Synthesis of Magnoshinin and Cyclogalgravin: Modified Stobbe Condensation Reaction

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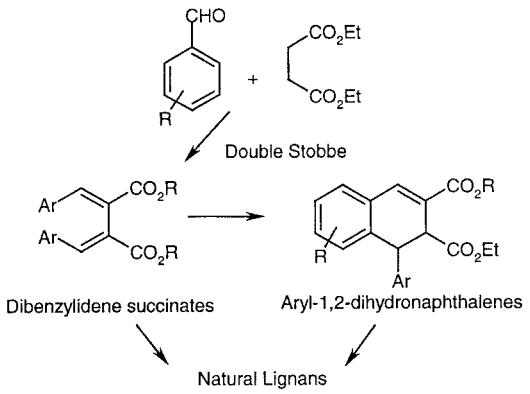
Abstract: The development of new methods for lignan synthesis is reported. A recently reported method for the preparation of 1-aryl-1,2-dihydronaphthalenes is exploited to prepare magnoshinin, a naturally occurring lignan, and cyclogalgravin (3,4-dehydrogalbulin), a derivative of a natural lignan.

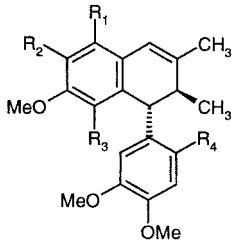
Key words: magnoshinin, cyclogalgravin, dehydrogalbulin, Stobbe condensation, 1,2-dihydronaphthalene, lignan

The double Stobbe condensation of a succinic diester with an aromatic aldehyde is a useful synthetic route for the construction of the basic lignan skeleton.[1–7] Two successive Stobbe condensation reactions of a succinate diester with an aromatic aldehyde generates an (*E*,*E*)-dibenzylidenesuccinate (Scheme 1) that is found in naturally occurring lignans such as phebalarin,[8] jatrodien,[9] and taiwanin.[10]



Scheme 1

Derivatives of (*E*,*E*)-dibenzylidenesuccinates (anhydrides and lactones) have also been found to undergo photochemical and thermal cyclizations followed by a 1,5-sigmatropic shift to give 1,2-dihydronaphthalene derivatives that are useful precursors to arylnaphthalene or aryltetralin lignans[11–18] (Scheme 1). Recently, we reported a modification of the classic double Stobbe condensation of succinic diesters with aromatic aldehydes that directly yields (*E*)-1-aryl-1,2-dihydronaphthalene derivatives rather than dibenzylidene succinates.[19] These aryldihydronaphthalenes have been shown to be very useful as intermediates in lignan synthesis,[19–22] and it occurred to us that the lignans magnoshinin **1** and cyclogalgravin **2** might also be prepared via such an intermediate.



Magnoshinon **1**; R_1, R_3, R_4 = OMe, R_2 = H
Cyclogalgravin **2**; R_1, R_3, R_4 = H, R_2 = OMe

Figure

Magnoshinin **1** was first isolated from the dry buds of *Magnolia salicifia* and was found to have anti-inflammatory effects.[23–25] To date, two synthetic routes to this compound have been reported in the literature.[24,25] One of these involved an interesting photochemical dimerization of (*E*)-asarone that produced magnoshinin in a single step, albeit in very low yield.[24] The other published synthesis involved an eight-step procedure that produced magnoshinin in good yield.[25]

Cyclogalgravin **2** (3,4-dehydrogalbulin) was obtained from the acid-catalyzed cyclization of galgravin, a lignan isolated from *Himantandra belgraveana*.[26–28] No reports were found in the literature for a synthesis of cyclogalgravin.

