from Et_2O–hexane to give 0.737 g of **12**, mp 134–136 °C dec. Chromatography of the mother liquor on 30 g of SiO_2 with 30% Et_2O–hexane gave an additional 0.843 g of crystalline **12** (total = 1.58 g, 51%). An analytical sample crystallized from Et_2O–hexane had mp 137–138 °C: $[\alpha]_D$ $CHCl_3$ +45.7°; IR (CH_2Cl_2) 3650, 1785, 1745, 1562, 1375 cm^{-1}; NMR δ 1.45 and 1.6 (two s, 6 H, $(CH_3)_2C$), 3.5 (br s, 1 H, OH), 4.55 (s, 1 H, $CHCO_2$), 4.74 (d, 1 H, J = 13 Hz, $O_2NCH_AH_B$), 4.96 (d, 1 H, J = 13 Hz, $O_2NCH_AH_B$), 5.2 (s, 2 H, CO_2CH_2), 5.85 (s, 1 H, C-5 H), 7.4 (s, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{18}N_2O_6S$: C, 52.45; H, 4.95; N, 7.65. Found: C, 52.45; H, 5.14; N, 7.62.

Benzyl 6-Nitromethylenepenicillanate (15) and *tert*-Butyl 7-Nitromethylenedeacetoxycephalosporanate (16). To a solution of 2 mmol of nitromethylcarbinol (**12** or **13**) in 40 mL of CH_2Cl_2 at −40 °C (argon) was added triethylamine (690 μL, 5 mmol), followed by dropwise addition of mesyl chloride (230 μL, 3 mmol) over 3 min. This mixture was stirred at −40 °C for 20 min. The mixture was diluted with 100 mL of CH_2Cl_2 and was washed with 40 mL of ice-cold 10% HCl solution, 40 mL of water, and 40 mL of saturated NaCl solution. After drying ($MgSO_4$), the solution was evaporated to give an oily crude product.

Compound **15** was purified by chromatography on 20 g of SiO_2 with 30% Et_2O–hexane and was obtained as a yellow oil (0.327 g, 47%): IR (CH_2Cl_2) 1776, 1745, 1530, 1375, 1350 cm^{-1}; NMR δ 1.4 and 1.55 (two s, 6 H, $(CH_3)_2C$), 4.65 (s, 1 H, $CHCO_2$), 5.2 (s, 2 H, CO_2CH_2), 6.15 (s, 1 H, C-5 H), 7.25 (s, 1 H, $=CHNO_2$), 7.35 (s, 5 H, C_6H_5). Anal. Calcd for $C_{16}H_{16}N_2O_5S$: C, 55.16; H, 4.64; N, 8.04. Found: C, 55.43; H, 4.97; N, 7.67.

Compound **16** was purified by preparative TLC (80% Et_2O–hexane) and it was obtained as a light-yellow solid, mp 152–154 °C dec (Et_2O–hexane), 0.335 g (55%): IR(CH_2Cl_2) 1776, 1720, 1535, 1370, 1345 cm^{-1}; NMR δ 1.5 (s, 9 H, $(CH_3)_3C$), 2.15 (s, 3 H, $CH_3C=$), 3.21 (d, 1 H, J = 18 Hz, SCH_AH_B), 3.56 (d, 1 H, J = 18 Hz, SCH_AH_B), 5.58 (br s, 1 H, C-7 H), 7.32 and 7.34 (two s, 1 H, $=CHNO_2$). Anal. Calcd for $C_{13}H_{16}N_2O_5S$: C, 49.99; H, 5.16; N, 8.97. Found: C, 49.93; H, 5.04; N, 8.96.

