Synthesis of Nitro and Amino *N*-Heterocycles *via* Ring Transformation of 2-Methyl-3-nitrochromone

Kaname Takagi*, Masaaki Tanaka, Yukitoshi Murakami, Kuniyoshi Ogura
Katsuyuki Ishii, Hikari Morita and Tomoji Aotsuka

Central Research Laboratories, Zeria Pharmaceutical Co., Konan-machi,
Osato-gun, Saitama 360-01, Japan

Received January 16, 1987

2-Methyl-3-nitrochromone (**1**) reacted with acid hydrazides, *S*-methylisothiourea, hydroxylamine and ethyl aminoethanoate to give the nitro derivatives of pyrazole **2**, pyrimidine **6**, isoxazole **11** and pyrrole **13**, respectively. These nitro compounds were reduced by catalytic hydrogenation to the corresponding amino derivatives. In the case of **2**, a rearrangement of the acyl group took place during the reduction. Substitution reactions of the 2-methylthio group in **6** were also described.

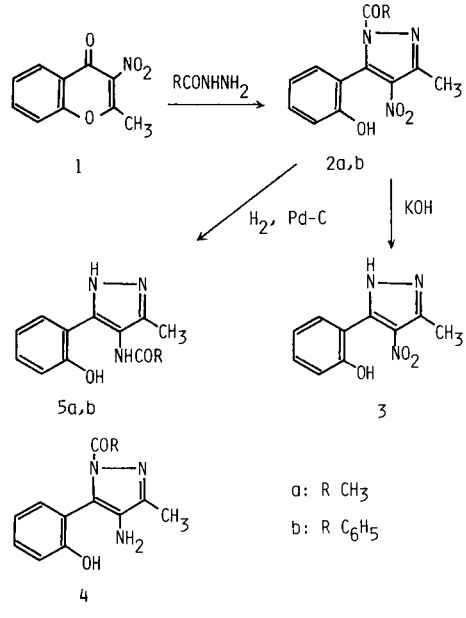
J. Heterocyclic Chem., **24**, 1003 (1987).

Previously, we reported that 2-methyl-3-nitrochromone (**1**) acted as an efficient Michael acceptor at the 2-position for nucleophiles such as hydrazines and amidines to give readily 3(5)-(2-hydroxyphenyl)-4-nitropyrazoles [1] and 4-(2-hydroxyphenyl)-5-nitropyrimidines [2], respectively. These nitro compounds were reduced to the corresponding amino derivatives, some of which exhibited potent analgesic activity and inhibitory effect for platelet aggregation [1]. The above results prompted us to examine reactions of **1** with different bifunctional nitrogen nucleophiles in order to prepare a variety of *N*-heterocyclic compounds. In these reactions, C^2, C^3 and carbonyl-C in **1** served effectively as a source of three carbons for the formation of an *N*-containing aromatic ring. This report describes the synthesis of new nitro and amino derivatives of pyrazole, pyrimidine, isoxazole and pyrrole starting from **1**.

Chromone **1** reacted with acid hydrazides under mild conditions to give pyrazoles. Treatment of **1** with acetic acid hydrazide and benzoic acid hydrazide in ethanol at room temperature for 5 hours gave 1-acetyl and 1-benzoyl-5-(2-hydroxyphenyl)-3-methyl-4-nitropyrazoles **2a,b** in 81 and 94% yields, respectively. The position of *N*-acyl group on the pyrazole ring of **2a,b** could not be distinguished by the spectral data. However, we propose the structures **2a,b** taking into consideration that the terminal amino group of the hydrazides might react at C^2 in **1**. Compounds **2a,b** were readily hydrolyzed in an alkaline solution to 3(5)-(2-hydroxyphenyl)-5(3)-methyl-4-nitropyrazole (**3**) which was previously synthesized from **1** and hydrazine [1] (Scheme 1).

