# Supporting Information for:

# "Synergic Asymmetric Organocatalysis (SAOc) of *Cinchona* Alkaloids and Secondary Amines in the Synthesis of Bicyclo[2.2.2]octan-2-ones"

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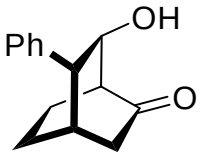
**General methods.** The $^{1}$H NMR and $^{13}$C NMR spectra were recorded at 200 MHz and 50 MHz respectively. The chemical shifts are reported in ppm downfield to TMS ($\delta = 0$) for $^{1}$H NMR and for $^{13}$C NMR relative to the central $CDCl_3$ resonance ($\delta = 77.5$). Flash chromatography (FC) was carried out using Merck silica gel 60 (230-400 mesh). The enantiomeric excess (*ee*) of the products was determined by HPLC (CHIRALPAK IC) and using a refractive index detector VARIAN RI 4.
**Materials.** Analytical grade solvents were used as received. All commercially available reagents were used as received. Compounds **1a, 1b, 2, I** and *cinchona* alkaloid catalysts **Q**, **QD** are commercially available and were used as received.
Aldehydes **1c-f** were prepared by DMP oxidation of the corresponding alcohols or by DIBAl-H reduction of the corresponding α-aryl acetonitriles. Catalyst **II** was a generous gift by Dr. Deborah A. Longbottom and Prof. Steven V. Ley. Compound **V** has been prepared according to standard literature procedure. [Abrunhosa, L. Delain-Bioton, A. C. Gaumont, M. Gulea, D. Masson and C. Serge *Tetrahedron* 2004, **60,** 9263. M. W. Paixao and J. A. Sehnem, *Tetrahedron: Asymmetry* 2006, **17,** 2793].

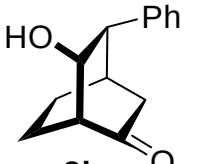
**General procedure for the preparation of bicyclo[2.2.2]octan-2-ones 3-8a-b:**

A mixture of **2** (0.5 mmol) and aldehyde **1a-f** was added to a suspension of catalyst **I**, **II** or **V** and *cinchona* alkaloid in the solvent (1mL). The reaction was stirred at rt or 30 °C for 1-3 days for catalyst **I** and up to 14 days for catalyst **V**. Water/ethyl acetate workup and FC afforded pure **3-8a** and **3-4b** as colorless crystalline solids.



**3a**

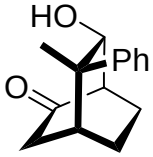
**3a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 88:12); flow rate 0.9 mL/min; $\tau_{major} = 24.8$ min; $\tau_{minor} = 29.5$ min.
**$^{1}$H NMR** δ ($CDCl_3$): 7.5-7.2 (m, 5H), 4.46 (dd, 1H, J = 3.4 Hz, J = 4.6 Hz), 3.0-2.9 (m, 1H), 2.57 (dd, 1H, J = 3.0 Hz, J = 6.0 Hz) 2.5-2.1 (m, 4H), 2.0-1.6 (m, 3H) 1.5-1.3 (m, 1H).
**$^{13}$C NMR** ($CDCl_3$): 207.0, 142.8, 129.2, 128.1, 127.1, 75.0, 53.5, 52.0, 46.0, 34.9, 20.7, 18.7.
$[\alpha]^{rt}_{D} = +9$ (sample with 87% *ee,* prepared as in table 1, entry 20); (c = 0.012 g/ 1 mL, *i*-PropOH)
**HRMS** calc. $C_{14}H_{16}NaO_2^+$: 239.1048; found: 239.1035.



**3b**

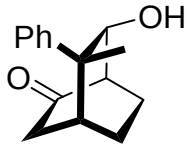
**3b:** (higher, less polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 88:12); flow rate 0.9 mL/min; $\tau_{major} = 9.85$ min; $\tau_{minor} = 10.00$ min.
**$^{1}$H NMR** δ ($CDCl_3$): 7.4-7.1 (m, 5H), 4.38 (dd, 1H, J = 3. Hz, J = 4. Hz), 3.0-2.8 (m, 1H), 2.55 (dd, 1H, J = 2.6 Hz, J = 5.2 Hz) 2.4-2.1 (m, 4H), 2.1-1.9 (m, 2H) 1.8-1.6 (m, 2H).
**$^{13}$C NMR** ($CDCl_3$): 216.6, 143.2, 129.2, 128.0, 127.1, 71.9, 53.3, 52.3, 39.8, 35.1, 27.2, 16.1.

