Formation of polyheterocyclic systems by reaction of 2-imino-4-methyl-2*H*-1-benzopyran-3-carbonitrile with active methylene compounds

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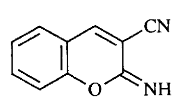
2-Imino-4-methyl-2*H*-1-benzopyran-3-carbonitrile undergoes [1,5] tautomerism in solution to 2-amino-4-methylidene-4*H*-1-benzopyran-3-carbonitrile. Reaction with one equivalent of compounds containing a reactive methylene group affords simple 4-methylbenzopyran derivatives, and a methylidene derivative (of [1]benzopyrano[2,3-*b*][1,8]naphthyridine). Reaction with two and three equivalents of malononitrile affords derivatives of [1]benzopyrano[2,3,4-de]quinoline and [1]benzopyrano[2,3,4-de][1,6]-naphthyridine, which had previously been formulated as bicyclic benzopyran derivatives. The X-ray crystal structure of ethyl 3-amino-2-cyano-3-(2-imino-4-methyl-2*H*-1-benzopyran-3-yl)prop-2-enoate has been determined, showing the presence of two molecules in the asymmetric unit.

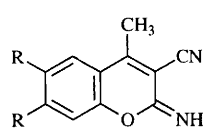
The inhibitory activity of dicyanomethylene derivatives against protein tyrosine kinase has led to considerable interest in the synthesis and reactions of these compounds.[1,2,3] 2-Imino-2*H*-benzopyran-3-carbonitrile **1** is very closely related to the benzylidenemalononitriles but it is quite unstable. We now describe the reactions of the more stable 4-methyl derivative, 2-imino-4-methyl-2*H*-1-benzopyran-3-carbonitrile **2a**.

The 4-methyl derivative **2a** was obtained in 1966 from the ethoxide catalysed reaction of 1-(2-hydroxyphenyl)ethanone with malononitrile.[4] Its hydrolysis to the oxo derivative **3** was described, but some related products were formulated incorrectly or incompletely. The correct formulations of these compounds (and also of new products obtained from the reactions of the imine **2a**) are now reported.

The NMR spectra of the monomeric imine **2a** show that in solution the compound quickly undergoes an interesting [1,5] tautomeric shift. When the ^{1}H and ^{13}C NMR spectra are recorded immediately on dissolution in [$^{2}H_6$]dimethyl sulfoxide, only one structure is present. However, after 2 h it is possible to detect the presence of a second tautomer, and after 48 h the solution contains a 1 : 1 mixture of the 4-methyl-2-imino compound **2a** and its 4-methylidene-2-amino tautomer **4a**.



1



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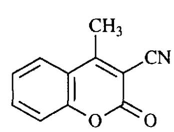

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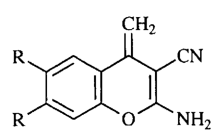
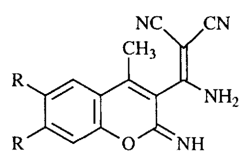


4

a R = H
b R = Me

In the original report of the synthesis of the 1 : 1 product **2a**, it was shown that replacement of ethoxide by catalytic piperidine resulted in the formation of the 1 : 2 product **5a**. It seems highly probable that this was formed *via* **2a**, and this is confirmed by the reaction of **2a** with malononitrile and catalytic piperidine to afford **5**. (The probable reaction pathway is outlined in Scheme 1.) The corresponding dimethyl compounds **2b** and **5b** are similarly obtained from 1-(2-hydroxy-4,5-dimethylphenyl)ethanone. They are less soluble than the unmethylated derivatives, and it is not possible to obtain an NMR spectrum of **2b** as a single tautomeric form; even when the spectrum is recorded immediately, the presence of the second tautomeric form **4b** is evident.

The reaction of **1** with malononitrile differs from the reaction of a benzopyran derivative with malononitrile previously described by the Van Allan group.[5] More recently, a compound **6** derived from the reaction of salicylaldehyde with malononitrile in 1 : 2 ratio has been described,[6] but its reactions were quite different, the lability of the 4-substituent being the dominant feature.



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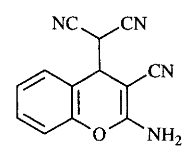
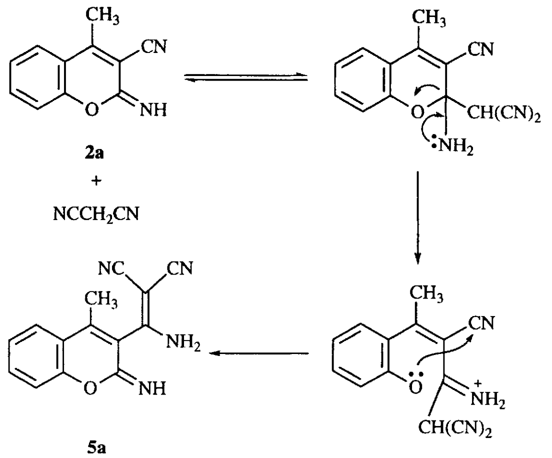


6

a R = H
b R = Me

The reaction of the 1 : 1 imine **2a** with malononitrile to form the 1 : 2 product **5a** is paralleled by the reaction of **2a** with benzoylacetonitrile, when the product formed is the benzoyl derivative **7**. Reaction of **2a** with methyl cyanoacetate in methanol affords the methyl ester **8**, but when this reaction is carried out in ethanol the ethyl ester **9** is obtained.

