Convenient Syntheses of Some Substituted 5*H*,11*H*-Pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridines and 7,9-Dioxa-3,4,6-triazabenzo[*de*]naphthacenes

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Benzopyran derivatives possess marked biological properties[1,2], a series of substituted pyridines show acaricidal, insecticidal, and herbicidal activities[3,4,5], and several pyrimidine derivatives are important analgesic and anti-inflammatory agents[6]. Compounds containing a combination of benzopyran and pyridine or benzopyran and pyrimidine units might therefore be expected to possess interesting properties. We investigated the synthesis of fused heterocycles of such types, namely, derivatives of 5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine **(3)** and of 7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene **(4)**.

6-Formyl-7-hydroxy-5-methoxy-2-methylchromone **(1)** was obtained from visnagin, a naturally occurring furobenzopyran, by oxidation (involving cleavage of the furan ring) with potassium dichromate/sulfuric acid[7]. Compound **1** in combination with malononitrile and, in part, other components was used for the syntheses of compounds **2, 3,** and **4** as depicted in the scheme under the conditions described in the experimental procedures.

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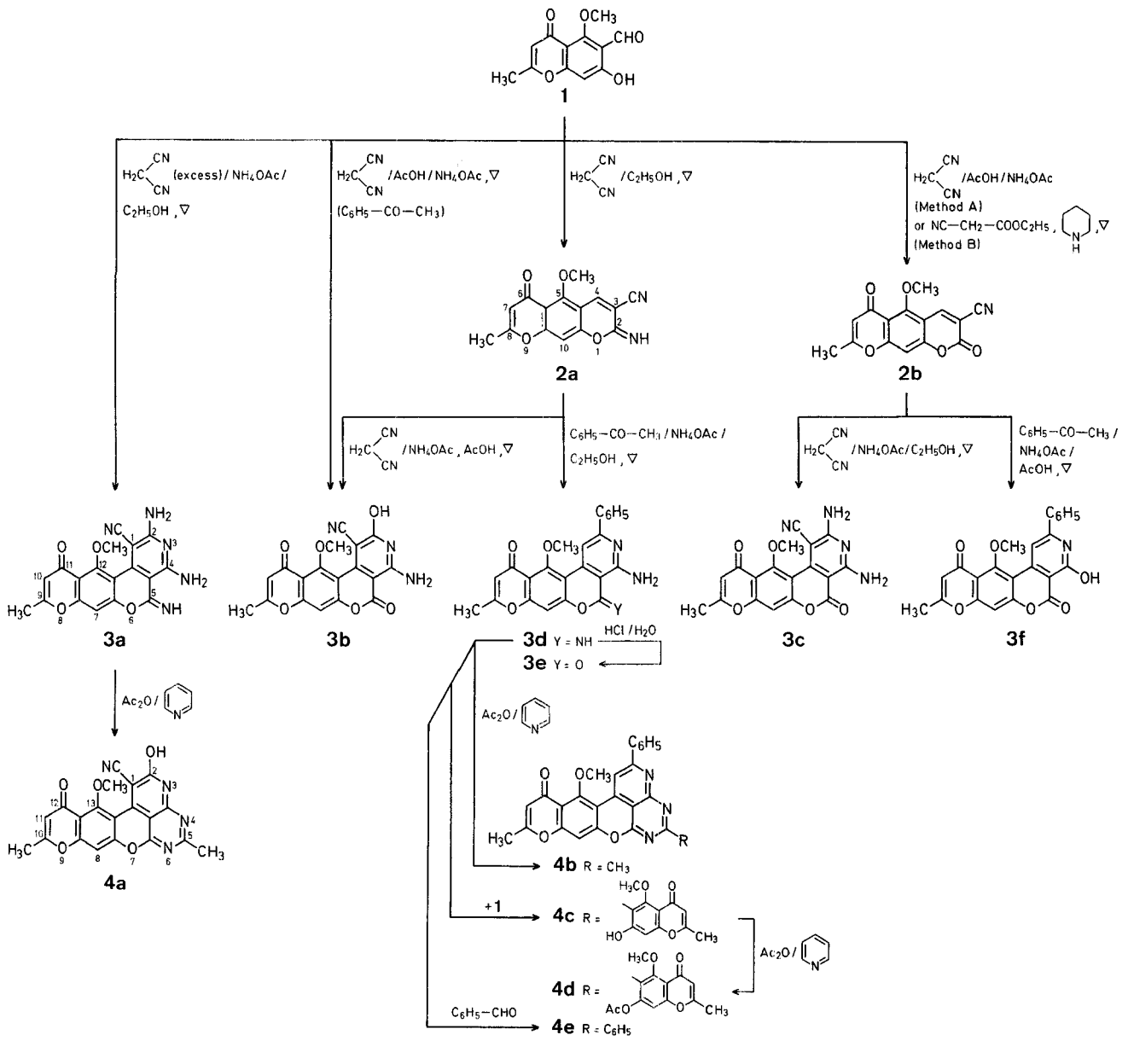

