropiophenone (**7a**) in 15% yield. The use of column chromatography on alumina with hexane as the eluent was necessary in order to obtain crystalline **7a**, mp 132–133°.

Anal. Calcd for $C_{27}H_{23}NO_4$: C, 76.22; H, 5.45; N, 3.29. Found: C, 76.37; H, 5.67; N, 3.27.

Saponification and decarboxylation of 3.5 g of **7a** in an ethanol solution of potassium hydroxide gave β-(1-isoquinolyl)-β-*p*-anisylpropiophenone (**7b**), mp 115–116° after chromatography (alumina, hexane) and recrystallization from benzene–hexane.

Anal. Calcd for $C_{25}H_{21}NO_2$: C, 81.72; H, 5.76; N, 3.81. Found: C, 81.60; H, 5.82; N, 3.84.

Cyclization of 0.36 g of **7b** by the action of 5 ml of 100% phosphoric acid at 120° for 2 hr gave 0.2 g of 1-*p*-anisyl-3-phenylpyrrolo[2,1-*a*]isoquinoline (**6e**), mp 118–119°, also in admixture with the sample of **6e** obtained by saponification and decarboxylation of **5c**. The infrared spectra of the two samples of **6e**, taken in chloroform solution, were superimposable.

Reaction of 1a with Methyl *p*-Nitrophenylpropiolate (3c). A mixture of 1.0 g (0.0049 mol) of **3c**, 2.0 g (0.0058 mol) of **1a**, 20 ml of methylene chloride, and 25 ml of ethanol was refluxed for 5 hr, a clear solution being formed near the end of this period. When cooled, the solution deposited 1.1 g of bright yellow crystals. Another 0.3 g of the same material was obtained by evaporation of the mother liquor to dryness, extraction of the residue with methylene chloride, and crystallization of the residue from ethanol. After repeated recrystallization from 95% ethanol, the yellow compound, methyl 1-*p*-nitrophenyl-3-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylate (**5d**), had mp 180–182°; nmr ($CDCl_3$) δ 3.45 (s, 3 H) and 6.7–8.5 (m, 15 H).

Anal. Calcd for $C_{26}H_{18}N_2O_4$: C, 73.92; H, 4.30; N, 6.63. Found: C, 73.90; H, 4.15; N, 6.74.

In the work-up of another reaction mixture, the mother liquor from the first crop of crystals of **5d** was concentrated to a small volume and placed in the refrigerator for 2 days. A crystalline compound, apparently 2-carbomethoxy-1-(*p*-nitrophenyl)-3-phenyl-3-hydroxy-13-cyano-3,13-dihydrobenzpyrrocoline-3,13-lactim (**4e**), mp 150–175° dec, was obtained. Attempts to recrystallize this material from 95% ethanol gave an insoluble compound, $(HNCO)_x$, and, from the filtrate, **5d**.

Proof of Structure of 5d. Saponification of 2.0 g of **5d**, effected by stirring it with a solution of 0.5 g of potassium hydroxide in 20 ml of 95% ethanol and 20 ml of methylene chloride at room temperature for 40 hr, gave 0.9 g of recovered **5d** and 0.75 g of 1-*p*-nitrophenyl-3-phenylpyrrolo[2,1-*a*]isoquinoline-2-carboxylic acid, mp 318.5–320.0° after crystallization from toluene–ethyl acetate.

Anal. Calcd for $C_{25}H_{16}N_2O_4$: C, 73.52; H, 3.95; N, 6.86. Found: C, 73.60; H, 4.25; N, 6.80.

Decarboxylation of 0.4 g of 1-*p*-nitrophenyl-3-phenylpyrrolo-[2,1-*a*]isoquinoline-2-carboxylic acid in the usual manner gave 0.2 g of dark red crystals (from carbon tetrachloride) of 1-*p*-nitrophenyl-3-phenylpyrrolo[2,1-*a*]isoquinoline (**6f**), mp 195–196°.

Anal. Calcd for $C_{24}H_{16}N_2O_2$: C, 79.10; H, 4.43; N, 7.69. Found: C, 79.40; H, 4.70; N, 7.49.

