

SYNTHESIS OF 5-OXO-5H-[1]BENZOPYRANO[4,3-b]PYRIDINE DERIVATIVES

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Abstract — 5-Oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxamides (2) were synthesized by the reaction of 4-oxo-4H-1-benzopyran-3-carbonitriles (1) with malonamide in the presence of sodium methoxide. Compounds (2) were also converted into carboxylic acids and tetrazole derivatives. The structures of 2 and their derivatives were confirmed by IR and NMR spectra and by X-ray crystallographic analysis.

The discovery that disodium cromoglycate possesses prophylactic properties for bronchial asthma, prompted many laboratories to search for similar antiallergic compounds including chromones, xanthenes, quinolones and many related ring systems¹.

Recently, we reported the synthesis and antiallergic activity of 5-oxo-5H-[1]benzopyrano[2,3-b]pyridines². In the course of the synthetic studies on these compounds, we found compounds possessing a ring system, 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine^{3,4} by reacting 4-oxo-4H-1-benzopyran-3-carbonitriles (1) with malonamide. There are reports that the reaction of 1 with some active methylene compounds affords 5-oxo-5H-[1]benzopyrano[2,3-b]pyridines⁵. However, there is no report on the synthesis of 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine derivatives by the reaction of 1 with malonamide.

We now report the preparation of these derivatives and the confirmation of their structures.

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Preparation of the 2-hydroxy-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxamides

When 6-isopropyl-4-oxo-4H-1-benzopyran-3-carbonitrile (1c) was reacted with malonamide in the presence of sodium methoxide in methanol under reflux, 2-hydroxy-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxamide (2c)⁺ was produced in 66% yield but an expected product, 2-hydroxy-7-isopropyl-5-oxo-5H-[1]benzo-pyrano[2,3-b]pyridine-3-carboxamide (3), was not obtained.

Similarly, the reaction of 1a,b,d with malonamide afforded 2a^{4a}, b,d in 56-76% yields (Table I).

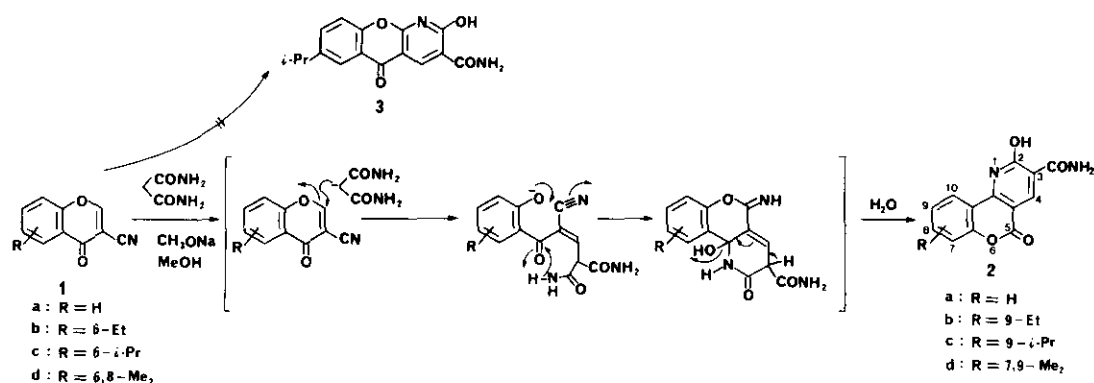


Chart 1

The mechanism of the reaction of 1 with malonamide in the presence of sodium methoxide in methanol, can be depicted as shown in Chart 1: the malonamide undergoes Michael addition to the γ -pyrone system with concomitant opening of the pyrone ring and the amide nitrogen attacks preferentially the carbonyl carbon to form a tricyclic imino intermediate which is subsequently followed by dehydration and hydrolysis to form 2.

On the other hand, when 6-ethyl-4-oxo-4H-1-benzopyran-3-carbonitrile (1b) reacted with malonamide in the presence of piperidine in methanol under reflux, 2,10-diethyl-8,16-dioxo-8H,16H-[1]dibenzopyrano[2,3-b][2,3-f][1,5]diazocine (4) was produced in 80% yield (Chart 2).

⁺The confirmation of structure is described in the following section.

