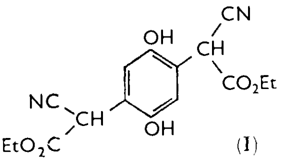
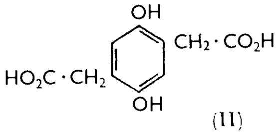
175. *The Chemistry of Colour Reactions. The Craven Reaction.*

By T. J. King and C. E. Newall.

The reaction of *p*-benzoquinone and 1,4-naphthaquinone with ethyl cyanoacetate in the presence of ammonia has been re-examined and the nature of the products formed is elucidated.

In 1931 Craven [1] reported that ethyl cyanoacetate reacted in alcoholic ammonia with a number of quinones, including *p*-benzoquinone and 1,4-naphthaquinone, to give intensely blue solutions. In some cases reaction products were isolated but no structures were assigned to them. In 1944, Wood and his co-workers [2] re-examined this reaction using *p*-benzoquinone and assigned to the end product, a sparingly soluble crystalline material, the quinol structure (I). This was reported as being coloured and difficult to purify. The structure assigned rested largely upon the fact that acid hydrolysed the compound in high yield to the quinol (II) together with the corresponding dilactone. The same compound was later isolated by Jeffreys [3] as a main component of the reaction between methoxy-*p*-benzoquinone and ethyl cyanoacetate in the presence of alkoxide ion. Largely because of the frequency (1672 cm.$^{-1}$) of the cabonyl stretching absorption, Jeffreys considered that the compound had the diamide structure (III).


(I)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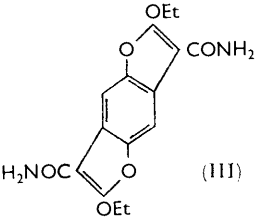
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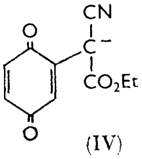
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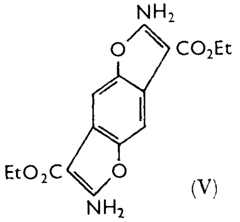
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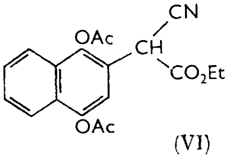
(VI)

There seems no reason to doubt the suggestion [3] that the colour produced in the Craven reaction is due to the resonating anion of a quinone of type (IV), whose formation would be predicted under the reaction conditions. With *p*-benzoquinone itself this compound undergoes further reaction with resulting loss of the blue colour and formation of a reddish coloured solid. If the initially formed blue solution is acidified the same solid is produced in reduced yield. The infrared absorption of the solid product shows the absence of nitrile function and thus the compound cannot have structure (I). The structure (III) we also believe to be incorrect and prefer the isomeric cyclisation product of (I), namely the bis-aminofuran (V), whose formation is chemically more acceptable than that of (III).

We do not accept Jeffrey's view that the infrared absorption is incompatible with such a structure. The carbonyl stretching frequency of ethyl β-aminocrotonate, in which the ester group is in a very similar environment, absorbs at 1660 cm.$^{-1}$, even lower than that observed for (V). Further, the NH stretching frequencies (3320 and 3440 cm.$^{-1}$) of the compound are too low to be due to an unbonded primary amide, [*e.g.*, *O*-methylsalicylamide, with the environment of the amide group similar to that of (III), shows bands at 3390

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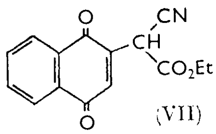
[1] Craven, *J.*, 1931, 1605.
[2] Wood, Colburn, Cox, and Garland, *J. Amer. Chem. Soc.*, 1944, **66**, 1540.
[3] Jeffreys, *J.*, 1959, 2153.

and 3515 cm.$^{-1}$] but are in good agreement with those expected for a hydrogen bonded primary amine. Finally, we have prepared, under relatively mild conditions, the tetra-acetate and tetrabenzoate of this Craven reaction product. These derivatives show no NH absorption. The di-acylation of a primary amide is normally difficult to achieve and thus the formation of these compounds is in better accord with the formulation of the product as an amine rather than an amide.

