effect of 3.1 for the hydrolysis of **1a** in strongly acidic media indicates that the rate-limiting step of the hydrolysis of this ester under these conditions is proton transfer from solvent to the double bond to form a carbonium ion which is subsequently rapidly attacked by water. Under mildly acidic conditions the α-acetoxystyrenes apparently hydrolyze via the normal $A_{AC}2$ mechanism of acid-catalyzed ester hydrolysis.[6] However, our studies with the acylenol **2** indicate that this compound hydrolyzes via rate-determining proton transfer to the double bond even in the mildly acidic pH region. The solvent deuterium isotope effect, 3.1 ± 0.1, for the hydrolysis of **2**, determined in the acidic pH region is similar to solvent deuterium isotope effects of 2.5–3.0 observed for the hydrolysis of ketene acetals[21] and vinyl ethers,[22] both of which hydrolyze by rate-determining protonation of the double bond. This isotope effect is also identical with that observed for hydrolysis of **1a** (see above) in the strong acid region of acidity.

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Registry No.—**1a**, 22390-98-3; **1b**, 22390-99-4; **1c**, 2206-94-2; **1d**, 22479-32-9; **1e**, 22391-00-0; **1f**, 22391-01-1; **2**, 62415-90-1; acetyl chloride, 75-36-5; $H_2{}^{18}O$, 14314-42-2; isopropenyl acetate-^{18}O, 62415-91-2; acetic acid-^{18}O, 60321-43-9; methylacetylene, 74-99-7; 1-ethoxy-2-phenylacetylene, 32569-84-9; $Hg(OAc)_2$, 1600-27-7; α-acetoxystyrene-^{18}O, 62415-92-3.

References and Notes

(1) NSF Predoctoral Fellow, 1972–1975.
(2) M. Novak and G. M. Loudon, *J. Am. Chem. Soc.*, **98**, 3591 (1976).
(3) (a) W. P. Jencks and J. Carriuolo, *J. Am. Chem. Soc.*, **82**, 675 (1960); (b) T. C. Bruice and M. F. Mayahi, *ibid.*, **82**, 3067 (1960); (c) T. C. Bruice, A. Donzel, R. W. Huffman, and A. R. Butler, *ibid.*, **89**, 2106 (1967); (d) L. doAmaral, K. Koehler, P. Bartenbach, T. Pletcher, and E. H. Cordes, *ibid.*, **89**, 3537 (1967); (e) G. M. Blackburn and W. P. Jencks, *ibid.*, **90**, 2638 (1968); (f) W. P. Jencks and M. Gilchrist, *ibid.*, **90**, 2622 (1968); (g) A. C. Satterthwait and W. P. Jencks, *ibid.*, **96**, 7018 (1974).
(4) (a) J. F. Kirsch and W. P. Jencks, *J. Am. Chem. Soc.*, **86**, 837 (1964); (b) J. T. Ryan and A. A. Humffray, *J. Chem. Soc. B*, 842 (1968); (c) B. Holmquist and T. C. Bruice, *J. Am. Chem. Soc.*, **91**, 2982, 2985 (1969).
(5) M. Novak and G. M. Loudon, *J. Org. Chem.*, preceding paper in this issue.
(6) D. S. Noyce and R. M. Pollack, *J. Am. Chem. Soc.*, **91**, 119 (1969).
(7) G. F. Hennion and J. A. Nieuwland, *J. Am. Chem. Soc.*, **56**, 1802 (1934).
(8) (a) M. L. Bender, *J. Am. Chem. Soc.*, **73**, 1626 (1951); (b) M. L. Bender, R. D. Ginger, and J. P. Unik, *ibid.*, **80**, 1044 (1958); (c) S. A. Shain and J. F. Kirsch, *ibid.*, **90**, 5848 (1968); (d) C. B. Sawyer and J. F. Kirsch, *ibid.*, **95**, 7375 (1973); (e) M. L. Bender, H. Matsui, R. J. Thomas, and S. W. Tobey, *ibid.*, **83**, 4193 (1961); (f) C. A. Bunton and D. A. Spatcher, *J. Chem. Soc.*, 1079 (1956).
(9) R. Tanaka and S. I. Miller, *Tetrahedron Lett.*, 1753 (1971).
(10) W. von Philipsborn, *Angew. Chem., Int. Ed. Engl.*, **10**, 472 (1971).
(11) D. Rittenburg and L. Ponticorvo, *Int. J. Appl. Radiat. Isot.*, **1**, 208 (1956).
(12) M. L. Bender and H. d'A. Heck, *J. Am. Chem. Soc.*, **89**, 1211 (1967).
(13) K. B. Wiberg, *Chem. Rev.*, **55**, 713 (1955).
(14) (a) A. J. Kirby in "Comprehensive Chemical Kinetics", Vol. 10, G. H. Bamford and C. F. H. Tipper, Ed., American Elsevier, New York, N.Y., 1972, p 57; (b) K. Yates, *Acc. Chem. Res.*, **4**, 136 (1971).
(15) K. Yates and R. A. McClelland, *J. Am. Chem. Soc.*, **89**, 2686 (1967).
(16) C. A. Bunto and T. Hadwick, *J. Chem. Soc.*, 3034 (1957); 943 (1961); 3248 (1958).
(17) P. Ballinger and F. A. Long, *J. Am. Chem. Soc.*, **82**, 795 (1960).
(18) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **75**, 4231 (1953).
(19) (a) M. L. Bender, *Chem. Rev.*, **60**, 53 (1960); (b) M. L. Bender, "Mechanisms of Homogeneous Catalysis, from Protons to Proteins", Wiley, New York, N.Y., 1971, pp 37–71.
(20) (a) C. A. Lane, *J. Am. Chem. Soc.*, **86**, 2521 (1964); (b) C. A. Lane, M. F. Cheung, and G. F. Dorsey, *ibid.*, **90**, 6492 (1968).
(21) (a) R. Herschfield, M. J. Yeager, and G. L. Schmir, *J. Org. Chem.*, **40**, 2940 (1975); (b) V. Gold and D. C. A. Waterman, *J. Chem. Soc.*, 839, 849 (1968).
(22) (a) G. M. Loudon, C. K. Smith, and S. E. Zimmerman, *J. Am. Chem. Soc.*, **96**, 465 (1974); (b) A. J. Kresge and H. J. Chen, *J. Am. Chem. Soc.*, **94**, 2819 (1972), and references cited therein.

