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Enantioselective total synthesis of chiricanine B

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Abstract—First enantioselective total synthesis of chiricanine B **1**, a novel naturally occurring 3-hydroxybenzopyran, has been achieved from readily available methyl 3,5-hydroxybenzoate **2**. The absolute stereochemistry was established via a Sharpless' asymmetric dihydroxylation (AD) reaction.

1. Introduction

2,2-Dimethyl-2*H*-benzopyran moiety is present in more than 4000 compounds including natural products and designed structures.[1] Examining the characteristics of these compounds reveals their diverse structural properties, and more importantly, their wide ranging biological actions, suggesting that derivatives of this benzopyran motif may be capable of interacting with a variety of cellular targets.[1] In particular, 3-hydroxybenzopyrans constitute an important class of these compounds due to their diverse range of interesting biological properties including protein kinase related cytotoxicity, antifungal activity, and antitumor activity.[2–6]

Chiricanine B **1**, a novel stilbene containing the 3-hydroxy-2,2-dimethylbenzopyran moiety, was isolated from the root bark of *Lonchocarpus chiricanus* that is well known for its insecticidal properties in Panama.[7] This stilbene derivative was identified as one of the substances responsible for the antifungal and larvicidal activities of the *L. chiricanus* dichloromethane extract.[7] Its structure was resolved on the basis of spectrometric methods but the absolute stereochemistry was not determined. The construction of the benzopyran ring was achieved by Steck in 1971 in the synthesis of racemic decurcinol.[8] Recently syntheses of non-racemic chiral 3-hydroxybenzopyrans were reported by several groups who used asymmetric enone epoxidation or Jacobson's chromene epoxidation.[9–11] In continuation of our work on the synthesis of naturally occurring 3-hydroxybenzopyrans,[12] herein we report the first enantioselective total synthesis of chiricanine B **1** via a Sharpless AD reaction (Fig. 1).[13]

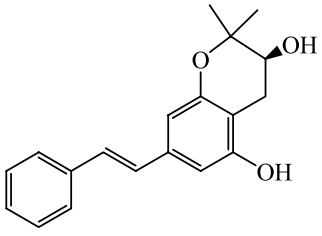

Figure 1. Chiricanine B **1**.

2. Results and discussion

The general strategic plan is summarized in Scheme 1; we envisioned that the desired chiricanine B **1** could be synthesized by a Wittig reaction. Next we focused on the construction of the 3-hydroxy benzopyan ring by treatment of the epoxide **10** under acidic conditions. The requisite chiral epoxide could be obtained by the application of Sharpless' AD reaction and then epoxidation. Further analysis indicated methyl 3,5-hydroxybenzoate **2** should be an ideal material.

The total synthesis of chiricanine B **1** is detailed in Scheme 2. The monobenzylated material **3** was readily available by selective extraction from a mixture of the dibenzylated product and diphenolic starting material **2**.[14] Then the remaining phenolic hydroxyl group was protected by a MOM group in 89% yield. After reduc-

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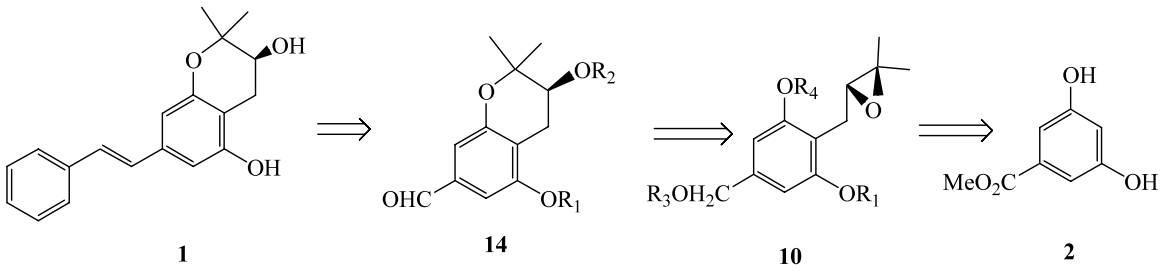


1 14 10 2

Scheme 1.

tion with $LiAlH_4$, the obtained alcohol **5** was converted to ether **6** in nearly quantitative yield.

