A NEW ROUTE TO QUINOLONE AND INDOLE SKELETONES VIA KETONE- AND ESTER-IMIDE CYCLODEHYDRATION REACTIONS

Guncheol Kim*† and Gyochang Keum

Organic Chemistry Division, Hanhyo Institutes of Technology, Jeonmin-Dong 461-6, Yusong-gu, Taejon 305-390, Korea

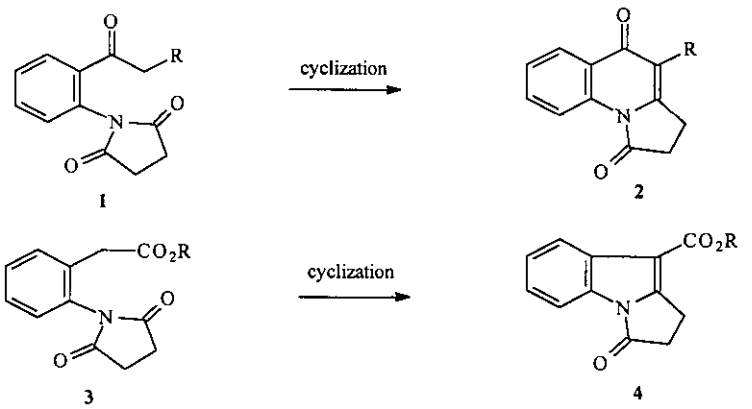
Abstract - Ketone-imide cyclodehydration reactions of aromatic succinimide and phthalimide (**7**, **8**) have afforded quinolone acids (**11**, **12**). Further transformation of the acids provided the corresponding esters (**13**, **14**) and vinylogous urethanes (**9**, **10**). Similarly, ester-imide cyclodehydration reactions of aromatic imide esters (**19**, **20**) have afforded indole acids (**23**, **24**).

Quinolones are well known compounds for antimicrobial[1] and antitumoral activities,[2] and quinolonecarboxylates have emerged as a major class of clinically useful and marketed antibacterial agents.[1] Enormous structural modifications around the skeletons have been developed by chemical alterations to improve therapeutic values of the agents.[3] As for the synthesis of quinolones, the quinolonecarboxylates have been commonly prepared by intramolecular condensation of properly functionalized enamines of aromatic halides.[3, 4a] On the other hand, quinolones which do not contain the 3-carboxylic group have been mainly prepared by intermolecular condensation of anilines with keto-esters followed by thermal cyclization [2, 4b, c] As we used a thioimide for cyclization to a pyrrolizidine structure,[5] we have tried to expand the cyclization reaction of imide toward quinolone or indole skeletones.

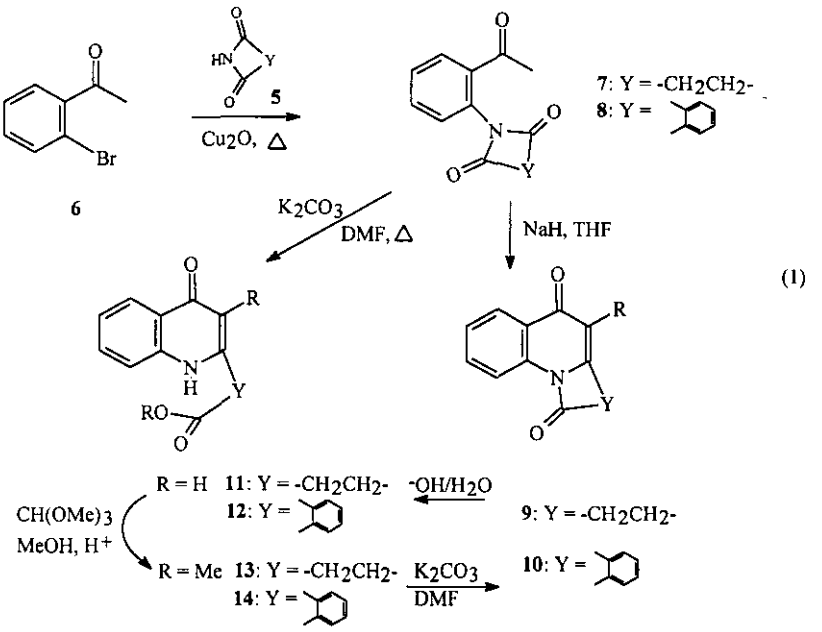
In this paper, we describe a new route to quinolone and indole derivatives by using aromatic keto-imide compounds. Cyclodehydration of a ketone-imide (**1**) with base was envisioned to afford 4-quinolones (**2**), and the same reaction of phenylacetate imides (**3**) would provide **4** which have indole moieties. Similar cyclodehydrations of carbonyl imides have been applied to provide vinylogous urethanes,[6] although activated thioimides were used for the purpose.