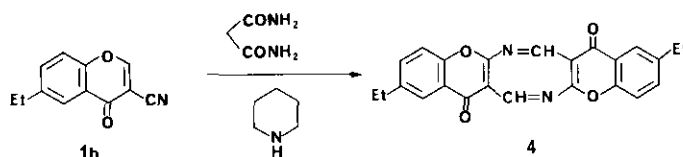


Chart 2

From these facts, the formation of 2 seemed to be a specific reaction due to malonamide in the presence of a strong base such as sodium methoxide.

Synthesis of 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine derivatives

To ascertain whether or not 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine derivatives possess antiallergic activity, we attempted to convert 2 into carboxylic acids and tetrazol derivatives.

Hydrolysis of 2c with 50% H_2SO_4 -AcOH gave 9-isopropyl-2-hydroxy-5-oxo-5H-[1]-benzopyrano[4,3-b]pyridine-3-carboxylic acid (5c) in 68% yield. Similarly, hydrolysis of 2a,b,d gave corresponding hydroxy acids (5a^{4a},b,d) in 74-77% yields. Further 5b was converted to the ethyl 2-chloro-9-ethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylate (6) in 54% yield by treatment with $POCl_3$ - PCl_5 and then with ethanol.

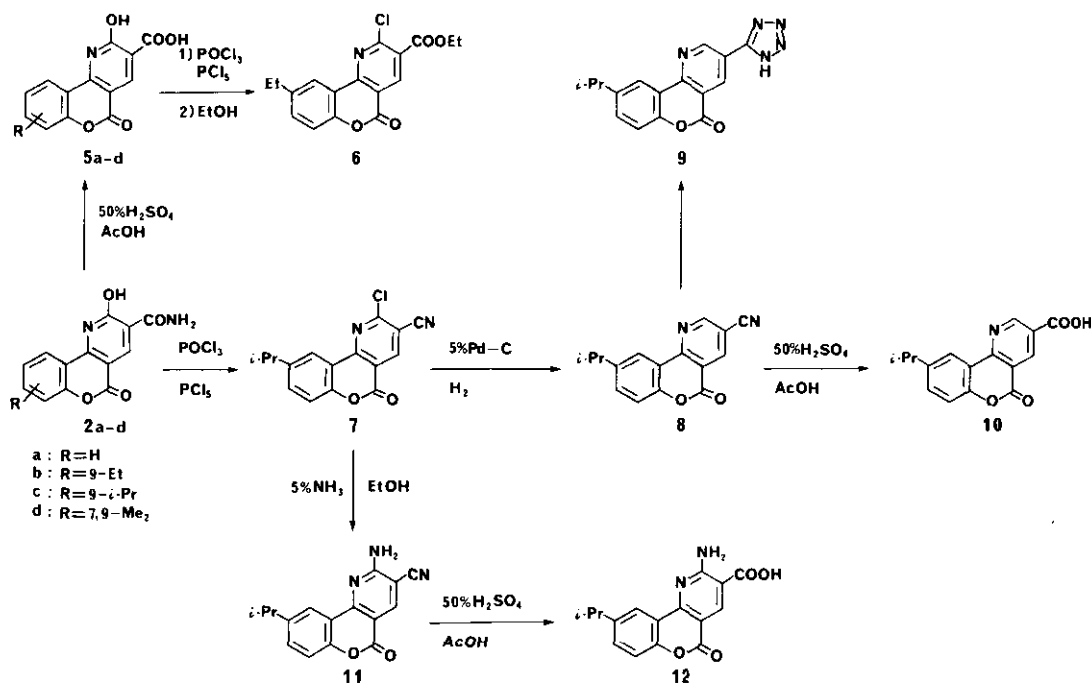


Chart 3

The compound (2c) was converted to 2-chloro-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (7) by treatment with $\text{POCl}_3\text{-PCl}_5$ at 120°C in 31% yield. Catalytic hydrogenation of 7 over 5% Pd-C in the presence of K_2CO_3 gave 9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (8) in 84% yield. By reacting 8 with $\text{NH}_4\text{Cl-NaN}_3$ in DMF 9-isopropyl-3-(1H-tetrazol-5-yl)-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine (9) was synthesized in 71% yield. Hydrolysis of 8 using 50% $\text{H}_2\text{SO}_4\text{-AcOH}$ afforded 9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic acid (10) in 64% yield. On the other hand, amination of 7 with NH_3/EtOH at 30°C gave 2-amino-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (11) in 94% yield. Hydrolysis of 11 using 50% $\text{H}_2\text{SO}_4\text{-AcOH}$ gave 2-amino-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic acid (12) in 57% yield (Chart 3).