Melting points are uncorrected. The mass spectra were run on a Varian Mat 112 spectrometer. The I.R. spectra were recorded on a Unicam SP 2000 spectrophotometer and the ^{1}H-N.M.R. spectra (at 60 MHz) on a Varian 360 spectrometer.

3-Cyano-2-imino-5-methoxy-8-methyl-6-oxo-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*']dipyran (2a):

To a stirred solution of malononitrile (3.3 g, 0.05 mol) and 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 11.7 g, 0.05 mol) in ethanol (50 ml) is added ammonium acetate (2.31 g, 0.03 mol). The mixture is stirred for 1 h, the precipitated product **2a** then isolated by suction, and recrystallized from ethanol; yield: 11.9 g (85%); yellow crystals, m.p. 217 °C.

$C_{15}H_{10}N_2O_4$	calc.	C 63.82	H 3.55	N 9.92
(282.3)	found	63.68	3.46	9.57

M.S. (70 eV): $m/e = 282$ (M^+).

I.R. (KBr): $\nu = 3260$; 2240; 1665 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): $\delta = 2.35$ (s, 3H); 4.10 (s, 3H); 6.18 (s, 1H); 6.98 (s, 1H); 8.22 ppm (s, 1H).

3-Cyano-2,6-dioxo-5-methoxy-8-methyl-2*H*,6*H*-benzo[1,2-*b*:5,4-*b*']dipyran (2b):

Method A: A mixture of 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 11.7 g, 0.05 mol), malononitrile (3.3 g, 0.05 mol), ammonium acetate (2.3 g, 0.03 mol), and acetic acid (20 ml) is stirred at room temperature for 1 h. The precipitated product is isolated by suction and recrystallized from ethanol to give **2b** as yellow crystals; yield: 11.3 g (80%); m.p. 225 °C.

Method B: A mixture of 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 11.7 g, 0.05 mol), ethyl cyanoacetate (5.6 g, 0.05 mol), piperidine (1 ml), and ethanol (50 ml) is refluxed for 1 h. The resultant precipitate is isolated by suction and recrystallized from ethanol to give **2b** as yellow crystals; yield: 12.0 g (85%); m.p. 225 °C.

$C_{15}H_9NO_5$	calc.	C 63.60	H 3.20	N 4.90
(283.2)	found	63.86	3.28	4.69

I.R. (KBr): $\nu = 2230$; 1715; 1660 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): $\delta = 2.42$ (s, 3H); 4.15 (s, 3H); 6.15 (s, 1H); 7.16 (s, 1H); 8.68 ppm (s, 1H).

1-Cyano-2,4-diamino-12-methoxy-9-methyl-11-oxo-5*H*,11*H*-pyrano[3',2':6,7][1]benzopyrano[3,4-*c*]pyridine (3a):

To a solution of 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 11.7 g, 0.05 mol) and malononitrile (4 g) in ethanol (50 ml) is added ammonium acetate (3 g). The mixture is refluxed for 1 h and then allowed to cool. The crystalline product is isolated by suction and recrystallized from ethanol to give **3a** as yellow crystals; yield: 12.7 g (70%); m.p. 235 °C.

$C_{18}H_{13}N_5O_4$	calc.	C 59.50	H 3.58	N 19.28
(363.3)	found	59.68	3.33	19.47

I.R. (KBr): $\nu = 3350$; 2210; 1660 cm^{-1}.