First, for the synthesis of quinolone derivatives, simple aromatic ketone imides (**7**) and (**8**) have been prepared by a coupling reaction of 2′-bromoacetophenone (**6**) with succinimide and phthalimide as described[7] in 84% and 99% yields respectively. The standard condition found for

Scheme 1

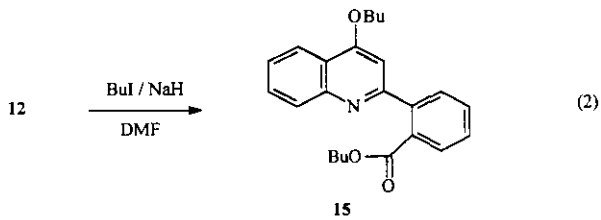


the desired cyclization was heating a solution of the ketone-imide (**7**) or (**8**) in DMF at 80-90 °C with 1.5 equivalents of potassium carbonate overnight. Quinolone acids (**11**) and (**12**) were obtained reproducibly in good yields[8a] (90% and 74% yields respectively). To isolate the reaction intermediate (**9**), compound (**7**) was treated with 1 equivalent of sodium hydride in anhydrous THF. Direct concentration followed by prompt silica gel column chromatography provided 24% yield of **9**,[8b] which was readily converted to **11** or **13** on the addition of a catalytic amount of

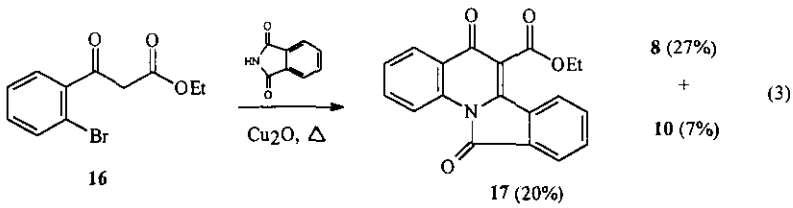


base in either aqueous or methanol solution. From the acid (**11**) was prepared ester (**13**) in 60% yield by treating with trimethyl orthoformate in MeOH in the presence of a catalytic amount of sulfuric acid, while **12** gave a mixture of **14** (17%) and **10** (79%) under the same conditions. Complete conversion of **14** to **10** in the mixture was observed by treating with K_2CO_3 in DMF. However, **13** was cyclized to **9** in less than 5% yield.

The quinoloneacid (**12**) was converted to quinoline derivatives by alkylation with alkyl halide and NaH in DMF. Methylation of **12** with methyl iodide afforded a mixture of products, *O*-methyl methyl ester (33%), *N*-methyl methyl ester (20%), and recyclized product (**10**) (30%). However, treatment with butyl iodide afforded only the *O*-alkylated 4-butoxyquinoline (**15**) in 87% yield.[9]



In order to prepare a precursor of new quinolonecarboxylate derivatives, we heated a neat mixture of ethyl bromobenzoylacetate[4a] (**16**) and phthalimide at 100 °C overnight. This reaction provided no trace of the expected precursor benzoylacetate imide. Instead, the imide (**8**) was separated as the major product (27%) along with **17**[8] (20%) and **10** (7%). The unexpected product (**17**) was assumed to be formed by a thermal cyclodehydration reaction after the coupling reaction. As for the formation of compounds (**17**) and (**10**), it is not clear whether

