# Supplementary Material (ESI) for Chemical Communications


**Ethyl 2-(4-nitrobenzenesulfonylamino)-5-methyl-3-[4-[(*tert*-butyldiphenylsilyloxy)methyl]-1-(4-toluenesulfonyl)-indol-3-yl]-4-hexenoate 9.**

Ethyl 2-azido-5-methyl-3-[4-[(*tert*-butyldiphenylsilyloxy)methyl]-1-(4-toluenesulfonyl)-indol-3-yl]-4-hexenoate (60 mg, 0.08 mmol) was dissolved in tetrahydrofuran (3 ml) containing triphenylphosphine (43 mg, 0.16 mmol) and water (0.16 ml, 0.16 mmol). The resulting solution was refluxed for 6h then cooled and concentrated *in vacuo*. The residual amine showed $\nu_{max}/cm^{-1}$ ($CHCl_3$) 3438, 2959, 1732, 1435 and 1372 (and no azide stretch at 2108 $cm^{-1}$). Without further purification, the crude amine was immediately dissolved in chloroform (1 ml) followed by the addition of 4-nitrobenzenesulfonyl chloride (21 mg, 0.10 mmol), pyridine (1 drop) and DMAP (2 mg). The resulting solution was stirred overnight at ambient temperature then cooled in ice and acidified using 2M hydrochloric acid. The organic phase was separated and the aqueous phase extracted with chloroform (2 x 2 ml). The combined organic solutions were washed with a equal volume of brine then dried ($MgSO_4$), filtered and evaporated. Silica gel chromatography (dichloromethane) then separated the *nosylate* **9** (33 mg, 43%) as an off-white solid and a *ca*. 3:2 mixture of diastereoisomers, which showed $\delta_H$ (400 MHz, $CDCl_3$) (major isomer) 7.95 (1H, d, *J* 8.4 Hz, ArH), 7.87 (2H, d, *J* 8.4, ArH), 7.70 (2H, d, *J* 8.2 Hz, ArH), 7.68-7.50 (7H, m, ArH), 7.38-7.00 (10H, m, ArH), 5.45 (1H, d, *J* 9.8 Hz, NH), 5.21 (1H, d, *J* 12.4 Hz, 1''-$H_a$), 5.18 (1H, d, *J* 10.1 Hz, 4-H), 4.97 (1H, d, *J* 12.4 Hz, 1"-$H_b$), 4.35 (1H, dd, *J* 9.8 and 3.2 Hz, 2-H), 3.86 (1H, dd, *J* 10.1 and 3.2 Hz, 3-H), 3.80-3.70 (2H, m, $OCH_2$), 2.24 (3H, s, TsMe), 1.62 (3H, s, Me), 1.24 (3H, s, Me), 0.96 (9H, s, $Me_3C$) and 0.81 (3H, t, *J* 7.1 Hz, $OCH_2CH_3$), m/z [ES] 893 ($M^+$, 100%) [Found: $M^+$, 893.2839. $C_{47}H_{51}N_3O_9S_2Si$ requires *M*, 893.2836].

**Ethyl (*6aRS, 9SR, 9aSR*)-6, 6a, 7, 8, 9, 9a-hexahydro-7,7-dimethyl-2-(4-toluenesulfonyl)-8-(4-nitrobenzenesulfonyl)isoindolo[4,5,6-cd]indole-9-carboxylate 10.**

The sulfonamide **9** (60 mg, 0.08 mmol) was dissolved in dry chloroform (2 ml) and the resulting solution cooled in ice. Triflic acid (20 μl) was added and the solution stirred without cooling for 1 h then quenched by the addition of 10% aqueous sodium carbonate (1 ml). The separated aqueous layer was extracted with dichloromethane (2 x 2 ml) and the combined organic solutions dried ($MgSO_4$), filtered and evaporated. Preparative tlc (EtOAc/petrol 1:2) then separated the *pyrrolidine* **10** (32 mg, 74%) as a pale yellow solid, m.p. 135~137°C, which showed $\nu_{max}/cm^{-1}$ ($CHCl_3$) 1730, 1440 and 1350, $\delta_H$ (400 MHz, $CDCl_3$) 8.22 (2H, d, *J* 8.3 Hz, ArH), 7.95 (2H, d, *J* 8.3, ArH), 7.88 (2H, d, *J* 8.2 Hz, ArH), 7.79 (1H, d, *J* 8.1, ArH), 7.45 (2H, d, *J* 8.2 Hz, ArH), 7.37-7.00 (2H, m, ArH), 6.90 (1H, dd, *J*

