Supplementary Material (ESI) for Chemical Communications

Supporting Information

Stoichiometric and Catalytic Reductive Aldol Cyclizations of Alkynediones Induced by Stryker's Reagent

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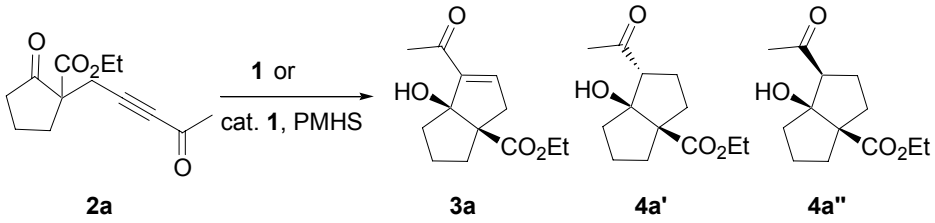
Contents:

General Experimental. Toluene was freshly distilled from CaH_2 under argon. Tetrahydrofuran (THF) was distilled from Na/Ph_2CO ketyl under argon. Prior to use in reactions, dry solvents were degassed by bubbling argon into the solvent for 30 minutes. $[Ph_3PCuH]_6$ **1** was synthesized.[1] All glassware and syringes used in the experiments were oven-dried at 120°C for at least 4 hours. Syringes were cooled in a dessicator. Over-dried glassware were assembled hot and allowed to cool under a stream of dry argon. Solvents and reagents in solution were transferred with syringes and cannulae using standard inert atmosphere techniques. Infrared spectra were recorded on a Bio-Rad FT-IR spectrometer as a solution in CH_2Cl_2 (DCM), from 4000 cm^{-1} to 400 cm^{-1}. Band intensities and features are designated as follows: s=strong, m=medium, w=weak, br=broad, sh=shoulder. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX 300, AV 400, DRX 500, or AV 600 spectrometers, operating at 300 MHz, 400 MHz, 500 MHz, or 600 MHz respectively for ^1H, and at 75 MHz, 100 MHz, 125 MHz, or 150 MHz respectively for ^{13}C. All spectra were calibrated at δ 7.26 or δ 0.00 ppm for ^1H spectra (residual $CHCl_3$ or TMS respectively), and δ 77.03 or δ 0.00 ppm for ^{13}C spectra. Spectral features are designated as follows: m=multiplet, q=quartet, t=triplet, d=doublet, s=singlet and br=broad. Low and high resolution mass spectra were recorded on a Finnigan MAT90 mass spectrometer. For each sample, high resolution mass spectral data was obtained for the molecular ion, or next largest fragment thereof. X-ray crystallographic analyses were obtained on a MAR Imaging Plate diffractometer.

Table 1, entry 1.1:



General experimental procedure A: Reductions using stoichiometric 1.

Reagent **1** (56 mg, 0.171 mmol) was transferred into an oven-dried 5 mL round-bottomed flask in a dry-box. The flask was capped with a septum, then removed from the dry-box. Anhydrous and degassed toluene (1 mL) was added and the solution was cooled to –40°C. Substrate **2a** (27.2 mg, 0.115 mmol) in 1 mL anhydrous and degassed toluene was added via cannula. The progress of the reaction was followed by TLC. After 15 min, the reaction was quenched by adding 1 mL saturated aqueous NH_4Cl and stirred for a further 2 hr, open to air. The resulting mixture was filtered through a silica gel pad and the pad was washed with EtOAc (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography (0 to 20% EtOAc in hexane) of the residue gave **3a** (14.8 mg, 54%) and mixture of **4a'** to **4a''** was 9:1 (3.56 mg, 13% overall isolated yield) as a colorless

[1] P. Chiu, Z. Li and C. M. Fung, *Tetrahedron Lett.* **2003**, *44*, 455.

oil.

Table 1, entry 1.2:

General experimental procedure B: Reductions using catalytic 1.

Reagent **1** (3.7 mg, 0.011 mmol) was transferred into an oven-dried 5 mL round-bottomed flask in a dry-box. The flask was capped with a septum, then removed from the dry-box. Anhydrous and degassed toluene (1 mL) was added and the solution was cooled to –40°C. To the solution was added PMHS (0.013 mL, 0.217 mmol), followed by substrate **2a** (25.0 mg, 0.106 mmol) in toluene (1 mL). The progress of the reaction was monitored by TLC. After 30 minutes, the reaction was quenched by adding 1 mL saturated aqueous NH_4Cl and stirring for further 2 hr, open to air. The resulting mixture was filtered through a silica gel pad and washed with EtOAc (10 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (5 mL x 2). The combined organic extracts were dried over $MgSO_4$ and concentrated. Flash chromatography (0 to 20% EtOAc in hexane) of the residue gave **3a** (14.7 mg, 58%), **4a'**(9.8 mg, 28%) and **4a"** (3.9 mg, 11%).

3a: R_f (40% EtOAc in hexane): 0.25; IR (DCM): 3547br (OH), 3063m, 2965m, 2920m, 2890m, 2875m, 1722s (ester C=O),[2] 1660s (enone C=O)[3], 1630m, 1370m, 1189s, 1141m, 1077m, 1029m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.80 (t, J = 2.7 Hz, 1H), 4.18 (m, 2H), 3.46 (dd, J = 20.0, 2.8 Hz, 1H), 3.36 (s, 1H), 2.57 (ddd, J = 6.3, 3.7, 2.8 Hz, 1H), 2.34 (s, 3H), 2.29 (dd, J = 20.0, 2.6 Hz, 1H), 2.22-2.10 (m, 1H), 2.01-1.96 (m, 1H), 1.93-1.88 (m, 1H), 1.65-1.60 (m, 1H), 1.43-1.40 (m, 1H), 1.27 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.1, 170.1, 145.3, 144.9, 94.1, 61.6, 61.1, 43.0, 40.8, 37.8, 27.4, 24.6, 14.2 ppm; LRMS (20 eV) *m/z* 238 [M^+, 13], 196 (5), 165 (92), 147 (13); HRMS (EI): Calculated for $C_{13}H_{18}O_4$ [M^+]: 238.1203. Found: 238.1205.

Determination of stereochemistry: The ester carbonyl stretch at significantly lower frequency (1722 cm^{-1}) which did not change upon high dilution indicates intramolecular hydrogen bonding with the hydroxyl group, which is possible only in the *cis*-fused diastereoisomer. Catalytic hydrogenation converted **3a** to **4a'**: and **4a"**, thus all three compounds have the same stereochemistry at the ring fusion.

4a': R_f (30% EtOAc in hexane): 0.34; IR (DCM): 3568br (OH), 2966m, 2879m, 1727sh (ester C=O),[2] 1702s (ketone C=O),[4] 1368m, 1203m, 1129m, 1021m, 942w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.20 (q, J = 7.1Hz, 2H), 3.53 (s, br, 1H), 3.07 (dd, J = 11.7, 7.0 Hz, 1H), 2.39 (m, 1H), 2.27 (s, 3H), 2.24-2.16 (m, 1H), 1.96-1.84 (m, 2H), 1.82-1.70 (m, 2H), 1.69-1.60 (m, 5H), 1.39-1.33 (m,

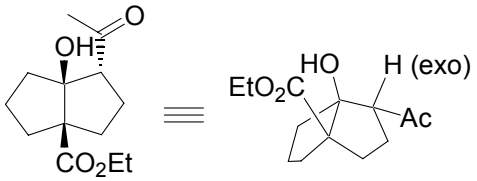
[2] For the series of compounds **3a-c**, **4a**, the ester C=O stretch is at significantly lower frequencies (<1723 cm^{-1}, with no change in frequency observed upon dilution), due to intramolecular hydrogen bonding in addition to angle deformation/steric strain for the ester at a quaternary or angular position

[3] For the series of compounds **3a-f,** the enone C=O stretch is at lower frequencies (<1660 cm^{-1}), due to intramolecular hydrogen bonding

[4] For compounds **4a**, **4d** and **4e**, the ketone C=O stretch is at lower frequencies (<1708 cm^{-1}, with no change in frequency observed upon dilution) due to intramolecular hydrogen bonding

1H), 1.30 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.9, 176.6, 92.1, 62.7, 62.6, 61.1, 36.9, 36.8, 34.0, 30.5, 24.5, 23.7, 14.2 ppm; LRMS (20 eV): *m/z* 240 [M^+, 1], 222 (12), 195 (7), 157 (100); HRMS (EI): Calculated for $C_{13}H_{20}O_4$ [M^+]: 240.1365. Found: 240.1362.

