Preparation of Alkyl-Substituted Indoles in the Benzene Portion. Part 5.[1] Efficient Preparative Procedure for 4-Substituted Indole Derivatives

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An effective and short synthetic method for 4-substituted indole derivatives was developed based on the two sequential reactions, *i.e.* nucleophilic addition of carbanions to common precursor molecules, 3-(1,3-dioxolan-2-yl)-1-[1-(phenylsulfonyl)- and 1-[(4-methylphenyl)sulfonyl]-3-pyrrolyl]-1-propanones (5a, b), followed by the acid-induced cyclization reaction of the resulting adducts to form 4-substituted 1-(phenylsulfonyl)- and 1-[(4-methylphenyl)-sulfonyl]indole derivatives (4a, b). This new method makes it possible readily to synthesize important intermediates, such as methyl 1-(phenylsulfonyl)indole-4-carboxylate (15), 4-formyl-1-(phenylsulfonyl)indole (16), and methyl 1-(phenylsulfonyl)indole-4-acetate (17) for numerous indole alkaloids, as well as a potent dopamine agonist, 4-[2-(dipropylamino)ethyl]indole (21).

Keywords indole synthesis; 4-substituted indole derivative; acid-induced indole cyclization; dopamine agonist; 4-[2-(dipropylamino)ethyl]indole

Indole derivatives with a 4-alkyl substituent have been considered to be an important class of precursor molecules in the synthesis of ergot alkaloids and related compounds,[2,3] including ergolines (*e.g.*, lergotrile and pergolide) which have dopamine agonist properties in the central nervous system. These are useful in the treatment of Parkinson's disease and for the inhibition of prolactin release.[4] In connection with our studies on the synthesis of ergot alkaloids, we have reported several methods for assembling the 4-substituted indole system by developing an acid-induced cyclization reaction on suitably modified pyrrole precursors.[1,5] In particular, the compounds (**3b**) in Chart 1 became important intermediates leading to 4-substituted 1-[(4-methylphenyl)sulfonyl]indoles (**4b**) in high yields.[5d] These tertiary alcohols (**3b**) were previously prepared from 3-acyl-1-[(4-methylphenyl)sulfonyl]pyrroles (**2b**), which were obtained by the Friedel–Crafts reaction[6] on 1-[(4-methylphenyl)sulfonyl]pyrrole (**1b**) with acylating agents and aluminum chloride.

This procedure, however, has the limitation that a necessary acyl halide is not always readily available or compatible with the Friedel–Crafts reaction conditions. To overcome this defect, we employed crystalline 1-(1-arylsulfonyl-3-pyrrolyl)-3-(1,3-dioxolan-2-yl)-1-propanone (**5a** and **5b**) as common intermediates, which could be allowed to react with carbon nucleophiles (R^-) having a variety of functional groups to give the corresponding tertiary alcohols (**3**). Here we report a short and efficient route to the intermediates (**5**), a general method for synthesizing 4-substituted 1-(arylsulfonyl)indoles (**4**) from **5**, and an application to the synthesis of a potent dopamine agonist, 4-[2-(dipropylamino)ethyl]indole (**21**).

Preparation of Compounds (5a, b) The common precursor compounds (**5a, b**) were synthesized according to two procedures as illustrated in Chart 2. The first is a route by way of 1-arylsulfonyl-3-formylpyrroles (**7a, b**),[7,8] whose economical preparation is still difficult. Since the Friedel–Crafts formylation of 1-(arylsulfonyl)pyrrole (**1**) with dichloromethyl butyl ether and aluminum chloride only affords a 2-formyl derivative,[6a] good methods for a facile and efficient access to the 3-formyl derivatives (**7**) are urgently required.[9] We devised a three-step method from readily available 3-acetyl compounds (**6a**[6b] and **6b**[5d]) using cheap reagents in the following way. Compounds (**6a, b**) were oxidized with selenium oxide to afford 3-ketoaldehyde derivatives, which were directly reduced to diols with excess sodium borohydride. The resulting diols were treated with sodium metaperiodate to give **7a** and **7b** in 85% and 82% overvall yields, respectively. The aldehydes (**7a, b**) were then reacted with 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide to yield the corresponding secondary alcohols, which, upon oxidation with manganese dioxide, afforded the desired compounds (**5a, b**) in 80% and 79% yields.

In order to minimize the number of steps to **5**, we developed another procedure, which utilized the nitro functionality as an aldehyde equivalent. For this purpose, 4-nitrobutyryl chloride (**8**) was prepared from *tert*-butyl acrylate (**11**) by modifying the original process starting with

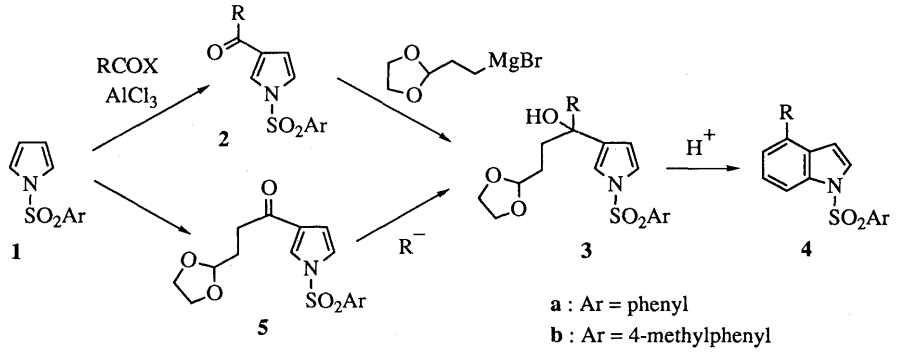


Chart 1

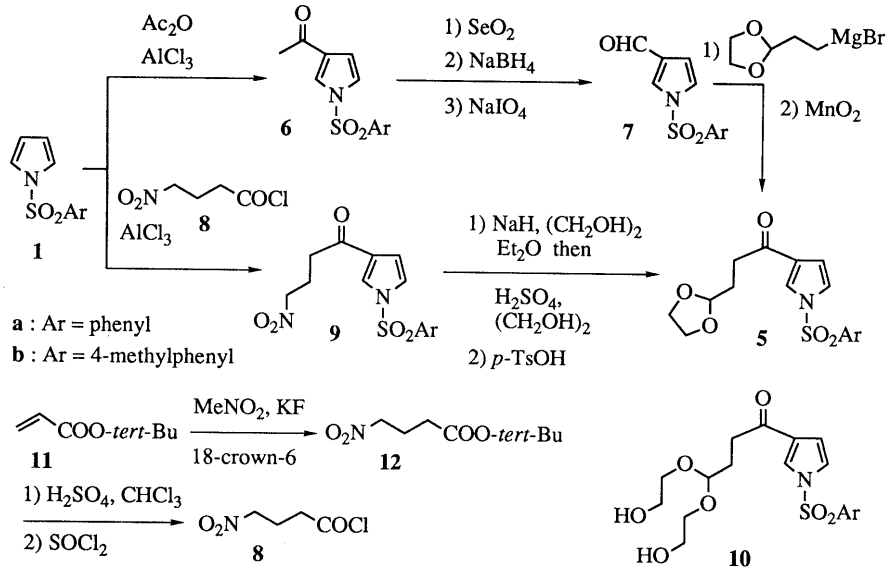
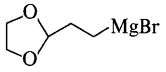
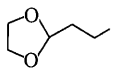
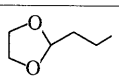
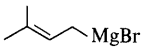
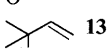
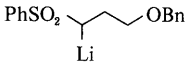
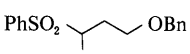
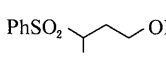
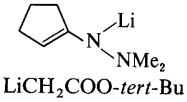
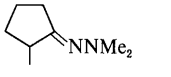
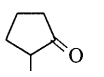
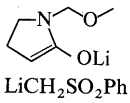
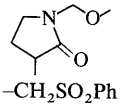
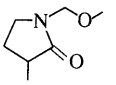