Notes

Quinoxaline Studies. 24.[1a] 3-(α-Cyano)benzyl-2(1*H*)-quinoxalinone *vs.* 2,3-Di(α-cyano)benzylquinoxaline. A Reinvestigation

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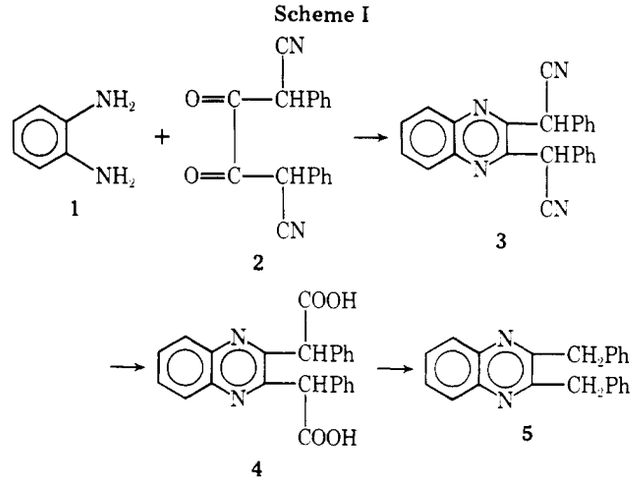
Dutt and Sen[2] reported the preparation of quinoxalines of structure **3** by condensation of *o*-phenylenediamine (**1**) with the diketone **2** prepared by condensation of diethyl oxalate with 2 mol of benzyl cyanide. In an effort to repeat this work for the purpose of preparing **4** and **5** (Scheme I) we found that the starting carbonyl compound used by Dutt and Sen was actually the 1:1 condensation product **6**, and their final condensation product was 3-(α-cyanobenzyl)-2(1*H*)-quinoxalinone (**7**). Our experiments also indicated that **2** would not condense with **1** to give **3**, but fortuitously synthesis of type **5** compounds has been recently reported.[3]

Interestingly, Dutt and Sen[2] claimed to have prepared 1,4-dicyano-1,4-diphenyl-2,3-butanedione (**2**) by a variation of the method of Volhard,[4] wherein diethyl oxalate was condensed with 2 equiv of benzyl cyanide with sodium in ethanol.