Determination of stereochemistry: The ester carbonyl stretch at significantly lower frequency (1702 cm^{-1}) which did not change upon high dilution indicates intramolecular hydrogen bonding with the hydroxyl group, which is possible only in the *cis*-fused ring system. The methine proton alpha to the acetyl group (δ_H 3.05 ppm) does not show any noe with the protons of the adjacent ring, indicating that the proton is *exo*, and the acetyl group must be anti with respect to the hydroxyl group (ref **4a"**).



4a": R_f (30% EtOAc in hexane): 0.39; IR (DCM): 3558br (OH), 2965s, 2931s, 2876m, 1708br (ester and ketone C=O),[5] 1365s, 1180m, 1132s, 909s cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.19 (q, J = 7.1 Hz, 2H), 3.72 (s, br, 1H), 2.74 (dd, J = 11.7, 7.0 Hz, 1H), 2.50 (dd, J = 13.1, 6.9, 2.8 Hz, 1H), 2.25 (s, 3H), 2.37-2.15 (m, 2H), 1.93-1.70 (m, 3H), 1.68-1.61 (m, 3H), 1.38 (ddd, J = 13.2, 11.2, 6.5 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.4, 176.7, 93.0, 62.7, 61.4, 61.0, 41.3, 36.6, 35.4, 30.9, 27.8, 22.9, 14.2 ppm; LRMS (20 eV): *m/z* 240 [M^+, 1], 220 (12), 157 (100), 129 (10); HRMS (EI): Calculated for $C_{13}H_{20}O_4$ [M^+]: 240.1358. Found: 240.1362.

Determination of stereochemistry: The ester carbonyl stretch at significantly lower frequency (1708 cm^{-1}) which did not change upon high dilution indicates intramolecular hydrogen bonding with the hydroxyl group, which is possible only in the *cis*-fused ring system. The methine proton alpha to the acetyl group showed noe with at least four protons in the adjacent ring (δ_H 2.74 ppm ↔ δ_H 1.38, 1.58, 1.83, 2.27) indicates that the proton is *endo*, hence the acetyl group must be syn with respect to the hydroxyl group (ref **4a'**).

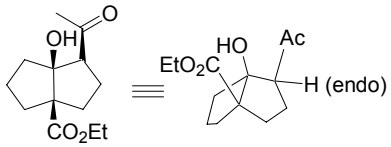
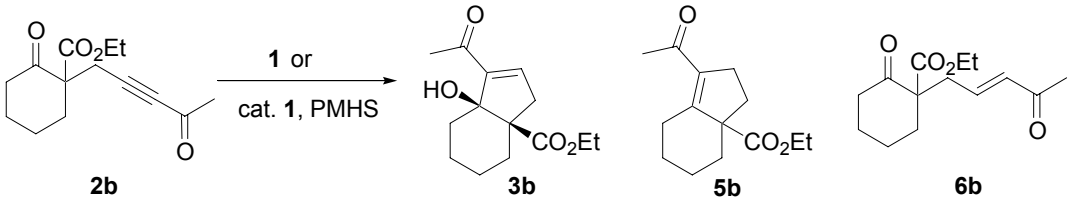


Table 1, entries 2.1, 2.2, 2.3:



[5] In the IR spectrum of **4a"**, the absorption at 1708 cm^{-1} is very broad and probably contains both the ester and ketone carbonyl absorptions whose frequencies are decreased by strong hydrogen bonding.

According to general procedure A, **2b** (49.9 mg, 0.200 mmol) was treated with **1** (97.9 mg, 0.300 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography (10-25% EtOAc in hexane), **3b** (24.2 mg, 48%) was obtained as white solid, and **5b** (7.55 mg, 16%) was obtained as a colorless oil.

According to general procedure A, reduction of **2b** (47.7 mg) at room temperature gave **3b** (26.8 mg, 60%) and **5b** (10.4 mg, 23%).

According to general procedure B, **2b** (35.2 mg, 0.141 mmol) was treated with **1** (4.6 mg, 0.014 mmol) and PMHS (0.02 mL, 3.33 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography, **3b** (19.9 mg, 56%) and **6b** (5.7 mg, 16%) were obtained.

3b: R_f (30% EtOAc in hexane): 0.22; mp = 66-68 °C; IR (DCM): 3574br (OH), 3064, 3064w, 2940m, 2860m, 1718s (ester C=O),[2] 1672s (enone C=O), 1613s, 1450m, 1370s, 1035m cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.83 (t, *J* = 2.7 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.12 (dd, *J* = 18.4, 2.3 Hz, 1H), 2.97 (s, br, 1H), 2.52 (dt, *J* = 13.4, 4.1 Hz, 1H), 2.32 (s, 3H), 2.28 (dd, *J* = 18.4, 3.1 Hz, 1H), 2.07 (dm, *J* = 13.8 Hz, 1H), 1.92 (ddd, *J* = 13.1, 12.5, 3.8 Hz, 1H), 1.73- 1.61 (m, 2H), 1.32-1.58 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.03-1.10 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.2, 174.6, 146.1, 83.7, 60.7, 55.9, 40.5, 34.6, 32.5, 27.7, 22.4, 21.6, 14.2 ppm; LRMS (20 eV) *m/z* 234 [M^+-H_2O, 8], 161 (16), 153 (100), 136 (77), 105 (47); HRMS (EI): Calculated for $C_{14}H_{20}O_3$ [M^+]: 234.1256. Found: 234.1255.

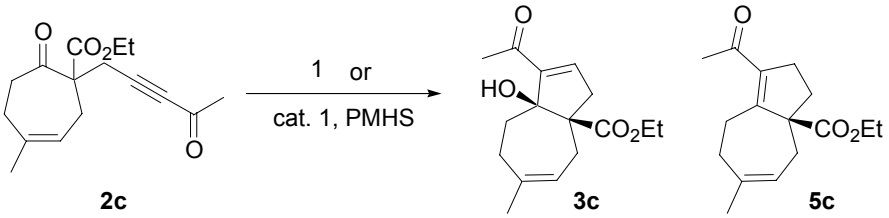
Structure determination: The structure and stereochemistry was unambiguously determined by crystallographic analysis. Crystals were obtained from a hexane and ethyl acetate solution. ***Crystal data***: [C_{14} H_{20} O_4] ; *M* = 252.30, Triclinic, *a* = 7.3680(15) Å, *b* = 9.1860(18) Å, *c* = 10.640(2) Å, V = 683.7(2) $Å^3$, T = 301 K, space group P $\bar{1}$, Z = 2, μ(Mo-Kα) = 0.089 mm^{-1}, 3246 reflections measured, 1933 unique (R_{int} = 0.0234) which were used in all calculations. R1= 0.0743 (all data). The final *wR*2 was 0.1917 (all data).

