

Towards the Synthesis of Dihydrooxepino[4,3-*b*]pyrrole Containing Natural Products via Cope Rearrangement of Vinyl Pyrrole Epoxides.

Alex Cameron,[†] Brendan Fisher,[†] Nicholas Fisk,[†] Jessica Hummel,[†] Jonathan M. White, Elizabeth H. Krenske,^{‡*} and Mark A. Rizzacasa.^{†*}

[†]*School of Chemistry, The Bio21 Institute, The University of Melbourne, Melbourne, Victoria, 3010, Australia.*

[‡]*School of Chemistry & Molecular Biosciences, The University of Queensland, Brisbane, QLD 4072, Australia.*

masr@unimelb.edu.au, e.krenske@uq.edu.au

Supporting Information

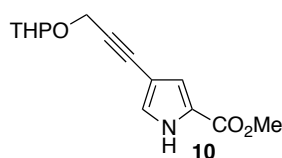
Experimental Section

General	S2
Preparation of alkyne 10	S2
Preparation of alkyne 11	S2
Preparation of alkene 12	S3
Preparation of alcohol 13	S3
Preparation of vinyl epoxide 14	S4
Preparation of vinyl epoxide 15	S5
Preparation of pyrrole 16	S5
Preparation of pyrrole 17	S6
Preparation of vinyl epoxide 19	S6
Preparation of vinyl epoxide 20	S7
Preparation of dihydrooxepine 21	S7
Preparation of dihydrooxepine 22	S8
Crystallography	S8
ORTEP of X-ray structure of dihydrooxepine 22	S9
Discussion of Cope transition state resonance contributors	S10
Computational data	S11-S17
Complete citation for Gaussian 09	S18
NMR spectra	S19-S30

General

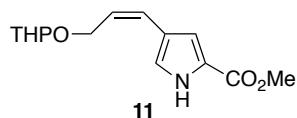
Proton nuclear magnetic resonance spectra (^1H NMR, 600, 500 or 400 MHz) and proton decoupled carbon nuclear magnetic resonance spectra (^{13}C NMR, 150, 125 or 100 MHz) were obtained in deuteriochloroform with residual chloroform as internal standard unless otherwise noted. Chemical shifts are followed by multiplicity, coupling constant(s) (J , Hz), integration, and assignments where possible. Optical rotations were recorded for a 1 mL solution and units are $\text{deg.cm}^2\text{g}^{-1}$. Flash chromatography was carried out on silica gel 60. Analytical thin layer chromatography (TLC) was conducted on aluminium-backed 2 mm thick silica gel 60 GF₂₅₄ and chromatograms were visualized with 20% w/w phosphomolybdic acid in ethanol. High resolution mass spectra (HRMS) were obtained by ionizing samples via electron spray ionization (ESI). Anhydrous THF, Et₂O and CH₂Cl₂ were dried using a solvent cartridge system. Dry methanol was distilled from magnesium methoxide. All other solvents were purified by standard methods. Petrol used refers to petroleum ether 40-60°C boiling range. All other commercially available reagents were used as received.

Alkyne 10.



To a solution of the iodide **8**¹ (4.625 g, 18.33 mmol) in DMF (30 mL) was added alkyne **9** (5.14 g, 36.7 mmol), NEt₃ (7.2 mL, 51.3 mmol), and (Ph₃P)₂PdCl₂ (1.96 g, 2.79 mmol). The solution was stirred for 15 min at rt and CuI (524 mg, 2.75 mmol) was added. The solution was then stirred for 15.5 h at rt then water was added and the mixture was extracted with ether. The combined organic extracts were washed with water and brine, then dried, filtered and solvents were evaporated. The crude residue was purified using flash chromatography (20% - 100% EtOAc/petrol) to afford the alkyne **10** (2.94 g, 61%) as a brown oil. IR: 3284, 2947, 2869, 1704, 1567, 1490, 1439, 1380, 1363, 1346, 1324, 1266, 1202, 1184, 1154, 1115, 1076, 1055, 1024, 1015, 987, 944, 927 cm^{-1} . ^1H NMR (400 MHz) δ 9.10 (br s, 1H), 7.11 (dd, J = 2.9, 1.4 Hz, 1H), 6.94 (t, J = 1.9 Hz, 1H), 4.88 (t, J = 3.4 Hz, 1H), 4.48 (d, J = 15.7 Hz, 1H), 4.41 (d, J = 15.7 Hz, 1H), 3.87-3.91 (m, 1H), 3.85 (s, 3H), 3.53-3.58 (m, 1H), 1.72-1.86 (m, 2H), 1.61-1.68 (m, 2H), 1.51-1.56 (m, 2H). ^{13}C NMR (100 MHz) δ 161.1, 126.5, 122.5, 118.1, 117.5, 106.3, 96.8, 84.2, 79.7, 62.0, 54.9, 51.7, 30.3, 25.4, 19.0. HRMS (ESI) calc. for C₁₄H₁₇NO₄ [$M + H$]⁺ = 264.1191, found 264.1230.

Alkene 11.

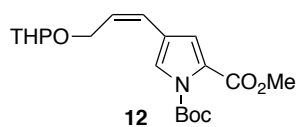


A suspension of Ni(OAc)₂•4H₂O (993 mg, 3.99 mmol) in EtOH (10 mL) was degassed and placed under an atmosphere of H₂ gas. A 5% solution of 2.5 M aq. NaOH in ethanol (4.3 mL) was added to NaBH₄ (163 mg, 37.8

