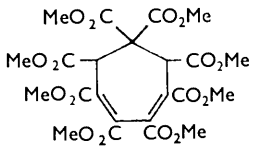
803. *The Reaction of Acetylenic Esters with Cyanoacetic Ester and Pyridine*

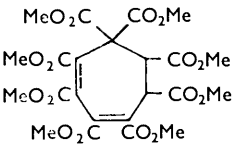
By P. Bamfield, A. Crabtree, and A. W. Johnson

Modified structures are suggested for the yellow and the blue adducts from dimethyl acetylenedicarboxylate, ethyl cyanoacetate, and pyridine, which were originally prepared and formulated by Diels.[1] The reaction of methyl phenylpropiolate, ethyl cyanoacetate, and pyridine leads to a 1 : 1 : 1-adduct in which the pyridine has suffered ring-fission. Various reactions of the adducts are discussed.

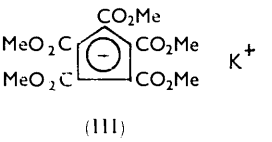
As a sequel to his detailed study of the reaction of dimethyl acetylenedicarboxylate with a variety of nitrogen heterocyclic compounds, Diels [1] examined the reaction of the acetylenic ester with malonic ester, cyanoacetic ester, and malonodinitrile in the presence of pyridine. In the case of dimethyl malonate, the two initial adducts which Diels obtained are now regarded [2,3] as compounds (I) and (II), and these, on treatment with potassium acetate, yield the salt (III). The acid corresponding to the salt (III) is of a strength comparable with that of hydrochloric acid [4] and several properties and derivatives of this acid have been recorded.[3,4]



(I)

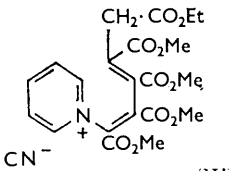


(II)

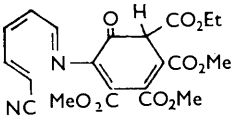


(III)

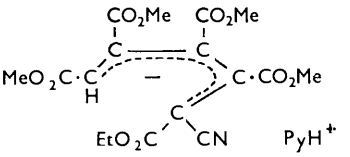
The reaction of dimethyl acetylenedicarboxylate with ethyl cyanoacetate in pyridine solution took a different course.[1] When the reaction was carried out at 0° the product was a yellow solid which contained ethyl cyanoacetate, pyridine, and the acetylenic ester in the ratio of 1 : 1 : 2. This product was formulated by Diels [1] as the salt (IV). When the reaction was carried out at a higher temperature or when the yellow adduct was heated or even kept at room temperature in an open vessel, it lost one equivalent of methanol and was converted into a blue adduct, formulated by Diels as structure (V).



(IV)



(V)

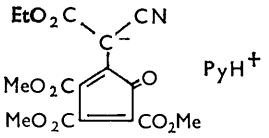


(VI)

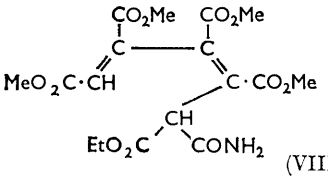
The rather improbable structures (IV) and (V) have also been revised [2] on the basis of spectral evidence to structures (VI) and (VII), respectively, a conclusion which, with one modification, we,[3,5] and also Professor R. C. Cookson and his colleagues,[3,6] reached on the basis of the chemical reactions as well as the physical properties of these compounds. The structures of the malonodinitrile adducts are analogous (CN for CO_2Et) to those of

[1] O. Diels, *Ber.*, 1942, **75**, 1452; O. Diels and U. Kock, *Annalen*, 1944, **556**, 38.
[2] E. Le Goff and R. B. LaCount, *J. Org. Chem.*, 1964, **29**, 423.
[3] P. Bamfield, R. C. Cookson, A. Crabtree, J. Henstock, J. Hudec, A. W. Johnson, and B. R. D. Whitear, *Chem. and Ind.*, 1964, 1313.
[4] R. C. Cookson, J. Hudec, and B. R. D. Whitear, *Proc. Chem. Soc.*, 1961, 117.
[5] A. Crabtree, Ph.D. Thesis, University of Nottingham, 1962.
[6] B. R. D. Whitear, Ph.D. Thesis, University of Southampton, 1962.

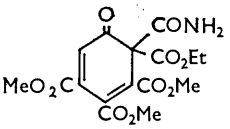
the cyanoacetic ester adducts. The yellow adduct (VI) from cyanoacetic ester, although it was a pyridinium salt, contained no ionic cyanide. Reaction of compound (VI) with cold formic acid or 80% sulphuric acid gave a colourless compound which was no longer a salt and in which the nitrile group had been hydrated to an amide. This product, which contained singlet peaks in the n.m.r. spectrum at 4·11 ($EtO_2C{\cdot}CH{\cdot}CONH_2$) and 3·18 τ ($=CH{\cdot}CO_2Me$), is now formulated as shown in structure (VIII).