The compound 5, 9, 10 and 12 exhibited antiallergic activity in a reaginic PCA test in rats³.

Confirmation of 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine skeleton.

To clarify the structures of 2 and their derivatives that possess the skeleton of 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine, we initially compared 6 derived from 2b with its structural isomer, ethyl 2-chloro-7-ethyl-5-oxo-5H-[1]benzopyrano[2,3-b]pyridine-3-carboxylate (14), which was synthesized by the reaction of ethyl 7-ethyl-2-hydroxy-5-oxo-5H-[1]benzopyrano[2,3-b]pyridine-3-carboxylate (13)^{2b} and $\text{POCl}_3\text{-PCl}_5$ in 66% yield (Chart 4). The IR spectrum of 6 exhibited the presence of lactone carbonyl at 1730 cm^{-1} ; 14 exhibited the presence of γ -pyrone carbonyl at 1660 cm^{-1} .

The ^1H and ^{13}C -NMR spectra of 6 and 14 are shown in Table II. In ^1H -NMR spectra, the chemical shift of C-10 hydrogen of 6 shifted lower field as compared with the C-6 hydrogen of 14. This is attributed to the effect of magnetic environment on the "bay" side⁶ of 6. In the ^{13}C -NMR spectrum, the presence of γ -pyrone carbonyl

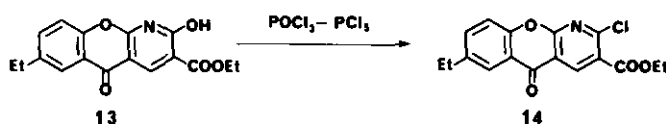
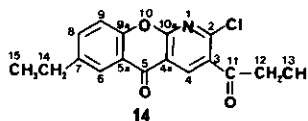
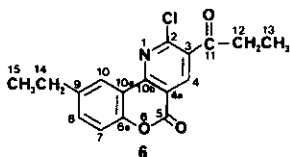


Chart 4

carbon of 14 was observed in 175.6 ppm, whereas the presence of the lactone carbonyl carbon of 6 was observed in 162.7 ppm. These chemical shifts are in agreement with those of xanthone derivatives⁷ and 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine derivatives^{4f}. Therefore these spectral data demonstrate that 6 possesses the 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine skeleton. Furthermore, we carried out X-ray crystallographic analysis of 10 derived from 2c. The crystal for X-ray crystallographic analysis was obtained after recrystallization from aqueous ethanol, and belongs to the orthorhombic space group $P 2_1 2_1 2_1$. The final R value was 0.086 for 628 effective reflections. The crystal data for 10 are shown in Table III.

A computer generated drawing of the structure of 10 is shown in Fig.1. The X-ray crystallographic data showed unambiguously that 10 possesses the skeleton of 5-oxo-5H-[1]benzopyrano[4,3-b]pyridine.

Table II ^1H -NMR and ^{13}C -NMR data for 6 and 14 (CDCl_3 , 100MHz)