1. Belanger, P. *Tetrahedron Lett.* **1979**, 2505.

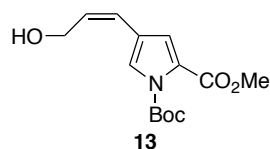
mmol) and this was degassed before adding to the suspension of $\text{Ni}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ and the solution turned black. Ethylenediamine (1.28 mL, 60.1 mmol) was added followed by a solution of the alkyne (422 mg, 1.60 mmol) in degassed ethanol (10 mL). The resultant solution was stirred at rt for 2.5 h then filtered through a plug of silica gel and celite with EtOAc as an eluent. The residue was purified by flash chromatography (20% EtOAc/petrol) to give the alkene **11** (283 mg, 66%) as a yellow oil: IR: 3293, 2945, 2868, 1670, 1568, 1488, 1439, 1389, 1353, 1315, 1285, 1265, 1233, 1199, 1113, 1076, 1066, 1022, 999, 963, 903 cm^{-1} . ^1H NMR (600 MHz) δ 9.73-9.68 (br m, 1H), 6.93 (d, $J = 1.2$ Hz, 1H), 6.85 (d, $J = 1.4$ Hz, 1H), 6.35-6.33 (m, 1H), 5.66-5.62 (m, 1H), 4.69 (t, $J = 3.7$ Hz, 1H), 4.49 (ddd, $J = 13.0, 5.8, 1.1$ Hz, 1H), 4.29 (ddd, $J = 13.0, 6.6, 1.0$ Hz, 1H), 3.89 (ddd, $J = 11.1, 8.1, 2.9$ Hz, 1H), 3.82 (s, 3H), 3.52-3.49 (m, 1H), 1.85-1.80 (m, 1H), 1.74-1.69 (m, 1H), 1.62-1.49 (m, 4H). ^{13}C NMR (150 MHz) δ 161.7, 125.5, 123.4, 123.1, 122.7, 122.4, 115.4, 98.3, 64.6, 62.3, 51.5, 30.7, 25.4, 19.5. HRMS (ESI) calc. for $\text{C}_{14}\text{H}_{19}\text{NO}_4$ $[\text{M} + \text{H}]^+$ 266.1387, found 266.1386.

Alkene 12.



To a solution of the alkene **11** (283 mg, 1.06 mmol) in CH_2Cl_2 (15 mL) at 0 °C was added di-*tert*-butyl dicarbonate (0.73 mL, 3.18 mmol) followed by a solution of 4-dimethylaminopyridine (6.5 mg, 0.053 mmol) and *i*- Pr_2NEt (1.1 mL, 6.32 mmol) in CH_2Cl_2 (5 mL) via cannula. The reaction was allowed to stir at 0 °C for 1.25 h and was then quenched with water. The organic layer was separated and the aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with brine, dried, filtered and the solvents were evaporated. Purification of the residue on silica gel with 10% EtOAc/petrol as the eluent afforded the pyrrole **12** (387 mg, 100%) as a colourless oil. IR: 3447, 2946, 1726, 1478, 1437, 1394, 1370, 1327, 1281, 1256, 1232, 1156, 1075, 1032, 975, 906 cm^{-1} . ^1H NMR (400 MHz) δ 7.27 (d, $J = 1.8$ Hz, 1H), 6.83 (d, $J = 1.9$ Hz, 1H), 6.27 (d, $J = 11.7$ Hz, 1H), 5.76 (dt, $J = 11.9, 6.0$ Hz, 1H), 4.69 (t, $J = 3.6$ Hz, 1H), 4.47 (ddd, $J = 13.1, 5.8, 1.8$ Hz, 1H), 4.27 (ddd, $J = 13.1, 6.7, 1.5$ Hz, 1H), 3.84 (s, 3H), 1.74 – 1.83 (m, 2H), 1.62 (dt, $J = 9.2, 3.4$ Hz, 2H), 1.59 (s, 9H), 1.56-1.51 (m, 2H). ^{13}C NMR (100 MHz) δ 161.2, 148.2, 128.0, 125.4, 122.3, 121.7, 121.1, 98.3, 85.0, 64.2, 62.4, 51.9, 30.7, 27.6, 25.4, 23.5, 19.5. HRMS (ESI) calc. for $\text{C}_{19}\text{H}_{27}\text{NO}_6$ $[\text{M} + \text{H}]^+$ 366.1911, found 366.1906.

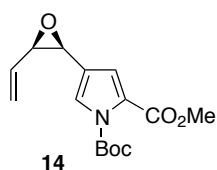
Alcohol 13.



The alkene **12** (59 mg, 0.161 mmol) was dissolved in methanol (10 mL) and camphorsulphonic acid (11 mg, 0.047 mmol) was added and the solution was stirred for 1.5 h at rt. A saturated aqueous solution of NaHCO_3 was added

and the solution was extracted with ether. The combined organic layers were dried, filtered and the solvents were evaporated to give the alcohol **13** (97%, 44 mg) as a yellow oil. IR: 3406, 2986, 2952, 1724, 1575, 1478, 1458, 1436, 1395, 1371, 1328, 1304, 1281, 1256, 1232, 1153, 1075, 1027, 953 cm^{-1} . ^1H NMR (400 MHz) δ 7.25 (d, J = 1.8 Hz, 1H), 6.81 (d, J = 1.9 Hz, 1H), 6.25 (dd, J = 11.6, 0.3 Hz, 1H), 5.78 (dt, J = 11.8, 6.0 Hz, 1H), 4.43 (dd, J = 6.3, 1.1 Hz, 2H), 3.85 (d, J = 0.5 Hz, 3H), 1.58 (d, J = 0.4 Hz, 9H). ^{13}C NMR (125 MHz) δ 161.1, 148.1, 130.3, 125.43, 125.38, 121.9, 121.5, 120.9, 85.2, 59.9, 52.0, 27.6. HRMS (ESI) calc. for $\text{C}_{14}\text{H}_{19}\text{NO}_5$ $[\text{M} + \text{Na}]^+$ 304.1155, found 304.1153.

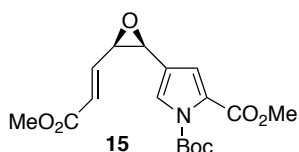
Epoxide 14.