The first steps of our synthetic strategy are shown in Scheme 2. The dihydronaphthalene esters **7** were prepared using a modification of our previously published method.[19] The (*E*)-benzylidene succinate diethyl esters **4** were synthesized using standard Stobbe conditions.[19] Condensation of **4a** with 2,4,5-trimethoxybenzaldehyde, and **4b** with 3,4-dimethoxybenzaldehyde, using lithium diisopropylamine (LDA) as base afforded the crude alcohols **5**. Quenching the reaction mixture at low temperature was necessary to avoid the formation of the dibenzylidene succinates. Immediate treatment of the crude alcohols **5** with trifluoroacetic acid (TFA) produced a 1:1 mixture of the corresponding *trans*-1,2-dihydronaphthalene diesters **6** and monoester acids **7**. Treatment of the crude mixtures of **6** and **7** with ethyl iodide and potassium carbonate in acetone gave the *trans*-1,2-dihydronaphthalene diethyl ester

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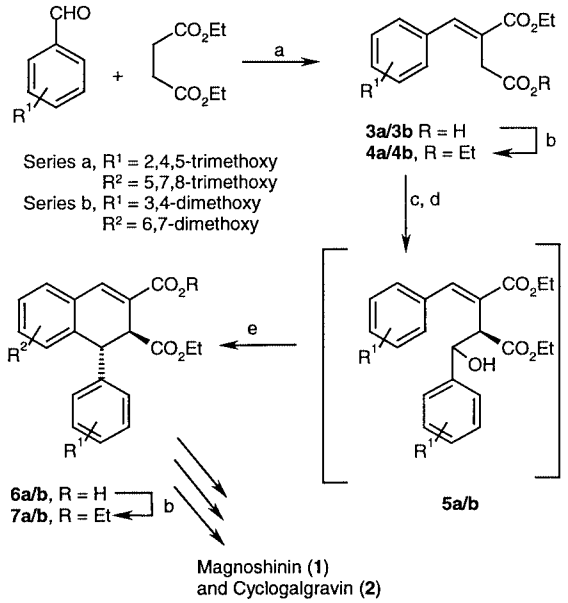
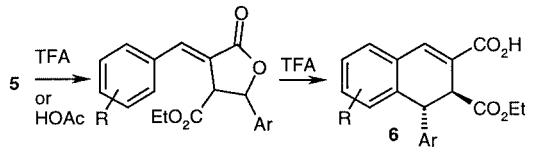
7 (**7a**, 56% yield from **4a**; **7b**, 46% from **4b**[19]). The formation of monoester acid **6** is probably due to partial lactonization of alcohol **5** on treatment with TFA, or perhaps during its workup with glacial acetic acid (Scheme 3).



a) EtONa, EtOH, reflux; b) EtI, K_2CO_3, acetone, reflux; c) LDA, THF, -70 °C; d) Ar^2CHO, -70 °C; e) TFA, rt.

Scheme 2

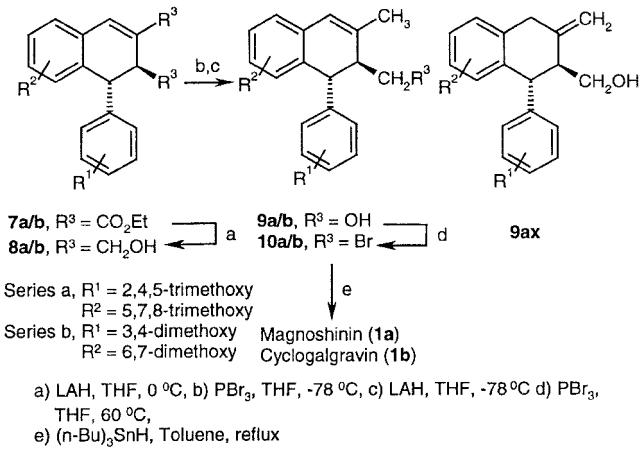


Scheme 3

The ester groups of **7** were reduced and deoxygenated in a stepwise fashion, as all attempts at a simultaneous reduction/deoxygenation failed. Reduction of **7** with lithium aluminum hydride (LAH) in tetrahydrofuran (THF) gave the unstable diols **8** (Scheme 4), which were immediately used for the next reaction without purification. Treatment of **8a** with PBr_3 in THF at –78 °C followed immediately by reduction with LAH at –78 °C gave alcohol **9a** (72%) along with a small amount (6%) of isomeric alcohol **9ax**. A similar reaction of **8b** gave only **9b** (64%) (Scheme 4).