Catalytic hydrogenation of **2a,b** over 5% palladium on charcoal (Pd-C) in ethanol did not give the corresponding 1-acyl-4-aminopyrazoles **4**, but 4-acylamino-3(5)-(2-hydroxyphenyl)-5(3)-methylpyrazoles **5a,b** (Scheme 1) which were formed by migration of the acyl group during the reduction. The structures of **5a,b** were determined on the basis of elemental analysis and spectral data. In particular, ^{1}H-nmr spectra of **5a,b** showed three broad deuterium-exchangeable signals (1H each) at lower magnetic field (see Experimental), and the signal corresponding to NH_2-protons was not observed. These findings indicate that the acyl group in **5a,b** is attached not to the nitrogen atom in the pyrazole ring, but to the amino group at 4-position. In fact, **5a** was identical with 4-acetamido-3(5)-(2-hydroxyphenyl)-5(3)-methylpyrazole synthesized from 3-acetamido-2-methylchromone and hydrazine [1].

Scheme 1



We previously described [2] that the reaction of **1** with thiourea in the presence of an alkali did not give the expected pyrimidinethione derivative because of the decomposition of the starting chromone **1**. However, upon treatment with *S*-methylisothiourea in the presence of triethylamine in hydroalcoholic medium, **1** readily underwent ring transformation to give 4-(2-hydroxyphenyl)-6-methyl-2-methylthio-5-nitropyrimidine (**6**) in 83% yield (Scheme 2). The structural assignment of **6** was based on elemental analysis and spectral data. Compound **6** was hydrolyzed to

Table I

Physical Data for Compounds **8a-j**

Compound No.	Yield %	Mp °C	Molecular Formula	Analyses Calcd. % / Found % C	H	N
8a	95	201-202	$C_{12}H_{12}N_4O_3$ (260.26)	55.38 / 55.12	4.65 / 4.63	21.53 / 21.40
8b	94	134-135	$C_{13}H_{14}N_4O_3$ (274.28)	56.93 / 56.60	5.15 / 5.12	20.43 / 20.53
8c	90	115-116	$C_{17}H_{20}N_4O_3$ (328.37)	62.18 / 61.88	6.14 / 6.10	17.06 / 17.04
8d	93	184-185	$C_{13}H_{14}N_4O_3$ (274.28)	56.93 / 56.71	5.15 / 5.09	20.43 / 20.49
8e	77	108-109	$C_{15}H_{18}N_4O_3$ (302.34)	59.59 / 59.42	6.00 / 6.00	18.53 / 18.40
8f	63	144-145	$C_{15}H_{18}N_4O_5$ (334.33)	53.88 / 53.71	5.43 / 5.46	16.76 / 16.66
8g	91	179-180	$C_{15}H_{16}N_4O_3$ (300.32)	59.99 / 59.80	5.37 / 5.37	18.66 / 18.60
8h	90	152-153	$C_{16}H_{18}N_4O_3$ (314.35)	61.13 / 61.05	5.77 / 5.77	17.83 / 17.77
8i	91	186-187	$C_{15}H_{16}N_4O_4$ (316.32)	56.96 / 56.69	5.10 / 5.11	17.71 / 17.57
8j	90	250-251	$C_{16}H_{19}N_5O_3$ (329.36)	58.35 / 58.01	5.82 / 5.77	21.27 / 21.15

