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PAPER

Ketosulfonyl indoles in the regiodefined synthesis of tryptophols and related indole derivatives†

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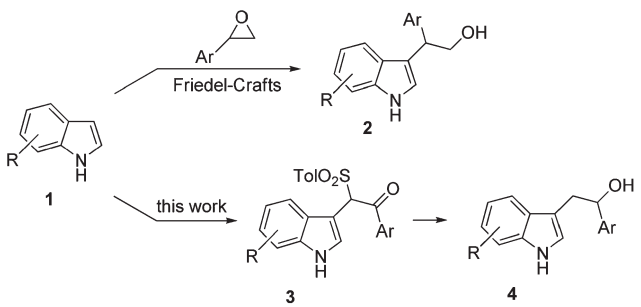
Reduction of ketosulfonyl indoles with sodium borohydride provides a ready entry to tryptophols in a regiocomplementary fashion with respect to the traditional oxirane ring-opening by indoles under Friedel–Crafts conditions. Compared to traditional β-ketosulfones, ketosulfonyl indoles show a peculiar behavior since they undergo a Lewis acid promoted elimination of the arylsulfonyl group allowing the preparation of indolyl-substituted 1,4-dicarbonyl derivatives.

Introduction

A considerable number of compounds containing the indole nucleus, both of synthetic and natural origin, are known for their outstanding pharmacological profile.[1] Tryptophol is a tryptophane metabolite featuring a C-3 hydroxyethyl side chain on the indole nucleus which is involved in some neuronal disorders such as sleeping sickness.[2] Tryptophol has been also recognized as one of the many components in extracts of marine origin and terrestrial *Streptomyces*.[3] Additionally, tryptophol derivatives are widely employed as pivotal intermediates for the synthesis of non-steroidal anti-inflammatory drugs (Etodolac, Pemedolac)[4] and 5-lipoxygenase inhibitors.[5] The whole body of approaches for the preparation of tryptophol derivatives generally enjoys the viable and fully exploited chemistry related to the indole synthesis. The Fischer indole reaction provides an exceptionally powerful method to access differently substituted systems, including those bearing a 3-(2-hydroxyethyl) moiety.[6] A different approach consists in the functionalization of indoles at C-3 through the Friedel–Crafts process involving a regioselective epoxide ring opening. The utilization of 2-aryloxiranes in such acid promoted reactions with indoles **1** invariably leads to the preferential formation of 2-(3-indolyl)-2-aryl-1-ethanols **2**, reflecting the higher stabilization pertaining to the incipient benzylic carbocations involved in the transition state (Scheme 1).[7] Chiral Lewis acids have been successfully used in such processes thus providing high level of enantioselection in the obtained tryptophols.[8] Interestingly, the observed regioselection is inverted when 2-alkyloxiranes are used for the same purpose.[9] The aim of the present work is to provide an efficient entry to regiocomplementary tryptophols **4** using a two-step procedure involving a preliminary installation of a C-3 side chain in the indole ring bearing a carbonyl function in a proper position as in ketosulfonyl indoles **3**, followed by its reduction to the hydroxy group. Besides, other applications of the newly prepared ketosulfonyl indoles **3** in the regiocomplementary synthesis of 1,4-dicarbonyl derivatives embedding the indole ring are reported.



Scheme 1 General synthetic strategy for tryptophols.

Results and discussion

The three-component coupling of indoles with aldehydes and arylsulfinic acids represents a straightforward way to access sulfonyl indoles which can be fruitfully employed as gramine equivalents in the preparation of functionalized indole derivatives.[10] The utilization of 2-oxoaldehyes **5** in the same reaction readily provides similar adducts that can be also considered as β-ketosulfonyl derivatives (Scheme 2).[11]

However, the presence of the indole nucleus brings about a significant change in the chemical properties of these ketosulfonyl indoles enabling different reaction pathways when they are treated with nucleophilic reagents. Ordinary β-ketosulfones

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† This paper is dedicated to Prof. Giuseppe Bartoli on the occasion of his retirement.

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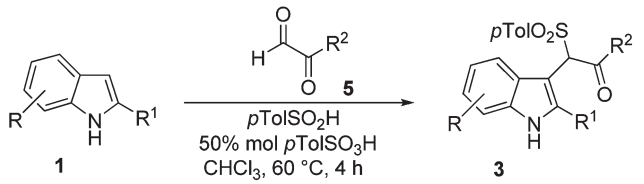
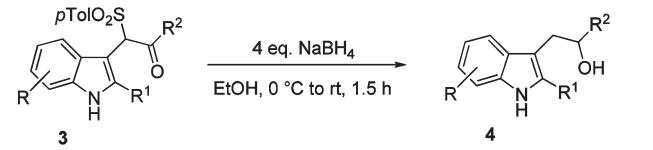


Scheme 2 Synthesis of ketosulfonyl indoles.

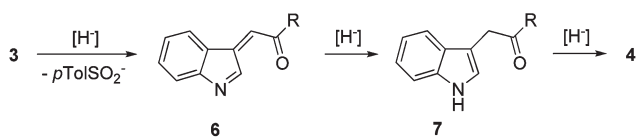
Table 1 Reduction of ketosulfonyl indoles



3a R = H; R^1= H; R^2 = 4-MePh
3b R = 7-Et; R^1= H; R^2 = Ph
3c R = H; R^1= Ph; R^2 = Ph
3d R = H; R^1= Me; R^2 = Ph
3e R = H; R^1= Me; R^2 = $Ph(CH_2)_2$
3f R = H; R^1= Ph; R^2 = 4-NO_2Ph
3g R = H; R^1= H; R^2 = 2-FPh
3h R = 5-CO_2Me; R^1= H; R^2 = 2-FPh

Entry	Substrate	Product	Yield[a] (%)
1	**3a**	**4a**	82
2	**3b**	**4b**	81
3	**3c**	**4c**	95
4	**3d**	**4d**	92
5	**3e**	**4e**	87
6	**3f**	**4f**	96
7	**3g**	**4g**	88
8	**3h**	**4h**	75

[a] Yield of pure isolated product.

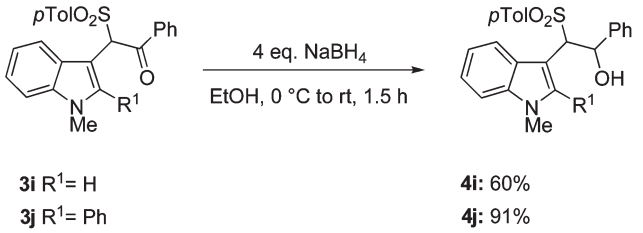


Scheme 3 Reductive pathway to tryptophols.

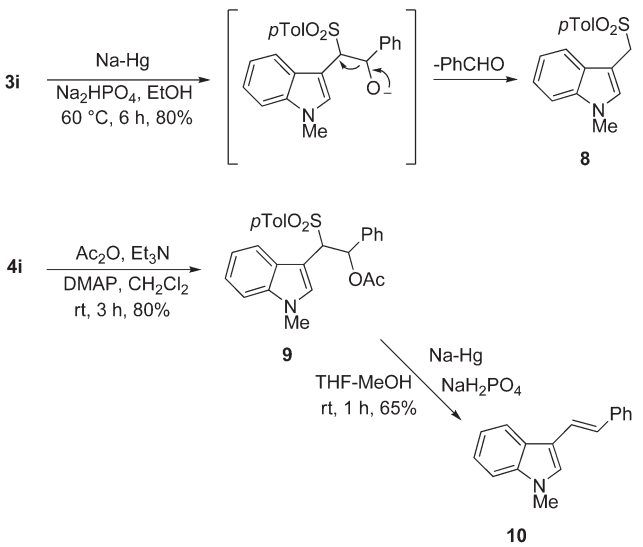
undergo to a simple reduction of the carbonyl moiety when made to react with complex hydride reagents leading to the corresponding β-hydroxysulfones.[12] Ketosulfonyl indoles **3** behave differently in the presence of $NaBH_4$ since reduction of the carbonyl group is coupled with removal of the arylsulfonyl group leading to the corresponding tryptophols **4** in excellent yields (Table 1).