(VII)

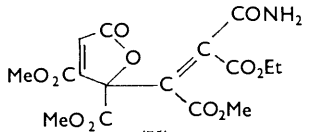


(VIII)

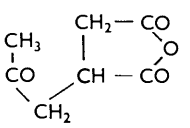


(IX)

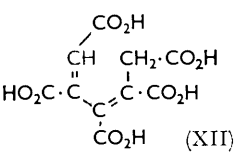
Treatment of the yellow adduct (VI) with hot formic acid or polyphosphoric acid results in cyclisation to give the pale yellow cyclohexadienone (IX) ($\lambda_{max.}$ 348 mμ; $\varepsilon_{max.}$ 12,000), the n.m.r. spectrum of which contains a singlet peak at 3·01 τ, equivalent to one olefinic hydrogen. This product can also be obtained from its precursor (VIII) by cyclisation with hot formic acid. The product (IX), on oxidation with cold nitric–sulphuric acid mixture, or with bromine in glacial acetic acid, gave a lactone presumed to be compound (X), which showed only end absorption in the ultraviolet. The n.m.r. spectrum of the lactone again showed the singlet at 2·89 τ corresponding to the single olefinic proton, and the infrared spectrum ($CHCl_3$ solution or KBr disc) contained peaks at 1800 and 1757 $cm.^{-1}$ associated with the unsaturated lactone system.[7] Hydrolysis of compound (IX) with strong hydrochloric acid gave a crystalline oxo-anhydride identified as acetonylsuccinic anhydride [8] (XI).



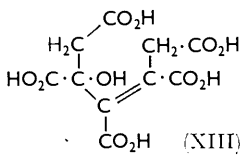
(X)



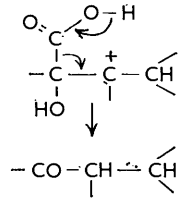
(XI)

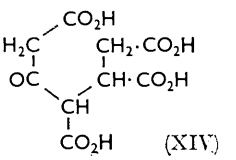


(XII)



(XIII)





(XIV)

This interesting conversion is visualised as a preliminary hydrolysis and decarboxylation of compound (IX) to the penta-1,3-diene-1,2,3,4,5-pentacarboxylic acid (XII), followed by an acid-catalysed hydration of the less-hindered double bond to compound (XIII). Decarboxylation and rearrangement proceed by the mechanism indicated, through the oxo-acid (XIV), to acetonylsuccinic anhydride (XI).

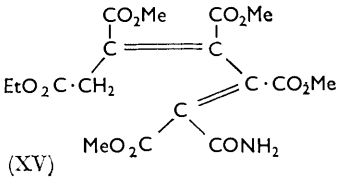
The structures (XV) and (XVI) advocated by Diels [1] for the formic acid rearrangement products from compound (IX) are incompatible with the n.m.r. data; moreover, compound (XVI) should exist as the tautomeric phenol.

The blue adduct from ethyl cyanoacetate, dimethyl acetylenedicarboxylate, and pyridine has been reformulated [2] as the pyridinium salt (VII) on spectral evidence. We

[7] Cf. R. N. Jones, C. L. Angell, T. Ito, and R. J. D. Smith, *Canad. J. Chem.*, 1959, **37**, 2007.

[8] H. R. Ing and W. H. Perkin, jun., *J.*, 1924, **125**, 1814; K. Alder and H. Söll, *Annalen*, 1949, **565**, 57.

accept this view [3] except that we regard the mesomeric fulvene (XVII) as making an important contribution to the overall structure. When the blue adduct is treated with cold formic acid a colourless insoluble pseudo-acid is obtained which can be reconverted



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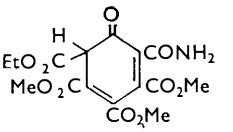

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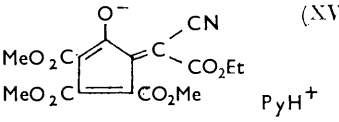
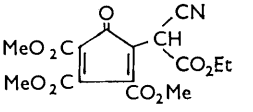
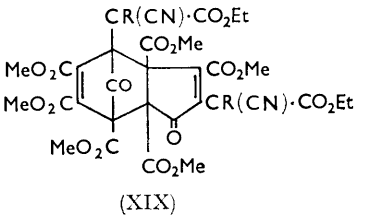


(XVII)



(XVIII)

into the blue salt (XVII) by the action of pyridine in acetonitrile. The colourless acid which also forms blue metallic salts can be regarded as the cyclopentadienone (XVIII), but the lack of colour and the low solubility led us to favour a dimeric structure such as (XIX; R = H) although several isomers of this structure are theoretically possible. Nitration of the presumed dimeric cyclopentadienone (XIX; R = H) gave two products. The first was a nitro-derivative regarded as compound (XIX; R = NO_2) and the second, which contained no nitrogen, has been formulated as the oxalylcyclopentadienone ester (XX). The latter compound has been characterised as its 2,4-dinitrophenylhydrazone and as the pale yellow quinoxaline (XXI) formed by condensation with *o*-phenylenediamine. The ready hydrolysis of an α-cyano-α-nitroacetic ester derivative to the corresponding oxalyl compound was to be expected, and it was found that the nitro-derivative (XIX; R = NO_2) could also be hydrolysed to the oxalyl compound with warm water.