Benzyl 6β-Nitromethylpenicillanate (17). Wilkinson's catalyst (0.116 g) was prereduced with H_2 at 45 psi in 20 mL of EtOH–benzene (1:1, degassed with argon prior to loading the catalyst). The nitroolefin **15** (0.116 g, 0.33 mmol) in 20 mL of degassed EtOH–benzene (1:1) was added, and the mixture was shaken with H_2 at 55 psi for 16 h. The mixture was concentrated to give a reddish-brown oil which was purified by preparative TLC to give 74 mg (64%) of **17** as an oil: IR (CH_2Cl_2) 1776, 1745, 1535, 1375 cm^{-1}; NMR δ 1.4 and 1.56 (two s, 6 H, $(CH_3)_2C$), 4.22 (m, 1 H, $J_{5,6}$ = 4 Hz, $J_{A,6}$ = 4.5 Hz, $J_{B,6}$ = 11 Hz, C-6 H), 4.42 (s, 1 H, $CHCO_2$), 4.63 (d of d, 1 H, $J_{6,A}$ = 4.5 Hz, $J_{A,B}$ = 15 Hz, $O_2NCH_AH_B$), 4.95 (d of d, 1 H, $J_{6,B}$ = 11 Hz, $J_{A,B}$ = 15 Hz, $O_2NCH_AH_B$), 5.15 (s, 2 H, CH_2O), 5.6 (d, 1 H, $J_{6,5}$ = 4 Hz, C-5 H), 7.35 (s, 5 H, C_6H_5); m/e 350 (M^+). Anal. Calcd for $C_{16}H_{18}N_2O_5S$: C, 54.84; H, 5.18; N, 8.0. Found: C, 55.17; H, 4.98; N, 7.69.

***tert*-Butyl 7β-Nitromethyldeacetoxycephalosporanate (19) and *tert*-Butyl 7α-Nitromethyldeacetoxycephalosporanate (18).** Hydrogenation of **16** (0.24 g, 0.77 mmol) under the same conditions used to prepare **17** afforded 0.111 g of **19** (46%) as an oil after preparative TLC (80% Et_2O–hexane): IR (CH_2Cl_2) 1776, 1720, 1560, 1360 cm^{-1}; NMR δ 1.5 (s, 9 H, $(CH_3)_3C$), 2.1 (s, 3 H, $CH_3C=$), 3.14 (d, 1 H, J = 18 Hz, SCH_AH_B), 3.47 (d, 1 H, J = 18 Hz, SCH_AH_B), 4.2–4.47 (m, 1 H, C-7 H), 4.65 (d of d, 1 H, $J_{7,A}$ = 4.5 Hz, $J_{A,B}$ = 15.5 Hz, $O_2NCH_AH_B$), 4.92 (d of d, 1 H, $J_{7,B}$ = 11 Hz, $J_{A,B}$ = 15.5 Hz, $O_2NCH_AH_B$), 4.99 (d, 1 H, $J_{7,6}$ = 4.5 Hz, C-6 H); m/e 314 (M^+). Anal. Calcd for $C_{13}H_{18}N_2O_5S$: C, 49.67; H, 5.77; N, 8.91. Found: C, 50.02; H, 6.09; N, 8.58. Compound **19** was also obtained in 31% yield through $NaBH_4$ reduction of **16** in EtOH.

The α-nitromethyl compound **18** was obtained in impure form as an oil in 11% yield by the hydrogenation of **16** and in ca. 14% yield through the $NaBH_4$ reduction of **16**: IR (CH_2Cl_2) 1775, 1715, 1560, 1360 cm^{-1}; m/e 314 (M^-).

7β-Hydroxy-7α-nitromethyldeacetoxycephalosporanic Acid (20). Alcohol **13** was dissolved in 5 mL of 100% formic acid and the solution was left at room temperature for 3 h. The solution was concentrated in vacuo to give a film. The residue was mixed with 10 mL of ice-cold 6% $NaHCO_3$ and the resulting mixture was throughly extracted with EtOAc. The aqueous phase at 0 °C was acidified with HCl and was extracted with EtOAc. The EtOAc extract was dried (Na_2SO_4) and concentrated to a film. Recrystallization from Et_2O–hexane afforded 11 mg of **20** as a tan powder which decomposed at ca. 160 °C: IR (CH_2Cl_2) 3500, 1780, 1725, 1555, 1360 cm^{-1}; NMR (Me_2SO-d_6) δ 1.98 (s, 3 H, $CH_3C=$), 3.27 (d, 1 H, J = 17 Hz, SCH_AH_B), 3.56 (d, 1 H, J = 17 Hz, SCH_AH_B), 4.82 (d, 1 H, J = 13.5 Hz, $O_2NCH_AH_B$), 5.12 (s, 1 H, C-6 H), 5.19 (d, 1 H, J = 13.5 Hz, $O_2NCH_AH_B$), 7.5 (s, 1 H, OH). Anal. Calcd for $C_9H_{10}N_2O_6S$: C, 39.41; H, 3.68; N, 10.22. Found: C, 39.24; H, 3.87; N, 10.19.