Although several groups have reported that Bn and MOM are *ortho*-metallation directing groups,[15–17] regioselective lithiation at the C-4 position of **6** and then coupling resulted in poor yield under the conditions described.[15] It was felt that TMEDA was indispensable for this reaction and the addition of HMPA can greatly improve the coupling yield.[18] Therefore, **6** was indeed regioselectively lithiated at C-4 position in THF:TMEDA (8:1/v) at −20°C and coupled with prenyl bromide in the presence of HMPA at −78°C to furnish **7** in good yield (70%).

Treatment of **7** with AD-mix-β in ButOH:H_2O (1:1/v) at 0°C for 36 h provided the desired product **8** in 72% yield with 97% ee. Diol **8** was converted to **9** by selective mesylation of the secondary alcohol followed by treatment of K_2CO_3 in methanol to effect ring closure in a simple one-pot procedure.[19] The construction of the 3-hydroxybenzopyran ring was achieved by selectively cleaving the benzyl group under H_2/Pd5%–C followed by the addition of HCOOH in 61% yield for these two steps. A fourth protecting group, acetyl, was introduced to mask the corresponding hydroxy group to give **11** in 82% yield. The TBDMS group was cleanly removed and the resultant alcohol **12** was oxidized by PCC/NaOAc in CH_2Cl_2 to produce aldehyde **13** uneventfully in 85% yield.

Wittig reaction of **13** in benzene furnished the stilbene **14** in 80% yield, with no *cis*-isomer being observed.[20,21] To explain this almost exclusive *trans*-selectivity, the planar transition state proposed by Vedejs can be adopted.[22] A model reaction carried out by treatment of benzaldehyde with the phosphonium salt under the same conditions confirmed the *trans*-selectivity (*trans*-stilbene:*cis*-stilbene = 8.5:1.5).

Finally, the Ac group and the MOM group were smoothly removed under base and acid conditions respectively in the same pot to afford **1** (76% yield). Spectroscopic data of **1** are identical with those reported.[7] Since the rotation direction of synthetic **1** is the same as the naturally occurring compound, the absolute configuration of chiricanine B is established as *S*.

In conclusion, the first enantioselective total synthesis of chiricanine B **1** (3.5% overall yield in 13 steps), has been achieved from methyl 3,5-dihydroxybenzoate **3**. The absolute stereochemistry was introduced by employing Sharpless' AD reaction. The synthetic route presented here allows access to the variety of compounds, which contain the chiral 3-hydroxybenzopyran ring.

