Supporting Information

A NEW APPROACH TO THE SYNTHESIS OF THE NATURAL PRODUCT ARIPUANIN

Aline S. Lazaro¹, Pedro H. Zana Ribeiro¹, Mirela I. Sairre², and Paulo M. Donate*¹

¹ *Departamento de Química, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Avenida Bandeirantes 3900, 14040-901, Ribeirão Preto, SP, Brazil*

² *Centro de Ciências Naturais e Humanas, Universidade Federal do ABC, Rua Santa Adélia 166, 09210-170, Santo André, SP, Brazil*

* Corresponding Author

E-mail: pmdonate@usp.br

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1. General information

All materials were obtained from commercial sources and were used as received unless stated otherwise. The catalyst Mn(salen) [(*R,R*)-(-)-*N,N'*-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride] was purchased from Acros Organics. NMR spectroscopy was performed on Bruker DRX-500, Bruker DRX-400 or Bruker DPX-300 instruments. TMS was used as internal standard. The chemical shifts are reported in ppm (δ), and the coupling constants (*J*) are given in Hertz (Hz). The following abbreviations were used to designate chemical shift multiplicities: d = doublet, dd = double doublet, ddd = double double doublet, m = multiplet, s = singlet, t = triplet, tt = triple triplet. HRMS were recorded on a VG AutoSpec instrument.

2. Synthetic procedures for compounds 3, 5, 6a and 1a/1b

(3E)-4-(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)but-3-en-2-one (3)

A solution of β -ionone (**2**) (2.1137 g, 11 mmol) and *N*-bromosuccinimide (2.3085 g, 13 mmol) in 100 mL of anhydrous toluene (carbon tetrachloride can also be used as solvent) was irradiated with a 100 W tungsten lamp for 1 hour.^[1] After cooling to room temperature and filtering, anhydrous sodium carbonate (2.5111 g, 24 mmol) and dimethylformamide (25 mL) were added to the filtrate, and the reaction mixture was stirred for 30 minutes. The solvent was distilled off and the resulting residue was extracted with ethyl ether (200 mL). The organic layer was washed with 5% aqueous HCl (100 mL) and saturated brine, and dried over anhydrous MgSO_4 . After solvent removal under reduced pressure, the residue was purified by column chromatography on silica gel using *n*-hexane:ethyl acetate (8:2) as eluent to give compound **3** (1.4640 g, 7.7 mmol, 70% yield) as a yellow liquid. The NMR characterization data are identical to the literature values.^[1] ^1H NMR (CDCl_3 , 500 MHz): δ 7.27 (d, $J = 16.4$ Hz, 1H), 6.21 (d, $J = 16.4$ Hz, 1H), 5.88 (m, 2H), 2.31 (s, 3H), 2.11 (d, $J = 2.1$ Hz, 2H), 1.91 (s, 3H), 1.08 (s, 6H). ^{13}C NMR (CDCl_3 , 75 MHz): δ 198.0, 141.5, 135.7, 132.5, 130.1, 129.4, 128.0, 39.8, 33.8, 27.1, 26.3, 26.3, 20.1.

^[1] Findlay, J. A.; MacKay, W. D. *Can. J. Chem.* **1971**, 49, 2369–2371.

(±)-(3E)-4-[1,4-dihydroxy-2,6,6-trimethylcyclohex-2-en-1-yl]but-3-en-2-one (5)

A solution of compound **3** (1.0471 g, 5.51 mmol) and Rose Bengal (0.0102 g, 0.010 mmol) in methanol (20 mL) was irradiated with a high-pressure sodium vapor lamp with continuous purge of dry oxygen for 24 hours. The temperature of the reaction mixture was controlled by an ice bath. The peroxy-derivative **4** was not isolated. The reaction flask was flushed with dry nitrogen. Thiourea (0.5024 g, 6.60 mmol) was added to the flask and the reaction mixture was stirred for 12 hours, at room temperature.^[2] After concentrating the mixture under reduced pressure, the resulting residue was purified by column chromatography on silica gel using ethyl ether:dichloromethane (7:3) as eluent to give compound **5** (0.6791 g, 3.03 mmol, 55% yield) as a colorless oil. The NMR characterization data are identical to the literature values.^[2] ¹H NMR (CDCl₃, 500 MHz): δ 6.75 (d, *J* = 15.8 Hz, 1H), 6.45 (d, *J* = 15.8 Hz, 1H), 5.68 (m, *J* = 2.4 Hz, *J* = 1.7 Hz, 1H), 4.30 (m, *J* = 7.3 Hz, *J* = 6.2 Hz, *J* = 2.4 Hz, *J* = 1.7 Hz, 1H), 2.30 (s, 3H), 1.82 (dd, *J* = 13.6 Hz, *J* = 7.3 Hz, 1H), 1.68 (ddd, *J* = 13.6 Hz, *J* = 6.2 Hz, *J* = 1.7 Hz, 1H), 1.65 (t, *J* = 1.7 Hz, 3H), 0.98 (s, 3H), 0.95 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz): δ 197.8, 147.5, 137.1, 130.2, 128.3, 77.5, 65.0, 42.1, 38.2, 28.2, 24.3, 24.3, 19.0.

