Reaction of 5-(Substituted-amino)oxazoles with *N*-Phenylmaleimide

Sadakatsu Shimada*

Production Technology Research Laboratories, Daiichi Seiyaku Co., Ltd., Kitakasai Edogawa-ku
Tokyo 134, Japan

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Reaction of 5-aminooxazoles with *N*-phenylmaleimide gave 7-hydroxy-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-diones and 7-amino-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-diones *via* tricyclic adducts. The ratio of the 7-hydroxy compound and 7-amino compound depended on the basicity of the leaving group of the adducts. The reaction of 5-acetaminooxazole with dienophiles is described.

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Many papers and patents dealing with the reaction of oxazoles with dienophiles, leading to pyridines, have been reported [1-2]. However, few reports on the reaction of 5-aminooxazoles with dienophiles have appeared before [3]. In previous work we reported a synthetic method of 3-aminopyridines from *N*-(1-cyanoethyl)acylamides with *N*-phenylmaleimide [4]. However, we could not isolate the tricyclic adduct which was assumed to be an intermediate of the reaction. This paper reports a synthesis of 3-hydroxypyridines by the reaction of 5-aminooxazole, which was prepared from *N*-(1-cyanoethyl)formamide and acetic anhydride in the presence of trifluoroacetic acid, with dienophiles, and also reports the aromatization of the adducts, which were prepared from 5-(substituted-amino)oxazoles and *N*-phenylmaleimide, affording 3-hydroxypyridines and 3-(substituted-amino)pyridines.

The reaction of *N*-(1-cyanoethyl)formamide (**1**) with *N*-phenylmaleimide in the presence of trifluoroacetic acid and acetic anhydride gave 7-hydroxy-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**5a**) and 7-acetamino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**6**) in 22% and 4% yields, respectively. The molecular formula of the compound (**5a**) was found $C_{14}H_{10}N_2O_3$ on the basis of its elemental analysis and mass spectrum. The infrared spectrum of **5a** showed characteristic peak at 3310 cm^{-1} attributable to a hydroxy group. The ^{1}H-nmr spectrum of **5a** revealed a singlet signal at δ 2.76 due to the methyl group and a singlet signal δ 8.83 due to the pyridine ring proton. From these observations, **5a** was assigned to be 7-hydroxy-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione. The structure of **5a** was further confirmed by the comparison of its spectral data with those of the sample prepared from 5-ethoxy-4-methyloxazole and *N*-phenylmaleimide. The structure of compound **6** was assigned to be 7-acetamino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine by its elemental analysis and spectral data (Experimental). In order to confirm this structural assignment, 7-amino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione [4] was heated with acetic anhydride to give **6** in 65% yield. The mechanism for the formation of **5a** and **6** is postulated to be as shown in Scheme 1. The following investigations were undertaken to identify the actual intermediates.

Treatment of a solution of *N*-(1-cyanoethyl)formamide (**1**) in trifluoroacetic acid with acetic anhydride at 60° for

