HETEROCYCLES, Vol. 55, No. 7, 2001, pp. 1291 - 1299, Received, 18th April, 2001

REACTION OF 1-BENZENESULFONYLINDOLE-2,3-DICARBOXYLIC ANHYDRIDE WITH WITTIG REAGENTS: SYNTHESIS OF PYRROLO[1,2-*a*]-INDOLES AND CYCLOPENT[*b*]INDOLE

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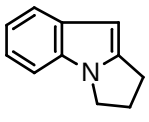
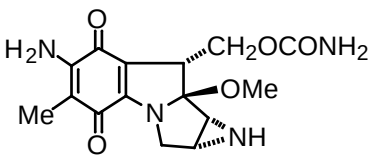
Abstract - Treatment of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride with methylenetriphenylphosphorane gave the corresponding ylide. After esterification of the carboxyl group and removal of the benzenesulfonyl group of the ylide, the obtained ylide was reacted with aldehydes to yield α,β-unsaturated ketones, which were converted to pyrrolo[1,2-*a*]indoles. We also examined the reactivity of the anhydride with (carbethoxymethylene)triphenylphosphorane and (carbethoxyethylidene)triphenylphosphorane.

Pyrrolo[1,2-*a*]indoles,[1-3] including mitomycin C, have received much attention because of their biological importance and were synthesized by reaction of 2-(benzotriazoylmethyl)indole with alkyl dihalide in the presence of a base,[4] Dieckmann condensation of 1-substituted indole–2-caboxylic acid ester,[5] radical cyclization of 1-substituted 3-formylindoles,[6] 2-(toluenesulfonyl)indoles,[7] and 2-bromoindoles.[8] Recently, we have reported a reaction of 1-benzylindole-2,3-dicarboxylic anhydride with methylene-triphenylphosphorane ($Ph_3P=CH_2$) and its application to the synthesis of cyclopent[*b*]indoles.[9] However, the pyrrolo[1,2-*a*]indoles were not prepared because debenzylation of the 1-benzylindole derivatives was quite difficult. In this paper we show a reaction of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride with Wittig reagents and its application to the synthesis of the pyrrolo[1,2-*a*]indoles.



