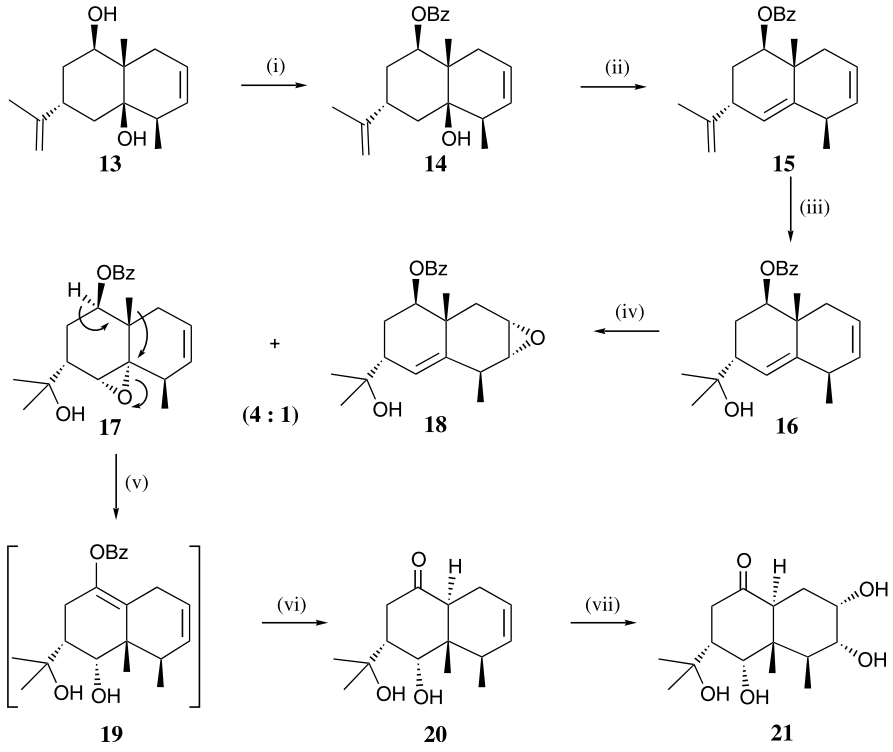
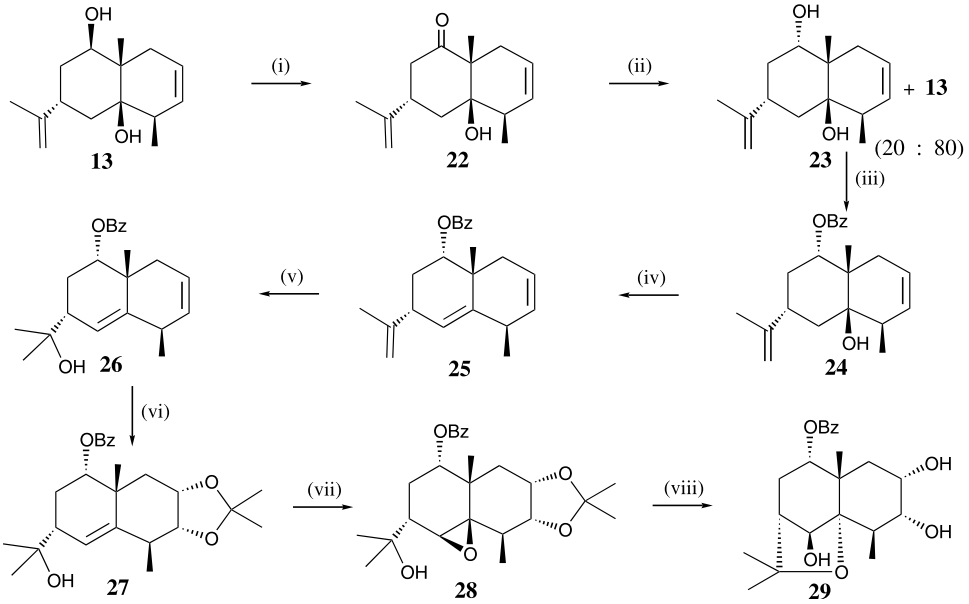