Scheme 1

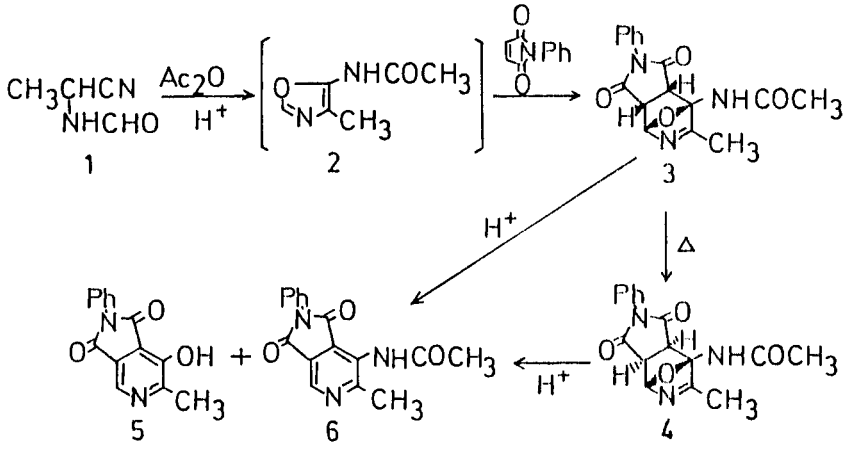


Table 1

Reaction of **1** with Dienophiles

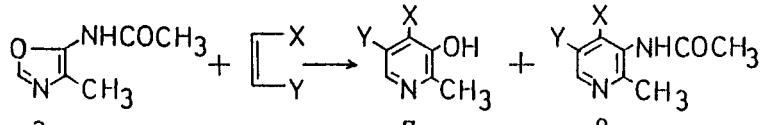
Dienophile X	Dienophile Y	Reaction conditions Temperature (°C)	Reaction conditions Time (hours)	Product (%) **7**	Product (%) **8**
COOMe	COOMe	110	44	47 [5]	5
CN	CN	110	44	11 [6]	0
CN	H	reflux	44	30 [a] [5]	3
				12 [b] [7]	0

[a] 4-Cyano-3-hydroxy-2-methylpyridine. [b] 5-Cyano-3-hydroxy-2-methylpyridine.

2 hours gave 5-acetamino-4-methyloxazole as hygroscopic solid in low yield. Then the structure was further confirmed by the Diels-Alder reaction of **2** with *N*-phenylmaleimide. 5-Acetamino-4-methyloxazole (**2**), allowed to react with *N*-phenylmaleimide at room temperature for 16 hours, gave endo 1-acetamino-4,8-diaza-3,5-dioxo-10-oxa-4-phenyltricyclo[5.2.1.$1^{1,5}$]dec-8-ene (**3**, endo adduct). Thermodynamically more stable exo adduct **4** was obtained by heating the endo adduct **3** under reflux in toluene for 6 hours. The configurations of the adducts were confirmed by the H,H-coupling constants in their ^{1}H-nmr spectra. In the ^{1}H-nmr spectrum of **4** the proton on the C_7 appeared at δ 6.14 as a singlet. In the ^{1}H-nmr spectrum of **3** the proton on the C_7 appeared at δ 6.12 as a doublet (J = 4 Hz). Therefore, the adducts can be assigned to formulas **3** and **4**. Treatment of **3** with acetic acid at 70° for 4 hours gave **5a** and **6** in 72% and 4% yields, respectively.

A similar reaction of **2** with dienophiles afforded 3-hydroxy, **7** and 3-acetaminopyridines **8** (Scheme 2). These results are listed in Table 1. These results indicate the preference of 3-hydroxy to 3-acetaminopyridines. In contrast with these results, the reaction of *N*-(1-cyanoethyl)formamide with *N*-phenylmaleimide in the absence of acetic anhydride gave 3-aminopyridines as the major product [4]. These facts indicate that the aromatization may be affected by the leaving group at the C_1 position of the adduct. Then the aromatization of 1-substituted-4,8-diaza-3,5-dioxo-10-oxa-4-phenyltricyclo[5.2.1.$0^{1,5}$]dec-8-enes was examined. Heating of 5-*N*-ethylanilino-4-methyloxazole [8] with *N*-phenylmaleimide in ethyl acetate under reflux for 6 hours gave 7-*N*-ethylanilino-6-methyl-2-phenylpyrrolo-[3,4-*c*]pyridine-1,3-dione (**11**), in which a molecule of water has been lost from the expected adduct **10**, in 64% yield (Scheme 3). The structural assignment for compound **11** was based on its ir, mass and ^{1}H-nmr spectra and elemental analysis (Experimental). 1-Benzyloxycarbonylamino adducts **13** were also prepared from benzyl oxazole-5-carbamates **12** and *N*-phenylmaleimide in a manner similar to the synthesis of **3** (Scheme 4). The aromatization of **13a** with acetic acid gave 7-hydroxy compound **5a** and 7-benzyloxy carbonylamino compound **14a** in 24% and 57% yields, respectively. In the case of adduct (**13b**) **5b**:**14b** were obtained in the ratio 1:2.2. The aromatization of 1-amino adduct **15**, which was prepared from **13** by the reductive cleavage, in acetic acid gave 7-amino compound **16** along with trace of 7-hydroxy compound. The results are summarized in Table 2. These results indicate that the relative rates of the elimination from the adducts by acetic