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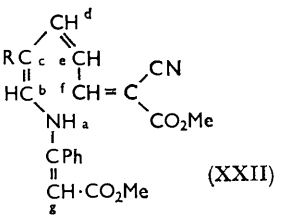
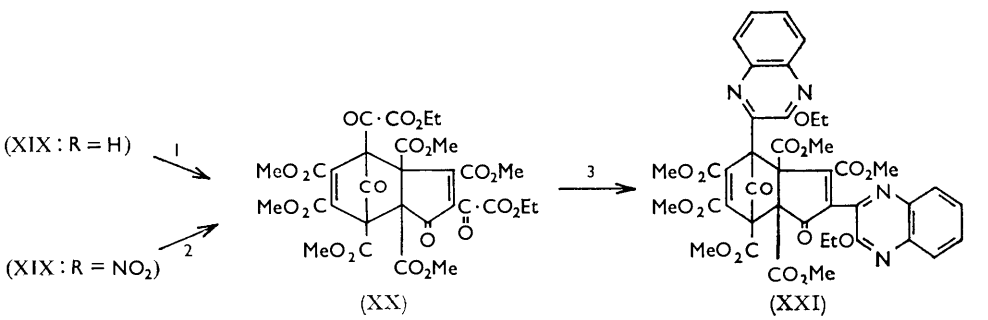


(XXII)



(XX)

(XXI)

Reagents: 1, HNO_3; 2, H_2O; 3, o-$C_6H_4(NH_2)_2$

It is known [9,10] that some cyclopentadienones form stable monomers, others are stable

[9] C. F. H. Allen, *Chem. Rev.*, 1945, **37**, 209; C. F. H. Allen and J. A. Van Allan, *J. Amer. Chem. Soc.*, 1950, **72**, 5165; P. L. Pauson and B. J. Williams, *J.*, 1961, 4162.
[10] C. F. H. Allen, *Chem. Rev.*, 1962, **62**, 653.

only in the dimeric form, and a third type exist as a temperature-dependent monomer–dimer equilibrium. The monomeric cyclopentadienones are usually highly coloured, whereas the dimers are colourless or yellow, which accords with the formulation of the pseudo-acid (XIX; R = H) as a dimer. Unfortunately this product was almost insoluble in common solvents and the tendency to depolymerise at higher temperatures precluded the accurate determination of the molecular weight. On the other hand, the sharp ester carbonyl bands at 1710 and 1735 cm.$^{-1}$ in the blue monomeric salt [(VII) or (XVII)] were replaced by bands at 1730 and 1755 cm.$^{-1}$ in the presumed dimer (XIX; R = H) and broad carbonyl bands between 1720—1765 and 1720—1760 cm.$^{-1}$ in the related compounds (XIX; R = NO_2) and (XX), respectively. The band at *ca.* 1765 cm.$^{-1}$ which has been assigned [10] to the transannular carbonyl group in dimeric cyclopentadienones (cyclopent-3-enone ring), shows up well in the spectrum of the quinoxaline derivative (XXI) and is also evident as an inflection in the spectra of compounds (XIX; R = NO_2) and (XX).

In an attempt to extend this reaction to other acetylenic esters, we have treated phenylpropiolic ester with ethyl cyanoacetate and pyridine, but have found that the reaction did not proceed in an analogous manner. Instead an orange adduct was obtained, the structure of which followed from determinations of the n.m.r. and mass spectra. The mass spectrum indicated a molecular formula $C_{19}H_{18}N_2O_4$ (*M*, 338) for the adduct, *i.e.*, a 1 : 1 : 1-adduct of the three compounds in which ester interchange (ethyl ⟶ methyl) of the cyanoacetic ester fragment had occurred. The interpretation of the n.m.r. spectrum ($CDCl_3$ solution) led to structure (XXII; R = H) for the adduct. The spectrum contained peaks at −0·9 (doublet, NH), 3·24 [triplet, 2 protons b and d in structure (XXII)], 4·06 (quartet, proton c), 3·53 (quartet, proton e), 2·30 (doublet, proton f), 2·58 (multiplet, 5 aromatic protons), 5·01 (singlet, proton g), 6·24 (singlet, 3-protons of ester methyl group), and 6·30 τ (singlet, 3 protons of ester methyl group). A series of decoupling experiments showed that six protons [a—f in (XXII)] were attached singly to adjacent atoms, *i.e.*, (a) was coupled to (b) or (d); (c) was coupled to (b) and (d); (e) was coupled to (f) and (b) or (d); (f) was coupled to (e), and that only couplings to adjacent protons were appreciable. The protons (b) and (d) had almost the same chemical shift and each was split into a quartet, but because of superposition these signals appeared as a triplet. Confirmation of structure (XXII; R = H) was obtained from the mass spectrum which showed the following fragment ions: *m/e* 323 (*p*-CH_3); 307 (*p*-OCH_3); 306 (*p*-CH_3OH with rearrangement); 279 (*p*-CO_2CH_3); 274 (*p*-$2CH_3OH$); 247 (*p*-CH_3OH–CO_2CH_3); 240 (*p*-$CH(CN)CO_2CH_3$); 219 [*p*-(CH_3OH + CO_2CH_3 + CO)]. Hydrolysis of the adduct (XXII; R = H) with concentrated hydrochloric acid for 2 days at room temperature gave acetophenone (2,4-dinitrophenylhydrazone) formed by hydrolysis of the enamine system. Analogous condensations have been carried out using β-picoline, nicotinic acid, and nicotinamide in place of pyridine, and cyanoacetic acid, and cyanoacetamide in place of ethyl cyanoacetate, the carboxylic acid groups being esterified during the reactions. In the case of the β-picoline, ethyl cyanoacetate, and methyl phenylpropiolate adduct (XXII; R = Me), n.m.r. examination showed the proton, H(f), to correspond to a doublet at 2·25 τ, thus indicating that the methyl group was present in the position shown in (XXII; R = Me) and not on the carbon atom adjacent to CH(f).