Formation of tryptophols **4** is the result of three distinct processes involving a base assisted elimination of *p*-toluenesulfinic acid with consequent formation of the alkylideneindolenine **6** that is reduced to ketoindole **7** and finally converted to tryptophol **4** by further reduction of the carbonyl group (Scheme 3).

The overall sequence may be obviously reverted since it is possible that reduction of the carbonyl group precedes the alkylideneindolenine formation and its reaction with excess of $NaBH_4$ even though the final result is unchanged. Although this strategy is particularly valuable to prepare 1-aryl derivatives **4**, it can be adopted also for straight chain analogues as demonstrated for the



Scheme 4 Reduction of *N*-methylketosulfonyl indoles.



Scheme 5 Reductive removal of the arylsulfonyl group using Na–Hg amalgam.

synthesis of compound **4e** (Table 1, entry 5). As reducing agent, $NaBH_4$ has been selected because of its mildness and chemoselectivity that allows survival of other reducible functional groups present in the molecule (Table 1, entries 6, 8). It is worth noting that protection of the indole nitrogen atom by methylation as in compounds **3i,j** prevents formation of the indolenine **6** allowing reduction of the sole carbonyl moiety leading to hydroxy derivatives **4i,j** (Scheme 4).

Reductive removal of the arylsulfonyl group from 1-phenyl-β-ketosulfones can be easily carried out exploiting the synergistic activating properties of the carbonyl and aromatic rings toward radical processes. When classical reaction conditions involving Na–Hg amalgam are used, the only notable process observed is formation of sulfonylmethylindole **8** from the parent functionalized indole **3i** (Scheme 5).[13]

Compound **8** is probably the result of a reductive process involving the carbonyl group followed by a retro-sulfonylaldol reaction. As a matter of fact, acylation of the hydroxy group in compound **3i** gives acetate **9** which cannot undergo to a retro condensation reaction and under classical Julia olefination conditions leads stereoselectively to the formation of (*E*)-alkenylindole **10**.[14]

Ketosulfonyl indoles **3** are rather insensitive also to other desulfonylation procedures involving radical intermediates such as reduction with Bu_3SnH which is on the contrary effective with other sulfonyl indoles.[10a,15] Under different radical

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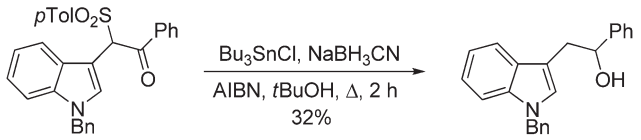
conditions proved to be adequate for particularly sensitive β-ketosulfones, compound **3k** is totally reduced to alcohol **4k** albeit in modest yield (Scheme 6).[16]

Alkylative displacement of the arylsulfonyl group represents a viable opportunity to implement the molecular carbon skeleton but with few notable exceptions, is effective only on selected substrates such as acetylenic, allylic and vinylic sulfones.[17] The carbocationic stabilizing effect pertaining to the indole ring has been already evidenced on simple sulfonyl indole and indazole derivatives.[18] However, to the best of our knowledge, no report on the behavior of a vicinal carbonyl group in such stabilization has been reported.[19] Interestingly, the same reaction conditions which are operative on sulfonyl indoles are also effective in the reaction of N-protected ketosulfonyl indoles **3i–m** with various nucleophilic reagents (Table 2). Utilization of silyl enol ethers and ketene acetals leads to the formation of regiodefined 1,4-dicarbonyl compounds and γ-ketoesters not accessible through a direct Friedel–Crafts process between indoles and 4-oxoalkenoates such as adducts **12a,b**. The regioselectivity displayed in the reaction of indoles with 4-oxoalkenoates is usually in favor of compound **13** which is the result of attack to the more electrophilic carbon atom (Scheme 7).[20]

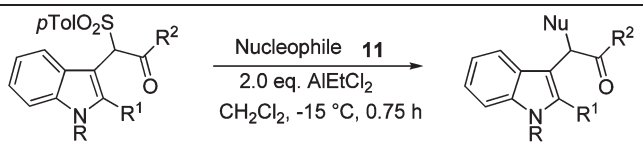
This result is regiocomplementary to that obtained in the reaction of ketosulfonyl indoles **3** with silyl ketene acetal **11b** leading to γ-ketoester **12c** (Table 2). It becomes even more difficult to make a distinction between electrophilic carbon atoms in unsymmetrical 1,4-enediones which roughly possess the same reactivity. Thus selective preparation of compound **12d** would be impossible using the Friedel–Crafts reaction of indoles with enediones. The synthetic value of the proposed approach, is further witnessed by the possibility of introducing butenolide



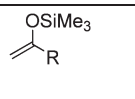
3k **4k**

Scheme 6 Reductive removal of the arylsulfonyl group under radical conditions.

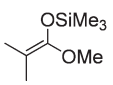
Table 2 Reaction of ketosulfonyl indoles with enol ethers and electron-rich aromatics[a]



3i-m **12**

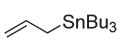


11a R= Bu^t
11b R= OMe

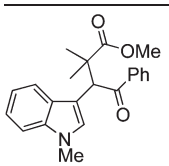


11c

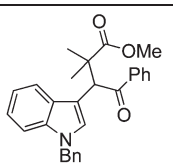
11d R= OSiMe$_3$
11e R= Me



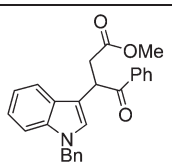
11f



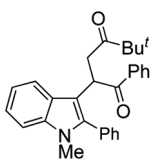
12a 58%



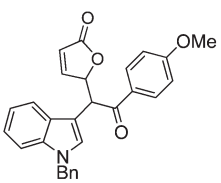
12b 76%



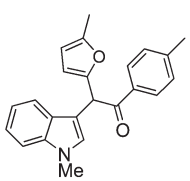
12c 53%



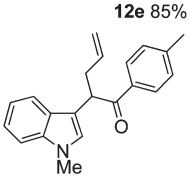
12d 92%



12e 85%



12f 80%



12g 75%

[a] Yield of pure isolated product.

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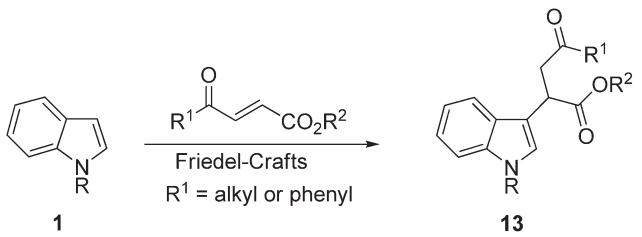
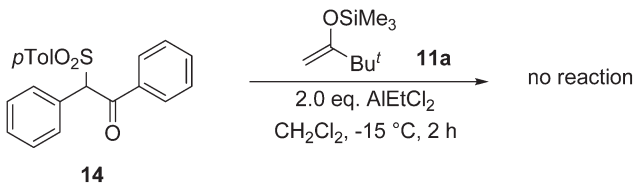


Scheme 7 Regioselective Friedel–Crafts reaction of indoles with enediones.



