

Reaction of Phthalic Anhydrides with Methyl Isocyanoacetate: A Useful Synthesis of 1,2-Dihydro-1-oxoisoquinolines¹⁾

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Nitro-1,2-dihydro-1-oxoisoquinoline-3-carboxylate compounds (**5a**, **b** and **9a**, **b**) were synthesized by the reaction of methyl isocyanoacetate with nitrophthalic anhydrides in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), followed by esterification with diazomethane and hydrolysis with HCl. In these reactions, the methylidenephthalide compound (**10**) was also obtained by hydrolysis of the oxazole-4-carboxylate compound (**8b**) due to the presence of the bulky *ortho* nitro group. Moreover, 1,2-dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylic acid (**16**) was prepared *via* the oxazole dicarboxylic acid compound (**15**) in good yield.

Keywords—methyl isocyanoacetate; phthalic anhydrides; methyl oxazole-4-carboxylates; methyl 1,2-dihydro-1-oxoisoquinoline-3-carboxylates; nitro-1,2-dihydro-1-oxoisoquinoline derivatives; 1,2-dihydro-1-oxoisoquinoline-3-carboxylic acid; methylidenephthalide; ring transformation

In our series of syntheses of amino acids and heterocyclic compounds using isocyano compounds, facile synthetic methods for a variety of pharmacologically interesting compounds have been described.³⁾ In the previous communication we reported the synthesis of methyl 1,2-dihydro-1-oxoisoquinoline-3-carboxylate derivatives by the reaction of methyl isocyanoacetate with phthalic anhydrides.⁴⁾

The isoquinoline compounds have been derived by means of the Gabriel-Colman reaction, which involves a base-catalyzed rearrangement of α -phthalimidoacetic acid esters.⁵⁾ Unfortunately, the reaction lacks generality because of the following limitations: 1) the rearrangement of α -phthalimidoacetic acid esters substituted with strong electron-withdrawing groups such as a nitro group does not occur; in such cases cleavage of the imido ring proceeds predominantly, 2) the isoquinoline derivatives derived from phthalimido compounds having substituents on the aromatic ring are generally obtained as a mixture of the position isomers.

Thus, it seemed worthwhile to try to overcome these limitations and to develop a new synthesis for the isoquinolines. In the present paper, we report in detail the reaction of phthalic anhydrides with methyl isocyanoacetate, which provides a general synthetic procedure for methyl 1,2-dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylates. Our previous report indicated that the reaction of 4-nitrophthalic anhydride (**1**) with methyl isocyanoacetate (**2**) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in tetrahydrofuran

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- 2) Location: 16-89 Kashima-3-chome, Yodogawa-ku, Osaka 532, Japan.
- 3) K. Matsumoto, *J. Agric. Chem. Soc. Japan*, **51**, R109 (1977); M. Suzuki, K. Nunami, T. Moriya, K. Matsumoto, and N. Yoneda, *J. Org. Chem.*, **43**, 4933 (1978), and references cited therein.
- 4) M. Suzuki, K. Nunami, K. Matsumoto, N. Yoneda, and M. Miyoshi, *Synthesis*, **1978**, 461.
- 5) a) S. Gabriel and J. Colman, *Chem. Ber.*, **33**, 980 (1900); b) C.F.H. Allen, *Chem. Revs.*, **47**, 284 (1950); W.J. Gensler, "Heterocyclic Compounds," Vol. 4, ed. by R.C. Elderfield John Wiley and Sons, Inc., New York, pp. 376-379; T. Nagase and Y. Yoneyoshi, Japan. Patent 7002382 (1970) [*C.A.*, **73**, 45168 (1970)].