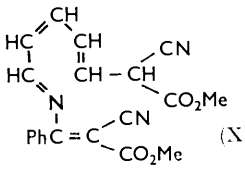
Many examples are known of the fission of the pyridinium ring by nucleophilic reagents,[11] but a particularly relevant example is the reaction product (XXIII) derived from pyridine, benzoyl chloride, and methyl cyanoacetate.[12] The possibility of a tautomeric structure corresponding to (XXII), *i.e.*, a secondary amine was apparently not considered by the German authors. We have repeated this preparation, and have shown that the n.m.r. spectrum of the product contains a sharp doublet at −1·89 τ (NH).

The reaction of methyl phenylpropiolate, ethyl cyanoacetate, and pyridine is considered

[11] E. Klingsberg, " Pyridine and its Derivatives," Part II, Interscience, New York and London, 1961, p. 58

[12] H. von Dobeneck and W. Goltzsche, *Chem. Ber.*, 1962, **95**, 1484.

to yield the zwitterion (XXIV; R = Ph) as a primary product, and this is followed by attack of the cyanoacetic ester anion with fission of the pyridine ring. Dimethyl acetylenedicarboxylate, in contrast, reacts with the cyanoacetic ester anion in preference to pyridine when both are present to yield the pyridinium salts (VI) and (VII). It is, however, well established that addition of dimethyl acetylenedicarboxylate and methyl



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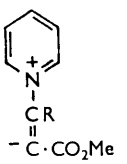
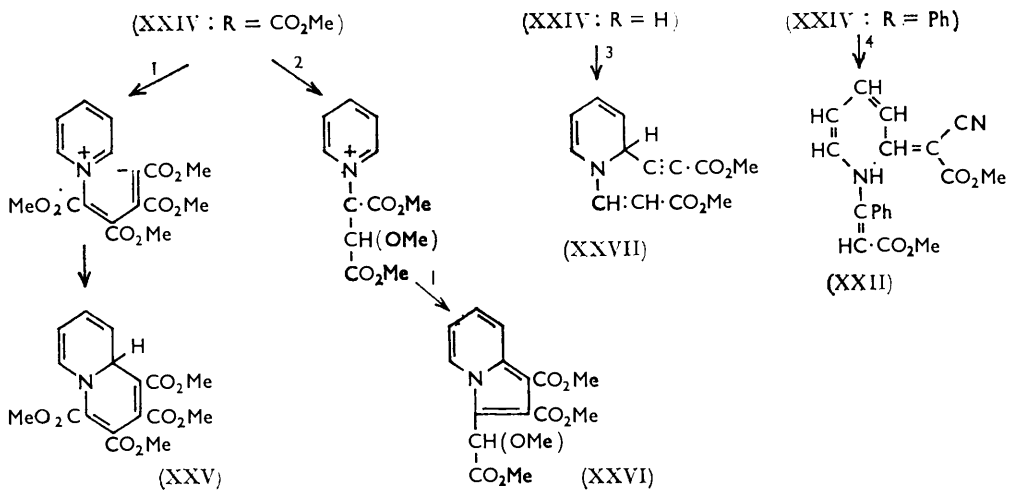


(XXIV)

Further reactions of compound (XXIV)



Reagents: 1, $(\ddot{C}\cdot CO_2Me)_2$. 2, H^+; OMe^-. 3, $^-C\ddot{C}\cdot CO_2Me$; H^+. 4, $^-CH(CN)\cdot CO_2Me$

propiolate to pyridine can occur, leading to the reactive zwitterions (XXIV; R = CO_2Me; H) which under different conditions yield derivatives of 9a*H*-quinolizine [13,14] (XXV), indolizine [14-16] (XXVI), or 1,2-dihydropyridine [15] (XXVII).

Experimental

Ultraviolet absorption spectra were determined on ethanolic solutions and infrared spectra on potassium bromide discs except where otherwise stated. N.m.r. spectra were determined on methylene dichloride solutions except where otherwise stated and were measured on an A.E.I. RS2 spectrometer using tetramethylsilane as an internal reference. Melting points were determined on a Kofler hot-stage apparatus.