Scheme 8 Attempt to use a β-ketosulfone bearing a simple phenyl group in the Lewis acid promoted substitution reaction.

frameworks and electron-rich aromatic systems (compounds **12e, f**) and the allyl moiety by reaction with allyltributyltin (compound **12g**). The peculiar behavior of the indole ring in determining the special reactivity of ketosulfonyl indoles **3** is further highlighted by a test experiment carried out on the parent β-ketosulfone **14** in which the indole nucleus is substituted by a phenyl ring (Scheme 8). Under the same reaction conditions which give valuable results for compounds **3i–m** the phenyl analogue **14** is totally unreactive.

Conclusions

Ketosulfonyl indoles **3** are structural analogs of β-ketosulfones but the presence of the indole ring introduces a peculiar reactivity, since it makes the arylsulfonyl group easily removable under basic and acidic conditions. Reduction of ketosulfonyl indoles with sodium borohydride allows the preparation of tryptophols in a regiocomplementary way compared to those obtained by oxirane ring-opening by indoles under Friedel–Crafts conditions. Furthermore, elimination of the arylsulfonyl group in *N*-alkylketosulfonyl indoles promoted by $AlEtCl_2$ allows the introduction in the molecular framework of weak nucleophilic reagents resulting in the synthesis of functionalized 1,4-dicarbonyl derivatives and other interesting compounds.

Experimental

General experimental

^{1}H NMR were recorded at 400 MHz on a Varian Mercury Plus 400.^{13}C NMR were recorded at 100 MHz. Microanalyses were performed with a CHNS-O analyzer Model EA 1108 from Fisons Instruments. Mass spectra were performed with a GC/MS system Agilent Technologies 6850 II/5973 Inert by means of the EI technique (70 eV). IR spectra were recorded with a Perkin-Elmer Paragon 500 FT-IR. All chemicals used were commercial.

Synthesis of ketosulfonyl indoles 3

Ketosulfonyl indoles **3** were prepared following a previously reported procedure using $CHCl_3$ as solvent at 60 °C as reported in Scheme 2.[11]

3a. Yield 61%. Pale brown solid, m.p. 92–94 °C. IR (Nujol) ν_{max}/cm^{-1}: 666, 743, 802, 845, 1287, 1605, 1674, 3364. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 6H), 6.48 (s, 1H), 7.03–7.24 (m, 7H), 7.33 (d, 1H, J = 7.8 Hz), 7.50 (d, 2H, J = 8.1 Hz), 7.63 (d, 1H, J = 7.8 Hz), 7.82 (d, 2H, J = 8.1 Hz), 8.53 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 21.9, 68.9, 104.0, 111.8, 118.8, 120.9, 123.0, 127.0, 129.1, 129.2, 129.4, 129.7, 130.4, 133.8, 134.2, 136.0, 144.9, 145.2, 191.1. Anal. Calcd for $C_{24}H_{21}NO_3S$ (403.49): C, 71.44; H, 5.25; N, 3.47. Found: C, 71.50; H, 5.34; N, 3.61.

3b. Yield 65%. White solid, m.p. 136–138 °C. IR (Nujol) ν_{max}/cm^{-1}: 671, 684, 704, 752, 811, 827, 988, 1277, 1596, 1683, 3337. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (t, 3H, J = 7.7 Hz), 2.34 (s, 3H), 2.82 (q, 2H, J = 7.7 Hz), 6.47 (s, 1H), 6.98–7.17 (m, 5H), 7.36 (t, 2H, J = 7.7 Hz), 7.43–7.53 (m, 4H), 7.89 (d, 2H, J = 8.1 Hz), 9.04 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.0, 21.9, 24.0, 69.1, 103.9, 116.4, 121.1, 121.4, 126.5, 126.8, 127.3, 128.9, 129.0, 129.1, 130.4, 134.0, 134.3, 135.1, 136.3, 144.9, 191.6. Anal. Calcd for $C_{25}H_{23}NO_3S$ (417.52): C, 71.92; H, 5.55; N, 3.35. Found: C, 72.09; H, 5.59; N, 3.29.

3c. Yield 62%. Yellow solid, m.p. 173–175 °C. IR (Nujol) ν_{max}/cm^{-1}: 648, 688, 702, 753, 1250, 1593, 1670, 3328. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.40 (s, 3H), 6.36 (s, 1H), 6.94 (t, 1H, J = 7.7 Hz), 7.07–7.15 (m, 3H), 7.20 (d, 2H, J = 8.1 Hz), 7.27 (d, 1H, J = 8.1 Hz), 7.34 (t, 1H, J = 7.7 Hz), 7.38–7.45 (m, 3H), 7.50–7.58 (m, 3H), 7.64–7.70 (m, 2H), 7.79 (d, 2H, J = 8.1 Hz), 8.48 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.9, 71.1, 100.7, 110.9, 121.0, 122.4, 123.0, 126.9, 128.6, 128.7, 129.3, 129.4, 129.5, 129.6, 130.6, 131.6, 133.6, 135.6, 135.9, 136.0, 140.4, 145.1, 190.3. Anal. Calcd for $C_{29}H_{23}NO_3S$ (465.56): C, 74.81; H, 4.98; N, 3.01. Found: C, 74.63; H, 5.07; N, 3.11.

3d. Yield 64%. White solid, m.p. 195–197 °C. IR (Nujol) ν_{max}/cm^{-1}: 685, 738, 994, 1267, 1596, 1683, 3319. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.28 (s, 3H), 2.36 (s, 3H), 6.23 (s, 1H), 6.96 (t, 1H, J = 7.7 Hz), 7.07 (t, 1H, J = 7.7 Hz), 7.13 (d, 2H, J = 8.1 Hz), 7.20–7.33 (m, 4H), 7.41–7.48 (m, 1H), 7.63 (d, 2H, J = 7.7 Hz), 7.79 (d, 2H, J = 8.1 Hz), 8.10 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.4, 21.8, 70.5, 99.9, 110.5, 118.8, 120.8, 122.1, 128.6, 128.9, 129.2, 130.5, 133.9, 135.0, 135.3, 135.9, 136.8, 144.8, 190.9. Anal. Calcd for $C_{24}H_{21}NO_3S$ (403.49): C, 71.44; H, 5.25; N, 3.47. Found: C, 71.56; H, 5.17; N, 3.39.

3e. Yield 67%. Red sticky oil. IR (neat) ν_{max}/cm^{-1}: 651, 698, 739, 817, 1596, 1715, 3315. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.09 (s, 3H), 2.35 (s, 3H), 2.64–2.96 (m, 4H), 5.27 (s, 1H), 6.90–6.96 (m, 1H), 7.00 (d, 2H, J = 7.7 Hz), 7.04–7.25 (m, 8H), 7.51 (d, 2H, J = 7.7 Hz), 8.24 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.0, 21.8, 29.8, 44.3, 73.7, 99.0, 110.6, 120.7, 122.1, 126.4, 128.5, 128.7, 129.3, 129.4, 129.9, 135.1, 135.3, 137.36, 140.4, 144.8, 200.4. Anal. Calcd for $C_{26}H_{25}NO_3S$ (431.55): C, 72.36; H, 5.84; N, 3.25. Found: C, 72.43; H, 5.92; N, 3.19.

3f. Yield 63%. Yellow solid, m.p. 183–185 °C. IR (Nujol) ν_{max}/cm^{-1}: 694, 706, 746, 759, 852, 1287, 1309, 1356, 1536, 1596, 1605, 1702, 3396. ^{1}H NMR (400 MHz, CD_3COCD_3) δ: 2.42 (s, 3H), 6.61 (s, 1H), 7.01 (t, 1H, J = 7.7 Hz), 7.13 (t, 1H,

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J = 7.7 Hz), 7.35 (d, 2H, J = 8.5 Hz), 7.39 (d, 1H, J = 8.1 Hz), 7.55–7.74 (m, 8H), 7.83 (d, 2H, J = 8.1 Hz), 8.02 (d, 2H, J = 8.5 Hz), 10.92 (bs, 1H). ^{13}C NMR (100 MHz, CD_3COCD_3) δ: 20.9, 70.9, 99.0, 111.5, 120.3, 122.0, 122.7, 123.6, 127.3, 129.3, 129.4, 129.5, 129.6, 129.7, 130.0, 131.5, 136.6, 136.7, 140.6, 141.1, 145.2, 150.5, 189.6. Anal. Calcd for $C_{29}H_{22}N_2O_5S$ (510.56): C, 68.22; H, 4.34; N, 5.49. Found: C, 68.31; H, 4.43; N, 5.56.