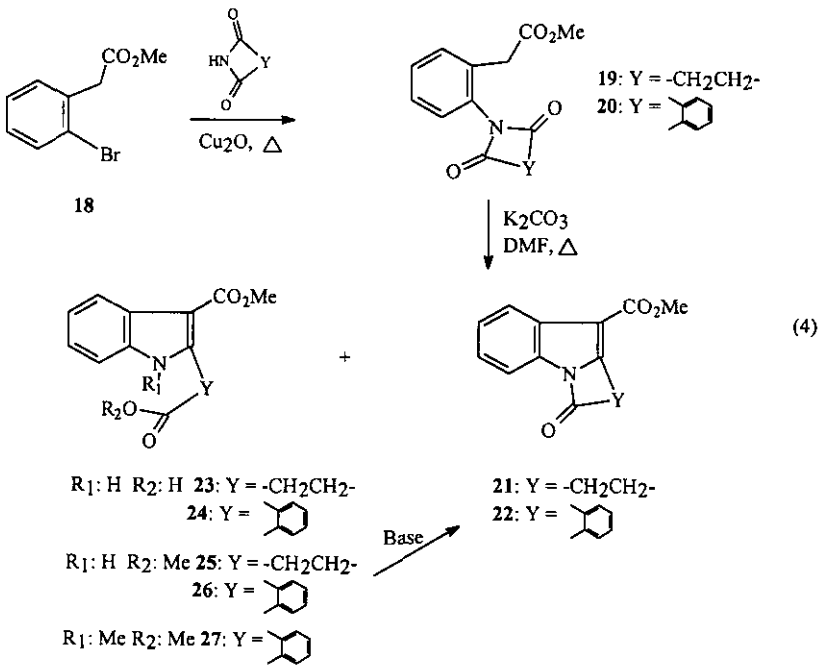


the deethoxycarbonylation of a keto ester group preceded the coupling step. We speculate, however, that the coupling reaction was followed by the deethoxycarbonylation process, from which were formed **10** as well as **8**. In contrast, the compound (**10**) was not detected at all from the coupling reaction of **6** and phthalimide as shown in eq. 1. The coupling reaction in the

absence of Cu_2O afforded the same products in much lesser yields.

For the construction of indole skeletons, precursors (**19**) and (**20**) have been prepared by the same reaction. Reactions of 2-bromophenylacetate with the imides were sluggish under even harsh conditions.[7] However, the reactions of compounds (**19**) and (**20**) under the standard condition, heating a DMF solution at 80-90 °C with 1.5 equivalents K_2CO_3 overnight, proceeded smoothly to afford the expected indole derivatives. A mixture of **21** and **23** (8% and 76% yields respectively) from **19** and compound (**24**) (89%) from **20** could be separated. Esters (**25**) and (**26**) were also readily obtained by esterifications of **23** and **24** as in the case of the quinolone acids (63% and 99% respectively). Conversion of **25** to **21** (36%) was much slower than that of **26** to **22**[8] (quantitative yield) with the base, K_2CO_3 in DMF, while direct addition of methyl iodide (2.4 equiv.) after heating **20** in DMF with the base afforded compound (**27**) (30% yield) as well as **22** (59% yield).

In summary, new quinolones and indoles have been prepared in moderate yields *via* cyclodehydration of carbonyl imides. Although several reliable pathways to the skeletones have been available, this new route will hopefully prove to be of valuable synthetic utility.



EXPERIMENTAL

General. All commercial chemicals were used as obtained without further purification, and all

solvents were carefully dried and distilled by standard methods prior to use. Column chromatography was carried out on silica gel 60 (E. Merck, 230-400 mesh) with the flash technique. Melting points were determined on a Rheometric Scientific Differential Scanning Calorimeter (DSC). NMR spectra were determined on a Bruker ARX 300 spectrometer. Chemical shifts are reported in δ ppm relative to $(CH_3)_4Si$ for ^1H and ^{13}C NMR. Coupling constants, J are reported in Hz. IR spectra (cm^{-1}) were obtained on a JASCO FT/IR-300E spectrometer. GCMS analysis was performed on a Hewlett-Packard 5890 series-MSD 5971series equipped with a capillary column (HP 1, 25 m). High resolution mass spectra (HRMS) were determined on a VG70-VSEQ mass spectrometer.