Scheme 2

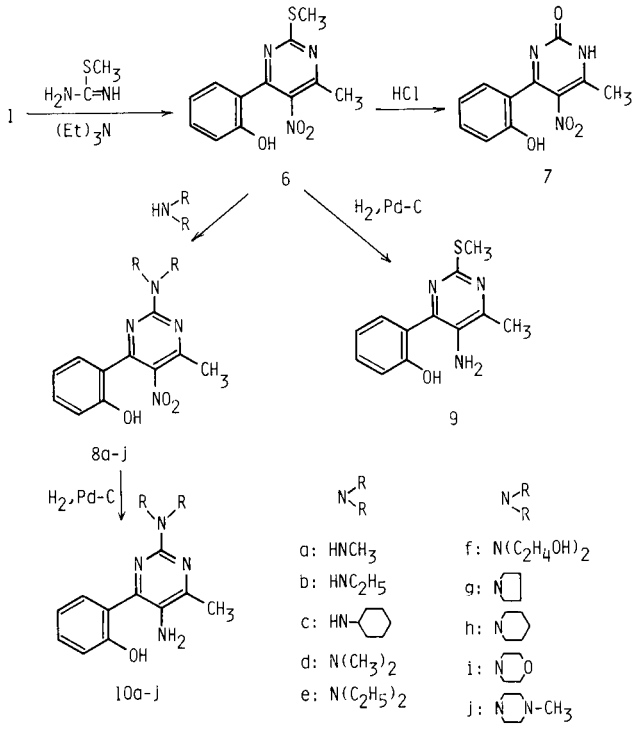


Table II

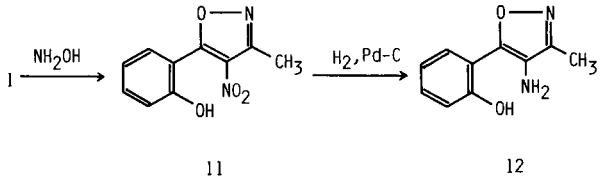
Spectral Data for Compounds **8a-k**

Compound No.	MS m/z M+	MS m/z M+-NO_2	IR (cm^{-1}) KBr NO_2	^{1}H-NMR (ppm) DMSO-d_6
8a	260	214	1550, 1343	2.54 (s, 3H, CH_3), 2.97 (d, J = 5 Hz, 3H, CH_3), 6.82-7.85 (m, 5H, aromatic and NH), 9.8-10.6 (br, 1H, OH)
8b	274	228	1553, 1337	1.25 (t, J = 7 Hz, 3H, CH_3CH_3), 2.47 (s, 3H, CH_3), 3.49 (m, 2H, CH_2CH_3), 5.3-6.1 (br, 1H, NH), 6.76-7.56 (m, 4H, aromatic), 10.9-11.7 (br, 1H, OH)
8c	328	282	1555, 1335	0.83-2.26 (m, 10H, -$(CH_2)_5$-), 2.46 (s, 3H, CH_3), 3.78 (br s, 1H, CH), 5.2-6.0 (br, 1H, NH), 6.71-7.54 (m, 4H, aromatic), 11.1-11.9 (br, 1H, OH)
8d	274	228	1567, 1342	2.54 (s, 3H, CH_3), 3.26 (s, 6H, $N(CH_3)_2$), 6.77-7.56 (m, 4H, aromatic), 9.7-10.5 (br, 1H, OH)
8e	302	256	1556, 1343	1.24 (t, J = 7 Hz, 6H, -$(CH_2CH_3)_2$), 2.48 (s, 3H, CH_3), 3.69 (q, J = 7 Hz, 4H, -$(CH_2CH_3)_2$), 6.73-7.55 (m, 4H, aromatic), 11.2-12.1 (br, 1H, OH)
8f	334	288	1556, 1345	2.52 (s, 3H, CH_3), 3.83 (s, 8H, -$(C_2H_4)_2$-), 4.5-5.2 (br, 2H, 2×OH), 6.80-7.52 (m, 4H, aromatic), 9.4-10.2 (br, 1H, OH)
8g	300	254	1553, 1332	1.91-2.13 (m, 4H, -CH_2CH_2-), 2.48 (s, 3H, CH_3), 3.40-3.81 (m, 4H, $N(CH_2)_2$), 6.70-7.43 (m, 4H, aromatic), 11.6-12.5 (br, 1H, OH)
8h	314	268	1550, 1347	1.68 (s, 6H, -$CH_2CH_2CH_2$-), 2.47 (s, 3H, CH_3), 3.85 (br s, 4H, $N(CH_2)_2$), 6.73-7.56 (m, 4H, aromatic), 9.9-10.7 (br, 1H, OH)
8i	316	270	1552, 1347	2.53 (s, 3H, CH_3), 3.80 (s, 4H, 2 × CH_2), 3.86 (s, 4H, 2 × CH_2), 6.80-7.57 (m, 4H, aromatic), 9.4-10.2 (br, 1H, OH)
8j	329	—	1548, 1344	2.45 (s, 3H, CH_3), 2.55 (s, 3H, CH_3), 2.63-2.87 (m, 4H, 2 × CH_2), 3.91-4.35 (m, 4H, 2 × CH_2), 6.80-7.70 (m, 4H, aromatic), 9.7-10.5 (br, 1H, OH)