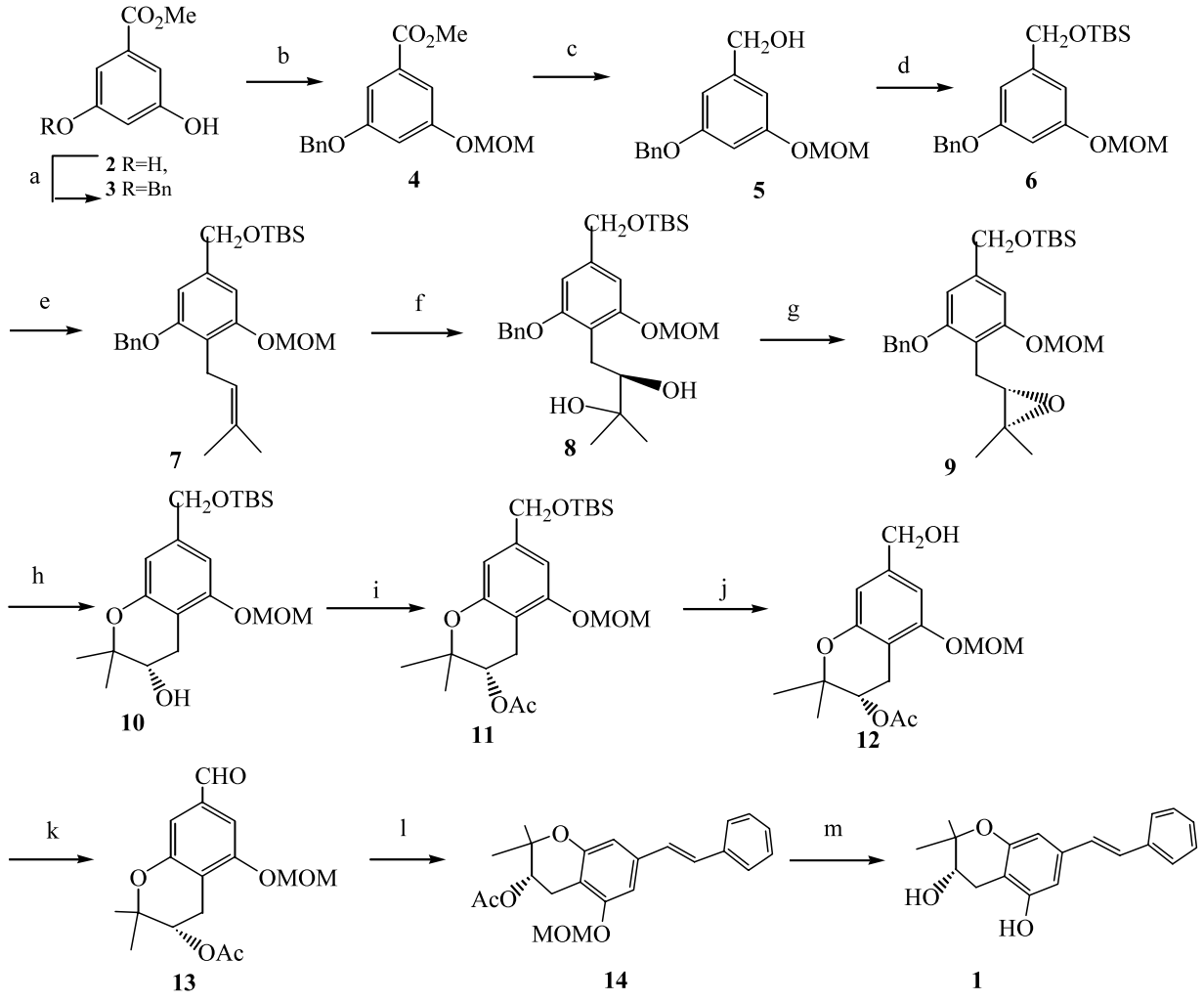
3. Experimental

3.1. General information

Melting points were measured on a Kofler hot stage apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on an Avance DRX200 or a Varian Mercury 300 BB spectrometer in $CDCl_3$ solution using TMS as the internal reference. IR spectra were obtained on a Nicolet AVATAR 360FT-IR spectrometer. Mass spectra were measured on a VG ZAB-HS or VG-7070 spectrometer by direct inlet at 70 eV. High resolution mass spectra were recorded on APEX™ II, ESI positive. Optical rotations were measured using sodium D line on a Perkin Elmer 341 polarimeter. The enantiomeric excess values were determined by chiral stationary phase HPLC analysis (Dikma Chiralcel OD 10U 250×4.6 M, hexane:2-propanol = 95:5, flow rate = 1 ml/min, detected at 254 nm on a Prostar330 detector). TLC monitored all reactions. Purification of products was conducted by flash column chromatography on silica gel (200–300 mesh) purchased from Yan Tai Yuan Bo Silica Gel Co.