3g. Yield 62%. White solid, m.p. 151–153 °C. IR (nujol) ν_{max}/cm^{-1}: 742, 752, 768, 863, 1267, 1608, 1676, 3419. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 6.50 (d, 1H, J = 2.5 Hz), 6.97–7.21 (m, 7H), 7.32 (d, 1H, J = 8.1 Hz), 7.42–7.54 (m, 4H), 7.84 (dt, 1H, J = 1.7, 7.7 Hz), 9.20 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 72.5, 72.6, 102.8, 111.8, 116.9, 117.2, 118.9, 120.7, 122.7, 124.9, 125.0, 125.3, 127.1, 127.3, 129.2, 130.2, 131.5, 131.6, 134.5, 135.7, 135.8, 136.1, 144.9, 160.4, 163.0, 189.4, 189.5. Anal. Calcd for $C_{23}H_{18}FNO_3S$ (407.06): C, 67.80; H, 4.45; N, 3.44. Found: C, 67.97; H, 4.38; N, 3.32.

3h. Yield 65%. Pale brown solid, m.p. 128–131 °C. IR (nujol) ν_{max}/cm^{-1}: 666, 756, 786, 821, 874, 803, 982, 1582, 1616, 1681, 1704, 3321. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 3.93 (s, 3H), 6.54 (d, 1H, J = 2.1 Hz), 7.02–7.09 (m, 1H), 7.12 (d, 2H, J = 8.1 Hz), 7.21 (t, 1H, J = 7.7 Hz), 7.33–7.38 (m, 2H), 7.46–7.55 (m, 3H), 7.83–7.91 (m, 2H), 8.10 (s, 1H), 8.90 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 52.2, 72.0, 72.1, 104.6, 111.5, 117.0, 117.2, 121.5, 122.9, 124.2, 125.0, 125.1, 126.8, 128.6, 129.4, 130.0, 131.5, 131.6, 134.3, 135.9, 136.0, 138.4, 145.3, 160.4, 163.0, 168.0, 189.2, 189.3. Anal. Calcd for $C_{25}H_{20}FNO_5S$ (465.49): C, 64.51; H, 4.33; N, 3.01. Found: C, 64.39; H, 4.39; N, 3.12.

3i. Yield 67%. White solid, m.p. 162–164 °C. IR (Nujol) ν_{max}/cm^{-1}: 643, 681, 710, 747, 988, 1269, 1594, 1682. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 3.70 (s, 3H), 6.48 (s, 1H), 7.06 (s, 1H), 7.11–7.18 (m, 3H), 7.21–7.32 (m, 2H), 7.39 (t, 2H, J = 7.7 Hz), 7.49–7.55 (m, 3H), 7.58 (dd, 1H, J = 0.9, 8.1 Hz), 7.92 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.9, 33.3, 68.9, 102.1, 109.9, 118.9, 120.7, 122.6, 127.3, 128.9, 129.0, 129.1, 130.4, 131.3, 134.0, 134.4, 136.4, 137.0, 144.9, 191.6. Anal. Calcd for $C_{24}H_{21}NO_3S$ (403.49): C, 71.44; H, 5.25; N, 3.47. Found: C, 71.60; H, 5.36; N, 3.55.

3j. Yield 65%. Pale grey solid, m.p. 170–172 °C. IR (Nujol) ν_{max}/cm^{-1}: 639, 682, 709, 738, 760, 790, 814, 844, 982, 1272, 1594, 1682. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.41 (s, 3H), 3.56 (s, 3H), 6.12 (s, 1H), 6.99 (t, 1H, J = 7.7 Hz), 7.11–7.30 (m, 8H), 7.33–7.44 (m, 3H), 7.47–7.62 (m, 4H), 7.75 (d, 2H, J = 7.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.9, 31.5, 71.2, 100.4, 109.5, 120.8, 122.5, 122.6, 126.1, 128.5, 128.7, 129.5, 129.7, 130.3, 130.6, 130.8, 131.7, 133.6, 135.8, 136.2, 137.4, 143.1, 144.9, 190.5. Anal. Calcd for $C_{30}H_{25}NO_3S$ (479.59): C, 75.13; H, 5.25; N, 2.92. Found: C, 75.18; H, 5.31; N, 2.99.

3k. Yield 64%. Red solid, m.p. 46–48 °C. IR (Nujol) ν_{max}/cm^{-1}: 666, 686, 740, 999, 1595, 1682. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 5.11 (d, 1H, J = 15.8 Hz), 5.24 (d, 1H, J = 15.8 Hz), 6.54 (s, 1H), 6.99–7.02 (m, 3H), 7.05 (d, 2H, J = 8.1 Hz), 7.18–7.30 (m, 6H), 7.40–7.48 (m, 4H), 7.55 (t, 1H, J = 7.3 Hz), 7.74–7.78 (m, 1H), 7.96 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 50.5, 68.9, 103.3, 110.3, 119.2, 120.9, 122.9, 127.0, 127.6, 128.0, 129.0, 130.6, 133.7, 134.0, 136.5, 136.6, 137.0, 144.8, 191.8. Anal. Calcd for $C_{30}H_{25}NO_3S$ (479.59): C, 75.13; H, 5.25; N, 2.92. Found: C, 75.01; H, 5.18; N, 2.87.

3l. Yield 65%. Red solid, m.p. 72–74 °C. IR (Nujol) ν_{max}/cm^{-1}: 666, 741, 1604, 1679. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.35 (s, 3H), 2.37 (s, 3H), 3.69 (s, 3H), 6.46 (s, 1H), 7.05 (s, 1H), 7.11–7.20 (m, 5H), 7.21–7.32 (m, 2H), 7.52 (d, 2H, J = 8.1 Hz), 7.59 (d, 1H, J = 8.1 Hz), 7.82 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 21.9, 33.3, 68.7, 102.3, 109.8, 118.9, 120.6, 122.5, 127.4, 129.0, 129.1, 129.7, 130.4, 131.3, 133.8, 134.4, 137.0, 144.9, 145.1, 191.1. Anal. Calcd for $C_{25}H_{23}NO_3S$ (417.52): C, 71.92; H, 5.55; N, 3.35. Found: C, 72.11; H, 5.63; N, 3.44.

3m. Yield 63%. White solid, m.p. 73–75 °C. IR (cm^{-1}, Nujol) ν_{max}/cm^{-1}: 666, 740, 813, 976, 1215, 1262, 1597, 1673. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 3.84 (s, 3H), 5.09 (d, 1H, J = 16.2 Hz), 5.24 (d, 1H, J = 16.2 Hz), 6.50 (s, 1H), 6.89 (d, 2H, J = 9.0 Hz), 6.98–7.07 (m, 5H), 7.15–7.32 (m, 6H), 7.45 (d, 2H, J = 7.7 Hz), 7.74–7.80 (m, 1H), 7.96 (d, 2H, J = 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.9, 50.5, 55.8, 68.5, 103.6, 110.3, 114.3, 119.3, 120.9, 122.9, 127.0, 127.6, 128.0, 128.9, 129.0, 129.3, 130.6, 130.7, 131.5, 133.7, 136.5, 137.1, 144.8, 164.4, 190.1. Anal. Calcd for $C_{31}H_{27}NO_4S$ (509.62): C, 73.06; H, 5.34; N, 2.75. Found: C, 73.18; H, 5.42; N, 2.83.