The deoxygenation of alcohol **9a** and **9b** was achieved by conversion to the corresponding bromide (**10a**, 49%) and (**10b**, 53%) with PBr_3 in THF followed by reduction with tri-*n*-butyl tin hydride to yield magnoshinin **1a** (99%), and cyclogalgravin **1b** (85%). Syntheses of magnoshinin and cyclogalgravin were completed in overall yield of 20% (from **4a**) and 9% (from **4b**), respectively. The present method should be applicable to the synthesis of other (*E*)-1,2-dihydronaphthalene lignans.

^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 FT instrument using $CHCl_3$ as internal standard, unless otherwise specified. Numbers in subscript in NMR chemical shift and coupling constant data, while not significant, serve to differentiate values that would otherwise be identical if the data were rounded to one less figure. Silicycle silica gel was used for all chromatography. HRMS/mass spectra were obtained on a VG Analytical 7070E-HF instrument.



a) LAH, THF, 0 °C, b) PBr_3, THF, -78 °C, c) LAH, THF, -78 °C d) PBr_3, THF, 60 °C,
e) $(n\text{-}Bu)_3SnH$, Toluene, reflux

Scheme 4

Benzylidenesuccinate Diester (4a)

Na metal (0.432 g, 18.8 mmol) was added to anhyd EtOH (20 mL) and heated at reflux under N_2 until the Na had completely reacted (approx. 30 min). The mixture was cooled to r.t. and a solution of diethyl succinate (3.1 mL, 18.6 mmol) and 2,4,5-trimethoxybenzaldehyde (3.23 g, 16.5 mmol) in anhyd EtOH (15 mL) was added quickly, with stirring. The reaction mixture was stirred at reflux for 21 h. Distilled H_2O (20 mL) was added to the reaction mixture, which was subsequently stripped of EtOH under reduced pressure. The mixture was poured into H_2O (20 mL) in a separatory funnel and extracted with EtOAc (3 × 20 mL). The organic layers were combined and washed with 5% $NaHCO_3$ (3 × 20 mL). The basic extracts were combined and acidified with 10% HCl and extracted with fresh EtOAc (3 × 20 mL). This second organic extract was washed with H_2O (10 mL), dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give crude product, a brown syrup of benzylidene monoester **3a** (5.08 g, 95 %). A small sample of the monoester was purified by chromatography on silica gel (50–100% EtOAc–hexanes).

3a

^1H NMR ($CDCl_3$): δ = 1.30 (t, 3H, *J* = 7.1 Hz), 3.50 (s, 2H), 3.78 (s, 3H), 3.79 (s, 3H), 3.88 (s, 3H), 4.26 (q, 2H, *J* = 7.1 Hz), 6.50 (s, 1H), 6.91 (s, 1H), 7.95 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 14.2, 34.4, 56.1, 56.3, 56.5, 61.3, 97.0, 113.2, 115.0, 123.7, 138.4, 142.9, 151.1, 152.7, 167.9, 177.3.

MS: *m/z* (%) = 278 (31), 128 (16), 101 (100), 73 (26).

HRMS: *m/z* calcd for $C_{16}H_{20}O_7$: 324.1209. Found: 324.1210.

The crude benzylidenesuccinate monoester **3a** (4.91 g, 15.1 mmol) was dissolved in acetone (30 mL), and solid K_2CO_3 (10.5 g, 75.7 mmol) was added to the mixture. After stirring the solution at r.t. for several minutes, ethyl iodide (2.4 mL, 30 mmol) was added and the solution was refluxed for 20 h. The solution was cooled, filtered, and the precipitate washed several times with acetone. The filtrate was evaporated to yield an orange oil, which was taken up in CH_2Cl_2, dried ($MgSO_4$), and evaporated. The solvent was removed under reduced pressure to yield an orange oil (4.80 g, 90%) as the crude product. The crude diester **4a** was purified by short path, high vacuum (0.1 mm Hg) distillation to give a viscous yellow oil (3.16 g, 59%).