Reaction of the lithium salt of 2-benzoyl-1,2-dihydroisoquinaldonitrile (0.03 mol) with methyl *p*-nitrocinnamate (0.03 mol) in ether–dioxane, initially at −10°, in a nitrogen atmosphere for 12 hr, with subsequent addition to water and Dry Ice, gave two layers. The organic layer, combined with the ether wash solutions of the aqueous layer, was dried and the ether distilled. The residue was dissolved in 50 ml of ethanol and treated with 30 ml of 10% hydrochloric acid. An insoluble hydrochloride salt of α-carbomethoxy-β-(1-isoquinolyl)-β-*p*-nitrophenylpropiophenone (**7c**) precipitated and was collected by filtration. Trituration of this salt with sodium bicarbonate solution and crystallization of the liberated base from methanol gave 1.6 g of **7c**, mp 144–145°.

Anal. Calcd for $C_{26}H_{20}N_2O_5$: C, 70.90; H, 4.58. Found: C, 70.87; H, 4.38.

A mixture of 0.4 g of **7c**, 30 ml of ethanol, and 2 ml of 10% hydrochloric acid was refluxed for 5 hr. The mixture was neutralized with potassium hydroxide solution and extracted with methylene chloride. Evaporation of the methylene chloride solution, dried over anhydrous magnesium sulfate, to dryness gave a residue of **7d**, which was mixed with 10 ml of 100% phosphoric acid and heated at 120° for 1 hr. The reaction mixture was cooled in an ice bath and neutralized with potassium hydroxide solution. Extraction with methylene chloride provided a red solid which was crystallized from carbon tetrahcloride to give 50 mg of **6f**, mp 195–196°. A mixture melting point with the sample of **6f** obtained previously showed no depression, and the infrared spectra of the two samples ($CHCl_3$) were superimposable.

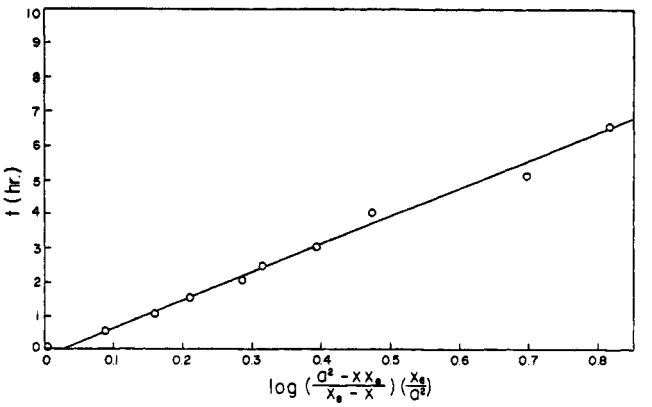


Figure 2. Plot of log $[(a^2 - xx_e)/(x_e - x)](x_e/a^2)$ *vs.* time for reaction of **1b** with **3a** at 41.00 ± 0.05°; concentration of **1b** = concentration of **3a** = 0.0172 *M*.

Kinetics Procedure for the Reactions of 1a, 1b, and 1c with 3a. In a three-necked flask equipped with a reflux condenser, a stopper, and a mechanical stirrer were placed 1.72×10^{-2} mol of a given 2-aroyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate, 30.0 ml of purified dimethylformamide, and 7.0 ml of 95% ethanol, and the flask and its contents were equilibrated in a constant-temperature bath. To this solution was added 3.00 ml (3.00 g, 1.72×10^{-2} mol) of ethyl phenylpropiolate from a micropipet. Zero time was defined as the instant of complete mixing of the reagents. At 1- or 2-hr intervals, a 2.00-ml aliquot of the reaction mixture was removed and added to 10 ml of saturated sodium bicarbonate solution in order to quench the reaction. The mixture was extracted thoroughly with ether, and the ether solution was concentrated to dryness. The residue was dissolved in a few milliliters of spectro-analyzed chloroform, and the flask was washed with small amounts of the same solvent. The combined chloroform solution was concentrated to exactly 2.00 ml and its infrared spectrum taken. The rates were determined by following the disappearance of the triple bond absorption at 2218 cm^{-1} for ethyl phenylpropiolate in a Beckman IR-10 spectrophotometer. A calibration curve was constructed by taking the infrared spectra of solutions of known concentrations of ethyl phenylpropiolate in spectroanalyzed chloroform at 2218 cm^{-1}. The plot was found to fit Beer's law very well. From the infrared spectrum of the aliquot and the calibration curve, the concentration of unchanged ethyl phenylpropiolate at each time, *t*, could be determined.