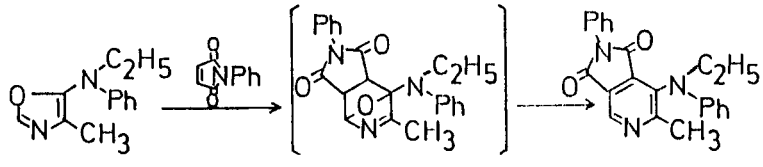
Scheme 2



2 7 8

a: X,Y=CO_2CH_3 a: X,Y=CO_2CH_3
b: X,Y=CN
c: X=CN,Y=H c: X=CN,Y=H
d: X=H,Y=CN

Scheme 3



9 10 11

Scheme 4

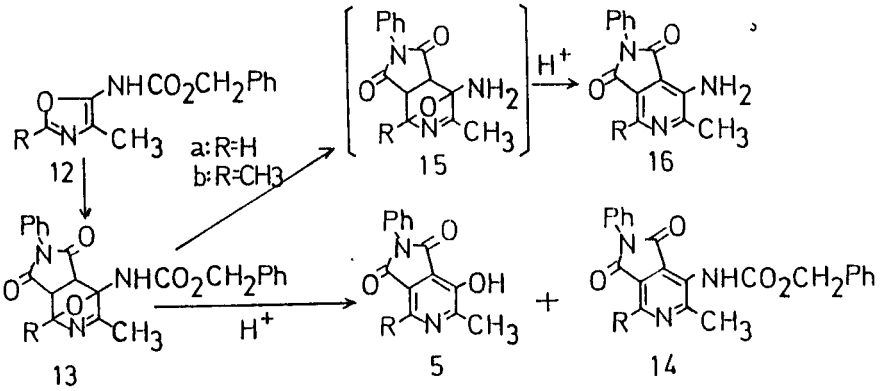
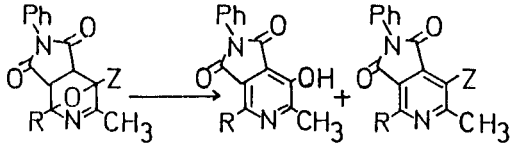


Table 2

Reaction of Adducts with Acetic Acid



	Substrate Z	R		Product (%) 7-Hydroxy	7-Z
3	CH_3CONH	H	endo	72	4
4	CH_3CONH	H	endo	65	10
10	($C_2H_5NC_6H_5$	H)		0	64
15a	(NH_2	H)		trace	67
15b	(NH_2	CH_3)		trace	67
13a	$C_6H_5CH_2OCONH$	H	endo	24	57
13b	$C_6H_5CH_2OCONH$	CH_3	endo	24	53

Adducts in parenthesis were not isolated.

acid seems to be in the order $RCONH_2 > RCOONH_2 = H_2O > R_2NH, NH_3$. The ratio of 3-hydroxypyridines and 3-(substituted-amino)pyridines depended on the basicity of the leaving group of the adducts.

EXPERIMENTAL

Melting points were determined on an electrically heated block and are uncorrected. The ^{1}H-nmr spectra were recorded on a JEOL JNM-PMX 60 or a Varian XL-200 spectrometer in deuteriochloroform solution unless otherwise stated. Chemical shifts are expressed as ppm downfield from tetramethylsilane as an internal standard. Infrared spectra were recorded on a Hitachi 260 spectrometer. Mass spectra were taken with a JEOL TMD 300 mass spectrometer.

7-Hydroxypyrrolo[3,4-*c*]pyridine-1,3-dione (**5a**) from **1**.

Trifluoroacetic acid (0.34 g, 30 mmoles) was added to a solution of *N*-(1-cyanoethyl)formamide (1.0 g, 10 mmoles) in 1,2-dichloroethane (1 ml) at 5°. The mixture was stirred at room temperature for 30 minutes. Acetic anhydride (20 ml) was added to the mixture. After being stirred for 2 hours at 60°, the mixture was concentrated to dryness under reduced pressure. The residue was heated with *N*-phenylmaleimide (1.73 g, 10 mmoles) in ethyl acetate (50 ml) at 45° for 24 hours. Removal of the solvent gave the mixture of 7-hydroxy-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**5a**) and 7-acetamino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**6**) which were separated by chromatography on silica in ethyl acetate. Yield and physical data for the product are as follows: **5a** was obtained in 22% yield as yellow plates (ethyl acetate), mp 229-230° dec; ir (potassium bromide): 3310, 1760 and 1690 cm^{-1}; ms: [m/z (relative intensity)] 254 (M^+, 100); ^{1}H-nmr: 2.76 (3H, s), 7.62 (5H, s), 8.83 (1H, s).