gave a mixture of methyl 5-(2-carboxy-4-nitrophenyl)- and 5-(2-carboxy-5-nitrophenyl)oxazole-4-carboxylate (**3**), which is very difficult to separate.⁴⁾ We have now carried out esterification of the 2-carboxyl group using diazomethane to separate the isomers of the oxazole compound. The resulting oxazole diester compound (**4**) was chromatographed on silica gel with CHCl_3 -AcOEt (4: 1) as an eluent. The first fraction afforded colorless crystals having mp 101–103° in 13% yield and the second fraction gave colorless crystals having mp 115–116.5° in 58% yield. From the nuclear magnetic resonance (NMR) data for the benzene ring protons, it appeared that the former product was **4b** and the latter product was **4a**. Namely, the aromatic proton signals of **4a** appeared at δ 7.99 (d, $J=9$ Hz, Ha), 8.53 (dd, $J=3$ and 9 Hz, Hb) and 8.65 (d, $J=3$ Hz, Hc) and those of **4b** were observed at δ 8.16 (d, $J=9$ Hz, Hf), 8.45 (dd, $J=2$ and 9 Hz, He) and 8.58 (d, $J=2$ Hz, Hd); Hc, which is located between the nitro and methoxycarbonyl groups, would appear at lower field than the other aromatic protons, while Ha would appear at the higher field⁶⁾ as shown in Chart 1. In this

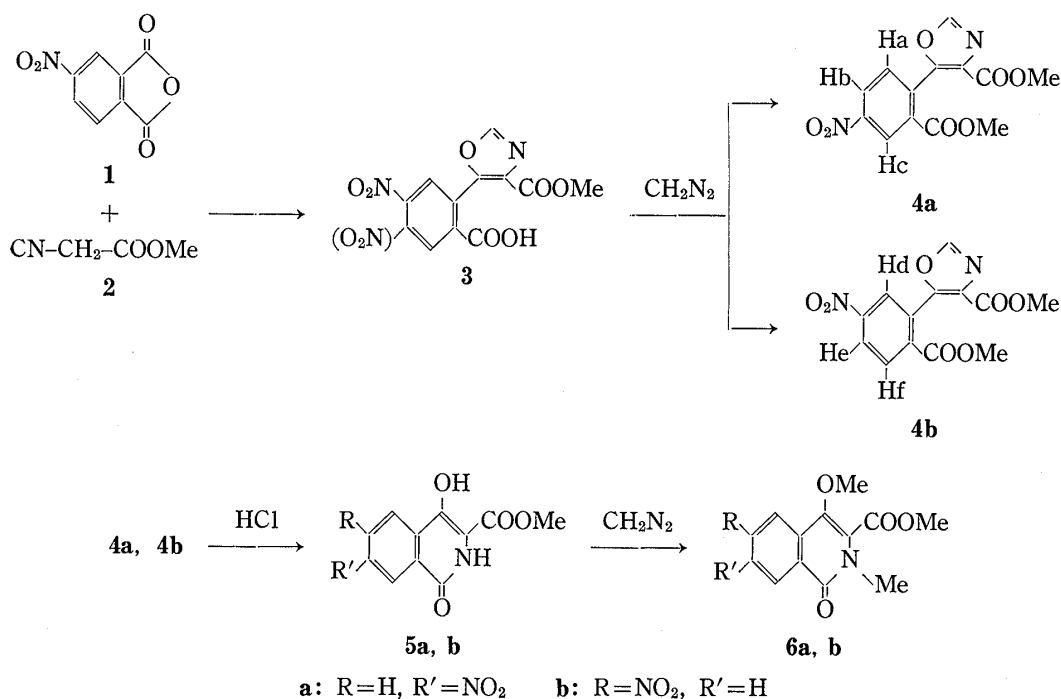


Chart 1

reaction, the compound **4a** was formed predominantly, because the electrophilicity of the carbonyl group adjacent to the *para* position with respect to the nitro group of compound **1** was stronger than that of the other carbonyl group located at the *meta* position. Subsequently, the separated compounds **4a** and **4b** were treated with 2N HCl-MeOH to afford the corresponding methyl 1,2-dihydro-4-hydroxy-7-nitro-1-oxoisoquinoline-3-carboxylate (**5a**) and methyl 1,2-dihydro-4-hydroxy-6-nitro-1-oxoisoquinoline-3-carboxylate (**5b**), respectively, in nearly quantitative yields. The structures of these compounds **5a** and **5b** were confirmed by spectral and analytical data. However, measurement of the NMR spectra for **5a** and **5b** was impossible because of their very poor solubility. Thus, in order to confirm the structures, **5a** and **5b** were converted to the O,N-dimethyl compounds (**6a** and **6b**) by treatment with diazomethane. In the NMR spectrum of **6a**, the chemical shift of the aromatic proton (position 8) located between the nitro and carbonyl groups was characteristically observed at lower field (δ 9.17) than the other aromatic protons.