We have also investigated the Craven reaction with 1,4-naphthaquinone. In this case the blue colour ($\lambda_{max.}$ 588 mμ) is stable almost indefinitely. Acidification of the blue solution and extraction with an organic solvent gave a red amorphous material ($\lambda_{max.}$ 508 mμ) which could not be purified and which was soluble in dilute aqueous base regenerating a blue colour. The red compound was readily reduced with zinc dust or catalytically, and a catalytically reduced sample was acetylated to give a crystalline product, $C_{19}H_{17}NO_6$, with the ultraviolet absorption of a substituted naphthalene. The infrared spectrum showed the presence of phenolic acetate groups, a saturated nitrile and an aliphatic ester. No NH or OH was present. This compound thus has structure (VI). The red amorphous product is thus clearly the quinone (VII). When this quinone was reductively acetylated with zinc and acetic acid–acetic anhydride a colourless product was isolated isomeric with (VI). The ultraviolet absorption of this was not that of an unconjugated naphthalene but was compatible with that of a naphthofuran. Nitrile absorption was absent from the infrared spectrum so the probable structures appeared to be (VIII) or (IX) with (VIII) preferred as being closest to the structure of the product from the *p*-benzoquinone reaction. The nuclear magnetic resonance spectrum of the compound is compatible with either of these structures and does not distinguish between them. The diacetate was characterised as a mono-*N*-methyl derivative and by further acetylation to a triacetate. The *N*-methyl derivative lost one of its acetyl groups when crystallised from ethanol–chloroform; the infrared spectrum showed that it was the phenolic acetate group which had been lost. Acid hydrolysis of the diacetate afforded 0·92 mol. ammonia and a good yield of the 5-hydroxybenzo[*g*]coumaran-2-one (X).[4]



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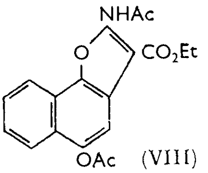
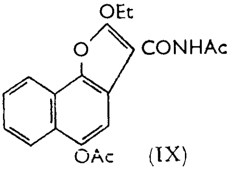


(VIII)



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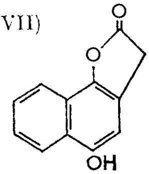

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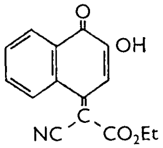

(XI)

The distinction between the structures (VIII) and (IX) was achieved by an analysis of the infrared spectrum. Only the aminofuran structure would show strong bonding of the hydrogen of the NH group. The NH stretching frequency of *N*-acetyl-*O*-methylsalicylamide, analogous to (IX), is a strong sharp band at 3355 cm.$^{-1}$, whereas the diacetate itself shows a broad weak band at 3300 cm.$^{-1}$ which was concentration independent. Ethyl *N*-acetylanthranilate (cf. VIII) also has a broad absorption peak at 3300 cm.$^{-1}$.

1,2-Naphthaquinone, which was reported by Craven as not giving a blue colour reaction, does do so, and the colour is stable in weak base. The free acid corresponding to the blue anion was amorphous but its infrared absorption was consistent with its having a structure

[4] McElvain and Engelhart, *J. Amer. Chem. Soc.*, 1944, **66**, 1077.

analogous to (XI), and after catalytic reduction the product showed ultraviolet absorption very similar to that of naphthalene-1,2-diol.

EXPERIMENTAL

Light petroleum refers to the fraction b. p. 40—60°. Infrared spectra were determined using either a Unicam S.P. 100 or Perkin-Elmer 237 instrument. Ultraviolet spectra were determined with a Perkin-Elmer 137 spectrophotometer on ethanolic solutions unless otherwise stated. N.m.r. spectra were measured at 60 Mc. with an A.E.I. (RS 2) spectrometer. M. p.s were determined on a Kofler hot-stage apparatus.

2,6-Diamino-3,7-diethoxycarbonylbenzo[1,2-b;4,5-b]*difuran* (V).—*p*-Benzoquinone (2 g.) and ethyl cyanoacetate (5 c.c.) in methanol (50 c.c.) were treated at room temperature with aqueous ammonia (10 c.c.; *d* 0·88). The solution became blue and then brown and after 5 min. it was diluted with water and acidified with dilute sulphuric acid. The precipitate so obtained was continuously extracted first with chloroform to remove impurities and then with acetone. The acetone extract afforded purple prisms (1·2 g.), m. p. 268—269°. The colour of the product was very variable some samples being light fawn (Found: C, 57·8, 57·7; H, 4·9, 5·0; N, 8·75, 8·25. Calc. for $C_{16}H_{16}N_2O_6$: C, 57·85; H, 4·85; N, 8·45%); $\lambda_{max.}$ (in tetrahydrofuran) 274 and 320 mμ (ε 28,000 and 23,000, respectively); $\nu_{max.}$ (in KBr) 1217s, 1549s, 1675vs, 3320ms, and 3440m cm.$^{-1}$.