An interesting feature of the ^{1}H NMR spectrum of the ethyl ester **9** is that the OCH_2 signal is a quartet of quartets; irradiation of the ester CH_3 signal reduces this to an AB quartet. This indicates that there is restricted rotation around the 3–3′ bond, within the NMR timescale, and the two hydrogen atoms are diastereotopic. The molecular structure of the ethyl ester **9** as determined by X-ray diffraction, is presented in Fig. 1. Two molecules are present in the asymmetric unit. The conformations of these are not quite enantiomeric (as they differ in the arrangement of the ethyl ester groups *relative to the*



Scheme 1

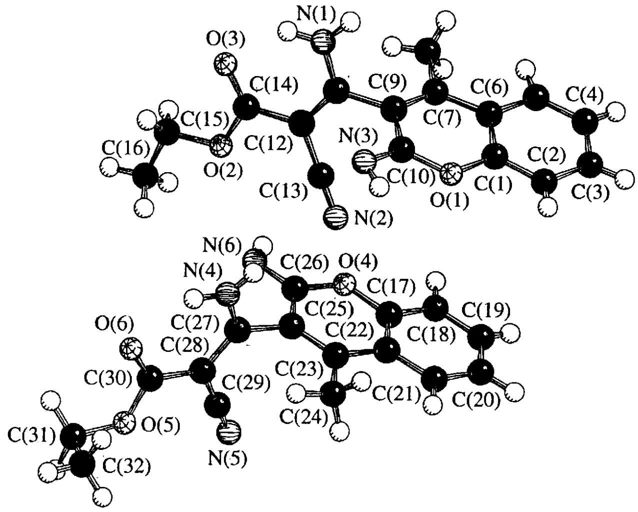
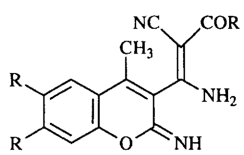


Fig. 1

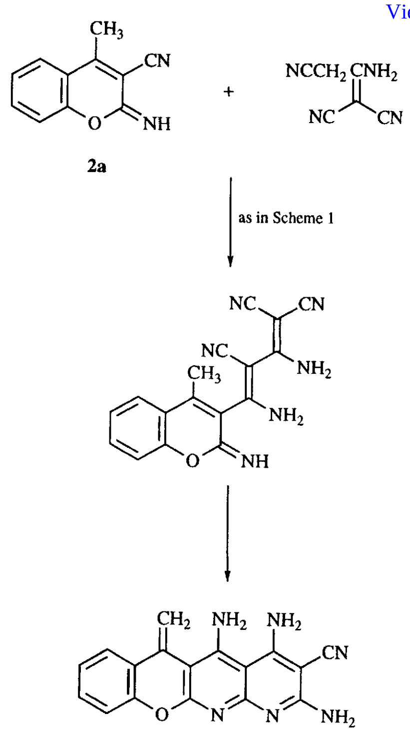


7 R = Ph
8 R = OMe
9 R = OEt

rest of the molecule), but they show that there is indeed restricted rotation about the 3–3′ bond. In solution, the flexibility of the ester group ensures that two enantiomers are present and that the ester CH_2 is diastereotopic.

The product formed from the reaction of the imine **2a** with 2-aminoprop-1-ene-1,1,3-tricarbonitrile ('malononitrile dimer') is the methylidene derivative **10**. Clearly this is derived from the methylidene tautomer **4a** rather than the methyl derivative **2a**. A possible mechanism for the reaction is outlined in Scheme 2. This involves the introduction of the exocyclic methylidene group early in the reaction sequence, but it is possible to visualise an alternative where this group is introduced later in the reaction.