The alcohol **13** (119 mg, 0.423 mmol) was dissolved in CH_2Cl_2 (10 mL) and a 0.1 M solution of dimethyldioxirane in acetone was added at 0 °C until all starting material was consumed. The solution was concentrated in vacuo to give the epoxide (100%, 126 mg) as a colourless oil. ^1H NMR (600 MHz) δ 7.24 (dd, J = 1.8, 0.8 Hz, 1H), 6.73 (dd, J = 1.3, 0.5 Hz, 1H), 3.93-3.93 (m, 1H), 3.79 (d, J = 0.3 Hz, 3H), 3.64-3.55 (m, 2H), 3.35-3.32 (m, 1H), 1.54 (dd, J = 1.2, 0.6 Hz, 9H). ^{13}C NMR (150 MHz) δ 161.0, 147.8, 125.4, 124.27, 124.24, 119.6, 119.0, 85.3, 77.2, 77.0, 76.8, 60.5, 58.3, 52.0, 27.6. To a solution of the crude epoxide (126 mg, 0.423 mmol) in CH_2Cl_2 (10 mL) was added NaHCO_3 (171 mg, 2.03 mmol) followed by Dess-Martin periodinane (180 mg, 0.424 mmol). The solution was stirred at rt for 1.25 h and was then quenched with a saturated aqueous solution of sodium thiosulphate and stirred for an additional 40 min. The solution was extracted with ether and the combined organic layers were dried with Na_2SO_4 , filtered and the solvents were evaporated to give the crude aldehyde (112 mg) which was used in the next step without additional purification. Methyltriphenylphosphonium bromide (757 mg, 2.12 mmol) was dissolved in THF (10 mL) and cooled to 0 °C before adding *t*-BuOK (213 mg, 1.90 mmol). The solution was stirred for 1.5 h and was then cooled to -78 °C and a solution of the above aldehyde (112 mg) in THF (10 mL) was added via cannula. The solution was stirred at -78 °C for 45 min then warmed to 0 °C and stirred for 20 min. The reaction was quenched with a saturated aqueous NH_4Cl and extracted with Et_2O . The combined organic layers were dried with Na_2SO_4 , filtered and the solvents were evaporated. The crude residue was purified by flash chromatography (10% EtOAc/petrol) to give the alkene (14 mg, 11%) as a yellow oil. IR: 2983, 1751, 1730, 1480, 1436, 1395, 1371, 1324, 1302, 1281, 1250, 1226, 1156, 1076, 984, 938, 846 cm^{-1} . ^1H NMR (400 MHz) δ 7.28 (dd, J = 1.9, 0.7 Hz, 1H), 6.78 (d, J = 1.9 Hz, 1H), 5.57-5.54 (m, 2H), 5.37-5.34 (m, 1H), 4.03 (d, J = 4.1 Hz, 1H), 3.84 (d, J = 0.5 Hz, 3H), 3.62-3.59 (m, 1H), 1.58 (d, J = 0.3 Hz, 9H). ^{13}C NMR (100 MHz): δ 161.0, 147.9, 132.1,

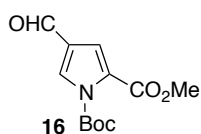
125.3, 124.5, 121.9, 120.1, 119.4, 85.1, 59.4, 53.8, 52.0, 27.6. HRMS (ESI) calc. for $C_{15}H_{19}NO_5$ [$M + Na$] $^+$ 316.1155, found 316.1152.

Epoxide 15.



To a solution of the crude epoxide above (129 mg, 0.434 mmol) dichloromethane (10 mL) was added $NaHCO_3$ (220 mg, 2.62 mmol) followed by Dess-Martin periodinane (224 mg, 0.528 mmol). The solution was stirred at rt for 1.5 h and was then quenched with a saturated aq. $Na_2S_3O_4$ and a saturated aqueous solution of $NaHCO_3$. Ether was added and the solution was stirred vigorously for an additional 90 min. The solution was extracted with ether and the combined organic extracts were washed with water, a 2M aq. $Na_2S_2O_3$ and a saturated aqueous solution of $NaHCO_3$, then dried with sodium sulphate and filtered. The solvents were evaporated to afford the crude aldehyde (124 mg) which was dissolved in CH_2Cl_2 (10mL). Methyl 2-(triphenylphosphoranylidene)acetate (290 mg, 0.868 mmol) was added and the solution was stirred for 50 min at room temperature. The solvents were evaporated and the crude residue was purified by flash chromatography (20% EtOAc/petrol) to afford the epoxide **15** (52 mg, 34%) as a yellow oil. IR: 3370, 2953, 1753, 1725, 1659, 1480, 1437, 1396, 1372, 1305, 1281, 1245, 1153, 1076, 1027, 978 cm^{-1} . 1H NMR (500 MHz) δ 7.30 (dd, J = 1.9, 0.7 Hz, 1H), 6.77 (d, J = 1.9 Hz, 1H), 6.58 (dd, J = 15.7, 7.8 Hz, 1H), 6.23 (dd, J = 15.7, 0.7 Hz, 1H), 4.14-4.14 (m, 1H), 3.85 (s, 3H), 3.74 (s, 3H), 3.72 (ddd, J = 7.8, 4.1, 0.7 Hz, 1H), 1.59 (s, 9H). ^{13}C NMR (125 MHz) δ 165.6, 160.9, 147.8, 141.2, 126.3, 125.7, 124.6, 118.96, 118.94, 85.3, 57.7, 54.6, 52.0, 51.8, 27.6. HRMS (ESI) calc. for $C_{17}H_{21}NO_7$ [$M + Na$] $^+$ 374.1210, found 374.1203.

Pyrrole 16.

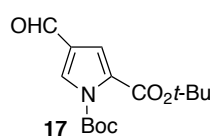


To a solution of the methyl 4-formyl-1*H*-pyrrole-2-carboxylate² (290 mg, 1.89 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added a solution of di-*t*-butyl dicarbonate (825 mg, 3.78 mmol) in CH_2Cl_2 (10 mL) via cannula. The solution was stirred for 10 min and a solution of DMAP (29 mg, 0.237 mmol) and *i*-Pr₂NEt (0.66 mL, 3.78 mmol) in CH_2Cl_2 (5 mL) was then added via cannula. The solution stirred at 0 °C for 2 h then quenched with water. The solution was extracted with EtOAc and the combined organic layers were washed with brine and dried with sodium sulphate, filtered, and solvents were evaporated. The crude residue was filtered through a plug of silica gel with 25% EtOAc/petrol as the eluent to afford the pyrrole **16** (396 mg, 83%) as a yellow oil. IR: 2985, 1763, 1732, 1687, 1564, 1486, 1460, 1437, 1417, 1372, 1340, 1283, 1260, 1232, 1151, 1114, 1078, 954, 910 cm^{-1} . 1H NMR (400 MHz) δ 9.83 (s, 1H), 7.88 (d, J = 1.7 Hz, 1H), 7.17 (d, J = 1.6 Hz, 1H), 3.87 (s, 3H), 1.60 (s, 9H). ^{13}C NMR (150 MHz): δ

2. Garrido, D. O. A.; Buldain, G.; Ojea, M. I.; Frydman, B. *J. Org. Chem.* **1988**, 53, 403.

184.9, 160.5, 147.3, 132.2, 127.0, 126.1, 116.9, 86.7, 52.3, 27.5. HRMS (ESI) calc. for C₁₂H₁₅NO₅ [M + Na]⁺ 276.0842, found 276.0840.

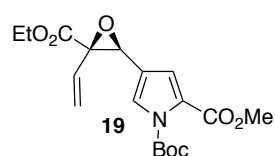
Pyrrole 17.