4-(2-hydroxyphenyl)-6-methyl-5-nitropyrimidin-2(1*H*)-one (**7**) in 94% yield on heating with aqueous hydrochloric acid in ethanol. The 2-methylthio group in **6** was also reacted with various amines. Heating of **6** with primary and secondary aliphatic amines in water afforded 2-(substitut-

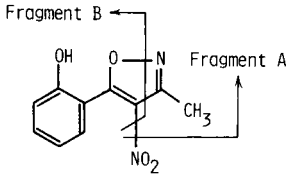
ed amino)-4-(2-hydroxyphenyl)-6-methyl-5-nitropyrimidines **8a-j** in good yields (Scheme 2, Table I and II). The nitropyrimidines **6** and **8a-j** were reduced to the corresponding 5-aminopyrimidines **9** and **10a-j** by catalytic hydrogenation over 5% Pd-C in ethanol.

Scheme 3



11 12

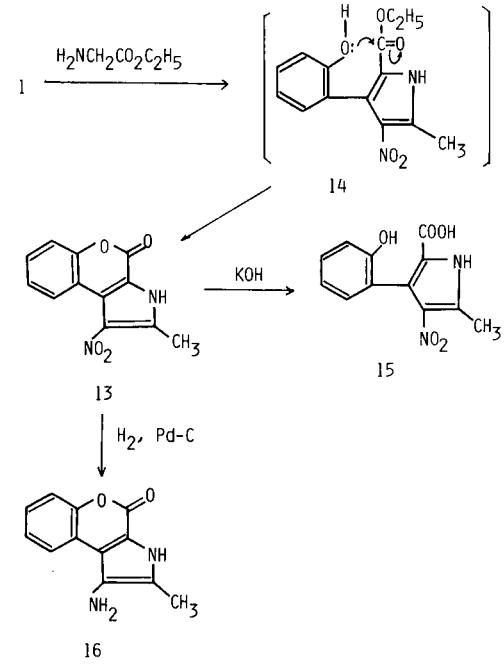
Figure 1



Fragment	m/z	Formula
M^+	220.0482	$C_{10}H_8N_2O_4$
A	174.0580	$C_{10}H_8NO_2$
B	133.0290	$C_8H_5O_2$

It is well known that reaction of alkylchromones with hydroxylamine gave 5-(2-hydroxyphenyl)isoxazoles [3,4]. The nitrochromone **1** also provided 5-(2-hydroxyphenyl)-3-methyl-4-nitroisoxazole (**11**) in 73% yield on heating with hydroxylamine liberated from its hydrochloride in ethanol (Scheme 3). The analytical and spectral data of **11** were consistent with the proposed structure. The high resolu-

Scheme 4



14 13 15 16

Table III

Physical and Spectral Data for Compounds **10a-j**

Compound No	Yield %	Mp °C	Molecular Formula	Analysis Calcd. % / Found % C	H	N	MS m/z M^+	IR (cm^{-1}) KBr
10a	41	159-160	$C_{12}H_{14}N_4O$ (230.27)	62.59 62.57	6.13 6.13	24.33 24.37	230	3390, 3260, 1600
10b	42	88-89	$C_{13}H_{16}N_4O$ (244.30)	63.91 63.89	6.60 6.63	22.94 23.18	244	3420, 3300, 1590
10c	67	138-140	$C_{17}H_{22}N_4O$ (298.39)	68.43 68.33	7.43 7.45	18.78 18.76	298	3410, 3360, 3330, 1615
10d	56	112-113	$C_{13}H_{16}N_4O$ (244.30)	63.91 63.70	6.60 6.58	22.94 22.98	244	3450, 3440, 1612, 1585
10e	49	120-121	$C_{15}H_{20}N_4O$ (272.35)	66.15 66.02	7.40 7.40	20.57 20.55	272	3420, 3350, 1625, 1590
10f	34	64-66	$C_{15}H_{20}N_4O_3$ (304.35)	59.19 58.88	6.62 6.65	18.41 18.24	304	3470, 3310, 3250, 1609
10g	55	191-192	$C_{15}H_{18}N_4O$ (270.34)	66.66 66.46	6.71 6.68	20.73 20.74	270	3400, 3330, 1613, 1590
10h	80	190-191	$C_{16}H_{20}N_4O$ (284.36)	67.58 67.40	7.09 7.05	19.71 19.70	284	3400, 3315, 1609, 1582
10i	69	146-147	$C_{15}H_{18}N_4O_2$ (286.34)	62.93 62.62	6.34 6.30	19.57 19.54	286	3400, 3330, 1613, 1590
10j	52	134-135	$C_{16}H_{21}N_5O$ (299.38)	64.19 64.37	7.07 7.11	23.40 23.58	299	3390, 3260, 1609, 1580