General procedure for the reduction of ketosulfonyl indoles 3

To a stirred solution of the appropriate ketosulfonyl indole **3** (1 mmol) in EtOH (10 mL) kept under nitrogen atmosphere at 0 °C, $NaBH_4$ (4 mmol) was added portionwise under stirring. After 1.5 h at room temperature, the reaction mixture was quenched by addition of a saturated solution of NH_4Cl (5 mL) and the aqueous phase extracted with CH_2Cl_2 (4 × 10 mL). The organic phase was dried over $MgSO_4$ and after evaporation of the solvent under reduced pressure the crude product thus obtained was purified by flash chromatography (hexanes–ethyl acetate 75 : 25).

4a. Yield 82%. Green viscous oil. IR (neat) ν_{max}/cm^{-1}: 819, 1041, 1515, 1620, 3054, 3417. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.33 (bs, 1H), 2.43 (s, 3H), 3.15 (dd, 1H, J = 9.0, 14.5 Hz), 3.26 (dd, 1H, J = 4.3, 14.5 Hz), 5.00 (dd, 1H, J = 4.3, 9.0 Hz), 6.93 (s, 1H), 7.17–7.31 (m, 4H), 7.32–7.40 (m, 3H), 7.69 (d, 1H, J = 8.1 Hz), 8.13 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 36.1, 74.1, 111.6, 112.2, 119.1, 119.7, 122.4, 123.5, 126.2, 127.8, 129.4, 136.6, 137.4, 141.5. MS (EI) m/z: 251[M$^+$, (5)], 130(100), 131(57), 121(8), 103(10), 91(15), 77(26). Anal. Calcd for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.82; N, 5.57. Found: C, 80.99; H, 6.92; N, 5.70.

4b. Yield 81%. Pink solid, m.p. 89–91 °C. IR (Nujol) ν_{max}/cm^{-1}: 698, 730, 751, 792, 818, 870, 910, 990, 1048, 1612, 3395, 3507. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.39 (t, 3H, J = 7.7 Hz), 2.19 (bs, 1H), 2.87 (q, 2H, J = 7.7 Hz), 3.11 (dd, 1H, J = 9.0, 14.5 Hz), 3.27 (dd, 1H, J = 3.8, 14.5 Hz), 5.02 (dd, 1H, J = 3.8, 9.0 Hz), 7.02 (s, 1H), 7.07–7.17 (m, 2H), 7.29–7.35 (m, 1H), 7.40 (t, 2H, J = 7.7 Hz), 7.44–7.50 (m, 2H), 7.52 (d, 1H, J = 7.7 Hz), 8.04 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 24.2, 36.4, 74.1, 112.7, 116.9, 120.1, 121.0, 123.0, 126.1, 126.9, 127.5, 127.7, 128.6, 135.5, 144.4. EI-MS: m/z 265[M$^+$, (11)],

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247(7), 158(100), 143(20), 115(7), 77(9). Anal. Calcd for $C_{18}H_{19}NO$ (265.35): C, 81.47; H, 7.22; N, 5.28. Found: C, 81.60; H, 7.12; N, 5.33.

4c. Yield 95%. White solid, m.p. 48–50 °C. IR (Nujol) ν_{max}/cm^{-1}: 699, 737, 823, 912, 1019, 1607, 3391, 3499. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.04 (bs, 1H), 3.25–3.36 (m, 2H), 5.13 (dd, 1H, J = 5.6, 8.1 Hz), 7.15–7.21 (m, 1H), 7.22–7.41 (m, 8H), 7.45 (t, 2H, J = 7.7 Hz), 7.56 (d, 2H, J = 7.7 Hz), 7.70 (d, 1H, J = 7.7 Hz), 8.27 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 35.6, 74.6, 109.0, 111.2, 119.5, 120.1, 122.7, 126.0, 127.7, 128.1, 128.6, 129.1, 129.4, 133.0, 136.2, 136.7, 144.4. EI-MS: m/z 313[M$^+$, (9)], 295(9), 207(34), 206(100), 204(33), 178(19), 77(10). Anal. Calcd for $C_{22}H_{19}NO$ (313.39): C, 84.31; H, 6.11; N, 4.47. Found: C, 84.10; H, 6.22; N, 4.15.

4d. Yield 92%. Pale yellow oil. IR (neat) ν_{max}/cm^{-1}: 705, 743, 811, 1031, 1597, 3401, 3497. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.17 (s, 3H), 2.19 (bs, 1H), 3.06–3.19 (m, 2H), 4.99 (dd, 1H, J = 6.0, 7.3 Hz), 7.10–7.21 (m, 2H), 7.24–7.42 (m, 6H), 7.58 (d, 1H, J = 7.7 Hz), 7.84 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 11.7, 35.4, 74.5, 107.4, 110.6, 118.3, 119.7, 121.5, 126.1, 127.6, 128.6, 129.1, 133.4, 135.5, 144.5. EI-MS: m/z 251[M$^+$, (6)], 144 (100), 115(6), 77(12). Anal. Calcd for $C_{17}H_{17}NO$ (251.32): C, 81.24; H, 6.82; N, 5.57. Found: C, 81.41; H, 7.73; N, 5.70.

4e. Yield 87%. Brown oil. IR (neat) ν_{max}/cm^{-1}: 742, 909, 943, 1052, 1602, 3026, 3058, 3301, 3402. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.85–1.98 (m, 3H), 2.38 (s, 3H), 2.69–2.84 (m, 2H), 2.86–3.00 (m, 2H), 3.87–3.99 (m, 1H), 7.07–7.35 (m, 8H), 7.50 (d, 1H, J = 7.7 Hz), 7.89 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.2, 32.6, 33.0, 38.8, 71.6, 107.9, 110.5, 118.4, 119.7, 121.5, 126.0, 128.6, 128.7, 129.1, 132.9, 135.6, 142.5. EI-MS: m/z 279 [M$^+$, (13)], 144(100), 130(6), 91(13), 77(7). Anal. Calcd for $C_{19}H_{21}NO$ (279.38): C, 81.68; H, 7.58; N, 5.01. Found: C, 81.79; H, 7.61; N, 4.92.

4f. Yield 96%. Yellow waxy solid. IR (Nujol) ν_{max}/cm^{-1}: 698, 740, 853, 1011, 1344, 1377, 1515, 1601, 3391. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.06 (bs, 1H), 3.27–3.38 (m, 2H), 5.15 (t, 1H, J = 6.8 Hz), 7.15–7.21 (m, 1H), 7.25 (t, 1H, J = 8.1 Hz), 7.33–7.46 (m, 8H), 7.66 (d, 1H, J = 8.1 Hz), 8.04 (d, 2H, J = 8.1 Hz), 8.27 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 35.3, 73.7, 107.6, 111.4, 119.1, 120.4, 122.9, 123.6, 126.7, 128.3, 128.4, 129.1, 129.2, 132.7, 136.1, 136.9, 147.4, 151.5. API-ES: m/z 359[M + H]$^+$, 381[M + Na]$^+$, 397[M + K]$^+$. Anal. Calcd for $C_{22}H_{18}N_2O_3$ (358.39): C, 73.73; H, 5.06; N, 7.82. Found: C, 73.90; H, 5.18; N, 7.70.