Anal. Calcd. for $C_{14}H_{10}N_2O_3$: C, 66.13; H, 3.96; N, 11.02. Found: C, 66.02; H, 4.21; N, 11.38.

7-Acetaminopyrrolo[3,4-*c*]pyridine-1,3-dione (**6**) from **1**.

Further elution of the mixture described in the preparation of **5a** with ethyl acetate gave 7-acetamino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**6**) (0.12 g, 4%) as colorless plates (ethyl acetate), mp 202-203°; ir (potassium bromide): 1775, 1720 and 1680 cm^{-1}; ms: [m/z (relative intensity)] 295 (M^+, 65), 253 (100); ^{1}H-nmr: 2.28 (3H, s), 2.67 (3H, s), 7.4-7.6 (5H, m), 8.2-8.4 (1H, broad), 8.97 (1H, s).

Anal. Calcd. for $C_{16}H_{13}N_3O_3$: C, 65.06; H, 4.44; N, 14.23. Found: C, 64.90; H, 4.60; N, 13.96.

5-Acetamino-4-methyloxazole (**2**).

a) From **1**.

Trifluoroacetic acid (0.34 g, 30 mmoles) was added to a stirred solution of *N*-(1-cyanoethyl)formamide (1.0 g, 10 mmoles) in 1,2-dichloroethane (1 ml). The mixture was stirred for 30 minutes at room temperature. Acetic anhydride (20 ml) was added dropwise with stirring to the mixture. After being stirred for 2 hours at 60°, the mixture was evaporated under reduced pressure to dryness. The residue was purified by silica gel chromatography in ethyl acetate. The fractions were concentrated to yield 0.29 g of **2** (21%) as a hygroscopic white solid; ir (potassium bromide): 1685 and 1660 cm^{-1}; ^{1}H-nmr: 2.15 (3H, s), 2.19 (3H, s), 7.70 (1H, s). The picrate of **2** was obtained as yellow crystals, mp 110-111° (benzene).

Anal. Calcd. for $C_{12}H_{12}N_5O_9$: C, 39.14; H, 3.11; N, 18.95. Found: C, 38.91; H, 3.24; N, 18.91.

b) From **12a**.

A solutoin of benzyl oxazole-5-carbamate [10] (2.32 g, 10 mmoles) in acetic anhydride (50 ml) was hydrogenated over 5% palladium on active carbon (4 g) for 2 hours at room temperature [9]. The catalyst was filtered off and the filtrates were evaporated *in vacuo*. The residue was purified on silica. The elution with ethyl acetate gave 0.53 g (38%) of **2**. The ir

and ^{1}H-nmr spectra were completely identical with those of the sample prepared from **1**.

endo Adduct **3** from **2**.

A mixture of **2** (1.40 g, 10 mmoles) and *N*-phenylmaleimide (1.73 g, 10 mmoles) in ethyl acetate (50 ml) was stirred at room temperature for 16 hours. The precipitates were filtered and washed with ethyl acetate (10 ml) to give 1.69 g (54%) of **3** as white needles, mp 192-194°; ir (potassium bromide): 1780 and 1720 cm^{-1}; ms: [m/z (relative intensity)] 313 (M$^+$, 3), 173 (100); ^{1}H-nmr: 1.95 (3H, s), 2.05 (3H, s), 3.80 (1H, dd, J = 4 Hz, J = 9 Hz), 3.87 (1H, d, J = 9 Hz), 6.05 (1H, d, J = 4 Hz), 7.0-7.6 (5H, m), 9.83 (1H, broad).

Anal. Calcd. for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.79; N, 13.41. Found: C, 61.32; H, 4.79; N, 13.59.

exo Adduct **4** from endo Adduct **3**.

A suspension of **3** (3.13 g, 10 mmoles) in toluene (50 ml) was refluxed for 5 hours. After removal of the solvent, the residue was recrystallized from chloroform-isopropyl ether (1:10) to give 1.60 g (51%) of exo adduct as white needles, mp 184-186°; ir (potassium bromide): 1780 and 1720 cm^{-1}; ms: [m/z (relative intensity)] 313 (M$^+$, 3), 173 (69), 98 (100); ^{1}H-nmr: 2.16 (1H, s), 2.20 (3H, s), 3.15 (3H, d, J = 7 Hz), 3.58 (1H, d, J = 7 Hz), 6.12 (1H, s), 7.6-8.0 (5H, m).