The sodium salt **21** was prepared in 91% yield by mixing **20** in EtOAc with 1.2 equiv of sodium 2-ethylhexanoate in EtOAc, followed by addition of Et_2O: IR (KBr) 1760 (br) cm^{-1}.

Acknowledgments. We thank Mrs. Janis Nelson, Dr. Michael Maddox, Mrs. Lilia Kurz, Dr. Laszlo Tökés, Mr. John Smith, and Mr. Vernon Hayashida of the Analytical Staff for their expert assistance.

Registry No.—**3**, 39126-59-5; **5**, 57792-75-3; **6**, 63599-56-4; **7**, 63599-57-5; **8**, 33610-06-9; **9**, 57792-76-4; **10**, 63599-58-6; **11**, 57792-79-7; **12**, 63641-44-1; **13**, 63599-59-7; **14**, 63599-60-0; **15**, 63599-61-1; **16**, 63599-62-2; **17**, 63625-58-1; **18**, 63599-63-3; **19**, 63625-59-2; **20**, 63599-64-4; **21**, 63625-60-5; *tert*-butyl 7β-aminocephalosporanate, 6187-87-7; dicyclohexylcarbodiimide, 538-75-0; nitromethane, 75-52-5.

Reference and Notes

(1) Contribution No. 486 from the Institute of Organic Chemistry and No. 6 in the series Studies in β-Lactams.
(2) Syntex Postdoctoral Fellow 1975–1976.
(3) Y. S. Lo and J. C. Sheehan, *J. Am. Chem. Soc.*, **94**, 8253 (1972).
(4) T. Jen, J. Frazee, and J. R. E. Hoover, *J. Org. Chem.*, **38**, 2857 (1973).
(5) J. C. Sheehan and Y. S. Lo, *J. Org. Chem.*, **38**, 3227 (1973).
(6) J. C. Sheehan and Y. S. Lo, *J. Org. Chem.*, **40**, 191 (1975).
(7) J. C. Sheehan, Y. S. Lo, J. Löliger, and C. C. Podewell, *J. Org. Chem.*, **39**, 1444 (1974).
(8) E. Roets, A. Vlietnck, and H. Vanderhaeghe, *J. Chem. Soc., Perkin Trans. 1*, 704 (1976).
(9) D. D. Perrin, W. L. F. Armarego, and D. D. Perrin, "Purification of Laboratory Chemicals", Pergamon, New York, N.Y., 1966, p 56.
(10) J. G. Moffatt, in "Techniques and Applications in Organic Synthesis. Oxidation", Vol. II, Marcel Dekker, New York, N.Y., 1971, p 1.
(11) E. J. Corey and C. U. Kim, *J. Am. Chem. Soc.*, **94**, 7586 (1972).
(12) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. I, Wiley, New York, N.Y., 1967, p 142.
(13) M. Fetizon, M. Golfier, and J.-M. Louis, *Chem. Commun.*, 1102 (1969).
(14) E. H. W. Bohme, H. E. Applegate, J. B. Ewing, P. T. Funke, M. S. Puar, and J. E. Dolfini, *J. Org. Chem.*, **38**, 230 (1973).
(15) S. L. Huang, K. Omura, and D. Swern, *J. Org. Chem.*, **41**, 3329 (1976).
(16) Yield based on starting alcohol **10**:**11**.
(17) R. E. Harmon, J. L. Parsons, D. W. Cooke, S. K. Gupta, and J. Schoolenberg, *J. Org. Chem.*, **34**, 3684 (1969).
(18) M. Freifelder, "Practical Catalytic Hydrogenation", Wiley-Interscience, New York, N.Y., 1971, p 207.