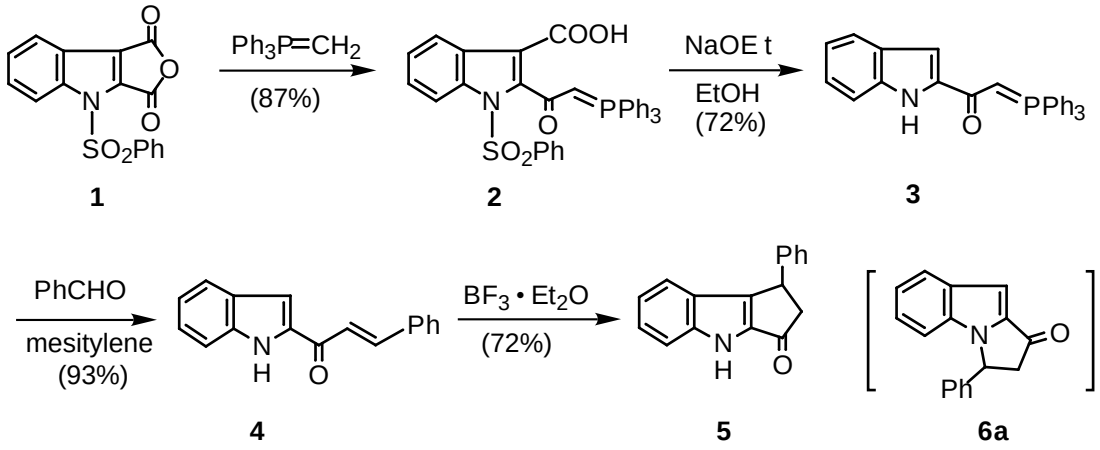
pyrrolo[1,2-*a*]indole



mitomycin C

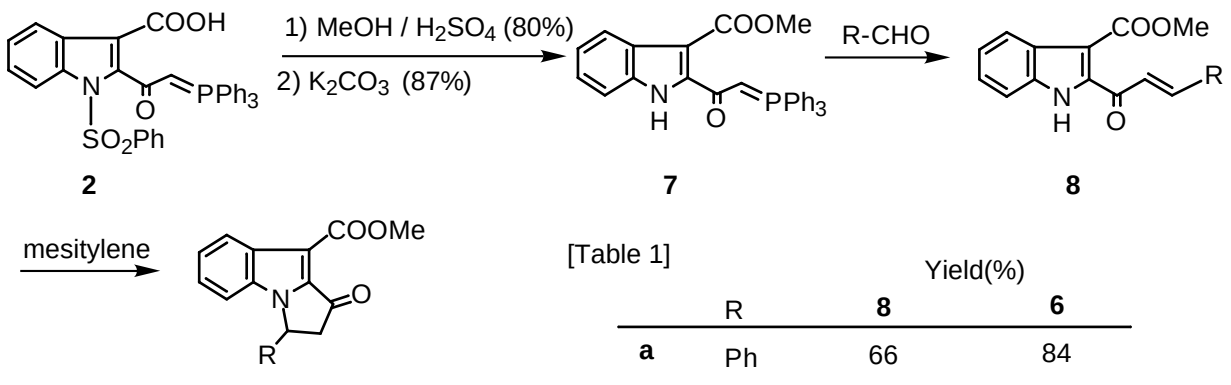
1-Benzenesulfonylindole-2,3-dicarboxylic anhydride (**1**) was reacted with $Ph_3P{=}CH_2$ to give a ylide (**2**)(87%), which was converted to 3-unsubstituted ylide (**3**) (72%) by treatment of sodium ethoxide. Reaction of **3** with benzaldehyde in refluxing mesitylene gave α,β-unsaturated ketone (**4**)[10] in 93% yield. Treatment of **4** with boron trifluoride etherate provided cyclopent[*b*]indol-3-one (**5**) in 72% yield. Several efforts were made to isolate the pyrrolo[1,2-*a*]indole (**6a**) under various conditions, but **6a** was not isolated. The cyclization of **4** to the 3-position of an indole is similar to our result[9] and Bergman's result.[11] However, if a substituent is positioned at the 3-position in an indole ring of **4**, cyclization of **4** to an indole nitrogen is given priority over the 3-position of that by this substituent. [Scheme 1]

[Scheme 1]



The ylide (**7**) was prepared from **2** by esterification (80%), followed by hydrolysis (87%). Reaction of **7** with benzaldehyde (R = Ph) provided α,β-unsaturated ketone (**8a**)(66%), which was led to pyrrolo[1,2-*a*]indole (**6a)** in 84% yield by heating in mesitylene. **6a** was also directly obtained from **7** in 74% yield. In a similar manner, **7** was reacted with aldehydes to give α,β-unsaturated ketones (**8b**,**c**), which were converted to the corresponding to pyrrolo[1,2-*a*]indoles (**6b**,**c**). [Scheme 2][Table 1]

[Scheme 2]