5b: R_f (25% EtOAc in hexane): 0.60; ^1H NMR (300 MHz, $CDCl_3$): δ 4.16 (q, *J* = 7.1 Hz, 2H), 3.40 (br, d, *J* = 14.2 Hz, 1H), 2.67 (m, 2H) 2.52 (dm, *J* = 12.5 Hz, 1H), 2.27 (s, 3H), 2.21 (m, 1H), 2.04 (m, 1H), 1.85 (m, 1H), 1.66 (m, 3H), 1.31 (m, 2H), 1.25 (t, *J* = 5.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 198.9, 175.1, 155.2, 60.8, 60.4, 38.4, 35.6, 32.2, 30.7, 29.7, 26.9, 23.5, 14.3 ppm. The spectra features were identical to previously obtained data.[6]

6b: R_f (25% EtOAc in hexane): 0.30; ^1H NMR (300 MHz, $CDCl_3$): δ 6.74 (m, 1H), 6.02 (dm, *J* = 16.0 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.73 (qd, *J* = 7.0, 1.4 Hz, 1H), 2.47 (m, 4H), 2.22 (s, 3H), 2.04 (m, 1H), 1.76 (m, 3H), 1.47 (td, *J* = 13.3, 4.6 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz NMR, $CDCl_3$): δ 206.7, 198.0, 170.1, 142.8, 133.9, 61.3, 60.5, 40.7, 37.7, 36.2, 27.2, 26.4, 22.2, 13.9 ppm. The spectra features were identical to previously obtained data.[2]

Table 1, entries 3.1-2:

[6] C. P. Szeto, M. Phil. Dissertation, The University of Hong Kong, Hong Kong, 2000.



2c **3c** **5c**

According to general procedure A, **2c** (32.6 mg, 0.118 mmol) was treated with **1** (57.8 mg, 0.177 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography (10-25% EtOAc in hexane), **3c** (15.7 mg, 48%) and **5c** (4.9 mg, 16%) were obtained as colorless oils.

According to general procedure B, **2c** (32.2 mg, 0.117 mmol) was treated with **1** (4.0 mg, 0.012 mmol) and PMHS (0.014 mL, 0.233 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography, **3c** (21.1 mg, 60%) and **5c** (1.8 mg, 6%) were obtained as colorless oils.

3c: R_f (30% EtOAc in hexane): 0.30; IR (DCM): 3692br (OH), 3055m, 2998s, 1722s (ester C=O),[2] 1656s (enone C=O),[3], 1551m, 1376m, 1197m, 1179m, 1097m, 1030w cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.98 (t, *J* = 2.7 Hz, 1H), 5.17 (m, 1H), 4.13 (qd, *J* = 7.1, 2.0 Hz, 2H), 3.72 (s, br, 1H), 3.07 (d, *J* = 13.5 Hz, 1H), 3.01 (dd, *J* = 19.4, 3.1 Hz, 1H), 2.67 (dd, *J* = 19.4, 2.4 Hz, 1H), 2.54 (m, 1H), 2.32 (s, 3H), 2.17-2.12 (m, 3H), 1.75 (m, 1H), 1.58 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.7, 174.4, 147.4, 143.7, 139.0, 119.3, 88.3, 61.5, 60.7, 39.4, 34.4, 31.4, 29.9, 27.2, 25.3, 14.1 ppm; LRMS (20 eV) *m/z* 278 [M^+, 1], 260 (30), 214 (15), 187 (100), 171 (17), 143 (24); HRMS (EI): Calculated for $C_{16}H_{22}O_4$ [M^+]: 278.1518. Found: 278.1516.

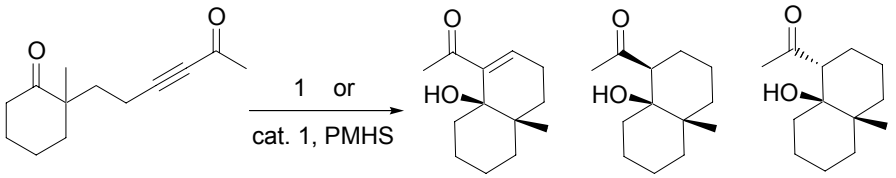
Structure determination: The structure was unambiguously determined by crystallographic analysis of its dinitrophenylhydrazone derivative. The **3c-2,4-DNP** derivative was synthesized from **3c** as follows. To a solution of the **3c** (31.4 mg, 0.113 mmol) in ethanol (0.75 mL) was added 2,4-dinitrophenylhydrazine (38.6 mg, 0.195 mmol) and 3N HCl (3 drops). The mixture was allowed to stir at room temperature overnight. Solvent was removed *in vacuo*. Ether (3mL) was added followed by 10% $NaHCO_3$ (1.5 mL). The aqueous layer was extracted by ether (3 x 3 mL) and dried over Na_2SO_4. Flash chromatography (10-25% EtOAc in hexane) of the residue gave **3c-2,4-DNP** (37.2 mg, 72%).

3c-2,4-DNP: R_f (30% EtOAc in hexane): 0.38; mp = 128°C, IR (DCM): 3691w (OH), 2959m, 2931m, 1723s (ester C=O),[2], 1618m, 1595m, 1337s, 1313w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 11.22 (s, 1H), 9.15 (d, *J* = 2.6 Hz, 1H), 8.31 (dd, *J* = 9.5, 2.6 Hz, 1H), 7.70 (d, *J* = 9.5 Hz, 1H), 6.61 (t, *J* = 2.9 Hz, 1H), 5.23 (d, *J* = 5.9 Hz, 1H), 4.37 (s, br, 1H), 4.23-4.11 (m, 2H), 3.16 (d, *J* = 16.9 Hz, 1H), 3.00 (dd, *J* = 19.0, 3.3 Hz, 1H), 2.75 (dd, *J* = 19.0, 2.6 Hz, 1H), 2.65 (d, br, *J* = 14.1 Hz, 1H), 2.41 (ddd, *J* = 14.1, 6.4, 2.8 Hz, 1H), 2.31 (s, 3H), 2.22 (d, *J* = 1.4 Hz, 1H), 1.62 (s, 2H), 1.56 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.8, 150.7, 144.3, 140.9, 139.8, 139.1, 138.4, 130.4, 130.0, 129.5, 123.6, 119.8, 115.9, 89.4, 62.1, 60.7, 39.4, 34.8, 31.5, 29.6, 25.4, 14.2, 13.8 ppm; LRMS (20eV): *m/z* 458 [M^+, 29], 440 (36), 423 (100), 405 (42), 367 (27), 331 (55), 316 (24), 274 (29), 258 (37), 212 (21); HRMS (EI): Calculated for $C_{22}H_{26}N_4O_7$ [M^+]: 458.1800 Found: 458.1801. Orange crystals were obtained from a hexane and ethyl acetate solution. ***Crystal data***: [$C_{22}H_{26}N_4O_7$] ;

M= 458.47, Triclinic, *a* = 7.460(2) Å, *b* = 8.609(2) Å, *c* = 18.302(4) Å, V = 1140.9(4) Å^3, T = 301 K, space group P $\bar{1}$, Z = 2, μ(Mo-Kα) = 0.101 mm^{-1}, 5057 reflections measured, 3078 unique (R_{int} = 0.0194) which were used in all calculations. R1= 0.0767 (all data). The final *wR*2 was 0.1912 (all data).

5c: R_f (20% EtOAc in hexane): 0.50; ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.42 (td, *J* = 5.8, 1.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.28 (m, 1H), 2.73-2.57 (m, 3H), 2.36-2.12 (m, 5H), 2.25 (s, 3H), 1.79 (m, 1H), 1.70 (s, 3H). 1.26 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ199.2, 174.9, 157.5, 140.8, 136.9, 120.6, 62.8, 62.8, 60.7, 35.2, 34.9, 32.2, 31.7, 30.5, 26.2, 25.9, 14.2 ppm. The spectra features were identical to previously obtained data.[7,8]

Table 1, entry 4:



According to general procedure A, **2d** (42.9 mg, 0.208 mmol) was treated with **1** (10.2 mg, 3.12 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography (10-25% EtOAc in hexane), **3d** (22.1 mg, 51%), **4d'** (5.7 mg, 13%) and **4d"** (1.3 mg, 3%) were obtained as colorless oils.