Two different types of plots were constructed to permit the calculation of specific rate constants. In the first, a typical plot for an uncomplicated second-order reaction was constructed. This was found to be linear for about 55–60% of reaction, as shown in Figure 1 for one experiment. In the second plot, for the reaction scheme

$$A + B \underset{k_1}{\overset{k}{\rightleftharpoons}} X$$

$\log [x_e(a^2 - xx_e)/a^2(x_e - x)]$ (in $A_0 = B_0$ case) or $\log [(A - \lambda_1)/(A - \lambda_2)]$ (in $A_0 \neq B_0$ case) was plotted *vs.* *t*. This gave a straight line for the entire equilibrium reaction. The terms for the first of these second- and first-order equilibrium plots are defined as follows:[14] ($a = A_0 = B_0$ = initial concentration of **1** and **3**, $x = A_0 - A = B_0 - B$, $x_e = A_0 - A_e$, $A = B$ = concentration of **1** and **3** at time *t*, A_e = concentration of **1** and **3** at equilibrium. A plot for a typical experiment where $A_0 = B_0$ is shown in Figure 2 and that for an experiment in which $A_0 \neq B_0$ in Figure 3. The data for the various experiments are summarized in Table I.

(14) (a) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," Wiley, New York, N. Y., 1953, pp 172–175; (b) G. E. Barrow, "Physical Chemistry," McGraw-Hill, New York, N. Y., 1966, Chapter 15.

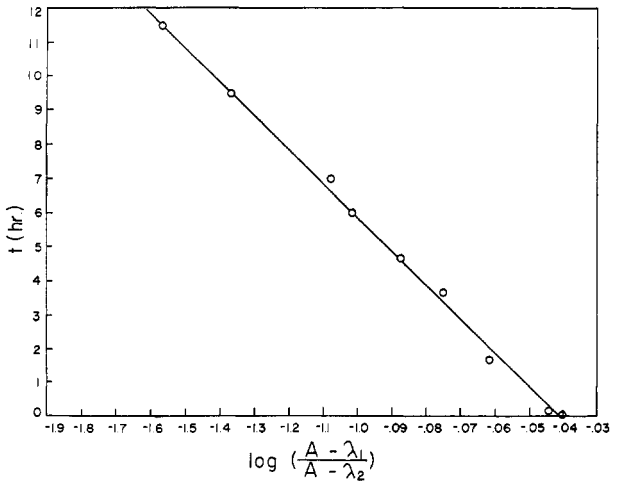


Figure 3. Plot of log $[(A - \lambda_1)/(A - \lambda_2)]$ *vs.* time for reaction of 2-benzoyl-1,2-dihydroisoquinoldonitrile hydrofluoroborate (**1a**) with ethyl phenylpropiolate (**3a**) at 34.40 ± 0.05°; concentration of **1a** = 0.021 *M*, concentration of **3a** = 0.0172 *M*.

Kinetics Procedure for the Reactions of 1a with 3b and 3c. All three phenylpropiolic acids and their esters used in this study show the characteristic –C≡≡C– stretch in the 2200–2300-cm^{-1} region of the infrared spectrum. Since other constituents present in the system do not absorb in this region, the base line method of analysis was employed. Two bands are observed in this region. The major band followed Beer's law over the concentration range used.[15] A Perkin-Elmer 237-B Infrared spectrometer was used. Sodium chloride cells of 0.4 mm thickness were used. The reaction cell had a 20-ml capacity and was jacketed completely. A Birkerd (Denmark) constant-temperature circulating water bath was used to maintain the reaction cell at 41.0 + 0.1°. The liquid–liquid continuous extraction apparatus used was modeled after that obtainable from the Scientific Apparatus Co.