Anal. Calcd. for $C_{16}H_{15}N_3O_4$: C, 61.34; H, 4.79; N, 13.41. Found: C, 61.24; H, 4.72; N, 13.16.

Aromatization of **3**.

A solution of **3** (3.13 g, 10 mmoles) in acetic acid (50 ml) was stirred at 80° for 2 hours. The reaction mixture was concentrated to dryness *in vacuo*. The residue was recrystallized from ethyl acetate to give **5a** (2.40 g, 72%) as yellow plates. **5a** was identified on the basis of the mixed fusion test and comparison of the spectral data with those of the sample prepared from **1**. Evaporation of the mother liquor described in the preparation of **5a** gave the mixture of **5a** and **6** which were separated by chromatography on silica in ethyl acetate. The minor component was eluted with ethyl acetate to give 0.12 g of 4% of 7-acetamino compound **6**.

Dimethyl 5-Hydroxypyridine-3,4-dicarboxylate (**7a**) from **2**.

A mixture of **2** (1.40 g, 10 mmoles) and dimethyl fumarate (3.0 g) in toluene (5 ml) was refluxed for 4 hours. After removal of the solvent, the residue was applied to a silica gel column. Elution with chloroform afforded **7a** (1.06 g, 47%) as colorless needles (methanol), mp 140-141°, (lit [5] mp 140-141°); ir (potassium bromide): 3450, 1745 and 1730 cm^{-1}; ms: [m/z (relative intensity)] 225 (M$^+$, 30), 193 (100); ^{1}H-nmr (DMSO-d$_6$): 2.18 (3H, s), 2.57 (3H, s), 3.97 (6H, s), 9.00 (1H, s).

Dimethyl 5-Acetaminopyridine-3,4-dicarboxylate (**8a**).

Further elution of the residue described in preparation of **7a** with chloroform gave 0.13 g (5%) of dimethyl 5-acetamino-6-methylpyridine-3,4-dicarboxylate (**8a**) as colorless needles (ethyl acetate), mp 127-129°; ir: 1720, 1690 1670 cm^{-1}; ^{1}H-nmr: 2.18 (3H, s), 2.57 (3H, s), 3.97 (6H, s), 9.00 (1H, s).

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: C, 54.13; H, 5.30; N, 10.53. Found: C, 54.22; H, 5.46; N, 10.37.

4,5-Dicyano-3-hydroxy-2-methylpyridine (**7b**) from **2**.

A mixture of **2** (1.0 g) and fumaronitrile (2.0 g) in toluene (20 ml) was refluxed for 44 hours. After removal of the solvent, the residue was purified by silica gel column chromatography. The fractions eluted with ethyl acetate afforded 0.16 g (11%) of **7b**, mp 189-190° (from benzene, lit [6] mp 189-190°). The ir and ^{1}H-nmr spectra were completely identical with those of the sample prepared by the method of Harris *et al.* [6].

5-Cyano-3-hydroxy-2-methylpyridine (**7d**).

A solution of **2** (1.40 g, 10 mmoles) in acrylonitrile (30 ml) was refluxed for 44 hours. After removal of the excess reagent, the residue was chromatographed on a silica gel column with ethyl acetate as an eluent afforded 0.16 g of **7d** (12%), mp 246-247° (lit [7] mp 246-247°); ir (potassium bromide): 3400, 2230 and 1600 cm^{-1}; ^{1}H-nmr (DMSO-d$_6$): 2.51 (3H, s), 7.39 (1H, d, J = 2 Hz), 8.26 (1H, d, J = 2 Hz). Compound **7d** was identical with the sample prepared by the method of Yoshikawa *et al.* [7].

3-Acetamino-4-cyano-2-methylpyridine (**8c**).

Further elution of the mixture described in preparation of **7d** with ethyl acetate gave 0.05 g (3%) **8c** as colorless needles, mp 164-165° (ethyl acetate); ir (potassium bromide): 2230 and 1665 cm^{-1}; ms: [m/z (relative intensity)] 275 (M$^+$, 5), 133 (100); ^{1}H-nmr: 2.30 (3H, s), 2.58 (3H, s), 7.49 (1H, d, J = 5 Hz), 8.68 (1H, d, J = 5 Hz).