According to general procedure B, **2d** (21.7 mg, 0.105 mmol) was treated with **1** (4.0 mg, 0.012 mmol) and PMHS (0.012 mL, 0.200 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography, **3d** (12.2 mg, 56%), **4d'** (3.5 mg, 16%) and **4d"** (2.0 mg, 9%) were obtained as colorless oils.

3d: R_f (20% EtOAc in hexane): 0.55; IR (DCM): 3481br (OH), 3051w, 2936s, 2930sh, 2866m, 1648s (enone C=O),[3] cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.86 (t, *J* = 3.8 Hz, 1H), 4.45 (s, 1H), 2.41 (m, 1H), 2.31 (s, 3H), 2.42-2.17 (m, 1H), 2.03-2.14 (m, 1H), 1.94 (d, *J* = 13.6 Hz, 1H), 1.87-1.62 (m, 2H), 1.57 (dd, *J* = 13.7, 3.4 Hz, 1H), 1.47 (m, 3H), 1.23 (d, *J* = 14.5 Hz, 1H), 1.18 (m, 1H), 0.94 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7, 143.4, 143.1, 74.3, 36.1, 35.8, 35.6, 29.5, 26.8, 24.0, 22.3, 21.4, 21.2 ppm; LRMS (20 eV): *m/z* 208 [M$^+$, 100], 190 (85), 175 (41), 152 (13); HRMS (EI): Calculated for $C_{13}H_{20}O_2$ [M$^+$]: 208.1463. Found: 208.1461.

Determination of stereochemistry: Catalytic hydrogenation converts **3d** to **4d'**and **4d"**. Thus all three compounds have the same stereochemistry at the fused rings. From the analysis of the nmr data of **4d'**and **4d"**, the ring fusion was determined to be *cis* (vide infra).

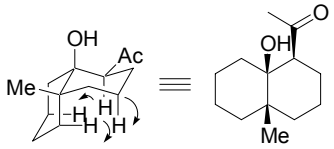
4d': R_f (30% EtOAc in hexane): 0.74; IR (DCM): 3477br (OH), 2938s, 2868sh, 1693s (ketone C=O),[4] 1450w, 1401w, 1363m, 1330m, 1188m, 1175m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08 (s, 1H), 3.23 (dd, *J* = 12.6, 3.5 Hz, 1H), 2.22 (s, 3H), 1.90-1.74 (m, 4H), 1.71-1.60 (m, 2H), 1.51-1.50 (m, 4H), 1.39-1.25 (m, 2H), 1.09-1. 02 (m, 2H), 0.99 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 216.8,

[7] P. Chiu, B. Chen and K. F. Cheng, *Tetrahedron Lett.* **1998**, *39*, 9229.

[8] B. Chen, Ph. D. Dissertation. The University of Hong Kong, Hong Kong, 2001.

73.7, 49.9, 37.4, 35.8, 33.8, 33.2, 31.8, 25.8, 24.0, 21.8, 21.3, 21.0 ppm; LRMS (20 eV): *m/z* 210 [M^+, 1], 192 (44), 177 (70), 154 (74), 149 (94), 134 (44), 112 (100); HRMS (EI): Calculated for $C_{13}H_{22}O_2$ [M^+]: 210.1620. Found: 210.1621.

Determination of stereochemistry: The only stereoisomer with a conformer that would have noe correlations of the axial methine proton alpha to the acetyl group (δ_H 3.23 ppm, J = 12.6, 3.5 Hz ↔ δ_H 1.38, 1.73 ppm) with protons of the adjacent ring and no noe with the angular methyl group is the one with all *syn* stereochemistry as shown



4d": R_f (30% EtOAc in hexane): 0.28; IR (DCM): 3617m, 3482br (OH), 2935s, 2868m, 1701s (ketone C=O),[4] 1683s, 1450m, 1362m cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.95 (s, br, 1H), 2.77 (dd, J = 12.2, 3.9 Hz, 1H), 2.20 (s, 3H), 1.97-1.89 (m, 1H), 1.88-1.80 (m, 2H), 1.72-1.68 (m, 2H), 1.65-1.43 (m, 6H), 1.33 (dm, J = 13.7 Hz, 1H), 1.11 (dm, J = 13.7, 1H), 1.05 (dm, J = 13.7 Hz, 1H), 1.00 (s, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 215.0, 75.3, 55.0, 38.0, 36.4, 33.1, 31.5, 28.4, 26.4, 22.5, 21.3, 20.9, 20.8 ppm; LRMS (20 eV): *m/z* 210 [M^+, 5], 192 (59), 177 (66), 149 (86), 112 (100); HRMS (EI): Calculated for $C_{13}H_{22}O_2$ [M^+]: 210.1617. Found: 210.1620.

Determination of stereochemistry: From the catalytic hydrogenation results, **4d"** must also have a *cis* ring fusion. The only other *cis* fused stereoisomer possible has the acetyl group *anti* to the hydroxyl group. This is confirmed by the observation of the noe correlation between the axial methine proton alpha to the acetyl group with the angular methyl group (δ_H 2.77, J = 12.2, 3.9 Hz ↔ δ 1.01) which shows that the relative stereochemistry of these groups is *syn*.

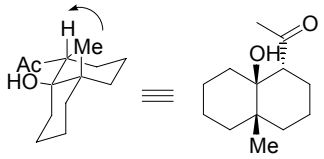
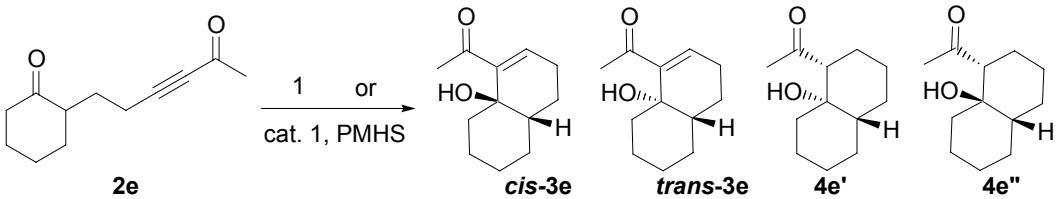


Table 1, entry 5:



According to general procedure A, **2e** (39.7 mg, 0.207 mmol) was treated with **1** (10.1 mg, 3.09 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography (10-25% EtOAc in hexane) ***cis*-3e** (19.7 mg, 49%), ***trans*-3e** (5.2 mg, 13%), **4e'** (4.5 mg, 11%) and **4e"** (1.2 mg, 3%) were obtained as colorless oils.

According to general procedure B, **2e** (26.8 mg, 0.140 mmol) was treated with **1** (5.0 mg, 0.015 mmol) and PMHS (0.017 mL, 0.283 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography, ***cis*-3e** (10.6 mg, 39%), ***trans*-3e** (3.0 mg, 14%), **4e'** (6.0 mg, 22%) and **4e"** (1.6 mg, 6%) were obtained as colorless oils.