6) The electron-withdrawing power of the substituents on the aromatic ring may be in the order hydrogen < oxazole < methoxycarbonyl < nitro.

Similarly, the reaction using 3-nitrophthalic anhydride (**7**) was investigated and methyl 5-(2-methoxycarbonyl-3-nitrophenyl)oxazole-4-carboxylate (**8a**) and methyl 5-(2-methoxycarbonyl-6-nitrophenyl)oxazole-4-carboxylate (**8b**) were separated by column chromatography in 31% and 60% yields, respectively. Subsequently, the oxazole compounds (**8a** and **8b**) were hydrolyzed with 2N HCl-MeOH to give the corresponding nitroisoquinoline compounds. As a result, methyl 1,2-dihydro-4-hydroxy-8-nitro-1-oxoisoquinoline-3-carboxylate (**9a**) was prepared in 91% yield from **8a**, but methyl 1,2-dihydro-4-hydroxy-5-nitro-1-oxoisoquinoline-3-carboxylate (**9b**) was formed in only 16% yield from **8b**; and interestingly, 3-(α -amino- α -methoxycarbonylmethylidene)-4-nitrophthalide hydrochloride (**10**) was obtained in 62% yield. The structure of compound **10** was confirmed by the spectral and elemental data as described later. The formation of **10** presumably occurs by intramolecular cyclization of the enol group, which resulted from cleavage of the oxazole ring, with the ester group, because the coplanarity of the benzene ring and oxazole ring was distorted owing to the bulkiness of the nitro group at the *ortho* position so that attack at the ester group by the amino group would be prevented. In the case of methyl 5-(2-carboxy-3,4,5,6-tetrachlorophenyl)oxazole-

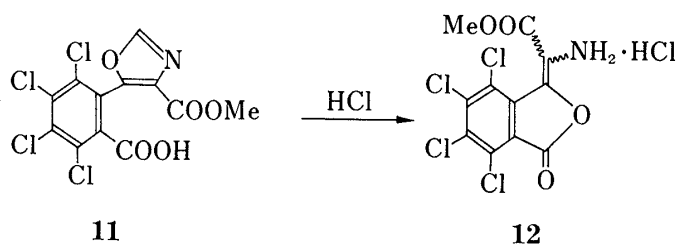
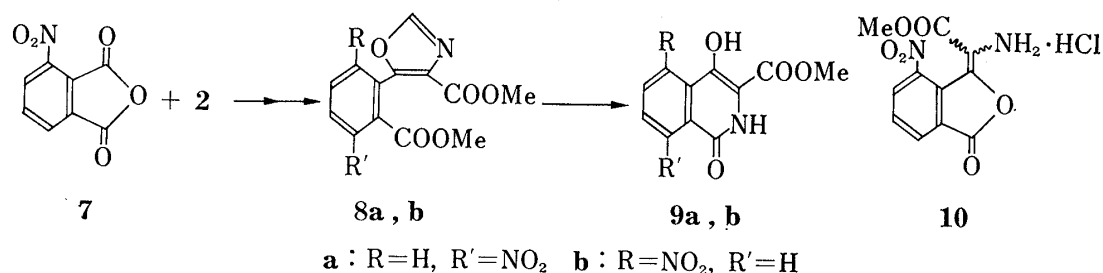