Scheme 3. *Reagents and conditions*: (i) C_6H_5COCl, Et_3N, DMAP, DCM, rt, 90%; (ii) $SOCl_2$, pyridine, −35°C, 85%; (iii) $Hg(OAc)_2$, cat. AcOH, THF:H_2O, rt, 75%; (iv) *m*CPBA, $NaHCO_3$, DCM, 83%; (v) $BF_3{\cdot}Et_2O$, DCM, 0°C, 80%; (vi) K_2CO_3, MeOH, rt, 95%; (vii) OsO_4, NMMO, CH_3COCH_3:H_2O, rt, 92%.

hydride led to a readily separable 4:1 mixture of **13** and the epimeric diol **23**. Although the stereoselectivity in this reaction to access desired **23** was not satisfactory, **13** could be recycled via **22** to build reasonable quantities of **23** (Scheme 4).[9] Monobenzoate **24** derived from **23** was dehydrated to furnish triene **25** regioselectively (Scheme 4). Oxymercuration of **25** was regioselective at the terminal olefinic moiety and readily led to the tertiary alcohol **26**.[9] Catalytic OsO_4-mediated dihydroxylation in **26** was stereoselective and acetonide protec-



Scheme 4. *Reagents and conditions*: (i) PCC, DCM, rt, 78%; (ii) $NaBH_4$, MeOH, 0°C, 90%; (iii) C_6H_5COCl, Et_3N, DMAP, DCM, rt, 87%; (iv) $SOCl_2$, pyridine, −35°C, 80%; (v) $Hg(OAc)_2$, cat. AcOH, THF:H_2O, rt, 70%; (vi) (a) OsO_4, NMMO, CH_3COCH_3:H_2O, rt, 95%; (b) CH_3COCH_3, Amberlyst, rt, 81%; (vii) *m*CPBA, $NaHCO_3$, DCM, 90%; (viii) TMSOTf, DCM, 0°C, 55%.

tion led to the polyfunctional **27** (Scheme 4). As the α-face of **27** was sterically shielded, epoxidation of **27** was stereoselective and furnished exclusively the β-epoxide **28**. Brief exposure of **28** to TMSOTf led to the contemplated tetrahydrofuran formation through epoxide opening and capture by the tertiary hydroxyl group to lead to agarofuran derivative **29**. The complete stereostructure of **29** was confirmed through its X-ray crystal structure determination.[10] Access to the agarofuran **29** with secured stereochemistry at eight stereogenic centers and five oxygen functionalities, particularly with C6 and C9 hydroxyl groups, makes our approach amenable to adaptation for the synthesis of many natural products of this family.

In summary, we have outlined a new approach to assemble rapidly, strategically functionalized eudesmanes from (−)-carvone employing RCM as the key step. Further transformations involving functional group amplification and rearrangements provide entry into polyoxyfunctionalized eremophilanes and agarofurans.