Chart 2

TABLE I. Synthesis of Variously Functionalized 4-Alkylindole Derivatives (**4a, b**) Using the Common Starting Materials (**3a, b**)

Run	Starting material	Nucleophile	3a, b		Cyclization[a] conditions	4a, b	
			R	Yield (%)		R	Yield (%)
1	**5a**			97	A		87
2	**5b**		 **13**	92	B		8[b]
3	**5a**	$LiC(SMe)_3$	$-C(SMe)_3$ **14**	91	D	–COOMe **15**	80
4	**5a**	MeSCHLiS(O)Me	MeSCHS(O)Me	—	B	–CHO **16**	69[c]
5	**5a**			99	B		81
6	**5b**			—	B		74[c]
7	**5a**	$LiCH_2COO$-*tert*-Bu	$-CH_2COO$-*tert*-Bu	98	C	$-CH_2COOMe$ **17**	91
8	**5a**	$LiCH_2CONPr_2$	$-CH_2CONPr_2$	96	B	$-CH_2CONPr_2$ **18**	93
9	**5a**			99	C		95
10	**5a**	$LiCH_2SO_2Ph$	$-CH_2SO_2Ph$	99	B	$-CH_2SO_2Ph$	97

a) Method A: *p*-TsOH in benzene, reflux; method B: 6% H_2SO_4 in 2-propanol, reflux; method C: 6% H_2SO_4 in MeOH, reflux; method D: H_2SO_4, $HgCl_2$ in MeOH–H_2O. *b*) This reaction gave compound (**19**) as a major product in 56% yield (Chart 3). *c*) Calculated from **5a** or **5b**.

methyl acrylate.[10] Michael addition[11] of nitromethane to **11** proceeded smoothly to provide *tert*-butyl 4-nitrobutyrate (**12**) in 71% yield. Treatment of **12** with a catalytic amount of sulfuric acid in refluxing chloroform gave the corresponding carboxylic acid, which was in turn converted into **8** on exposure to thionyl chloride in 90% yield. The resulting **8** was reacted with **1a** and **1b** in the presence of aluminum chloride[6,8] to obtain the 3-acylated products (**9a, b**) in 96% and 97% yields, respectively. These were then subjected to the Nef reaction[12] using ethylene glycol, followed by treatment with *p*-toluenesulfonic acid to afford directly the objective ketoacetals (**5a, b**) in 76% and 82% yields. The latter treatment was to effect a clean conversion of contaminants (**10a, b**), formed in small amounts as by-products during the Nef reaction, into the final compounds (**5a, b**). Thus the requisite compounds (**5a, b**) were prepared in only two operations from **1a, b**.

Synthesis of 4-Substituted Indole Derivatives Addition reactions of a variety of carbon nucleophiles to the carbonyl group of **5a** and **5b** proceeded readily to give the tertiary alcohols (**3a, b**), which were transformed into 4-substituted indole derivatives (**4a, b**) by treatment with acid (Table I). Indole cyclization conditions involved refluxing either in 6% sulfuric acid–containing alcohol[5c] or in benzene in the presence of *p*-toluenesulfonic acid.[5b]

In run 3, compound (**14**) obtained by the reaction with lithium tris(methylthio)methylide[13] was directly converted to methyl 1-(phenylsulfonyl)indole-4-carboxylate (**15**) in 80% yield *via* methanolysis of the tris(methylthio)methyl unit to the carboxylate function with the aid of mercuric chloride in addition to the usual acid condition. In run 4, the reaction of **5a** with the lithium salt of methyl methylsulfinylmethyl sulfide[14] provided an inseparable mixture of the diastereomers and the reagent employed,

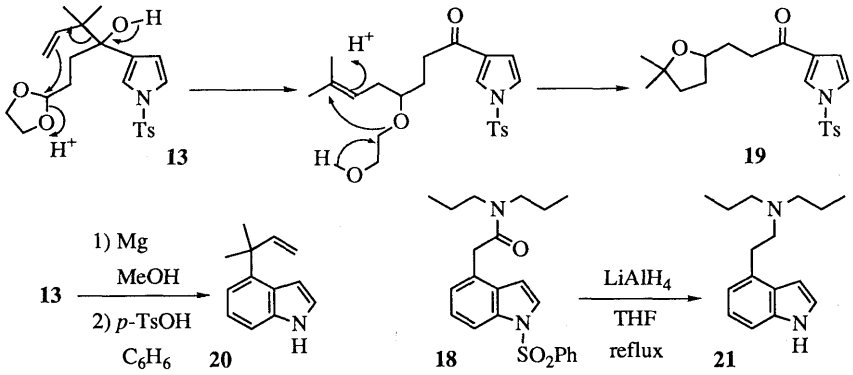


Chart 3

which was therefore submitted to the subsequent indole ring cyclization reaction, giving 4-formyl-1-(phenylsulfonyl)-indole (**16**) in 69% yield based on **5a**. The formyl group was saved from acetalization by the use of a bulky alcohol, 2-propanol in this reaction, and no detectable amount of a diisopropylacetal derivative was recognized.[15] The reaction in run 6 was also conducted in 2-propanol for the same reason as in run 4, and afforded 1-[(4-methylphenyl)sulfonyl]-4-(2-oxocyclopentyl)indole in 74% yield, calculated from **5b**. In run 7, the *tert*-butyl acetate moiety efficiently introduced during the carbanion reaction was converted completely to the methyl acetate unit by the cyclization reaction with 6% sulfuric acid in methanol.

The treatment of compound (**13**) in run 2 with 6% sulfuric acid–2-propanol provided the target molecule, 4-(1,1-dimethyl-2-propenyl)-1-[(4-methylphenyl)sulfonyl]indole in only 8% yield, together with a 56% yield of the compound (**19**), which was probably generated by the acid-promoted rearrangement of the 1,1-dimethyl-2-propenyl group, followed by the formation of the tetrahydrofuran ring (Chart 3).[5c] However, 4-(1,1-dimethyl-2-propenyl)-indole (**20**) was obtained in 73% yield from **13**, when the *p*-toluenesulfonyl group of **13** was removed in advance with magnesium in methanol at room temperature[5c] in order to enhance nucleophilicity of the pyrrole ring, and the resulting compound was refluxed for a few minutes in benzene in the presence of a catalytic amount of *p*-toluenesulfonic acid.