tion mass analysis of **11** assured the orientation of N-O bond in the isoxazole ring as shown in Figure 1. The compound **11** was converted to the 4-amino derivative **12** by catalytic hydrogenation.

Reaction of **1** with ethyl aminoethanoate in the presence of sodium ethoxide in boiling ethanol afforded 2-methyl-1-nitropyrrolo[2,3-*c*][1]benzopyran-4-one (**13**) [5] which was presumably formed *via* the intermediate phenolic ester **14** (Scheme 4). A similar attempt to condense **1** with aminoacetonitrile under the same conditions provided many unidentified product. The lactone structure of **13** was supported by elemental analysis, spectral data and its ring opening reaction to 3-(2-hydroxyphenyl)-5-methyl-4-nitropyrrole-2-carboxylic acid (**15**) in an aqueous sodium hydroxide solution. Reduction of **13** by catalytic hydrogenation over 5% Pd-C gave the corresponding amino derivative **16**.

EXPERIMENTAL

Melting points were determined using a Yanagimoto micro melting point apparatus and are uncorrected. Analyses were done by Perkin-Elmer Model 240B elemental analyser. Nuclear magnetic resonance (^{1}H-nmr) spectra were measured with a JNMPMX 60 spectrometer (JEOL) with tetramethylsilane as an internal standard. Mass spectra (ms) were taken on a JMS-DX 300 spectrometer (JEOL). Infrared (ir) spectra were recorded from potassium bromide discs on a JASCO A-102 spectrophotometer.

1-Acyl-5-(2-hydroxyphenyl)-3-methyl-4-nitropyrazoles **2a,b**.

A mixture of **1** (2.1 g, 10 mmoles) and acetic acid hydrazide or benzoic acid hydrazide (11 mmoles) in ethanol (40 ml) was stirred at room temperature for 5 hours. After removal of the solvent under reduced pressure, the residue was treated with water to give a crystalline solid which was collected and recrystallized from benzene/*n*-hexane (**2a**) or ethanol/water (**2b**).

Compound **2a** was obtained in 80% yield (2.1 g) mp 109-111°; ir: ν cm^{-1} 1765, 1360, ^{1}H-nmr (deuteriochloroform): δ 2.06 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 7.13-7.77 (m, 4H, aromatic), 11.9-13.0 (br, 1H, OH); ms: m/z 261 (M^+).

Anal. Calcd. for $C_{12}H_{11}N_3O_4$: C, 55.17; H, 4.24; N, 16.09. Found: C, 54.95; H, 4.20; N, 16.08.

Compound **2b** was obtained in 93% yield (3.0 g) mp 156-157°; ir: ν cm^{-1} 1710, 1360, ^{1}H-nmr (deuteriochloroform): δ 2.07 (s, 3H, CH_3), 7.19-8.07 (m, 9H, aromatic), 11.3-13.7 (br, 1H, OH); ms: m/z 323 (M^+).

Anal. Calcd. for $C_{17}H_{13}N_3O_4$: C, 63.15; H, 4.05; N, 13.00. Found: C, 63.13; H, 4.07; N, 12.90.

Hydrolysis of **2a,b** to 3(5)-(2-Hydroxyphenyl)-5(3)-methyl-4-nitropyrazole (**3**).