Synthesis of Quinolizinones by the Condensation of Ylidenemalonodinitriles with Quinoline 1-Oxide

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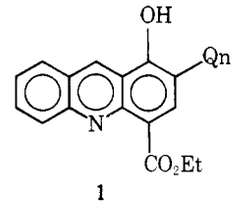
Several years ago we reported that quinoline 1-oxide reacts with diethyl glutaconate in the presence of acetic anhydride to yield the substituted acridine **1**, the product of a 2,3-annelation on the quinoline nucleus.[1] The inherently more likely



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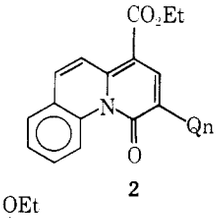

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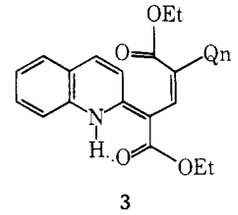

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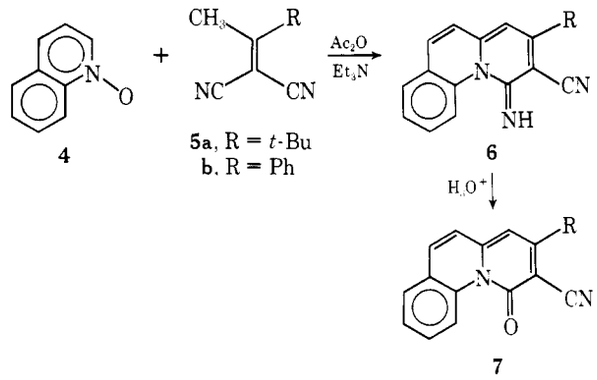
2,1-annelation, which would have given the 4-quinolizinone **2**, was not observed presumably because of the intramolecularly hydrogen-bonded nature of the probable intermediate **3**.[2]

We now wish to report that 2,1-annelations on the quinoline nucleus leading to α-quinolizinones (**7**)[3] can be achieved by

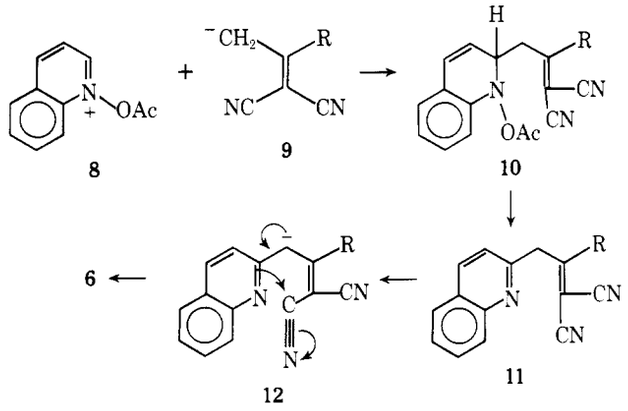


4 **5a**, R = *t*-Bu; **b**, R = Ph **6** **7**

means of condensation of quinoline 1-oxide (**4**) with suitably substituted ylidenemalonodinitriles (**5**).[4] Previously reported syntheses of α-quinolizinones involved ring closures on 2-substituted pyridines or quinolines.[5]

For example, 3,3-dimethyl-2-butylidenemalonodinitrile (**5a**) affords, after hydrolysis on the intermediate imine **6**, 3-*tert*-butyl-2-cyano-1*H*-benzo[*c*]quinolizin-1-one (**7a**). Attempts to isolate the imine or the corresponding quinolizinium salt in pure form were unsuccessful. It was also found that the R group of the ylidenemalonodinitrile could not contain α-hydrogen atoms, otherwise a complex mixture of products was obtained.

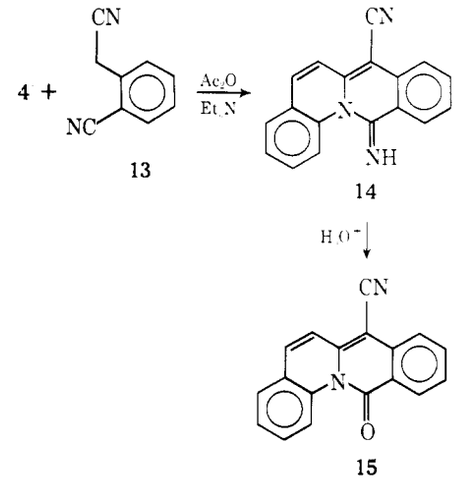
The use of triethylamine as a proton scavenger markedly improved the yields of the reaction. In its absence yields were typically less than 10%; in its presence yields were 60% or better. The amine could play an important role in three stages of the reaction: (1) generation of carbanion **9** which reacts with 1-acetoxyquinolinium ion **8** to give intermediate **10**, (2) base-promoted elimination of the elements of acetic acid from



8 **9** **10** **11** **12**

10 to yield 2-substituted quinoline **11**,[6] and (3) generation of carbanion **12** which closes on nitrogen to give imine **6**.