Advantages of the present indole synthesis are as follows. (1) Common precursor compounds (**5a** and **5b**) are readily available from **1a, b**, and are crystalline materials, which can be stored in a large amount. (2) Various kinds of carbanion reagents can be reacted with **5a** or **5b** and this versatility makes it possible to synthesize in only a few steps and in good overall yields 4-substituted indole derivatives having complex carbon side chains that are otherwise hardly accessible. (3) The synthesized indole derivatives (**4a, b**) carry *N*-protecting groups, so that they are far more stable than the indoles without protecting groups, and compatible with various derivatization reactions at the 4-substituents. At any time, *N*-sulfonyl groups of **4a, b** could be easily removed with magnesium in methanol,[5c] by alkaline hydrolysis, or by reduction with lithium aluminum hydride, depending on the reactivity of the functional groups on the alkyl side chains introduced and modified. (4) Compounds (**15**,[2d,16] **16**,[2c,17] and **17**)[18] are all of great value as important synthetic intermediates leading to many biologically active indole alkaloids.[17b,19]

Utility of the present method was confirmed by applying it to the synthesis of 4-[2-(dipropylamino)-ethyl]indole (**21**), a potent dopamine agonist.[20] Treatment of the above compound (**18**) (run 8) with lithium aluminum hydride under reflux for 2.5 h effected both reduction of carboxamide and removal of the protecting group to produce **21** in 85% yield, making 51% overall yield from **1a** in only five steps.[21] When amide enolates having suitable alkyl side chains are employed as a nucleophile (as in run 9), it should be possible to prepare compounds containing many kinds of 4-indolylethylamine fragment, which are required to elucidate the active portion in the ergolines responsible for their dopamine-like action.[21b]

In summary, we were able to attain a two-step synthesis of the 4-substituted indole system from the common intermediates (**5a, b**). Our method presented here offers a short and efficient approach to the regiospecific formation of 4-alkylindoles.

Experimental

Melting points were determined on Yanagimoto micro-melting point apparatus and are not corrected. Mass spectra (MS) and high resolution MS (HRMS) were recorded on a Hitachi RMS-4 or M-80B instrument at an ionizing voltage of 70 eV. Liquid secondary ion MS (LSIMS) were measured with a Hitachi M-90 using *m*-nitrobenzyl alcohol as the matrix. Infrared (IR) spectra were taken on a Hitachi 215 spectrophotometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were obtained on a Varian EM 390 (90 MHz) spectrometer in $CDCl_3$ with tetramethylsilane (TMS) as an internal reference. Column chromatography was conducted on silica gel, Fuji Davison BW 200 and preparative thin-layer chromatography (PTLC) was carried out on glass plates (20 × 20 cm) coated with Merck silica gel 60 PF_{254} (1 mm thick) (PTLC) or Merck Al_2O_3 60 PF_{254} (type E) (1 mm thick) (Al_2O_3 PTLC). Usual work-up refers to washing of the organic layers with water or brine, drying over anhydrous Na_2SO_4, and evaporating off the solvents under reduced pressure.

3-Formyl-1-(phenylsulfonyl)pyrrole (7a) A suspension of SeO_2 (888 mg, 8.00 mmol) in dioxane (10 ml) and H_2O (0.4 ml) was refluxed with stirring for 0.5 h to make a clear solution. After cooling of the above solution, a solution of 3-acetyl-1-(phenylsulfonyl)pyrrole (**6a**)[6] (500 mg, 2.00 mmol) in dioxane (4 ml) was added and the mixture was refluxed for 4 h. The reaction mixture was filtered through a Celite bed to remove the precipitated black solid, which was washed with CH_2Cl_2. The filtrate was concentrated *in vacuo* and the residue (730 mg) was dissolved in EtOH (18 ml). To this was added $NaBH_4$ (228 mg, 6.00 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. Saturated NH_4Cl–H_2O was added to this and the whole was extracted with CH_2Cl_2. Usual work-up and purification by column chromatography (5% MeOH–CH_2Cl_2) afforded 1-[1-(phenylsulfonyl)-3-pyrrolyl]-1,2-ethanediol (465.5 mg, 87%) as a colorless syrup. MS *m/z*: 267 (M^+). ^{1}H-NMR δ: 2.65—3.82 (4H, m), changed with D_2O to [3.51 (1H, dd, J=12, 7.5 Hz), 3.67 (1H, dd, J=12, 3.5 Hz)], 4.60 (1H, dd, J=7, 3.5 Hz), 6.18 (1H, dd, J=3.5, 1.5 Hz), 6.98—7.20 (2H, m), 7.28—7.94 (5H, m). A solution of $NaIO_4$ (432.5 mg, 2.02 mmol) in H_2O (3 ml) was added to a solution of the above diol

(432.5 mg, 1.62 mmol) in Et_2O (12 ml) at 0 °C, and the mixture was stirred at the same temperature for 40 min. H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by column chromatography [hexane–EtOAc (3 : 1)] gave **7a**[7] (373 mg, 98%) as a colorless amorphous solid. *Anal.* Calcd for $C_{11}H_9NO_3S$: C, 56.16; H, 3.86; N, 5.96. Found: C, 56.15; H, 4.02; N, 6.20. MS *m/z*: 235 (M^+). IR (KBr) cm^{-1}: 1680. ^{1}H-NMR δ: 6.66 (1H, dd, J=3.5, 1.5 Hz), 7.14 (1H, dd, J=3.5, 2 Hz), 7.38—7.69 (3H, m), 7.76 (1H, dd, J=2, 1.5 Hz), 7.81—8.03 (2H, m), 9.77 (1H, s). 2,4-Dinitrophenylhydrazone: Red needles, mp 186—187 °C (CH_2Cl_2–MeOH). *Anal.* Calcd for $C_{17}H_{13}N_5O_6S$: C, 49.16; H, 3.15; N, 16.86. Found: C, 48.90; H, 3.15; N, 16.67.

3-Formyl-1-[(4-methylphenyl)sulfonyl]pyrrole (7b) Similarly prepared from **6b** *via* 1-[1-(4-methylphenyl)sulfonyl-3-pyrrolyl]-1,2-ethanediol. The diol: 86% from **6b**. Colorless syrup. HRMS Calcd for $C_{13}H_{15}NO_4S$: 281.0722. Found: 281.0736. ^{1}H-NMR δ: 2.27 (3H, s), 3.41 (1H, dd, J=12, 7 Hz), 3.56 (1H, dd, J=12, 4 Hz), 3.69—4.36 (2H, br s, OH), 4.54 (1H, dd, J=7, 4 Hz), 6.15 (1H, dd, J=3, 1.5 Hz), 6.97—7.16 (2H, m), 7.16, 7.66 (A_2B_2, J=8.5 Hz). The aldehyde (**7b**): 95% from the diol. Colorless amorphous solid. *Anal.* Calcd for $C_{12}H_{11}NO_3S$: C, 57.81; H, 4.45; N, 5.62. Found: C, 57.65; H, 4.44; N, 5.74. MS *m/z*: 249 (M^+). IR (KBr) cm^{-1}: 1680. ^{1}H-NMR δ: 2.37 (3H, s), 6.65 (1H, dd, J=3.5, 1.5 Hz), 7.17 (1H, dd, J=3.5, 2 Hz), 7.29 and 7.80 (A_2B_2, J=8.5 Hz), 7.81 (1H, dd, J=2, 1.5 Hz), 9.80 (1H, s). 2,4-Dinitrophenylhydrazone: Orange fine needles, mp 235—237 °C (CH_2Cl_2–MeOH). *Anal.* Calcd for $C_{18}H_{15}N_5O_6S$: C, 50.34; H, 3.52; N, 16.31. Found: C, 50.14; H, 3.53; N, 16.14.