A solution of **2a,b** (1 mmole) and potassium hydroxide (0.4 g, 7 mmoles) in water (10 ml) was heated on a water bath for 20 minutes and then acidified by addition of 10% hydrochloric acid with cooling. The precipitates were collected by filtration and washed with 5% sodium bicarbonate solution and water. Recrystallization from ethanol/water gave **3** (0.18 g, 82% from **2a**; 0.17 g, 78% from **2b**), mp 201-202°. The ir spectra and melting points of these samples coincided with those of an authentic sample [1].

4-Acylamino-3(5)-(2-hydroxyphenyl)-5(3)-methylpyrazoles **5a,b**.

A solution of **2a,b** (5 mmoles) in ethanol (50 ml) was stirred under a hydrogen atmosphere over 5% Pd-C (0.3 g) at room temperature. The catalyst was removed by filtration and the filtrate was concentrated under reduced pressure. The residual oily product was triturated in benzene/*n*-hexane (1:1, v/v) to give a crystalline solid which was recrystallized from benzene/ethanol.

Compound **5a** was obtained in 52% yield (0.6 g) mp 164-165°; ir: ν cm^{-1} 3340, 3230, 1642; ^{1}H-nmr (DMSO-d_6): δ 2.05 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 6.69-7.87 (m, 4H, aromatic), 9.21 (br s, 1H, NH), 10.9-11.7 (br, 1H, CONH), 12.6-13.4 (br, 1H, OH); ms: m/z 231 (M^+). The ir spectrum and melting point of this compound coincided with those of an authentic sample [1].

Compound **5b** was obtained in 65% yield (0.95 g) mp 261-262°; ir: ν cm^{-1} 3400, 3270, 1640; ^{1}H-nmr (DMSO-d_6): δ 2.20 (s, 3H, CH_3), 6.59-8.30 (m, 9H, aromatic), 9.75 (br s, 1H, NH), 10.8-11.6 (br, 1H, CONH), 12.8-13.4 (br, 1H, OH); ms: m/z 293 (M^+).

Anal. Calcd. for $C_{17}H_{15}N_3O_2$: C, 69.69; H, 5.16; N, 14.34. Found: C, 69.81; H, 5.03; N, 14.56.

4-(2-Hydroxyphenyl)-6-methyl-2-methylthio-5-nitropyrimidine (**6**).

A mixture of **1** (2.1 g, 10 mmoles), *S*-methylisothiourea sulfate (2.8 g, 20 mmoles) and triethylamine (3.0 g, 30 mmoles) in ethanol/water (1:3, v/v, 80 ml) was heated at 60° for 30 minutes with stirring. The reaction mixture was concentrated under reduced pressure and the precipitates separated were collected, washed with water and recrystallized from ethanol/water to yield **6** (2.3 g, 83%) as yellow leaflets, mp 159-160°; ir: ν cm^{-1} 1609, 1528, 1353; ^{1}H-nmr (deuteriochloroform): δ 2.59 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 6.79-7.59 (m, 4H, aromatic), 10.7-11.2 (br, 1H, OH); ms: m/z 277 (M^+), 231 (M^+-NO_2).

Anal. Calcd. for $C_{12}H_{11}N_3O_3S$: C, 51.98; H, 4.00; N, 15.15. Found: C, 51.91; H, 3.99; N, 15.20.

4-(2-Hydroxyphenyl)-6-methyl-5-nitropyrimidin-2(1*H*)-one (**7**).

A solution of **6** (1.4 g, 5 mmoles) and concentrated hydrochloric acid (20 ml) in ethanol (20 ml) was refluxed for 6 hours. The reaction mixture was concentrated to a half volume and neutralized by addition of sodium bicarbonate with cooling. The precipitates were collected, washed with water and recrystallized from dimethylformamide/water to yield **7** (1.1 g, 89%) as orange prisms, mp 262-263°; ir: ν cm^{-1} 1656, 1593, 1523; ^{1}H-nmr (DMSO-d_6): δ 2.57 (s, 3H, CH_3), 6.78-7.63 (m, 4H, aromatic); the signals of NH and OH were not observed clearly; ms: m/z 247 (M^+), 201 (M^+-NO_2).

Anal. Calcd. for $C_{11}H_9N_3O_4$: C, 53.44; H, 3.67; N, 17.00. Found: C, 53.26; H, 3.55; N, 17.34.