^{1}H NMR ($CDCl_3$): δ = 1.23 (t, 3H, *J* = 7.1 Hz), 1.30 (t, 3H, *J* = 7.1 Hz), 3.47 (s, 2H), 3.77 (s, 3H), 3.80 (s, 3H), 3.89 (s, 3H), 4.15 (q, 2H, *J* = 7.1 Hz), 4.24 (q, 2H, *J* = 7.1 Hz), 6.50 (s, 1H), 6.91 (s, 1H), 7.94 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 14.2_6, 14.3_1, 34.4, 56.1, 56.3_7, 56.4_4, 60.9, 61.0, 97.0, 113.2, 115.4, 124.7, 137.8, 142.8, 150.9, 152.7, 167.6, 171.8.

MS: *m/z* (%) = 352 (M^+, 100), 279 (23), 205 (70), 191 (28), 175 (21).

HRMS: *m/z* calcd for $C_{18}H_{24}O_7$: 352.1522. Found: 352.1529.

Benzylidenesuccinate Diester (4b)

This compound was prepared as described previously.[19]

Dihydronaphthalene Diester 7a and Monoester Acid 6a

A solution of benzylidenesuccinate diester **4a** (0.947 g, 2.69 mmol) in THF (5 mL) was added at –70 °C to lithium diisopropylamide (3.5 mmol) in THF (5 mL) through a plug of activated alumina (1.01 g); rinsing with THF (2.5 mL). Upon addition of the diester, the solution turned dark orange, which persisted until the reaction was quenched. The solution was stirred under N_2 for 10 min. 2,4,5-Trimethoxybenzaldehyde (1.04 g, 5.28 mmol) was dissolved in anhyd THF (10 mL) with heating, and added quickly to the reaction mixture through a plug of activated alumina (1.07 g); rinsing with THF (5 mL). The solution was stirred at –70 °C for 1 h. The reaction was quenched at –70 °C with glacial HOAc (1 mL), at which point the solution turned pale yellow. The solution was allowed to warm slowly to r.t.

Distilled H_2O (20 mL) was added to the reaction mixture and the solution extracted with EtOAc (3 × 25 mL). The combined organic layers were extracted with 20% HCl (2 × 25 mL), 5% $NaHCO_3$ (2 × 25 mL), and finally washed with H_2O (10 mL). The organic layers were dried ($MgSO_4$) and the solvent was removed under reduced pressure to give an orange oil (2.66 g), which was immediately dissolved in TFA (4 mL) and stirred at r.t. for 1 h. The reaction mixture was poured into 5% $NaHCO_3$ and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with 5% $NaHCO_3$ (3 × 10 mL) and H_2O (10 mL), dried ($MgSO_4$), filtered, and evaporated. NMR spectroscopy indicated the presence of at least three compounds. A small portion (0.258 g) was purified by flash column chromatography on silica gel (100 mL) using 30% EtOAc–hexanes (300 mL), then 40% EtOAc–hexanes (600 mL) to afford first 2,4,5-trimethoxybenzaldehyde, followed by the dihydronaphthalene diester **7a**. The dihydronaphthalene diester was obtained as a yellow amorphous solid. The dihydronaphthalene monoester acid **6a** was eluted with 100% EtOAc as a yellow wax.

The remaining crude product mixture was dissolved in acetone (17 mL), and K_2CO_3 (2.15 g) and ethyl iodide (0.5 mL) were added to the solution. The mixture was stirred at reflux for 3.5 h, cooled to r.t., and filtered. The precipitate was washed several times with acetone. The filtrate was evaporated, dissolved in CH_2Cl_2, dried ($MgSO_4$) and evaporated under reduced pressure to yield a brown amorphous solid. The crude mixture was purified by flash column chromatography over silica gel (100 mL) (30–50% EtOAc–hexanes) affording the dihydronaphthalene **7a** (0.798 mg, 56% overall yield).