***cis*-3e**: R_f (30% EtOAc in hexane): 0.54; IR (DCM): 3505br (OH), 3059w, 2940s, 2863m, 1650s (enone C=O),[3] 1226m, 1159m, 1024m, 957w, 561w cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 6.89 (t, J = 3.6, 3.6 Hz, 1H), 4.39 (s, 1H), 2.37-2.34 (m, 2H), 2.37-2.30 (m, 3H), 2.08-2.02 (m, 1H), 1.92 (d, J = 13.8 Hz, 1H), 1.88-1.78 (m, 2H), 1.77-1.71 (m, 1H), 1.62-1.56 (m, 2H), 1.47-1.45 (m, 1H), 1.41-1.34 (m, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.2, 144.3, 143.9, 72.2, 39.4, 34.0, 27.4, 26.7, 26.6, 24.3, 21.5, 21.0 ppm; LRMS (20 eV): *m/z* 194 [M^+, 50], 176 (52), 161 (18), 151 (100) 138 (40), 133 (14); HRMS (EI): Calculated for $C_{12}H_{18}O_2$ [M^+]: 194.1307. Found: 194.1362.
Determination of stereochemistry: Catalytic hydrogenation converts ***cis*-3e** into **4e"**. Thus these two compounds have the same stereochemistry at the ring fusion. The ring junction was deduced to be cis in ***cis*-3e** by the inference from the *cis* stereochemistry of **4e"** (vide infra)**.**

***trans*-3e**: R_f (30% EtOAc in hexane): 0.62; IR (DCM): 3540br (OH), 3055w, 2937s, 2861m, 1660s (enone C=O),[3] 1227m, 960s cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ 6.72 (m, 1H), 2.95 (s, 1H), 2.29 (s, 3H), 2.29-2.27 (m, 2H), 2.21 (d, J = 13.6 Hz, 1H), 1.83 (qt, J = 13.4, 4.1 Hz, 1H), 1.73 (dm, J = 10.7 Hz, 1H), 1.68 (dd, J = 12.6, 4.0 Hz, 1H), 1.63 (m, 1H), 1.53 (dm, J = 13.4 Hz, 1H), 1.24-1.38 (m, 4H), 1.10 (td, J = 13.4, 4.1 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ 202.7, 145.7, 141.0, 69.1, 43.9, 35.5, 27.5, 27.1, 27.1, 26.3, 23.9, 21.5 ppm; LRMS (20 eV): *m/z* 194 [M^+, 28], 176 (100), 161 (29), 151 (61), 138 (13); HRMS (EI): Calculated for $C_{12}H_{18}O_2$ [M^+]: 194.1307. Found: 194.1307.
Determination of stereochemistry: Catalytic hydrogenation converts ***trans*-3e** into **4e'**. Thus these two compounds have the same stereochemistry at the ring fusion. The ring junction was deduced to be *trans* in ***trans*-3e** by inference from the stereochemistry of **4e'** whose structure had been previously determined.[8]

4e': ^1H NMR (300 MHz, $CDCl_3$): δ 3.47 (d, J = 1.3 Hz, 1H), 2.43 (dd, J = 12.4, 3.7 Hz, 1H), 2.19 (s, 3H), 1.81-1.63 (m, 6H), 1.55-1.41 (m, 3H), 1.33 (dt, J = 13.1, 3.9 Hz, 1H), 1.26 (m, 3H), 1.18 (ddd, J = 16.3, 16.3, 3.8 Hz, 1H), 1.09 (ttd, J = 12.2, 3.5, 1.2 Hz, 1H) ppm. The spectra features were identical to previously obtained data.[9]

4e": R_f (40% EtOAc in hexane): 0.50; IR (DCM): 3684w, 3599br (OH), 3488w, 2936s, 2864m, 1702s (ketone C=O),[4] 1303m cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 3.05 (s, br, 1H), 2.42 (dd, J = 13.1, 3.7 Hz, 1H), 2.20 (s, 3H), 2.00 (dt, J = 13.2, 4.8 Hz, 1H), 1.88-1.79 (m, 2H), 1.73-1.51 (m, 6H), 1.48-1.34 (m, 5H), 1.26 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 214.1, 73.8, 61.0, 43.4, 31.4, 28.2, 27.1, 27.0, 26.5, 25.6, 21.3, 20.1 ppm; LRMS (20 eV): *m/z* 196 [M^+, 14], 178 (62), 135 (100), 120 (26), 111 (43), 98 (47); HRMS (EI): *m/z* calcd for $C_{12}H_{20}O_2$ [M^+]: 196.1455. Found: 196.1463.
Determination of stereochemistry: The ring fusion must be *cis* since no other *trans*-fused decalin

[9] P. Chiu, C. P. Szeto, Z. Geng and K. F. Cheng, *Org. Lett.* **2001,** 3, 1901.

isomer (other than **4e'**) would have the methine proton alpha to the acetyl group (δ_H 2.42, J = 13.1, 3.7 Hz) in the axial position. The noe correlation of this proton with the proton at the ring junction (δ_H 2.42 ↔ 1.58) is only possible when both protons are exo, thus the acetyl group must be *anti* with respect to the hydroxyl group.

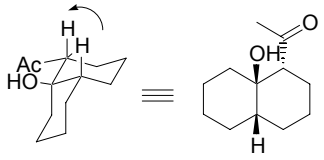
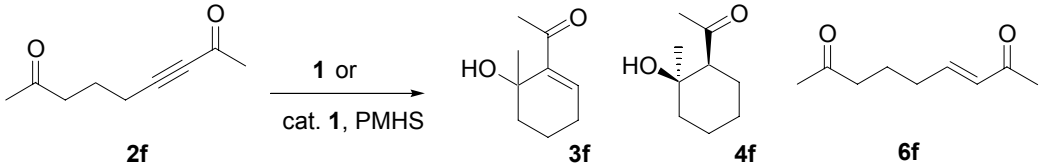


Table 1, entries 6.1-2:



According to general procedure A, **2f** (29.9 mg, 0.197 mmol) was treated with **1** (9.6 mg, 0.295 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography (15-25% EtOAc in hexane), **3f** (18.8 mg, 62%) and **4f** (4.0 mg, 13%) were obtained as colorless oils.

According to general procedure B, **2f** (32.0 mg, 0.211 mmol) was treated with **1** (6.9 mg, 0.021 mmol) and PMHS (0.025 mL, 0.421 mmol) in 1.5 mL anhydrous toluene. After workup and flash chromatography, **3f** (14.9 mg, 46%), and **6f** (7.8 mg, 24%) were obtained as colorless oils.

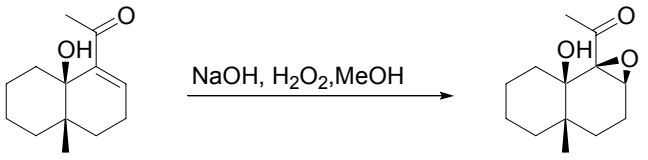
3f: R_f (30% EtOAc in hexane): 0.51; IR (DCM): 3503br (OH), 2946w, 2915sh, 1652s (enone C=O),[3] 1622sh, 1468m, 1388m, 1320m, 1220w, 897w cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.91 (t, J = 4.0 Hz, 1H), 4.52 (s, br, 1H), 2.31 (s, 3H), 2.29 (m, 2H), 1.83-1.71 (m, 3H), 1.65-1.56 (m, 1H), 1.43 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ 202.1, 143.6, 143.4, 70.1, 37.7, 28.6, 26.7, 26.4, 19.0 ppm; LRMS (20 eV): *m/z* 154 [M^+, 16], 125 (66), 97 (63), 83 (70); HRMS (EI): Calculated for $C_9H_{14}O_2$ [M^+]: 154.0996. Found: 154.0994.