To a solution of 4-formyl-1*H*-pyrrole-2-carboxylic acid¹ (140 mg, 1.00 mmol) in CH₂Cl₂ (20 mL) was added *O*-*tert*-butyl-*N,N*-diisopropylisourea (650 mg, 3.25 mmol). The solution was stirred for 18 h then filtered through a plug of Celite with dichloromethane as the eluent. The crude residue was purified by flash chromatography (20% EtOAc/petrol) to afford the *t*-butyl ester (123 mg, 63%) as a yellow oil. IR: 3274, 2979, 1705, 1663, 1559, 1501, 1477, 1443, 1416, 1395, 1367, 1389, 1357, 1213, 1157, 1110, 986, 963, 849, 831, 760, 746, 734 cm⁻¹. ¹H-NMR (600 MHz; CDCl₃): δ 9.83 (s, 1H), 9.52 (br s, 1H), 7.51 (s, 1H), 7.23 (s, 1H), 1.56 (s, 9H). ¹³C NMR (151 MHz; CDCl₃): δ 185.9, 160.7, 128.5, 127.2, 126.4, 113.8, 82.2, 28.2. HRMS calc. for C₁₀H₁₃NO₃ [M + H]⁺ 196.0968, found 196.0967.

To a solution of the above *t*-butyl ester (123 mg, 0.626 mmol) in CH₂Cl₂ (5 mL) at 0 °C was added a solution of di-*tert*-butyl dicarbonate (410 mg, 1.88 mmol) in CH₂Cl₂ (10 mL) via cannula. The solution was stirred for 10 min and a solution of DMAP (8 mg, 0.07 mmol) and *i*-Pr₂NEt (0.33 mL, 1.9 mmol) in CH₂Cl₂ (5 mL) was then added via cannula. The solution stirred at 0 °C for 1.5 h then quenched with water. The solution was extracted with ethyl acetate and the combined organic layers were washed with water and brine and dried with MgSO₄, filtered, and solvents were evaporated. The crude residue was purified by flash chromatography (10% EtOAc/petrol) to afford the pyrrole (116 mg, 63%) as a yellow oil. IR: 2982, 1764, 1723, 1687, 1562, 1479, 1459, 1417, 1395, 1371, 1341, 1286, 1242, 1155, 1113, 1080, 1036, 910, 846, 823, 779, 732 cm⁻¹. ¹H NMR (400 MHz): δ 9.82 (s, 1H), 7.84 (d, *J* = 1.8 Hz, 1H), 7.12 (d, *J* = 1.8 Hz, 1H), 1.60 (s, 9H), 1.55 (s, 9H). ¹³C NMR (100 MHz): δ 185.1, 159.0, 147.4, 132.2, 128.9, 125.9, 116.5, 86.3, 82.1, 28.0, 27.6. HRMS (ESI) calc. for C₁₅H₂₁NO₅ [M+Na]⁺ 318.1312, found: 318.1310.

Vinyl epoxide 19.

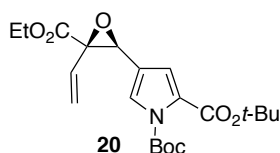


A solution of *n*-BuLi in hexanes (2.0 M, 1.78 mL, 3.55 mmol) was added to a solution of *i*-Pr₂NH (0.49 mL, 3.55 mmol) and HMPA (0.61 mL, 3.55 mmol) in THF (2.5 mL) at -78 °C this was allowed to warm to rt. The reaction was then cooled to -100 °C and a solution of ester **18**³ (681 mg, 3.55 mmol) in THF (2 mL) at -78 °C was transferred to the reaction via a cooled cannula. A solution of the aldehyde (300 mg, 1.18 mmol) in THF (4 mL) at -78 °C was then added to the reaction via cooled cannula. The reaction mixture was stirred for 1.5 h at -100 °C and for 45 min at -78 °C and

3. Hudlicky, T.; Fleming, A.; Radesca, L. *J. Am. Chem. Soc.* **1989**, *111*, 6691.

was then quenched with a saturated aq. NH_4Cl . The solution was allowed to warm to rt before extracting with ether. The combined organic layers were washed with water and brine, dried with sodium sulphate, filtered, and the solvents evaporated. The crude residue was purified by flash chromatography (10% EtOAc/petrol) to afford the vinyl epoxide **19** (316 mg, 73%) as a yellow oil. IR: 2983, 1726, 1585, 1479, 1459, 1436, 1394, 1370, 1327, 1306, 1276, 1255, 1232, 1152, 1075, 1045.6, 987, 951 cm^{-1} . ^1H NMR (600 MHz): δ 7.19 (1H, d, $J = 1/9$ Hz), 6.68 (1H, d, $J = 1.8$ Hz), 6.00 (1H, dd, $J = 17.3, 10.9$ Hz), 5.44 (1H, dd, $J = 17.3, 1.0$ Hz), 5.35 (1H, dd, $J = 11.0, 1.2$ Hz), 4.24–4.19 (2H, m), 4.15 (1H, s), 3.76 (3H, s), 1.50 (9H, s), 1.26 (3H, t, $J = 7.1$ Hz). ^{13}C NMR (150 MHz): δ 168.8, 160.8, 147.8, 127.4, 125.5, 125.1, 120.5, 119.5, 117.8, 85.3, 62.9, 62.0, 59.4, 51.9, 27.5, 14.0. HRMS (ESI) calc. for $\text{C}_{18}\text{H}_{23}\text{NO}_7$ $[\text{M} + \text{Na}]^+$ 388.1367, found 388.1368.

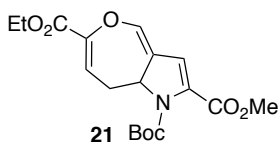
Vinyl epoxide **20**.



A solution of *n*-BuLi in hexanes (1.1 M, 4.0 mL, 4.4 mmol) was added to a solution of *i*-Pr₂NH (0.5 mL, 3.57 mmol) and HMPA (0.63 mL, 3.64 mmol) in THF (20 mL) at -78° and the solution was allowed to warm to 0°C . The reaction was then cooled to -100°C and a solution of ester **18** (703 mg, 3.64 mmol) in THF (5 mL) was cooled to -78°C and transferred to the reaction via cooled cannula. A solution of the aldehyde **17** (308 mg, 1.08 mmol) in THF (5 mL) was cooled to -78°C and transferred to the reaction via cooled cannula. The reaction was stirred for 2 h at -100°C and was then quenched with a saturated aq. NH_4Cl . The solution was allowed to warm to rt before extracting with Et₂O. The combined organic layers were washed with water and brine, dried with sodium sulphate, filtered, and the solvents evaporated. The crude residue was purified by flash chromatography (10% EtOAc/petrol) to afford the vinyl epoxide **20** (239 mg, 53%) as a yellow oil.