7a

^{1}H NMR ($CDCl_3$): δ = 1.17 (t, 3H, *J* = 7.1 Hz), 1.27 (t, 3H, *J* = 7.1 Hz), 3.50 (s, 3H), 3.51 (s, 3H), 3.82 (s, 3H), 3.87 (s, 3H), 3.89 (s, 3H), 3.93 (s, 3H), 3.97 (d, 1H, *J* = 1.1 Hz), 4.06 (m, 2H), 4.17 (m, 2H), 5.45 (d, 1H, *J* = 1.1 Hz), 6.02 (s, 1H), 6.40 (s, 1H), 6.51 (s, 1H), 8.05 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 14.2, 14.4, 33.0, 44.5, 55.9, 56.1, 56.2, 56.8, 57.2, 60.5, 60.6, 60.8, 95.4, 98.1, 114.2, 114.6, 121.9, 122.1, 131.5, 132.3, 140.6, 142.6, 148.7, 151.3, 154.0, 155.6, 167.2, 172.3.

MS: *m/z* (%) = 530 (M^+, 64), 456 (83), 412 (25), 410 (32), 381 (48).

HRMS: *m/z* calcd for $C_{28}H_{34}O_{10}$: 530.2151. Found: 530.2133.

Monoester 6a

^{1}H NMR ($CDCl_3$): δ = 1.17 (t, 3H, *J* = 7.0 Hz), 3.50 (s, 3H), 3.51 (s, 3H), 3.82 (s, 3H), 3.88 (s, 3H), 3.89 (s, 3H), 3.92 (s, 3H), 3.95 (s, 1H), 4.07 (m, 2H), 5.45 (s, 1H), 5.99 (s, 1H), 6.40 (s, 1H), 6.50 (s, 1H), 8.16 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 14.2, 33.2, 44.1, 55.9, 56.1, 56.2, 56.8, 57.3, 60.7, 61.0, 95.4, 98.1, 114.3, 114.5, 120.9, 121.6, 132.5, 134.0, 140.6, 142.7, 148.9, 151.3, 154.4, 156.1, 171.8, 172.2.

MS: *m/z* (%) = 502 (M^+, 26), 456 (55), 454 (100), 411 (33), 408 (64), 393 (34), 168 (78).

HRMS: *m/z* calcd for $C_{26}H_{30}O_{10}$: 502.1838. Found: 502.1806.

Dihydronapthalene 7b

This compound was prepared as described previously.[19]

Dihydronaphthalene Diol 8a

Dihydronaphthalene diester **7a** (0.530 g, 1.0 mmol) was dissolved in freshly distilled THF (16 mL), cooled to 0 °C, and then a slurry of LAH (0.10 g, 2.63 mmol) in THF (4 mL) was slowly added. The reaction mixture was stirred at 0 °C under N_2 for 30 min and worked up by Fieser's method.[29] In succession, H_2O (0.10 mL), 15% NaOH (0.10 mL) and H_2O (0.30 mL) were added to the reaction mixture followed by EtOAc. The solution was dried ($MgSO_4$), filtered, and the solvent was removed under reduced pressure to afford a cloudy, colorless oil (0.547 g, 100%). This compound was unstable and had to be reacted quickly in the next step without purification.

^{1}H NMR ($CDCl_3$): δ = 2.59 (dd, 1H, *J* = 6.3, 7.9 Hz), 3.35 (s, 3H), 3.51 (dd, 1H, *J* = 7.3, 9.9 Hz), 3.52 (s, 3H), 3.62 (dd, 1H, *J* = 6.3, 9.9 Hz), 3.81 (s, 3H), 3.83 (s, 6H), 3.87 (s, 3H), 3.90 (d, 1H, *J* = 13.1 Hz), 4.06 (d, 1H, *J* = 13.1 Hz), 4.80 (s, 1H), 6.14 (s, 1H), 6.41 (s, 1H), 6.50 (s, 1H), 6.83 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 32.4, 45.2, 55.8 (CH_3), 56.1_4, 56.1_8, 56.7, 57.1, 60.6, 65.8, 67.0, 95.9, 97.9, 114.1, 115.9, 119.0, 123.1, 130.7, 136.0, 140.9, 142.5, 148.2, 150.8, 152.0, 153.0 (C).

MS: *m/z* (%) = 444 (8), 428 (100), 398 (63), 397 (38), 383 (49), 352 (71), 337 (47).