4-Amino-1-cyano-2-hydroxy-12-methoxy-9-methyl-5,11-dioxo-5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine (3b):

From **2a**: A mixture of malononitrile (4 g), compound **2a** (11.7 g), ammonium acetate (3 g), and acetic acid (20 ml) is heated on a boiling water bath and then allowed to cool. The solid product is isolated by suction and recrystallized from acetic acid to give **3b** as yellow crystals; yield: 11.4 g (75%); m.p. >300 °C.

$C_{18}H_{11}N_3O_6$	calc.	C 59.18	H 3.01	N 11.51
(365.3)	found	58.88	3.14	11.78

I.R. (KBr): ν=3380; 2200; 1740; 1660; 1640 cm^{-1}.

From **1**: A mixture of malononitrile (2 g), 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 7 g, ~0.03 mol), ammonium acetate (3 g), and acetic acid (20 ml) is heated on a boiling water bath for 1 h. The solid product is isolated by suction; yield: 7.6 g (70%); m.p. >300 °C.

2,4-Diamino-1-cyano-12-methoxy-9-methyl-5,11-dioxo-5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine (3c):

From **2b**: A mixture of compound **2b** (6 g, ~0.02 mol), malononitrile (4 g, 0.066 mol), ammonium acetate (3 g, ~0.04 mol), and ethanol (50 ml) is refluxed for 1 h and then allowed to cool. The precipitated product is isolated by suction and recrystallized from methanol to give **3c** as yellow crystals; yield: 6.2 g (80%); m.p. 255 °C.

$C_{18}H_{12}N_4O_5$	calc.	C 59.34	H 3.30	N 15.38
(364.3)	found	58.99	3.55	15.17

I.R. (KBr): ν=2210; 1720; 1660 cm^{-1}.

4-Amino-5-imino-12-methoxy-9-methyl-11-oxo-2-phenyl-5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine (3d):

A mixture of compound **2a** (8 g, ~0.03 mol), acetophenone (6 ml, 0.05 mol), ammonium acetate (5 g, 0.06 mol), and ethanol (50 ml) is refluxed for 1 h and then allowed to cool. The precipitated golden-yellow product **3d** is isolated by suction and recrystallized from ethanol; yield: 7.3 g (65%); m.p. 240 °C.

$C_{23}H_{17}N_3O_4$	calc.	C 69.17	H 4.26	N 10.52
(399.4)	found	69.10	4.60	10.30

M.S. (70 eV): m/e=399 (M^+).

I.R. (KBr): ν=3350; 1660 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ=2.35 (s, 3H); 4.04 (s, 3H); 6.10 (s, 1H); 6.88 (s, 1H); 7.35–7.7 ppm (m, 6H).

The direct conversion **1**→**3d** gives unsatisfactory results. In an attempt, malononitrile (2 g, 0.03 mol), compound **1** (7 g, 0.03 mol), acetophenone (3.2 g, 0.03 mol), and ammonium acetate (3 g) were heated in boiling ethanol for 2 h. The mixture was filtered while hot and the filtrate allowed to cool to give **4c** as yellow crystals which were recrystallized from ethanol; yield: 2.2 g (12%). The residue on the filter from filtration of the reaction mixture was recrystallized from benzene to give **3d**; yield 20%. The substance which was unsoluble in hot benzene was recrystallized from ethanol to give **3a**; yield: 0.9 g (8%).

4-Amino-12-methoxy-5,11-dioxo-2-phenyl-5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine (3e):

To a mixture of compound **3d** (3 g, ~0.08 mol) and ethanol (10 ml) is added hydrochloric acid (3 ml). The mixture is refluxed for 1 h and then allowed to cool. The precipitated product is isolated and recrystallized from acetone to give **3e** as yellow crystals; yield: 1.5 g (50%); m.p. >300 °C.

$C_{23}H_{16}N_2O_5$	calc.	C 69.00	H 4.00	N 7.00
(400.4)	found	69.06	4.31	6.74

I.R. (KBr): ν=1715; 1660 cm^{-1}.

^{1}H-N.M.R. (DMSO-d_6/TMS_{int}): δ=2.45 (s, 3H); 3.96 (s, 3H); 6.15 (s, 1H); 6.72 (s, 1H); 7.3–7.7 ppm (m, 6H).