^[2] Serra, S.; Barakat, A.; Fuganti, C. *Tetrahedron: Asymmetry* **2007**, *18*, 2573–2580.

(±)-(3*E*)-4-[1,4-Dihydroxy-2,3-epoxy-2,6,6-trimethylcyclohexan-1-yl]but-3-en-2-one (6a)

A solution of the catalyst Mn(salen) (2 mg, 0.03 mmol) and compound **5** (0.7402 g, 3.30 mmol) in dichloromethane (25 mL) was vigorously stirred for 30 minutes at room temperature. Then, a solution of *m*-CPBA (1.1390 g, 6.60 mmol) in dichloromethane (120 mL) was added, and the reaction mixture was stirred for 3 hours at room temperature. The excess acid was decomposed with 10% sodium bisulfite solution (100 mL). The resulting mixture was extracted with dichloromethane, washed with 5% aqueous NaHCO₃ and saturated brine, and dried over anhydrous MgSO₄. After solvent removal under reduced pressure, the residue was purified by column chromatography on silica gel using ethyl ether:dichloromethane (7:3) as eluent to give compound **6a** (0.4755 g, 1.98 mmol, 60% yield) as a white solid (mp 132–133 °C). About 0.25 g of unconverted starting material was also recovered with good purity; thus, the ratio of the epoxide **6a** to the starting material was 6:4. ¹H NMR analysis of the reaction mixture did not detect the presence of the epoxy-derivative **6b** [3.41 (d, *J*_{3,4} = 2.3 Hz, 1H)]. ¹H NMR (CDCl₃, 500 MHz): δ 6.80 (d, *J* = 15.3 Hz, 1H), 6.68 (d, *J* = 15.3 Hz, 1H), 4.16 (ddd, *J* = 10.9 Hz, *J* = 6.1 Hz, *J* = 1.8 Hz, 1H), 3.46 (d, *J*_{3,4} = 1.8 Hz, 1H), 2.26 (s, 3H), 1.50 (dd, *J* = 13.5 Hz, *J* = 10.9 Hz, 1H), 1.41 (dd, *J* = 13.5 Hz, *J* = 6.1 Hz, 1H), 1.25 (s, 3H), 0.95 (s, 3H), 0.80 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz): δ 197.5, 144.9, 130.0, 75.0, 65.7, 65.6, 65.5, 40.0, 37.1, 28.8, 24.0, 23.6, 21.7. HRMS *m/z* calculated for C₁₃H₂₀O₄: 240.1362, found: 240,1346.

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3. Copies of NMR spectra

^1H NMR and ^{13}C NMR for (3*E*)-4-(2,6,6-trimethylcyclohexa-1,3-dien-1-yl)but-3-en-2-one (3)

¹H NMR and ¹³C NMR for (±)-(3E)-4-[1,4-dihydroxy-2,6,6-trimethylcyclohex-2-en-1-yl]but-3-en-2-one (5)

^1H NMR and ^{13}C NMR for $(\pm)$ -(3*E*)-4-[1,4-dihydroxy-2,3-epoxy-2,6,6-trimethylcyclohexan-1-yl]but-3-en-2-one (6a)

¹H NMR (400 MHz) for (±)-aripuanin or {(±)-1-[(*IE*)-3-hydroxybuten-1-yl]-2,6,6-trimethylcyclohexane-1,2,4-triol} (mixture of 1a + 1b)

^{13}C NMR (125 MHz) for $(\pm)$ -aripuanin or $\{(\pm)\text{-}1\text{-}[(E)\text{-}3\text{-hydroxybuten-1-yl}]\text{-}2,6,6\text{-trimethylcyclohexane-1,2,4-triol}\}$ (mixture of 1a + 1b)