$[\alpha]^{rt}_D$ = +14 (sample with 76% ee, prepared using L-proline); (c = 0.033 g/ 1 mL, *i*-PrOH)
**HRMS** calc. $C_{14}H_{16}NaO_2^+$: 239.1048; found: 239.1035.



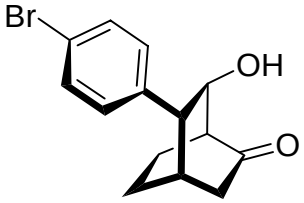
**4a**

**4a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 90:10); flow rate 0.9 mL/min; $\tau_{major}$ = 16.70 min; $\tau_{minor}$ = 20.90 min.
**$^1$H NMR** δ ($CDCl_3$): 7.4-7.0 (m, 5H), 4.5-4.4 (m, 1H), 2.7-2.5 (m, 2H), 2.4-2.2 (m, 3H) 1.7-1.4 (m, 4H), 1.10 (s, 3H).
$[\alpha]^{rt}_D$ = +4 (sample with 44% ee, prepared as in table 1, entry 6); (c = 0.013 g/ 1 mL, *i*-PrOH).
**HRMS** calc. $C_{15}H_{18}NaO_2^+$: 253.1204; found: 253.0067.



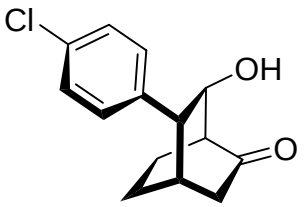
**4b**

**4b:** (higher, less polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 90:10); flow rate 0.9 mL/min; $\tau_{major}$ = 11.90 min; $\tau_{minor}$ = 13.20 min.
**$^1$H NMR** δ ($CDCl_3$): 7.5-7.1 (m, 5H), 4.5-4.4 (m,1H), 2.8-2.6 (m, 1H), 2.5-2.4 (m, 1H) 2.4-2.0 (m, 3H), 1.8-1.5 (m, 4H), 1.41 (s, 3H).
$[\alpha]^{rt}_D$ = +10 (sample with 33% ee, prepared as in table 1, entry 6); (c = 0.013 g/ 1 mL, *i*-PrOH).
**HRMS** calc. $C_{15}H_{18}NaO_2^+$: 253,1204; found: 253,1198.
**$^{13}$C NMR** of the mixture of the two diasteroisomers ($CDCl_3$): 216.8, 216.6, 151.0, 150.0, 129.0, 128.8, 126.4, 126.3, 126.3, 125.9, 79.0, 72.8, 53.6, 52.9, 46.3, 44.8, 43.4, 41.5, 37.0, 36.5, 26.2, 25.7, 22.2, 21.7, 21.0, 15.8.



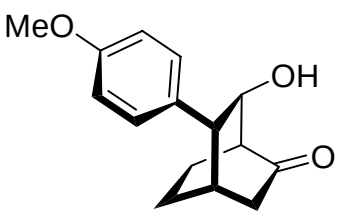
**5a**

**5a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 89:11); flow rate 0.9 mL/min; $\tau_{major}$ = 23.45 min; $\tau_{minor}$ = 29.90 min.
**$^1$H NMR** δ ($CDCl_3$): 7.49 (d, 2H, J=8.4 Hz), 7.15 (d, 2H, J=8.6 Hz), 4.37 (m,1H), 2.9-2.8 (m, 1H), 2.6-2.5 (m, 1H), 2.5-2.2 (m, 3H), 2.0-1.4 (m, 4H), 1.3-1.2 (s, 1H).
**$^{13}$C NMR** ($CDCl_3$): 214.9, 159.5 141.7, 132.2, 129.7, 75.5, 52.9, 52.0, 46.0, 34.6, 20.7, 18.8.
$[\alpha]^{rt}_D$ = +1 (sample with 90%ee, prepared as in table 2, entry 1) (c= 0.006 g/ 1 mL, *i*-PrOH).
**HRMS** calc. $C_{14}H_{15}BrNaO_2^+$: 317.0153; found: 317.0065.



**6a**

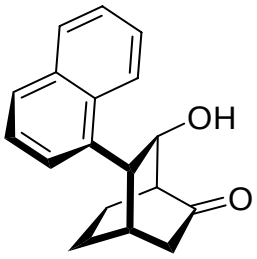
**6a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK IC column (hexane/*i*-PrOH 89:11); flow rate 0.9 mL/min; $\tau_{major}$ = 23.15 min; $\tau_{minor}$ = 29.00 min.
**$^1$H NMR** δ ($CDCl_3$): 7.4-7.2 (m, 4H), 4.38 (dd, 1H, J = 4.4 Hz, J = 3.4 Hz), 2.9-2.8 (m, 1H), 2.6-2.5 (dd, 1H, J = 2.8 Hz, J = 5.8 Hz ), 2.5-2.3 (m, 3H), 2.0-1.4 (m, 5H) .
**$^{13}$C NMR** ($CDCl_3$): 215.5, 141.2, 132.7, 129.3, 129.0, 74.8, 52.5, 51.8, 45.8, 34.6, 20.5, 18.5.
$[\alpha]^{rt}_D$ = +16 (sample with 40% *ee*, from screening tests); (c= 0.007 g/ 1 mL, *i*-PrOH)
**HRMS** calc. $C_{14}H_{15}ClNaO_2^+$: 273,0658; found: 273,0665.