Carbon	^{13}C -NMR	Proton	^1H -NMR	Carbon	^{13}C -NMR	Proton	^1H -NMR
C-5	162.7 (s) ^{a)}			C-5	175.6 (s)		
C-11	159.2 (s)			C-10a	*162.5 (s) ^{c)}		
C-6a	*155.6 (s) ^{b)}			C-11	*159.2 (s) ^{c)}		
C-2	*153.2 (s) ^{b)}			C-2	**153.7 (s) ^{d)}		
C-10b	151.4 (s)			C-9a	**153.2 (s) ^{d)}		
C-10a	144.8 (s)			C-7	141.8 (s)		
C-4	142.4 (d)	C ₄ -H	9.13 (1H, s)	C-4	141.6 (d)	C ₄ -H	9.26 (1H, s)
C-9	141.3 (s)			C-8	135.9 (d)	C ₈ -H	7.80 (1H, dd, J=2&8Hz)
C-8	133.5 (d)	C ₈ -H	7.56 (1H, dd, J=2&8Hz)	C-6	124.6 (d)	C ₆ -H	8.23 (1H, d, J=2Hz)
C-3	126.2 (s)			C-3	123.7 (s)		
C-10	123.8 (d)	C ₁₀ -H	8.40 (1H, d, J=2Hz)	C-5a	120.9 (s)		
C-7	116.9 (d)	C ₇ -H	7.36 (1H, d, J=8Hz)	C-9	118.0 (d)	C ₉ -H	7.60 (1H, d, J=8Hz)
C-4a	115.3 (s)			C-4a	114.5 (s)		
C-12	62.3 (t)	C ₁₂ -H	4.53 (2H, q, J=7Hz)	C-12	62.1 (t)	C ₁₂ -H	4.53 (2H, q, J=7Hz)
C-14	28.1 (t)	C ₁₄ -H	2.83 (2H, q, J=7Hz)	C-14	28.0 (t)	C ₁₄ -H	2.85 (2H, q, J=7Hz)
C-15	15.4 (q)	C ₁₅ -H	1.31 (3H, t, J=7Hz)	C-15	15.1 (q)	C ₁₅ -H	1.33 (3H, t, J=7Hz)
C-13	14.0 (q)	C ₁₃ -H	1.45 (3H, t, J=7Hz)	C-13	14.0 (q)	C ₁₃ -H	1.46 (3H, t, J=7Hz)

a) Abbreviations given in parentheses denote signal patterns observed in off-resonance experiments.

b)-d) Assignments may be interchangeable.

Table III. Crystal data for compound(10)

Crystal Data	
Formula	C ₁₆ H ₁₃ NO ₄
Formula Weight	283.3
Crystal System	Orthorhombic
Cell Dimension	a=13.067(2) Å
	b=14.825(2) Å
	c=6.879(2) Å
Cell Volume	1850.2(3) Å ³
Number of Formulas in the Unit Cell	4
Calculated Density	1.41 g.cm ⁻³
Space Group	P2 ₁ 2 ₁ 2 ₁

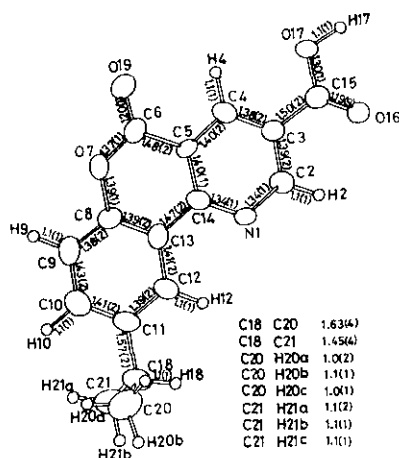


Fig. 1 ORTEP drawing of the structure for 10

Numbering for 10 is tentative.

EXPERIMENTAL

All melting points were determined on a micro melting point apparatus (Yanagimoto) and are uncorrected. The following instruments were used to obtain physical data : NMR spectra, a Varian T-60 and a Varian XL-100 spectrometer; IR spectra, a Hitachi 215 grating infrared spectrometer. In the NMR spectra, chemical shifts are given on the δ (ppm) scale with tetramethylsilane as an internal standard and coupling constants (J) are given in Hz. The following abbreviations are used: s=singlet, bs=broad singlet, d=doublet, dd=double doublet, t=triplet, q=quartet, m=multiplet.

2-Hydroxy-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxamide (2c);

General Procedure for 2a-d.

A mixture of malonamide (1.02 g), 28% CH₃ONa-MeOH solution (4.0 ml) and methanol (30 ml) was heated at 40°C for 10 min. To the solution, 1c (0.213 g) was added and the mixture was heated under reflux for 30 min. The deposited crystals were

collected and washed with methanol to afford yellow crystals. Recrystallization from acetic acid gave yellow prisms(2c), mp >300°C, Yield 0.31 g (66%). IR $\nu_{\text{max}}^{\text{nujol}}$ cm^{-1} : 3320, 3150, 1730, 1665. NMR(DMSO- d_6) δ : 1.33(6H, d, J=7 Hz), 3.10(1H, quintet, J=7 Hz), 7.56(1H, d, J=8 Hz), 7.86(1H, dd, J=8 & 2 Hz), 8.05, 8.95(2x1H, br), 8.75(1H, d, J=2 Hz) 9.03(1H, s).