4f: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.94 (d, J = 2.3 Hz, 1H), 2.46 (dd, J = 10.8, 5.1 Hz, 1H), 2.21 (s, 3H), 1.65-1.82 (m, 5H), 1.48 (dm, J = 11.0 Hz, 1H), 1.25 (m, 1H), 1.18 (m, 1H), 1.18 (s, 3H) ppm. The spectra features were identical to previously obtained data.[9]

6f: ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.66 (m, 1H), 5.96 (m, 1H), 2.37 (t, J = 7.2 Hz, 2H), 2.13 (m, 5H), 2.05 (s, 3H), 1.65 (qt, J = 7.2 Hz, 2H) ppm. The spectra features were identical to literature values.[10]

Epoxidation of 3d

[10] D. F. Cauble, J. D. Gipson and M. J. Krische, *J. Am. Chem. Soc*. **2003**, 125, 1110.s



3d **8**

To a solution of **3d** (0.011 g, 0.058 mmol) in MeOH (1 mL) was added 10% NaOH (0.013 mL, 0.032 mmol) and 50% H_2O_2 (0.01 mL, 0.347 mmol). The reaction was stirred at room temperature and diluted with ether. The organic phase was washed with water (3 x 1 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo*. The residue was purified by flash chromatography (10% EtOAc in hexane) to afford epoxide **8** (0.012g, 90%) as a white solid.

8: R_f (30% EtOAc in hexane): 0.61; IR (DCM):): 3463br (OH), 2971s, 2934m, 2869m, 1693s (ketone C=O),[11] 1360m cm^{-1}; 3463 (OH), 2971, 2934, 2869, 1693s (ketone C=O),[4] 1360 cm^{-1}; ^{1}H NMR (300 MHz): δ 3.61 (s, br, 1H), 3.22 (d, *J* = 2.3 Hz, 1H), 2.15 (s, 3H), 2.17-1.89 (m, 3H), 1.70 (ddd, *J* = 14.0, 4.8, 4.7 Hz, 1H), 1. 91-1. 36 (m, 6H), 1.28 (m, 1H), 1.16 (m, 1H), 0.92 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 210.8, 77.6, 72.8, 66.44, 57.6, 35.5, 35.3, 32.0, 27.8, 26.9, 22.2, 21.2, 21.0, 20.9 ppm; LRMS (20 eV): *m/z* 224 [M^+, 1], 112 (100); HRMS (EI): *m/z* calcd $C_{13}H_{20}O_3$ [M^+]: 224.1412 Found: 224.1412.

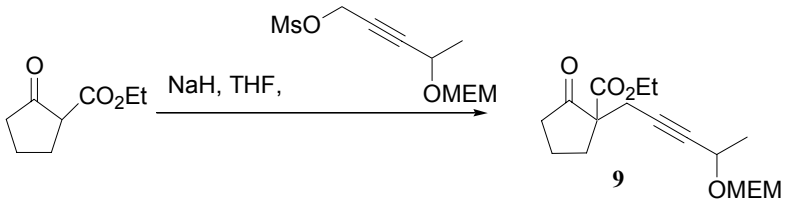
Determination of stereochemistry: Stereochemically, both due to possible directing effects of the hydroxyl group and the preference of the incoming reagent to approach from the exo face suggested that the epoxide is exo. This is confirmed by the considering the minimized conformations of both the epoxide isomers.[12] The minimized conformation of the epoxide with relative stereochemistry as shown in **8** has the methine proton of the epoxide and the vicinal methylene group with dihedral angles of 51º and 63º, which should have ^{3}J couplings in the order of 1-3 Hz. This is what is observed (δ_H 3.22, *J*= 2.3 Hz). The endo epoxide isomer has been calculated to have the corresponding methine proton of the epoxide and the vicinal methylene group with dihedral angles dihedral angles of 93º and 21º, which would be expected to have ^{3}J couplings in the order of 7 Hz.

Preparation of Alkynedione Substrates

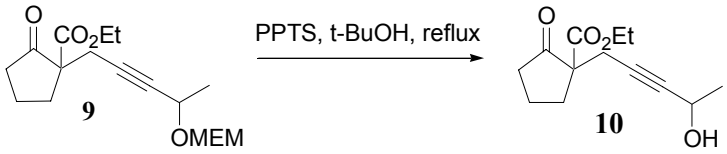
Preparation of alkynedione **2a**

[11] The ketone C=O stretch at significantly lower frequencies (1693 cm^{-1}) with no change observed in frequency upon dilution, is due to intramolecular hydrogen bonding in addition to angle deformation/steric strain for the ketone at very hindered position.

[12] The conformations of the epoxide isomers were optimized computationally by DFT calculations using the B3LYP/6-31G(d) model. We thank Ms. Lihong Hu and Dr. G. H. Chen of the Department of Chemistry, The University of Hong Kong for doing the calculations.



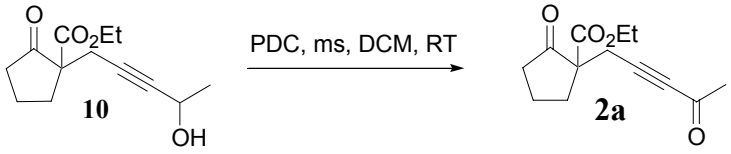
To a suspension of NaH (60% in oil, 0.158 g, 6.583 mmol, washed by pentane three times) in THF (10 mL) was added ethyl 2-oxocyclopentane carboxylate (0.42 mL, 2.843 mmol). The reaction was stirred at room temperature for 30 min and mesylate (1.060 g, 3.984 mmol) in THF (5 mL) was added. The reaction mixture was allowed to stir at room temperature overnight. The crude mixture was quenched by sat. NH_4Cl (20 mL) and extracted with ether (3 x 10mL). The combined organics were washed with brine (10 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography (10% EtOAc in hexane) to afford **9** (1.545 g, 72%) as a colourless oil. **9**: R_f (40% EtOAc in hexane): 0.58; IR (DCM): 2986m, 2932m, 2893m, 2250w (C≡C), 1753s (cyclopentanone C=O), 1727s (ester C=O),[13] 1449m, 1102s, 1031s cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.90 (d, J = 7.0 Hz, 1H), 4.65 (d, J = 7.0 Hz, 1H), 4.43 (q, J = 6.6 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 3.77-3.70 (m, 1H), 3.64-3.58 (m, 1H), 3.55-3.52 (m, 2H), 3.37 (s, 3H), 2.71 (dd, J = 3.5, 1.9 Hz, 2H), 2.51-2.41 (m, 2H), 2.29-2.22 (m, 2H), 2.11-1.19 (m, 2H), 1.38 (d, J = 6.7 Hz, 3H), 1.24 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.7, 170.4, 92.9, 82.1, 80.7, 71.7, 67.2, 61.7, 61.5, 59.0, 58.9, 38.4, 32.6, 23.4, 22.3, 19.8, 14.0 ppm; LRMS (20 eV): *m/z* 221 [M^+-OMEM, 221], 193 (46), 177 (18), 164 (25), 147 (44), 125 (17), 119 (6); HRMS (EI): *m/z* calcd for $C_{13}H_{17}O_3$ [M^+-OMEM]: 221.1175. Found: 221.1178.



A mixture of PPTS (0.058 g, 0.229 mmol) and **9** (0.619 g, 1.879 mmol) in t-BuOH (20 mL) was refluxed for 3 hr. The reaction mixture was cooled to room temperature and water (5 mL) was added. The reaction mixture was extracted by ether (3 x 30 mL), dried over $MgSO_4$ and evaporated *in vacuo.* The residue was purified by flash chromatography (20% EtOAc in hexane) to afford **10** (0.331 g, 74%) as a colourless oil. **10**: R_f (30% EtOAc in hexane): 0.22; IR (DCM): 3600br (OH), 2982m, 2936m, 2892m, 2877m, 1752s (cyclopentanone C=O), 1727s (ester C=O),[13] 1376w, 1326m, 1230m, 898w cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.42 (s, br, 1H), 4.12 (q, J = 7.1 Hz, 1H), 2.68 (d, J = 1.9 Hz, 2H), 2.48-2.40 (m, 2H), 2.29-2.20 (m, 2H), 2.09-1.98 (m, 2H), 1.35 (d, J = 6.6 Hz, 3H), 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 213.4, 170.5, 84.8, 79.6, 61.7, 58.9, 58.1, 38.3, 32.6, 24.5, 23.3, 19.7, 14.0 ppm; LRMS (20 eV): *m/z* 238 [M^+, 4], 220 (4), 164 (53), 147 (100); HRMS (EI):

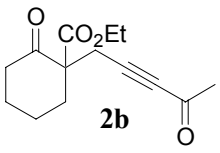
[13] The ester C=O stretch is at lower frequencies (<1727 cm^{-1}) due to angle deformation/steric strain for the ester at a quaternary or angular position.

m/z calcd for $C_{13}H_{18}O_4$ [M^+]: 238.1200. Found: 238.1205.