Preparation of 3-(1,3-Dioxolan-2-yl)-1-[1-(phenylsulfonyl)-3-pyrrolyl]-1-propanone (5a) from 7a A solution of **7a** (202 mg, 0.859 mmol) in THF (5 ml) was treated at −20 °C for 10 min under an Ar atmosphere with the Grignard reagent (1.83 ml, 1.72 mmol), prepared from Mg (90 mg, 3.70 mg atom) and 2-(1,3-dioxolan-2-yl)ethyl bromide (0.66 ml, 5.87 mmol) in THF (3.4 ml). The reaction was quenched with saturated NH_4Cl–H_2O and the whole was extracted with CH_2Cl_2, Usual work-up and purification by PTLC [benzene–EtOAc (3 : 2)] yielded 3-(1,3-dioxolan-2-yl)-1-[1-(phenylsulfonyl)-3-pyrrolyl]-1-propanol (283 mg, 98%) as colorless prisms, mp 80.5—81.5 °C (CH_2Cl_2–MeOH). *Anal.* Calcd for $C_{16}H_{19}NO_5S$: C, 56.96; H, 5.68; N, 4.15. Found: C, 56.97; H, 5.68; N, 4.43. MS *m/z*: 337 (M^+). ^{1}H-NMR δ: 1.57—1.99 (4H, m), 2.57 (1H, d, J=4.5 Hz, OH), 3.66—4.07 (4H, m), 4.46–4.73 (1H, m), 4.84 (1H, dd, J=4, 4 Hz), 6.24 (1H, dd, J=2.5, 2.5 Hz), 7.07 (2H, d, J=2.5 Hz), 7.29—7.94 (5H, m). A mixture of the above alcohol (166 mg, 0.492 mmol) and MnO_2 (644 mg, 7.41 mmol) in benzene (6 ml) was heated under reflux with stirring for 1 h. The mixture was filtered through a Celite bed, then the filtrate and CH_2Cl_2 washings were combined and evaporated *in vacuo*. The residue was purified by PTLC [hexane–EtOAc (3 : 2)] and recrystallization from Et_2O–hexane to afford **5a** (135 mg, 82%), colorless prisms, mp 61—62 °C. *Anal.* Calcd for $C_{16}H_{17}NO_5S$: C, 57.30; H, 5.11; N, 4.18. Found: C, 57.20; H, 5.09; N, 4.23. MS *m/z*: 335 (M^+). IR (KBr) cm^{-1}: 1668. ^{1}H-NMR δ: 2.04 (2H, dt, J=4.5, 7.5 Hz), 2.84 (2H, t, J=7.5 Hz), 3.67—4.07 (4H, m), 4.91 (1H, t, J=4.5 Hz), 6.66 (1H, dd, J=3.5, 1.5 Hz), 7.11 (1H, dd, J=3.5, 2 Hz), 7.38—7.73 (3H, m), 7.73 (1H, dd, J=2, 1.5 Hz), 7.78—8.02 (2H, m).

Preparation of 3-(1,3-Dioxolan-2-yl)-1-[1-[(4-methylphenyl)sulfonyl]-3-pyrrolyl]-1-propanone (5b) from 7b Prepared similarly *via* 3-(1,3-dioxolan-2-yl)-1-[1-[(4-methylphenyl)sulfonyl]-3-pyrrolyl]-1-propanol. The alcohol: 98% from **7b**. Colorless syrup. MS *m/z*: 351 (M^+). ^{1}H-NMR δ: 1.52—2.02 (4H, m), 2.37 (3H, s), 2.64 (1H, br s, OH), 3.66—4.06 (4H, m), 4.46—4.72 (1H, m), 4.83 (1H, dd, J=4, 4 Hz), 6.23 (1H, dd, J=2.5, 2.5 Hz), 7.05 (2H, d, J=2.5 Hz), 7.23 and 7.69 (A_2B_2, J=8.5 Hz). **5b**: 81% from the above alcohol. Colorless prisms, mp 86—87 °C (Et_2O–hexane). *Anal.* Calcd for $C_{17}H_{19}NO_5S$: C, 58.44; H, 5.48; N, 4.01. Found: C, 58.20; H, 5.47; N, 4.05. MS *m/z*: 349 (M^+). IR (KBr) cm^{-1}: 1673. ^{1}H-NMR δ: 2.04 (2H, dt, J=4.5, 7.5 Hz), 2.40 (3H, s), 2.84 (2H, t, J=7.5 Hz), 3.67—4.08 (4H, m), 4.91 (1H, t, J=4.5 Hz), 6.65 (1H, dd, J=3.5, 1.5 Hz), 7.29 and 7.77 (A_2B_2, J=8.5 Hz), 7.59 (1H, dd, J=3.5, 2 Hz), 7.66—7.77 (1H, m).

***tert*-Butyl 4-Nitrobutyrate (12)** A mixture of *tert*-butyl acrylate (**11**) (10.00 g, 78.0 mmol), 99% $MeNO_2$ (95.32 g, 156 mmol), 18-crown-6 (0.62 g, 2.34 mmol), and KF (0.45 g, 7.75 mmol) was heated at 90 °C with stirring for 6 h, then cooled to 0 °C. Saturated NH_4Cl–H_2O was added and the mixture was extracted with Et_2O. The extract was worked up as usual, though evaporation was conducted below 30 °C. The residue was distilled at atmospheric pressure to recover $MeNO_2$ (63.76 g), followed by distillation under reduced pressure to yield **12** (10.42 g, 71%) as a colorless oil, bp 111—113 °C (8 mmHg) or 54—58 °C (0.02 mmHg) [lit.[22] 56—63 °C (0.15 mmHg)]. GC-MS *m/z*: 189 (M^+). IR (neat) cm^{-1}: 1731, 1567, 1554, 1373. ^{1}H-NMR δ: 1.43 (9H, s), 2.01—2.50 (4H, m), 4.42 (2H, t, J=6.5 Hz); and di-*tert*-butyl 4-nitroheptanedioate (2.20 g, 18%) as colorless viscous oil, bp 115—120 °C (0.02 mmHg) [lit.[22] 142—148 °C (0.05 mmHg)]. GC-MS *m/z*: 317 (M^+). IR (neat) cm^{-1}: 1730, 1555, 1373. ^{1}H-NMR δ: 1.41 (18H, s), 1.87—2.42 (8H, m), 4.34—4.77 (1H, m).

4-Nitrobutyryl Chloride (8) A mixture of *tert*-butyl 4-nitrobutyrate (**12**) (10.19 g, 53.9 mmol) and 95% H_2SO_4 (0.17 g, 1.65 mmol) in $CHCl_3$ (30 ml, freshly distilled over P_2O_5) was refluxed for 5 h. After cooling, the $CHCl_3$ solution was washed with brine and separated. The aqueous layer was extracted with Et_2O and the combined organic solution was worked up as usual. $SOCl_2$ (5.90 ml, 80.9 mmol) was added to the resulting carboxylic acid (7.23 g) at 0 °C and the mixture was heated at 80—85 °C for 1 h. Excess $SOCl_2$ was evaporated off and residual traces of $SOCl_2$ were removed azeotropically with benzene (10 ml). The residue was distilled under reduced pressure to give **8** (7.35 g, 90%) as a pale yellow oil, bp 61—63 °C (0.03 mmHg) [lit.[10] 70 °C (0.03 mmHg)]. IR (neat) cm^{-1}: 1792, 1561, 1552. ^{1}H-NMR δ: 2.35 (2H, tt, J=6.5, 6.5 Hz), 3.09 (2H, t, J=6.5 Hz), 4.45 (2H, t, J=6.5 Hz).