o-Cyanophenylacetonitrile (**13**), a compound which is structurally related to the ylidenemalonodinitriles, was also found to annelate quinoline 1-oxide in the presence of acetic anhydride–triethylamine. In this case the imine **14** could be isolated; acid-catalyzed hydrolysis of **14** afforded the known compound 7-cyano-12*H*-dibenzo[*b*,*f*]quinolizin-12-one (**15**).[7]



13 **14** **15**

Experimental Section

Melting points, uncorrected, were determined on a Mel-Temp device. Infrared spectra were recorded on a Perkin-Elmer 467 instrument using KBr disks. ^{1}H NMR spectra were determined on a Varian A-60D spectrometer and mass spectra were determined on a Finnegan 3100D instrument. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

The ylidenemalonodinitriles were prepared by the Knoevenagel condensation of the appropriate ketone with malonodinitrile.[8]

3-*tert*-Butyl-2-cyano-1*H*-benzo[*c*]quinolizin-1-one Monohydrate (7a). To a solution of 4.35 g (30.0 mmol) of quinoline 1-oxide and 6.12 g (60.0 mmol) of acetic anhydride in 20 mL of dry glyme was added slowly with stirring at room temperature under N_2 a solution of 4.44 g (30.0 mmol) of 3,3-dimethyl-2-butylidenemalonodinitrile and 6.05 g (60.0 mmol) of triethylamine in 20 mL of dry glyme. After the addition was complete (ca. 1 h), the deep red mixture was stirred for an additional 2 h.

Methanol (10 mL) was added and the mixture was refluxed for 1 h in order to remove unreacted acetic anhydride. All volatile material was then removed on the rotary evaporator. The residue was taken up in 50 mL of 5% aqueous acetic acid containing 2 drops of 48% hydrobromic acid, and the resulting mixture was heated under reflux for 2 h.

The solid which formed upon cooling was recrystallized from 50% aqueous acetic acid to yield 5.02 g (60.4%) of reddish-brown powder: mp 247–248 °C; IR (KBr) 2210 (CN) and 1655 cm^{-1} (α-pyridone C=O[9]); NMR (CF_3CO_2D) δ 1.62 (s, 9 H, *t*-Bu) and 7.5–8.0 ppm (m, 7 H, aromatic); mass spectrum (70 eV) *m/e* 276 (100, M^+), 219 (11, $M^+ - C_4H_9$), 192 (40, $M^+ - C_5H_{10}N$), 129 (51, $C_9H_7N^+$), and 128 (63, $C_9H_6N^+$).

Anal. Calcd for $C_{18}H_{16}N_2O \cdot H_2O$: C, 73.45; H, 6.17; N, 9.51. Found: C, 73.71; H, 5.88; N, 9.46.

2-Cyano-3-phenyl-1*H*-benzo[*c*]quinolizin-1-one (7b). This compound was prepared by the same method as that described for compound **7a**. 1-Phenylethylidenemalonodinitrile (4.35 g, 30.0 mmol) yielded 6.02 g (68.2%) of dark reddish powder: mp 275–277 °C; IR (KBr) 2205 (CN) and 1655 cm^{-1} (α-pyridone C=O[9]); mass spectrum (70 eV) *m/e* 296 (43, M^+), 269 (5, $M^+ - HCN$), 145 (51, $C_9H_9N_2^+$), 129 (72, $C_9H_7N^+$) and 77 (100, $C_6H_5N^+$).

Anal. Calcd for $C_{20}H_{12}N_2O$: C, 81.07; H, 4.08; N, 9.45. Found: C, 80.93; H, 4.13; N, 9.41.

7-Cyano-12*H*-dibenzo[*b*,*f*]quinolizin-12-one Imine (14). A solution containing 4.35 g (30.0 mmol) of quinoline 1-oxide, 6.12 g (60.0 mmol) of acetic anhydride, 4.26 g (30.0 mmol) of freshly distilled *o*-cyanophenylacetonitrile, and 6.05 g (60.0 mmol) of triethylamine dissolved in 50 mL of dry glyme was refluxed under nitrogen for 3 h. Methanol (10 mL) was added and the mixture was refluxed for an additional hour.