3.2. Methyl 3-benzyloxy-5-methoxymethoxybenzoate 4

A solution of **3** (3.37 g, 13 mmol) in THF (60 ml) was cooled to 0°C under Ar. Then NaH (60%, 626 mg, 15.6 mmol) was added slowly. After the hydrogen evolution was over, MOMCl (1.14 ml, 15.6 mmol) was dropped via syringe and the reaction mixture was allowed to warm to rt 4 h later, the reaction mixture was quenched by the slow addition of water (5 ml) and was further extracted with ether (3×100 ml). The combined organic layers were washed by brine, dried over $MgSO_4$, filtered, and concentrated to afford yellowish oil. Flash chromatography (16:1 petrol ether/ethyl acetate) provided **4** (3.49 g, 89%) as colorless oil. ^1H NMR (200



Scheme 2. *Reagents and conditions*: (a) BnBr, K_2CO_3, acetone, reflux, 3 h, 51%; (b) NaH, MOMCl, THF, 0°C to rt, 4 h, 89%; (c) $AlLiH_4$, Et_2O, 0°C to rt, 4 h, 91%; (d) TBDMSCl, imidazole, DMF, rt, 1 h, 98%; (e) *n*-BuLi, TMEDA, THF, −20°C to 0°C, 1 h, then HMPA, prenyl bromide, −78 to 0°C, 2 h, 70%; (f) BuOH–H_2O (1:1), AD-mix-β, $NH_2SO_2CH_3$, 0°C, 36 h, 72%; (g) (1) MsCl, pyridine, CH_2Cl_2, rt, 12 h; (2) K_2CO_3, CH_3OH, reflux, 4 h, 65% for two steps; (h) (1) Pd 5%–C, H_2, EtOAc, rt, 4 h; (2) HCOOH, EtOAc, rt, overnight, 61% for two steps; (i) pyridine, Ac_2O, DMAP(cat.), rt, 4 h, 82%; (j) TBAF, THF, rt, 1 h, 99%; (k) PCC, NaOAc silica gel, CH_2Cl_2, rt, 4 h, 85%; (l) *n*-BuLi, benzene, $Ph_3P^+CH_2C_6H_5Cl^-$, rt, 3 h, 80%; (m) (1) K_2CO_3, CH_3OH, rt, overnight; (2) 3N HCl, CH_3OH, reflux, 1 h, 76% for two steps.

MHz): 3.47 (s, 3H), 3.90 (s, 3H), 5.08 (s, 2H), 5.18 (s, 2H), 6.86–6.89 (m, 1H), 7.30–7.46 (m, 7H). IR (film): 1722, 1597, 1150, 1025, 767, 698. EIMS, *m*/*z* (%): 302 (M^+, 19), 271 (11), 135 (13), 91 (100), 45 (66).

3.3. 3-Benzyloxy-5-methoxymethoxybenzyl alcohol 5

To a 0°C slurry of $LiAlH_4$ (595 mg, 15.7 mmol) in anhydrous ether (60 ml), **4** (3.15 g, 104 mmol) was added under Ar. The slurry was allowed to warm to ambient temperature and stirred for 3 h. Then the reaction was quenched by Et_2O:H_2O/10:1. The organic phase was extracted with Et_2O (3×100 ml), washed by water (10 ml) and brine, dried over Na_2SO_4, concentrated. Flash chromatography (2:1 petrol ether/ethyl acetate) gave **5** (2.59 g, 91%) as a white powder. Mp = 62–63°C. ^{1}H NMR (200 MHz, $CDCl_3$, δ ppm): 1.80 (br. 1H), 3.38 (s, 3H), 4.53 (s, 2H), 4.96 (s, 2H), 5.08 (s, 2H), 6.53 (s, 1H), 6.58 (s, 2H), 7.23–7.36 (m, 5H). IR (KBr): 3347, 3261, 2919, 1590. EIMS, *m*/*z* (%): 274 (M^+, 27), 149 (48), 91 (100), 45 (35).

