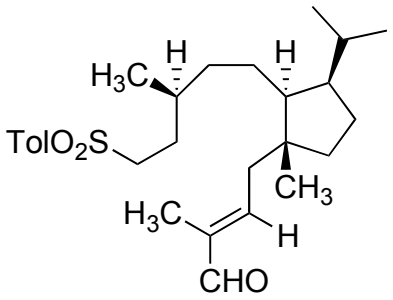
Strategies for the Synthesis of Fusicoccanes via Nazarov Reactions of Dolabelladienones. Total Synthesis of (+)-Fusicoauritone

David R. Williams, Leslie A. Robinson, C. Richard Nevill and Jayachandra P. Reddy*

Department of Chemistry, Indiana University, Bloomington, IN, 47405-7102, U.S.A.

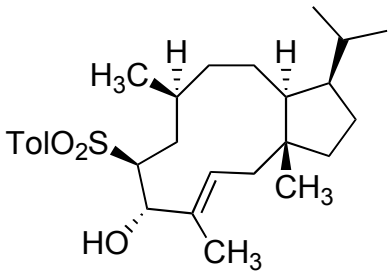
Supporting Information

Spectral data for identification of key compounds **16**, **17ab**, **18**, **22**, **23**, **24ab**, and **1** and ORTEP illustrations from the X-ray diffraction study of **25**. ^{1}H NMR spectra of synthetic and natural fusicoauritone (**1**).

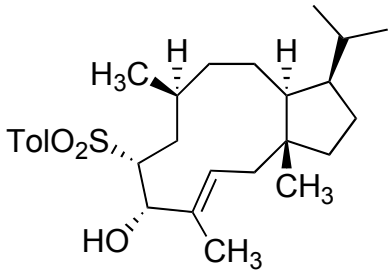


16

*Spectral characterization of **16** as a colorless oil:* IR (film) 2960, 2880, 1680, 1640, 1600, 1470, 1320, 1150, 1090 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$ δ 9.42 (s, 1H), 7.78 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 6.53 (m, 1H), 3.06 (m, 2H), 2.46 (s, 3H), 2.35 (AB of ABX, J_{AB} = 15.2 Hz, J_{AX} = 7.0 Hz, J_{BX} = 7.0 Hz, $\Delta\nu_{AB}$ = 63.4 Hz, 2H), 1.75 (s, 3H), 1.75 (m, 2H), 1.60–1.12 (m, 12H), 1.00 (s, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H), 0.81 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 195.3 (d), 152.6 (d), 144.6 (s), 140.6 (s), 136.3 (s), 129.9 (d), 128.0 (d), 54.5 (t), 50.8 (d), 48.4 (d), 46.3 (s), 41.6 (t), 37.6 (t), 37.1 (t), 32.9 (d), 29.6 (d), 29.1 (t), 27.4 (t), 23.2 (q), 22.2 (q), 22.0 (q), 21.9 (t), 21.6 (q), 19.2 (q), 9.6 (q); MS (CI, *m/z*, relative intensity) 429 (15), 361 (32), 319 (19), 207 (42), 157 (63), 123 (53), 95 (99); HRMS calcd for $M^{+\bullet}$ +1: 447.2935, found: 447.2940.



17A (Major)

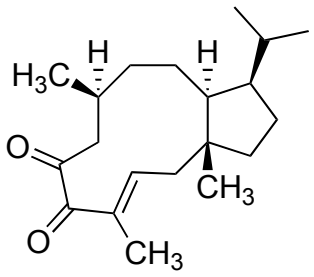


17B (Minor)

*Spectral characterization of **17A** (Major Isomer):* mp 171–172 °C; IR ($CHCl_3$) 3505, 3015, 2960, 1600, 1460, 1385, 1380, 1290, 1140, 1090 cm^{-1}; ^1H NMR (300 MHz,

$CDCl_3$) δ 7.82 (m, 2H), 7.39 (m, 2H), 5.60 (dd, J = 12.3 Hz, J = 3.0 Hz, 1H), 4.67 (s, 1H, –OH), 4.39 (d, J = 10.2 Hz, 1H), 3.00 (m, 1H), 2.48 (s, 3H), 2.24 (1/2 AB of ABX, J_{AB} = 12.7 Hz, 1H), 1.94–1.72 (m, 2H), 1.72–0.90 (m, 13H), 1.68 (s, 3H), 0.92 (s, 3H), 0.84 (d, J = 5.9 Hz, 3H), 0.80 (d, J = 6.2 Hz, 3H), 0.47 (d, J = 7.0 Hz, 3H); MS (25 eV, *m/z*, relative intensity) 361 (4), 319 (3), 273 (5), 229 (3), 137 (5), 123 (5), 95 (8), 69 (100); HRMS calcd for $M^{+\bullet}$: 446.2856, found: 446.2848.