Scheme I



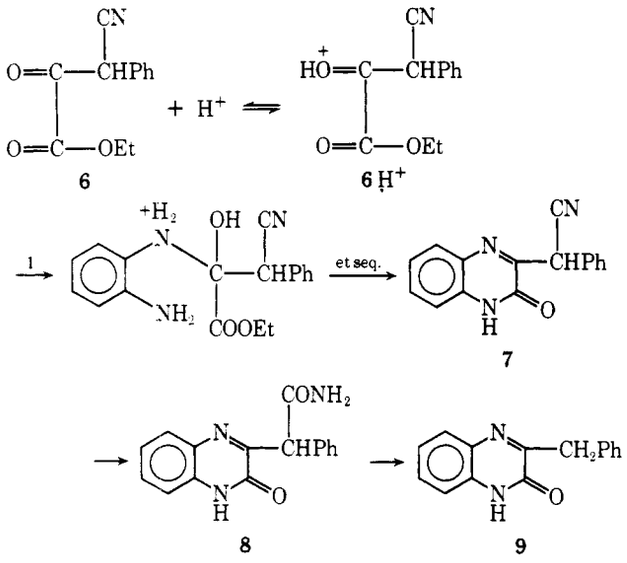
But in contrast to Volhard's procedure, Dutt and Sen omitted the ethanol. Repetition of both procedures showed that Volhard prepared **2**, but that Dutt and Sen had prepared ethyl phenylcyanopyruvate (**6**). Formation of **6** in the absence of EtOH and an excess of benzyl cyanide is probably the consequence of precipitating the sodium salt of **6** formed by interaction of 1 equiv each of diethyl oxalate and benzyl cyanide,

thus interdicting further alkylation of **6**. Compound **6** is better prepared by the method of Adams and Calvery.[5]

Condensation of **6** with **1** by the reported procedure in either cold HOAc or hot EtOH gave **7** monohydrate. In hot HOAc the hydrolysis product, 3-(α-carboxamido)benzyl-2(1*H*)-quinoxalinone (**8**) was, however, obtained. Complete hydrolysis with spontaneous decarboxylation of either cyanide **7** or amide **8** gave the known 3-benzyl-2(1*H*)-quinoxalinone (**9**).[6]

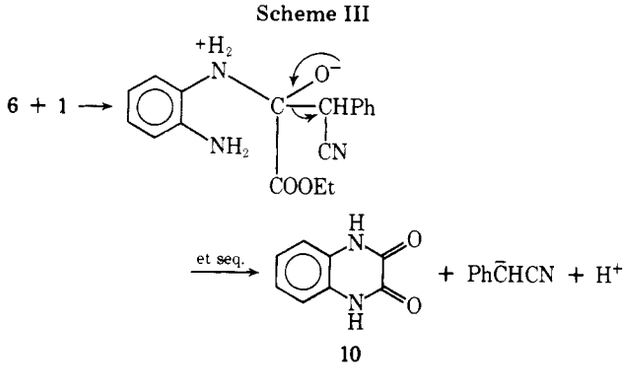
Obviously, condensations of **1** with **6** in HOAc and EtOH proceed via the classical "addition–elimination" (A–E) sequence (Scheme II) about the keto group of **6**, wherein water is eliminated in the second (E) step of the reaction.

Scheme II



Surprisingly, in the aprotic solvent THF, the second step of the A–E sequence referred to above results in elimination of the relatively stable cyanobenzyl carbanion (instead of water), with formation of 2,3(1*H*,4*H*)-quinoxalinedione (**10**)! This reaction is outlined in Scheme III.