2-Carboxyethyl-4-quinolone (11) To a 10 mL of DMF solution of ketone imide (**7**) (1.50 g, 6.91 mmol) was added K_2CO_3 (1.43 g, 10.37 mmol). After stirring at 80 - 90 °C overnight, the solvent was removed under vacuum. The residue was dissolved in H_2O and loaded on Dowex 50X8-400 (H^+) ion exchange resin. After washing with H_2O, 1N HCl and H_2O, the resin was eluted with 1N NH_4OH. Removal of solvent under vacuum provided quinolone acid (**11**) (1.35 g, 90 %) as a brownish solid: mp 205 °C (EtOAc); ^1H NMR (CD_3OD) δ 8.19 (dd, J =8.1, 1.1, 1H), 7.67 (ddd, J =8.3, 7.0, 1.4, 1H), 7.57 (d, J =8.3, 1H), 7.37 (ddd, J =8.1, 6.9, 1.1, 1H), 6.26 (s, 1H), 2.99, 2.66 (2t, J =7.2, 4H); ^{13}C NMR (CD_3OD) δ 181.0, 179.5, 157.0, 141.7, 133.9, 126.1, 125.6, 119.7, 109.0, 36.7, 31.4; IR (KBr) 1641, 1599, 1558, 1504, 1413 cm^{-1}; HRMS(EI) calcd for $C_{12}H_{11}NO_3$ (M^+) 217.2242, found 217.2248.

2-(2′-Carboxyphenyl)-4-quinolone (12) Quinolone acid (**12**) was prepared by the same procedure of **11** from **8** in 74 % yield, and HCl salt of **12** was obtained as a white solid in aqueous media by acidification with 3N HCl. Spectra of **12** as a free amine: mp 225 °C (EtOAc); ^1H NMR (CD_3OD) δ 8.21 (d, J = 8.4, 1H), 7.75-7.6 (m, 3H), 7.5 (m, 3H), 7.35 (m, 1H), 6.50 (s, 1H); ^{13}C NMR (CD_3OD) δ 180.5, 176.2, 155.2, 141.9, 134.0, 133.5, 131.1, 130.6, 130.2, 130.0, 129.1, 126.0, 125.3, 120.1, 110.5; IR (KBr) 3398 (br), 1639, 1581, 1510, 1469, 1388 cm^{-1}; HRMS(EI) calcd for $C_{16}H_{11}NO_3$ (M^+) 247.2530, found 247.2537.

2-Carbomethoxyethyl-4-quinolone (13) The quinolone acid (**11**) (140 mg, 0.64 mmol) was dissolved in MeOH (2 mL) and was treated with trimethyl orthoformate (106 mL, 2.46 mmol) and H_2SO_4 (cat. amount). After stirring overnight at reflux, the reaction mixture was concentrated under reduced pressure. H_2O was added and the solution was extracted with CH_2Cl_2. The extracts were dried over $MgSO_4$, and the solvent was removed on the rotatory evaporator. Purification of the mixture by chromatography on silica gel (CH_2Cl_2:MeOH=10:1) gave the quinolone ester (**13**) (90 mg, 60 %) as a white solid: mp 167 °C (EtOAc); ^1H NMR ($CDCl_3$)

δ 12.6 (s, 1H), 8.38 (d, *J* =8.1, 1H), 7.74 (d, *J* =8.3, 1H), 7.61 (ddd, *J* =1.2, 8.1, 8.3, 1H), 7.35 (t, *J* =8.3, 1H), 6.29 (s, 1H), 3.62 (s, 3H), 3.07 (t, *J* =7.4, 2H), 2.83 (t, *J* =7.4, 2H); ^{13}C NMR ($CDCl_3$) δ 179.6, 173.4, 152.6, 140.2, 132.2, 125.5, 124.8, 124.0, 117.9, 108.2, 52.2, 32.8, 28.9; IR (KBr) 1732, 1638, 1600, 1546, 1498, 1442, 1201 cm^{-1}; MS (M-MeOH+1) 200; HRMS(EI) calcd for $C_{13}H_{13}NO_3$ (M^+) 231.2511, found 231.2518.