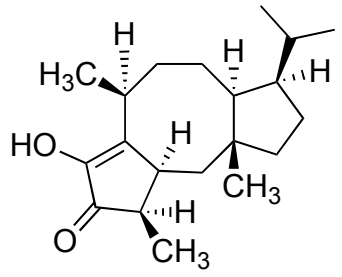
*Spectral characterization of **17B** (Minor Product) (same IR and MS/HRMS as above):* ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.0 (m, 1H), 4.57 (m, 1H), 3.40 (s, 1H), 2.86 (m, 1H), 2.18 (m, 1H), 1.00 (s, 3H), 0.85 (d, J = 5.9 Hz, 3H).



18

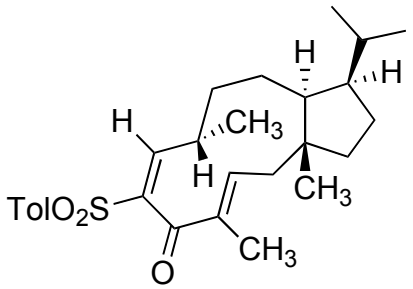
*Spectroscopic characterization of diketone **18**:* IR (film) 2950, 1705, 1665, 1635, 1450, 1380, 1375, 1210, 1000 cm^{-1}; UV ($CHCl_3$) λ_{max} 360 (63); ^{1}H NMR(300 MHz, $CDCl_3$) δ 6.64 (m, 1H), 2.47 (AB of ABX, J_{AB} = 12.9 Hz, J_{AX} = 12.5 Hz, J_{BX} = 2.7 Hz, $\Delta\nu_{AB}$ = 184.5 Hz, 2H), 2.34 (AB of ABX, J_{AB} = 14.1 Hz, J_{AX} = 11.6 Hz, J_{BX} = 4.1 Hz, $\Delta\nu_{AB}$ = 26.7 Hz, 2H), 1.85 (s, 3H), 1.80 (m, 1H), 1.62–1.32 (m, 7H), 1.31–1.12 (m, 4H), 1.09 (s, 3H), 0.98 (d, J = 7.0 Hz, 3H), 0.87 (d, J = 5.9 Hz, 3H), 0.81 (d, J = 5.9 Hz, 3H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 208.0, 199.2, 153.2, 134.6, 53.5, 49.4, 45.7, 45.4, 44.7, 41.4, 34.1, 28.3, 27.7, 26.4, 23.8, 22.2, 22.1, 21.0, 20.9, 10.1; MS (CI, NH_3, *m/z*, relative

intensity) 305 (11), 304 (19), 289 (17), 262 (19), 261 (100), 233 (35), 215 (52), 195 (28); HRMS (CI, NH_3) calcd for [$M^{+\bullet}$ +1]: 305.2482, found: 305.2477.



