A concise and chemoenzymatic synthesis of (−)-gabosine A, a carba-sugar enone from *Streptomycetes*

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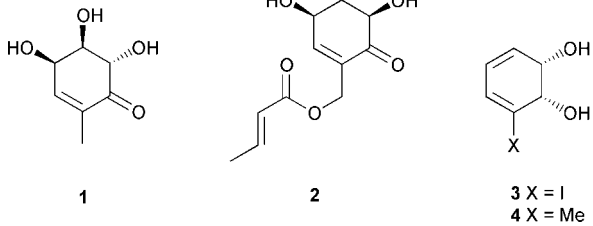
The title compound 1 has been prepared, for the first time, in six steps and a completely stereo-controlled fashion from the *cis*-1,2-dihydrocatechol 3. The starting material is a readily available and enantiopure compound that can be obtained in large quantity *via* toluene dioxygenase (TDO) mediated dihydroxylation of iodobenzene.

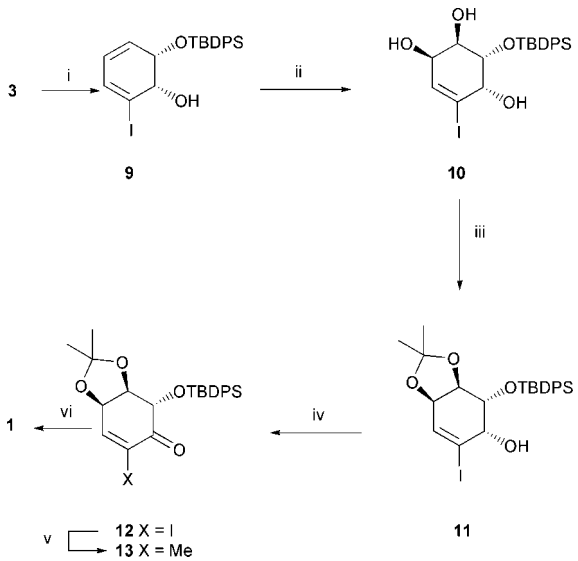
(−)-Gabosine A (**1**)[1] is one of more than a dozen structurally related and generally base-sensitive compounds[1–4] isolated by Zeeck and others during chemical screening of different *Streptomycetes* strains for new secondary metabolites. Although such carba-sugars are similar in their molecular architectures to shikimic acid, biosynthetic studies[5] have revealed that their origins are distinct and involve a pentose phosphate pathway with cyclisation of a heptulose phosphate intermediate. Certain of the gabosines exhibit plant growth regulating effects,[6] DNA-binding properties[4] and/or anti-bacterial behaviour,[2] while congener **2** [(−)-COTC], which was isolated from the culture broth of *Streptomyces griseoporeus* by Umezawa and co-workers,[7] acts as a glyoxalase I inhibitor and, as such, has potential as a tumour-selective anti-cancer agent.[8] As a consequence of their unusual structures and promising biological profiles, these carba-sugars have been the subject of various synthetic studies[9–15] but a route to the title compound **1** has not been reported to date. Consequently, we now describe a concise (six step) and chemoenzymatic synthesis of (−)-gabosine A from the *cis*-1,2-dihydrocatechol **3**, a material readily prepared in large quantity and enantiopure form by toluene dioxygenase mediated dihydroxylation of iodobenzene.[16]

Like congener **3**, diol **4** is readily prepared by analogous means although now from toluene and this latter metabolite seemed the more obvious precursor to target **1**. Indeed, our initial studies were focussed on exploiting compound **4** for this purpose. While the sterically less hindered C-1 hydroxyl group within diol **4** could be selectively protected as the corresponding TBDPS ether (Scheme 1), reaction of product **5** with OsO_4 under the UpJohn conditions afforded a complex mixture of products from which only the triol **6** (7%) could be isolated. No doubt there is a lack of selectivity associated with this dihydroxylation reaction (*viz.* both double bonds within diene



5 react with OsO_4),[17] which contributes to the complexity of the process. The TBDPS protecting group migration associated with the conversion **4** → **6** was not detected initially but revealed through subsequent chemistry. In particular, after selective protection of the newly introduced and *cis*-related hydroxyl groups as the corresponding TBDMS ethers, so as to afford tris(silyl ether) **7**, the remaining free hydroxyl group was subject to oxidation under Swern conditions. Spectroscopic analysis of the ensuing product **8** (*ca.* 10% *ex.* **6**) established, *inter alia*, that the carbonyl moiety was not conjugated with the carbon–carbon double bond (ν_{max} 1748 cm^{-1}) and led to the conclusion that the structure of this ketone is as illustrated.