Scheme III



Experimental Section[7]

α,α'-Dicyanodibenzyl diketone (2) was prepared by the Volhard[4] procedure. Yellow material (29%) was obtained: mp 285–287 °C from HOAc–H_2O (1:1, 100 mL/g) (lit.[2] mp 132 °C); green powder, mp 279 °C from amyl alcohol (150 mL/g) (lit.[4] mp 270 °C); IR (KBr) 3300 (OH), 2300 (CN), 1530 cm^{-1} (C=C); NMR (Me_2SO) δ 7.29–8.15 (m, 10, aromatic), 9.35 (s, 2, OH).

Anal. Calcd for $C_{18}H_{12}N_2O_2$: C, 74.98; H, 4.19; N, 9.72. Found: C, 74.63; H, 4.38; N, 9.43 (lit.[2] N, 9.4; lit.[4] C, 75.11; H, 4.27; N, 9.89).

Ethyl Phenylcyanopyruvate (6). The Dutt and Sen[2] "modified" procedure for **2** was used, wherein the above procedure for the preparation of **2** was altered by omitting EtOH solvent, Na being added directly to a solution of diethyl oxalate and benzyl cyanide: mp 126–128 °C from EtOH–H_2O (1:1, 10 mL/g) (lit.[2] mp 132 °C, lit.[5] mp 130 °C); lit.[5] preparation mmp 125–127 °C.

Anal. Calcd for $C_{12}H_{11}O_3N$: N, 6.45 (lit.[2] N, 9.4).

3-(α-Cyano)benzyl-2(1*H*)-quinoxalinone (7). A solution of 2.8 g (0.014 mol) of **6**, 1.2 g (0.011 mol) of **1**, and 20 mL of HOAc was stirred for 0.5 h at 25 °C, diluted with water, and filtered to give 2.6 g (85%) of yellow solid: mp 222–223 °C; mp 215–217 °C from HOAc–H_2O (1:1, 150 mL/g), mp 217–218 °C from EtOH–H_2O (1:1, 100 mL/g) (lit.[2] mp 227 °C for alleged **3**); IR (KBr) 4000–2700 (NH, OH), 2170 (CN), 1650 (CO), 1600 cm^{-1} (NH bend).

Anal. Calcd for $C_{16}H_{11}N_3O{\cdot}H_2O$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.82; H, 4.57; N, 15.15.

The same weights of **1** and **6** in 20 mL of boiling EtOH for 0.5 h gave the same results as above.

Anal. Found: C, 68.86; H, 4.15; N, 15.30.

After drying at 78 °C (1 mm), the samples had mp 219–220 °C; analysis then showed the substance to be a hemihydrate which regained its original weight upon standing in air; IR (KBr) 3400 (NH, OH), 2180 (CN), 1650 (CO), 1600 cm^{-1} (NH bend); UV max 372 nm (ε 11 111), 356 (infl), 290 (infl), 226 (21 111), 200 (end absorption).

Anal. Calcd for $C_{16}H_{11}N_3O{\cdot}\frac{1}{2}H_2O$: C, 71.10; H, 4.47; N, 15.54. Found: C, 70.95; H, 4.22; N, 15.61.

3-(α-Carboxamido)benzyl-2(1*H*)-quinoxalinone (8). Method A. Refluxing **7** in HOAc (20 mL/g) for 3 h gave 44% of yellow **8**: mp 297–299 °C; mp 301–303 °C from HOAc–H_2O (1:1, 60 mL/g); IR (KBr) 3360–3180 (NH), 1650 cm^{-1} (CO); UV max 340 nm (ε 5571), 282 (5352), 254 (infl), 229 (16 571), 200 (end absorption); NMR (Me_2SO) δ 5.51 (s, 1, CH), 7.25–7.90 (m, 12, aromatics, NH_2).

Anal. Calcd for $C_{16}H_{13}N_3O_2$: C, 68.81; H, 4.69; N, 15.04. Found: C, 68.55; H, 4.75; N, 15.13.

Method B. Refluxing a solution of 2.4 g of **1** and 5.6 g of **6** in 40 mL of HOAc for 3 h gave 29% of **8**, melting point and mixture melting point as above.