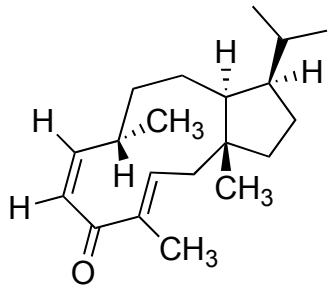
19

*Spectral characterization of **19**:* IR ($CHCl_3$) 3410, 2960, 1695, 1460, 1390, 1385, 1250, 1050, 910 cm^{-1}; UV ($CHCl_3$) λ_{max} 379 (5,750), 270 (12,650); ^1H NMR (300 MHz, $CDCl_3$) δ 5.88 (br s, 1H, –OH), 2.99 (m, 1H), 2.85 (m, 1H), 2.61 (dq, J = 6.0 Hz, J = 6.4 Hz, 1H), 2.01 (AB of ABX, J_{AB} = 13.1 Hz, J_{AX} = 2.7 Hz, J_{BX} = 0.4 Hz, $\Delta\nu_{AB}$ = 15.5 Hz, 2H), 1.90–1.15 (m, 11H), 1.11 (d, 7.4 Hz, 3H), 1.09 (s, 3H), 1.07 (d, J = 7.0 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.6 Hz, 3H); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 204.4, 161.5, 147.2, 55.2, 54.1, 49.8, 47.2, 45.9, 41.7, 38.3, 32.6, 32.0, 27.6, 27.0, 26.2, 24.1, 22.4, 21.8, 21.4, 10.5; MS (CI, NH_3, *m/z*, relative intensity) 305 (15), 261 (32), 191 (18), 165 (46), 140 (41), 125 (68), 109 (37), 95 (58); HRMS (CI, NH_3) calcd for [$M^{+\bullet}$ +1]: 305.2482, found, 305.2481.



22

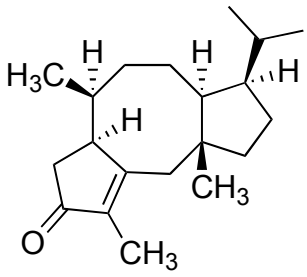
*Spectral characterization of **22**:* R_f = 0.3 (20% EtOAc/hexanes); mp 184 °C (dec.); IR (film) 2950, 1640, 1600, 1460, 1380, 1305, 1250, 1220, 1150 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 6.88 (d, *J* = 11.5 Hz, 1H), 6.72 (dd, *J* = 10.7 Hz, *J* = 1.1 Hz, 1H), 2.54–2.47 (m, 1H), 2.43 (s, 3H), 2.37 (d, *J* = 14.3 Hz, 1H), 2.07 (d, *J* = 14.3 Hz, 1H), 1.80–1.70 (m, 2H), 1.79 (s, 3H), 1.67–0.95 (m, 9H), 1.03 (s, 3H), 0.93 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.05, 152.13, 148.92, 144.29, 142.15, 138.95, 137.47, 129.59, 128.31, 48.01, 46.50, 45.34, 42.82, 42.63, 35.79, 32.62, 26.51, 25.99, 24.40, 24.21, 23.44, 21.62, 20.68, 20.44, 11.07; MS (CI, NH_3, *m/z*, relative intensity) 443 (79), 287 (67), 149 (57), 107 (89), 91 (100); HRMS (CI, NH_3) calcd for [$M^{+\bullet}$ +1] 443.2622, found: 443.2619.



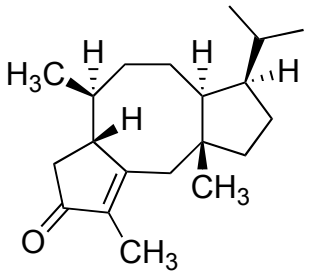
23

*Spectral characterization of **23** as a colorless oil:* R_f = 0.45 (20% EtOAc/hexanes); IR (film) 2940, 1645, 1450, 1385, 1305, 1250, 1210, 1165, 1070, 940, 785, 735; ^1H NMR (400 MHz, $CDCl_3$) 6.68 (ddd, *J* = 11.8 Hz, *J* = 2.9 Hz, *J* = 1.4 Hz, 1H), 5.99 (d, *J* = 11.8 Hz, 1H), 5.70 (t, *J* = 11.4 Hz, 1H), 2.67 (m, 1H), 2.40 (dd, *J* = 14.5 Hz, *J* = 12.1 Hz, 1H), 2.05 (d, *J* = 14.5 Hz, 1H), 1.81 (s, 3H), 1.76–1.21 (m, 11H), 1.04 (s, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) 200.27, 146.85, 143.39, 139.15, 128.52, 48.94, 46.10, 44.97, 43.38, 42.94, 36.04, 31.64,

26.67, 26.30, 24.13, 23.95, 22.79, 21.63, 20.65, 11.33; MS (CI, NH_3, *m/z*, relative intensity) 289 (8), 245 (13), 109 (42), 84 (100); HRMS (CI, NH_3) calcd for [$M^{+\bullet}$ +1]: 289.2533, found: 289.2510.