4-Hydroxy-12-methoxy-9-methyl-5,11-dioxo-2-phenyl-5*H*,11*H*-pyrano[3′,2′:6,7][1]benzopyrano[3,4-*c*]pyridine (3f):

A mixture of compound **2b** (4 g, ~0.015 mol), acetophenone (3 ml, 0.025 mol), ammonium acetate (2.5 g, 0.03 mol), and acetic acid (20 ml) is heated on a boiling water bath for 1 h and then allowed to cool. The precipitated product is isolated by suction and recrystallized from acetic acid to give **3f** as yellow crystals; yield: 3.4 g (60%); m.p. >300 °C.

$C_{23}H_{15}NO_6$	calc.	C 68.83	H 4.74	N 3.49
(401.4)	found	68.95	4.96	3.80

I.R. (KBr): ν=1760; 1660; 1640 cm^{-1}.

1-Cyano-2-hydroxy-13-methoxy-5,10-dimethyl-12-oxo-12*H*-7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene (4a):

A mixture of compound **3a** (5 g, ~0.014 mol), acetic anhydride (10 ml), and pyridine (2 ml) is heated on a boiling water bath for 1 h. The solid product is isolated by suction and washed with ethanol to give **4a** as yellow crystals; yield: 2.67 g (50%); m.p. >300 °C.

$C_{20}H_{12}N_4O_5$	calc.	C 61.85	H 3.09	N 14.43
(388.3)	found	62.03	3.22	14.09

13-Methoxy-5,10-dimethyl-12-oxo-2-phenyl-12*H*-7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene (4b):

Acetic anhydride (6 ml) is added to a solution of compound **3d** (5 g, 0.0125 mol) in pyridine (10 ml) and the mixture is heated on a boiling water bath for 1 h. The deep-orange crystalline product is isolated and recrystallized from acetic acid; yield: 2.9 g (55%); m.p. >300 °C.

$C_{25}H_{17}N_3O_4$	calc.	C 70.92	H 4.02	H 9.93
(423.4)	found	70.81	4.32	9.73

5-(7-Hydroxy-5-methoxy-2-methyl-4-oxo-4*H*-1-benzopyran-6-yl)-13-methoxy-10-methyl-2-phenyl-12-oxo-12*H*-7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene (4c):

A mixture of 6-formyl-7-hydroxy-5-methoxy-2-methylchromone (**1**; 2 g, 8.54 mmol), compound **3d** (3 g, 7.51 mmol), pyridine (2 ml), and acetic anhydride (6 ml) is heated on a boiling water bath for 1 h. The solid product is isolated by suction and recrystallized from chloroform; yield: 2.77 g (60%); m.p. 208–210 °C.

$C_{35}H_{23}O_8$	calc.	C 68.51	H 3.75	N 6.85
(613.6)	found	68.49	3.93	6.59

I.R. (KBr): ν=3400; 1660 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ=2.32 (s, 3H); 2.38 (s, 3H); 4.02 (s, 3H); 4.08 (s, 3H); 6.09 (s, 1H); 6.12 (s, 1H); 7.2, 7.7 ppm (m, 8H).

5-(7-Acetoxy-5-methoxy-2-methyl-4-oxo-4*H*-1-benzopyran-6-yl)-13-methoxy-10-methyl-12-oxo-2-phenyl-12*H*-7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene (4d):

A mixture of compound **4c** (1 g), acetic anhydride (5 ml), and pyridine (2 ml) is heated on the boiling water bath for 1 h. The solid product is isolated by suction and recrystallized from chloroform to give **4d** as yellow crystals; yield: 0.85 g (80%); m.p. >300 °C.

$C_{37}H_{25}N_3O_9$	calc.	C 67.79	H 3.82	N 6.64
(655.6)	found	67.82	4.02	6.59

I.R. (KBr): ν=1780; 1660 cm^{-1}.

13-Methoxy-10-methyl-12-oxo-2,5-diphenyl-12*H*-7,9-dioxa-3,4,6-triazabenzo[*de*]naphthacene (4e):

A mixture of compound **3d** (1 g), benzaldehyde (0.5 ml), ammonium acetate (1 g), and ethanol (50 ml) is heated for 0.5 h. The solid product is isolated by suction and recrystallized from chloroform to give **4e** as yellow crystals; yield: 0.85 g (70%); m.p. 225 °C.

$C_{30}H_{19}N_3O_4$	calc.	C 74.23	H 3.92	N 8.66
(485.5)	found	74.42	4.09	8.51

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