Acknowledgements

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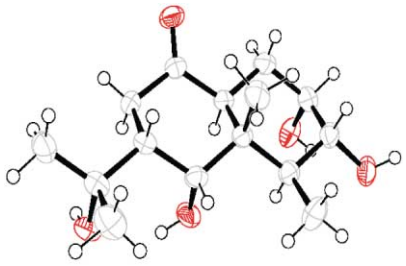
9. All new compounds reported here were duly characterized on the basis of spectroscopic data (IR, ^{1}H and ^{13}C NMR) and elemental analyses. Data for **29**: mp 213–214°C; $[\alpha]_D=-11.1$ (*c* 0.45, $CHCl_3$), IR (cm^{-1}) 3438, 1711; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, $J=7.2$ Hz, 2H), 7.58 (t, $J=7.5$ Hz, 1H), 7.47 (t, $J=7.5$ Hz, 2H), 5.10 (d, $J=7.5$ Hz, 1H), 4.70 (br s, 1H), 4.30 (d, $J=9.9$ Hz, 1H), 3.91 (br s, -OH), 3.69 (d, $J=9.6$ Hz, 1H), 2.71 (ddd, $J=16.5$, 7.5, 4.2 Hz, 1H), 2.46–2.43 (br m, -OH), 2.36–2.20 (m, 2H), 1.99–1.93 (m, 2H), 1.79 (br s, -OH), 1.48 (s, 6H), 1.32 (s, 3H), 1.31 (d, $J=7.8$ Hz, 3H), 1.17 (dd, $J=12.9$, 4.5 Hz, 1H); ^{13}C NMR (75 MHz) δ 166.1, 132.9, 130.4, 129.7, 128.5, 83.5, 79.7, 76.9, 75.9, 75.8, 65.9, 47.8, 46.9, 45.4, 35.8, 30.6, 25.5, 25.3, 25.1, 14.9; HRMS calcd for 413.1940 (M+Na). Found: 413.1945. **28**: $[\alpha]_D=-19.0$ (*c* 1.0, $CHCl_3$); IR (cm^{-1}) 3452, 1718, 1273; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, $J=7.8$ Hz, 2H), 7.57 (t, $J=7.8$ Hz, 1H), 7.45 (t, $J=7.8$ Hz, 2H), 4.96 (dd, $J=11.7$, 3.6 Hz, 1H), 4.51–4.44 (m, 1H), 4.18–4.16 (m, 1H), 3.13 (s, 1H), 2.19–1.92 (m, 4H), 1.77–1.73 (m, 2H), 1.52 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 1.22 (d, $J=7.8$ Hz, 3H), 1.15 (s, 3H); ^{13}C NMR (75 MHz) δ 165.9, 133.1, 130.2, 129.6, 128.4, 107.9, 79.5, 75.9, 72.1, 71.3, 65.4, 64.2, 44.8, 38.8, 37.6, 32.3, 28.5, 26.2, 26.1, 24.0, 19.8, 16.0; HRMS calcd for 453.2253 (M+Na). Found 453.2291. **26**: mp 146.5–147.5°C; $[\alpha]_D=-4.1$ (*c* 1.2, $CHCl_3$); IR (cm^{-1}) 3351, 1715, 1273; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, $J=8.1$ Hz, 2H), 7.58 (t, $J=7.5$ Hz, 1H), 7.46 (t, $J=7.5$ Hz, 2H), 5.66 (s, 2H), 5.64 (s, 1H), 5.22 (dd, $J=12.3$, 3.6 Hz, 1H), 2.97 (d, $J=6.9$ Hz, 1H), 2.43–2.38 (m, 2H), 2.18 (dd, $J=4.5$, 3.6 Hz, 1H), 2.02–1.98 (m, 1H), 1.51 (q, $J=12$ Hz, 1H), 1.25 (d, $J=7.5$ Hz, 3H), 1.24 (s, 3H), 1.23 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (75 MHz) δ 166.4, 146.1, 132.9, 132.2, 130.6, 129.5, 128.4, 123.8, 122.2, 79.3, 72.4, 46.0, 39.7, 38.9, 34.9, 27.9, 27.1, 25.9, 24.8, 21.4; HRMS calcd for 363.1936 (M+Na), Found 363.1970. **21**: mp 189–191°C; $[\alpha]_D=-42.8$ (*c* 1.05, MeOH); IR (cm^{-1}) 3413, 1696, 1025; ^{1}H NMR (300 MHz, MeOH-d_4) δ 4.06 (s, 1H), 3.87 (d, $J=2.7$ Hz, 1H), 3.25–3.17 (m, 2H), 2.67 (t, $J=13.5$ Hz, 1H), 2.34–2.19 (m, 2H), 1.87–1.81 (m, 2H), 1.51 (dt, $J=13.5$, 2.4 Hz, 1H), 1.32 (s, 3H), 1.12 (s, 3H), 0.91 (d, $J=6.6$ Hz, 3H), 0.54 (s, 3H); ^{13}C NMR (75 MHz) δ 216.7, 74.2, 73.7, 72.0, 69.7, 47.5, 46.6, 44.9, 38.1, 35.7, 28.8, 28.4, 27.6, 14.0, 10.5; HRMS calcd for 309.1678 (M+Na). Found 309.1692. **17**: $[\alpha]_D=-62.5$ (*c* 1.2, $CHCl_3$); IR (cm^{-1}) 3479, 1717, 1275; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, $J=6.9$ Hz, 2H), 7.56 (t, $J=6.9$ Hz, 1H), 7.44 (t, $J=7.2$ Hz, 2H), 5.67–5.62 (br s, 2H), 5.24 (dd, $J=12$, 4.5 Hz, 1H), 3.31 (d, $J=3$ Hz, 1H), 2.29–1.96 (m, 3H), 1.91–1.87 (m, 2H), 1.79–1.67 (m, 1H),