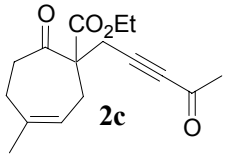


To a suspension of PDC (0.622 g, 1.653 mmol) and MS 4Å (1 g) in DCM (20 mL) was added **I-3** (0.197 g, 8.269 mmol) in DCM (5 mL) at 0°C. The reaction mixture was stirred at room temperature for 1.5 hr. The reaction mixture was diluted with ether (20 mL) and filtered through a celite pad (1 inch). The pad was washed with ether and the combined filtrate was concentrated *in vacuo*. The residue was purified by flash chromatography (20% EtOAc in hexane) to afford **2a** (0.1718 g, 88%) as a colourless oil. **2a**: R_f (30% EtOAc in hexane): 0.54; IR (DCM): 2982m, 2978m, 2890m, 2216m (C≡C), 1754s (cyclopentanone C=O), 1728s (ester C=O),[13] 1677s (ynone C=O), 1229s, 1152m, 1026m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (q, *J* = 7.1 Hz, 2H), 2.88 (d, *J* = 17.5 Hz, 1H), 2.78 (d, *J* = 17.5 Hz, 1H), 2.52-2.43 (m, 2H), 2.25 (s, 3H), 2.33-2.03 (m, 4H), 1.25 (t, *J* = 7.1 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.8, 184.0, 169.8, 88.6, 82.7, 61.9, 58.4, 37.9, 32.7, 32.6, 23.4, 19.7, 13.9 ppm; LRMS (20 eV): *m/z* 236 [M^+, 21], 221 (10), 207 (36), 190 (52), 179 (27), 163 (100), 147 (26), 135 (66), 121 (29); HRMS (EI): *m/z* calcd for $C_{13}H_{16}O_4$ [M^+]: 236.1051. Found: 236.1049.

Alkynediones **2b** and **2c** were synthesized by routes similar to the synthesis of **2a**, starting from ethyl 2-oxocyclohexanecarboxylate and ethyl 4-methyl-7-oxocyclohept-3-enecarboxylate[14] respectively.



2b: colourless oil. R_f (30%EtOAc in hexane): 0.29; IR (DCM): 2951m, 2870w, , 2215m (C≡C), 1721s (ester C=O),[13] 1712s (ketone C=O), 1678s (ynone C=O) 1440m, 1204m cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.22 (q, *J* = 7.1 Hz, 2H), 2.87 (d, *J* = 17.5 Hz, 1H), 2.70 (d, *J* = 17.5 Hz, 1H), 2.64 (dq, *J* = 13.5, 3.0 Hz, 1H), 2.50-2.40 (m, 2H), 2.28 (s, 3H), 2.07-1.98 (m, 1H), 1.80-1.75 (m, 2H), 1.68-1.52 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 205.3, 184.3, 170.0, 88.8, 83.5, 61.9, 59.8, 40.6, 35.6, 32.7, 27.2, 25.0, 22.2, 14.6 ppm; LRMS (20 eV) *m/z* 250 [M^+, 6], 221 (16), 204 (57), 177 (100), 162 (17), 141 (25), 133 (20), 113 (15); HRMS (EI): *m/z* calcd for $C_{14}H_{18}O_4$ [M^+]: 250.1205. Found: 250.1203.

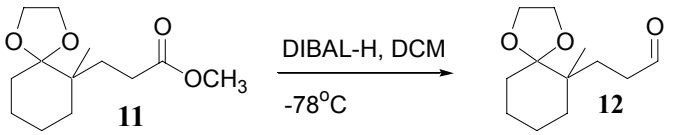


2c: colourless oil. R_f (30% EtOAc in hexane): 0.60; IR (DCM): 2979m, 2943m, 2214w (C≡C), 1736s (ester C=O), 1713s (ketone C=O), 1675s (ynone C=O), 1467w, 1446m, 1418w, 1361m, 1230m, 1202m cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.46 (td, *J* = 6.6, 1.0Hz, 1H), 4.16 (qd, *J* = 7.1, 2.6Hz, 2H), 3.29-3.07 (m, 2H), 3.02 (d, *J* = 17.4Hz, 1H), 2.71 (d, *J* = 17.4Hz, 1H), 2.54-2.50 (m, 1H) 2.39 (ddd, *J* = 17.2, 5.8, 5.8Hz, 1H), 2.27 (s, 3H), 2.21 (ddd, *J* = 17.3, 10.4, 4.9Hz, 1H), 1.68 (s, 3H), 1.23 (t, *J* = 7.1Hz, 3H) ppm; ^{13}C NMR (100MHz, $CDCl_3$): δ 206.4, 184.2, 169.6, 139.1, 119.7, 89.4, 83.2, 63.9, 61.9, 39.2, 32.7, 31.2, 30.2, 25.2, 24.2, 14.0 ppm; LRMS (20 eV): *m/z* 276 [M^+, 5], 233 (24), 203 (20),

[14] B. C. Pan, H. Y. Chang, G. L. Cai and Y. S. Guo, *Pure & Appl. Chem.* **1989**, 61, 389.

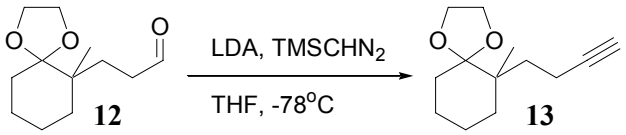
195 (41), 187 (32), 159 (23), 149 (100), 121 (22); HRMS (EI): *m/z* calcd for $C_{16}H_{20}O_4$ [M^+]: 276.1362. Found: 276.1362.

Preparation of alkynedione **2d**



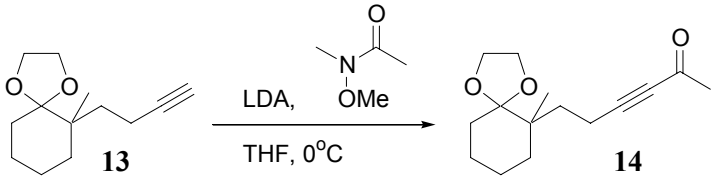
11 **12**

A solution of **11**[15] (3.002 g, 12.40 mmol) in DCM (120 mL) at –78°C was treated with 1 M DIBAL-H (17.0 mL, 17.00 mmol) for 2 hr. The reaction was quenched with saturated aqueous sodium potassium tartrate (30 mL) and extracted with DCM (3 x 30 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash chromatography (25% EtOAc in hexane) to afford **13** (2.261g, 86%) as a colourless oil. **12**: R_f (40% EtOAc in hexane): 0.60; IR (DCM): 2939s, 2888m, 2870m, 2831m, 1708s (aldehyde C=O), 1176m, 1127m, 1091m cm^{-1}; ^1H NMR (400 MHz): δ 9.75 (t, *J* =1.8 Hz, 1H), 3.95-3.87 (m, 4H), 2.43-2.36 (m, 2H), 1.79-1.70 (m, 2H), 1.59-1.53 (m, 4H), 1.41 (s, 4H), 0.91 (s, 3H) ppm; ^{13}C NMR (100 MHz): δ 203.3, 112.7, 64.9, 64.6, 40.6, 39.2, 34.8, 30.4, 27.0, 23.5, 20.8, 19.5 ppm; LRMS (20 eV): *m/z* 212 [M^+, 6], 184 (37), 169 (100), 155 (40), 127 (14), 113 (24); HRMS (EI): *m/z* calcd $C_{12}H_{20}O_3$ [M^+]: 212.1412. Found: 212.1400.