2-(Substituted amino)-4-(2-hydroxyphenyl)-6-methyl-5-nitropyrimidines **8a-j**.

A solution of **6** (1.4 g, 5 mmoles) in 40% aqueous solution (10 ml) of an appropriate aliphatic amine (Scheme 2) was heated under reflux for 2 hours (in the reactions with diethylamine and diethanolamine, the heating was continued for 24 hours to complete the reactions). The reaction mixture was acidified by addition of 10% hydrochloric acid with cooling and the whole was extracted with chloroform. The organic layer was washed with water, dried over anhydrous sodium sulfate and evaporated to give a crystalline solid which was recrystallized from ethanol/water to yield **8a-j** (Table I and II).

Catalytic Hydrogenation of **6** and **8a-j** to the Corresponding 5-Aminopyrimidines **9** and **10a-j**.

A solution of **6** or **8a-j** (3 mmoles) in ethanol (50 ml) was stirred under a hydrogen atmosphere over 5% Pd-C (0.3 g) at room temperature. The catalyst was removed by filtration and the filtrate was concentrated under reduced pressure to give a residue which was recrystallized from ethanol/water to yield **9** or **10a-j**.

Compound **9** was obtained in 61% yield (0.45 g) mp 164-165°; ir: ν cm^{-1} 3410, 3340; ^{1}H-nmr (DMSO-d_6): δ 2.47 (s, 3H, CH_3), 2.57 (s, 3H, CH_3), 3.6-4.2 (br, 2H, NH_2), 6.83-8.00 (m, 4H, aromatic), 11.20 (br s, 1H, OH); ms: m/z 247 (M^+).

Anal. Calcd. for $C_{12}H_{13}N_3OS$: C, 58.28; H, 5.30; N, 16.99. Found: C, 58.21; H, 5.16; N, 17.25.

The data for **10a-j** are given in Table III.

5-(2-Hydroxyphenyl)-3-methyl-4-nitroisoxazole (**11**).

Hydroxylamine hydrochloride (0.84 g, 12 mmoles) was added to an ethanolic potassium hydroxide solution (0.6 g of potassium hydroxide in 40 ml of ethanol) and the mixture was stirred at room temperature for 20 minutes. Chromone **1** (2.1 g, 10 mmoles) was then added and the mixture was refluxed for 24 hours. After removal of the solvent, the residue was treated with water to give a crystalline solid which was recrystallized from ethanol/water to yield **11** (1.6 g, 73%), mp 202-204°; ^{1}H-nmr (DMSO-d_6): δ 2.53 (s, 3H, CH_3), 6.74-7.73 (m, 4H, aromatic), 10.62 (br s, 1H, OH); ms: m/z 220 (M^+), 174 (M^+-NO_2), 133 (M^+-NO_2 and CH_3CN).

Anal. Calcd. for $C_{10}H_8N_2O_4$: C, 54.55; H, 3.66; N, 12.72. Found: C, 54.44; H, 3.65; N, 12.77.

4-Amino-5-(2-hydroxyphenyl)-3-methylisoxazole (**12**).

A mixture of **11** (2.2 g, 10 mmoles) and 5% Pd-C (0.6 g) in ethanol (100 ml) containing concentrated hydrochloric acid (2 ml) was treated under a hydrogen atmosphere in the same manner as described for the preparation of **10a-j**. The crude reduction product was recrystallized from ethanol/ether to give **12** as the monohydrochloride (1.1 g, 49%), mp 150-152°; ^{1}H-nmr (DMSO-d_6): δ 2.42 (s, 3H, CH_3), 6.80-7.79 (m, 4H, aromatic), 8.0-9.7 (br, 4H, N^+H_3 and OH); ms: m/z 190 (M^+), 149 (M^+-CH_3CN), 121 (M^+-CH_3CN and CNH_2).

Anal. Calcd. for $C_{10}H_{10}N_2O_2$·HCl: C, 52.99; H, 4.89; N, 12.36. Found: C, 52.87; H, 5.01; N, 12.48.

2-Methyl-1-nitropyrrolo[2,3-*c*][1]benzopyran-4-one (**13**).