4-Nitro-1-[1-(phenylsulfonyl)-3-pyrrolyl]-1-butanone (9a) $AlCl_3$ (944 mg, 7.08 mmol) was added to a solution of **8** (751 mg, 5.00 mmol) in $ClCH_2CH_2Cl$ (6 ml) at 0 °C. The mixture was stirred for 10 min, then a solution of **1a** (489 mg, 2.36 mmol) in $ClCH_2CH_2Cl$ (4 ml) was added and stirring was continued at 0 °C for 1 h. The mixture was poured into ice-cold H_2O and extracted with CH_2Cl_2. The organic solution was washed successively with 8% NH_4OH, 0.1 N citric acid–H_2O, saturated $NaHCO_3$–H_2O and H_2O, and dried over Na_2SO_4. After evaporation of the solvent, the residue was purified by column chromatography [hexane–CH_2Cl_2 (1 : 2)], and recrystallization from Et_2O–hexane give **9a** (731 mg, 96%) as colorless prisms, mp 69.5—70 °C. *Anal.* Calcd for $C_{14}H_{14}N_2O_5S$: C, 52.16; H, 4.38; N, 8.69. Found: C, 52.17; H, 4.39; N, 8.76. MS *m/z*: 322 (M^+). IR (KBr) cm^{-1}: 1677, 1553, 1380. ^{1}H-NMR δ: 2.34 (2H, tt, J=6.5, 6.5 Hz), 2.88 (2H, t, J=6.5 Hz), 4.45 (2H, t, J=6.5 Hz), 6.63 (1H, dd, J=3, 1.5 Hz), 7.12 (1H, dd, J=3, 2 Hz), 7.31—7.71 (3H, m), 7.71 (1H, dd, J=2, 1.5 Hz), 7.80—8.02 (2H, m).

1-[1-(4-Methylphenyl)sulfonyl-3-pyrrolyl]-4-nitro-1-butanone (9b) 97% yield from **1b**. Colorless needles, mp 81.5—82.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{15}H_{16}N_2O_5S$: C, 53.56; H, 4.79; N, 8.33. Found: C, 53.45; H, 4.80; N, 8.43. MS *m/z*: 336 (M^+). IR (KBr) cm^{-1}: 1680, 1556, 1372. ^{1}H-NMR δ: 2.33 (2H, tt, J=6.5, 6.5 Hz), 2.40 (3H, s), 2.87 (2H, t, J=6.5 Hz), 4.45 (2H, t, J=6.5 Hz), 6.62 (1H, dd, J=3, 1.5 Hz), 7.10 (1H, dd, J=3, 2 Hz), 7.30 and 7.76 (A_2B_2, J=8.5 Hz), 7.69 (1H, dd, J=2, 1.5 Hz).

Preparation of 3-(1,3-Dioxolan-2-yl)-1-[1-(phenylsulfonyl)-3-pyrrolyl]-1-propanone (5a) from 9a To a stirred mixture of **9a** (144 mg, 0.447 mmol) and $HOCH_2CH_2OH$ (2 ml) in Et_2O (4 ml) was added 60% NaH (36 mg, 0.900 mmol) at 0 °C under an Ar atmosphere, and stirring was continued at 0 °C for 10 min and at room temperature for 5 min. The solution was cooled to 0 °C and 20% H_2SO_4–$HOCH_2CH_2OH$ (2 ml) was added. After stirring for 10 min, the mixture was poured into ice-cold $NaHCO_3$–H_2O–CH_2Cl_2, and extracted with CH_2Cl_2. The extract was worked up as usual. The resulting residue (182 mg) was dissolved in benzene (6 ml) and stirred with *p*-TsOH·H_2O (10 mg, 0.053 mmol) at room temperature for 1.5 h. Then saturated $NaHCO_3$–H_2O was added, and the whole was extracted with CH_2Cl_2 and worked up as usual. Purification by PTLC [hexane–CH_2Cl_2 (1 : 4)] gave **5a** (114 mg, 76%), colorless needles, mp 66—66.5 °C (Et_2O–hexane), along with the recovered starting material (**9a**) (12 mg, 8%).

Preparation of 3-(1,3-Dioxolan-2-yl)-1-[1-(4-methylphenyl)sulfonyl-3-pyrrolyl]-1-propanone (5b) from 9b Prepared similarly in 82% yield, along with the recovered **9b** in 5% yield.

Formation of 3 from 5 The preparation of **14** (run 3) is described as a typical example. A solution of tris(methylthio)methane (97 mg, 0.629 mmol) in THF (3 ml) was treated with 15% BuLi in hexane (0.40 ml, 0.630 mmol) under an Ar atmosphere at −80—−70 °C for 30 min. To this was added a solution of **5a** (70 mg, 0.209 mmol) in THF (3 ml) at −70 °C, and the mixture was stirred at −70—−50 °C for 1 h. The reaction was quenched by addition of saturated NH_4Cl–H_2O, and the whole was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (2 : 1)] yielded **14** (93 mg, 91%) as a colorless syrup. MS *m/z*: 489 (M^+). ^{1}H-NMR δ: 1.08—1.83 (2H, m), 1.94 (9H, s), 1.94—2.54 (2H, m), 3.63 (1H, s, OH), 3.63—4.03 (4H, m), 4.76 (1H, dd, J=4, 4 Hz), 6.44 (1H, dd, J=3, 1.5 Hz), 7.03 (1H, dd, J=3, 2 Hz), 7.22 (1H, dd, J=2, 1.5 Hz), 7.29—7.68 (3H, m), 7.68—7.94 (2H, m).

3a [R=2-(1,3-Dioxolan-2-yl)ethyl] (Run 1) Obtained in 97% yield from **5a** by treatment with 2-(1,3-dioxolan-2-yl)ethylmagnesium bromide (3.5 eq) in THF at −20 °C for 15 min under an Ar atmosphere. Colorless

syrup. MS *m/z*: 437 (M^+). ^{1}H-NMR δ: 1.20—2.02 (8H, m), 3.33 (1H, s, OH), 3.58—4.01 (8H, m), 4.74 (2H, dd, J=4, 4 Hz), 6.12 (1H, dd, J=2.5, 2.5 Hz), 7.05 (2H, d, J=2.5 Hz), 7.29—7.68 (3H, m), 7.68—7.91 (2H, m).

13 (Run 2) Obtained in 92% yield from **5b** using the Grignard reagent prepared from Mg and 3-methyl-2-butenyl bromide.[5c] Colorless syrup. MS *m/z*: 419 (M^+). IR (film) cm^{-1}: 1632. ^{1}H-NMR δ: 0.93 (6H, s), 1.19—2.06 (4H, m), 2.37 (3H, s), 2.63 (1H, s, OH), 3.64—4.03 (4H, m), 4.76 (1H, dd, J=4.5, 4.5 Hz), 4.91 (1H, dd, J=17, 1.5 Hz), 5.00 (1H, dd, J=11, 1.5 Hz), 5.91 (1H, dd, J=17, 11 Hz), 6.11 (1H, dd, J=2.5, 2.5 Hz), 7.00 (2H, d, J=2.5 Hz), 7.22 and 7.67 (A_2B_2, J=8.5 Hz).