Yellow Adduct (VI) *from Ethyl Cyanoacetate and Methyl Acetylenedicarboxylate.*—This was prepared from dimethyl acetylenedicarboxylate (17 ml.) and ethyl cyanoacetate (12 g.) in methanol (65 ml.) following Diels and Kock.[1] The product was crystallised from methanol and formed pale yellow needles, m. p. 124° (Found: C, 55·7; H, 5·0; N, 5·8. Calc. for $C_{22}H_{24}N_2O_{10}$: C, 55·4; H, 5·1; N, 5·9%), $\lambda_{max.}$ 229 and 370 mμ ($\varepsilon_{max.}$ 12,900 and 17,400); $\lambda_{infl.}$ 250 mμ ($\varepsilon_{infl.}$ 10,700); $\nu_{max.}$ 1735 (ester C=O), 2180 (CN) cm.$^{-1}$.

[13] L. M. Jackman, A. W. Johnson, and J. C. Tebby, *J.*, 1960, 1579.
[14] R. M. Acheson, *Adv. Heterocyclic Chem.*, 1963, **1**, 125.
[15] A. Crabtree, A. W. Johnson, and J. C. Tebby, *J.*, 1961, 3497; cf. T. Agawa and S. I. Miller, *J. Amer. Chem. Soc.*, 1961, **83**, 449.
[16] O. Diels and R. Meyer, *Annalen*, 1934, **513**, 129; cf. V. Boekelheide and K. Fahrenholtz, *J. Amer. Chem. Soc.*, 1961, **83**, 458; R. Huisgen, *Proc. Chem. Soc.*, 1961, 357.

Action of Cold Formic Acid on the Yellow Adduct.—The yellow adduct (500 mg.) in 98% formic acid was kept at room temperature for 14 days, after which the precipitated solid (20 mg.) was separated and crystallised from 50% aqueous methanol when it formed colourless needles, m. p. 150° (lit.,[1] 148°) (Found: C, 49·1; H, 5·4; N, 3·2. Calc. for $C_{17}H_{21}NO_{11}$: C, 49·2; H, 5·1; N, 3·4%), $\lambda_{infl.}$ 224 mμ ($\varepsilon_{infl.}$ 13,300); $\nu_{max.}$ 3350 and 3455 ($CONH_2$) cm.$^{-1}$. The n.m.r. spectrum showed peaks at 3·18 (singlet; 1 olefinic proton), 4·11 (singlet; 1 aliphatic proton), 5·77 (quartet; methylene of ethyl ester), 6·16, 6·25, 6·35 (singlets, total of four methyl ester groups) and 8·76 τ (triplet; methyl of ethyl ester).

Action of 80% *Sulphuric Acid on the Yellow Adduct.*—The yellow adduct (8·5 g.) was dissolved in 80% (w/w) sulphuric acid (100 g.) with stirring at room temperature. The stirring was continued overnight and the resulting clear yellow solution poured into cold water (200 ml.). The solution was extracted continuously with chloroform for 24 hr. and the solvent removed from the extract leaving a brown tar. This was slurried with acetone (50 ml.) and the solid separated and washed with water. The colourless product, m. p. 150°, was identical with that obtained in the previous experiment.

Action of Hot Formic Acid on the Yellow Adduct.—The yellow adduct (70·5 g.) was thoroughly mixed with formic acid (300 ml. of 98%) and the yellow solution heated under reflux for 6 hr. The excess formic acid was removed by distillation, and the residue mixed with methanol (50 ml.), filtered, and washed with more methanol (50 ml.). The yellow solid (12 g.) was air-dried and crystallised from ethanol when it formed pale yellow needles (9·4 g.), m. p. 189°, raised to 190—191° (lit.,[1] 173°) after recrystallisation (Found: C, 49·9; H, 4·3; N, 3·8. Calc. for $C_{16}H_{17}NO_{10}$: C, 50·1; H, 4·45; N, 3·65%), $\lambda_{max.}$ 272 and 352 mμ ($\varepsilon_{max.}$ 10,990 and 12,000) $\nu_{max.}$ (in $CHCl_3$) 3180, 3280, and 3370 ($CONH_2$) cm.$^{-1}$. The n.m.r. spectrum showed peaks at 3·01 (singlet; 1 olefinic proton), 5·77 (quartet; methylene of ethyl ester), 6·18 (singlet; 3 protons of 1 methyl ester), 6·26 (singlet; 6 protons of 2 methyl esters), and 8·74 τ (triplet; methyl of ethyl ester).

Cyclisation of the Yellow Adduct with Polyphosphoric Acid.—The yellow adduct (10 g.) was added to polyphosphoric acid[17] (from 18 ml. syrupy phosphoric acid and 38 g. phosphorus pentoxide) at 95—100° and stirred at this temperature for 1 hr. The hot solution was poured into iced water (200 ml.), a small amount of precipitated solid was separated and the filtrate neutralised with ammonium hydroxide. A little tar was separated and the filtrate kept for 3 days, after which the pale yellow solid which had separated was removed, and washed with water (50 ml.). The product (3·1 g.) was dried at 70° and crystallised from ethanol when it formed pale yellow needles (600 mg.), m. p. 187—189°, identical with the product of the previous experiment.