9-Hydrogen(2a), 9-ethyl(2b), and 7,9-dimethyl(2d) were prepared employing the same procedure. Yield and mp are listed in Table I.

2,10-Diethyl-8,16-dioxo-8H,16H-[1]dibenzopyrano[2,3-b][2,3-f][1,5]diazocine(4).

A mixture of 1b (0.199 g), malonamide (0.130 g), piperidine (0.2 ml), and ethanol (30 ml) was refluxed for 30 min. The deposited crystals were filtered and washed with ethanol to afford yellow crystals. Recrystallization from DMF gave yellow needles (4), mp 279-280°C, Yield 0.32 g (80 %). Anal. Calcd. for $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}_4$: C, 71.98; H, 5.03; N, 7.00. Found: C, 72.15; H, 5.22; N, 7.24. IR $\nu_{\text{max}}^{\text{nujol}}$ cm^{-1} : 1665, 1655, 1615. NMR(CF_3COOD) δ : 1.43 (6H, t, J=7 Hz), 3.00(4H, q, J=7 Hz), 7.86(2H, d, J=8 Hz), 8.10(2H, dd, J=8 & 2 Hz), 8.31(2H, d, J=2 Hz), 9.98, 10.03(2x1H, s).

2-Hydroxy-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic Acid(5c). General Procedure for 5a-d.

A mixture of 2c (0.15 g) and 50% H_2SO_4 -AcOH (1:1) solution (7 ml) was heated with stirring at 120°C for 6 h. The reaction mixture was diluted with water and the deposited white solids were collected. Recrystallization from acetic acid gave colorless prisms(5c), mp 294-296°C, yield 0.102 g (68 %). IR $\nu_{\text{max}}^{\text{nujol}}$ cm^{-1} : 1735, 1710, 1620. NMR(DMSO- d_6) δ : 1.30(6H, d, J=7 Hz), 3.06 (1H, quintet, J=7 Hz), 7.50(1H, d, J=8 Hz), 7.83(1H, dd, J=8 & 2 Hz), 8.66 (1H, d, J=2 Hz), 8.80 (1H, s). 9-Hydrogen(5a), 9-ethyl(5b) and 7,9-dimethyl compound(5d) were prepared employing the same procedure. Yield and mp are listed in Table I.

Table I. 2-Hydroxy-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxamides (2) and 2-hydroxy-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic acids (5)

Compd.	mp (°C)	Re- crystn. solvent	Yield (%)	Formula	Analysis (%)					
					Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
2a	> 300	AcOH	68	C ₁₃ H ₈ N ₂ O ₄	60.94	3.15	10.93	60.62	3.47	11.05
2b	> 300	AcOH	76	C ₁₅ H ₁₂ N ₂ O ₄	63.38	4.26	9.86	63.27	4.40	9.71
2c	> 300	AcOH	66	C ₁₆ H ₁₄ N ₂ O ₄	64.42	4.73	9.39	64.26	4.65	9.29
2d	> 300	AcOH	56	C ₁₅ H ₁₂ N ₂ O ₄	63.38	4.26	9.86	63.33	4.35	9.68
5a	> 300	AcOH	75	C ₁₃ H ₇ NO ₅	60.71	2.74	5.45	60.42	2.66	5.75
5b	> 300	AcOH	74	C ₁₅ H ₁₁ NO ₅	63.16	3.89	4.91	63.11	3.85	5.16
5c	294-296	AcOH	68	C ₁₆ H ₁₃ NO ₅	64.21	4.38	4.68	63.85	4.45	4.46
5d	> 300	DMF	77	C ₁₅ H ₁₁ NO ₅	63.16	3.89	4.91	62.87	3.90	5.29

Ethyl 2-Chloro-9-ethyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylate (6)