IR: 2971, 1738, 1478, 1456, 1306, 1280, 1232, 1217, 1156, 1122, 1078, 1046, 987, 908, 849, 823, 776, 731, 676 cm^{-1} . ^1H NMR (400 MHz; CDCl_3): δ 7.24–7.23 (m, 1H), 6.73 (d, $J = 1.8$ Hz, 1H), 6.08–6.01 (m, 1H), 5.51–5.39 (m, 2H), 4.31 (t, $J = 8.5$ Hz, 3H), 4.19 (s, 1H), 3.82 (s, 3H), 1.57 (d, $J = 0.2$ Hz, 9H), 1.09–1.04 (m, 2H), 0.06 (d, $J = 0.4$ Hz, 9H). ^{13}C NMR (100 MHz): δ 169.0, 159.4, 147.9, 127.4, 127.1, 125.1, 120.5, 119.2, 117.4, 85.0, 81.4, 63.0, 62.1, 59.7, 28.1, 27.6, 14.1. HRMS (ESI) calc. for $\text{C}_{21}\text{H}_{29}\text{NO}_7$ $[\text{M} + \text{Na}]^+$ 430.18362, found 430.18321.

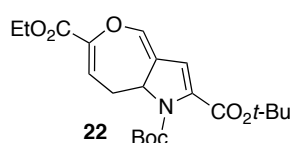
Dihydrooxepine **21**.



A solution of divinyl epoxide **19** (340 mg, 0.933 mmol) in degassed CCl_4 (5 mL) in a pressure tube was heated and stirred at 150°C for 2 h. The solvents were evaporated and the crude residue was purified using flash chromatography (20% EtOAc/petrol) to afford the dihydrooxepine **21** (279

mg, 83%) as a colourless solid. m.p. 92.2 – 93.8 °C. IR: 2980, 1707, 1648, 1587, 1477, 1437, 1389, 1368, 1336, 1268, 1214, 1168, 1124, 1060, 1046, 979, 953, 938, 917 cm^{-1} . ^1H NMR (500 MHz) δ 6.69 (d, J = 2.8 Hz, 1H), 6.42-6.39 (m, 1H), 6.18 (s, 1H), 4.72-4.69 (m, 1H), 4.28 (q, J = 7.1 Hz, 2H), 3.83 (s, 3H), 3.21 (ddd, J = 15.2, 9.7, 3.0 Hz, 1H), 2.31 (ddd, J = 15.2, 9.2, 3.3 Hz, 1H), 1.47 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz) δ 162.64, 162.53, 152.5, 142.7, 135.2, 134.9, 126.6, 117.3, 113.2, 82.2, 61.8, 61.0, 52.2, 33.9, 28.1, 14.2. HRMS (ESI) calc. for $\text{C}_{18}\text{H}_{24}\text{NO}_7$ $[\text{M} + \text{H}]^+$ 366.1547, found 366.1548.

Dihydrooxepine 22.



A solution of the divinyl epoxide **20** (239 mg, 0.549 mmol) in degassed CCl_4 (2 mL) in a pressure tube was heated and stirred to 150 °C for 1.5 h. The solvents were evaporated, the crude residue was recrystallised from petrol, and the mother liquor was purified using flash chromatography

(10% EtOAc/petrol) to afford the dihydrooxepine **22** (143 mg, 60%) as a colourless solid. m.p. 140.4-140.1 °C. IR: 2971, 1738, 1650, 1579, 1448, 1367, 1275, 1228, 1217, 1166, 1126, 1061, 1017, 896, 852, 770 cm^{-1} . ^1H NMR (400 MHz): δ 6.66 (d, J = 2.8 Hz, 1H), 6.39 (dd, J = 9.7, 3.2 Hz, 1H), 6.13 (s, 1H), 4.66 (dt, J = 9.1, 2.9 Hz, 1H), 4.27 (q, J = 7.1 Hz, 2H), 3.20 (ddd, J = 15.2, 9.7, 3.0 Hz, 1H), 2.29 (ddd, J = 15.2, 9.2, 3.3 Hz, 1H), 1.52 (s, 9H), 1.47 (s, 9H), 1.33 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz): δ 162.7, 160.5, 152.6, 142.6, 136.9, 134.5, 126.8, 117.4, 113.3, 81.94, 81.87, 61.8, 61.2, 33.9, 28.15, 28.11, 14.2. HRMS (ESI) calc. for $\text{C}_{21}\text{H}_{29}\text{NO}_7$ $[\text{M} + \text{H}]^+$ 408.2017, found 408.2014.

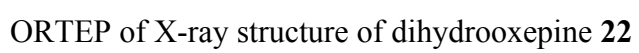
Crystallography. Intensity data were collected on a CCD diffractometer using Cu-K α radiation (graphite crystal monochromator λ = 1.54184 Å). The temperature during data collection was maintained at 130.0(1). The structure was solved by direct methods (SHELXT) and difference Fourier synthesis.⁴ Thermal ellipsoid plots were generated using the program ORTEP-3⁵ integrated within the WINGX⁶ suite of programs. The structure has been deposited at the Cambridge Crystallographic Data Centre and assigned the CCDC deposit code: 1429575.

Crystal data for **XX**. $\text{C}_{21}\text{H}_{29}\text{NO}_7$, M = 407.45, T = 130.0(2) K, λ = 1.54184 Å, Triclinic, space group $P-1$ a = 6.1386(2), b = 8.8450(3), c = 20.0476(7) Å, α = 100.943(3)° β = 95.193(3)° γ = 92.110(3)° V = 1062.70(6) Å³, Z = 2, D_c = 1.273 Mg M^{-3} $\mu(\text{Cu-K}\alpha)$ = 0.792 mm^{-1} , $F(000)$ = 436, crystal size 0.40 x 0.10 x 0.05 mm. θ_{max} = 77.09°, 21646 reflections measured, 4469 independent reflections (R_{int} = 0.0357) the final R = 0.0366 [$I > 2\sigma(I)$, 4003 data] and $wR(F^2)$ = 0.0993 (all data) GOOF = 1.051.