Chart 2

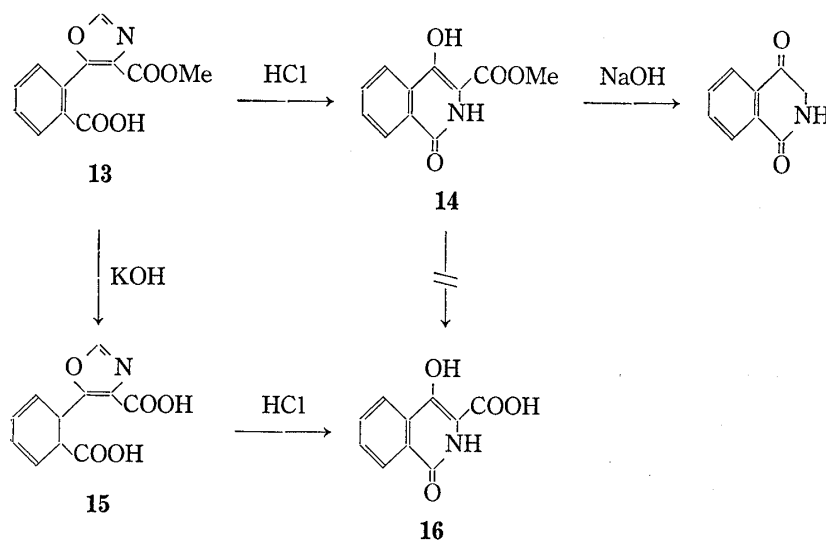


Chart 3

4-carboxylate (**11**) derived from 3,4,5,6-tetrachlorophthalic anhydride which has a bulky chlorine atom at the *ortho* position, only the lactone compound (**12**) was formed in good yield by the subsequent acid hydrolysis of **11**.

Furthermore, we have investigated the synthesis of 1,2-dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylic acid (**16**), which would be a versatile intermediate for pharmacologically interesting compounds. Though direct saponification of methyl 1,2-dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylate (**14**) was carried out, the desired compound (**16**) was not obtained because of accompanying decarboxylation.^{5a)} As an alternative approach to obtain the carboxylic acid (**16**), methyl 5-(2-carboxyphenyl)oxazole-4-carboxylate (**13**) was allowed to saponify in the first step to give 5-(2-carboxyphenyl)oxazole-4-carboxylic acid (**15**) in high yield. Subsequent acid treatment of **15** afforded isoquinoline-3-carboxylic acid (**16**) in high yield, as shown in Chart 3.

Experimental

Melting points are uncorrected and were measured with a Yamato melting point apparatus. Infrared (IR) spectra were recorded with a Shimadzu IR-27G spectrophotometer and NMR spectra with a Hitachi Perkin-Elmer R-20A high resolution NMR spectrometer using tetramethylsilane as an internal standard. Mass spectra (MS) were determined on a Hitachi RMU-6M spectrometer. Column chromatography was carried out on silica gel (Kieselgel 60, 0.063–0.200 mm, E. Merck).

Methyl 5-(2-Methoxycarbonyl-4-nitrophenyl)oxazole-4-carboxylate (4a) and Methyl 5-(2-Methoxycarbonyl-5-nitrophenyl)oxazole-4-carboxylate (4b)—A mixture of methyl 5-(2-carboxy-4-nitrophenyl)oxazole-4-carboxylate and methyl 5-(2-carboxy-5-nitrophenyl)oxazole-4-carboxylate (**3**) was obtained as a syrup by reaction of 4-nitrophthalic anhydride (**1**) (5.79 g, 30 mmol) with **2** (2.97 g, 30 mmol) in the presence of DBU (4.56 g, 30 mmol) according to a method similar to that described in the previous paper.⁴⁾ This mixture was dissolved in MeOH (30 ml) and ethereal diazomethane (1.1 eq.) was added at room temperature. The solution was evaporated *in vacuo* and the resulting residue was subjected to silica gel column chromatography (220 g) using CHCl₃–AcOEt (4:1) as an eluent. The separated isomers were purified by recrystallization from appropriate solvents. **4a**: colorless prisms from AcOEt, 5.30 g (58%). mp 115–116.5°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3100, 1740, 1720, and 1525. NMR (in DMSO-*d*₆) δ : 8.67 (1H, s, oxazole-H), 8.65 (1H, d, *J*=3 Hz, C₃-H), 8.53 (1H, dd, *J*=9 and 3 Hz, C₅-H), 7.99 (1H, d, *J*=9 Hz, C₆-H), 3.80 (3H, s, OCH₃), and 3.70 (3H, s, OCH₃). Anal. Calcd. for C₁₃H₁₀N₂O₇: C, 50.99; H, 3.29; N, 9.15. Found: C, 50.83; H, 3.31; N, 9.11. **4b**: colorless prisms from AcOEt–hexane, 1.19 g (13%). mp 101–103°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3120, 1735, and 1530. NMR (in DMSO-*d*₆) δ : 8.64 (1H, s, oxazole-H), 8.58 (1H, d, *J*=2 Hz, C₆-H), 8.45 (1H, dd, *J*=9 and 2 Hz, C₄-H), 8.16 (1H, d, *J*=9 Hz, C₃-H), 3.77 (3H, s, OCH₃), and 3.71 (3H, s, OCH₃). Anal. Calcd. for C₁₃H₁₀N₂O₇: C, 50.99; H, 3.29; N, 9.15. Found: C, 50.97; H, 3.31; N, 9.12.