A mixture of 5b (0.27 g), PCl₅ (0.15 g) and POCl₃ (10 ml) was heated with stirring at 110°C for 16 h. After POCl₃ was removed in vacuo, the residue was dissolved in ethanol (3 ml) and heated at 60°C for 10 min. The precipitated colorless solid was filtered and purified by chromatography on silica gel (25 g). From the fraction eluted with CHCl₃ a white solid was obtained, which was recrystallized from isopropyl ether-CHCl₃ to give colorless needles (6), mp 136-138°C, yield 0.170 g (54 %). Anal. Calcd. for C₁₇H₁₄ClNO₄: C, 61.54; H, 4.25; N, 4.22. Found: C, 61.25; H, 4.15; N, 4.56. IR $\nu_{\text{max}}^{\text{nujol}}$ cm⁻¹: 1742, 1730. NMR data were shown in Table II.

2-Chloro-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (7)

A mixture of 2c (1.5 g), PCl₅ (2.3 g) and POCl₃ (30 ml) was heated at 120°C for 17 h. After POCl₃ was removed in vacuo, the residue was extracted with CHCl₃. The CHCl₃ layer was washed well with H₂O and dried over Na₂SO₄. Evaporation of CHCl₃ gave a residue, which was submitted to chromatography on silica gel (40 g). From the fraction eluted with CHCl₃ a white solid was obtained, which was recrystallized from CH₃CN to give colorless needles (7), mp 175-177°C, yield 0.472 g (31 %). Anal. Calcd. for C₁₆H₁₁ClN₂O₂: C, 64.32; H, 3.71; N, 9.37. Found: C, 64.09; H, 3.53; N, 9.64. IR $\nu_{\text{max}}^{\text{nujol}}$ cm⁻¹: 2220, 1730, 1580. NMR (CDCl₃) δ : 1.36 (6H, d, J=7 Hz), 3.13 (1H, quintet, J=7 Hz), 7.43 (1H, d, J=9 Hz), 7.70 (1H, dd, J=9 & 2 Hz), 8.43 (1H, d, J=2 Hz), 8.96 (1H, s).

9-Isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (8)

A solution of 7 (0.298 g) in THF (30 ml) was hydrogenated with H_2 in the presence of 5 % Pd-C (30 mg) and K_2CO_3 (0.100 g) at room temperature. The catalyst was then filtered and the filtrate was evaporated. The residue was dissolved in $CHCl_3$ and chromatographed on silica gel (30 g). From the fraction eluted with $CHCl_3$ a white solid was obtained, which was recrystallized from isopropyl ether to give colorless needles (8), mp 186-188°C, yield 0.222 g (84 %). Anal. Calcd. for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.58; N, 10.60. Found: C, 72.84; H, 4.43; N, 10.48. IR ν_{max}^{nujol} cm^{-1} : 2220, 1730, 1585. NMR($CDCl_3$) δ : 1.36 (6H, d, J=7 Hz), 3.13 (1H, quintet, J=7 Hz), 7.40 (1H, d, J=8 Hz), 7.66 (1H, dd, J=8 & 2 Hz), 8.53 (1H, d, J=2 Hz), 8.95 (1H, d, J=2 Hz), 9.28 (1H, d, J=2 Hz).

9-Isopropyl-3-(1H-tetrazol-5-yl)-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine (9)

A mixture of 8 (0.150 g), NH_4Cl (0.075 g), NaN_3 (0.075 g), and DMF (15 ml) was heated with stirring at 120°C for 2 h. The reaction mixture was evaporated to dryness. 10% HCl solution was added to the residue and the deposited solid was collected. Recrystallization from ethanol gave colorless prisms (9), mp 236-238°C (dec.). yield 0.123 g (71%). Anal. Calcd. for $C_{16}H_{13}N_5O_2$: C, 62.53; H, 4.26; N, 22.79. Found: C, 62.62; H, 4.38; N, 22.38. IR ν_{max}^{nujol} cm^{-1} : 1730, 1680, 1605. NMR ($DMSO-d_6$) δ : 1.33 (6H, d, J=7 Hz), 3.13 (1H, quintet, J=7 Hz), 7.46 (1H, d, J=8 Hz), 7.73 (1H, dd, J=8 & 2 Hz), 8.46 (1H, d, J=2 Hz), 9.18 (1H, d, J=2 Hz), 9.76 (1H, d, J=2 Hz).