**7a**

**7a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 89:11); flow rate 0.9 mL/min; $\tau_{major}$ = 44.2 min; $\tau_{minor}$ = 56.2 min.

**$^1$H NMR** δ ($CDCl_3$): 7.25 (d, 2H, J = 8.4 Hz), 6.90 (d, 2H, J = 8.8 Hz), 4.39 (dd,1H, J = 3.2 Hz, J = 4.6 Hz), 3.81 (s, 3H), 2.86 (m, 1H), 2.6-2.5 (m, 1H), 2.5-2.2 (m, 3H), 2.0-1.3 (m, 5H).
**$^{13}$C NMR** ($CDCl_3$): 214.3, 134.7, 129.0, 114.7, 112.7, 75.6, 55.9, 53.0, 52.2, 35.1, 20.9, 18.8.
$[\alpha]^{rt}_D$ = +7 (sample with 82% *ee*, prepared as in table 2, entry 3); (c= 0.009 g/ 1 mL, *i*-PrOH).
**HRMS** calc. $C_{15}H_{18}NaO_3^+$: 269.1154; found: 269.1061.

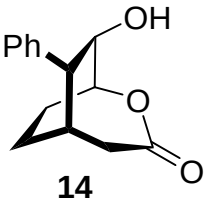


**8a**

**8a:** (lower, more polar diastereoisomer) The *ee* was determined by HPLC using CHIRALPAK column (hexane/*i*-PrOH 89:11); flow rate 0.9 mL/min; $\tau_{minor}$ = 20.7 min; $\tau_{major}$ = 24.9 min.
**$^1$H NMR** δ ($CDCl_3$): 8.1-7.3 (m, 7H), 4.9-4.7 (m,1H), 3.8-3.7 (m, 1H), 2.7-2.6 (m, 2H), 2.5-1.2 (m, 7H).
**$^{13}$C NMR** ($CDCl_3$):208.3, 137.7, 134.8, 132.5, 129.7, 128.1, 126.9, 126.3, 125.5, 123.5, 121.4, 73.6, 52.0, 49.5, 45.7, 34.9, 20.7, 19.0.
$[\alpha]^{rt}_D$ = +19 (sample with 82% *ee,* prepared as in table 2, entry 3) (c= 0.008 g/ 1 mL, *i*-PrOH).
**HRMS** calc. $C_{18}H_{18}NaO_2^+$: 289.1204; found: 289.1128.

**Procedure for the synthesis of 14 from 3a.**

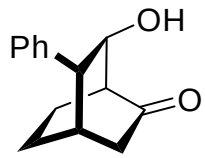
Compound **3a** (200 mg, racemate) was dissolved in $CH_2Cl_2$ (5 mL), the solution cooled at 4 °C and 3-chloroperbenzoic acid (4 eq.) was added portionwise. After 2 h a TLC check showed that no starting material was left. The reaction mixture was diluted with EtOAc (20 mL), washed with saturated sodium thiosulphate solution (5 mL) and brine (5 mL). Flash Chromatograpy (petrol ether: ethyl acetate 1:1) afforded pure **14** in 81% yield.