12 **13**

To a solution of LDA (10.52 mmol) at –78°C, was added $TMSCHN_2$ (2 M in hexane solution, 5.0 mL, 10.0 mmol) dropwise. After stirring for 30 min, a solution of **12** (1.715 g, 8.092 mmol) in THF (10 mL) was added dropwise at –78°C. The mixture was stirred at this temperature for 1 hr and then refluxed for a further 3 hr. The reaction was quenched by cold water, extracted by ether (3 x 20 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography (10% EtOAc in hexane) on triethylamine-treated silica gel to afford **13** (0.909 g, 54%) as a colourless oil. The spectral features were identical to previously obtained data.[16]



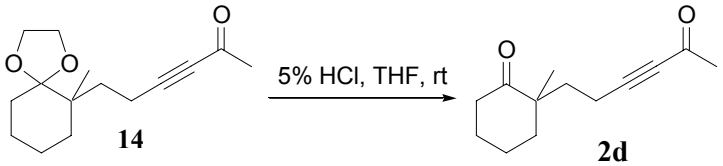
13 **14**

To a solution of **13** (0.235 g, 1.129 mmol) in THF (10 mL) was added 1.53 M *n*-BuLi (1.1 mL, 1.683

[15] M. Takahashi, K. Dodo, Y. Hashimoto and R. Shirai *Tetrahedron Lett.* **2000**, *41*, 2111.

[16] T. C. McKenzie, *Synthesis* **1977**, 9, 608

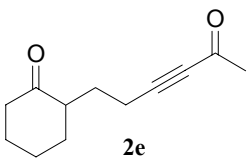
mmol). The solution was stirred for 1 hr followed by the addition of N-methoxy-N-methylacetamide (0.194 g, 1.921 mmol). The reaction was quenched by sat. NH_4Cl (20 mL) and extracted with ether (3 x 20 mL). The combined organics were dried over $MgSO_4$ and concentrated *in vacuo*. The crude was purified by flask chromatography (10% EtOAc) on the triethylamine-treated silica gel to afford **14** as a colourless oil (0.152 g, 54%). **14**: R_f (20% EtOAc in hexane): 0.54; IR (DCM): 2995m, 2943m, 2971m, 2210 w (C≡C), 1673s (ynone C=O), 1566w, 1513w cm^{-1}; ^1H NMR (400 MHz): δ 3.95-3.88 (m, 4H), 2.26-2.20 (m, 2H), 2.28 (s, 3H), 1.67-1.83 (m, 2H), 1.59-1.53 (m, 4H), 1.42 (d, J = 2.5 Hz, 4H), 0.92 (s, 3H) ppm; ^{13}C NMR (100 MHz): δ 112.7, 85.8, 67.6, 64.9, 64.7, 41.0, 34.5, 34.3, 30.4, 23.5, 20.8, 19.2, 13.3 ppm; LRMS (20eV): *m/z* 250 [M^+, 6], 207 (19), 169 (100), 113 (24), 99 (57); HRMS (EI): *m/z* calcd $C_{15}H_{22}O_3$ [M^+]: 250.1569. Found: 250.1569.



14 **2d**

A solution of **14** (0.152 g, 0.610 mmol) in THF (5 mL) was treated with 5% HCl (5 mL) at room temperature. The reaction mixture was neutralized by 50% Na_2CO_3, extracted with ether (3 x 5 mL) and dried over $MgSO_4$. The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography (25% EtOAc in hexane) to afford **2d** (0.123 g, 98%) as a colourless oil. **2d**: R_f (30% EtOAc in hexane): 0.46; IR (DCM): 2992w, 2940m, 2971w, 2211m (C≡C), 1701s (ketone C=O), 1671s (ynone C=O), 1559w, 1507w cm^{-1}; ^1H NMR (300 MHz): δ 2.41-2.38 (m, 2H), 2.35 (dd, J = 11.0, 4.5 Hz, 1H), 2.29 (s, 3H), 2.21 (ddd, J = 17.0, 10.4, 5.6 Hz, 1H), 1.96 (ddd, J = 13.9, 10.4, 5.6 Hz, 1H), 1.85-1.70 (m, 6H), 1.69-1.60 (m, 1H), 1.09 (s, 3H) ppm; ^{13}C NMR (75 MHz): δ 214.8, 184.8, 93.5, 81.4, 48.1, 39.0, 38.7, 35.9, 32.7, 27.4, 22.4, 21.0, 14.1 ppm; LRMS (20eV): *m/z* 206 [M^+, 2], 193 (2), 163 (3), 145 (5), 135 (3), 125 (4), 119 (7), 112 (100); HRMS (EI): *m/z* calcd $C_{13}H_{18}O_2$ [M^+]: 206.1308 Found: 206.1307.

Alkynediones **2e** and **2f** were synthesized by routes similar to the synthesis of **2d**, starting from ethyl 3-(1,4-dioxaspiro[4.5]dec-6-yl)propionaldehyde [17], and ethyl 4-(2-methyl[1,3]dioxolan-2-yl)butyraldehyde respectively.[18]



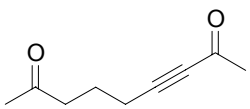
2e

2e: colourless oil; R_f (40% EtOAc in hexane): 0.59; IR (DCM): 2941m, 2865w, 2211m (CC), 1707s (ketone C=O), 1673s (ynone C=O) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.39 (t, J = 7.2 Hz, 1H), 2.42-2.37 (m, 2H), 2,35-2.29 (m, 1H), 2.26 (s, 3H), 2.10-1.99 (m, 3H), 1.84-1.83 (m, 1H), 1.69-1.63 (m, 2H), 1.42-1.28 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.3, 184.7, 93.4, 81.5, 49.0, 42.1, 34.0,

[17] G. Pandey, S. Hajra and M. K. Ghorai, *J. Org. Chem.* **1997**, *62,* 5966.

[18] F. Ameer, R. G. F. Giles, I. R. Green and K. S. Nagabhushana, *Synth. Comm.* **2002**, *32,* 369.

32.7, 279, 27.6, 25.0, 16.7 ppm; LRMS (20 eV): *m/z* 192 [M^+, 16], 159 (7), 149 (42), 131 (16), 121 (100); HRMS (EI): *m/z* calcd for $C_{12}H_{16}O_2$ [M^+]: 192.1150. Found: 192.1146.



2f

2f: colourless oil. R_f (30% EtOAc in hexane): 0.26; IR (DCM): 2963m, 2947w, 2900w, 2212m (CC), 1714s (ketone C=O), 1674s (ynone C=O), 1360w, 1233w, 1160m, 964w cm^{-1}; ^1H NMR (400 MHz): δ 2.57 (t, *J* = 7.1 Hz, 2H), 2.40 (t, *J* = 6.9 Hz, 2H), 2.30 (s, 3H), 2.15 (s, 3H), 1.83 (quint, *J* = 7.0 Hz, 2H) ppm; ^{13}C NMR (100 MHz): δ 211.0, 188.2, 96.1, 85.3, 45.3, 36.2, 33.5, 24.9, 21.6 ppm; LRMS (20 eV): *m/z* 152 [M^+, 4], 137 (10), 109 (31), 95 (24); HRMS (EI): *m/z* calcd $C_9H_{12}O_2$ [M^+]: 152.0837. Found: 152.837.