The following general procedure was used.

a. 2-Benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate (**1a**) was placed in the reaction cell together with a magnetic stirrer and 15 ml of ethanol.

b. The phenylpropiolate ester to be studied was dissolved in spectrograde methylene chloride and taken up in a syringe.

c. Half an hour was allowed for the cell to reach thermal equilibrium.

d. The ester in solution was injected into the reaction cell, t_0 being taken as corresponding to the time when half the ester had been added.

e. At time = t, the reaction was quenched by addition of the solution to 50 ml of slightly alkaline aqueous solution at 0°.

f. A 100-ml sample of spectrograde methylene chloride was placed in the flask of the extraction apparatus, 20 ml in the extractor, and then the aqueous mixture was added to the extractor. The methylene chloride in the flask was heated to its reflux temperature and the extractor was allowed to operate for 20 hr (the aqueous layer was cloudy to begin with, as part of the mixture oiled out during the quenching step. After the extraction, the aqueous layer was clear.)

g. The organic layer was drained into the flask, and the solvent was removed by distillation. A 100-ml sample of anhydrous benzene was added to the residue and distilled. This procedure was repeated until the benzene distilled at 80°. The flask was not allowed to go dry at this temperature, but was cooled to room temperature, and the remaining benzene was removed under reduced pressure at room temperature.

h. The residue was adjusted to exactly 10 ml with spectrograde methylene chloride.

i. Three aliquots (300 μl) were treated separately by slowly scanning the 2500–2000-cm^{-1} region of the infrared spectrum. From the average value for absorbance, the concentration was read from the calibration curve.

Calibration curves were made by using an identical procedure except for the presence of 2-benzoyl-1,2-dihydroisoquinaldonitrile hydrofluoroborate.

A check on possible polymerization of the alkyne esters was made by refluxing their solutions at the reaction temperature corresponding to the longest time period used in the given reaction. When the ir spectrum was taken, no evidence of polymerization was detected; that is, the concentration of the ester was unchanged.

Efficiency of extraction was checked as follows: an aliquot of a mock reaction mixture was removed before the quenching step; it was diluted with enough methylene chloride so that the ethanol present constituted less than 5% of the resulting solution (in order not to fog the sodium chloride windows of the ir cells used). The concentration was determined by the ir method and compared with that of the remainder of the reaction mixture, which was worked up as usual. Within experimental accuracy, extraction proved to be complete.

The specific rate constants were calculated graphically by use of the second-order rate law where the two reactants are present in unequal concentrations.[14]

$$k = \frac{\frac{1}{a-b} x \ln \frac{b(a-x)}{a(b-x)}}{t} \text{ l. mol}^{-1} \text{ sec}^{-1}$$

Every point on the graph represents a different run; hence the quantity plotted along the ordinate was

$$\frac{1}{a-b} x \ln \frac{b(a-x)}{a(b-x)}$$

rather than

$$\ln \frac{b(a-x)}{a(b-x)}$$

The results are summarized in Table I.

Appendix

Rate Law for Reaction A + B ⇌ X, where $A_0 \neq B_0$. By a derivation which parallels that described by Benson,[16] one obtains the rate expression

$$-\left(\frac{1}{\lambda_1 - \lambda_2}\right) \log \frac{(A-\lambda_1)}{(A-\lambda_2)} = k_1 t + 1$$

which, by further manipulation, gives

$$\frac{1}{\lambda_1 - \lambda_2} \log \frac{(A-\lambda_1)(A_0-\lambda_2)}{(A-\lambda_2)(A_0-\lambda_1)} = -k_1 t$$

The various terms are defined as follows

$$\lambda_1 = \frac{r + \sqrt{r^2 + 4\delta}}{2}$$

$$\lambda_2 = \frac{r - \sqrt{r^2 + 4\delta}}{2}$$

$$N - M = r = \left[(A_0 - B_0) - \left(\frac{A_e^2 - A_e N}{A_0 - A_e}\right)\right]$$

$MA_0 = \delta$, which is a constant for the given reaction.

$$M = \frac{k_{-1}}{k_1} = \frac{1}{K_e}$$

$A_0 - B_0 = N$, a constant for a reaction under consider-

(15) According to Bellamy, such additional bands are observed in certain conjugated acetylenic esters, although their origin is not definitely known. Some chemists attribute them to mechanical coupling effects; others, to overtones or combination bands: L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Wiley, New York, N. Y., 1966, p 60.

(16) S. W. Benson, "The Foundations of Chemical Kinetics," McGraw-Hill, New York, N. Y., 1960, pp 29–31.

ation. A_0, B_0, and A_e = initial and equilibrium concentrations of reagents. The complete derivation, as tailored to the system under consideration, can be found in Hung's dissertation.[17]

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(17) William Mo-wei Hung, Doctoral Dissertation, University of Massachusetts, Aug 1970.