3.4. (3-Benzyloxy-5-methoxymethoxybenzyl) *tert*-butyldimethyl silyl ether 6

To a solution of **5** (2.50 g, 9.1 mmol) in DMF (3 ml) was added imidazole (1.24 g, 18.2 mmol) and TBDMSCl (1.51 g, 10 mmol) successively at ambient temperature. After 1 h, the reaction mixture was diluted with ether (90 ml), washed by water (5 ml) and brine, dried over $MgSO_4$ and concentrated. Flash chromatography (32:1 petrol ether/ethyl acetate) afforded **6** (3.46 g, 98%) as colorless oil. ^{1}H NMR (200 MHz): 0.10 (s, 6H), 0.93 (s, 9H), 3.48 (s, 3H), 4.69 (s, 2H), 5.05 (s, 2H), 5.15 (s, 2H), 6.58–6.59 (m, 1H), 6.64 (s, 2H), 7.34–7.46 (m, 5H). IR (film): 2953, 1597, 1456, 1371, 1254, 1147, 961, 838, 778. EIMS, *m*/*z* (%): 388 (M^+, 1), 331 (42), 301 (36), 269 (10), 225 (14), 91 (100), 45 (20).

3.5. (3-Benzyloxy-4-prenyl-5-methoxymethoxybenzyl) *tert*-butyl-dimethyl silyl ether 7

A solution of BuLi in petrol ether (2.5 M, 3.94 ml, 9.90 mmol) was added dropwise to a stirred solution of **6** (3.20 g, 8.25 mmol) in THF: TMEDA (40 ml:5 ml) under Ar at −20°C. The reaction mixture was allowed to stand at −20 ~ 0°C for 1 h. Then the solution was cooled to −78°C, followed by the addition of HMPA (0.5 ml) and prenyl bromide (1.14 ml, 9.90 mmol). The reaction mixture was stirred for another 2 h between −78°C and 0°C. Finally, water (5 ml) was added and the product extracted with Et_2O. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (99:1 petrol/ethyl acetate), which afforded **7** (3.16 g, 70%) as a yellow oil. ^{1}H NMR (200 MHz): 0.10 (s, 6H), 0.96 (s, 9H), 1.68 (s, 3H), 1.73 (s, 3H), 3.44 (d, $J=7.2$ Hz, 2H), 3.50 (s, 3H), 4.78 (s, 2H), 5.10 (s, 2H), 5.21 (s, 2H), 6.67 (s, 1H), 6.73 (s, 1H), 7.34–7.47 (m, 5H). IR (film): 2929, 1589, 1434, 1065, 838. EIMS, m/z (%): 456 (M^+, 12) 399 (11) 387 (32) 91 (90) 45 (100). Calcd for (M+H): 457.2769. Found 457.2768.

3.6. (*R*)-(3-Benzyloxy-4-(2,3-dihydroxy-3-methylbutyl)-5-methoxymethoxybenzyl) *tert*-butyl-dimethyl silyl ether 8

A 50 ml flask, equipped with a magnetic stirrer, was charged with *t*-BuOH (5 ml), water (5 ml), and AD-mix-β (1.4 g). Stirring at rt produced two clear phases. Methane sulfonamide (104 mg, 1.1 mmol) was added and the mixture was cooled to 0°C whereupon some of the dissolved salts precipitated. Olefin **7** (456 mg, 1 mmol) was added at once, and the heterogeneous slurry was stirred vigorously at 0°C for 36 h. While the mixture was stirred at 0°C, solid sodium sulfite (1.5 g) was added and the mixture was allowed to warm to room temperature and stirred for 30 min. Ethyl acetate (10 ml) was added to the mixture. After separation of the layers, the aqueous phase was further extracted with EtOAc (3×15 ml). The combined organic layers were washed with 2N KOH (5 ml) thoroughly, dried over anhydrous $MgSO_4$ and concentrated. This crude product was purified by flash chromatography (2:1 petrol/ethyl acetate) to afford **8** (353 mg, 72%) as a colorless oil. $[\alpha]_D^{20}=+6$ (c 1.1, $CHCl_3$). 97% e.e., ret. time = 7.723 min for the (*R*)-isomer and 8.701 min for the (*S*)-isomer. ^{1}H NMR (200 MHz): 0.10 (s, 6H), 0.94 (s, 9H), 1.21 (s, 6H), 2.48 (br., 1H), 2.73 (br., 1H), 2.77 (dd, $J=13.8$ Hz, 10.4 Hz, 1H), 3.03 (dd, $J=13.8$ Hz, 2 Hz, 1H), 3.49 (s, 3H), 3.52–3.62 (m, 1H), 4.71 (s, 2H), 5.10 (s, 2H), 5.21 (s, 2H), 6.71 (s, 1H), 6.76 (s, 1H), 7.35–7.41 (m, 5H). IR (film): 3412, 2928, 1588, 1068, 838, 777; EIMS, m/z (%): 490 (M^+, 3) 91 (100) 45 (95). Calcd for (M+NH_4): 508.3089. Found: 508.3099.