4g. Yield 88%. White solid, m.p. 108–110 °C. IR (Nujol) ν_{max}/cm^{-1}: 739, 756, 810, 829, 1005, 1071, 1616, 3402. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.94 (bs, 1H), 3.01 (dd, 1H, J = 9.0, 14.5 Hz), 3.27 (dd, 1H, J = 3.8, 14.5 Hz), 5.28 (dd, 1H, J = 3.4, 9.0 Hz), 6.98–7.26 (m, 6H), 7.34 (d, 1H, J = 7.7 Hz), 7.52 (dt, 1H, J = 1.3, 7.7 Hz), 7.61 (d, 1H, J = 7.7 Hz), 8.79 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 35.0, 67.9, 111.5, 111.8, 115.2, 115.4, 119.1, 119.5, 122.2, 123.6, 124.4, 127.4, 127.5, 127.8, 128.7, 128.8, 131.7, 131.8, 136.7, 158.8, 161.2. EI-MS: m/z 255 [M$^+$, (6)], 130(100), 103(7), 77(12). Anal. Calcd for $C_{16}H_{14}FNO$ (255.29): C, 75.28; H, 5.53; N, 5.49. Found: C, 75.23; H, 5.66; N, 5.50.

4h. Yield 75%. White solid, m.p. 142–144 °C. IR (Nujol) ν_{max}/cm^{-1}: 747, 759, 816, 979, 1377, 1616, 1682, 3395. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.15 (dd, 1H, J = 7.7, 14.5 Hz), 3.26 (dd, 1H, J = 5.1, 14.5 Hz), 3.88 (s, 3H), 4.45 (bs, 1H), 5.30–5.38 (m, 1H), 7.01–7.08 (m, 1H), 7.16 (t, 1H, J = 7.7 Hz), 7.21–7.30 (m, 2H), 7.43 (d, 1H, J = 8.5 Hz), 7.60–7.65 (m, 1H), 7.79 (d, 1H, J = 8.5 Hz), 8.36 (s, 1H), 10.36 (bs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 35.4, 51.9, 68.3, 111.8, 111.9, 114.3, 115.5, 115.7, 121.7, 122.5, 123.3, 125.0, 125.1, 126.0, 126.2, 128.5, 128.6, 129.3, 129.4, 133.5, 133.6, 140.1, 159.4, 161.8, 168.4. EI-MS: m/z 313[M$^+$, (5)], 295(5), 188(100), 174(21), 129 (36), 102(9), 77(12). Anal. Calcd for $C_{18}H_{16}FNO_3$ (313.32): C, 69.00; H, 5.15; N, 4.47. Found: C, 69.22; H, 5.23; N, 4.34.

4i. Diastereomeric mixture d.r. 7 : 3. Yield 60%. White solid, m.p. 133–135 °C. IR (Nujol) ν_{max}/cm^{-1}: 741, 816, 1129, 1280, 1594, 3403. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (s, 2.1H), 2.36 (s, 0.9H), 2.99 (bs, 1H), 3.60 (s, 0.9H), 3.80 (s, 2.1H), 4.67 (s, 0.7H), 4.82 (d, 0.3H, J = 9.4 Hz), 5.77 (d, 0.3H, J = 9.4 Hz), 5.96 (s, 0.7H), 6.75–6.91 (m, 2H), 6.98–7.30 (m, 10H), 7.41 (d, 0.6H, J = 8.1 Hz), 7.56 (d, 1.4H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.7, 21.8, 33.1, 33.4, 68.8, 70.3, 70.8, 74.1, 100.4, 104.1, 109.3, 117.9, 118.9, 119.6, 119.8, 121.6, 121.9, 125.5, 126.2, 127.3, 127.8, 128.1, 128.2, 128.3, 128.5, 129.0, 129.1, 129.3, 129.4, 129.6, 130.1, 131.4, 134.9, 135.1, 136.0, 136.3, 140.1, 144.8, 144.9. EI-MS: m/z 249(12), 144 (100), 77(16). Anal. Calcd for $C_{24}H_{23}NO_3S$ (405.51): C, 71.09; H, 5.72; N, 3.45. Found: C, 71.27; H, 5.81; N, 3.59.

4j. Diastereomeric mixture d.r. 1 : 1. Yield 91%. White waxy solid. IR (Nujol) ν_{max}/cm^{-1}: 700, 739, 814, 925, 1134, 1594, 3478. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 1.5H), 2.41 (s, 1.5H), 3.19 (s, 1.5H), 3.29 (s, 1.5H), 4.20 (dd, 0.5H, J = 1.3, 3.4 Hz), 4.37 (dd, 0.5H, J = 1.3, 10.3 Hz), 5.72 (d, 0.5H, J = 7.7 Hz), 5.98–6.04 (m, 1.5H), 6.14–6.23 (m, 1H), 6.93–7.39 (m, 16H), 8.09–8.15 (m, 0.5H), 8.41–8.47 (m, 0.5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 21.9, 30.9, 31.0, 72.0, 72.4, 72.7, 100.8, 102.9, 109.4, 109.6, 120.5, 120.8, 122.2, 122.4, 122.8, 124.3, 126.1, 126.8, 127.1, 127.9, 128.0, 128.1, 128.3, 128.5, 128.6, 128.9, 129.0, 129.3, 129.4, 129.8, 129.9, 130.1, 130.2, 130.6, 130.9, 135.8, 136.1, 137.2, 137.5, 140.6, 140.8, 142.4, 144.0, 144.4, 144.7. EI-MS: m/z 325(8), 220(100), 204(19), 77 (14). Anal. Calcd for $C_{30}H_{27}NO_3S$ (481.61): C, 74.82; H, 5.65; N, 2.91. Found: C, 74.70; H, 5.55; N, 2.99.

Reduction of ketosulfonyl indole 3i with Na–Hg amalgam

5% Na–Hg amalgam (0.9 g) and Na_2HPO_4 (2 mmol) were added at room temperature to a stirred solution of ketosulfonyl indole **3i** (0.5 mmol, 0.20 g) in dry EtOH (5 mL). After stirring for 6 h at 60 °C, the mixture was filtered through a short pad of florisil, that was subsequently washed with CH_2Cl_2 (3 × 3 mL). The crude product obtained after removal of the solvent was purified by column chromatography (hexanes–ethyl acetate 80 : 20) giving 0.12 g (80%) of sulfonyl indole **8** as a white solid, m.p. 118–120 °C. IR (cm^{-1}, Nujol) ν_{max}/cm^{-1}: 692, 732, 808, 1137, 1286, 1614. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 3.74 (s, 3H), 4.49 (s, 2H), 6.95–7.03 (m, 2H), 7.14–7.23 (m, 4H), 7.25–7.28 (m, 1H), 7.57 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 33.2, 54.7, 101.3, 109.6, 118.9, 120.0, 122.2, 127.8, 128.8, 129.7, 130.6, 135.8, 136.9, 144.6. EI-MS: m/z 299[M$^+$, (1)], 144(100), 128(5), 115(6), 91(9), 77 (7). Anal. Calcd for $C_{17}H_{17}NO_2S$ (299.39): C, 68.20; H, 5.72; N, 4.68. Found: C, 68.41; H, 5.83; N, 4.77.