After allowing the mixture to cool to room temperature, the yellow solid which had formed was filtered off, washed with a few milliliters of glyme, dried, and recrystallized from acetone to afford 3.85 g (47.7%) of yellow needles: mp 214–215 °C; IR (KBr) 3280 (=NH) and 2195 cm^{-1} (CN).

Anal. Calcd for $C_{18}H_{11}N_3$: C, 80.28; H, 4.12; N, 15.60. Found: C, 80.51; H, 4.01; N, 15.64.

7-Cyano-12*H*-dibenzo[*b*,*f*]quinolizin-12-one (15). A solution of 2.0 g (7.4 mmol) of imine **14** in 20 mL of 5% aqueous acetic acid (plus

one drop of 48% hydrobromic acid) was heated under reflux for 4 h. The resulting solid was recrystallized from 50% aqueous acetic acid to yield 1.28 g (64%) of yellow powder; mp 189–190 °C [lit.[5] mp 190 °C]; IR (KBr) 2200 (CN) and 1675 cm^{-1} (α-pyridone CO).

Registry No.—**4,** 1613-37-2; **5a,** 13017-53-3; **5b,** 5447-87-0; **7a,** 63702-22-7; **7b,** 63702-23-8; **13,** 3759-28-2; **14,** 63702-24-9; **15,** 63702-25-0.

References and Notes

(1) J. E. Douglass and D. Koottungal, *J. Org. Chem.*, **37,** 2913 (1972).
(2) (a) A. L. Borror and A. F. Haeberer, *J. Org. Chem.*, **30,** 243 (1965); (b) J. E. Douglass and J. M. Wesolosky, *ibid.*, **36,** 1165 (1971); (c) J. E. Douglass and H. D. Fortner, *J. Heterocycl. Chem.*, **10,** 115 (1973).
(3) The designation α indicates that the carbonyl group is adjacent to the nitrogen atom. This is to avoid the confusion which arises from the numbering of the various benzoquinolizinones; e.g., both 4*H*-quinolizin-4-one and 1*H*-benzoquinolizin-1-one and α-quinolizinones.
(4) E. Campaigne and S. W. Schneller, *Synthesis*, 705 (1976).
(5) (a) T. Kappe, M. Hariri, and F. S. G. Soliman, *Arch. Pharm. (Weinheim, Ger)*, **309,** 684 (1976); (b) G. R. Newkome, J. M. Robinson, and M. S. Bhacca, *J. Org. Chem.*, **38,** 2235 (1973); (c) H. N. Al-Jallo and F. W. Al-Azami, *J. Heterocycl. Chem.*, **10,** 139 (1973); (d) C. K. Bradsher and J. P. Sherer, *J. Org. Chem.*, **32,** 733 (1967).
(6) For a discussion of the mechanism of this type of reaction, see A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic N-Oxides", Academic Press, New York, N.Y., 1971.
(7) (a) E. Ochiai and S. Suzuki, *Pharm. Bull.*, **5,** 405 (1957); (b) C. K. Bradsher, Duke University, private communication.
(8) F. S. Prout, *J. Org. Chem.*, **18,** 928 (1953).
(9) A. R. Katritzky and R. A. Jones, *J. Chem. Soc.*, 2947 (1960).

Reaction of Kojic Acid and Its Derivatives with Acrylonitrile. A New Look at an Old Problem

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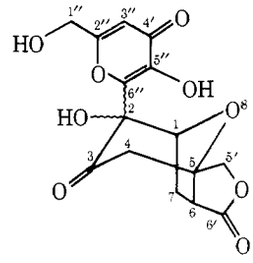
The reaction of kojic acid (**1**) with acrylonitrile was initially studied by Woods[1] and later extensively investigated by Hurd and co-workers,[2] who examined the reaction of various 3-hydroxy-4-pyrones with acrylonitrile and acrylate esters. Unidentified, yet well-characterized products involving two molecules of pyrone and one molecule of acrylonitrile or acrylate ester were formed in these reactions rather than the expected simple Michael addition products. Hurd and Trofimenko[3] later focused their attention on the reaction of α-deoxykojic acid (**2**) with acrylonitrile in an effort to solve this intriguing structural problem. Structure **3** was suggested as the product of this reaction on the basis of experimental findings and a complex mechanistic rationale. We now wish to report structural assignments for the reaction products of kojic acid (**1**) and its derivatives with acrylonitrile and acrylate esters, proposing a general reaction mechanism for their formation and revising the structure of the α-deoxykojic acid–acrylonitrile reaction product.