In an effort to circumvent the difficulties described above the readily prepared TBDPS derivative **9**[18] of compound **3** was converted (Scheme 2), by previously established procedures[18] and *via* triol **10**, into the acetonide **11** (78% overall yield from **3**). The success of this sequence, as compared with the equivalent shown in Scheme 1, derives, at least in part, from the strong difference in nucleophilicity between the two double bonds within compound **9**. As a consequence, only the non-halogenated double bond is subject to dihydroxylation. Oxidation of compound **11** to the corresponding ketone **12** (85%) proceeded smoothly under Swern conditions and the presence of a conjugated cyclohexenone



Scheme 1 *Reagents and conditions*: (i) TBDPSCl (1.1 mol equiv.), imidazole (3.2 mol equiv.), CH_2Cl_2, 18 °C, 1.5 h; (ii) OsO_4 (cat.), NMMNO (1.5 mol equiv.), acetone–H_2O (1 : 1 v/v), 60 °C, 1 h; (iii) TBDMSOTf (2 mol equiv.), Et_3N (3 mol equiv.), CH_2Cl_2, −78 to 18 °C, 1 h; (iv) oxalyl chloride (5 mol equiv.), DMSO (10 mol equiv.), −78 °C, 1 h, then Et_3N (10 mol equiv.), −78 to −10 °C, 0.5 h.

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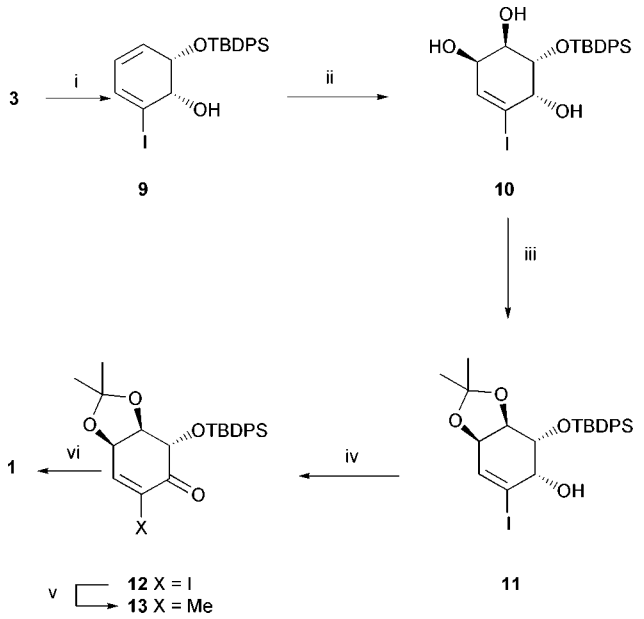

Scheme 2 *Reagents and conditions*: (i) TBDPSCl (1.1 mol equiv.), imidazole (3 mol equiv.), CH_2Cl_2, 18 °C, 7 h; (ii) OsO_4 (cat.), NMMNO (1.3 mol equiv.), acetone–H_2O (3 : 1 v/v), 0–4 °C, 30 h; (iii) 2,2-dimethoxypropane (neat), *p*-TsOH (cat.), 18 °C, 3 h, then Et_3N (0.27 mol equiv.); (iv) oxalyl chloride (2.5 mol equiv.), DMSO (5 mol equiv.), −78 °C, 1 h, then Et_3N (5.2 mol equiv.), −78 to −10 °C, 0.5 h; (v) MeMgCl (2.2 mol equiv.), $FeCl_3$ (10 mol.%), NMP (9 mol equiv.), THF, 0 °C, 0.5 h; (vi) HCl (trace of 2 M aq. solution), methanol, 18 °C, 96 h, then $(Me_2N)_3S^+F_2SiMe_3^-$ (4.8 mol equiv.), THF, 18 °C, 0.5 h.