HRMS: *m/z* calcd for $C_{24}H_{30}O_8$ (M^+ – 18): 446.1940. Found: 446.1940.

Dihydronaphthalene Diol 8b

Dihydronaphthalene diester **7b** (0.296 g, 0.601 mmol) was reduced with LAH (0.048 g, 2.01 mmol) as described above to afford a colorless oil (0.210 g, 86.4%).

^{1}H NMR ($CDCl_3$): δ = 2.72 (dt, 1H, *J* = 4.3 Hz), 3.64 (d, 2H, *J* = 7.3 Hz), 3.77 (s, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 3.88 (s, 3H), 4.04_8 (d, 1H, *J* = 12.8 Hz), 4.06_1 (d, 1H, *J* = 2.5 Hz), 4.13_5 (d, 2H, *J* = 12.8 Hz), 6.47_3 (dd, 1H, *J* = 2.0_5, 8.2 Hz), 6.47_9 (s, 1H), 6.60 (s, 1H), 6.62_6 (d, 1H, *J* = 2.0_5 Hz), 6.69 (d, 1H, *J* = 8.2 Hz), 6.70 (s, 1H).

^{13}C NMR ($CDCl_3$): δ = 45.1, 47.4, 55.8_1, 55.8_3, 55.8_9, 56.0, 64.7, 66.3, 110.0, 110.9_8, 111.0_7, 112.6, 119.7, 125.3, 125.9, 128.12, 136.1, 136.4, 147.5, 147.9, 148.6, 148.7.

MS: *m/z* (%) = 386 (M^+, 35), 368 (100), 337 (34), 325 (42), 307 (54), 151 (40).

HRMS: *m/z* calcd $C_{22}H_{26}O_6$: 386.1729. Found: 386.1738.

Dihydronaphthalene Alcohol 9a

Dihydronaphthalene diol **8a** (0.447 g, 1 mmol) was dissolved in freshly distilled THF (15 mL) in a flask flushed with N_2 and cooled to –78 °C. PBr_3 (0.201 mg, 0.74 mmol) in THF (2 mL) was added, the solution stirred at –78 °C for 1 h, then a slurry of LAH (80 mg, 2.1 mmol) in THF (4 mL) was added to the reaction mixture. The mixture was slowly warmed to 0 °C (1.5 h), refluxed for 25 min, and then worked up using Fieser's method.[29] In succession, H_2O (0.35 mL), 15% NaOH (0.35 mL) and H_2O (0.9 mL) were added to the reaction mixture followed by EtOAc. The solution was dried ($MgSO_4$), filtered, and stripped of solvent under reduced pressure to give an oil (0.40 g). The crude reaction mixture was purified by flash silica gel column chromatography (50–70% EtOAc–hexanes). The conjugated alcohol (0.309 g, 72%) was obtained as a pale yellow oil that slowly crystallized.

Mp 128.0–130.0 °C (hexane–EtOAc).

^{1}H NMR ($CDCl_3$): δ = 1.77 (d, 3H, *J* = 1.4 Hz), 2.37 (dd, 1H, *J* = 4.5, 8.6 Hz), 3.39 (s, 3H), 3.42 (dd, 1H, *J* = 8.6, 10.5 Hz), 3.56 (s, 3H), 3.64 (dd, 1H, *J* = 4.5, 10.5 Hz), 3.84 (s, 6H), 3.85 (s, 3H), 3.92 (s, 3H), 4.98 (s, 1H), 6.25 (s, 1H), 6.41 (s, 1H), 6.53 (s, 1H), 6.63 (d, 1H, *J* = 1.4 Hz).

^{13}C NMR ($CDCl_3$): δ = 23.4, 31.7, 49.3, 56.1, 56.2, 56.3, 57.0, 57.1, 60.5, 64.1, 96.3, 98.2, 114.0, 117.0, 117.3, 124.6, 129.6, 132.6, 141.3, 142.8, 148.0, 150.5, 151.0, 152.1.

MS: *m/z* (%) = 430 (M^+, 41), 412 (100), 399 (76), 397 (50), 384 (37), 352 (35).