3.7. (*S*)-(3-Benzyloxy-4-(2,3-oxy-3-methylbutyl)-5-methoxymethoxybenzyl) *tert*-butyl-dimethyl silyl ether 9

To a solution of **8** (220 mg, 0.45 mmol) in CH_2Cl_2 (3 ml), pyridine (0.073 ml, 0.90 mmol) and MsCl (0.052 ml) was added at 0°C. Then the reaction mixture was stirred for 12 h at rt. After completion of the reaction, the volatiles were evaporated and the residue were dissolved in MeOH (5 ml) and treated with K_2CO_3 (124 mg, 0.90 mmol) by refluxing for 4 h. The solvent was removed under vaccuo and the residue was diluted by Et_2O (30 ml), washed by water (2 ml), dried ($MgSO_4$), and concentrated. The residue was purified by flash chromatography (8:1 petrol/ethyl acetate), which afforded **9** (138 mg, 65%) as colorless oil. $[\alpha]_D^{21}=-6$ (c 1.2, $CHCl_3$). ^{1}H NMR (200 MHz): 0.09 (s, 6H), 0.94 (s, 9H), 1.24 (s, 3H), 1.31 (s, 3H), 2.83 (dd, $J=12.8$ Hz, 4.2 Hz, 1H), 2.97–3.02 (m, 1H), 3.14 (dd, $J=12.8$ Hz, 4.2 Hz, 1H), 3.48 (s, 3H), 4.69 (s, 2H), 5.09 (s, 2H), 5.19 (s, 2H), 6.67 (s, 1H), 6.74 (s, 1H), 7.34–7.40 (m, 5H). IR (film): 3414, 2928, 1590, 1114, 1072. EIMS, m/z (%): 472 (M^+, 4), 415 (18), 91 (100), 45 (28). Calcd for (M+NH_4): 490.2983, Found: 490.2995.

3.8. (*S*)-2,2-Dimethyl-3-hydroxy-5-methoxymethoxy-7-(*tert*-butyl-dimethyl)silyloxybenzopyan 10

5% Pd/C (100 mg) was suspended in EtOAc (6 ml) and hydrogen was pumped into the slurry to saturate. Then the solution of **9** (120 mg, 0.254 mmol) in EtOAc was charged and the solution was stirred under a hydrogen atmosphere for another 3 h at rt. After the hydrogenlization was over, HCOOH (0.5 ml) was added to complete the cyclization. 5% Pd/C was filtered through a short pad of silica gel. EtOAc was evaporated and the residue was purified by flash chromatography (4:1 petrol/ethyl acetate) to give the desired **10** (73.2 mg, 61%) as colorless oil. $[\alpha]_D^{20}=-12$ (c 1.1, $CHCl_3$). ^{1}H NMR (200 MHz): 0.10 (s, 6H), 0.94 (s, 9H), 1.30 (s, 3H), 1.36 (s, 3H), 2.70 (dd, $J=17.4$ Hz, 5.4 Hz, 1H), 2.92 (dd, $J=17.4$ Hz, 5.0 Hz, 1H), 3.48 (s, 3H), 3.74–3.82 (m, 1H), 4.65 (s, 2H), 5.18 (s, 2H), 6.52 (s, 1H), 6.63 (s, 1H). IR (film): 3406, 2927, 1098, 838, 777. Calcd for (M+H): 383.2248, Found: 383.2255.