moiety within this product was readily discerned spectroscopically (ν_{max} 1705 cm^{-1}). The necessary replacement of iodine by a methyl group was attempted at this point. However, all efforts to effect such a conversion (*viz.* **12** → **13**) using palladium(0) catalysed cross-coupling reactions with tetramethyltin, dimethylzinc or methylmagnesium chloride failed. In stark contrast, reaction of compound **12** with 2.2 mol equiv. of methylmagnesium chloride in the presence of iron(III) chloride under the very mild conditions (0 °C) developed by Cahiez and Avedissian[19] proved highly effective and provided, in just 0.5 h, target **13** in 94% yield. Treatment of the latter compound with methanolic HCl at room temperature for extended periods then gave gabosine A (**1**) (85%). The synthetic sample of (−)-gabosine A proved identical, as judged by appropriate spectroscopic comparisons, with material obtained by Zeeck and co-workers.[1] In particular, the optical rotations of the synthetic {$[\alpha]_D$ − 131 (c = 0.27 in methanol)} and natural {$[\alpha]_D$ − 132 (c = 1 in methanol)} materials were in excellent agreement.

The present study serves to emphasize the utility of *cis*-1,2-dihydrocatechols like **3** as starting materials in chemical synthesis and their potential as versatile precursors to the biologically significant gabosines and related carba-sugars. Furthermore, the capacity for replacement of the iodine atom within intermediates such as the α-iodoenone **12** by carbon-based groups other than simple methyl (and especially under the mild cross-coupling conditions defined above)[20] offers the possibility for accessing a wide range of carba-sugars, including the interesting anti-mitotic agent tricholomenyn B.[21] Work aimed at pursuing such possibilities is now underway in our laboratories.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer using deuterochloroform as solvent. Infrared spectra were recorded using KBr plates on either a Perkin–Elmer 683 or 1800 FTIR instrument. Mass spectral analyses were carried out in electron-impact mode and on a VG Micromass 7070F double-focussing spectrometer. Thin layer chromatographic analyses were carried out on aluminium-backed 0.2 mm thick silica gel 60 GF_{254} plates supplied by Merck while flash chromatographic purifications were conducted according to the method of Still *et al.*[22] using Merck silica gel 60 (230–400 mesh) as adsorbent. All solvents and common reagents were purified by established procedures.[23]

Syntheses

(1*S*,2*R*,3*R*,6*R*)-6-{[(1,1-Dimethylethyl)diphenylsilyl]oxy}-5-methylcyclohex-4-ene-1,2,3-triol (6). (1,1-Dimethylethyl)-diphenylsilyl chloride (TBDPSCl; 2.42 g, 8.82 mmol) was added, dropwise, to a magnetically stirred solution of the diol **4** (1.01 g, 8.02 mmol) and imidazole (1.75 g, 25.65 mmol) in dry CH_2Cl_2 (15 ml) maintained at 18 °C under a nitrogen atmosphere. Stirring was continued for a further 1.5 h, then the reaction mixture was poured into water (20 ml). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 20 ml) and the combined organic extracts were washed with NaCl (1 × 80 ml of a saturated solution) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the TBDPS ether **5**[24] (2.92 g, 99%) as a pale yellow oil. HRMS: m/z 364.1864 ($M^{\cdot+}$); $C_{23}H_{28}O_2Si$ requires 364.1859; δ_H 7.73–7.67 (complex m, 4H), 7.48–7.36 (complex m, 6H), 5.78–5.72 (complex m, 1H), 5.68–5.66 (complex m, 1H), 5.49–5.45 (complex m, 1H), 4.47–4.45 (complex m, 1H), 3.79 (dd, J = 5.6 and 5.5 Hz, 1H), 2.67 (d, J = 5.1 Hz, 1H, OH), 1.87 (s, 3H, CH_3), 1.09 (s, 9H, 3 × CH_3); m/z 364 ($M^{\cdot+}$, 7), 346 [$(M - H_2O)^+$, 1], 307 (5), 289 (76), 229 (100), 199 (96), 77 (30).