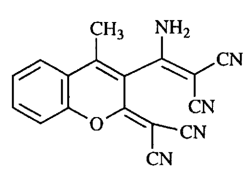
Apart from the 1:2 reaction product **5a**, the original piperidine-catalysed reaction of 1-(2-hydroxyphenyl)ethanone with an excess of malononitrile had also afforded two other products. The structural formula **11** was ascribed to one of these (molecular formula $C_{17}H_9N_5O$), while the partial structural formula **13** was suggested for the other (molecular



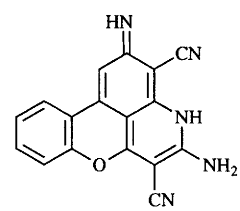
10

Scheme 2

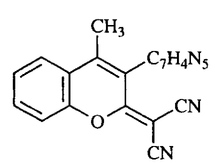
formula $C_{20}H_{11}N_6O$). The NMR spectra show at once that neither of these formulations is correct, since the methyl/methylidene group of the compound formulated as **11** is incorporated into an unsaturated ring, and in the compound '**13**' the methyl group is attached to a tetrahedral carbon. In fact, both of these compounds are tetracyclic structures, the compound **11** ($C_{17}H_9N_5O$) being correctly formulated as **12**, while the compound **13** ($C_{20}H_{11}N_6O$) is correctly formulated as **14**. Mechanisms for the formation of **12** and **14** are suggested in Scheme 3.



11



12



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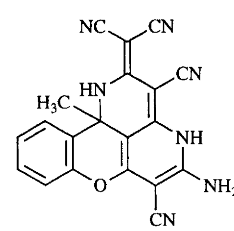
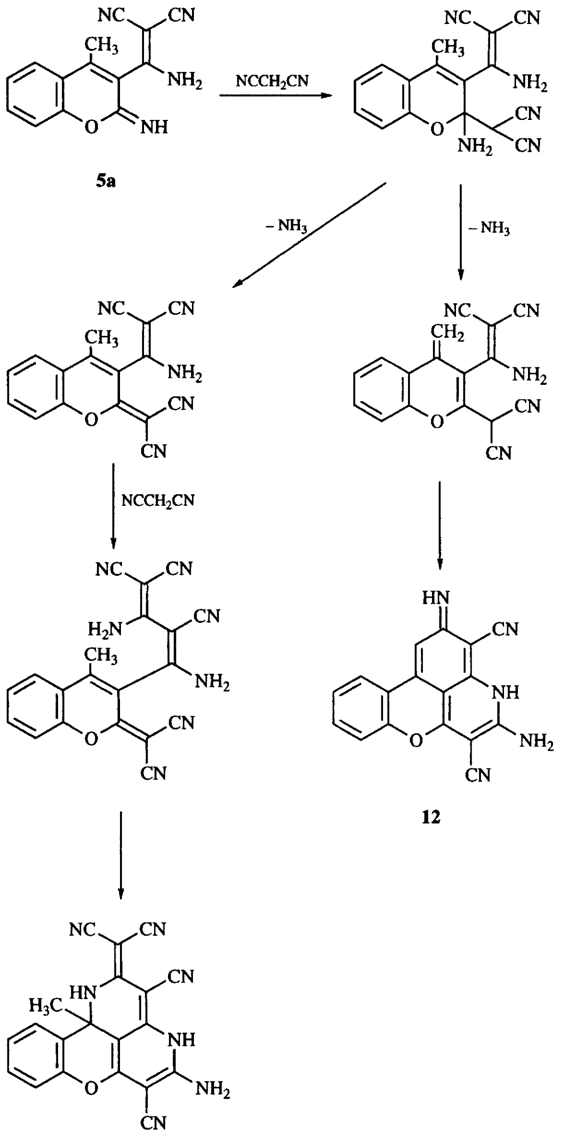
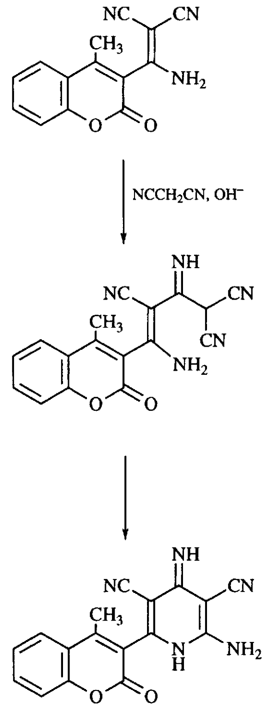


14

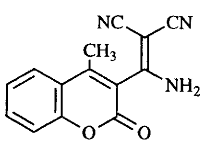
It was noted that the compound now formulated as **14** was also obtained from the reaction of the imine derivative **5a** with malononitrile. The reaction of the corresponding oxo derivative **15** with malononitrile in sodium hydroxide afforded a compound $C_{17}H_{11}N_5O_2$ for which the benzopyrano formulation **16** was suggested.[4] NMR spectra confirm that this is a 2-oxo-1-benzopyran-2-yl derivative **17**. The mechanism involved is a simple one, outlined in Scheme 4.