Anal. Calcd. for $C_9H_9N_3O$: C, 61.70; H, 9.07; N, 24.02. Found: C, 61.84; H, 9.19; N, 23.97.

4-Cyano-3-hydroxy-2-methylpyridine (**7c**).

Further elution of the mixture described in preparation of **8c** with ethyl acetate gave 0.40 g (30%) of **7c** as colorless prisms, mp 235-237° (methanol). Compound **7c** was identified on the basis of the mixed melting points and comparison of the spectral data with those of synthesized standard [5].

7-*N*-Ethylanilinopyrrolo[3,4-*c*]pyridine-1,3-dione (**11**).

A solution of **9** [8] (2.0 g, 10 mmoles) and *N*-phenylmaleimide (1.73 g, 10 mmoles) in ethyl acetate (50 ml) was refluxed for 6 hours. After removal of the solvent, the residue was recrystallized from ethyl acetate to give **2**. 30 g (64%) of **11** as red prisms, mp 139-140°; ir (potassium bromide): 1760 and 1720 cm^{-1}; ms: [m/z (relative intensity)] 357 (M$^+$, 99), 342 (100); ^{1}H-nmr: 1.37 (3H, t), 2.50 (3H, s), 3.92 (2H, q), 6.5-7.5 (5H, m), 7.42 (5H, s), 9.00 (1H, s).

Anal. Calcd. for $C_{22}H_{19}N_3O_3$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.71; H, 5.28; N, 11.66.

endo Adduct **13a** from **12a**.

A mixture of benzyl 4-methyloxazole-5-carbamate (**12a**) [10] (2.32 g, 10 mmoles) and *N*-phenylmaleimide (1.73 g, 10 mmoles) in ethyl acetate (50 ml) was stirred at room temperature for 24 hours. The crystals separated were filtered and washed with ethyl acetate (10 ml) to give endo adduct **13a** (1.58 g, 39%) as white needles, mp 182-183°; ir (potassium bromide): 1720 cm^{-1}; ms: [m/z (relative intensity)] 405 (M$^+$, 2), 173 (100); ^{1}H-nmr (DMSO-d$_6$): 2.03 (3H, s), 3.35 (1H, dd, J = 4 Hz, J = 10 Hz), 3.92 (1H, d, J = 10 Hz), 5.12 (2H, s), 6.03 (1H, d, J = 4 Hz), 9.31 (1H, broad).

Anal. Calcd. for $C_{22}H_{19}N_3O_5$: C, 65.18; H, 4.72; N, 10.34. Found: C, 64.96; H, 4.75; N, 10.36.

endo Adduct **13b** from **12b**.

A mixture of benzyl 2,4-dimethyloxazole-5-carbamate (**12b**) [10] (2.46 g, 10 mmoles) and *N*-phenylmaleimide (1.73 g, 10 mmoles) in ethyl acetate (50 ml) was stirred for 24 hours at room temperature. The precipitates which separated were filtered and washed with ethyl acetate (10 ml) to give 2.35 g (56%) of endo adduct **13b** as white needles, mp 197-199°; ir (potassium bromide): 1720 cm^{-1}; ms: [m/z (relative intensity)] 419 (M$^+$, 1), 173 (100); ^{1}H-nmr: 1.90 (3H, s), 2.05 (3H, s), 3.62 (1H, d, J = 7.5 Hz), 4.05 (1H, d, J = 7.5 Hz), 5.20 (2H, s), 7.2-7.7 (10H, m), 7.50 (1H, broad).

Anal. Calcd. for $C_{23}H_{21}N_3O_5$: C, 65.86; H, 5.05; N, 10.02. Found: C, 65.40; H, 5.08; N, 9.84.

Aromatization of **13a**.

A solution of endo adduct **13a** (2.03 g, 5 mmoles) in acetic acid (50 ml) was stirred for 40 hours at room temperature. Evaporation of the reaction mixture under reduced pressure gave a mixture of **5** and **14a** which was separated by chromatography on silica in chloroform methanol (9:1). Elution with chloroform-methanol (9:1) afforded 1.10 g of 7-benzyloxycarbonylamino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**14a**) (57%) as white needles, mp 192-193° (ethyl acetate); ir (potassium bromide): 1780, 1740 and 1710 cm^{-1}; ms: [m/z (relative intensity)] 387 (M$^+$, 19), 279 (100); ^{1}H-nmr: 2.72 (3H, s), 5.25 (2H, s), 7.3-7.6 (10H, m), 9.00 (1H, s).