2-(2′-Carbomethoxyphenyl)-4-quinolone (14) In the esterification of acid (**12**) following the same procedure of **13**, ester (**14**) was obtained in 17 % yield while cyclized compound (**10**) was obtained in 79 % yield. Data of **14**: mp 201 °C (EtOAc); ^{1}H NMR (CD_3OD) δ 8.33 (d, *J* =7.8, 1H), 8.11 (dd, *J* =7.5, 1.5, 1H), 7.8-7.5 (m, 5H), 7.44 (t, *J* =7.6, 1H), 6.30 (s, 1H), 3.73 (s, 3H); ^{13}C NMR (CD_3OD) δ 169.7, 166.0, 156.9, 139.7, 134.9, 133.7, 133.1, 131.4, 131.3, 131.2, 129.5, 127.9, 124.0, 120.3, 119.9, 106.4, 52.9, 29.8; IR (KBr) 2506, 1712, 1643, 1596, 1495, 1364, 1284 cm^{-1}; MS (M-MeOH) 248; HRMS(EI) calcd for $C_{17}H_{13}NO_3$ (M^+) 279.2951, found 279.2960.

5-Oxo-5*H*-isoindolo[2,3-*a*]quinolin-11-one (10) Cyclized compound (**10**) was obtained in 79 % yield (with 17% of ester (**14**)) in the esterifcation process of acid (**12**), and ester (**14**) was converted to **10** completely by the following procedure. To a 3 mL solution of quinolone ester (**14**) (57 mg, 0.204 mmol) in DMF was added K_2CO_3 (42.3 mg, 0.306 mmol). After stirring at rt overnight, the solvent was removed under high vacuum. The residue was chromatographed on silica gel with 3:1 solution of hexane-ethyl acetate to afford quinolone lactam (**10**) (50 mg, quantitative yield) as a yellow solid: mp 267 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 9.11 (d, *J* =8.6, 1H), 8.29 (dd, *J* =1.5, 8.0, 1H), 7.98 (d, *J* =7.4, 1H), 7.86 (d, *J* =7.5, 1H), 7.76 (m, 2H), 7.67 (dt, *J* =1.1, 8.5, 1H), 6.76 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 179.9, 166.0, 145.9, 137.6, 135.1, 134.5, 134.4, 132.3, 128.8, 126.8, 125.7, 125.2, 124.7, 121.7, 117.7, 106.8; IR (film) 1739, 1650, 1580, 1479, 1407 cm-1; MS (M+1) 248; HRMS(EI) calcd for $C_{16}H_9NO_2$ (M^+) 247.2530, found 247.2537.

2,3-Dihydro-3-oxo-1*H*-pyrrolo[1,2-*a*]quinolin-9-one (9) Ester (**13**) was cyclized to **9** in less than 5 % yield under the same condition as that of the synthesis of **10**. The following procedure gave a better yield. To a 5 mL of THF solution of imide (**7**) (1.04 g, 4.80 mmol) was added NaH (288 mg of a 60 % dispersion in oil, 7.2 mmol) at 0 °C. After stirring at rt for 4 h, the solvent was removed on the rotatory evaporator. The residue was chromatographed on silica gel with 1:2 solution of hexane-ethyl acetate and then ethyl acetate to give lactam (**9**) (Rf = 0.1 in hexane : ethyl acetate = 1:2, 228 mg, 24 %) as a white solid: mp 195 °C (Hexane); 1H NMR ($CDCl_3$) δ 9.08 (d, *J* =8.6, 1H), 8.32 (dd, *J* =7.9, 1.3, 1H), 7.70 (dt, *J* =8.4, 1.4, 1H), 7.50 (t, *J* = 7.8, 1H), 6.25 (s, 1H), 3.20 (m, 2H), 2.92 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 179.2, 175.6, 155.1, 136.9, 133.3, 126.8, 126.6, 125.5, 118.1, 109.3, 53.7, 29.4, 23.1; IR (film) 1759, 1635, 1595, 1471, 1265, 1145,

1084 cm^{-1}; MS (M+1) 200; HRMS(EI) calcd for $C_{12}H_9NO_2$ (M^+) 199.2090, found 199.2096.