Methyl 5-(2-Methoxycarbonyl-3-nitrophenyl)oxazole-4-carboxylate (8a) and Methyl 5-(2-Methoxycarbonyl-6-nitrophenyl)oxazole-4-carboxylate (8b)—A similar reaction using 3-nitrophthalic anhydride (**7**) (5.79 g, 30 mmol) and **2** (2.97 g, 30 mmol) in the presence of DBU (4.56 g, 30 mmol) was carried out to give **8a** and **8b**. **8a**: colorless needles from ether, 2.8 g (31%). mp 123–125°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3100, 1735, 1720, and 1540. NMR (in DMSO-*d*₆) δ : 8.65 (1H, s, oxazole-H), 8.34 (1H, dd, *J*=8 and 2 Hz, C₄-H), 8.20 (1H, dd, *J*=8 and 2 Hz, C₆-H), 7.89 (1H, t, *J*=8 Hz, C₅-H), and 3.76 (6H, s, 2OCH₃). Anal. Calcd. for C₁₃H₁₀N₂O₇: C, 50.99; H, 3.29; N, 9.15. Found: C, 50.91; H, 3.30; N, 9.15. **8b**: colorless needles from AcOEt, 5.51 g (60%). mp 142–144°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3100, 1735, 1710, and 1535. NMR (in DMSO-*d*₆) δ : 8.70 (1H, s, oxazole-H), 8.44 (1H, dd, *J*=8 and 2 Hz, C₅-H), 8.35 (1H, dd, *J*=8 and 2 Hz, C₃-H), 7.96 (1H, t, *J*=8 Hz, C₄-H), 3.72 (3H, s, OCH₃), and 3.62 (3H, s, OCH₃). Anal. Calcd. for C₁₃H₁₀N₂O₇: C, 50.99; H, 3.29; N, 9.15. Found: C, 50.85; H, 3.32; N, 9.10.

Methyl 1,2-Dihydro-4-hydroxy-7-nitro-1-oxoisoquinoline-3-carboxylate (5a)—Compound **4a** (0.612 g, 2 mmol) was dissolved in a mixture of MeOH (6 ml) and conc. HCl (1.2 ml) and the solution was stirred for 6 hr at room temperature. The resulting precipitates were collected by suction and washed with H₂O and MeOH. Recrystallization from dimethylformamide gave **5a** as yellow needles (0.51 g, 97%). mp 278–280° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3150, 1690, and 1660. Anal. Calcd. for C₁₁H₈N₂O₆: C, 50.00; H, 3.05; N, 10.60. Found: C, 49.79; H, 3.15; N, 10.43.

Methyl 1,2-Dihydro-4-hydroxy-6-nitro-1-oxoisoquinoline-3-carboxylate (5b)—Compound **4b** (0.612 g, 2 mmol) was treated as described above to give **5b**, which was recrystallized from dimethylformamide to afford yellow needles (0.52 g, 99%). mp >280°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm⁻¹: 3150, 1690, and 1655. Anal. Calcd. for C₁₁H₈N₂O₆: C, 50.00; H, 3.05; N, 10.60. Found: C, 49.91; H, 2.97; N, 10.48.