Nitric Acid Oxidation of the Cyclised Yellow Adduct.—The cyclised product (IX) (2 g.) in concentrated sulphuric acid (25 ml.) at 0° was treated with concentrated nitric acid (0·8 ml.) and the mixture kept at 6° for 3 hr. The resulting pale yellow solution was poured into iced water (150 ml.) and kept at 0° for a further hour, after which it was extracted with ether (3 × 75 ml.). The ethereal extract was washed and dried and the solvent removed to give a colourless *solid* which crystallised from ethanol as colourless prisms, m. p. 121—122° (Found: C, 48·1; H, 4·2; N, 3·3. $C_{16}H_{17}NO_{11}$ requires C, 48·1; H, 4·3; N, 3·5%), $\lambda_{infl.}$ 223 and 253 mμ ($\varepsilon_{infl.}$ 13,600 and 7570); $\nu_{max.}$ 1707 (amide C=O), 1745 (ester C=O), 1757, and 1800 (αβ-unsaturated γ-lactone C=O) 3175 and 3450 ($CONH_2$) cm.$^{-1}$. The n.m.r. spectrum showed the following signals: 2·89 (singlet; 1 olefinic proton); 5·65 (quartet; methylene of ethyl ester); 6·17 (singlet; 2 methyl esters); 6·24 (singlet; one methyl ester), and 8·48 τ (triplet; methyl of ethyl ester).

Bromine Oxidation of Cyclised Yellow Adduct.—The cyclised product (1 g.) was dissolved in warm acetic acid (10 ml.) and bromine (0·3 ml.) was added. The mixture was heated on a water-bath for 10 min., cooled, and poured into water (30 ml.). The product was extracted with ether and the extract washed and dried and the solvent removed. The residue was washed with a little ether and then separated when it was obtained as a colourless solid (142 mg.), m. p. 118—120°, identical with the product from the foregoing experiment.

Acid Hydrolysis of the Cyclised Yellow Adduct.—The cyclised product (IX) (3 g.) was mixed with concentrated hydrochloric acid (100 ml.) and heated under reflux for 6 hr. The pale yellow solution was evaporated to dryness under reduced pressure and the residue slurried with acetone (50 ml.). The insoluble ammonium salts were separated and the solvent

[17] G. M. Badger and W. F. H. Sasse, *J.*, 1957, 4.

removed from the filtrate. The residue slowly solidified and the product crystallised from ethanol to give colourless needles (600 mg.) of acetonylsuccinic anhydride, m. p. **93**—**94°** (lit.,[8] 95—96°) (Found: C, 54·3; H, 5·3. Calc. for $C_7H_8O_4$: C, 53·8; H, 5·2%), $\nu_{max.}$ 1705 (ketonic C=O), 1780 and 1845 (anhydride C=O) cm.$^{-1}$. The n.m.r. spectrum showed signals at 7·78 (singlet; methyl ketone), 6·87 τ (multiplet corresponding to the remaining 5 aliphatic protons). The product was identical with an authentic specimen.[18]

Yellow Adduct from Malonodinitrile and Methyl Acetylenedicarboxylate.—Prepared following Diels and Kock,[1] the adduct had m. p. 161—162° (lit., 162—163°) (Found: C, 55·6; H, 4·15; N, 9·4. Calc. for $C_{20}H_{12}N_3O_8$: C, 55·95; H, 4·45; N, 9·8%), $\lambda_{max.}$ 262 and 352 mμ ($\varepsilon_{max.}$ 5510 and 22,610) $\nu_{max.}$ 1730 (ester C=O), 2,165, and 2,190 (CN groups).

Blue Adduct (VII) *from Ethyl Cyanoacetate and Dimethyl Acetylenedicarboxylate.*—Dimethyl acetylenedicarboxylate (17 ml.), ethyl cyanoacetate (12 g.), and methanol (65 ml.) were stirred at room temperature and a solution of pyridine (12 ml.) in acetic acid (12 ml.) was added during 15 min. The temperature of the mixture rose almost to the b. p. of the solvent, and the product was heated under reflux for 30 min., cooled, and the precipitated adduct separated. After crystallisation from acetonitrile it formed deep blue needles, m. p. 173° (lit.,[1] 173—174°) (Found: C, 57·0; H, 4·5; N, 6·25. Calc. for $C_{21}H_{20}N_2O_9$: C, 56·75; H, 4·55; N, 6·35%), $\lambda_{max.}$ 257, 317, and 625 mμ ($\varepsilon_{max.}$ 17,780, 20,400, and 1660); $\nu_{max.}$ 1735 (ester C=O) and 2195 (CN) cm.$^{-1}$.