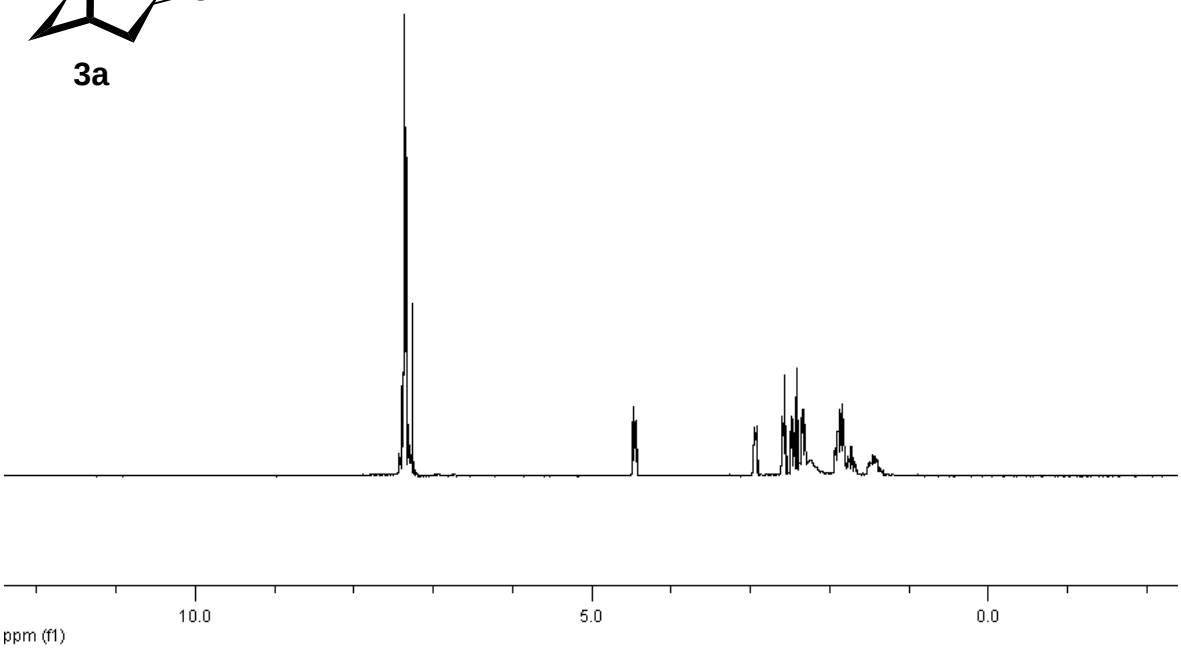
**14**

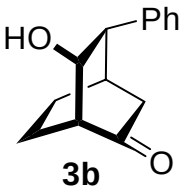
**$^1$H NMR** δ ($CDCl_3$): 7.5-7.2 (m, 5H), 5.1-5.3 (m,1H), 3.73 (ddd, 1H, J = 2.2 Hz, J = 5.4 Hz, J = 11.6 Hz), 3.6-3.5 (m, 1H), 3.1-2.9 (m, 1H), 2.8-2.6 (m, 2H), 2.1-1.8 (m, 3H), 1.8-1.4 (m, 2H).
**$^{13}$C NMR** ($CDCl_3$): 172.0, 136.9, 129.2, 127.1, 126.8, 82.2, 67.3, 41.8, 38.0, 27.7, 25.8, 25.4.
**HRMS** calc. $C_{14}H_{16}NaO_3^+$: 255.0997; found: 255.1017.