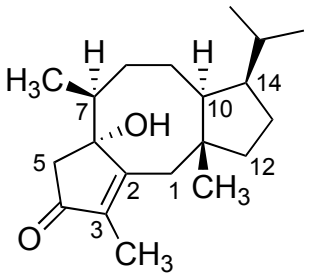
24A



24B

*Spectroscopic characterization of **24A**:* R_f = 0.3 (20% EtOAc/hexanes); IR (film) 2925, 1695, 1625, 1450, 1380 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.82 (d, *J* = 12.4 Hz, 1H), 2.73 (m, 1H), 2.40 (m, 1H), 2.34 (dd, *J* = 18.3 Hz, *J* = 6.1, 1H), 2.12 (m, 2H), 2.10 (dd, *J* = 18.3 Hz, *J* = 4.0 Hz, 1H), 2.02 (d, *J* = 12.4 Hz, 1H), 1.70 (d, *J* = 2.2 Hz, 3H), 1.70–1.13 (m, 9H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.80 (d, *J* = 6.7 Hz, 3H), 0.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) 209.20, 175.78, 138.77, 49.36, 48.00, 47.70, 47.06, 43.61, 43.43, 35.98, 29.31, 28.22, 27.39, 24.68, 24.29, 22.06, 21.61, 19.86, 19.76, 9.87; MS (CI, NH_3, *m/z*, relative intensity) 289 (27), 245 (37), 137 (100), 81 (27); HRMS (CI, NH_3) calcd for [$M^{+\bullet}$ +1]: 289.2533, found: 289.2503.

*Spectroscopic characterization of **24B** (same IR and MS/HRMS as above):* ^1H NMR (400 MHz, $CDCl_3$) δ 2.88 (d, *J* = 12.3 Hz, 1H), 2.64 (dd, *J* = 18.2 Hz, *J* = 6.5 Hz, 1H), 2.33 (d, *J* = 18.2 Hz, 1H), 2.26 (m, 1H), 2.07 (dd, *J* = 12.3 Hz, *J* = 3.7 Hz, 1H), 1.90 (m, 3H), 1.78–1.17 (m, 9H), 1.73 (d, *J* = 2.1 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 0.98 (s, 3H), 0.86 (d, *J* = 6.8 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H).



Fusicoauritone (**1**)

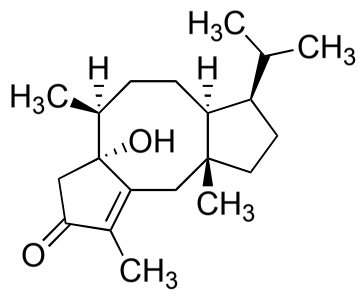
*Characterization of Synthetic **1**:* R_f 0.28 (30% EtOAc/hexanes); $[\alpha]_D^{24}$ +13.3 (*c* 0.21, $CHCl_3$); IR (film) 3445, 2970, 2935, 2880, 1702, 1468, 1390, 1050, 1020, 975, 955 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.71 (d, *J* = 12.8 Hz, 1H), 2.46 (d, *J* = 18.4 Hz, 1H), 2.27 (d, *J* = 18.4 Hz, 1H), 2.22 (d, *J* = 13.2 Hz, 1H), 2.19–2.10 (m, 3H), 2.05 (s, 1H), 1.73 (s, 3H), 1.71–1.55 (m, 6H), 1.30–1.25 (m, 3H), 1.11 (d, *J* = 7.2 Hz, 3H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.8, 173.6, 139.6, 83.1, 48.5, 47.2, 46.9, 44.3, 44.0, 40.3, 33.4, 30.2, 28.0, 24.5, 24.4, 22.9, 20.0, 19.5, 17.6, 9.5; MS (CI, NH_3) *m/z* (relative intensity) 304 (M^+), 179 (100), 137 (80), 95 (72); HRMS (CI, NH_3) calcd for $C_{20}H_{33}O_2$ [M^++1]: 305.2475, found: 305.2471.