3a [R=3-Benzyloxy-1-(phenylsulfonyl)-1-propyl] (Run 5) Obtained in 99% yield from **5a** by treatment with the reagent (6 eq), prepared from BuLi and 1-benzyloxy-3-(phenylsulfonyl)propane, in THF at −77—−67 °C for 20 min under an Ar atmosphere. Colorless syrup. LSIMS: 626 [$(M+H)^+$]. ^{1}H-NMR δ: 2.73—3.40 (2H, m), 3.52 (1H, br t, J=4.5 Hz), 3.65—3.92 (4H, m), 4.03, 4.17 (total 2H, both s), 4.38, 4.63 (total 1H, both s, OH), 4.56—4.87 (1H, m), 5.74, 5.99 (total 1H, both dd, J=3, 1.5 Hz), 6.89—8.00 (17H, m).

3a [R=*tert*-butyloxycarbonylmethyl] (Run 7) Obtained in 98% yield from **5a** by treatment with the lithium enolate (5 eq) of *tert*-butyl acetate in THF at −80—−70 °C for 40 min under an Ar atmosphere. Colorless needles, mp 132—133 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{22}H_{29}NO_7S$: C, 58.52; H, 6.47; N, 3.10. Found: C, 58.50; H, 6.39; N, 3.09. MS *m/z*: 451 (M^+). IR (KBr) cm^{-1}: 1700. ^{1}H-NMR δ: 1.23 (9H, s), 1.23—2.03 (4H, m), 2.57 (2H, s), 3.62—4.02 (4H, m), 4.40 (1H, s, OH), 4.74 (1H, dd, J=4, 4 Hz), 6.15 (1H, dd, J=2.5, 2.5 Hz), 7.04 (2H, d, J=2.5 Hz), 7.29—7.66 (3H, m), 7.66—7.91 (2H, m).

3a [R=*N,N*-Dipropylcarbamoylmethyl] (Run 8) Obtained in 96% yield from **5a** by treatment with the lithium enolate (5 eq.) of *N,N*-dipropylacetamide in THF at −85—−70 °C for 30 min under an Ar atmosphere. Colorless syrup. MS *m/z*: 478 (M^+). IR ($CHCl_3$) cm^{-1}: 1617. ^{1}H-NMR δ: 0.74 (3H, t, J=7.5 Hz), 0.85 (3H, t, J=7.5 Hz), 1.10—2.07 (8H, m), 2.46 (1H, d, J=15 Hz), 2.71 (1H, d, J=15 Hz), 2.86—3.47 (4H, m), 3.61—4.03 (4H, m), 4.66—4.88 (1H, m), 6.16 (1H, dd, J=2.5, 2.5 Hz), 6.25—6.47 (1H, br s, OH), 7.04 (2H, d, J=2.5 Hz), 7.30—7.67 (3H, m), 7.70—7.92 (2H, m).

3a [R=1-Methoxymethyl-2-oxo-3-pyrrolidinyl] (Run 9) Obtained in 99% yield from **5a** by treatment with the lithium enolate (3 eq) of 1-methoxymethyl-2-oxo-pyrrolidine[23] in THF at −85—−70 °C for 30 min under an Ar atmosphere. Colorless syrup. MS *m/z*: 464 (M^+). IR ($CHCl_3$) cm^{-1}: 1680. ^{1}H-NMR δ: 1.30—2.30 (6H, m), 2.76 (1H, dd, J=10, 2.5 Hz), 2.87—3.44 (2H, m), 3.02, 3.21 (3H, both s), 3.63—4.08 (4H, m), 4.50 (2H, s), 4.83 (1H, dd, J=4, 4 Hz), 5.67 (1H, s, OH), 6.13—6.30 (1H, m), 6.96—7.19 (2H, m), 7.32—7.69 (3H, m), 7.69—7.93 (2H, m).

3a [R=(Phenylsulfonyl)methyl] (Run 10) Obtained in 99% yield from **5a** by treatment with (phenylsulfonyl)methyl lithium (3 eq) in THF at −78—−65 °C for 30 min under an Ar atmosphere. Colorless needles, mp 131—132 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{23}H_{25}NO_7S_2$: C, 56.19; H, 5.13; N, 2.85. Found: C, 55.93; H, 5.15; N, 2.87. MS *m/z* (relative intensity): 350 ($M^+ - SO_2Ph$, 3), 332 (5), 249 (15), 234 (9), 194 (12), 141 (26), 94 (19), 87 (33), 77 (100), 73 (59). ^{1}H-NMR δ: 1.07—2.21 (4H, m), 3.54 (2H, s), 3.61—4.00 (4H, m), 4.13 (1H, dd, J=3.5, 3.5 Hz), 4.60 (1H, s, OH), 5.70 (1H, dd, J=3, 1.5 Hz), 6.79 (1H, dd, J=3, 2.5 Hz), 7.07 (1H, dd, J=2.5, 1.5 Hz), 7.18—7.71 (8H, m), 7.71—7.94 (2H, m).

Indole Cyclization of 3 to Form 4 Preparation of methyl 1-(phenylsulfonyl)indole-4-carboxylate (**15**) by method D (run 3) is described as a typical example. A 9.5% solution (3 ml) of H_2SO_4 in MeOH–H_2O (9 : 1) was added to a solution of **14** (41 mg, 0.084 mmol) and $HgCl_2$ (46 mg, 0.169 mmol) in MeOH (1.5 ml), and the mixture was refluxed for 4 h. After cooling, inorganic material was filtered off through a Celite bed and washed with CH_2Cl_2. The filtrate was washed with saturated $NaHCO_3$–H_2O and worked up as usual. Purification by PTLC [hexane–EtOAc (2 : 1)] and recrystallization from CH_2Cl_2–MeOH gave **15** (21 mg, 80%) as colorless prisms, mp 145—146 °C. *Anal.* Calcd for $C_{16}H_{13}NO_4S$: C, 60.94; H, 4.16; N, 4.44. Found: C, 60.85; H, 4.16; N, 4.53. MS *m/z*: 315 (M^+). IR (KBr) cm^{-1}: 1729. ^{1}H-NMR δ: 3.92 (3H, s), 7.26—7.63 (3H, m), 7.32 (1H, dd, J=8, 8 Hz), 7.34 (1H, d, J=4 Hz), 7.66 (1H, d, J=4 Hz), 7.73—7.96 (2H, m), 7.94 (1H, d, J=8 Hz), 8.20 (1H, d, J=8 Hz).

4-[2-(1,3-Dioxolan-2-yl)ethyl]-1-(phenylsulfonyl)indole (4a) [R=2-(1,3-Dioxolan-2-yl)ethyl] (Run 1) Obtained in 87% yield from the corresponding **3a** by refluxing with *p*-TsOH–H_2O (0.28 eq) in benzene for 15 min (method A). Colorless syrup. HRMS Calcd for $C_{19}H_{19}NO_4S$: 357.1035. Found: 357.1030. ^{1}H-NMR δ: 1.81—2.13 (2H, m), 2.76—3.04 (2H, m), 3.68—4.08 (4H, m), 4.84 (1H, t, J=4.5 Hz), 6.72 (1H, d, J=4 Hz), 7.01 (1H, br d, J=8 Hz), 7.20 (1H, dd, J=8, 8 Hz), 7.20—7.53 (3H, m), 7.53 (1H, d, J=4 Hz), 7.69—7.96 (2H, m), 7.82 (1H, d, J=8 Hz).