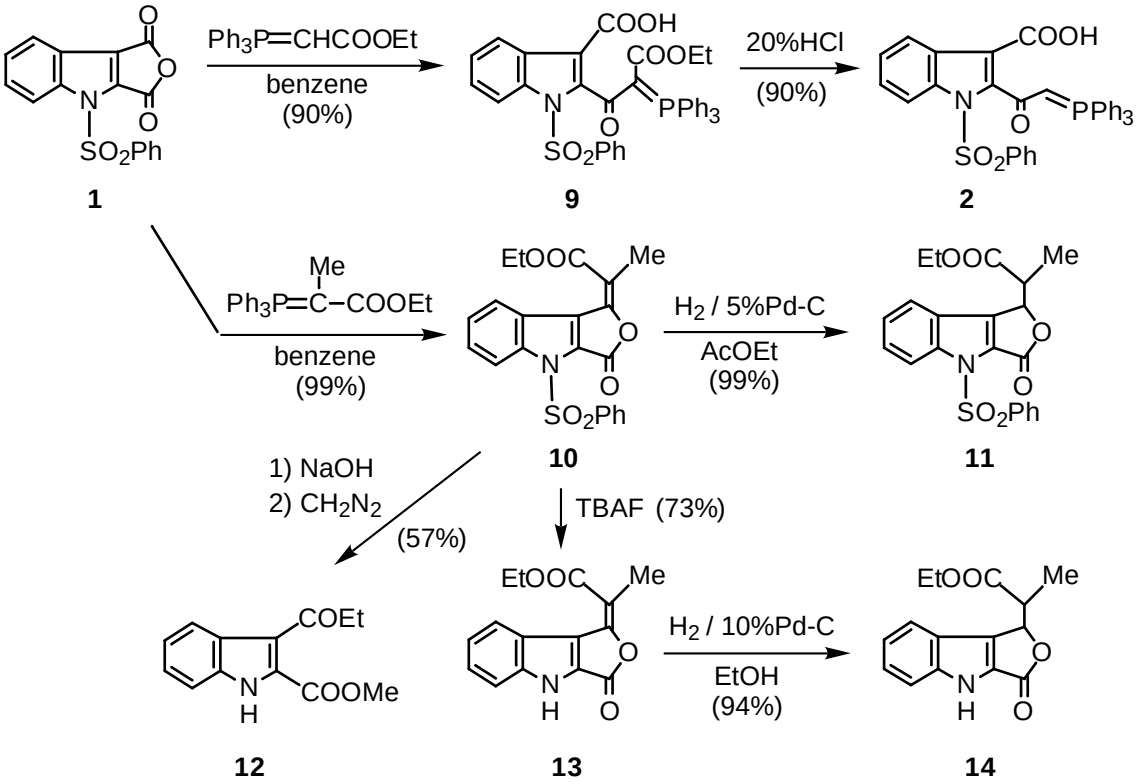
a: R = Ph, **b**: R = Me, **c**: R = H

[Table 1]

		Yield(%)	
	R	**8**	**6**
a	Ph	66	84
b	Me	63	67
c	H	51	17

The ylide (**2**) was also obtained from **1** with (carbethoxyethylidene)triphenylphosphorane (Ph_3P=CHCOOEt) in hot benzene, followed by acid treatment in 81% yield. However, (carbethoxyethylidene)triphenylphosphorane, a disubstituted stabilized ylide, reacted with a carbonyl group at the 3-position in **1** to give the enol lactone (**10**) as the sole product, which was converted to lactone (**11**) by catalytic hydrogenation over 5% palladium on activated carbon in high yield. **10** was changed to methyl 3-propionoylindole-2-carboxylte (**12**) by basic hydrolysis treatment, followed by diazomethane in 57% yield. Treatment of **10** with teterabutylammonium fluoride (TBAF)[13] gave the debenzylated product (**13**), which was also transformed to the lactone (**14**) by catalytic hydrogenation over 10% palladium on activated carbon in high yield. The stereochemistry of the carbon-carbon bond in **13** was assigned on the basis that the proton of the 8-position (δ 8.20) in **13** appeared in lower field compared with the proton (δ 7.20-7.68) in **14**.[9,14]

[Scheme 3]



EXPERIMENTAL

Melting points were determined on Yanagimoto micromelting point apparatus and are uncorrected. The ^{1}H-NMR spectra were determined on a JEOL JNM-GSX 270 spectrometer using tetramethylsilane as an internal standard. The IR spectra were recorded with a JASCO FT/IR-7000 spectrophotometer. The high MS were recorded on a JOEL JMX-HX100 spectrometer. Column chromatography was performed on E. Merck silica gel 60 (70-230 mesh or 230-400 mesh). Tetrahydrofuran (THF) was distilled from sodium and benzophenone prior to use. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride prior to use.

[2-(1-Benzenesulfonyl-3-carboxyindol-2-yl)-2-oxoethylidene]triphenylphosphorane (2)

From methylenetriphenylphosphorane

A solution of 1-benzenesulfonylindole-2,3-dicarboxylic anhydride (**1**) [12] (0.98 g, 3 mmol) in THF (60 mL) was added to a solution of methylenetriphenylphosphorane [prepared from methyltriphenylphosphonium bromide (3.24 g, 9.1 mol) and *n*-butyllithium (5.8 mL of a 1.56 M *n*-hexane solution, 9 mmol) at rt for 20 min] in THF (15 mL) at 0℃ under argon and the mixture was stirred for 3 h. The reaction mixture was acidified with 10% hydrochloric acid and extracted with CH_2Cl_2. The organic extracts were washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (CH_2Cl_2 : MeOH = 50 : 1) to give [2-(1-benzenesulfonyl-3-carboxyindol-2-yl)-2-oxoethylidene]triphenylphosphorane (**2**) (1.57 g, 87%) as a pale yellow solid, mp 163-165℃ (*n*-hexane-$CHCl_3$). IR (Nujol) ν: 1773, 1694, 1542 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 7.16-7.84 (26H, m, aromatic protons), 8.10 (1H, dt, *J* = 8, 1 Hz, H-7 or H-4), 8.36 (1H, dt, *J* = 8, 1 Hz, H-4 or H-7). HRMS *m/z* (M^+) calcd for $C_{35}H_{27}NO_5PS$: 604.1347. Found: 604.1342.