# Copies of $^{1}$H NMR Spectra

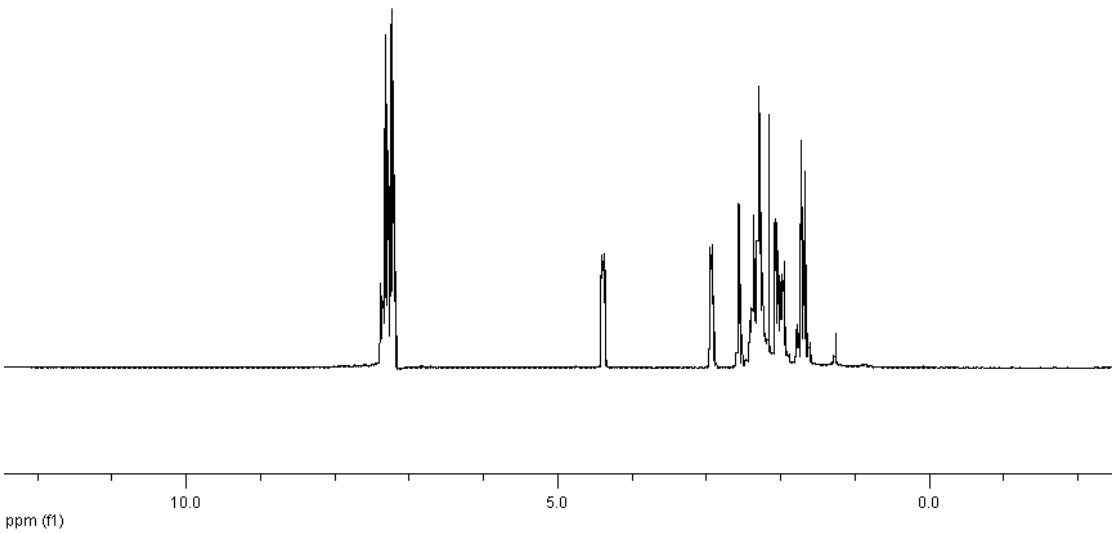


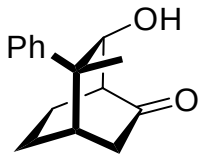

**3a**



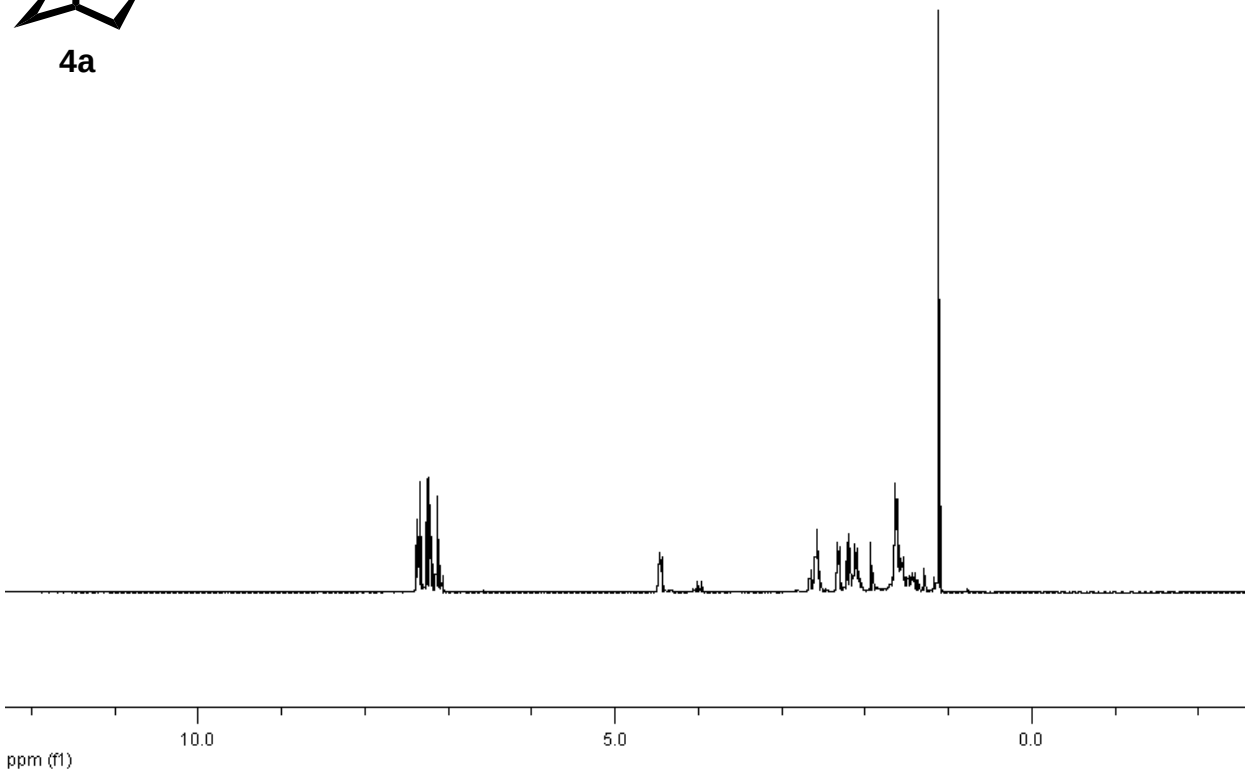



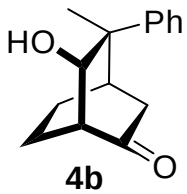