Scheme 3



Scheme 4



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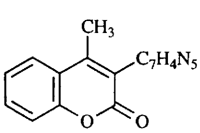

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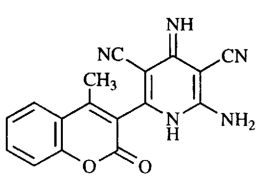

17

Experimental

Melting points were determined in capillary tubes on a Gallenkamp apparatus and are uncorrected. IR spectra (Nujol) were recorded on a Perkin-Elmer spectrophotometer, and UV spectra on a Unicam UV4-100 instrument. NMR spectra were recorded in ppm on a Bruker MSL 300 instrument, using [$^2H_6$]dimethyl sulfoxide as solvent. *J* Values are given in Hz.

2-Imino-4-methyl-2*H*-1-benzopyran-3-carbonitrile 2a

Prepared using catalytic ethoxide according to the literature method, the colourless crystalline nitrile **2a** had mp 142–143 °C (lit.,[4] mp 150 °C) (Found: C, 71.4; H, 4.3; N, 15.3. Calc. for $C_{11}H_8N_2O$: C, 71.7; H, 4.4; N, 15.2%), ν_{max}/cm^{-1} 3307 (NH), 2224 (C≡N) and 1660; δ_H 2.59 (3 H, s, CH_3), 7.20 (1 H, dd, *J* 1.3, 8.0, ArH), 7.31 (1 H, dt, *J* 1.3, 8.0, ArH), 7.62 (1 H, dt, *J* 1.3, 8.0, ArH), 7.76 (1 H, dd, *J* 8.0, 1.3, ArH) and 8.64 (1 exchangeable H, br s, NH), δ_C 17.6 (CH_3), 102.8 (C-3), 114.8 (C≡N), 115.7 (C-8), 118.0 (C-4a), 124.1 (C-6), 126.7 (C-5), 134.0 (C-7), 151.7 (C-8a), 152.6 (C-4) and 155.6 (C-2).

When the NMR solution was set aside for 48 h, it became a 1 : 1 mixture of **2a** and its tautomer *2-amino-4-methylidene-*4H-1-*benzopyran-*3-*carbonitrile* **4a**, δ_H 4.57 (1 H, s, H^a of =CH_2), 5.17 (1 H, s, H^b of =CH_2), 7.11 (1 H, dd, *J* 1.4, 7.7, ArH), 7.23 (1 H, dt, *J* 7.7, 1.4, ArH), 7.40 (1 H, dt, *J* 1.4, 7.7, ArH), 7.6 (2 exchangeable H, br s, partially concealed, NH_2) and 7.82 (1 H, dd, *J* 1.4, 7.7, ArH), δ_C 62.0 (C-3), 92.5 (=CH_2), 116.8 (C-8), 117.8 (C≡N), 119.2 (C-4a), 123.7 (C-6), 125.1 (C-5), 130.1 (C-7), 130.3 (C-4), 148.2 (C-8a) and 160.3 (C-2). The tautomeric mixture had λ_{max}(MeOH)/nm 206, 225, 290, 300 and 345.

Preparation of 3-amino-2-cyano-3-(2-imino-4-methyl-2*H*-1-benzopyran-3-yl)prop-2-enenitrile 5a from 2-imino-4-methyl-2*H*-1-benzopyran-3-carbonitrile 2a

A mixture of the imine **2a** (0.46 g, 2.5 mmol) and malononitrile (0.165 g, 2.5 mmol) in ethanol (35 cm^3) was heated to dissolve, then cooled to 20 °C and piperidine (0.06 cm^3) added. The mixture was set aside for 3 days, after which the amine **5a** crystallised. The colourless crystals were filtered off, dried and recrystallised from methanol (0.39 g, 62%), mp 230 °C (decomp.) (lit.,[4] mp, 230 °C), λ_{max}(MeOH)/nm 202, 222 and 277; ν_{max}/cm^{-1} 3299, 3222, (NH, NH_2), 2219, 2207 (C≡N) and 1644; δ_H 2.29 (3 H, s, CH_3), 7.21 (1 H, dd, *J* 1.3, 8.0, ArH), 7.30 (1 H, dt, *J* 1.3, 8.0, ArH), 7.56 (1 H, dt, *J* 1.3, 8.0, ArH), 7.73 (1 H, dd, *J* 1.3, 8.0, ArH), 8.38 (1 exchangeable H, s, =NH), 8.96 (1 exchangeable H, br s, NH) and 9.06 (1 exchangeable H, br s, NH); δ_C 14.9 (CH_3), 50.1 (C-2), 115.0 (C≡N), 115.4 (C-8′), 116.4

(C≡N), 118.9 (C-3′), 121.8 (C-4′), 121.8 (C-4a′), 124.0 (C-6′), 125.9 (C-5′), 132.3 (C-7′) and 168.4 (C-3).