From (carbethoxymethylene)triphenylphosphorane

A solution of the anhydride (**1**)(0.98 g, 3 mmol) and (carbethoxymethylene)triphenylphosphorane (1.04 g, 3 mmol) in benzene (30 mL) was refluxed for 1 h under argon. The reaction mixture was concentrated to give a residue, which was purified by column chromatography (CH_2Cl_2 : MeOH = 50:1) to give [2-(1-benzenesulfonyl-3-carboxyindol-2-yl)-1-ethoxycarbonyl-2-oxoethylidene]triphenylphosphorane (**9**) (1.83 g, 90%) as a white solid, mp 188-190°C (decomp)(*n*-hexane-$CHCl_3$). IR (Nujol) ν: 1675, 1542 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 0.48 (3H, t, *J* = 7 Hz, CH_2CH_3), 3.62-3.75 (2H, m, CH_2CH_3), 7.20-8.15 (24H, m, aromatic protons). *Anal.* Calcd for $C_{38}H_{30}NO_7PS$: C, 67.55; H, 4.88; N, 2.07. Found: C, 67.46; H, 4.54; N, 2.03.

A suspension of [2-(1-benzenesulfonyl-3-carboxyindol-2-yl)-1-ethoxycarbonyl-2-oxoethylidene]triphenylphosphorane (**9**) (1.35 g, 2 mmol) in 20% hydrochloric acid (40 mL) was refluxed for 3.5 h under argon. The reaction mixture was neutralized to pH 7 with 10% sodium hydroxide solution, and extracted with $CHCl_3$. The combined extracts were washed with water, dried over Na_2SO_4, and concentrated to give a residue, which was purified by column chromatography ($CHCl_3$: MeOH = 50 : 1) to yield **2** (1.09 g, 90%).

[2-(Indol-2-yl)-2-oxoethylidene]triphenylphosphorane (3)

The ylide (**2**) (1.57 g, 2.6 mmol) was added to a solution of sodium (359 mg, 16 mmol) in EtOH (25 mL). The mixture was refluxed for 5 h and neutralized with 10% hydrochloric acid. The precipitates were collected by filtration to yield [2-(indol-2-yl)-2-oxoethylidene]triphenylphosphorane (**3**) (0.78g, 72%) as a pale yellow solid, mp 206℃ (decomp) (*n*-hexane-CH_2Cl_2). IR (Nujol) ν: 3180, 1505 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ: 4.50 (1H, d, *J* = 24 Hz, $CHPPh_3$), 6.85 (1H, br s, H-3), 6.92-7.80 (20H, m, aromatic protons). *Anal.* Calcd for $C_{28}H_{22}NOP$: C, 80.18; H, 5.29; N, 3.33. Found: C, 79.93; H, 5.34; N, 3.51.

(*E*)-1-(Indol-2-yl)-3-phenyl-2-propen-1-one (4)

A solution of [2-(indol-2-yl)-2-oxoethylidene]triphenylphosphorane (**3**) (754 mg, 1.8 mmol) and benzaldehyde (0.20 mL, 2.0 mmol) in mesitylene (9 mL) was refluxed for 3 h under argon. The solvent was evaporated off to give a residue, which was purified by column chromatography (*n*-hexane : AcOEt =

5 : 1) to afford (*E*)-1-(indol-2-yl)-3-phenyl-2-propen-1-one (**4**) (414 mg, 93%) as a yellow solid, mp 222-225°C (MeOH)(lit.,[10] mp 226-227°C). IR (Nujol) ν: 3280, 1651 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 7.16-7.50 (7H, m, aromatic protons), 7.54 (1H, d, *J* = 16 Hz, COCH=C*H*Ph), 7.64-7.78 (3H, m, aromatic protons), 7.92 (1H, d, *J* = 16 Hz, COC*H*=CH), 9.38 (1H, br s, NH). *Anal.* Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.54; H, 5.53; N, 5.59.