**3b**



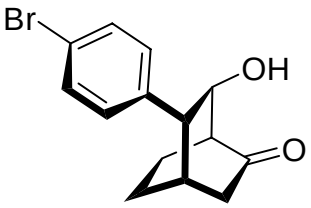



**4a**

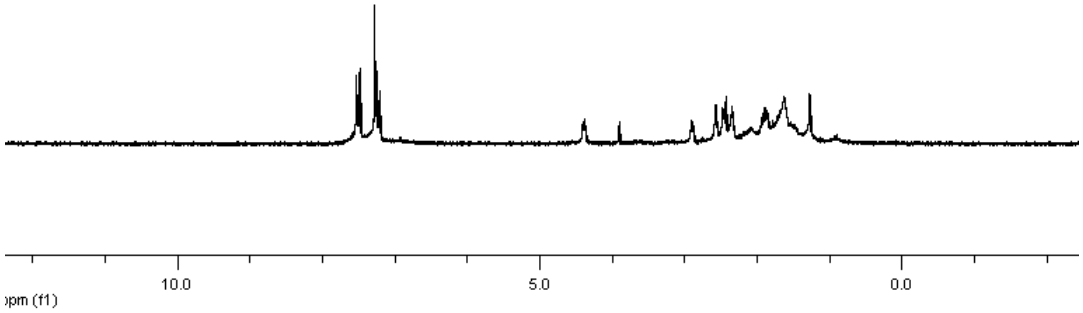


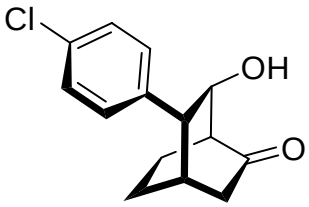




**4b**

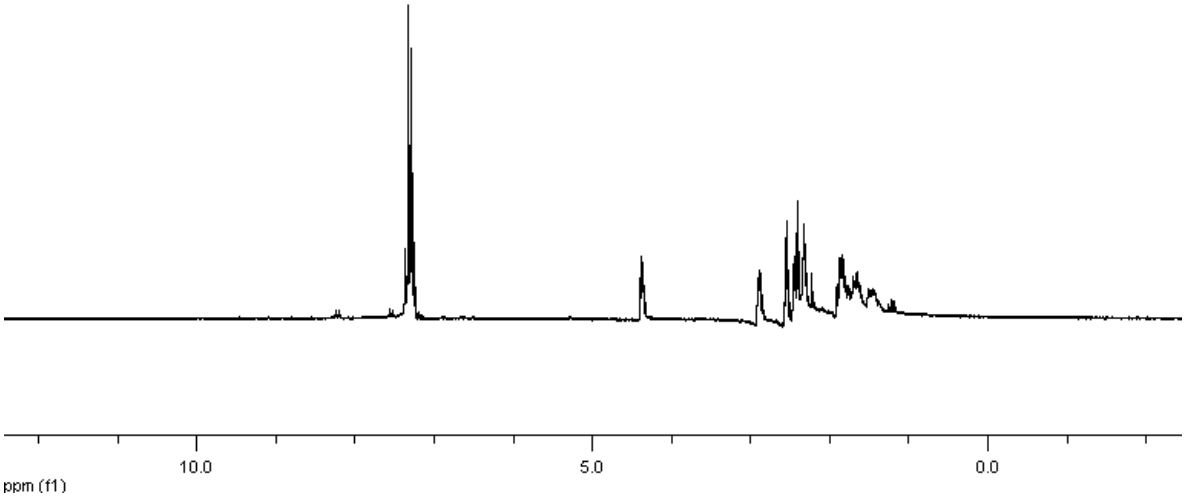


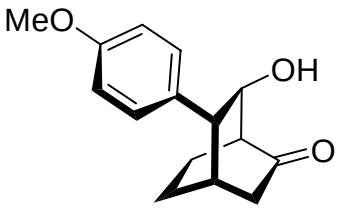