This unstable material was used immediately in the next step of the reaction sequence. Osmium tetroxide (3 ml of a 2.5 wt% solution in 2-methylpropan-2-ol) was added to a magnetically stirred solution of compound **5** (2.92 g, 8.02 mmol) and *N*-methylmorpholine-*N*-oxide (NMMNO; 1.41 g, 12.03 mmol) in a mixture of acetone–water (120 ml of a 3 : 1 v/v mixture) maintained at 0 °C. The resulting solution was heated at 60 °C for 1 h, then cooled and poured into sodium metabisulfite (100 ml of a 20 wt% aq. solution). The resulting mixture was extracted with CH_2Cl_2 (6 × 200 ml) and the combined organic extracts dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a dark brown oil. Subjection of this material to flash chromatography (silica gel, 3 : 2 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.4) afforded the triol **6** (231 mg, 7%) as a clear colourless oil. $[\alpha]_D$ − 86 (c 0.7 in $CHCl_3$); HRMS: m/z 362.1706 ($M - 2\ H_2O)^{\cdot+}$; $C_{23}H_{26}O_2Si$ requires 362.1702; ν_{max} 3400, 2956, 2930, 1110 cm^{-1}; δ_H 7.73–7.61 (complex m, 4H), 7.49–7.39 (complex m, 6H), 5.53 (d, J = 4.3 Hz, 1H), 4.40 (m, 1H), 4.18 (d, J = 3.8 Hz, 1H), 4.12 (m, 1H), 3.80 (m, 1H), 2.61 (br s, 1H, OH), 1.41 (s, 3H, CH_3), 1.06 (s, 9H, 3 × CH_3); δ_C 137.3 (C), 135.9 (CH), 135.8 (CH), 133.2 (C), 132.6 (C), 129.9 (CH), 129.7 (CH), 127.7 (CH), 127.5 (CH), 124.9 (CH), 72.5 (CH), 70.2 (CH), 69.2 (CH), 66.3 (CH), 27.0 (CH_3), 21.4 (CH_3), 19.7 (C); m/z 362 [$(M - 2\ H_2O)^{\cdot+}$, 5], 323 {$[M - (H_2O + C_4H_9)]^+$, 41}, 245 (63), 227 (40), 199 (100).

(1*S*,2*R*,5*R*,6*S*)-5,6-Bis-{[(1,1-dimethylethyl)dimethylsilyl]oxy}-2-{[(1,1-dimethylethyl)diphenylsilyl]oxy}-3-methylcyclohex-3-enol (7). (1,1-Dimethylethyl)dimethylsilyl trifluoromethanesulfonate (TBDMSOTf; 85 mg, 0.32 mmol) was added dropwise to a magnetically stirred solution of triol **6** (64 mg, 0.16 mmol) and Et_3N (49 mg, 0.48 mmol) in CH_2Cl_2 (5 ml) maintained at −78 °C under a nitrogen atmosphere. The reaction mixture was allowed to warm to 18 °C over *ca.* 0.5 h, then stirred at this temperature for a further 0.5 h. The resulting solution was poured into sodium carbonate (10 ml of a saturated aqueous solution) and diluted with CH_2Cl_2 (5 ml). The separated aqueous phase was extracted with CH_2Cl_2

(3 × 10 ml) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 10 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.6) afforded the title alcohol **7** (58 mg, 58%) as a clear, colourless oil. $[\alpha]_D$ − 92 (*c* 0.9 in $CHCl_3$); HRMS: *m/z* 569.2942 ($M - C_4H_9)^+$; $C_{31}H_{49}O_4Si_3$ requires 569.2939; ν_{max} 2954, 2929, 2983, 2857, 1103, 1070, 1047, 879, 835, 776, 701 cm^{-1}; δ_H 7.71–7.66 (complex m, 4H), 7.46–7.34 (complex m, 6H), 5.24 (m, 1H), 4.46–4.42 (complex m, 2H), 4.08–4.05 (complex m, 1H), 3.86 (dd, *J* = 5.6 and 3.9 Hz, 1H), 2.70 (br s, 1H, OH), 1.50 (s, 3H, CH_3), 1.11 (s, 9H, 3 × CH_3), 0.88 (s, 9H, 3 × CH_3), 0.71 (s, 9H, 3 × CH_3), 0.06 (s, 6H, 2 × CH_3), −0.01 (s, 3H, CH_3), −0.08 (s, 3H, CH_3); δ_C 136.1 (CH), 136.0 (CH), 133.5 (C), 133.1 (C), 130.0 (CH), 129.9 (CH), 127.7 (CH), 127.6 (CH), 126.3 (CH), 73.1 (CH), 71.9 (CH), 71.5 (CH), 67.3 (CH), 27.2 (CH_3), 26.2 (CH_3), 25.8 (CH_3), 20.6 (CH_3), 19.6 (C), 18.4 (C), 18.1 (C), −4.3 (CH_3), −4.6 (CH_3), −5.1 (CH_3), (two signals obscured or overlapping); *m/z* 569 [$(M - C_4H_9)^+$, 40] 452 (82), 437 (57), 73 (100).