1.43 (s, 3H), 1.40 (s, 3H), 1.30 (s, 3H), 1.24 (d, $J=7.8$ Hz, 3H); ^{13}C NMR (75 MHz) δ 165.9, 132.9, 130.6, 129.5, 128.4, 123.4, 76.6, 74.2, 66.3, 58.9, 41.8, 39.0, 35.9, 34.2, 27.9, 27.7, 23.7, 18.5, 16.5; HRMS calcd for 379.1885 (M+Na). Found 379.1907. **16**: $[\alpha]_D=-33.1$ ($c=1.0$, $CHCl_3$); IR (cm^{-1}) 3489, 1715, 1275; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, $J=7.5$ Hz, 2H), 7.56 (d, $J=6.6$ Hz, 1H), 7.45 (t, $J=6.6$ Hz, 2H), 5.66 (s, 1H), 5.60 (s, 2H), 5.16 (t, $J=6.9$ Hz, 1H), 2.96 (d, $J=6.3$ Hz, 1H), 2.38 (br s, 1H), 2.17–2.12 (m, 1H), 1.99–1.95 (m, 3H), 1.31 (s, 6H), 1.27 (s, 3H), 1.25 (d, $J=7.5$ Hz, 3H); ^{13}C NMR (75 MHz) δ 166.3, 145.8, 132.8, 131.5, 129.5, 128.4, 122.8, 121.7, 78.0, 73.3, 44.8, 37.8, 37.6, 37.0, 27.9, 27.6, 25.6, 24.2, 21.0; HRMS calcd for 363.1936 (M+Na). Found 363.1956. **13**: $[\alpha]_D=-66.2$ (c 0.8, $CHCl_3$); IR (cm^{-1}) 3321, 1455; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.63–5.60 (m, 1H), 5.48–5.46 (m, 1H), 4.73 (s, 2H), 3.59–3.55 (m, 1H), 3.14–3.07 (br s, -OH), 2.75–2.72 (m, 1H), 2.18–2.12 (m, 2H), 1.81–1.63 (m, 4H), 1.74 (s, 3H), 1.46 (dd, $J=8.7$, 3.3 Hz, 1H), 1.21 (s, 3H), 1.15 (d, $J=7.5$ Hz, 3H); ^{13}C NMR (75 MHz) δ 149.2, 131.4, 121.0, 109.0, 78.5, 75.7, 43.5, 42.2, 39.3, 35.5, 34.0, 33.9, 21.1, 21.0, 16.0; HRMS calcd for 259.1674 (M+Na). Found 259.1695. **12**: $[\alpha]_D=+75.9$ ($c=0.83$, $CHCl_3$); IR (cm^{-1}) 3343, 1455; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.47 (br s, 1H), 5.36 (d, $J=9.9$ Hz, 1H), 4.74 (s, 2H), 3.63 (br s, 1H), 3.09 (d, $J=6.6$ Hz, 1H), 2.97 (s, 1H), 2.68–2.65 (m, 1H), 2.45 (m, 1H), 2.18 (d, $J=17.7$ Hz, 1H), 1.84–1.81 (m, 2H), 1.75 (s, 3H), 1.31–1.23 (m, 1H), 1.16 (s, 3H), 0.99 (d, $J=7.5$ Hz, 3H); ^{13}C NMR (75 MHz) δ 149.5, 130.6, 122.8, 109.1, 77.4, 76.1, 39.2, 38.5, 36.1, 33.9, 33.5, 31.9, 20.9, 18.8, 13.2; HRMS calcd for 259.1674 (M+Na). Found 259.1683.