**5a**



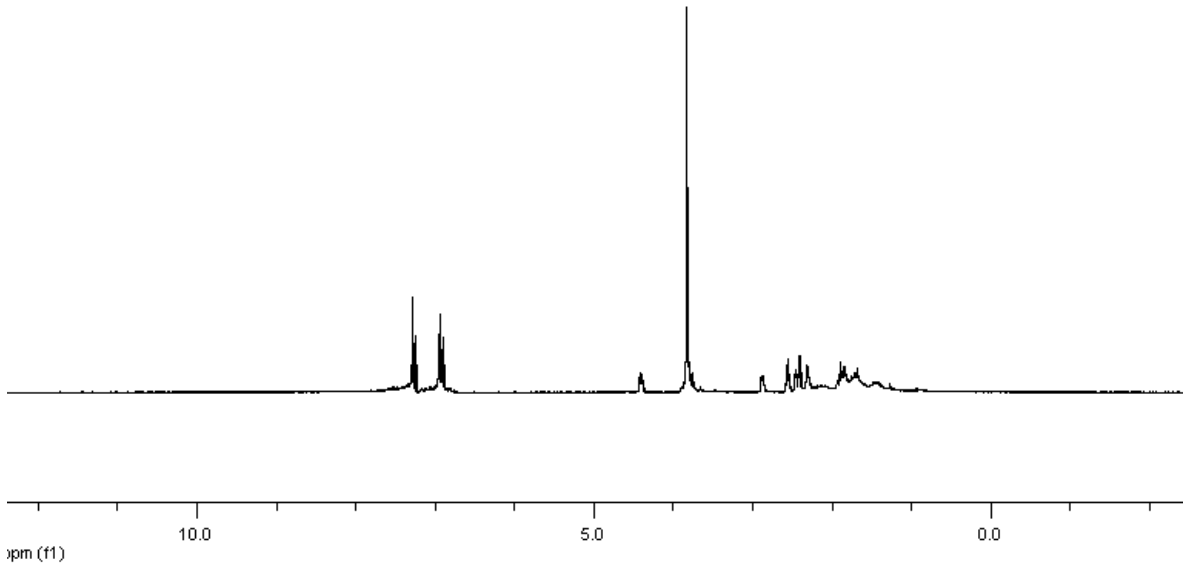



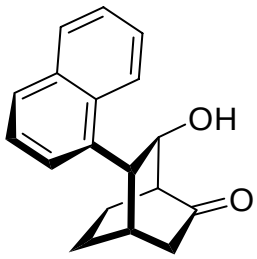

**6a**



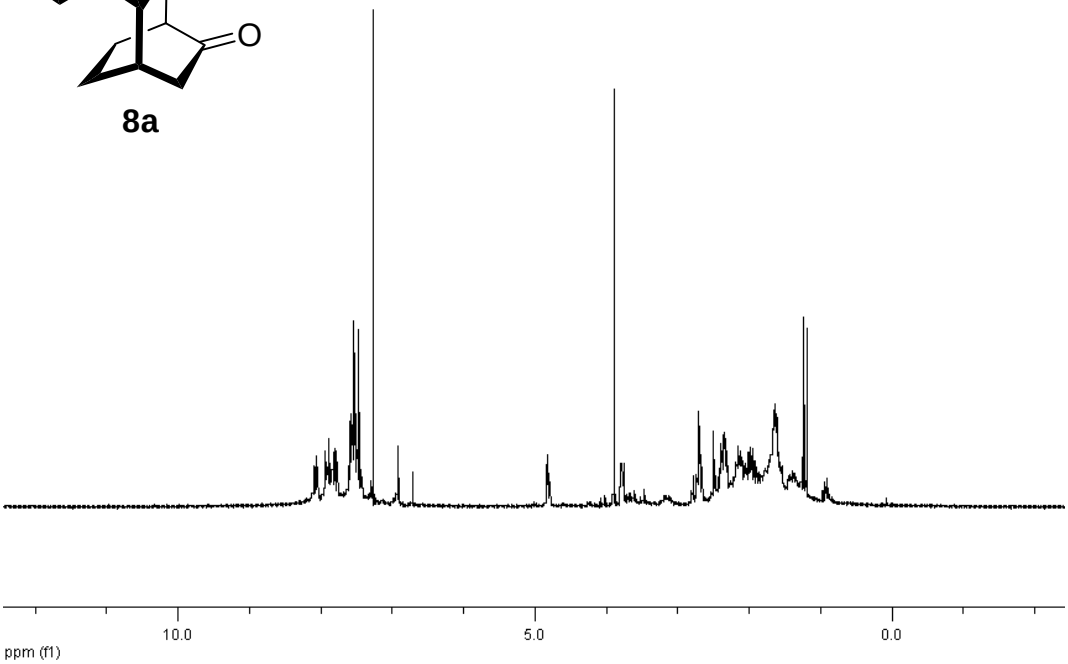


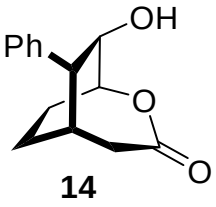