(2*R*,5*R*,6*R*)-5,6-Bis-{[(1,1-dimethylethyl)dimethylsilyl]oxy}-2-{[(1,1-dimethylethyl)diphenylsilyl]oxy}-3-methylcyclohex-3-enone (8). Dimethyl sulfoxide (52 mg, 0.67 mmol) was added, dropwise, to a magnetically stirred solution of oxalyl chloride (43 mg, 0.34 mmol) in dry CH_2Cl_2 (4 ml) maintained at −78 °C under an atmosphere of nitrogen. After 0.5 h, a solution of alcohol **7** (42 mg, 0.067 mmol) in CH_2Cl_2 (3 ml) was added, dropwise, to the reaction mixture. After a further 1 h, a solution of Et_3N (68 mg, 0.67 mmol) in CH_2Cl_2 (2 ml) was added dropwise and the resulting homogenous solution stirred at −78 °C for 20 min, then for a further 10 min at −10 °C. The reaction mixture was then diluted with CH_2Cl_2 (20 ml) and sodium bicarbonate (20 ml of a saturated aqueous solution). The separated aqueous phase was extracted with CH_2Cl_2 (3 × 40 ml) and the combined organic extracts washed with brine (2 × 100 ml), dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a pale yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 10 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.5) afforded ketone **8** (41 mg, 98%) as a clear, colourless oil. $[\alpha]_D$ −41 (*c* 2.4 in $CHCl_3$); HRMS: *m/z* 624.3488 ($M^{\cdot+}$); $C_{35}H_{56}O_4Si_3$ requires 624.3486; ν_{max} 2929, 2856, 1748, 1472, 1428, 1361, 1256, 1112, 837, 779, 702 cm^{-1}; δ_H 7.71–7.67 (complex m, 4H), 7.44–7.32 (complex m, 6H), 5.40 (d, *J* = 3.0 Hz, 1H), 4.84 (s, 1H), 4.41 (d, *J* = 3.2 Hz, 1H), 4.36 (m, 1H), 1.55 (s, 3H, CH_3), 1.09 (s, 9H, 3 × CH_3), 0.84 (s, 9H, 3 × CH_3), 0.80 (s, 9H, 3 × CH_3), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3), −0.01 (s, 3H, CH_3), −0.08 (s, 3H, CH_3); δ_C 204.5 (C), 136.3 (CH), 136.1 (CH), 133.6 (C), 132.9 (C), 129.7 (CH), 127.5 (CH), 127.4 (CH), 126.5 (CH), 78.8 (CH), 74.4 (CH), 72.2 (CH), 27.0 (CH_3), 25.9 (CH_3), 25.8 (CH_3), 20.2 (CH_3), 19.8 (C), 18.2 (C), −4.5 (CH_3), −4.8 (CH_3), −4.9 (CH_3), (four signals obscured or overlapping); *m/z* 624 ($M^{\cdot+}$, 4), 567 [$(M - C_4H_9)^+$, 69], 539 (12), 435 (36), 275 (63), 73 (100).