2-(2'-Carbobutoxyphenyl)-4-butoxyquinoline (15) To a 2 mL solution of quinolone acid (12) (249 mg, 0.94 mmol) in DMF was added NaH (113 mg of a 60 % dispersion in oil, 2.82 mmol) at 0 °C. After stirring at rt for 30 min, n-butyl iodide (0.32 mL, 2.8 mmol) was added, and the mixture was stirred overnight at rt. The solvent was removed under vacuum. To the residue was added ethyl acetate, and the organic solution was washed with saturated $NaHCO_3$ solution. The organic layer was dried over $MgSO_4$, and the solvent was removed on the rotatory evaporator. The residue was chromatographed on silica gel (Hexane/EtOAc = 4:1) to yield compound (15) (309 mg, 87%): mp 57 °C (Hexane); ^1H NMR ($CDCl_3$) δ 8.21 (d, J =8.6, 1H), 8.01 (d, J =8.4, 1H), 7.87 (d, J =8.3, 1H), 7.8-7.4 (m, 5H), 6.88 (s, 1H), 4.21 (t, J =6.4, 2H), 4.02 (t, J =6.5, 2H), 1.94 (m, 2H), 1.62 (m, 2H), 1.21 (m, 2H), 1.03 (t, J =7.3, 3H), 0.94 (m, 2H), 0.59 (t, J =7.3, 3H); ^{13}C NMR ($CDCl_3$) δ 169.1, 161.9, 160.4, 149.1, 142.2, 132.2, 131.2, 130.10, 130.05, 130.0, 129.3, 128.6, 125.6, 122.0, 120.6, 101.0, 68.5, 165.2, 31.2, 30.6, 19.6, 19.1, 14.1, 13.6; IR (KBr) 2956, 1723, 1574, 1107, 1063 cm^{-1}; MS (M+1) 378; HRMS(EI) calcd for $C_{24}H_{27}NO_3$ (M^+) 377.4833, found 377.4849.

12-Carboethoxy-5-oxo-5*H*-isoindolo[2,3-*a*]-quinolin-11-one (17) Phthalimide (0.90 g, 6.0 mmol), ethyl bromobenzoylacetate (1.10 g, 4.06 mmol) and Cu_2O (1.34 g, 9.3 mmol) were heated at 100 °C overnight. After cooling to rt, the reaction mixture was filtered through a pad of silica gel, eluting with 1:1 solution of hexane-ethyl acetate. The filtrate was evaporated and chromatographed on silica gel (hexane:ethyl acetate = 3:1 then 2:1) to afford quinolone carboxylate (17) (259 mg, 20%), ketone imide (8) (265 mg, 27%) and quinolone (10) (71 mg, 7%). Data of 17: mp 188 °C (Hexane); ^1H NMR ($CDCl_3$) δ 9.16 (d, J =8.6, 1H), 8.32 (dd, J =1.5, 8.1, 1H), 8.1-7.7 (m, 5H), 7.45 (dt, J =1.0, 8.0, 1H), 4.59 (q, J =7.1, 2H), 1.47(t, J =7.1, 3H); ^{13}C NMR ($CDCl_3$) δ 176.8, 165.8, 165.1, 142.9, 137.4, 135.0, 134.4, 133.6, 132.8, 129.0, 127.1, 126.2, 125.6, 124.3, 123.7, 117.9, 62.8, 14.4; IR (film) 1731, 1633, 1480, 1404, 1297 cm^{-1}; MS (M+1) 320; HRMS(EI) calcd for $C_{19}H_{13}NO_4$ (M^+) 319.3165, found 319.3173.

2-(2'-Carboxyphenyl)-3-carbomethoxyindole (24) To a DMF solution (2 mL) of ester imide (20) (275 mg, 0.93 mmol) was added K_2CO_3 (193 mg, 1.40 mmol). After stirring at 80 - 90 °C overnight, the solvent was removed under high vacuum. The residue was chromatographed on silica gel (CH_2Cl_2:CH_3OH = 7:1) to provide indole acid (24) (245 mg, 89%) as a white solid. HCl salt form of 24 was also obtained by acidifing with 1N HCl until precipitation complete. The white precipitate was filtered and dried under vacuum. Product was obtained as a white solid (258 mg, 86%). Spectra of 24 as a free amine: mp 313 °C (EtOAc, decomp); ^1H NMR (CD_3OD)