1-Phenyl-3-oxo-1,2,3,4-tetrahydrocyclopent[*b*]indole (5)

Boron trifluoride etherate (26 μL, 0.4 mmol) was added to a solution of (*E*)-1-(indol-2-yl)-3-phenyl-2-propen-1-one (**4**)(25 mg, 0.1 mmol) in CH_2Cl_2 (3 mL) under argon and the mixture was refluxed for 1 h. The reaction mixture was basified with saturated aqueous $NaHCO_3$ solution and extracted with $CHCl_3$. The combined extracts were washed with water, dried over Na_2SO_4, and evaporated. The residue was purified by column chromatography ($CHCl_3$) to give 1-phenyl-3-oxo-1,2,3,4-tetrahydrocyclopent[*b*]indole (5) (18 mg, 72%) as a white solid, mp 245-248°C (AcOEt). IR (Nujol) ν: 3204, 1678 cm^{-1}; ^{1}H-NMR(DMSO-d_6) δ: 2.71 (1H, dd, *J* = 18, 3 Hz), 3.49 (1H, dd, *J* = 18, 7 Hz), 4.74 (1H, dd, *J* = 7, 3 Hz), 6.98-7.50 (9H, m, aromatic protons), 11.67 (1H, br s, NH). *Anal.* Calcd for $C_{17}H_{13}NO$: C, 82.57; H, 5.30; N, 5.66. Found: C, 82.50; H, 5.48; N, 5.56.

[2-(3-Methoxycarbonylindol-2-yl)-2-oxoethylidene]triphenylphosphorane (7)

A solution of the ylide (**2**)(600 mg, 1.0 mmol) and conc. sulfuric acid (1 mL) in MeOH (10 mL) refluxed for 11 h. The solution was basified with 10% KOH solution and extracted with CH_2Cl_2. The combined extracts were washed with water, dried over Na_2SO_4, and concentrated to provide a residue, which was purified by column chromatography (CH_2Cl_2 : AcOEt = 5:1) to give [2-(3-methoxycarbonylindol-2-yl)-2-oxoethylidene]triphenylphosphorane (494 mg, 80%) as a pale yellow solid, mp 106-107°C (*n*-hexane-CH_2Cl_2). IR (Nujol) ν: 1720, 1538 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.60 (3H, s, OCH_3), 4.08 (1H, d, *J* = 24 Hz, C*H*=PPh_3), 7.24-8.24 (24H, m, aromatic protons). HRMS *m/z* (M^+) calcd for $C_{36}H_{29}NO_5PS$: 618.1504. Found: 618.1479.

A solution of [2-(3-methoxycarbonylindol-2-yl)-2-oxoethylidene]triphenylphosphorane (477 mg, 0.8 mmol) and K_2CO_3 (442 mg, 3.2 mmol) in MeOH (24 mL) and H_2O (6 mL) was refluxed for 30 min. Water was added to the mixture and the aqueous mixture was extracted with CH_2Cl_2. The extracts were washed with water, dried over Na_2SO_4, concentrated, and purified by column chromatography (CH_2Cl_2 : AcOEt = 2:1) to give **7** (331 mg, 87%) as a pale yellow solid, mp 247-248°C (decomp)(*n*-hexane-CH_2Cl_2). IR (Nujol) ν: 3194, 1693, 1527 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.97 (3H, s, OCH_3), 6.18 (1H, d, *J* = 26 Hz, C*H*=PPh_3), 7.16-8.18 (19H, m, aromatic protons), 10.20 (1H, br s, NH). *Anal.* Calcd for $C_{30}H_{24}NO_3P$: C, 75.46; H, 5.07 ; N, 2.93. Found: C, 75.16; H, 5.21; N, 3.08.

(*E*)-1-(3-Methoxycarbonylindol-2-yl)-3-phenyl-2-propen-1-one (8a)

A solution of the ylide (**7**) (48 mg, 0.1 mmol) and benzaldehyde (11 μL, 0.11 mmol) in toluene (1.0 mL) was refluxed for 23 h. The solvent was evaporated off to afford a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 5:1) to give (*E*)-1-(3-methoxycarbonylindol-2-yl)-3-phenyl-2-propen-1-one (**8a**) (20 mg, 66%) as a yellow solid, mp 158-161℃ (MeOH). IR (Nujol) ν: 3292, 1711, 1647 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 4.03 (3H, s, OCH_3), 7.26-7.72 (8H, m, aromatic protons), 7.90 (1H, d, *J* = 16 Hz, COC*H*=CH), 8.14 (1H, d, *J* = 16 Hz, COCH=C*H*Ph), 8.19 (1H, d, *J* = 8, 1 Hz, H-4), 9.99

(1H, br s, NH). *Anal.* Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95 ; N, 4.59. Found: C, 74.50; H, 5.14; N, 4.62.