Synthesis of 2-imino-4,6,7-trimethyl-2*H*-1-benzopyran-3-carbonitrile 2b

Sodium (0.4 g) dissolved in ethanol (10 cm^3) was added to a mixture of 1-(2-hydroxy-4,5-dimethylphenyl)ethanone (3.28 g, 20 mmol) and malononitrile (1.32 g, 20 mmol) in ethanol (20 cm^3). The mixture was heated for 5 min, then set aside at room temperature for 3 h. The colourless *product* which separated was essentially pure; when recrystallised from methanol, it had mp 197–198 °C (3.20 g, 75%) (Found: C, 73.2; H, 5.65; N, 13.0. $C_{13}H_{12}N_2O$ requires C, 73.6; H, 5.7; N, 13.2%), ν_{max}/cm^{-1} 3290 (NH), 2225 (C≡N), 1662. The NMR, determined 40 min after dissolution, showed that the imine **2b** was present to the extent of 75%, with the tautomeric *2-amino-6,7-dimethyl-4-methylidene-4H-1-benzopyran-3-carbonitrile* **4b** present to the extent of 25%. The imine **2b** present had δ_H 2.28 (3 H, s, CH_3), 2.49 (3 H, s, CH_3), 2.52 (3 H, s, CH_3), 6.96 (1 H, s, ArH), 7.45 (1 H, s, ArH), 8.43 (1 exchangeable H, s, NH) and δ_C 17.4 (CH_3), 18.6 (CH_3), 19.7 (CH_3), 101.4 (C-3), 115.0 (C≡N), 115.5 (C-4a), 116.1 (C-8), 126.4 (C-5), 132.5 (C-6), 144.0 (C-7), 150.8 (C-8a), 152.2 (C-4), 155.2 (C-2), while the tautomeric *amine* **4b** had δ_H 2.25 (3 H, s, CH_3), 2.26 (3 H, s, partially concealed, CH_3), 4.75 (1 H, s, H^a of =CH_2), 5.06 (1 H, s, H^b of =CH_2), 6.86 (1 H, s, ArH), 7.52 (1 H, s, ArH), 7.50 (2 exchangeable H, br s, NH_2); δ_C 18.8 (CH_3), 19.2 (CH_3), 62.0 (C-3), 91.2 (=CH_2), 116.3 (C≡N), 117.0 (C-8), 117.9 (C-4a), 123.8 (C-5), 130.3 (C-6), 132.2 (C-7), 138.9 (C-4), 146.2 (C-8a) and 160.3 (C-2). The tautomeric mixture had λ_{max}(MeOH)/nm 209, 231, 297, 306 and 364.

Synthesis of 3-amino-2-cyano-3-(2-imino-4,6,7-trimethyl-2*H*-1-benzopyran-3-yl)prop-2-enenitrile 5b

A mixture of 1-(2-hydroxy-4,5-dimethylphenyl)ethanone (1.64 g, 10 mmol) and malononitrile (0.66 g, 10 mmol) in ethanol (25 cm^3) was heated to dissolve, and then cooled to 20 °C. Piperidine (0.6 g) was added, and the solution set aside for 48 h. The material which separated was a mixture of unchanged ketone and 3-amino-2-cyano-3-(2-imino-4,6,7-trimethyl-2*H*-1-benzopyran-3-yl)prop-2-enenitrile **5b**. The *latter*, purified by recrystallation from methanol, was colourless crystals (1.14 g, 41%) mp 260 °C (decomp.) (Found: C, 68.7; H, 5.1; N, 19.9. $C_{16}H_{14}N_4O$ requires C, 69.0; H, 5.1; N, 20.1%); ν_{max}/cm^{-1} 3309, 3276 (NH, NH_2), 2215, 2202 (C≡N) and 1649; δ_H 2.26 (3 H, s, CH_3), 2.27 (3 H, s, CH_3), 2.30 (3 H, s, CH_3), 7.03 (1 H, s, ArH), 7.48 (1 H, s, ArH), 8.21 (1 exchangeable H, br s, NH), 8.96 (1 exchangeable H, s, NH) and 9.02 (1 exchangeable H, s, NH); δ_C 15.0 (CH_3), 18.7 (CH_3), 19.5 (CH_3), 50.3 (C-2), 115.1 (C≡N), 115.9 × 2 (C-8′, C≡N), 116.3 (C-3′), 132.0 (C-7′), 141.6 (C-4′), 142.1 (C-8a′), 150.7 (C-2′) and 168.5 (C-3).