4. Sheldrick, G.M., *Acta Cryst.* **2008**, A64, 112.

5. Farrugia, L. J.; *J. Appl. Cryst.* **1997**, 30, 565.

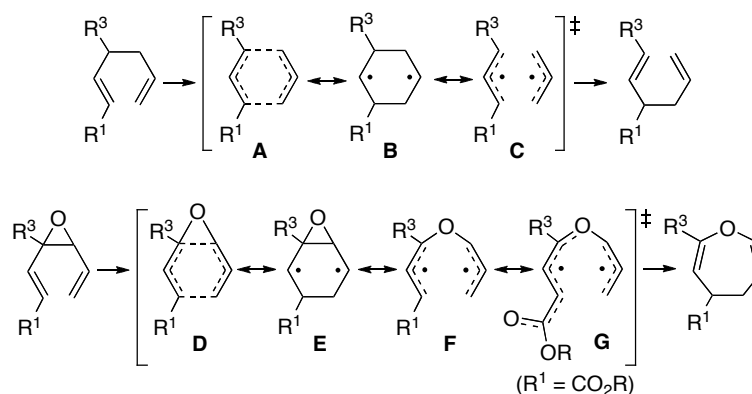
6. Farrugia, L. J.; *J. Appl. Cryst.* **1999**, 32, 837.



Discussion of Cope transition state resonance contributors

Scheme S1 shows the resonance contributors for Cope rearrangement transition states of acyclic 1,5-dienes and divinyl epoxides. The presence of a π -acceptor substituent at R^3 lowers the barrier for the Cope rearrangements of both 1,5-dienes (as reported previously⁷) and divinyl epoxides (this work). This is because a π -acceptor substituent at R^3 stabilizes resonance contributors **C** (or **F**) and also provides stabilization due to conjugation with the developing double bond. A π -acceptor substituent at the terminus (R^1) of an acyclic diene raises the barrier for rearrangement, due to the loss of conjugation.⁷ In divinyl epoxides, by contrast, the opposite effect is observed, where an ester group at R^1 lowers the rearrangement barrier by 1 kcal/mol. This likely reflects the involvement of a new resonance contributor, **G**, containing an extended conjugated π system.

SCHEME S1. Cope transition state resonance contributors for acyclic 1,5-dienes and divinyl epoxides.



7. Hrovat, D. A.; Beno, B. R.; Lange, H.; Yoo, H-Y; Houk, K. N.; Borden, W. T. *J. Am. Chem. Soc.* **1999**, *121*, 10529.

Computational data

Geometries listed below were computed with M06-2X/6-311+G(d,p) in Gaussian 09, using the SMD implicit solvent model to simulate solvation in CCl₄. The ultrafine integration grid was used. The computations employed restricted M06-2X (RM06-2X). In order to check for any diradical character, the transition states were reoptimized with unrestricted UM06-2X using the guess=(mix,always) keyword. The transition states thus obtained had identical energies to those from the RM06-2X calculations reported below.

Underneath the Cartesian coordinates for each species are listed the following energies (in Hartree):

M06-2X potential energy incorporating solvation corrections (E)

M06-2X Gibbs free energy in solution at a standard state of 1 mol/L (G)

S1

C	0.742333	0.629559	0.321999
C	-0.742335	0.629565	0.321996
H	-1.225616	1.149711	1.146496
H	1.225615	1.149702	1.146501
O	0.000004	1.477031	-0.546386
C	-1.545738	-0.441674	-0.303378
H	-1.157317	-0.874311	-1.220329
C	-2.693112	-0.868465	0.213098
H	-3.099849	-0.434654	1.121649
H	-3.260550	-1.665379	-0.252588
C	1.545731	-0.441686	-0.303370
H	1.157297	-0.874342	-1.220307
C	2.693117	-0.868461	0.213092
H	3.099866	-0.434632	1.121629
H	3.260552	-1.665378	-0.252590

0 imaginary frequencies
E = -308.542079
G = -308.445923

TS-S1

H	-0.385434	-2.268916	1.419286
C	-0.518596	-1.247210	1.078956
C	0.420309	-0.294151	1.454370
H	1.323790	-0.578300	1.984361
C	0.420309	0.971246	0.880262
C	0.420309	0.971246	-0.880262
C	0.420309	-0.294151	-1.454370
C	-0.518596	-1.247210	-1.078956
H	1.061947	1.774010	1.226586
H	1.323790	-0.578300	-1.984361
H	-1.546051	-0.928500	-0.986286
H	-0.385434	-2.268916	-1.419286
H	-1.546051	-0.928500	0.986286
O	-0.596596	1.355600	0.000000
H	1.061947	1.774010	-1.226586

1 imaginary frequency
E = -308.503184
G = -308.404962

Chair TS for Cope rearrangement of S1

H	2.267509	1.442922	0.221139
C	1.355981	0.887527	0.437094
C	0.182623	1.428157	-0.136676
H	0.304311	2.227609	-0.861309
C	-1.071489	0.812287	-0.241740
C	-0.899371	-0.869454	-0.351649
C	0.316924	-1.354536	0.156362
C	1.514846	-0.840446	-0.365282
H	-1.783143	1.256017	-0.930592
H	0.306496	-1.533650	1.229966
H	1.558791	-0.603101	-1.425204
H	2.461445	-1.184443	0.043095
H	1.334433	0.528361	1.458393
O	-1.685663	-0.171799	0.571364
H	-1.361620	-1.140528	-1.295059

1 imaginary frequency

E = -308.476937

G = -308.381672

S2

C	-0.113583	0.435182	0.081540
C	-0.921417	-0.823821	0.192626
H	-0.375594	-1.757676	0.077375
O	-0.527889	-0.067378	1.327144
C	1.341176	0.240733	-0.274728
C	-2.356322	-0.866537	-0.146587
H	-2.925582	0.043461	0.011096
C	-2.928490	-1.964084	-0.630013
H	-2.362580	-2.878136	-0.782115
H	-3.980228	-1.983270	-0.889860
C	-0.693943	1.725224	-0.375073
H	-0.367469	2.061390	-1.352832
C	-1.533985	2.439957	0.362702
H	-1.930561	3.380250	-0.001386
H	-1.838110	2.108786	1.349968
O	1.882906	0.836241	-1.168997
O	1.931716	-0.681270	0.478260
C	3.302208	-0.952302	0.159519
H	3.386450	-1.330149	-0.859992
H	3.626175	-1.704921	0.873546
H	3.899771	-0.046593	0.263021