9-Isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic Acid (10)

A mixture of 8 (0.250 g) and 50% H_2SO_4 -AcOH (1:1) solution (10 ml) was heated with stirring at 120°C for 15 h. The reaction mixture was diluted with water and a white solid was obtained. Recrystallization from ethanol gave colorless prisms (10), mp 260-262°C. yield 0.170 g (64%). Anal. Calcd. for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.95. Found: C, 67.59; H, 4.60; N, 5.09. IR ν_{max}^{nujol} cm^{-1} : 1725, 1700. NMR ($DMSO-d_6$) δ : 1.30 (6H, d, J=6 Hz), 3.13 (1H, quintet, J=6 Hz), 7.46 (1H, d, J=8 Hz), 7.76 (1H, dd, J=8 & 2 Hz), 8.46 (1H, d, J=2 Hz), 8.96 (1H, d, J=2 Hz), 9.56 (1H, d, J=2 Hz).

2-Amino-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carbonitrile (11)

A solution of 5% NH_3 -EtOH (10 ml) was added to a solution of 7 (0.340 g) in CHCl_3 (25 ml) and the mixture was stirred at 30°C for 3 h. After the solvent was removed in vacuo, the residue was extracted with CHCl_3 . The CHCl_3 layer was washed with water and dried over Na_2SO_4 . Evaporation of CHCl_3 gave a residue which was submitted to chromatography on silica gel (30 g). From the fraction eluted with CHCl_3 a white solid was obtained which was recrystallized from CH_3CN to give colorless prisms (11), mp $273\text{--}275^\circ\text{C}$. yield 0.30 g (94%). Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_2$: C, 68.80; H, 4.69; N, 15.05. Found: C, 68.84; H, 4.63; N, 14.76. IR $\nu_{\text{max}}^{\text{nujol}} \text{ cm}^{-1}$: 3300, 3200, 1718, 1620. NMR (CDCl_3 - CF_3COOD) δ : 1.36 (6H, d, $J=7$ Hz), 3.31 (1H, quintet, $J=7$ Hz), 7.60 (1H, d, $J=9$ Hz), 7.95 (1H, dd, $J=9$ & 2 Hz), 8.43 (1H, d, $J=2$ Hz), 9.13 (1H, s).

2-Amino-9-isopropyl-5-oxo-5H-[1]benzopyrano[4,3-b]pyridine-3-carboxylic Acid (12)

A mixture of 11 (0.217 g) and 50% H_2SO_4 -AcOH (1:1) solution (10 ml) was heated with stirring at 120°C for 4 h. The reaction mixture was poured into water and the deposited solid was collected and recrystallized from DMF to give colorless prisms (12), mp $260\text{--}264^\circ\text{C}$ (dec.). yield 0.131 g (57%). Anal. Calcd. for $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.14; H, 4.57; N, 9.48. IR $\nu_{\text{max}}^{\text{nujol}} \text{ cm}^{-1}$: 3400, 3300, 1725, 1650. NMR ($\text{DMSO}-d_6$) δ : 1.30 (6H, d, $J=7$ Hz), 3.10 (1H, quintet, $J=7$ Hz), 7.41 (1H, d, $J=8$ Hz), 7.70 (1H, dd, $J=8$ & 2 Hz), 8.36 (1H, d, $J=2$ Hz), 8.86 (1H, s).

Ethyl 2-Chloro-7-ethyl-5-oxo-5H-[1]benzopyrano[2,3-b]pyridine-3-carboxylate (14)

A mixture of 13 (0.278 g), PCl_5 (0.17 g) and POCl_3 (10 ml) was heated at 110°C for 15 h. After the POCl_3 was removed in vacuo, the residue was dissolved in ethanol (3 ml) and heated at 60°C for 10 min. The resulting deposited solid was collected by filtration. Recrystallization from ethanol gave colorless needles (14), mp $161\text{--}162^\circ\text{C}$. yield 0.215 g (66%). Anal. Calcd. for $\text{C}_{17}\text{H}_{14}\text{ClNO}_4$: C, 61.54; H, 4.25; N, 4.22. Found: C, 61.24; H, 4.08; N, 4.29. IR $\nu_{\text{max}}^{\text{nujol}} \text{ cm}^{-1}$: 1745, 1660. NMR data were shown in Table II.

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