The base-catalyzed addition of acrylonitrile to kojic acid (**1**) provided the necessary data for solving this structural problem. In accordance with Hurd's observations, product[4] **4,** mp 264–265 °C, is formed on acid workup and analyzes for $C_{15}H_{14}O_9$. Compound **4** gives a positive ferric chloride test and is easily acetylated. Its infrared spectrum shows a strong hydroxyl band at 2.94 μm, carbonyl bands at 5.63 and 5.78 μm, and pyrone bands at 6.02, 6.18, and 6.36 μm. Under appropriate conditions, a labile nitrogen-containing intermediate (**7**) can be isolated.[2] Its infrared spectrum shows carbonyl



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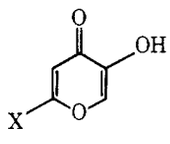
bands at 5.76 and 5.93 μm, and **7** is smoothly converted to **4** under acidic conditions.[2] On the basis of key ^1H and ^{13}C NMR studies (Tables I and II) and the data obtained by Hurd, we have assigned **4** the following tricyclic structure.

Compound **4** is a rigid 2,2-disubstituted 8-oxabicyclo[3.2.1]octan-3-one containing a cis fused γ-lactone ring at carbon atoms 5 and 6 whose structure is uniquely described by ^1H NMR and ^{13}C NMR data. The presence of a pyrone moiety in the molecule is substantiated by the appearance of an olefin signal in the ^1H NMR spectrum at δ 6.90 and an allylic methylene signal at δ 4.77. Two distinct AB patterns are present and can be assigned to the H-4 (J_{AB} = 14 Hz) and H-5′ (J_{AB}, Hz) protons of the molecule. The broad doublet at δ 5.60 can be assigned H-1 on the basis of its chemical shift and the coupling (J = 7 Hz) of this bridgehead proton to the exo H-7 proton. As anticipated,[5] the coupling of H-1 to the endo H-7 proton is small (J < 2 Hz). The H-7 signals appear as a complex ABXY pattern as a result of coupling with H-1 and H-6. H-7(exo), as expected,[5] is coupled with H-7(endo) (J_{AB} = 14 Hz) and is weakly coupled (J = 4 Hz) to the trans-oriented H-6 proton. A larger coupling constant (J = 10 Hz) results from the cis relationship of H-7(endo) and H-6.

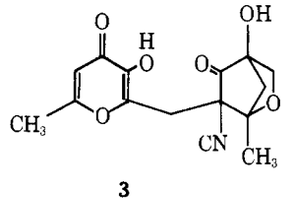
^{13}C NMR further strengthens the structural assignment for **4.** The chemical shifts of the pyrone carbon atoms (C-1″–C-6″) correspond to those reported for kojic acid.[6] The presence of two additional carbonyl groups (C-3 and C-6′) and four saturated carbon atoms bound to oxygen (C-1, C-2, C-5, C-5′) is confirmed by the ^{13}C chemical shifts. ^{13}C–^1H coupling further demonstrates that two of these carbon atoms bound to oxygen are tertiary (C-5, C-2), one is secondary (C-1), and one is primary (C-5′). The chemical shifts and ^{13}C–^1H coupling of the remaining carbon atoms (C-4, C-7, and C-6) are also consistent with the structure of **4.**

A mechanistic pathway leading to **4** is shown in Scheme I. The reaction is initiated with an ionic (4 + 2) cyclization[7] involving kojic acid (**1**) and acrylonitrile to afford bicyclic intermediate[8] **5** which enolizes to relieve the electrostatic interactions[9] present in cyclic α-diketones. As a result, only the ketone moiety α to the bridge (which cannot enolize) is susceptible to nucleophilic attack. Base-catalyzed addition of another molecule of kojic acid occurs at this site to generate **6.**[10] Addition[11] of the hydroxymethyl group of **6** to the exo nitrile functionality then generates imidolactone **7** which was originally isolated by Hurd.[2] Acid workup of **7** yields tricyclic structure **4.**

The other reaction products of γ-pyrones with acrylonitrile and acrylate esters[2] can be explained by the same general mechanism. The reaction of α-deoxykojic acid (**2**) with acrylonitrile yields, as reported by Hurd,[2] two products **8** and **9** in



1, X = CH_2OH
2, X = CH_3



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