4-(1,1-Dimethyl-2-propenyl)-1-[(4-methylphenyl)sulfonyl]indole (4b) [R=1,1-Dimethyl-2-propenyl] (Run 2) Obtained in 8% yield from **13**, together with **19** (56%) by refluxing in 6% H_2SO_4 in 2-propanol for 1.5 h (method B). Colorless syrup. MS *m/z*: 339 (M^+). IR ($CHCl_3$) cm^{-1}: 1633. ^{1}H-NMR δ: 1.44 (6H, s), 2.30 (3H, s), 4.98 (1H, dd, J=18, 1 Hz), 4.99 (1H, dd, J=10, 1 Hz), 6.04 (1H, dd, J=18, 10 Hz), 6.81 (1H, d, J=4 Hz), 7.04—7.31 (4H, m), 7.46 (1H, d, J=4 Hz), 7.70 (2H, A_2B_2, J=8.5 Hz), 7.70—7.97 (1H, m). **19**: Colorless syrup. MS *m/z*: 375 (M^+). IR ($CHCl_3$) cm^{-1}: 1677. ^{1}H-NMR δ: 1.19 (3H, s), 1.22 (3H, s), 1.37—2.16 (6H, m), 2.40 (3H, s), 2.52—3.13 (2H, m), 3.96 (1H, dddd, J=6.5, 6.5, 6.5, 6.5 Hz), 6.65 (1H, dd, J=3.5, 1.5 Hz), 7.09 (1H, dd, J=3.5, 2.5 Hz), 7.29 and 7.77 (A_2B_2, J=8.5 Hz), 7.68—7.79 (1H, m).

4-Formyl-1-(phenylsulfonyl)indole (16) (Run 4) A solution of methyl methylsulfinylmethyl sulfide (210 mg, 1.69 mmol) in THF (5 ml) was treated with 15% BuLi in hexane (1.0 ml, 1.60 mmol) under an Ar atmosphere at −20 °C for 30 min. The mixture was cooled to −80 °C, a solution of **5a** (80 mg, 0.239 mmol) in THF (3 ml) was added, and the whole was stirred at −80—−40 °C for 1.5 h. The reaction was quenched with NH_4Cl–H_2O, the whole was extracted with CH_2Cl_2, and the extract was worked up as usual. The crude residue (240 mg) was dissolved in 6% H_2SO_4–2-propanol (12 ml) and the mixture was refluxed for 30 min, poured into ice-cold $NaHCO_3$–H_2O, extracted with CH_2Cl_2 and worked up as usual. Purification by PTLC [hexane–EtOAc (6 : 1)] and recrystallization from CH_2Cl_2–hexane afforded **16** (47 mg, 69%) as colorless prisms, mp 101.5—102 °C. *Anal.* Calcd for $C_{15}H_{11}NO_3S$: C, 63.15; H, 3.89; N, 4.91. Found: C, 62.98; H, 3.84; N, 4.92. MS *m/z* (relative intensity): 285 (M^+, 54), 144 (10), 143 (14), 141 (41), 117 (12), 116 (11), 89 (20), 77 (100). IR (KBr) cm^{-1}: 1694. ^{1}H-NMR δ: 7.25—7.56 (5H, m), 7.59—7.75 (1H, m), 7.71 (1H, d, J=3.5 Hz), 7.75—7.96 (2H, m), 8.24 (1H, dd, J=8, 1 Hz), 10.11 (1H, s).

4-[3-Benzyloxy-1-(phenylsulfonyl)-1-propyl]-1-(phenylsulfonyl)indole (4a) [R=3-Benzyloxy-1-(phenylsulfonyl)-1-propyl] (Run 5) Obtained in 81% yield from the corresponding **3a'** by method B. Colorless syrup. HRMS Calcd for $C_{30}H_{27}NO_5S_2$: 545.1329. Found: 545.1330. ^{1}H-NMR (55 °C) δ: 2.15—3.67 (4H, m), 4.08 (1H, d, J=12 Hz), 4.26 (1H, d, J=12 Hz), 4.69 (1H, dd, J=10.5, 3.5 Hz), 6.30 (1H, d, J=3.5 Hz), 7.32 (1H, d, J=3.5 Hz), 6.84—8.03 (18H, m).

1-[(4-Methylphenyl)sulfonyl]-4-(2-oxocyclopentyl)indole (4b) [R=2-Oxocyclopentyl] (Run 6) A solution of cyclopentanone *N,N*-dimethylhydrazone[24] (115 mg, 0.911 mmol) in THF (3 ml) was treated with 15% BuLi in hexane (0.58 ml, 0.911 mmol) under an Ar atmosphere at −60—−45 °C for 1 h. It was cooled at −80°C, a solution of **5b** (80 mg, 0.229 mmol) in THF (2 ml) was added dropwise to it, and the mixture was stirred at −80—−60 °C for 40 min. Saturated NH_4Cl–H_2O and saturated $NaHCO_3$–H_2O were added and the whole was extracted with CH_2Cl_2. Usual work-up and PTLC [benzene–EtOAc (1 : 1)] afforded 5 mg (6%) of recovered **5b** and 113 mg of the crude adduct. A solution of the latter in 6% H_2SO_4 in 2-propanol (6 ml) was heated under reflux for 30 min. After cooling, the mixture was poured into ice-cold $NaHCO_3$–H_2O and extracted with CH_2Cl_2. Usual work-up, followed by successive PTLC [hexane–EtOAc (3 : 1)] and [hexane–CH_2Cl_2 (1 : 2)] yielded **4b** [R=2-oxocyclopentyl] (60 mg, 74%) as a colorless syrup. HRMS Calcd for $C_{20}H_{19}NO_3S$: 353.1085. Found: 353.1092. IR (KBr) cm^{-1}: 1740. ^{1}H-NMR δ: 1.70—2.73 (6H, m), 2.30 (3H, s), 3.34—3.73 (1H, m), 6.53 (1H, d, J=3.5 Hz), 6.91 (1H, d, J=7.5 Hz), 7.06—7.32 (1H, m), 7.15 and 7.71 (A_2B_2, J=8.5 Hz), 7.52 (1H, d, J=3.5 Hz), 7.85 (1H, d, J=7.5 Hz).

Methyl 1-(Phenylsulfonyl)indole-4-acetate (17) (Run 7) Obtained in 91% yield from the corresponding **3a** by refluxing in 6% H_2SO_4–MeOH for 2.5 h (method C). Colorless prisms, mp 65—66 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{17}H_{15}NO_4S$: C, 61.99; H, 4.59; N, 4.25. Found: C, 61.95; H, 4.58; N, 4.43. MS *m/z*: 329 (M^+). IR (KBr) cm^{-1}: 1739. ^{1}H-NMR δ: 3.63 (3H, s), 3.78 (2H, s), 6.70 (1H, d, J=3.5 Hz), 7.09 (1H, dd, J=8, 1.5 Hz), 7.24 (1H, dd, J=8, 8 Hz), 7.24—7.55 (3H, m), 7.55 (1H, d, J=3.5 Hz), 7.73—8.00 (3H, m).