^{13}C NMR (101 MHz, $CDCl_3$) **Spectral Data Comparison of Natural and Synthetic Fusicoauritone (1)**

Carbon Number	Natural 1	Synthetic 1
1	40.3	40.3
2	173.3	173.6
3	139.7	139.6
4	(212.8*)	207.8*
5	44.0	44.0
6	83.1	83.1
7	33.4	33.4
8	30.2	30.2
9	22.9	22.9
10	48.6	48.5
11	46.9	46.9
12	44.3	44.3
13	24.5	24.5

14	47.3	47.2
15	28.1	28.0
16	20.0	20.0
17	24.5	24.4
18	17.6	17.6
19	9.5	9.5
20	19.6	19.5

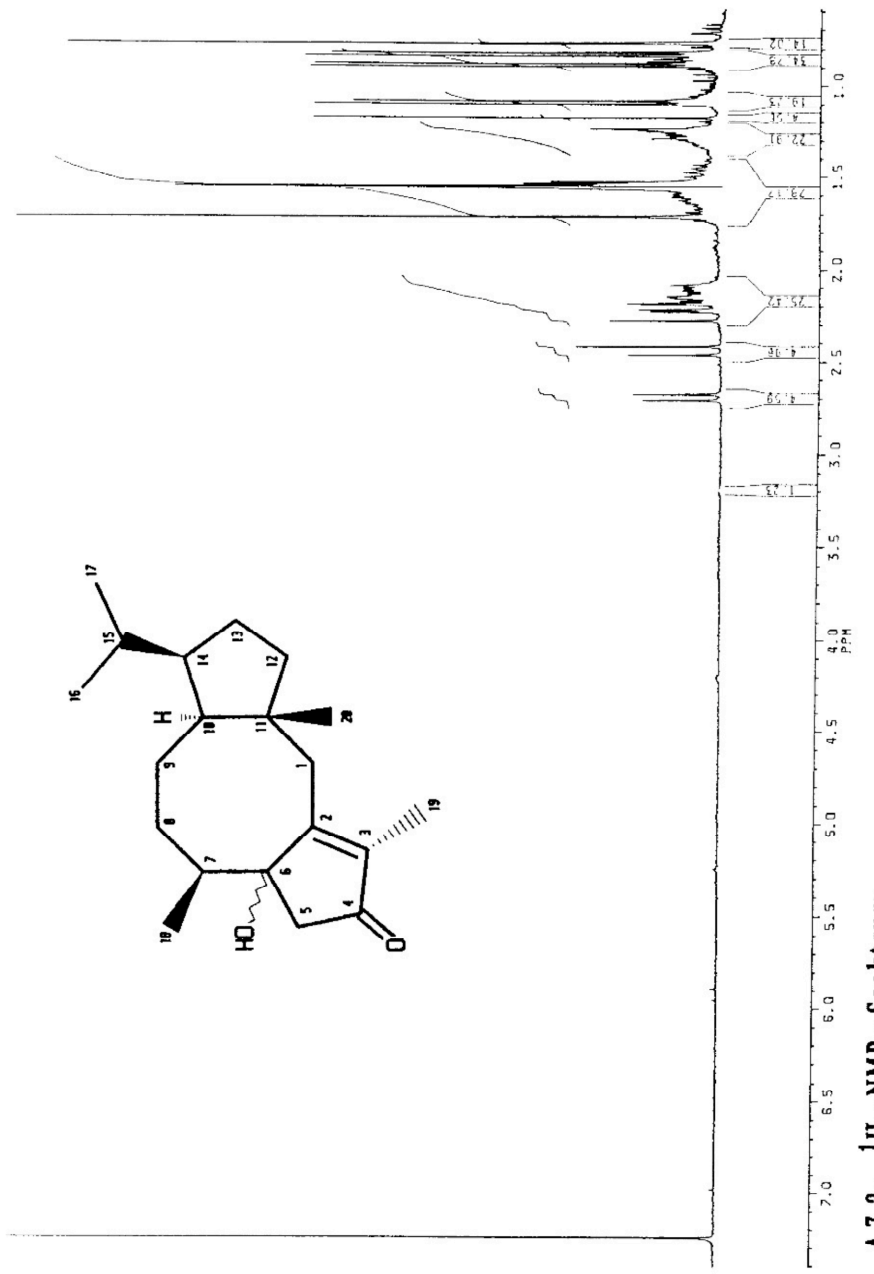
*The carbonyl carbon signal δ 212.8 was not directly observed in the ^{13}C NMR spectrum of natural fusicoauritone (**1**). Its value was taken from the HMBC data.



1

Synthetic Fusicoauritone

^{1}H NMR (400 MHz, $CDCl_3$)



A7.2: ^{1}H - NMR - Spektrum