Synthesis of 3-amino-2-benzoyl-3-(2-imino-4-methyl-2*H*-1-benzopyran-3-yl)prop-2-enenitrile 7

A mixture of the imine **2a** (0.92 g, 5 mmol) and benzoylacetonitrile (0.73 g, 5 mmol) in ethanol (40 cm^3) was heated to dissolve, then cooled to 20 °C, and piperidine (0.03 cm^3) added. The mixture was set aside for 24 h, and the material which crystallised was filtered off, dried and recrystallised from methanol. The recrystallised colourless *product* had mp 160–161 °C (1.10 g, 67%) (Found: C, 72.95; H, 4.35; N, 12.55. $C_{20}H_{15}N_3O_2$ requires C, 72.9; H, 4.6; N, 12.8%); λ_{max}(MeOH)/nm 204, 222 and 323; ν_{max}/cm^{-1} 3298, 3180 (NH_2, NH), 2204 (C≡N), 1651 (C=O); δ_H 2.33 (3 H, s, CH_3), 7.22–7.78 (9 H, m, 5 ArH and 4 ArH), 8.37 (1 exchangeable H, s, =NH), 9.66 (1 exchangeable H, br s, NH), 10.85 (1 exchangeable H, br s, NH); δ_C 15.0 (CH_3), 81.2 (C-2), 115.3 (ArCH), 119.1 (C≡N), 120.4 (C-3′), 123.3 (C-4a′), 123.8 (ArCH), 125.8 (ArCH), 127.5 × 2 (ArCH), 128.1 × 2 (ArCH), 131.2 (ArCH), 131.9 (ArCH), 139.2 (ArC), 141.2 (C-4), 152.5 (C-8a′), 153.2 (C-2′), 168.5 (C-3) and 191.2 (C=O).

Synthesis of alkyl 3-amino-2-cyano-3-(2-imino-4-methyl-2*H*-1-benzopyran-3-yl)prop-2-enoates 8 and 9

A mixture of the imine **2a** (0.92 g, 5 mmol), methyl cyanoacetate (0.50 g, 5 mmol) and piperidine (0.06 cm^3) in methanol (50 cm^3) was heated on a water-bath for 5 min and then set aside at room temperature for two days. The colourless product, which was filtered off, dried and recrystallised from methanol, had mp 189–191 °C (0.85 g, 60%) (Found: C, 63.4; H, 4.55; N, 14.5. $C_{15}H_{13}N_3O_3$ requires C, 63.6; H, 4.6, N, 14.8%); λ_{max}(MeOH)/nm 210, 279 and 323; ν_{max}/cm^{-1} 3338, 3180br (NH_2, NH), 2211 (C≡N), 1668 (C=O) and 1634; δ_H 2.26 (3 H, s, CH_3), 3.73 (3 H, s, OCH_3), 7.22 (1 H, d, *J* 1.2, 7.8, ArH), 7.30 (1 H, dt, *J* 1.2, 7.8, ArH), 7.54 (1 H, dt, *J* 1.2, 7.8, ArH), 7.72 (1 H, dd, *J* 1.2, 7.8, ArH), 8.31 (1 exchangeable H, s, =NH), 9.04 (1 exchangeable H, s, NH) and 9.18 (1 exchangeable H, s, NH); δ_C 14.9 (CH_3), 51.2 (OCH_3), 71.3 (C-2), 115.2 (C-8′), 118.2 (C≡N), 119.1 (C-3′), 123.3 (C-4a′), 123.8 (C-6′), 125.7 (C-5′), 131.9 (C-7′), 141.0 (C-4′), 152.5 (C-8a′), 153.1 (C-2′), 166.4 (C-3) and 167.2 (C=O)

The ethyl ester **9**, obtained as colourless *crystals* when the above preparation was carried out in ethanol, had mp 188–190 °C (1.16 g, 78%) (Found: C, 64.45; H, 5.0; N, 13.9. $C_{16}N_{15}N_3O_3$ requires C, 64.6; H, 5.1; N, 14.1%); λ_{max}(MeOH)/nm 204, 278 and 323; ν_{max}/cm^{-1} 3415, 3359, 3296, 3208 (NH, NH_2), 2199 (C≡N), 1688 (C=O) and 1656; δ_H 1.27 (3 H, t, *J* 7.0, OCH_2CH_3), 2.26 (3 H, s, CH_3), 4.19 (2 H, ABqq, *J* 7, 12, OCH_2), 7.21 (1 H, d, *J* 1.2, 7.8, ArH), 7.29 (1 H, t, *J* 1.2, 7.8, ArH), 7.55 (1 H, t, *J* 1.2, 7.8, ArH), 7.72 (1 H, dd, *J* 1.2, 7.8, ArH), 8.30 (1 exchangeable H, s, =NH), 9.02 (1 exchangeable H, br s, NH) and 9.18 (1 exchangeable H, br s, NH); δ_C 14.3 (CH_3), 14.9 (CH_3), 59.8 (OCH_2), 72.0 (C-2), 115.2 (C-8′), 118.2 (C≡N), 119.1 (C-3′), 123.3 (C-4a′), 123.7 (C-6′), 125.7 (C-5′), 131.9 (C-7′), 141.0 (C-4′), 152.4 (C-8a′), 153.1 (C-2′), 167.4 (C-3) and 167.2 (C=O).