3.9. (*S*)-3-Acetyloxy-2,2-dimethyl-5-methoxymethoxy-7-(*tert*-butyl-dimethyl)silyloxybenzopyan 11

A solution of **10** (65 mg, 0.170 mmol) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was added DMAP(5 mg) and stirred at ambient temperature for 8 h. Then the reaction mixture was diluted with EtOAc (3×10 ml), washed by water (1 ml) and brine, dried over Na_2SO_4, concentrated in vacuo. A flash chromatography (8:1 petrol ether/ethyl acetate) afforded **11** (59 mg, 82%) as a colorless oil. $[\alpha]_D^{20}=-9$ (c 0.8, $CHCl_3$). ^{1}H NMR (300 MHz): 0.12 (s, 6H), 0.97 (s, 9H), 1.33 (s, 3H), 1.35 (s, 3H), 2.10 (s, 3H), 2.72 (dd, $J=15.8$ Hz, 5.2 Hz, 1H), 3.01 (dd, $J=15.8$ Hz, 5.4 Hz, 1H), 3.49 (s, 3H), 4.68 (s, 2H), 5.05 (t, $J=5.2$ Hz, 1H), 5.19 (s, 2H), 6.55 (s, 1H), 6.66 (s, 1H). IR (film): 2928, 1739, 1059. EIMS, m/z (%): 424 (M^+, 3), 381 (15), 367 (47), 45 (94).

3.10. (*S*)-3-Acetyloxy-2,2-dimethyl-5-methoxymethoxy-benzopyanyl-7-methanol 12

A solution of **11** (54 mg, 0.127 mmol) in THF (3 ml) was added a solution of *t*-BAF in THF (1 M, 0.19 ml, 0.19 mmol) and the reaction mixture was stirred for 2 h

at ambient temperature. After the evaporation of the solvent, the residue was purified by a flash chromatography (2:1 petrol/ethyl acetate) to give **12** (39 mg, 99%) as colorless oil. $[\alpha]_D^{20}=+5$ (*c* 0.5, $CHCl_3$). ^1H NMR (300 MHz): 1.20 (s, 3H), 1.23 (s, 3H), 1.71 (br., 1H), 1.96 (s, 3H), 2.61 (dd, $J=17.8$ Hz, 5.0 Hz, 1H), 2.89 (dd, $J=17.8$ Hz, 5.4 Hz, 1H), 3.36 (s, 3H), 4.50 (s, 2H), 4.94 (t, $J=5.2$ Hz, 1H), 5.09 (s, 2H), 6.46 (s, 1H), 6.56 (s, 1H). IR (film): 3411, 1737, 1587, 1151. EIMS, *m*/*z* (%): 310 (M^+, 4), 45 (100).

3.11. (*S*)-3-Acetyloxy-2,2-dimethyl-5-methoxymethoxybenzopyanyl-7-methanal 13

To a 25 ml flask, equipped with a magnetic stirrer, PCC (45 mg, 0.20 mmol), anhydrous NaOAc (10 mg, 0.11 mmol), silica gel (10 mg) and CH_2Cl_2 (4 ml) were added and stirred at ambient temperature. A solution of **12** (39 mg, 0.126 mmol) in CH_2Cl_2 (1 ml) was dropped and the reaction mixture was stirred for 4 h. After filtration, the volatiles were evaporated and the residue was purified through flash chromatography (8:1 petrol/ethyl acetate), which afford the **13** (33 mg, 85%) as a colorless oil. $[\alpha]_D^{20}=+21$ (*c* 1.5, $CHCl_3$). ^1H NMR (300 MHz): 1.23 (s, 3H), 1.26 (s, 3H), 1.99 (s, 3H), 2.68 (dd, $J=18.6$ Hz, 4.8 Hz, 1H), 2.96 (dd, $J=18.6$ Hz, 5.2 Hz, 1H), 3.40 (s, 3H), 4.96 (t, $J=5.0$ Hz, 1H), 5.15 (s, 2H), 6.95 (s, 1H), 7.06 (s, 1H), 9.76 (s, 1H). IR (film): 3387, 2924, 1738, 1697, 1067. Calcd for ($M+NH_4$): 326.1598. Found: 326.1599.