The above product was stirred with pyridine and excess of acetic anhydride for 48 hr. at room temperature. The precipitate was collected and crystallised from ethanol–chloroform to give the *tetra-acetate* as needles, m. p. 230—235° (decomp.) (Found: C, 57·3; H, 4·75; N, 5·4. $C_{24}H_{24}N_2O_{10}$ requires C, 57·6; H, 4·85; N, 5·6%). The compound had the expected nuclear magnetic resonance absorption. The *tetrabenzoate* was prepared in a similar way using benzoyl chloride and formed needles, m. p. 242—245° (Found: C, 70·5; H, 4·45; N, 3·45. $C_{44}H_{32}N_2O_{10}$ requires C, 70·6; H, 4·3; N, 3·75%). The ultraviolet, infrared, and nuclear magnetic spectra of this derivative were completely compatible with its formulation as the tetrabenzoate of (V). When the crude reaction mixture from the benzoylation was diluted with water and heated at 100° for 2 hr. the *dibenzoate* was isolated as yellow needles from chloroform–methanol, m. p. 309—310° (Found: C, 66·3; H, 4·25; N, 4·9. $C_{30}H_{24}N_2O_8$ requires C, 66·6; H, 4·5; N, 5·2%) The dibenzoate was also obtained in low yield from the action of lithium aluminium hydride on the tetrabenzoate, and its presence in hydrolysates of the tetrabenzoate was demonstrated by thin layer chromatography.

Craven Reaction with 1,4-*Naphthaquinone*.—1,4-Naphthaquinone (1·6 g.) and ethyl cyanoacetate (2·5 c.c.) in methanol (30 c.c.) were treated with aqueous ammonia (10 c.c.; *d* 0·88). After 10 min. the deep blue solution was diluted with water and washed twice with ether. The blue solution was then acidified with dilute sulphuric acid and the red precipitate was collected in ether. When the solution was shaken with dilute ammonia the aqueous layer became blue and the ether layer could be shown to contain no involatile material. Evaporation of the red ether solution gave a red amorphous solid which could not be purified. It showed $\lambda_{max.}$ 282 and 508 mμ. In basic ethanol its blue solution had $\lambda_{max.}$ 291, 315, and 588 mμ.

α-*Cyano*-1,4-*diacetoxy*-2-*naphthylacetate* (VI).—The amorphous red product from the above reaction in ether (50 c.c.) was shaken with hydrogen at room temperature and pressure in the presence of palladised charcoal until absorption of hydrogen ceased. The solution was filtered, acetic anhydride was added (50 c.c.), the ether was removed under reduced pressure and one drop of concentrated sulphuric acid was added. After 3 hr. at room temperature, water (300 c.c.) was added and after 1 hr. more, the precipitate was collected. The *diacetate* crystallised, with some difficulty at first, from ether–light petroleum as needles, m. p. 115—116° (Found: C, 63·9; H, 4·8; N, 3·9. $C_{19}H_{17}NO_6$ requires C, 64·2; H, 4·8; N, 3·95%); $\lambda_{max.}$ 226, 287, and 323 mμ (ε 69,000, 7000, and 900, respectively); $\nu_{max.}$ (in KBr) included 1180vs, 1370s, 1610m, 1755s, 1783vs, and 2250m cm.$^{-1}$.

2-*Acetamido*-5-*acetoxy*-3-*ethoxycarbonylnaphtho*[1,2-b]*furan* (VIII).—The crude product from the Craven reaction with naphthaquinone was dissolved in acetic acid (25 c.c.), and acetic anhydride (25 c.c.), and zinc powder (1 g.), and concentrated sulphuric acid (5 drops) were added. The mixture was boiled gently for 4 hr. and the colourless solution was filtered and poured into water. After 2 hr. the precipitate was collected and crystallised from methanol–chloroform to give the *naphthofuran* (325 mg.) as needles, m. p. 182—183° (Found: C, 63·9;

H, 4·95; N, 4·0%; *M* (Rast) 360. $C_{19}H_{17}NO_6$ requires C, 64·2; H, 4·8; N, 3·9%, *M* 355); $\lambda_{max.}$ 245 and 337 mμ (ε 48,600 and 4600, respectively); $\nu_{max.}$ (in CCl_4) included 1590s, 1610vs, 1680s, 1775s, and 3300w, broad cm.$^{-1}$.