(*E*)-1-(3-Methoxycarbonylindol-2-yl)-2-buten-1-one (8b)

A mixture of the ylide (**7**) (334 mg, 0.7 mmol), $NaHCO_3$ (88 mg, 1.1 mmol), and acetaldehyde (0.78 mL, 0.11 mmol) in CH_2Cl_2 (7.0 mL) was stirred for 28 h. The insoluble material was filtered off and the filtrate was evaporated off to give a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 5:1) to give (*E*)-1-(3-methoxycarbonylindol-2-yl)-2-buten-1-one (**8b**) (108 mg, 63%) as a yellow solid, mp 124-125℃ (*n*-hexane-AcOMe). IR (Nujol) ν: 3304, 1714, 1652 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 2.02 (3H, dd, *J* = 6.5, 1 Hz, CH_3), 4.01 (3H, s, OCH_3), 7.19 (1H, dd, *J* = 15, 6.5 Hz, COCH=C*H*CH_3), 7.24-7.48 (4H, m, aromatic protons), 8.15 (1H, dd, *J* = 8, 1 Hz, H-4), 9.72 (1H, br s, NH). *Anal.* Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39 ; N, 5.76. Found: C, 69.19; H, 5.34; N, 5.77.

(*E*)-1-(3-Methoxycarbonylindol-2-yl)-2-propen-1-one (8c)

A mixture of the ylide (**7**) (954 mg, 2.0 mmol), $NaHCO_3$ (252 mg, 3.0 mmol), and 37% formalin (0.22 mL, 2.9 mmol) in CH_2Cl_2 (20 mL) was stirred for 2 h. Water was added to the mixture and the aqueous solution was extracted with CH_2Cl_2. The extracts were washed with water, dried over Na_2SO_4, concentrated to give a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 5:1) to give (*E*)-1-(3-methoxycarbonylindol-2-yl)-2-propen-1-one (**8c**) (232 mg, 51%) as a yellow solid, mp 112-113℃ (*n*-hexane-AcOMe). IR (Nujol) ν: 3324, 1715, 1644 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 4.01 (3H, s, OCH_3), 5.91 (1H, dd, *J* = 11, 2 Hz, COCH=C*H*$_2$), 6.55 (1H, dd, *J* = 17, 2 Hz, COCH=C*H*$_2$), 7.25-7.50 (3H, m, aromatic protons), 7.55 (1H, dd, *J* = 17, 11 Hz, COC*H*=CH_2), 8.16 (1H, br d, *J* = 8 Hz, H-4), 9.53 (1H, br s, NH). *Anal.* Calcd for $C_{13}H_{11}NO_3$: C, 68.11; H, 4.84; N, 6.11. Found: C, 68.11; H, 4.89; N, 6.19.

Methyl 2,3-Dihydro-3-phenyl-1-oxo-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (6a)

From (*E*)-1-(3-Methoxycarbonylindol-2-yl)-3-phenyl-2-propen-1-one (8a)

A suspension of (*E*)-1-(3-methoxycarbonylindol-2-yl)-3-phenyl-2-propen-1-one (**8a**) (31 mg, 0.1 mmol) in mesitylene (0.5 mL) was refluxed for 5 h. The solvent was evaporated off to afford a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 3:1) to give **6a** (26 mg, 84%) as a yellow solid, mp 196-198℃ (MeOH). IR (Nujol) ν: 1720, 1700 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 3.13 (1H, dd, *J* = 18, 4 Hz), 3.75 (1H, dd, *J* = 18, 8 Hz), 4.02 (3H, s, CH_3), 5.79 (1H, dd, *J* = 8, 4 Hz), 6.92-7.40 (8H, m, aromatic protons), 8.37 (1H, dt, *J* = 8, 1 Hz, H-4). *Anal.* Calcd for $C_{19}H_{17}NO_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.66; H, 5.09; N, 4.69.

From [2-(3-Methoxycarbonylindol-2-yl)-2-oxoethylidene]triphenylphosphorane (7)

A solution of [2-(3-methoxycarbonylindol-2-yl)-2-oxoethylidene]triphenylphosphorane (**7**) (144 mg, 0.3 mmol) and benzaldehyde (33 μL, 0.33 mmol) in mesitylene (1.5 mL) was refluxed for 3.5 h. The solvent was evaporated off to afford a residue, which was purified by column chromatography (*n*-hexane : AcOEt = 3:1) to give **6a** (69 mg, 74%).