Methyl 1,2-Dihydro-4-methoxy-2-methyl-7-nitro-1-oxoisoquinoline-3-carboxylate (6a)—Ethereal diazomethane (1.1 eq.) was added to a suspension of **5a** (0.2 g, 0.76 mmol) in MeOH (10 ml) and the solution was evaporated *in vacuo*. The resulting residue was subjected to silica gel column chromatography (20 g)

using benzene-AcOEt (9: 1) as an eluent, and recrystallization from AcOEt-hexane gave **6a** as yellow needles (0.13 g, 59%). mp 153–155°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1730 and 1660. NMR (in CDCl_3) δ : 9.17 (1H, d, $J=3$ Hz, $\text{C}_8\text{-H}$), 8.45 (1H, dd, $J=9$ and 3 Hz, $\text{C}_6\text{-H}$), 7.86 (1H, d, $J=9$ Hz, $\text{C}_5\text{-H}$), 4.06 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), and 3.51 (3H, s, NCH_3). Anal. Calcd. for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_6$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.62; H, 4.16; N, 9.62.

Methyl 1,2-Dihydro-4-methoxy-2-methyl-6-nitro-1-oxoisoquinoline-3-carboxylate (6b)—Compound **5b** (0.2 g, 0.76 mmol) was treated as described above to give **6b**, which was recrystallized from AcOEt-hexane as yellow needles (0.13 g, 59%). mp 133–135°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1725 and 1660. NMR (in CDCl_3) δ : 8.52 (1H, d, $J=9$ Hz, $\text{C}_8\text{-H}$), 8.51 (1H, d, $J=2$ Hz, $\text{C}_5\text{-H}$), 8.20 (1H, dd, $J=9$ and 2 Hz, $\text{C}_7\text{-H}$), 4.02 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), and 3.50 (3H, s, NCH_3). Anal. Calcd. for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_6$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.39; H, 4.10; N, 9.66.

Methyl 1,2-Dihydro-4-hydroxy-8-nitro-1-oxoisoquinoline-3-carboxylate (9a)—Compound **8a** (0.612 g, 2 mmol) was treated as described above to give **9a**, which was recrystallized from dimethylformamide as yellow needles (0.48 g, 91%). mp 257–260° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3180, 1700, 1660, and 1550. Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_6$: C, 50.00; H, 3.05; N, 10.60. Found: C, 49.81; H, 3.11; N, 10.51.

Hydrolysis of 8b—Compound **8b** (0.612 g, 2 mmol) was suspended in a mixture of MeOH (6 ml) and conc. HCl (1.2 ml) and the mixture was stirred for 6 hr at room temperature. The precipitates were collected by suction, washed with MeOH, and then recrystallized from dimethylformamide to give methyl 1,2-dihydro-4-hydroxy-5-nitro-1-oxoisoquinoline-3-carboxylate (**9b**) as yellow needles (0.085 g, 16%). mp 261–262° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3140, 1690, 1650, and 1550. Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{N}_2\text{O}_6$: C, 50.00; H, 3.05; N, 10.60. Found: C, 49.87; H, 3.06; N, 10.49. The filtrate was concentrated *in vacuo* and the resulting residue was recrystallized from MeOH-ether to give 3-(α -amino- α -methoxycarbonylmethylidene)-4-nitrophthalide hydrochloride (**10**) as colorless needles (0.37 g, 62%). mp 161–167° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1760, 1720, 1680, and 1600. NMR (in $\text{DMSO}-d_6$) δ : 8.6–7.8 (3H, m, arom-H), 7.2–6.1 (3H, broad, $\text{NH}_2\cdot\text{HCl}$), and 3.94 (3H, s, OCH_3). MS m/e : 264 ($\text{M}^+ - \text{HCl}$). Anal. Calcd. for $\text{C}_{11}\text{H}_9\text{ClN}_2\text{O}_6 \cdot 3/2\text{H}_2\text{O}$: C, 40.31; H, 3.69; Cl, 10.82; N, 8.54. Found: C, 40.23; H, 3.57; Cl, 10.51; N, 8.52.

Methyl 5-(2-Carboxy-3,4,5,6-tetrachlorophenyl)oxazole-4-carboxylate (11)—The reaction of 3,4,5,6-tetrachlorophthalic anhydride (4.29 g, 15 mmol) with **2** (1.5 g, 15 mmol) was carried out in the presence of DBU (2.28 g, 15 mmol) using a method similar to that described in the previous paper⁴ to give **11**, which was recrystallized from AcOEt-hexane as colorless needles (5.27 g, 91%). mp 208–211°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1750 and 1730. NMR (in $\text{DMSO}-d_6$) δ : 8.79 (1H, s, oxazole-H) and 3.31 (3H, s, OCH_3). Anal. Calcd. for $\text{C}_{12}\text{H}_5\text{Cl}_4\text{NO}_5$: C, 37.43; H, 1.30; Cl, 36.83; N, 3.63. Found: C, 37.52; H, 1.28; Cl, 37.01; N, 3.52.