0 imaginary frequencies

E = -536.404174

G = -536.271018

TS-S2

C	3.014196	-0.579618	0.180569
C	1.956864	-1.203375	0.825595
C	0.696890	-1.257350	0.245787
O	0.472246	-0.732163	-1.026999
C	0.068150	0.351073	-0.246237
C	-1.377365	0.458932	0.106351
O	-1.839846	1.363786	0.753672
C	0.938952	1.410585	0.004519
C	2.240653	1.378794	-0.459974
O	-2.093909	-0.560551	-0.369294
C	-3.491414	-0.526635	-0.062517
H	3.933889	-0.405522	0.728742
H	2.009527	-1.442922	1.882532
H	-0.123955	-1.835827	0.654862
H	0.617779	2.126681	0.752308
H	2.416405	0.986272	-1.449879
H	2.934732	2.143046	-0.128162

H	3.131925	-0.744611	-0.879500
H	-3.913894	-1.417847	-0.519681
H	-3.645871	-0.541629	1.016895
H	-3.950019	0.369340	-0.481705

1 imaginary frequency
E = -536.368034
G = -536.232343

S3

C	-3.847677	1.721366	-0.508057
C	-2.963798	0.942747	0.106234
C	-2.777709	-0.477558	-0.256723
O	-2.459707	-1.383671	0.789322
C	-1.460005	-1.165460	-0.196048
C	-0.236906	-0.470860	0.240561
C	0.943506	-0.652490	-0.348506
H	-3.483686	-0.868833	-0.986157
H	-1.312949	-1.996196	-0.881861
H	-2.344124	1.332039	0.908093
H	-4.481660	1.339563	-1.302649
H	-3.964127	2.764277	-0.238661
H	-0.314236	0.217007	1.078015
H	1.078868	-1.340002	-1.175979
C	2.135623	0.093385	0.117071
O	3.214446	-0.228176	-0.608320
O	2.158357	0.886652	1.024085
C	4.427014	0.437277	-0.245259
H	5.186180	0.060492	-0.926184
H	4.317432	1.516417	-0.357638
H	4.693248	0.206354	0.786703

0 imaginary frequencies
E = -536.409677
G = -536.276615

TS-S3

C	0.649791	1.586697	0.080610
C	1.820001	1.316561	0.778301
C	2.758299	0.427595	0.276419
O	2.595499	-0.151498	-0.981073
C	2.106161	-1.177704	-0.164334
C	0.751877	-1.303706	0.077104
C	-0.153913	-0.371590	-0.423830
H	-0.134870	2.150535	0.574877
H	1.919199	1.582525	1.825274
H	3.723977	0.265797	0.742812
H	0.440452	-1.994673	0.853540
H	-0.048830	-0.043677	-1.446222
C	-1.536721	-0.384452	0.106442
H	0.712057	1.727690	-0.988074
H	2.831272	-1.931589	0.119839
O	-2.367261	0.317173	-0.680621
O	-1.892052	-0.921487	1.126722
C	-3.720996	0.404559	-0.231803
H	-4.243663	0.995869	-0.979855
H	-4.165161	-0.588685	-0.157193
H	-3.770918	0.894943	0.741316

1 imaginary frequency
E = -536.372612
G = -536.237323

S4

C	-0.349493	-1.402828	-0.350912
C	-1.404156	-0.519379	-0.722674
C	-0.872493	0.741363	-0.785825
N	0.462108	0.668044	-0.456992
C	0.787600	-0.653791	-0.186089
C	-2.807681	-0.889497	-1.006031
O	-3.683773	0.171461	-1.333165
C	-3.936497	-0.526195	-0.112856
C	-3.745823	0.222723	1.144386
C	-4.558171	0.080956	2.186464
C	1.234584	1.831961	-0.241494
O	2.108437	1.641929	0.727851
C	3.092330	2.673684	0.880387
C	2.176807	-1.137516	-0.093336
O	2.219038	-2.345800	0.479423
C	3.510331	-2.960777	0.518996
H	-4.813307	-1.168713	-0.146794
O	1.049708	2.847716	-0.848043
O	3.145019	-0.566453	-0.525764
H	-2.939426	-1.784878	-1.609641
H	-2.898134	0.900022	1.186188
H	-5.412906	-0.587738	2.150732
H	-4.394039	0.625643	3.108716
H	-0.398626	-2.477442	-0.262621
H	-1.330918	1.691894	-1.006995
H	3.739417	2.340953	1.687324
H	3.661938	2.781169	-0.042810
H	2.613518	3.618045	1.137787
H	3.909730	-3.076610	-0.489144
H	3.358693	-3.932814	0.981872
H	4.197851	-2.360892	1.115816

0 imaginary frequencies
E = -895.838181
G = -895.641295

TS-S4

C	-0.423224	-1.430573	-0.764095
C	0.610285	-0.666224	-0.313353
N	0.174232	0.653845	-0.174511
C	-1.215868	0.713808	-0.435416
C	-1.579196	-0.596234	-0.890545
C	1.868542	-1.159883	0.281758
O	2.255367	-2.299658	-0.303489
C	3.399816	-2.929683	0.279947
C	0.928773	1.820475	-0.153003
O	0.447152	2.899788	0.077769
C	-2.900519	-1.052391	-0.903430
O	-3.953894	-0.154162	-0.735410
C	-3.777666	-0.730249	0.535198
H	-4.437717	-1.559554	0.762716
O	2.200024	1.589755	-0.452117
C	3.076354	2.713586	-0.312743
C	-3.042748	-0.054190	1.508471
C	-2.344329	1.104997	1.158809
O	2.443251	-0.651175	1.208224
H	-3.160968	-2.028881	-1.297056
H	-2.820843	-0.598812	2.420008
H	-2.894106	1.833339	0.575375
H	-1.666241	1.540602	1.885472
H	-1.538527	1.614235	-0.935975
H	-0.385513	-2.502062	-0.892908
H	4.067102	2.341404	-0.559685
H	2.785241	3.508731	-0.998963