Action of Cold Formic Acid on the Blue Adduct (XIX; R = H).—A solution of the adduct (20 g.) in cold formic acid (50 ml. of 98%) was stirred overnight. The precipitated solid (11·1 g.) was separated, and washed with formic acid (3 × 10 ml.) until the washings were no longer coloured. The solid was dissolved in hot formic acid and the solution cooled, when the product was obtained as a colourless amorphous solid, m. p. 219—221° (lit.,[1] 219—221°) (Found: C, 52·6; H, 4·5; N, 3·8. Calc. for $C_{32}H_{30}N_2O_{18}$: C, 52·6; H, 4·15; N, 3·85%), $\nu_{max.}$ 1730, 1755 (>C=O), and 2260 (CN) cm.$^{-1}$.

Reaction of the Cyclopentadienone Dimer (XIX; R = H) *with Nitric Acid.*—The foregoing product (XIX; R = H) (5 g.) was warmed with concentrated nitric acid (40 ml.) until solution was complete (30 min.). The solution was cooled and the water was added dropwise to precipitate the product, which was separated and washed with water (50 ml.). It was dried *in vacuo* over P_2O_5 and then the product (5·2 g.) was dissolved in 1 : 1 chloroform–methanol (150 ml.). The solvent was evaporated, the volume being kept at *ca.* 50 ml. by the addition of more methanol, and the crystalline solid obtained on cooling was separated (0·25 g.). The *nitro-derivative* (XIX; R = NO_2) formed pale yellow plates, m. p. 130—131° from chloroform–methanol (Found: C, 46·8; H, 3·65; N, 6·8. $C_{16}H_{14}N_2O_{11}$ requires C, 46·8; H, 3·4; N, 6·8%), $\lambda_{infl.}$ 249 and 310 mμ ($\varepsilon_{infl.}$ 11,500 and 1620); $\nu_{max.}$ 1765 (ketonic C=O), 1740 (ester C=O), 1595, and 1330 (NO_2) cm.$^{-1}$.

The methanolic mother-liquors from this preparation were diluted with water (50 ml.) and heated under reflux for 1 hr. After cooling, the precipitated *solid* (XX) was separated and dried. It was crystallised from chloroform–methanol and formed pale yellow plates, m. p. 238—239° (Found: C, 50·7; H, 3·7. $C_{30}H_{28}O_{20}$ requires C, 50·85; H, 4·0%), $\lambda_{infl.}$ 250 and 310 mμ; $\varepsilon_{infl.}$ 4800 and 880, $\nu_{max.}$ 1760 (ketonic C=O), 1740, and 1720 (ester C=O) cm.$^{-1}$. The n.m.r. spectrum (CH_2Cl_2 containing trifluoroacetic acid) showed signals at 5·46 (quartet; methylene of ethyl ester), 6·03, 6·20, 6·23 (singlets; three methyl esters), and 8·53 τ (triplet; methyl of ethyl ester). The 2,4-*dinitrophenylhydrazone* formed pale yellow prisms, m. p. 238°, from chloroform–methanol (Found: C, 47·0; H, 3·5; N, 10·1. $C_{42}H_{36}N_8O_{26}$ requires C, 47·1; H, 3·4; N, 10·5%), $\lambda_{max.}$ (in 10% $CHCl_3$–CH_3OH) 250 and 343 mμ ($\varepsilon_{max.}$ 16,660 and 22,390); $\lambda_{max.}$ (in 10% $CHCl_3$–CH_3OH + 2 drops N-NaOH) 250, 350, and 530 mμ ($\varepsilon_{max.}$ 16,980, 5,500, and 25,100).

The α-oxo-ester (XX) (1 g.) was suspended in boiling ethanol (75 ml.) and a solution of *o*-phenylenediamine (300 mg.) in acetic acid (10 ml.) was added. The mixture was heated under reflux for 20 hr. and then cooled. The precipitated yellow solid was separated, washed with ethanol (20 ml.), and then dried in air. The *bisquinoxalyl derivative* (XX) (326 mg.) was crystallised from aqueous *NN*-dimethylformamide when it was obtained as a pale yellow powder, m. p. ≮360° (Found: N, 6·95. $C_{42}H_{56}N_4O_{16}$ requires N, 6·6%), $\nu_{max.}$ 1730 (ester C=O) and 1765 (ketonic C=O) cm.$^{-1}$.

[18] S. Ruhemann and K. C. Browning, *J.*, 1898, **73**, 727.

Adduct (XXII) *from Methyl Phenylpropiolate, Ethyl Cyanoacetate, and Pyridine.*—A mixture of pyridine (0·8 ml.) and glacial acetic acid (0·8 ml.) was added to a solution of methyl phenylpropiolate (1·5 ml.) and ethyl cyanoacetate (1 ml.) in methanol (15 ml.) and the mixture was heated under reflux for 17 hr. The deep red solution was adsorbed on alumina (25 g.), dried at 80°, and the alumina then continuously extracted with light petroleum (b. p. 60—80°, 100 ml.) until the extract was no longer coloured. On cooling, the *product* was obtained as orange needles which, after crystallisation from methanol, had m. p. 156—157° (Found: C, 67·1; H, 5·5; N, 8·4. $C_{19}H_{18}N_2O_4$ requires C, 67·45; H, 5·35; N, 8·3%), $\lambda_{max.}$ 298 and 444 mμ ($\varepsilon_{max.}$ 9220 and 59,620) $\lambda_{infl.}$ 244 mμ ($\varepsilon_{infl.}$ 9380); $\nu_{max.}$ 1710 (ester C=O) and 2225 (CN) cm.$^{-1}$.