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Synthesis of 3-phenylethenylindole 10

Ac_2O (1.5 mmol, 0.15 g) and Et_3N (1.75 mmol, 0.17 g) were sequentially added to a stirred solution of alcohol **4i** (0.75 mmol, 0.30 g) in dry CH_2Cl_2 (10 mL) at 0 °C. The reaction mixture was stirred at room temperature for 3 h and then diluted with CH_2Cl_2 (10 mL). After washing with 1 N HCl (3 × 10 mL) and brine (10 mL), the organic phase was dried over $MgSO_4$ and after evaporation of the solvent under reduced pressure the crude product thus obtained was purified by flash chromatography (hexanes–ethyl acetate 85 : 15) giving 0.27 g (80%) of pure acetate **9** as a white solid, m.p. 65–75 °C. IR (Nujol) ν_{max}/cm^{-1}: 740, 816, 1227, 1596, 1740. ^1H NMR (400 MHz, $CDCl_3$) diastereomeric mixture d.r. 1 : 1 δ: 1.94 (s, 1.5H), 2.17 (s, 1.5H), 2.29 (s, 1.5H), 2.34 (s, 1.5H), 3.61 (s, 1.5H), 3.83 (s, 1.5H), 4.69 (d, 0.5H, J = 1.2 Hz), 5.13 (d, 0.5H, J = 9.8 Hz), 6.69–7.71 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.4, 21.5, 21.7, 21.8, 33.2, 33.5, 67.8, 67.9, 71.8, 74.0, 101.4, 103.1, 109.4, 109.5, 119.9, 120.0, 121.9, 122.0, 125.3, 125.8, 126.6, 127.9, 128.2, 128.4, 128.5, 128.6, 128.7, 128.8, 129.1, 129.2, 129.5, 130.5, 131.4, 135.4, 136.7, 137.7, 138.0, 144.2, 144.7, 169.6, 169.7. EI-MS: *m/z* 291(20), 249(19), 220(13), 186(100), 144 (47), 77(28). Anal. Calcd for $C_{26}H_{25}NO_4S$ (447.55): C, 69.78; H, 5.63; N, 3.13. Found: C, 69.61; H, 5.75; N, 3.19.

To a stirred solution of acetate **9** (0.56 mmol, 0.25 g) in 1 : 1 v/v THF–MeOH (10 mL), NaH_2PO_4 (2.25 mmol, 0.27 g) and 5% Na–Hg amalgam (0.95 g) were added at room temperature. After stirring for 1 h at room temperature, the mixture was filtered through a short pad of florisil, that was subsequently washed with CH_2Cl_2 (20 mL). The crude product obtained after removal of the solvent was purified by column chromatography (hexanes–ethyl acetate 95 : 5) giving 0.085 g (65%) of alkenyl indole **10** as a white solid, m.p. 97–99 °C. IR (neat) ν_{max}/cm^{-1}: 729, 811, 849, 954, 1071. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.80 (s, 3H), 7.12 (d, 1H, J = 16.7 Hz), 7.19–7.42 (m, 8H), 7.54 (d, 2H, J = 7.7 Hz), 8.02 (d, 1H, J = 7.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.2, 109.9, 114.2, 120.3, 120.5, 121.8, 122.5, 125.0, 125.9, 126.4, 126.7, 128.8, 128.9, 137.9, 138.9. EI-MS: *m/z* 233 [M^+, (100)], 217(38), 189(11), 115(10). Anal. Calcd for $C_{17}H_{15}N$ (233.31): C, 87.52; H, 6.48; N, 6.00. Found: C, 87.71; H, 6.35; N, 5.89.

Desulfonylation–reduction of ketosulfonyl indole 3k

Reaction was carried out as previously reported[16] on compound **3k** (0.5 mmol, 0.24 g) leading to 0.052 g (32%) of alcohol **4k** as a yellow sticky oil. IR (neat) ν_{max}/cm^{-1}: 700, 740, 1048, 1182, 1357, 1613, 3030, 3391. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.48 (bs, 1H), 3.14 (dd, 1H, J = 8.5, 14.5 Hz), 3.23 (dd, 1H, J = 4.7, 14.5 Hz), 4.97–5.03 (m, 1H), 5.25 (s, 2H), 6.93 (s, 1H), 7.05–7.16 (m, 3H), 7.20 (t, 1H, J = 7.3 Hz), 7.23–7.38 (m, 6H), 7.39–7.43 (m, 2H), 7.65 (d, 2H, J = 7.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 36.2, 50.2, 74.2, 110.0, 111.4, 119.4, 119.5, 122.2, 126.2, 127.1, 127.5, 127.6, 127.8, 128.5, 128.6, 129.0, 136.9, 137.8, 144.6. EI-MS: *m/z* 327[M^+, (8)], 221 (18), 220(87), 129(9), 91(100). Anal. Calcd for $C_{23}H_{21}NO$ (327.42): C, 84.37; H, 6.46; N, 4.28. Found: C, 84.55; H, 6.51; N, 4.38.

General procedure for the reaction of ketosulfonyl indoles 3 with nucleophiles in the presence of Lewis acid

To a stirred solution of ketosulfonyl indole **3** (1 mmol) in dry CH_2Cl_2 (14 mL) kept under nitrogen atmosphere at −15 °C, the nucleophile (1.5 mmol) and $AlEtCl_2$ (2 mmol) were subsequently added under stirring. After 0.75 h 2 N HCl (12 mL) was added to the reaction mixture and the aqueous phase extracted with CH_2Cl_2 (3 × 10 mL). The organic phase was dried over Na_2SO_4 and after evaporation of the solvent under reduced pressure, the crude product that was purified by flash chromatography (hexanes–ethyl acetate 95 : 5).

12a. Yield 58%. White waxy solid. IR (Nujol) ν_{max}/cm^{-1}: 694, 725, 1151, 1601, 1678, 1731. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.29 (s, 3H), 1.48 (s, 3H), 3.63 (s, 3H), 3.69 (s, 3H) 5.39 (s, 1H), 6.87 (s, 1H), 7.17–7.31 (m, 5H), 7.33–7.41 (m, 1H), 7.78 (d, 1H, J = 8.1 Hz), 7.88 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.6, 27.3, 33.1, 46.1, 50.5, 52.2, 107.9, 109.7, 119.2, 119.9, 122.0, 128.5, 128.6, 130.0, 132.5, 137.2, 137.5, 178.8, 199.9. EI-MS: *m/z* 349[M^+, (20)], 248(100), 244 (97), 220(51), 184(49) 144(34), 105(38), 77(44), 42(16). Anal. Calcd for $C_{22}H_{23}NO_3$ (349.42): C, 75.62; H, 6.63; N, 4.01. Found: C, 75.51; H, 6.68; N, 3.93.

12b. Yield 76%. White solid, m.p. 44–47 °C. IR (Nujol) ν_{max}/cm^{-1}: 691, 722, 1148, 1595, 1677, 1731. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.28 (s, 3H), 1.43 (s, 3H), 3.62(s, 3H), 5.22 (s, 2H), 5.36 (s, 1H), 6.80–6.86 (m, 2H), 6.92 (s, 1H), 7.11–7.28 (m, 8H), 7.33–7.40 (m, 1H), 7.73–7.79 (m, 1H), 7.83 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.5, 27.4, 45.8, 50.2, 51.0, 52.2, 109.0, 110.3, 119.4, 120.2, 122.2, 126.5, 127.7, 128.4, 128.5, 128.7, 128.9, 129.7, 132.5, 136.8, 137.4, 178.7, 199.9. EI-MS: *m/z* 425[M^+, (4)], 324(28), 320(25), 105(16), 91 (100) 77(15). Anal. Calcd for $C_{28}H_{27}NO_3$ (425.52): C, 79.03; H, 6.40; N, 3.29. Found: C, 79.19; H, 6.55; N, 3.38.

12c. Yield 53%. Yellow viscous oil. IR (neat) ν_{max}/cm^{-1}: 690, 725, 1146, 1597, 1681, 1730. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.86 (dd, 1H, J = 4.7, 17.1 Hz), 3.44 (dd, 1H, J = 9.9, 17.1 Hz), 3.65 (s, 3H), 5.20 (d, 2H, J = 3.4 Hz), 5.38 (dd, 1H, J = 4.7, 9.9 Hz), 6.90–6.97 (m, 3H), 7.12–7.25 (m, 6H), 7.34 (d, 2H, J = 7.7 Hz), 7.42–7.49 (m, 1H), 7.72–7.78 (m, 1H), 7.99 (d, 2H, J = 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 37.9, 41.0, 50.2, 52.0, 110.3, 112.2, 119.1, 120.1, 122.5, 126.8, 126.9, 127.3, 127.8, 128.6, 128.9, 129.0, 133.0, 136.5, 137.0, 137.3, 173.1, 199.0. EI-MS: *m/z* 397[M^+, (4)], 292(41), 105(6), 91(100) 77(12). Anal. Calcd for $C_{26}H_{23}NO_3$ (397.47): C, 78.57; H, 5.83; N, 3.52. Found: C, 78.40; H, 5.97; N, 3.60.