***N,N*-Dipropyl-1-(phenylsulfonyl)indole-4-acetamide (18) (Run 8)** Obtained in 93% yield from the corresponding **3a** by refluxing in 6% H_2SO_4–2-propanol for 20 min (method B). Colorless needles, mp 91.5—92.5 °C (CH_2Cl_2–hexane) and colorless prisms, mp 99.5—100.5 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{22}H_{26}N_2O_3S$: C, 66.31; H, 6.58; N, 7.03. Found: C, 66.46; H, 6.61; N, 7.00. MS *m/z* (relative intensity): 398 (M^+, 54), 270 (22), 257 (7), 215 (9), 157 (14), 141 (15), 130 (27), 129 (59), 128 (100), 86 (90), 77 (87), 43 (94). IR (KBr) of needles cm^{-1}: 1650, 1633. IR (KBr) of prisms cm^{-1}: 1633, 1623. ^{1}H-NMR δ: 0.73 (3H, t, J=7.5 Hz), 0.83 (3H, t, J=7.5 Hz), 1.11—1.82 (4H, m), 3.13 (2H, t, J=7.5 Hz), 3.24

(2H, t, J=7.5 Hz), 3.86 (2H, s), 6.76 (1H, d, J=4 Hz), 7.05 (1H, d, J=8 Hz), 7.22 (1H, dd, J=8, 8 Hz), 7.33—7.50 (3H, m), 7.53 (1H, d, J=4 Hz), 7.74—8.00 (3H, m).

4-(1-Methoxymethyl-2-oxo-3-pyrrolidinyl)-1-(phenylsulfonyl)indole (4a) [R=1-Methoxymethyl-2-oxo-3-pyrrolidinyl] (Run 9) Obtained in 95% yield from the corresponding **3a** by refluxing in 6% H_2SO_4–MeOH for 10 min (method C). Colorless syrup. HRMS Calcd for $C_{20}H_{20}N_2O_4S$: 384.1143. Found: 384.1130. IR ($CHCl_3$) cm^{-1}: 1696. ^{1}H-NMR δ: 1.90—2.74 (2H, m), 3.34 (3H, s), 3.39—3.71 (2H, m), 3.99 (1H, dd, J=9, 9 Hz), 4.74 (2H, s), 6.65 (1H, d, J=3.5 Hz), 7.03 (1H, d, J=7 Hz), 7.23 (1H, dd, J=7, 7 Hz), 7.23—7.55 (3H, m), 7.55 (1H, d, J=3.5 Hz), 7.68—7.99 (3H, m).

1-(Phenylsulfonyl)-4-(phenylsulfonylmethyl)indole (4a) [R=(Phenylsulfonyl)methyl] (Run 10) Obtained in 97% yield from the corresponding **3a** by refluxing in 6% H_2SO_4–2-propanol for 30 min (method B). Colorless prisms, mp 146—147 °C (CH_2Cl_2–hexane). *Anal.* Calcd for $C_{21}H_{17}NO_4S_2$: C, 61.29; H, 4.16; N, 3.40. Found: C, 61.33; H, 4.20; N, 3.41. HRMS Calcd for $C_{21}H_{17}NO_4S_2$: 411.0599. Found: 411.0590. MS m/z (relative intensity): 411 (M^+, 6), 270 (100), 130 (30), 129 (35), 102 (17), 77 (86), 51 (34). ^{1}H-NMR δ: 4.49 (2H, s), 6.39 (1H, d, J=4 Hz), 6.95 (1H, d, J=8 Hz), 7.03—7.68 (9H, m), 7.19 (1H, dd, J=8, 8 Hz), 7.71—7.96 (2H, m), 7.96 (1H, d, J=8 Hz).

Synthesis of 4-(1,1-Dimethyl-2-propenyl)indole (20) from 13 Applying the reported procedure,[5c] **13** (51 mg, 0.122 mmol) was reductively deprotected with Mg (73 mg, 3.042 mg atom) in MeOH (5 ml). Purification by PTLC [hexane–EtOAc (5 : 3)] gave the corresponding pyrrole derivative (30 mg, 93%) as a colorless syrup. MS m/z: 265 (M^+). IR ($CHCl_3$) cm^{-1}: 1633. ^{1}H-NMR δ: 0.99 (3H, s), 1.01 (3H, s), 1.34—2.20 (4H, m), 2.33 (1H, s, OH), 3.63—4.04 (4H, m), 4.81 (1H, dd, J=4.5, 4.5 Hz), 4.98 (1H, dd, J=19, 1.5 Hz), 5.01 (1H, dd, J=10, 1.5 Hz), 5.92—6.04 (1H, m), 6.04 (1H, dd, J=19, 10 Hz), 6.50—6.71 (2H, m), 8.32 (1H, br s, pyrrole NH). A solution of the above compound (29 mg, 0.109 mmol) and p-TsOH·H_2O (4 mg, 0.021 mmol) in benzene (4 ml) was refluxed for 3 min, then cooled. Saturated $NaHCO_3$–H_2O was added and the mixture was extracted with CH_2Cl_2. Usual work-up and purification by PTLC [hexane–EtOAc (14 : 1)] afforded colorless crystalline **20** (16 mg, 79%), mp 55—57 °C. Attempted recrystallization from various solvents failed. HRMS Calcd for $C_{13}H_{15}N$: 185.1204. Found: 185.1199. IR ($CHCl_3$) cm^{-1}: 3500, 1637. ^{1}H-NMR δ: 1.54 (6H, s), 5.03 (1H, dd, J=10.5, 1.5 Hz), 5.07 (1H, dd, J=17.5, 1.5 Hz), 6.18 (1H, dd, J=17.5, 10.5 Hz), 6.68 (1H, dd, J=3, 2 Hz), 6.93—7.30 (4H, m), 7.93 (1H, br s, NH).

4-[2-(Dipropylamino)ethyl]indole (21) A suspension of **18** (38.5 mg, 0.097 mmol) and $LiAlH_4$ (37 mg, 0.966 mmol) in THF (3.5 ml) was refluxed with stirring for 2.5 h. After cooling in an ice bath, it was quenched with saturated Rochelle salt in H_2O and the mixture was extracted with CH_2Cl_2. After usual work-up, the resulting residue was purified by Al_2O_3 PTLC [hexane–EtOAc (19 : 1)], and recrystallization from MeOH–H_2O afforded **21** (20 mg, 85%) as colorless prisms, mp 77—77.5 °C. *Anal.* Calcd for $C_{16}H_{24}N_2$: C, 78.64; H, 9.90; N, 11.46. Found: C, 78.62; H, 9.98; N, 11.51. MS m/z (relative intensity): 244 (M^+, 7), 215 (5), 213 (8), 144 (49), 130 (67), 114 (100), 86 (46), 77 (18), 72 (66), 43 (69). ^{1}H-NMR δ: 0.88 (6H, t, J=7.5 Hz), 1.29—1.77 (4H, m), 2.33—2.68 (4H, m), 2.68—3.20 (4H, m), 6.46—6.62 (1H, m), 6.87 (1H, dd, J=6.5, 2 Hz), 6.94—7.26 (3H, m), 8.41 (1H, br s, NH).

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