3.12. (*S*)-3-Acetyloxy-5-methoxymethoxy-2,2-dimethyl-7-(2-phenylethenyl)benzopyan 14

To the slurry of phosphonium salt (42.7 mg, 0.11 mmol) in benzene (4 ml) flushed with Ar, was added 0.1 ml of *n*-BuLi in petrol (2.3 M, 0.048 ml, 0.11 mmol). The colored solution was stirred at ambient temperature for 1 h, after which the solution of **13** in benzene (1 ml) was dropped via syringe. After stirring overnight, the reaction was quenched by water (1 ml), extracted with ether (3×10 ml), washed and concentrated. The residue was purified by a flash chromatography (32:1 petrol/ethyl acetate) to afford the desired **14** (32 mg, 80%) as a colorless oil. $[\alpha]_D^{20}=-6$ (*c* 0.8, $CHCl_3$). ^1H NMR (300 MHz): 1.33 (s, 3H), 1.35 (s, 3H), 2.08 (s, 3H), 2.73 (dd, $J=18.2$ Hz, 5.0 Hz, 1H), 2.96 (dd, $J=18.2$ Hz, 5.2 Hz, 1H), 3.40 (s, 3H), 5.05 (t, $J=5.0$ Hz, 1H), 5.24 (s, 2H), 6.74 (s, 1H), 6.82 (s, 1H), 9.76 (s, 1H). IR (film): 3393, 2932, 1737, 1057. Calcd for (M+H): 383.1853. Found: 383.1851.

3.13. (*S*)-3,5-Dihydroxy-2,2-dimethyl-7-(2-phenylethenyl)benzopyan 1

In a 25 ml flask, a solution of **14** (20 mg, 0.05 mmol) in methanol (4 ml) was added K_2CO_3 (28 mg, 0.20 mmol) and the reaction mixture was stirred overnight. After the Ac group was smoothly removed, 3 M HCl (2 ml) was charged and the solution was refluxed for 20 min whereupon the MOM group was easily cleaved. Then methanol was evaporated and the residue was diluted with EtOAc, washed by saturated $NaHCO_3$, water and brine, dried and concentrated. The crude product was purified (2:1 petrol/ethyl acetate) to furnish **1** (11 mg, 76%) as a yellow amorphous powder. $[\alpha]_D^{20}=-12$ (*c* 0.9, $CHCl_3$) [lit.[7] $[\alpha]_D^{20}=-9$ (*c* 0.3, $CHCl_3$). ^1H NMR (300 MHz): 1.33 (s, 3H), 1.39 (s, 3H), 2.73 (dd, $J=17.1$ Hz, 5.0 Hz, 1H), 2.94 (dd, $J=17.1$ Hz, 4.8 Hz, 1H), 3.85 (t, $J=5.0$ Hz, 1H), 4.86 (br., 1H), 6.54 (s, 1H), 6.65 (s, 1H), 6.94 (d, $J=15.9$ Hz, 1H), 7.03 (d, $J=16.5$ Hz, 1H), 7.25 (t, $J=7.5$ Hz, 1H), 7.35 (t, $J=7.2$ Hz, 2H), 7.48 (d, $J=7.5$ Hz, 2H). ^{13}C NMR (75 MHz), δ 22.24, 24.48, 26.28, 69.25, 77.20, 105.02, 106.23, 107.99, 126.50, 126.50, 127.64, 128.06, 128.67, 128.76, 128.76, 137.14, 137.26, 153.93, 154.54. IR (film): 3402, 2924, 1070, 745, 632, 517. FAB-MS: 296 (M^+, 55), 303 (M+Li, 20), 319 (M+Na, 10), 225 (40), 202 (58), 76 (44). Calcd for (M+H): 297.1485. Found: 297.1485.

Acknowledgements

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