Cyclopropanes. II. An Electrophilic Addition with Nucleophile Retention[1]

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Abstract: The cyclopropane hydrocarbon **11** was synthesized as an analogy with the previous case **3**, to test the importance of polar *vs.* steric effects in cyclopropane cleavage. Unlike **3**, the major cleavage products of **11** with HBr exhibited Markovnikov direction. They also showed exclusive retention of nucleophile. These results are rationalized in terms of a unified picture of cyclopropane cleavages.

Electrophilic addition to cyclopropanes has aroused considerable interest in recent years, since it involves a nearly unique opportunity to study the stereoelectronic effects in σ-bond cleavage as well as an unusual system of strained bonding orbitals. Experimentally it is possible to discern not only the sites of electrophile and nucleophile attachment across a cleaved σ-bond but also their stereochemistry. Each may bond *via* retention or inversion of configuration (of a cyclopropane carbon) with respect to that of the bond cleaved. The four possible stereochemical results may be symbolized, with R = retention, I = inversion, as (RR), (RI), (IR), (II), the electrophile first followed by the nucleophile. These are shown in Figure 1 for a generalized cyclopropane.

Theoretical calculations on protonation of cyclopropanes implicate two kinds of initial species (intermediates?), arising from edge protonation and corner protonation, of roughly comparable energy[3] and presumably readily interconvertible by minor shifts in nuclear positions.[4a] These are summarized in Figure 1. Edge protonation of the bond cleaved leads to two possible products, reversed in site of attachment of electrophile–nucleophile but both exhibiting electrophile retention. Corner protonation can occur with H^+ oriented on either side and nucleophile attack at either of the other two cyclopropane carbons, opening either bond adjacent to the protonated corner carbon. Hence either retention or inversion of the electrophile (H^+) may be observed: the first case is the corner-protonated species nearest in geometry to (and interconvertible to) the edge-protonated species above; the second case is the corner-protonated species nearest in geometry to one edge-protonated at the bond *adjacent* to that which is finally cleaved. Thus if edge protonation precedes equilibration to a corner-protonated species electrophile inversion can proceed by edge protonation at one bond, equilibration to a corner-protonated species, and collapse with nucleophile to cleave the adjacent bond. The edge-protonated species is seen as a proton embedded in the σ-bond orbital, in the plane of the ring. The corner-protonated variant is essentially equivalent to the midpoint of a Wagner–Meerwein rearrangement, *i.e.*, of the corner-protonated carbon passing across the other two carbons; its two modes of collapse with nucleophile correspond to completion of a 1,2-shift in either direction.[4b]

Each species may collapse in two ways by nucleophile attack, the edge-protonated version at either end of the protonated bond, breaking only that bond in either case, the corner protonation by breaking either of the two adjacent bonds but nucleophile ultimately sited upon one of the other two carbons. The choice of mode is usually dictated by the residual preference in the complex cation for carbonium ion stabilization at one carbon site or the other (tertrary > secondary > primary; allylic > saturated; etc.), but the preference differential is presumably less in the complex cation than in "free" carbonium ions. Backside attack of nucleophile is the usual observation, leading to inversion at the nucleophile site, but the first clear case of

(1) Previous paper: J. B. Hendrickson and R. K. Boeckman, Jr., *J. Amer. Chem. Soc.*, **91**, 3269 (1969).

(2) National Institutes of Health Predoctoral Fellow, 1969–1970.

(3) (a) T. Yonezawa, K. Shimiza, and H. Kato, *Bull. Chem. Soc. Jap.*, **46**, 1302 (1967); (b) J. D. Petke and J. L. Whitten, *J. Amer. Chem. Soc.*, **90**, 3338 (1968); (c) H. Fischer, H. Kollmar, H. O. Smith, and K. Miller, *Tetrahedron Lett.*, 5821 (1968); (d) G. Klopman, *J. Amer. Chem. Soc.*, **91**, 89 (1969).

(4) (a) Since the distinction between the two species is geometrically small and the energy difference may indeed be only a few kilocalories per mole, the distinction may be unimportant. The electron-rich bent σ bond is the obvious place of attack, stereoelectronically, and subsequent passage through corner-protonated geometry can give observed products, as indicated in Figure 1. (b) The corner-protonated species may be envisioned as an sp^2 carbon bearing hydrogen, with its p orbital embedded in the midpoint of a π orbital between the other two carbons.