A mixture of **1** (2.1 g, 10 mmoles) and ethyl aminoethanoate hydrochloride (2.1 g, 15 mmoles) in an ethanolic sodium ethoxide solution (0.7 g of sodium in 50 ml of anhydrous ethanol) was refluxed for 5 hours. After evaporation of the solvent under reduced pressure, the residue was dissolved in water and the solution was acidified with 10% hydrochloric acid. The precipitates were collected, washed with water and recrystallized from ethanol/chloroform to give **13** (0.81 g, 33%), mp 305-307°; ir: ν cm^{-1} 3200, 1690, 1560, 1350; ^{1}H-nmr (DMSO-d_6): δ 2.68 (s, 3H, CH_3), 7.11-8.63 (m, 4H, aromatic), 13.2-14.0 (br, 1H, NH); ms: m/z 244 (M^+), 197 (M^+-NO_2 and H).

Anal. Calcd. for $C_{12}H_8N_2O_4$: C, 59.07; H, 3.30; N, 11.48. Found: C, 58.71; H, 3.15; N, 11.61.

3-(2-Hydroxyphenyl)-5-methyl-4-nitropyrrole-2-carboxylic Acid (**15**).

A suspension of **13** (0.24 g, 1 mmole) in 5% sodium hydroxide solution (15 ml) was heated on a water-bath for 2 hours. After cooling, the reaction mixture was acidified by addition of concentrated hydrochloric acid and the precipitates were collected, washed with cold water and recrystallized from water to yield **15** (0.19 g, 73%), mp > 300°; ir: ν cm^{-1} 3380, 1680, 1370; ^{1}H-nmr (DMSO-d_6): δ 2.65 (s, 3H, CH_3), 6.67-7.40 (m, 4H, aromatic), 8.6-9.7 (br, 1H, NH), 12.63 (br s, 2H, 2 × OH); ms: m/z 262 (M^+).

Anal. Calcd. for $C_{12}H_{10}N_2O_5$: C, 54.97; H, 3.84; N, 10.68. Found: C, 54.76; H, 3.68; N, 10.68.

1-Amino-2-methylpyrrolo[2,3-*c*][1]benzopyran-4-one (**16**).

A mixture of **13** (0.5 g, 2 mmoles) and 5% Pd-C (0.2 g) in ethanol (100 ml) was treated under a hydrogen atmosphere in the same manner as described for the preparation of **10a-j**. Recrystallization from ethanol gave **16** (0.19 g, 44%), mp 259-261°; ir: ν cm^{-1} 3390, 3340, 3200, 1690; ^{1}H-nmr (DMSO-d_6): δ 2.30 (s, 3H, CH_3) 4.16 (s, 2H, NH_2), 7.11-8.50 (m, 4H, aromatic), 11.7-12.2 (br, 1H, NH); ms: m/z 214 (M^+).

Anal. Calcd. for $C_{12}H_{10}N_2O_2$: C, 67.28; H, 4.71; N, 13.08. Found: C, 67.39; H, 4.68; N, 12.86.

REFERENCES AND NOTES

[1] K. Takagi, M. Tanaka, Y. Murakami, H. Morita and T. Aotsuka, *Eur. J. Med. Chem.*, **21**, 65 (1986).

[2] M. Tanaka, Y. Murakami, H. Morita and K. Takagi, *Chem. Pharm. Bull.*, **33**, 2129 (1985).

[3] G. P. Ellis, ed, "Chromenes, Chromanones and Chromones", John Wiley and Sons, Inc, New York, London, Sydney and Toronto, 1977, pp 599-600.

[4] Recently, it was reported that the reaction of chromone with hydroxylamine in an alkaline solution gave several products, mainly ring-opened oxime and isoxazole derivatives: V. Szabó, J. Borbély, E. Theisz, J. Borda and G. Janzsó, *Tetrahedron*, **40**, 413 (1984), and references cited therein.

[5] An analogous result was reported in the reaction of 3-nitrochromone with ethyl aminoethanoate: G. Haas, J. L. Stanton and T. Winkler, *J. Heterocyclic Chem.*, **18**, 619 (1981).