H	3.054832	3.082771	0.712725
H	3.559942	-3.837759	-0.296055
H	4.270556	-2.277153	0.209956
H	3.210094	-3.170808	1.326575

l imaginary frequency
E = -895.794053
G = -895.594946

S5

C	1.963019	-0.596259	0.345425
C	1.080108	-1.613513	0.604713
C	0.197260	-1.715585	-0.508756
C	0.580590	-0.766813	-1.420129
N	1.654080	-0.079804	-0.904157
C	-0.908437	-2.683453	-0.672468
C	-2.344526	-2.298574	-0.620673
C	-2.761923	-0.907311	-0.388614
C	-3.892137	-0.592099	0.241046
C	2.155914	1.087680	-1.527437
O	2.169506	1.225440	-2.716374
C	3.217425	-0.288768	1.055458
O	4.220075	0.141260	0.545577
O	-1.676158	-2.571025	-1.851286
O	2.532664	1.972249	-0.626141
C	3.236669	3.112038	-1.138151
O	3.119908	-0.617781	2.347908
C	4.323939	-0.481158	3.108970
H	-3.050614	-3.067392	-0.318263
H	-0.683074	-3.705658	-0.376455
H	-2.104593	-0.116148	-0.738110
H	-4.586747	-1.343600	0.599364
C	-4.244522	0.827714	0.477908
H	1.102280	-2.242987	1.481222
H	0.166263	-0.497738	-2.378623
H	3.495679	3.706990	-0.266635
H	4.137516	2.787254	-1.659017
H	2.596035	3.679246	-1.812885
H	5.103684	-1.129317	2.707148
H	4.066256	-0.779357	4.122170
H	4.668128	0.553146	3.093903
O	-5.421126	0.930474	1.109440
O	-3.579174	1.779226	0.155704
C	-5.853669	2.262611	1.397927
H	-6.810438	2.159730	1.903905
H	-5.133056	2.763351	2.045394
H	-5.969691	2.833316	0.476064

0 imaginary frequencies
E = -1123.705521
G = -1123.470765

TS-S5

C	-0.593226	-1.922343	-0.935607
C	0.741357	-2.123943	-0.446300
C	1.315577	-0.907736	-0.262072
N	0.417202	0.088329	-0.659010
C	-0.817322	-0.502440	-1.007153
C	2.537492	-0.628940	0.525151
O	2.727572	0.349592	1.195339
C	0.694459	1.407351	-1.000708
O	1.994620	1.609555	-1.150715
C	2.393413	2.977742	-1.289996
C	-1.604012	-2.867099	-0.845772
O	-2.934135	-2.519018	-1.030892
C	-2.849108	-2.477430	0.371306

C	-2.614782	-1.274529	1.004350
C	-2.376452	-0.129803	0.225320
O	3.390549	-1.657855	0.441464
C	4.556357	-1.552960	1.264367
O	-0.170147	2.228065	-1.170818
H	-3.144294	-3.385008	0.883717
H	-1.388302	-3.929170	-0.796061
H	-2.410753	-1.277489	2.069313
H	-3.031642	0.005253	-0.626263
C	-2.012665	1.125735	0.934641
H	-1.331273	-0.028158	-1.830615
H	1.180849	-3.066262	-0.156200
H	3.478206	2.958036	-1.355329
H	1.963890	3.409555	-2.193833
H	2.078785	3.549182	-0.416384
H	5.132045	-2.455946	1.076345
H	5.135790	-0.670164	0.993065
H	4.275114	-1.493561	2.316451
O	-2.656675	2.180718	0.430237
O	-1.227942	1.187236	1.847958
C	-2.260420	3.449348	0.952383
H	-2.854637	4.188102	0.419710
H	-2.460481	3.502522	2.023325
H	-1.198469	3.610734	0.765768

l imaginary frequency
E = -1123.661095
G = -1123.422724

S6

C	2.889641	-0.452334	0.212933
C	1.916434	0.257419	-0.688704
O	2.610909	-0.900856	-1.094442
H	2.283583	1.175171	-1.142566
C	4.212703	0.247915	0.410442
O	4.697895	0.443761	1.493790
O	4.747373	0.653892	-0.736568
C	5.984097	1.368433	-0.623744
H	6.274392	1.613571	-1.642007
H	5.844671	2.276494	-0.036437
H	6.740835	0.741788	-0.151798
C	2.460379	-1.302569	1.348767
H	2.607779	-0.873391	2.333566
C	1.948685	-2.516202	1.187436
H	1.836921	-2.953063	0.201216
H	1.646965	-3.110785	2.041523
C	0.456066	0.161545	-0.525663
C	-0.319084	-0.953306	-0.713712
N	-1.627599	-0.616482	-0.465960
C	-1.692493	0.725924	-0.119364
C	-0.416712	1.226409	-0.157962
H	-0.151903	2.259400	0.009532
H	-0.055639	-1.964078	-0.978064
C	-2.643138	-1.598901	-0.385030
O	-2.647950	-2.575870	-1.076722
O	-3.504942	-1.302831	0.567402
C	-4.695513	-2.102760	0.589995
H	-5.301062	-1.696224	1.395259
H	-5.218932	-2.012475	-0.362055
H	-4.447069	-3.145620	0.785037
C	-2.959300	1.476858	-0.080379
O	-3.985004	1.134123	-0.610888
O	-2.806839	2.634980	0.570044
C	-3.954063	3.490718	0.572418

H	-4.246107	3.739017	-0.448389
H	-3.651144	4.386073	1.109316
H	-4.787851	3.007012	1.082072

0 imaginary frequencies
E = -1123.699590
G = -1123.465526

TS-S6

C	-1.485581	0.661497	-0.408799
N	-1.481415	-0.723834	-0.224734
C	-0.206985	-1.230504	-0.542599
C	0.531551	-0.124112	-1.071044
C	-0.292520	1.043161	-0.938919
C	-2.567110	-1.584134	-0.079562
O	-3.710621	-0.971566	-0.347601
C	-4.894997	-1.718513	-0.045704
C	1.918064	-0.116850	-1.190859
O	2.651492	-1.275773	-0.965181
C	2.747931	-0.647376	0.282521
C	1.881423	-1.009499	1.314151
C	0.859020	-1.917737	1.057491
C	-2.488352	1.543973	0.226073
O	-3.126124	1.265303	1.206807
C	3.944647	0.202658	0.545422
O	4.750231	0.283748	-0.514086
C	5.918291	1.092779	-0.338730
O	4.148839	0.758938	1.593878
O	-2.439559	-2.742820	0.217974
O	-2.541481	2.727298	-0.392796
C	-3.391987	3.701255	0.221851
H	2.460471	0.707731	-1.640157
H	1.902983	-0.396912	2.207734
H	1.118258	-2.781339	0.458330
H	0.118871	-2.104610	1.827904
H	-0.200471	-2.214725	-0.984284
H	5.639152	2.121114	-0.106972
H	6.535976	0.694420	0.466480
H	6.452149	1.045878	-1.284439
H	0.008155	2.065199	-1.114454
H	-5.723667	-1.063948	-0.302525
H	-4.931162	-2.631829	-0.639139
H	-4.922127	-1.963157	1.016346
H	-3.308354	4.594239	-0.392157
H	-4.422880	3.347242	0.240571
H	-3.060048	3.906924	1.240176

1 imaginary frequency
E = -1123.658304
G = -1123.421192

Complete citation for Gaussian 09

Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford CT, 2009.