(1*S*, 6*S*)-6-{[(1,1-Dimethylethyl)diphenylsilyl]oxy}-2-iodocyclohexa-2,4-dien-1-ol (9). (1,1-Dimethylethyl)diphenylsilyl chloride (3.96 ml, 15.2 mmol) was added dropwise to a magnetically stirred solution of diol **3** (3.30 g, 13.8 mmol) and imidazole (2.83 g, 41.6 mmol) in dry CH_2Cl_2 (70 ml) maintained at 18 °C under a nitrogen atmosphere. Stirring was continued for 7 h, then the reaction mixture was poured into water (90 ml). The separated aqueous layer was extracted with CH_2Cl_2 (2 × 100 ml) and the combined organic layers were washed with NaCl (1 × 100 ml of a 50% v/v aq. solution) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to give the title compound **9**[18] (6.40 g, 97%) as a light yellow oil. δ_H 7.78–7.38 (complex m, 10H), 6.62 (d, *J* = 5.5 Hz, 1H), 5.65 (dd, *J* = 9.6 and 3.5 Hz, 1H), 5.54 (dd, *J* = 9.6 and 5.5 Hz, 1H), 4.51 (m, 1H), 4.08 (d, *J* = 6.0 Hz, 1H), 2.80 (br m, 1H), 1.09 (br s, 9H). This unstable material was used immediately in the next step of the reaction sequence.

(3a*R*,4*R*,5*S*,7a*R*)-4-{[(1,1-Dimethylethyl)diphenylsilyl]oxy}-3a,4,5,7a-tetrahydro-6-iodo-2,2-dimethyl-1,3-benzodioxol-5-ol (11). Osmium tetroxide (4.0 ml of a 2.5 wt% solution in 2-methylpropan-2-ol, 0.47 mmol) was added, dropwise, to a magnetically stirred solution of alcohol **9** (3.84 g, 8.06 mmol) and *N*-methylmorpholine-*N*-oxide (1.22 g, 10.4 mmol) in acetone–water (200 ml of a 3 : 1 v/v mixture) maintained at 0 °C. The resulting solution was warmed to 4 °C, stirred at this temperature for 30 h, then treated with sodium metabisulfite (100 ml of a 20% w/v aq. solution). After 1 h the reaction mixture was concentrated under reduced pressure and the residue thus obtained was partitioned between diethyl ether (500 ml) and NaCl (300 ml of a 50% w/v aq. solution). The separated aqueous phase was extracted with diethyl ether (2 × 500 ml) and the combined ethereal fractions were washed with HCl (500 ml of a 10% v/v aq. solution), then brine (1 × 500 ml) before being dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford the triol **10**[18] (4.00 g, 98%) as a tan-coloured oil. This unstable material was used immediately in the next step of the reaction sequence.

p-TsOH (8 mg, 0.421 mmol) was added to a magnetically stirred solution of triol **10** (4.00 g, 7.84 mmol) in dry 2,2-dimethoxypropane (50 ml) maintained at 18 °C under a nitrogen atmosphere. After 3 h the reaction mixture was treated with Et_3N (300 μl, 2.15 mmol) and the resulting mixture concentrated under reduced pressure. The residue so-formed was dissolved in diethyl ether (300 ml) then washed with NaOH (1 × 90 ml of a 1 M aq. solution) and water (1 × 90 ml). The separated aqueous phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure and the residue subjected to flash chromatography (silica gel, 1 : 10 v/v ethyl acetate–hexane elution) to afford, after concentration of the appropriate fractions (R_f 0.3), the title acetonide **11**[18] (3.67 g, 85%) as a clear, colourless oil. $[\alpha]_D$ +19 (*c* 1.4 in $CHCl_3$); HRMS: *m/z* 535.0800 ($M - CH_3)^+$; $C_{24}H_{28}IO_4Si$ requires 535.0802; ν_{max} 3556, 2932, 1428, 1131, 1113, 1052 cm^{-1}; δ_H 7.73–7.62 (complex m, 4H), 7.49–7.38 (complex m, 6H), 6.53 (m, 1H), 4.48 (m, 1H), 4.29 (dd, *J* = 5.4 and 3.5 Hz, 1H), 4.20 (app t, *J* = *ca.* 5.4 Hz, 1H), 4.06–4.02 (complex m, 1H), 2.40 (d, *J* = 8.6 Hz, 1H), 1.26 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 1.09 (s, 9H, 3 × CH_3); δ_C 137.1 (CH), 136.0 (CH), 135.6 (CH), 132.3 (C), 130.2 (CH), 130.1 (CH), 128.1 (CH), 127.9 (CH), 109.8 (C), 104.9 (C), 75.2 (CH), 73.8 (CH), 72.2 (CH), 71.8 (CH), 27.6 (CH_3), 26.9 (CH_3), 26.1 (CH_3), 19.4 (C), (one signal obscured or overlapping); *m/z* 536 and 535 [$(M - CH_3)^+$, <1 and <1], 436 and 435 (21 and 50), 199 [$(C_{12}H_{11}SiO)^{\cdot+}$, 100].