Synthesis of 1,3,12-triamino-11-methylidene-11*H*-[1]benzopyrano[2,3-*b*][1,8]naphthyridine-2-carbonitrile 10

A mixture of the imine **2a** (0.92 g, 5 mmol) and 2-aminoprop-1-ene-1,1,3-tricarbonitrile (0.66 g, 5 mmol) in ethanol (50 cm^3) containing piperidine (0.06 cm^3) was heated for 5 min after dissolution and then set aside for 24 h. Evaporation of the mixture under reduced pressure afforded a viscous residue which partly solidified. Trituration with methanol gradually afforded a mustard yellow solid which was filtered off, dried and recrystallised from methanol to give the *product* **10**, mp > 330 °C (1.09 g, 69%) (Found: C, 62.3; H, 3.8; N, 25.2. $C_{17}H_{12}N_6O\cdot 2/3\ H_2O$ requires C, 62.2; H, 4.1; N, 25.6%); λ_{max}(MeOH)/nm 202, 264 and 323; ν_{max}/cm^{-1} 3340br, 3250br (NH_2), 2200 (C≡N) and 1651; δ_H 5.74 (1 H, s, H^a of =CH_2), 6.64 (2 exchangeable H, s, NH_2), 6.91 (2 exchangeable H, s, NH_2), 7.06 (2 exchangeable H, s, NH_2) 7.10 (1 H, s, H^b of =CH_2), 7.13 (1 H, dd, *J* 1.3, 7.8, ArH), 7.31 (1 H, dt, *J* 1.3, 7.8, ArH), 7.33 (1 H, dt, *J* 1.3, 7.8, ArH), 7.78 (1 H, dd, *J* 1.3, 7.8, ArH); δ_C 71.2 (C-2), 95.8 (C-12a), 97.2 (C-11a), 107.7 (=CH_2), 116.4 (C≡N), 116.5 (C-7), 123.6 (C-10a), 123.8 (C-9), 124.1 (C-10), 128.8 (C-8), 129.8 (C-11), 149.3 (C-6a), 156.0 (C-4a), 156.7 (C-12)*, 157.1 (C-5a), 157.7 (C-1)* and 159.5 (C-3)* (*assignments interchangeable).

Synthesis of 5-amino-2-imino-2,4-dihydro[1]benzopyrano-[2,3,4-*de*]quinoline-3,6-dicarbonitrile 12 and 5-amino-2-dicyanomethylidene-11b-methyl-1,2,4,11b-tetrahydro[1]benzopyrano[2,3,4-*de*][1,6]naphthyridine-3,6-dicarbonitrile 14

The compounds **12** and **14** (previously formulated incorrectly as **11** and **13**) were prepared according to the literature method.[4] A solution of 1-(2-hydroxyphenyl)ethanone (5 cm^3) and malononitrile (2.6 g) in ethanol (10 cm^3) containing piperidine (0.12 cm^3) was heated on a boiling water-bath for 5 min. The insoluble light brown solid which separated from the hot solution was the *product* **12** (mp > 330 °C) (dimethylformamide) (Found: C,

Table 1 Crystallographic data for compound **9**

Mol. formula	$C_{16}H_{15}N_3O_3$
M_r	297.31
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 9.915(4) Å
	b = 10.759(5) Å
	c = 14.338(6) Å
	α = 95.37(4)°
	β = 98.49(2)°
	γ = 96.11(2)°
Volume	1494.8(11) Å^3
Z	4
D_c	1.321 g cm^{-3}
Adsorption coefficient	0.094 mm^{-1}
F(000)	624
Crystal size	0.6 × 0.3 × 0.3 mm
θ range	1.44 to 24.98°
Total data measured	4770
Total data unique	4579 [R(int) = 0.0172]
Number of parameters	493
Goodness-of-fit on F^2	1.050
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0558, R_w = 0.1357
R indices (all data)	R_1 = 0.1030, R_w = 0.1619
Largest diff. peak and hole	0.322 and −0.312 e Å^{-3}

68.25; H, 3.0; N, 23.1. Calc. for $C_{17}H_9N_5$: C, 68.2; H, 3.0; N, 23.4%); λ_{max}(MeOH)/nm 202, 226, 264, 294, 305 and 361; ν_{max}/cm^{-1} 3463, 3435, 3363, 3261 (NH_2, NH) 2220, 2212 (C≡N), 1673 and 1651; δ_H 7.12 (1 exchangeable H, br s, NH), 7.12 (1 H, s, ArH), 7.13 (1 exchangeable H, br s, partly concealed, NH), 7.46 (1 H, dt, J 1.3, 7.6, ArH), 7.48 (1 H, dd, J 1.3, 7.6, ArH), 7.62 (1 H, dt, J 1.3, 7.6, ArH), 7.95 (1 H, dd, J 1.3, 7.6, ArH); δ_C 72.6 (C-6), 84.2 (C-11b), 100.9 (C-1), 101.1 (C-3), 114.1 (C≡N), 116.7 (C≡N), 117.7 (C-8), 118.4 (C-11a), 123.8 (C-10), 125.8 (C-11), 130.4 (C-11b), 132.1 (C-9), 150.1 (C-7a), 153.3 (C-3a), 157.4 (C-2), 159.7 (C-5) and 160.4 (C-6a).