7.5 and 3.3 Hz, ArH), 4.73 (1H, d, *J* 9.5 Hz, 9-H), 3.86 (2H, q, *J* 7.1 Hz, $OCH_2$), 3.57 (1H, dd, *J* 9.5 and 4.1 Hz, 9a-H), 2.80-2.65 (2H, m, 6-$CH_2$), 2.28 (3H, s, TsMe), 2.03 (1H, td, *J* 12.2 and 4.1, 6a-H), 1.60 (3H, s, Me), 1.54 (3H, s, Me) and 0.99 (3H, t, *J* 7.1 Hz, $OCH_2CH_3$), $\delta_C$ (100 MHz, $CDCl_3$) 174.2 (CO), 169.6, 150.0, 146.5, 145.1, 135.6 (all ArC), 134.9 (ArCH), 132.4 (ArC), 130.0 (ArCH), 129.7 (ArC), 129.2, 128.4 (both ArCH), 127.1 (ArC), 125.5, 124.1, 120.2, 111.5 (all ArCH), 60.2 ($OCH_2$), 58.7, 46.5, 35.6 (all CH), 28.9 ($CH_2$), 28.8, 26.6 (both Me), 25.8 (7-C), 23.6 and 21.6 (both Me), m/z [ES] 637 ($M^+$, 12%) and 618 ($M^+$-Et, 100) [Found: $M^+$, 637.1555. $C_{31}H_{31}N_3O_8S_2$ requires *M*, 637.1552].

**α-Cyclopiazonic acid 1**

To a stirred solution of the foregoing pyrrolidine **10** (25 mg, 0.04 mmol) in dry dimethylformamide (2 ml) was added lithium hydroxide (7.5 mg, 0.16 mmol) followed by thioglycolic acid (80 μl, 0.08 mmol). The resulting solution was stirred at ambient temperature for 4 h then diluted with ether (2 ml) and water (2 ml). The layers were separated and the aqueous layer extracted with ether (2 x 2 ml). The combined organic solutions were washed with saturated aqueous sodium carbonate (3 x 2 ml) then dried ($MgSO_4$), filtered and evaporated. The residue was purified by preparative tlc (EtOAc/petrol 1:2) to give *(6aRS, 9aSR, 9SR) ethyl 6,6a,7,8,9,9a-hexahydro-7,7-dimethylisoindolo[4,5,6-cd]indole-9-carboxylate **11*** (9 mg, 80%) as an off-white solid of indeterminate melting point, which showed $\delta_H$ (400 MHz, $CDCl_3$) 8.12 (1H, br s, NH), 7.23 (1H, s, ArH), 7.20-7.05 (2H, m, ArH), 6.90-6.85 (1H, m, ArH), 4.59 (1H, d, *J* 10.3 Hz, 9-H), 3.72-3.68 (2H, m, $OCH_2$), 3.50-3.47 (1H, m, 9a-H), 3.02-2.95 (2H, m, 6-$CH_2$), 2.50-2.40 (1H, m, 6a-H), 1.62 (3H, s, Me), 1.51 (3H, s, Me) and 0.96 (3H, t, *J* 7.2 Hz, $OCH_2CH_3$), m/z [APCI] 299 ($M^+$+H, 100%) and 279 ($M^+$-Et, 65) [Found: $M^+$+H, 299.1768. $C_{18}H_{23}N_2O_2$ requires *M*, 299.1764].

The product **11** (7 mg, 0.02 mmol) was immediately dissolved in dry dichloromethane (2 ml) containing diketene (1 drop) and potassium *t*-butoxide (20 mg).The resulting solution was refluxed for 48 h then cooled and the volatiles evaporated. Preparative tlc of the residue (EtOAc/petrol 3:2) separated *α-cyclopiazonic acid* **1** (3 mg, 65%) as a colourless solid, m.p. of 238-242°C [authentic: m.p. 244-245°C (Tocris sample); mixed m.p. 240-242°C], $\delta_H$ (400 MHz, $CDCl_3$) 8.05 (1H, br s, NH), 7.19 (1H, s, ArH), 7.18-7.05 (2H, m, ArH), 6.85 (1H, d, *J* 7.0 Hz, ArH), 4.00 (1H, d, *J* 11.1 Hz), 3.60 (1H, dd, *J* 11.1 and 5.8 Hz), 3.02-2.95 (2H, m), 2.60-2.50 (1H, m), 2.38 (3H, s, Me), 1.57 (3H, s, Me) and

1.45 (3H, s, Me), m/z [APCI] 337 ($M^+$+H, 100%) [Found: $M^+$+H, 337.1548. $C_{20}H_{21}N_2O_3$ requires *M*, 337.1547].