(3a*R*,4*R*,7a*R*)-4-{[(1,1-Dimethylethyl)diphenylsilyl]oxy}-3a,7a-dihydro-6-iodo-2,2-dimethyl-1,3-benzodioxol-5(4*H*)-one (12). Dimethyl sulfoxide (200 μl, 2.81 mmol) was added, dropwise, to a magnetically stirred solution of oxalyl chloride (118 μl, 1.35 mmol) in dry CH_2Cl_2 (4 ml) maintained at −78 °C under a nitrogen atmosphere. After 0.5 h a solution of compound **11** (300 mg, 0.545 mmol) in dry CH_2Cl_2 (3 ml) was added dropwise to the reaction mixture. After a further 1 h a solution of Et_3N (392 μl, 2.81 mmol) in CH_2Cl_2 (1 ml) was added and the resulting homogeneous solution was stirred at −78 °C for 20 min and then for a further 10 min after warming to −10 °C. The reaction mixture was then diluted with CH_2Cl_2 (20 ml) and $NaHCO_3$ (20 ml of a saturated aq. solution). The separated organic phase was washed with water (2 × 20 ml) and brine (2 × 20 ml), then dried ($MgSO_4$), filtered and concentrated under reduced pressure to yield the title compound **12** (269 mg, 90%) as a clear colourless oil. $[\alpha]_D$

+9.4 (*c* 5.0 in $CHCl_3$); HRMS: *m/z* 533.0643 $(M - CH_3)^+$; $C_{24}H_{26}IO_4Si$ requires 533.0645; ν_{max} 2932, 1705, 1223, 1113, 1069 cm^{-1}; δ_H 7.70–7.66 (complex m, 2H), 7.59–7.56 (complex m, 2H), 7.46–7.35 (complex m, 7H), 4.77 (m, 1H), 4.44 (m, 2H), 1.29 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.06 (s, 9H, 3 × CH_3); δ_C 188.8 (C), 151.6 (CH), 135.9 (CH), 132.4 (C), 131.9 (C), 130.1 (CH), 130.0 (CH), 127.8 (CH), 127.7 (CH), 111.7 (C), 102.9 (C), 78.2 (CH), 73.6 (CH), 72.2 (CH), 27.7 (CH_3), 26.8 (CH_3), 26.6 (CH_3), 19.4 (C) (one peak due to sp^2-hybridised carbon obscured or overlapping); *m/z* 534 and 533 $[(M - CH_3)^+$, *ca.* 1 and 1], 492 and 491 (20 and 36), 434 and 433 (20 and 34), 406 and 405 (20 and 40), 307 and 306 (36 and 100), 199 $[(C_{12}H_{11}SiO)^{\cdot+}$, 30].