The second, more soluble product **14** separated when the filtered reaction mixture was cooled and set aside. Recrystallised (slowly) from dimethyl sulfoxide (instead of nitrobenzene as in the original preparation) as pale yellow crystals, it had mp >330 °C (Found: C, 65.6; H, 3.1; N, 26.6. Calc. for $C_{20}H_{11}N_7O$: C, 65.7; H, 3.0; N, 26.9%); λ_{max}(MeOH)/nm 202, 239 and 318; ν_{max}/cm^{-1} 3420, 3321, 3215 (NH_2, NH), 2214s, 2191 (C≡N) and 1650; δ_H 1.44 (3 H, s, CH_3), 4.05 (3 exchangeable H, br s, NH, NH_2), 7.34 (1 H, dd, J 1.7, 7.5, ArH), 7.44 (1 H, dt, J 1.7, 7.5, ArH), 7.50 (1 H, dt, J 1.7, 7.5, ArH), 7.71 (1 H, d, J 1.7, 7.5, ArH), 7.78 (1 exchangeable H, s, NH); δ_C 30.5 (CH_3), 40.7 (C-11b), 48.5 (C-3), 66.4 (C-1′), 71.2 (C-6), 96.3 (C-11c), 112.7 (C≡N), 115.9 (C≡N), 116.9 (C-8), 118.37 (C≡N), 118.39 (C≡N), 124.5 (C-11a), 126.1 × 2 (C-9, C-11), 129.9 (C-10), 147.2 (C-7a), 148.4 (C-6a), 155.8 (C-3a), 156.6 (C-2) and 158.9 (C-5).

Synthesis of 2-amino-4-imino-6-(4-methyl-2-oxo-2*H*-1-benzopyran-3-yl)-1,4-dihydropyridine-3,5-dicarbonitrile 17

The compound **17** (previously formulated incorrectly as **16**) was prepared according to the literature method.[4] 3-Amino-2-cyano-3-(4-methyl-2-oxo-2*H*-1-benzopyran-3-yl)prop-2-enenitrile **15** (obtained by hydrolysis of the imine **6a**) (0.9 g) was gently heated with malononitrile (0.7 g) and aq. sodium hydroxide (10%, 5 cm^3) for 5 min. The colourless solid product, collected and washed with acetic acid, was the pyridine derivative **17**, mp >330 °C, ν_{max}/cm^{-1} 3442, 3338, 3237 (NH_2, NH), 2219 (C≡N), 1688 (C=O) and 1657; δ_H 2.36 (3 H, s, CH_3), 7.46–7.59 (6 H, m, 2 ArH and 4 NH), 7.75 (1 H, t, J 7.5, ArH), 7.95 (1 H, d, J 7.5, ArH); δ_C 15.7 (CH_3), 71.4 (C-3), 84.0 (C-5), 114.8 (C≡N), 115.5 (C≡N), 116.6 (C-8′), 119.0 (C-3′), 123.7 (C-4a′), 125.0 (C-6′), 126.3 (C-5′), 132.9 (C-7′), 150.4 (C-8a′), 152.3 (C-4′), 158.1 × 2 (C-2, C-6), 161.0 (C=O), 162.2 (C=NH).

Crystal structure determination of 9

Data were collected on an Enraf-Nonius CAD-4 diffractometer (Mo radiation, graphite monochromator, ω-2θ scans) at 20 °C. Crystal data and experimental parameters are summarised in Table 1. The final cell parameters were determined using the Celdim routine. Decay and absorption were minimal and no correction was applied during data processing. The data were reduced to give the number of unique reflections and those with $|F| \geq 4\sigma|F|$ were then used in structure solution and refinement.

The structure was solved by automatic direct methods using SHELXS-86.[7] The hydrogen atoms were treated in two different ways during refinement. All hydrogen atoms except those on the two methyl groups of the esters were located from subsequent difference Fourier maps and refined with individual temperature factors. The hydrogen atoms of the two methyl groups were placed geometrically with temperature factors dependent on the parent carbon atoms. The structure was refined by full-matrix least-squares analysis on F^2 with SHELXL.[8] The non-hydrogen atoms were refined anisotropically and the hydrogen atoms with individual temperature factors, to a final R value of 5.6%.

Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1996, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/2.

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