5-*Acetoxy*-3-*ethoxycarbonyl*-2-*methylacetamidonaphtho*[1,2-b]*furan*.—The above diacetate (190 mg.) in methyl iodide (5 c.c.) was stirred with silver oxide (500 mg.) for 4 days. The solvent was evaporated and the residue was extracted with ether and crystallised from ether–light petroleum to give the *N-methyl derivative* as colourless needles (97 mg., 46%), m. p. 154—156° (Found: *N*-Me 3·8. $C_{20}H_{19}NO_6$ requires *N*-Me 4·05%), the nuclear magnetic resonance spectrum showed a singlet (3 proton intensity) at τ 6·58 absent from the spectrum of the unmethylated product. The infrared spectrum showed no band attributable to N–H.

When this compound was crystallised twice from chloroform–methanol 3-*ethoxycarbonyl*-5-*hydroxy*-2-*methylacetamidonaphtho*[1,2-b]*furan* was formed, needles, m. p. 209—210°, (86%) (Found: C, 66·3; H, 5·15; *N*-Me, 3·85. $C_{18}H_{17}NO_5$ requires C, 66·05; H, 5·25; *N*-Me, 4·65%), no max. near 1775 cm.$^{-1}$ but absorption at 3590 cm.$^{-1}$ (OH).

5-*Acetoxy*-2-*diacetamido*-3-*ethoxycarbonylnaphtho*[1,2-b]*furan*.—The above diacetate was acetylated by acetic anhydride in pyridine for 4 days at room temperature. The *product*, isolated in the usual way crystallised from ether–light petroleum in laths (69%), m. p. 139—140° (Found: C, 63·15; H, 4·9; N, 3·7. $C_{21}H_{19}NO_7$ requires C, 63·4; H, 4·8; N, 3·55%). The nuclear magnetic resonance spectrum, showed two peaks corresponding to MeCO intensity 6 protons and 3 protons. The infrared spectrum showed no band corresponding to NH.

Acid Hydrolysis of the Diacetate (VIII).—The diacetate (VIII) (61 mg.) was boiled with aqueous alcoholic hydrochloric acid [concentrated acid (5 c.c.), water (5 c.c.), ethanol (1 c.c.)] for 4 hr. The mixture was then diluted, extracted with ether, and purified by distillation and sublimation to give prisms, m. p. 201—202° identical with an authentic sample of 5-hydroxybenzo[g]coumaran-2-one.

A similar hydrolysis mixture was basified and the ammonia liberated was distilled and titrated in the usual way (0·92 mol.).

N-*Acetyl*-O-*methylsalicylamide*.—*O*-Methylsalicylamide (568 mg.) was boiled with acetyl chloride (20 ml.) for 16 hr. The solvent was evaporated in a vacuum and the residue crystallised from aqueous ethanol to give the *acetate* as prisms (60%), m. p. 82—83° (Found: C, 62·4; H, 5·95; N, 7·1. $C_{10}H_{11}NO_3$ requires C, 62·2; H, 5·75; N, 7·25%), $\nu_{max.}$ (in CCl_4) included 3350ms, sharp cm.$^{-1}$.

Craven Reaction on 1,2-*Naphthaquinone*.—The reaction mixture from 1,2-naphthaquinone (160 mg.), ethyl cyanoacetate (124 mg.), and ammonia in ethanol rapidly became a blue-violet colour; $\lambda_{max.}$ 252, 315, 377, and 572 mμ. The free " acid " was isolated as an amorphous orange powder by the same method as was employed for the 1,4-naphthaquinone product. It could not be purified but the light absorption properties were $\lambda_{max.}$ 255, 337, and 380 mμ, $\nu_{max.}$ (in CCl_4) included 1420ms, 1655s, 1730s, 2215w, and 3425wm cm.$^{-1}$. An acidified ethanol solution became colourless on treatment with zinc dust and then showed $\lambda_{max.}$ 238, 307, and 345 mμ, the ratios of the intensities were approximately 9 : 1 : 1, respectively.

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