Anal. Calcd. for $C_{22}H_{17}N_3O_4$: C, 68.21; H, 4.22; N, 10.85. Found: C, 67.74; H, 4.63; N, 10.48.

Further elution of the mixture with ethyl acetate gave 0.30 g (24%) of **5a**.

Aromatization of **13b**.

7-Benzyloxycarbonylamino-2,6-dimethyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**14b**) (53%) and 7-hydroxy-2,6-dimethyl-2-phenylpyrrolo-[3,4-*c*]pyridine-1,3-dione (**5b**) (24%) were obtained from **13b** with acetic acid in a manner similar to the synthesis of **14a** and **5a** from **13a**. Physical data for the products are as follows: **14b** was obtained as white prisms, mp 136-137° (ethyl acetate); ir (potassium bromide): 1775, 1720 and 1695 cm^{-1}; ms: [m/z (relative intensity)]: 4.01 (M^+, 10), 293 (100); ^{1}H-nmr: 2.67 (3H, s), 2.88 (3H, s), 5.22 (2H, s), 7.38 (5H, s), 7.5-7.8 (1H, broad), 7.3-7.6 (5H, m).

Anal. Calcd. for $C_{23}H_{19}N_3O_4$: C, 68.65; H, 4.76; N, 10.44. Found: C, 68.75; H, 4.56; N, 10.44.

Compound **5b** was obtained as yellow plates, mp 215-217° (ethyl acetate); ir (potassium bromide): 3430, 1700 and 1700 cm^{-1}; ms: [m/z (relative intensity)] 268 (M^+, 100); ^{1}H-nmr: 2.70 (3H, s), 2.80 (3H, s), 7.60 (5H, s).

Anal. Calcd. for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 67.01; H, 4.33; N, 10.24.

7-Aminopyrrolo[3,4-*c*]pyridine-1,3-dione (**16a**) from **13a**.

A solution **13a** (2.05 g, 5 mmoles) in glacial acetic acid (50 ml) was hydrogenated over 5% palladium on active carbon (1 g) for 8 hours at room temperature. After removal of the catalyst, the filtrate was evaporated *in vacuo*. The residue was chromatographed on a silica gel column. The major component was eluted with ethyl acetate to give 7-amino-6-methyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**16a**) (0.85 g, 67%) as yellow crystals (ethyl acetate), mp 280°; ir (potassium bromide): 3460, 3360, 1740 and 1700 cm^{-1}; ms: [m/z (relative intensity)] 253 (M^+, 100); ^{1}H-nmr (DMSO-d_6): 2.53 (3H, s), 6.51 (2H, broad), 7.52 (5H, s), 8.21 (1H, s).

Anal. Calcd. for $C_{14}H_{11}N_3O_2$: C, 66.40; H, 4.38; N, 16.59. Found: C, 66.49; H, 4.43; N, 16.49.

The minor component was not isolated.

7-Aminopyrrolo[3,4-*c*]pyridine-1,3-dione (**16b**) from **13b**.

A solution of **13b** (2.10 g, 5 mmoles) in glacial acetic acid (50 m) was shaken with hydrogen over 5% palladium on active carbon (2 g) at room temperature for 5 hours. The catalyst was filtered off and washed with acetic acid. The filtrate was concentrated under reduced pressure, and the residue was chromatographed on a silica gel column. The component was eluted with ethyl acetate to afford 0.89 g (67%) of 7-amino-4,6-dimethyl-2-phenylpyrrolo[3,4-*c*]pyridine-1,3-dione (**16b**) as yellow crystals, mp 267° dec; ir (potassium bromide): 3460, 3360, 1740 and 1700 cm^{-1}; ms: [m/z (relative intensity)] 267 (M^+, 100); ^{1}H-nmr (DMSO-d_6): 2.49 (3H, s), 2.60 (3H, s), 6.2-6.4 (2H, broad), 7.51 (5H, s).

Anal. Calcd. for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.19; H, 4.90; N, 15.73.

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