Methyl 2,3-Dihydro-3-methyl-1-oxo-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (6b)

A suspension of (*E*)-1-(3-methoxycarbonylindol-2-yl)-2-buten-1-one (**8b**) (49 mg, 0.2 mmol) in mesitylene (2 mL) was refluxed for 5.5 h. The solvent was evaporated off to afford a residue, which was

purified by column chromatography (*n*-hexane : AcOEt = 1:1) to give methyl 2,3-dihydro-3-methyl-1-oxo-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (**6b**) (33 mg, 67%) as a yellow solid, mp 126-127°C (MeOH). IR (Nujol) ν: 1729, 1702 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.71 (3H, d, *J* = 7 Hz, CH_3), 2.87 (1H, dd, *J* = 19, 3 Hz, one of CH_2), 3.50 (1H, dd, *J* = 19, 7.5 Hz, one of CH_2), 3,99 (3H, s, CH_3), 4.89-5.02 (1H, m), 7.31-7.55 (3H, m, aromatic protons), 8.38 (1H, dt, *J* = 8, 1 Hz, H-4). *Anal.* Calcd for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.19; H, 5.34; N, 5.77.

Methyl 2,3-Dihydro-1-oxo-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (6c)

A suspension of (*E*)-1-(3-methoxycarbonylindol-2-yl)-2-propen-1-one (**8c**) (23 mg, 0.1 mmol) in mesitylene (3 mL) was refluxed for 2 h. The solvent was evaporated off to afford a residue, which was purified by column chromatography ($CHCl_3$) to give methyl 2,3-dihydro-1-oxo-1*H*-pyrrolo[1,2-*a*]indole-9-carboxylate (**6c**) (4 mg, 17%) as a solid, mp 160-161°C (MeOH). IR (Nujol) ν: 1733, 1703 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 3.30 (2H, dd, *J* = 6.5, 5.5 Hz), 3.99 (3H, s, CH_3), 4.49 (2H, t, *J* = 6.5 Hz), 7.33-7.51 (3H, m, aromatic protons), 8.37 (1H, dt, *J* = 8, 1 Hz, H-4). HRMS *m/z* (M^+) calcd for $C_{13}H_{11}NO_3$: 229.0739. Found: 229.0751.

Ethyl (*E*)-2-(4-Benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]indol-1-ylidene)-propionate (10)

A solution of the anhydride (**1**) (654 mg, 2 mmol) and (carbethoxyethylidene)triphenylphosphorane (796 mg, 2.2 mmol) in benzene (20 mL) was refluxed for 1 h under argon. The reaction mixture was evaporated off to give a residue, which was purified by column chromatography (CH_2Cl_2) to afford ethyl (*E*)-2-(4-benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]indol-1-ylidene)propionate (**10**) (817 mg, 99%) as a pale yellow solid, mp 192-193°C (AcOEt). IR (Nujol) ν: 1790, 1720 and 1632 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.36 (3H, t, *J* = 7 Hz, CH_2CH_3), 2.24 (3H, s, CH_3), 4.41 (2H, q, *J* = 7 Hz, CH_2CH_3), 7.36-7.66 (6H, m, aromatic protons), 7.97 (br d, *J* = 8 Hz, H-8 or H-5), 8.11-8.18 (2H, m, SO_2Ph), 8.40 (1H, dd, *J* = 9, 1 Hz, H-5). *Anal.* Calcd for $C_{21}H_{17}NO_6S$: C, 61.31; H, 4.16; N, 3.40. Found: C, 61.37; H, 4.27; N, 3.24.

Ethyl 2-(4-Benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]-indol-1-yl)propionate (11)

A suspension of ethyl (*E*)-2-(4-benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]indol-1-ylidene)-propionate (**10**) (164 mg, 0.4 mmol) and 5% Pd-C (16 mg) in AcOEt (12 mL) was stirred for 30 h under hydrogen. The catalyst was removed by filtration through Celite and the filtrate evaporated off. The residue was purified by column chromatography (*n*-hexane : AcOEt = 3:1) to give ethyl 2-(4-benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]-indol-1-yl)propionate (**11**) (164 mg, 99%) as a white solid, mp 96-97°C (EtOH). IR (Nujol) ν: 1785 and 1736 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.03 (3H, d, *J* = 7 Hz, $CHCH_3$), 1.22 (3H, t, *J* = 7 Hz, CH_2CH_3), 3.16 (1H, dq, *J* = 7, 5 Hz, $CHCH_3$), 4.20 (2H, q, *J* = 7, CH_2CH_3), 5.88 (1H, d, *J* = 5 Hz, OC*H*), 7.34-7.66 (6H, m, aromatic protons), 8.10-8.16 (2H, m, SO_2Ph), 8.39 (1H, br d, *J* = 8 Hz, H-5 or H-8). *Anal.* Calcd for $C_{21}H_{19}NO_6S$: C, 61.01; H, 4.63; N, 3.39. Found: C, 61.00; H, 4.63; N, 3.47.