(3*aR*,4*R*,7*aR*)-4-{[(1,1-Dimethylethyl)diphenylsilyl]oxy}-3a,7a-dihydro-2,2,6-trimethyl-1,3-benzodioxol-5(4*H*)-one (13). A solution of methyl magnesium chloride (160 μL of a 3 M solution in THF, 0.48 mmol) was added, dropwise, to a magnetically stirred solution of α-iodoenone **12** (120 mg, 0.22 mmol) and iron(III) chloride (4 mg, 0.02 mmol) in a mixture of THF (5 ml) and *N*-methylpyrrolidinone (NMP; 195 mg, 1.97 mmol) maintained at 0 °C under a nitrogen atmosphere. The resulting mixture was stirred at this temperature for a further 0.5 h, then diluted with water (10 ml). The reaction mixture was extracted with CH_2Cl_2 (3 × 10 ml) and the organic extracts were combined, dried ($MgSO_4$), filtered and concentrated under reduced pressure to afford a light yellow oil. Subjection of this material to flash chromatography (silica gel, 1 : 10 v/v ethyl acetate–hexane elution) and concentration of the appropriate fractions (R_f 0.3) afforded the title enone **13** (90 mg, 94%) as a colourless oil. $[\alpha]_D$ −30 (*c* 0.8 in $CHCl_3$); HRMS: *m/z* 421.1831 $(M - CH_3)^+$; $C_{25}H_{29}O_4Si$ requires 421.1835; ν_{max} 2931, 2858, 1705, 1112, 1066, 702 cm^{-1}; δ_H 7.75–7.64 (complex m, 4H), 7.44–7.32 (complex m, 6H), 6.43 (dq, J = 3.9 and 0.7 Hz, 1H), 4.81–4.77 (complex m, 1H), 4.44–4.40 (complex m, 1H), 4.31 (d, J = 6.3 Hz, 1H), 1.77 (dd, J = 1.5 and 1.4 Hz, 3H, CH_3), 1.34 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.11 (s, 9H, 3 × CH_3); δ_C 196.1 (C), 136.2 (C), 136.1 (CH), 136.0 (CH), 133.0 (C), 132.9 (C), 129.8 (CH), 129.7 (CH), 127.5 (CH), 127.4 (CH), 110.8 (C), 78.8 (CH), 75.2 (CH), 71.5 (CH), 27.8 (CH_3), 26.9 (CH_3), 26.5 (CH_3), 19.5 (C), 15.9 (CH_3), (one signal obscured or overlapping); *m/z* 421 $[(M - CH_3)^+$, 1], 379 (42), 321 (100), 293 (78), 227 (45), 199 (49).

(4*R*,5*R*,6*S*)-4,5,6-Trihydroxy-2-methyl-2-cyclohexen-1-one [(−)-gabosine A, 1]. HCl (1 drop of a conc. aq. solution) was added to a magnetically stirred solution of compound **13** (12 mg, 0.027 mmol) in methanol (2 ml) maintained at 18 °C under a nitrogen atmosphere. The resulting mixture was stirred at this temperature for 96 h, then concentrated under reduced pressure to afford a light yellow oil. ^1H NMR analysis of this oil suggested the presence of a *ca.* 1 : 2 mixture of the target compound **1** and its 6-TBDPS ether so it was dissolved in THF (3 ml), then tris(dimethylamino)sulfonium difluorotrimethylsilicate[25] (35 mg, 0.13 mmol) was added in portions. The resulting mixture was stirred at 18 °C for 0.5 h, then concentrated under reduced pressure to afford a pale yellow oil that was subject to flash chromatography (silica gel, 1 : 10 v/v methanol–chloroform elution). Concentration of the appropriate fractions (R_f 0.3) then gave gabosine A (**1**) (3.7 mg, 85%) as a pale yellow oil. $[\alpha]_D$ −131 (*c* 0.27 in methanol); HRMS: *m/z* 158.0582 $(M^{\cdot+})$; $C_7H_{10}O_4$ requires 158.0579; ν_{max} 3292, 2919, 1686 cm^{-1}; λ_{max} (methanol) 222 nm (ε 7200); δ_H (600 MHz) 6.75 (qd, $J_{3,7}$ = 1.5 and $J_{3,4}$ = 5.6 Hz, 1H, H-3), 4.38 (m, 1H, H-4), 4.32 (d, $J_{6,5}$ = 10.0 Hz, 1H, H-6), 3.73 (dd, $J_{5,6}$ = 10.0 and $J_{5,4}$ = 4.0 Hz, 1H, H-5), 1.82 (dd, $J_{7,3}$ = 1.5 and $J_{7,4}$ = 0.9 Hz, 1H, 7-CH_3); δ_C = 200.5 (C, C-1), 143.0 (CH, C-3), 136.9 (C, C-2), 75.1 (CH, C-6), 73.9 (CH, C-5), 67.4 (CH, C-4), 15.6 (CH_3, 7-CH_3); *m/z* 158 $(M^{\cdot+}$, 2), 140 (31), 111 (79), 98 (100), 70 (74).

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