Acid Hydrolysis of the Methyl Phenylpropiolate Adduct.—The foregoing adduct (1·0 g.), concentrated hydrochloric acid (50 ml.), and ether (100 ml.) were stirred at room temperature for 2 days. The ethereal layer was separated, dried, and then treated with a solution of 2,4-dinitrophenylhydrazine hydrochloride (0·5 g.) in ethanol (15 ml.) and warmed to 30°. Next day, the orange needles which had separated were removed and dried in air (383 mg.) when they had m. p. 247—249° and were identical with the 2,4-dinitrophenylhydrazone of acetophenone (lit., m. p. 250°).

Other Adducts from Methyl Phenylpropiolate.—(*a*) *With ethyl cyanoacetate and β-picoline.* Prepared from β-picoline (1 g.) as described above for the pyridine adduct but using a reflux period of 24 hr., the *adduct* (XXII; R = Me) formed orange-red needles (methanol), m. p. 182—184° (Found: C, 67·7; H, 5·65; N, 7·75. $C_{20}H_{20}N_2O_4$ requires C, 68·15; H, 5·7; N, 7·95%), $\lambda_{max.}$ 300 and 445 mμ ($\varepsilon_{max.}$ 6340 and 59,270); $\lambda_{infl.}$ 244 mμ ($\varepsilon_{infl.}$ 9990); $\nu_{max.}$ 1710 (ester C=O) and 2225 (CN) cm.$^{-1}$. The n.m.r. spectrum contained a singlet peak at 7·97 (CH_3 derived from β-picoline), and a doublet at 2·25 τ [H(f) in (XXII; R = Me)].

(*b*) *With ethyl cyanoacetate and nicotinic acid.* Prepared from nicotinic acid (1·2 g.) as described above for the pyridine adduct but using a reflux period of 48 hr., the *adduct* (0·11 g.) formed orange prisms (from methanol), m. p. 175—176° (Found: C, 64·0; H, 5·25; N, 7·0. $C_{21}H_{20}N_2O_6$ requires C, 63·65; H, 5·1; N, 7·05%), $\lambda_{max.}$ 432 mμ ($\varepsilon_{max.}$ 29,440) $\lambda_{infl.}$ 241, 265, and 300 mμ; ($\varepsilon_{infl.}$ 11,680, 8890, and 7280); $\nu_{max.}$ 1705 [ester (C=O) and 2225 (CN) cm.$^{-1}$].

(*c*) *With ethyl cyanoacetate and nicotinamide.* Prepared from nicotinamide (1·2 g.) as described above for the pyridine adduct, but using a reflux period of 20 hr., the *product*, after crystallisation from chloroform–light petroleum, formed orange-yellow needles, m. p. 165° (Found: C, 63·1; H, 5·5. $C_{20}H_{19}N_3O_5$ requires C, 63·0; H, 5·0%), $\lambda_{max.}$ 438 mμ ($\varepsilon_{max.}$ 32,000); $\lambda_{infl.}$ 246, 270, and 304 mμ ($\varepsilon_{infl.}$ 11,280, 9360, and 8150); $\nu_{max.}$ 1700 (ester and amide C=O), 2210 (CN), 3180, 3345, and 3425 ($CONH_2$) cm.$^{-1}$.

(*d*) *With cyanoacetic acid and pyridine.* Prepared as above from cyanoacetic acid (1 g.), ethanol as solvent and a reflux period of 18 hr., the *product* after crystallisation from ethanol, formed orange-red prisms, m. p. 147—149° (Found: C, 68·6; H, 6·15; N, 7·55. $C_{21}H_{22}N_2O_4$ requires C, 68·85; H, 6·65; N, 7·65%), $\lambda_{max.}$ 298 and 444 mμ ($\varepsilon_{max.}$ 10,020 and 59,730); $\lambda_{infl.}$ 244 mμ ($\varepsilon_{infl.}$ 10,450). The n.m.r. spectrum contained signals at 5·73, 5·75 (quartets; methylenes of ethyl esters), and 8·72 τ (triplet; two methyls of ethyl esters).

(*e*) *With cyanoacetamide and pyridine.* Prepared from cyanoacetamide (1 g.) as described above but using a reflux period of 48 hr., the *product*, after crystallisation from aqueous acetone, formed brownish-yellow plates, m. p. 203—205° (Found: C, 66·6; H, 5·3; N, 12·6. $C_{18}H_{17}N_3O_3$ requires C, 66·85; H, 5·3; N, 13·0%), $\lambda_{max.}$ 301 and 444 mμ ($\varepsilon_{max.}$ 9110 and 53,460); $\lambda_{infl.}$ 244 mμ ($\varepsilon_{infl.}$ 9480); $\nu_{max.}$ 1686 (amide C=O), 2210 (CN), 3220, 3330, and 3480 ($CONH_2$) cm.$^{-1}$.

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