Methyl 3-Propionylindol-2-carboxylate (12)

A suspension of ethyl 2-(4-benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-b]-indol-1-yl)propionate (**10**) (62 mg, 0.15 mmol) in 3N NaOH solution and MeOH (1:2) (2 mL) was refluxed for 1 h. The mixture was acidified with 10% hydrochloric acid, extracted with CH_2Cl_2. The extracts were washed with water, dried over Na_2SO_4, concentrated to give a residue. The residue was treated with diazomethane to provide a crude ester, which was purified by column chromatography (*n*-hexane : AcOEt = 5:1) to afford methyl 3-propionylindol-2-carboxylate (**12**) (20 mg, 57%) as a pale yellow solid,, mp 98-99 °C (*n*-hexane-ether). IR (Nujol) ν: 3302, 1725, 1644 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.25 (3H, t, *J* = 7 Hz, CH_2CH_3), 3.08 (2H, q, *J* = 7 Hz, CH_2CH_3), 3.98 (3H, s, OCH_3), 7.20-7.97 (4H, m, aromatic protons), 9.26 (1H, br s, NH). *Anal.* Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.54; H, 5.74; N, 6.05.

Ethyl (*E*)-2-(1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-ylidene)propionate (13)

To a solution of ethyl (*E*)-2-(4-benzenesulfonyl-1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-ylidene)-propionate (**10**) (411 mg, 1 mmol) in THF (40 mL) was added 1M TBAF in THF (1.0 mL, 1 mmol) at -30°C and the mixture was stirred for 0.5 h. The reaction mixture was acidified with 1% hydrochloric acid and extracted with CH_2Cl_2. The extracts were washed with water, dried over Na_2SO_4, and evaporated in vacuo. The residue was separated by chromatography (CH_2Cl_2) to afford ethyl (*E*)-2-(1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-ylidene)propionate (**13**) (198 mg, 73%) as a pale yellow solid, mp 194-195°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3264, 1756 and 1635 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.40 (3H, t, *J* = 7 Hz, CH_2CH_3), 2.26 (3H, s, CH_3), 4.43 (2H, q, *J* = 7 Hz, CH_2CH_3), 7.25-7.55 (3H, m, aromatic protons), 8.20 (1H, dd, *J* = 8, 0.5 Hz, H-4), 9.54 (1H, br s, NH). *Anal.* Calcd for $C_{15}H_{13}NO_4$: C, 66.41; H, 4.83; N, 5.17. Found: C, 66.38; H, 4.89; N, 5.15.

Ethyl 2-(1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-yl)propionate (14)

A suspension of ethyl (*E*)-2-(1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-ylidene)propionate (**13**) (109 mg, 0.4 mmol) and 10% Pd-C (33 mg) in EtOH (12 mL) was stirred at 40°C for 1 h under hydrogen. The catalyst was removed by filtration through Cerite and the filtrate evaporated off. The residue was purified by chromatography (*n*-hexane : AcOEt = 3:1) to give ethyl 2-(1,3-dihydro-3-oxo-4*H*-furo[3,4-*b*]indol-1-yl)propionate (**14**) (103 mg, 94%) as a white solid, mp 134-135°C (*n*-hexane-AcOEt). IR (Nujol) ν: 3242 and 1724 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, d, *J* = 7 Hz, $CHCH_3$), 1.31 (3H, t, *J* = 7 Hz, CH_2CH_3), 3.14 (1H, dq, *J* = 7, 6 Hz, $CHCH_3$), 4.29 (2H, q, *J* = 7, CH_2CH_3), 6.04 (1H, d, *J* = 6 Hz, OC*H*), 7.20-7.68 (4H, m, aromatic protons), 10.06 (1H, br s, NH). *Anal.* Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.93; H, 5.57; N, 5.14.

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