HRMS: *m/z* calcd for $C_{24}H_{30}O_7$: 430.1991. Found: 430.1949.

Dihydronaphthalene Alcohol 9b

Dihydronaphthalene diol **8b** (0.182 g, 0.471 mmol) in THF (5 mL) was brominated (PBr_3, 0.113 g, 0.417 mmol) and reduced (LAH, 0.045 g, 1.186 mmol) as described above to give a colorless oil (0.113 g, 64%).

^{1}H NMR ($CDCl_3$): δ = 1.79 (d, 3H, *J* = 1.4 Hz), 2.47 (ddd, 1H, *J* = 1.8, 4.2, 8.8 Hz), 3.43 (dd, 1H, *J* = 8.8, 10.7 Hz), 3.68 (dd, 1H, *J* = 4.2, 10.7 Hz), 3.77 (s, 3H), 3.77 (s, 3H), 3.80 (s, 3H), 3.87 (s, 3H), 4.16 (d, 1H, *J* = 1.8 Hz), 6.25 (d, 1H, *J* = 1.4 Hz), 6.53 (dd, 1H, *J* = 2.0_4, 8.3 Hz), 6.61 (s, 2H), 6.63 (d, 1H, *J* = 2.0_4 Hz), 6.69 (d, 1H, *J* = 8.3 Hz).

^{13}C NMR ($CDCl_3$): δ = 22.7, 44.5, 50.9, 55.7_8, 55.8, 55.8_7, 55.9_1, 62.9, 109.2, 111.0, 112.9, 119.5, 123.8, 126.8_2, 126.9_5, 133.1, 137.8, 147.3, 147.7, 147.9, 148.7.

MS: *m/z* (%) = 370 (M^+, 43), 352 (20), 339 (100), 324 (23), 308 (19).

HRMS: *m/z* calcd for $C_{22}H_{26}O_5$: 370.1780. Found: 370.1768.

Dihydronaphthalene Bromide 10a

A solution of dihydronaphthalene alcohol **9a** (50 mg, 0.116 mmol) in freshly distilled THF (3 mL) was warmed to 60 °C and a solution of PBr_3 (25 mg, 0.092 mmol) in THF (1 mL) was added. The solution was stirred at 60 °C under N_2 for 1 h. The reaction mixture was cooled to r.t., 5% $NaHCO_3$ (2 mL) was added, and the mixture extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo. Chromatography on silica gel (30–50% EtOAc–hexanes) gave a solid (28 mg, 49%).

Mp 144.0–146.0 °C (hexane–EtOAc).

^{1}H NMR ($CDCl_3$): δ = 1.76 (d, 3H, *J* = 1.5 Hz), 2.57 (ddd, 1H, *J* = 1.0, 3.9, 10.6 Hz), 3.09 (dd, 1H, *J* = 10.2, 10.6 Hz), 3.47 (dd, 1H, *J* = 3.9, 10.2 Hz), 3.53 (s, 3H), 3.54 (s, 3H), 3.84 (s, 3H), 3.85_7, (s, 3H), 3.86 (s, 3H), 3.93 (s, 3H), 5.20 (d, 1H, *J* = 1.0 Hz), 6.18 (s, 1H), 6.42 (s, 1H), 6.52 (s, 1H), 6.62 (q, 1H, *J* = 1.5 Hz).

^{13}C NMR ($CDCl_3$): δ = 23.0, 33.1, 35.3, 47.6, 56.1, 56.2, 56.3, 57.0, 57.2, 60.9, 96.3, 98.6, 114.1, 116.6, 117.9, 123.2, 129.1, 133.2, 141.7, 142.8, 148.3, 151.2, 151.3, 152.6.

MS: *m/z* (%) = 494 (M^+, 33), 412 (100), 397 (52), 245 (92), 181 (69).

HRMS: *m/z* calcd for $C_{24}H_{29}O_6{}^{81}Br$: 494.1127. Found: 494.1117.