Hydrolysis of 11—Compound **11** (0.77 g, 2 mmol) was dissolved in a mixture of MeOH (6 ml) and conc. HCl (1.2 ml) and the solution was stirred for 6 hr at room temperature. The solvent was evaporated *in vacuo* and the resulting crystals were recrystallized from MeOH-ether to give 3-(α -amino- α -methoxycarbonylmethylidene)-4,5,6,7-tetrachlorophthalide hydrochloride (**12**) as colorless needles (0.71 g, 90%). mp 177–183° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1810 and 1750. MS m/e : 355 ($\text{M}^+ - \text{HCl}$). Anal. Calcd. for $\text{C}_{11}\text{H}_6\text{Cl}_5\text{NO}_4$: C, 33.57; H, 1.53; Cl, 45.05; N, 3.56. Found: C, 33.35; H, 1.74; Cl, 44.61; N, 3.38.

Saponification of Methyl 1,2-Dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylate (14)—Compound **14**⁴ (0.22 g, 1 mmol) was added to a solution of NaOH (0.16 g, 4 mmol) in 50% aqueous MeOH (6 ml) and the solution was refluxed for 5 hr. The solution was acidified with 10% HCl and the resulting precipitates were collected by suction and washed with H_2O to give 1,4-dioxo-1,2,3,4-tetrahydroisoquinoline (0.11 g, 68%). mp 255° (dec.) (Lit.,^{5a} >250°). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 1640 and 1600. NMR (in $\text{DMSO}-d_6$ and CF_3COOD) δ : 8.3–7.3 (4H, m, arom-H) and 2.55 (2H, broad, CH_2). MS m/e : 161 (M^+). Anal. Calcd. for $\text{C}_9\text{H}_7\text{NO}_2$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.00; H, 4.45; N, 8.47.

5-(2-Carboxyphenyl)oxazole-4-carboxylic Acid (15)—Methyl 5-(2-carboxyphenyl)oxazole-4-carboxylate (**13**)⁴ (2.47 g, 10 mmol) was added to a solution of KOH (2.24 g, 40 mmol) in MeOH (15 ml) and the solution was stirred for 3 hr at 50°. Water (10 ml) was added to this solution and the solvent was evaporated *in vacuo*. The resulting residue was acidified with conc. HCl (3 ml) and the crystals obtained were collected by suction then washed with H_2O . Recrystallization from 50% aqueous EtOH gave **15** as colorless prisms (2.15 g, 92%). mp 198–202° (dec.). IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3120, 1720, and 1680. NMR (in $\text{DMSO}-d_6$) δ : 8.47 (1H, s, oxazole-H) and 8.1–7.5 (4H, m, arom-H). Anal. Calcd. for $\text{C}_{11}\text{H}_7\text{NO}_5$: C, 56.66; H, 3.03; N, 6.01. Found: C, 56.38; H, 3.12; N, 6.01.

1,2-Dihydro-4-hydroxy-1-oxoisoquinoline-3-carboxylic Acid (16)—A mixture of **15** (1.8 g, 7.8 mmol), conc. HCl (3 ml), and MeOH (15 ml) was stirred for 6 hr at room temperature, the same treatment was applied and recrystallization from MeOH gave **16** as colorless needles (1.4 g, 88%). mp >280°. IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1} : 3150 and 1645. NMR (in $\text{DMSO}-d_6$) δ : 9.3–8.3 (2H, broad, NH and OH) and 8.4–7.5 (4H, m, arom-H). MS m/e : 205 (M^+). Anal. Calcd. for $\text{C}_{10}\text{H}_7\text{NO}_4$: C, 58.54; H, 3.44; N, 6.83. Found: C, 58.18; H, 3.49; N, 6.82.

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