δ 8.06 (d, *J* =7.1, 1H), 7.81 (d, *J* =7.0, 1H), 7.40 (m, 3H), 7.17 (m, 3H), 3.60 (s, 3H); ^{13}C NMR (CD_3OD) δ 177, 168.5, 147.7, 138, 137.3, 133.6, 132.7, 130.9, 130.6, 130.0, 128.7, 123.9, 122.9, 122.6, 113.0, 105.3, 51.8; IR (KBr) 1677, 1549, 1451, 1208 cm^{-1}; HRMS(EI) calcd for $C_{17}H_{13}NO_4$ (M^+) 295.2945, found 295.2953.

2-Carboxyethyl-3-carbomethoxyindole (23) 76%; mp 111 °C (EtOAc); ^{1}H NMR (CD_3OD) δ 7.98 (m, 1H), 7.34 (m, 1H), 7.13(m, 2H), 3.90 (s, 3H), 3.40 (t, *J* =7.7, 2H), 2.72 (t, *J* =7.7, 2H); ^{13}C NMR (CD_3OD) δ 178.0, 167.6, 148.1, 135.6, 127.5, 122.7, 121.8, 121.4, 111.7, 103.4, 51.1, 34.5, 23.9; IR (KBr) 3294, 1722, 1656, 1547, 1456, 1198, 1091 cm^{-1}; HRMS(EI) calcd for $C_{13}H_{13}NO_4$ (M^+) 247.2505, found 247.2511.

2-Carbomethoxyethyl-3-carbomethoxyindole (25) The compounds (**25**, **26**) were prepared as described in the preparation of **13** and **14** in 61% and 99% yields respectively. mp 85 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 9.21 (s, 1H), 8.10 (m, 1H), 7.34 (m, 1H), 7.20 (m, 2H), 3.93 (s, 3H), 3.69 (s, 3H), 3.49 (t, *J* =6.2, 2H), 2.81 (t, *J* =6.2, 2H); ^{13}C NMR ($CDCl_3$) δ 174.9, 166.3, 146.6, 134.6, 126.7, 122.7, 121.7, 121.5, 111.0, 104.1, 52.0, 50.8, 33.1, 22.1; IR (film) 1725, 1695, 1680, 1548, 1456 cm^{-1}; MS (M-MeOH+1) 230; HRMS(EI) calcd for $C_{14}H_{15}NO_4$ (M^+) 261.2774, found 261.2781.

2-(2′-Carbomethoxyphenyl)-3-carbomethoxyindole (26) mp 158 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 8.95 (br s, 1H), 8.17 (d, *J* =7.9, 1H), 7.92 (dd, *J* =7.6, 1.4, 1H), 7.6-7.3 (m, 3H), 7.3-7.1 (m, 3H), 3.70 (s, 3H), 3.64 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.0, 166.4, 144.4, 135.8, 133.8, 131.6, 131.5, 130.0, 129.0, 127.2, 122.9, 121.8, 121.7, 111.6, 104.7, 52.3, 50.8; IR (film) 3300 (br), 1726, 1447, 1286, 1210, 1130, 1087 cm^{-1}; MS (M-MeOH) 278; HRMS(EI) calcd for $C_{18}H_{15}NO_4$ (M^+) 309.3214, found 309.3222.