Dihydronaphthalene Bromide 10b

Alcohol **9b** (50 mg, 0.135 mmol) was brominated in THF (5 mL) using PBr_3 (100 mg, 0.369 mmol) in THF (1 mL) as described above to give a yellow oil (31 mg, 53%) after chromatography.

^{1}H NMR ($CDCl_3$): δ = 1.81 (d, 3H, *J* = 1.2 Hz), 2.62 (dt, 1H, *J* = 2.7, 10.4 Hz), 3.15 (t, 1H, *J* = 10.4 Hz), 3.51 (dd, 1H, *J* = 3.2, 10.1 Hz), 3.78 (s, 3H), 3.81 (s, 3H), 3.82 (s, 3H), 3.88 (s, 3H), 4.33 (d, 1H, *J* = 2.1 Hz), 6.27 (br s, 1H), 6.53 (dd, 1H, *J* = 2.0, 8.2 Hz), 6.63 (br s, 3H), 6.71 (d, 1H, *J* = 8.3 Hz).

^{13}C NMR ($CDCl_3$): δ = 22.2, 35.2, 45.3, 55.8 (2 × CH_3), 55.9_4, 55.9_6, 109.2, 111.0, 113.1, 119.7, 124.4, 126.0, 126.4, 133.0, 136.6, 147.5, 148.0, 148.2, 148.7.

MS: *m/z* (%) = 434 (M^+, 8), 432 (M^+, 10).

HRMS: *m/z* calcd for $C_{22}H_{25}O_4{}^{79}Br$: 432.0936. Found: 432.0917.

Magnoshinin 1a

A solution of **10a** (63 mg, 0.127 mmol) and tri-*n*-butyltin hydride (0.2 mL, 0.74 mmol) in toluene (5 mL) was refluxed under N_2 for 12 h. Evaporation of the solvent in vacuo and chromatography on silica gel (50% EtOAc–hexanes) gave a colorless oil (53 mg, 99%).

The ^{1}H NMR ($CDCl_3$) spectrum was identical with that previously published.[23]

^{13}C NMR ($CDCl_3$): δ = 19.1, 22.8, 36.8, 40.6, 56.1_1, 56.1_7, 56.4, 56.9, 57.1, 60.6, 96.2, 98.2, 113.9, 114.2, 117.4, 125.2, 130.0, 138.7, 141.6, 142.7, 147.8, 150.7_9, 150.8_4, 151.8.

MS: *m/z* (%) = 414 (M^+, 100), 399 (16), 384 (21), 383 (36), 368 (32), 246 (22), 231 (39).

HRMS: *m/z* calcd for $C_{24}H_{30}O_6$: 414.2042. Found: 414.2029.

Cyclogalgravin 1b

Dihydronaphthalene bromide **10b** (0.030 g, 0.069 mmol) was reduced with tri-*n*-butyltin hydride (1.1 mL, 0.402 mmol) in toluene (5 mL) as described above to give a colorless oil (20.9 mg, 85%) after chromatography (40% EtOAc–hexanes).

^{1}H NMR ($CDCl_3$): δ = 1.08 (d, 3H, *J* = 7.1 Hz), 1.80 (d, 3H, *J* = 1.4 Hz), 2.38 (dq, 1H, *J* = 3.2, 7.1 Hz), 3.67 (d, 1H, *J* = 3.2 Hz), 3.77_7 (s, 3H), 3.78_0 (s, 3H), 3.82 (s, 3H), 3.88 (s, 3H), 6.14 (br, 1H), 6.55_8 (s, 1H), 6.55 (dd, 1H, *J* = 2.0, 8.1 Hz), 6.62 (s, 1H), 6.66 (d, 1H, *J* = 2.0 Hz), 6.71 (d, 1H, *J* = 8.1 Hz).

The ^{13}C NMR ($CDCl_3$) spectrum was identical to that previously published.[28]

MS. *m/z* (%) = 354 (M^+, 100), 352 (14), 340 (13), 339 (57), 324 (20), 308 (15), 216 (17), 165 (16).

HRMS: *m/z* calcd for $C_{22}H_{26}O_4$: 354.1831. Found: 354.1833.

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