12d. Yield 92%. White waxy solid. IR (Nujol) ν_{max}/cm^{-1}: 688, 702, 722, 740, 942, 972, 1156, 1596, 1682, 1704. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.23(s, 9H), 2.80 (dd, 1H, J = 3.0, 18.0 Hz), 3.52 (s, 3H), 4.24 (dd, 1H, J = 11.1, 18.0 Hz), 5.22 (dd, 1H, J = 3.0, 11.1 Hz), 7.12–7.19 (m, 3H), 7.20–7.37 (m, 5H), 7.53–7.61 (m, 5H), 7.81 (d, 1H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 26.8, 31.1, 40.0, 40.4, 44.2, 109.0, 109.7, 120.2, 120.6, 122.2, 126.5, 128.2, 128.9, 129.1, 129.2, 130.9, 131.6, 132.5, 136.7, 137.5, 139.0, 198.8, 214.9. EI-MS: *m/z* 423[M^+, (5)], 318(38), 234(20), 217(8), 105 (10), 77(13), 57(100), 41(13). Anal. Calcd for $C_{29}H_{29}NO_2$ (423.55): C, 82.24; H, 6.90; N, 3.31. Found: C, 82.30; H, 6.88; N, 3.39.

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12e. Diastereomer A. Yield 63%. White solid, m.p. 70–73 °C. IR (Nujol) ν_{max}/cm^{-1}: 741, 810, 830, 843, 807, 1022, 1082, 1170, 1211, 1574, 1601, 1671, 1755, 3052. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.80 (s, 3H), 4.97 (d, 1H, J = 8.1 Hz), 5.20 (d, 1H, J = 15.8 Hz), 5.27 (d, 1H, J = 15.8 Hz), 5.90 (d, 1H, J = 8.1 Hz), 6.02 (d, 1H, J = 6.0 Hz), 6.82 (d, 2H, J = 8.5 Hz), 6.93–6.99 (m, 2H), 7.05 (s, 1H), 7.15–7.29 (m, 6H), 7.38 (d, 1H, J = 6.0 Hz), 7.60–7.65 (m, 1H), 7.91 (d, 2H, J = 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 48.2, 50.4, 55.7, 84.1, 107.3, 110.6, 114.0, 118.9, 120.7, 122.3, 122.9, 126.8, 127.0, 128.0, 128.2, 128.7, 129.0, 131.3, 137.0, 137.1, 156.7, 163.9, 173.0, 194.9. API-ES: m/z 438 $[M + H]^+$, 460 $[M + Na]^+$, 476$[M + K]^+$, 897 $[2M + Na]^+$. Anal. Calcd for $C_{28}H_{23}NO_4$ (437.49): C, 76.87; H, 5.30; N, 3.20. Found: C, 76.95; H, 5.23; N, 3.31. *Diastereomer B*. Yield 22%. Yellow sticky oil. IR (Nujol) ν_{max}/cm^{-1}: 741, 810, 830, 843, 807, 1022, 1082, 1170, 1211, 1574, 1601, 1671, 1755, 3052. ^1H NMR (400 MHz, $CDCl_3$) δ: 3.79 (s, 3H), 5.00 (d, 1H, J = 7.7 Hz), 5.21 (d, 1H, J = 16.2 Hz), 5.27 (d, 1H, J = 16.2 Hz), 5.74 (d, 1H, J = 7.3 Hz), 6.10 (dd, 1H, J = 1.2, 5.6 Hz), 6.81 (d, 2H, J = 8.9 Hz), 6.93–7.00 (m, 2H), 7.10 (s, 1H), 7.15–7.28 (m, 6H), 7.68 (d, 1H, J = 5.6 Hz), 7.70–7.74 (m, 1H), 7.90 (d, 2H, J = 8.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 48.4, 50.4, 55.7, 84.7, 108.6, 110.5, 114.0, 118.9, 120.5, 122.2, 122.6, 126.8, 127.2, 127.9, 128.4, 128.8, 129.0, 131.3, 137.0, 137.2, 156.0, 163.9, 173.1, 195.5. API-ES: m/z 438 $[M + H]^+$, 460$[M + Na]^+$, 476$[M + K]^+$, 897$[2M + Na]^+$. Anal. Calcd for $C_{28}H_{23}NO_4$ (437.49): C, 76.87; H, 5.30; N, 3.20. Found: C, 77.01; H, 5.40; N, 3.15.

12f. Yield 80%. Yellow sticky oil. IR (neat) ν_{max}/cm^{-1}: 741, 960, 1154, 1189, 1606, 1682, 3054. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.26 (s, 3H), 2.37 (s, 3H), 3.73 (s, 3H), 5.87 (d, 1H, J = 3.0 Hz), 5.98 (d, 1H, J = 3.0 Hz), 6.23 (s, 1H), 7.00 (s, 1H), 7.13 (t, 1H, J = 7.7 Hz), 7.17–7.32 (m, 4H), 7.63 (d, 1H, J = 8.1 Hz), 7.96 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9, 21.9, 33.1, 44.6, 106.6, 109.4, 109.6, 110.1, 119.2, 119.6, 122.1, 127.1, 128.6, 129.2, 129.5, 134.0, 137.3, 144.0, 151.4, 151.8, 196.0. EI-MS: m/z 343[M^+, (2)], 224(100), 180(11), 119 (5), 91(7). Anal. Calcd for $C_{23}H_{21}NO_2$ (343.42): C, 80.44; H, 6.16; N, 4.08. Found: C, 80.59; H, 6.12; N, 4.20.

12g. Yield 75%. Yellow oil. IR (neat) ν_{max}/cm^{-1}: 742, 914, 1014, 1181, 1332, 1473, 1606, 1677, 3056. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.34 (s, 3H), 2.62–2.73 (m, 1H), 2.92–3.04 (m, 1H), 3.69 (s, 3H), 4.88–5.00 (m, 2H), 5.09 (d, 1H, J = 17.1 Hz), 5.78–5.91 (m, 1H), 6.89 (s, 1H), 7.13–7.20 (m, 3H), 7.21–7.30 (m, 2H), 7.75 (dd, 1H, J = 0.9, 8.1 Hz), 7.90 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 21.8, 33.0, 38.1, 44.3, 109.7, 112.9, 116.4, 119.0, 119.5, 122.0, 127.0, 127.5, 128.9, 129.4, 134.5, 137.0, 137.3, 143.7, 199.4. EI-MS: m/z 303[M^+, (11)], 262(16), 234(13), 184(100) 168(20), 91(9). Anal. Calcd for $C_{21}H_{21}NO$ (303.40): C, 83.13; H, 6.98; N, 4.62. Found: C, 83.01; H, 7.10; N, 4.77.

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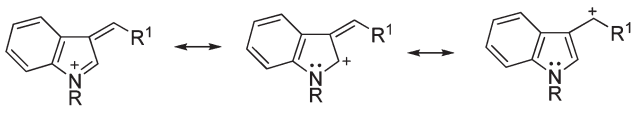
19 The carbocationic nature of the intermediate obtained upon treatment of compounds **3** with Lewis acids is probably due to the retaining of the aromatic character of the pyrrole ring in structure **C**



A **B** **C** (aromatic)

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