**7a**



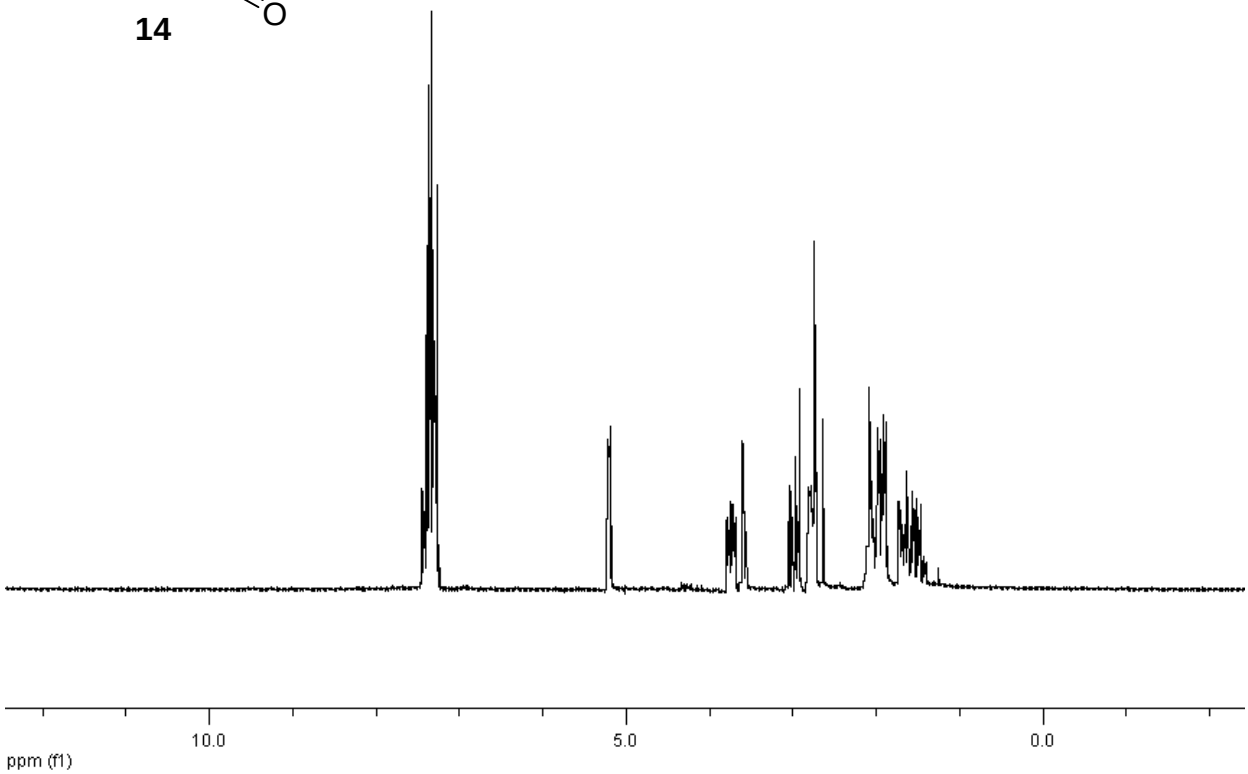



**8a**




**14**



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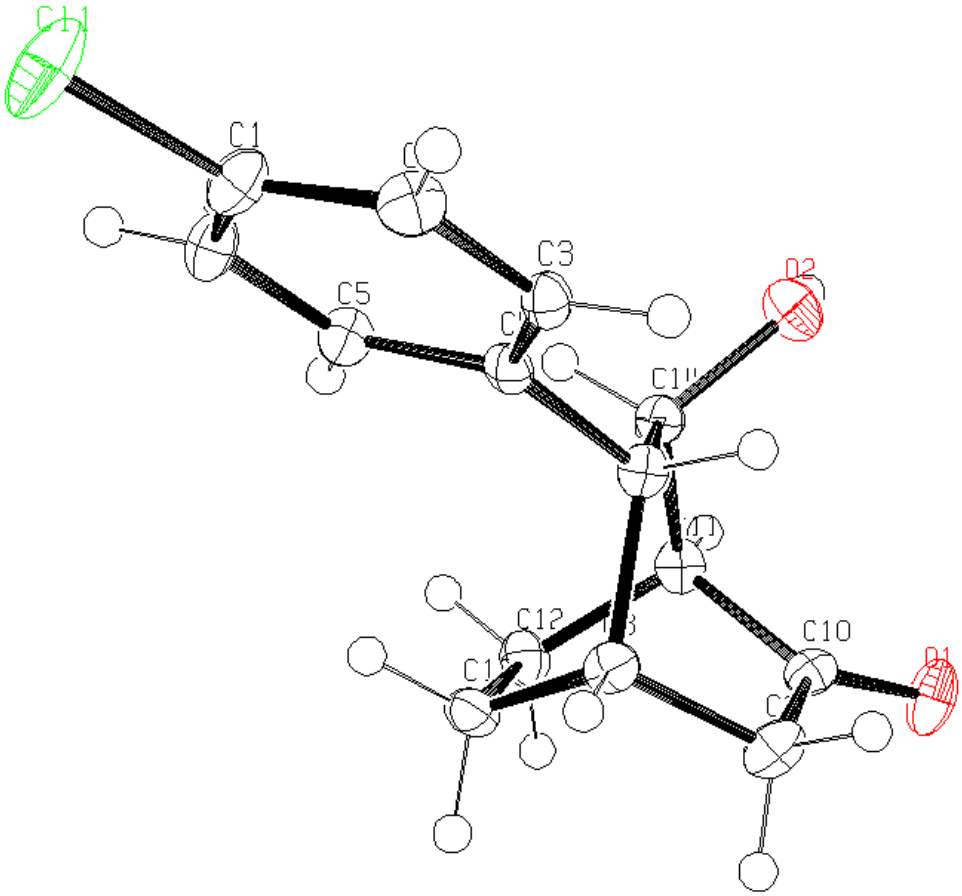


CCDC 701756 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033