3-Benzyl-2(1*H*)-quinoxalinone (9). Method A. A suspension of **8** in 6 N HCl (66 mL/g) was refluxed for 6 h to give 78% of yellow **9**, mp 199–202 °C. The crude product was treated with Darco and Filteraid in 4.5 N NH_4OH solution, filtered, and reprecipitated with 6 N HCl to give white **9**: mp 199–202 °C; mp 200–201 °C (lit.[6] mp 196 °C) from Me_2CO (50 mL/g); IR (KBr) 1650 cm^{-1} (CO); UV max 344 nm (ε 7176), 334 (infl), 282 (6588), 254 (infl), 229 (21 647), 200 (end absorption); NMR (Me_2SO) δ 4.2 (s, 2, CH_2), 7.0–8.0 (m, 10, aromatics, OH).

Anal. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86. Found: C, 76.26; H, 5.14; N, 11.52.

Method B. Hydrolysis of **8** in boiling 2 N KOH for 6 h gave 44% yield of white **9**: mp 196–200 °C; mp 201–202 °C from EtOH–H_2O (1:1, 100 mL/g); same mixture melting point, IR, UV, and NMR as cited above.

Anal. Found: C, 76.05; H, 5.09; N, 11.74.

2,3(1*H*,4*H*)-Quinoxalinedione (10). Method A. A solution of 5.6 g (0.028 mol) of **6** and 2.4 g (0.022mol) of **1** in 40 mL of boiling THF for 1 h gave 2.0 g (56%) of yellow solid: mp <360 °C; mp <360 °C from EtOH (200 mL/g) (lit.[8] mp <360 °C); IR (KBr) 3050–2800 (NH), 1660 cm^{-1} (CO); UV (0.1 N NaOH) max 342 nm (ε 11 000), 327 (16 800), 315 (13 440), 264 (infl), 200 (end absorption) [lit.[8] 340 (11 000), 326 (14 500), 315 (12 000)]; NMR (Me_2SO) δ 7.3 (s, 4, aromatics) 12.0 (s, 2, NH).

Method B. Preparation of **10** by the method of Newbold and Spring[8] gave **10** of the same melting point, mixture melting point, IR, UV, and NMR as cited above.

Registry No.—**1**, 95-54-5; **2**, 10471-29-1; **3**, 62212-27-5; **6**, 6362-63-6; **7**, 38036-61-2; **8**, 62212-21-9; **9**, 24949-43-7; **10**, 15804-19-0.

References and Notes

(1) (a) Part 23 of this series: G. H. Fisher, H. R. Moreno, J. E. Oatis, Jr., and H. P. Schultz, *J. Med. Chem.*, **18**, 746 (1975). (b) Abstracted from the M.S. Thesis of M.M., 1973.

(2) (a) S. Dutt and N. K. Sen, *J. Chem. Soc.*, **121**, 2663 (1922); (b) J. C. E. Simpson, "Condensed Pyridazine and Pyrazine Rings", Vol. 5, "The Chemistry of Heterocyclic Compounds", A. Weissberger, Ed., Interscience, New York, N.Y., 1953, p 212.

(3) M. Chaykovsky, M. H. Lin, and A. Rosowsky, *J. Org. Chem.*, **37**, 2018 (1972).

(4) J. Volhard, *Justus Liebigs Ann. Chem.*, **282**, 4 (1894).

(5) R. Adams and H. O. Calvery, "Organic Syntheses", Collect. Vol. II, A. H. Blatt, Ed., Wiley, New York, N.Y., 1943, p 287.

(6) A. H. Cook and C. A. Perry, *J. Chem. Soc.*, 394 (1943).

(7) Melting points, uncorrected, were determined on a Thomas-Hoover apparatus. Spectra were recorded as follows: UV, Jasco ORD/UV in 95% EtOH at concentrations of ~5 mg/L in 1-cm quartz cells; ^1H NMR, Hitachi Perkin-Elmer R-20, 60 MHz, 34 °C, δ in parts per million from internal Me_4Si; IR, Beckman IR-10. Elemental analyses were performed by PCR, Inc., Gainesville, Fla.

(8) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 519 (1948), and references cited therein.