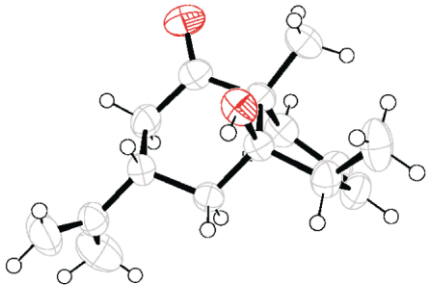
10. X-Ray crystal structure determination: X-ray data were collected at 293 K on a SMART CCD–BRUKER diffractometer with graphite monochromated MoKα radiation ($\lambda=0.7107$ Å). Structure was solved by direct methods (SIR92). Refinement was by full-matrix least-squares procedures on F^2 using SHELXL-97. The non-hydrogen atoms were refined anisotropically whereas hydrogen atoms were refined isotropically. **Compound PNB derivative of 12**: $C_{22}H_{27}O_5N$, MW = 385.45, crystal system: monoclinic, space group: $P2(1)$, cell parameters: $a=8.265$ (2), $b=13.123$ (3), $c=18.829(5)$ Å, $\beta=94.113(5)$, $V=2037.09(6)$ Å^3, $Z=4$, $D_{calcd}=1.257$ g cm^{-3}, $F(000)=824.0$, $\mu=0.09$ mm^{-1}. Total number of l.s. parameters = 721, $R_1=0.0576$ for 6673, $F_o>4\sigma(F_o)$ and 0.0797 for all 8820 data. $WR_2=0.1213$, GOF = 1.123. Restrained GOF = 1.123 for all data. There are two molecules in an asymmetric unit. An ORTEP diagram with only one molecule is shown in Scheme 2. (CCDC 214302). **Compound 21**: $C_{15}H_{26}O_5$, MW = 286.37, colorless crystal, Crystal system: monoclinic, space group: $P2(1)$, cell parameters: $a=7.6151(6)$, $b=12.361(1)$, $c=16.356(1)$ Å, $V=1539.76$ Å^3, $Z=4$, $D_{calcd}=1.235$ g cm^{-3}, $F(000)=624.0$, $\mu=0.09$ mm^{-1}. Total number of l.s. parameters = 285, $R_1=0.0385$ for 2927, $F_o>4\sigma(F_o)$ and 0.0417 for all 53125 data. $WR_2=0.0925$, GOF = 1.086. Restrained GOF = 1.086 for all data (CCDC 214303).



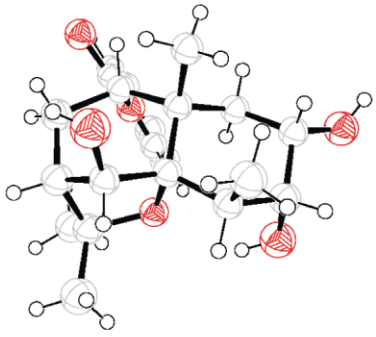
ORTEP diagram of **21**

Compound 22: $C_{15}H_{22}O_2$, MW = 234.34, colorless crystal, crystal system: monoclinic, space group: $P2(1)$, cell parameters: $a=10.305(2)$, $b=10.916(2)$, $c=12.805(3)$ Å, $\beta=108.436(4)$, $V=1366.75(6)$ Å^3, $Z=4$, $D_{calcd}=1.139$ g cm^{-3}, $F(000)=512.0$, $\mu=0.07$ mm^{-1}. Total number of l.s. parameters = 315, $R_1=0.0565$ for 4301, $F_o>4\sigma(F_o)$ and 0.0739 for all 5368 data. WR2 = 0.1254, GOF = 1.106, restrained GOF = 1.106 for all data. There are two molecules in an asymmetric unit. (CCDC 214304).

Compound 29: $C_{22}H_{30}O_6$, MW = 390.48, crystal system: monoclinic, space group: $P2(1)$, cell parameters: $a=8.198(2)$, $b=15.354(4)$, $c=16.138$ (4) Å, $\beta=94.364$ (5), $V=2025.55$ Å^3, $Z=4$, $D_{calcd}=1.28$ g cm^{-3}, $F(000)=840.0$, $\mu=0.09$ mm^{-1}. Total number of l.s. parameters = 239, $R_1=0.0897$ for 5614, $F_o>4\sigma(F_o)$ and 0.1226 for all 7976 data. $wR_2=0.2182$, GOF = 1.025, Restrained GOF = 1.025 for all data. There are two molecules in an asymmetric unit. (CCDC 214305).



ORTEP diagram of **22**



ORTEP diagram of **29**