11-Carbomethoxy-5-oxo-5*H*-isoindolo[2,3-*a*]indole (22) To a 3 mL of DMF solution of indole ester (**26**) (37 mg, 0.12 mmol) was added K_2CO_3 (25 mg, 0.18 mmol). After stirring at rt overnight, the solvent was removed under high vacuum. The residue was chromatographed on silica gel with 4:1 solution of hexane-ethyl acetate to afford indole lactam (**22**) (33 mg, quantitative yield) as a yellow solid: mp 197 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 8.30 (dd, *J* =6.9, 0.7, 1H), 7.97 (dd, *J* =7.9, 0.8, 1H), 7.89 (dt, *J* =7.0, 0.8, 1H), 7.76 (dt, *J* =7.5, 0.8, 1H), 7.57 (dt, *J* =7.6, 0.9, 1H), 7.41 (dt, *J* =7.5, 1.0, 1H), 7.32 (dt, *J* =7.9, 1.1, 1H), 7.22 (dt, *J* =7.9, 1.0, 1H), 4.01 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 164.2, 162.8, 143.5, 134.5, 133.5, 133.4, 132.7, 131.3, 130.4, 126.8, 125.9, 125.3, 124.7, 123.2, 113.1, 108.8, 51.7; IR (film) 1748, 1712, 1596, 1442, 1360, 1283 cm^{-1}; MS (M+1) 278; HRMS(EI) calcd for $C_{17}H_{11}NO_3$ (M^+) 277.2792, found 277.2800.

1-Methyl-2-(2′-carbomethoxyphenyl)-3-carbomethoxyindole (27) Direct addition of MeI

(681 mg, 4.8 mmol) to the resulting reaction mixture of **20** (580 mg, 2.0 mmol) afforded compound (**22**) (330 mg, 59 %) as well as **27** (190 mg, 30 %). Data of **27**: mp 141 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 8.22 (m, 1H), 8.14 (dd, *J* = 7.6, 1.6, 1H), 7.64 (dt, *J* =7.5, 1.6, 1H), 7.55 (dt, *J* =7.5, 1.6, 1H), 7.4-7.2 (m, 4H), 3.68 (s, 3H), 3.64 (s, 3H), 3.49(s, 3H); ^{13}C NMR ($CDCl_3$) δ 166.5, 165.5, 146.4, 136.7, 133.2, 131.9, 131.5, 131.1, 130.3, 129.2, 126.5, 122.6, 121.9, 121.8, 109.6, 104.6, 52.2, 50.6, 30.6; IR (film) 2949, 1727, 1696, 1469, 1397, 1265, 1193, 1103 cm^{-1}; MS (M) 323; HRMS(EI) calcd for $C_{19}H_{17}NO_4$ (M^+) 323.3483, found 323.3492.

9-Carbomethoxy-2,3-dihydro-3-oxo-1*H*-pyrrolo[1,2-*a*]indole (21) The ester (**25**) (207 mg, 0.79 mmol) was allowed to react as in the preparation of **22** to afford **21**(71 mg, 36 %): mp 155 °C (Hexane); ^{1}H NMR ($CDCl_3$) δ 8.07 (m, 2H), 7.36 (m, 2H), 3.94 (s, 3H), 3.43 (m, 2H), 3.13 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 172.2, 164.9, 152.6, 132.1, 130.5, 125.4, 124.6, 121.8, 113.7, 106.1 51.6, 34.2, 21.7; IR (KBr) 1756, 1699, 1588, 1434, 1340, 1218, 1149, 1110, 1076 cm^{-1}; MS (M+1) 230; HRMS(EI) calcd for $C_{13}H_{11}NO_3$ (M^+) 229.2352, found 229.2359.

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Present address: Department of Chemistry, Chungnam National University, Taejon 305-764, Korea

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7. T. Yamamoto and Y. Kurata, *Can. J. Chem.*, 1983, **61**, 86. Heating the neat mixture of **6** and each imide at 100 °C for 2 days provided **7** and **8** respectively. The mixture of **18** and succinimide was heated at 230 °C for 36 h yielding 21% of **19**, while that of **18** and phthalimide yielding 47% of **20** under 210 °C heating for 1 day.
8. (a) We assume that the water liberated in the process of dehydration should already attack the vinylogous urethane intermediates (**9**, **10**, **21**, and **22**) to give the corresponding acids. (b) We assume that treatment with NaH in anhydrous THF would afford a lesser chance of the presence of H_2O in the reaction condition.
9. Butylation of **11** with BuI also afforded 4-butoxyquinoline butyl ester as a single product in *ca.* 60% yield. A single intermediate detected during the alkylation with BuI was confirmed to be a 4-butoxyquinoline acid, which indicated that *O*-alkylation should be followed by esterification. Though we have not tried halides other than the two discussed, we assume higher halides than MeI would follow the same trend.[2c]

Received, 28th October, 1996