Supporting Information

Combination iminium, enamine and copper(I) cascade catalysis: A carboannulation for the synthesis of cyclopentenes

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1. General Experimental

All reactions were performed under an atmosphere of dry nitrogen unless otherwise stated. All glass apparatus was oven dried and cooled under vacuum before use.

1) Solvents and Reagents
Bulk solutions were evaporated under reduced pressure using a Büchi rotary evaporator. Reagents used were obtained from commercial suppliers or redistilled. Petroleum ether refers to distilled light petroleum of fraction (40-65 °C). Anhydrous methanol was distilled over Mg. Pyrrolidine was distilled over KOH. Anhydrous NMP was purchased from Aldrich.

2) Chromatography
Flash column chromatography was carried out using Merck Kiesegel 60 silica gel (230-400 mesh). Thin-layer chromatography (TLC) was carried out using Merck Kiesegel 60 F_{254} (230-400 mesh) fluorescent treated silica which were visualised under UV light (250nm) or by staining with aqueous potassium permanganate solutions as appropriate.

3) Spectra
All \(^1\text{H}\) and \(^13\text{C}\) NMR spectra were recorded using Bruker 500 MHz or Bruker 400 MHz spectrometers and use ppm for measurement against a TMS internal standard. Chemical shifts (\(\delta\)) are given in parts per million (ppm), and coupling constants (\(J\)) are given in Hertz (Hz). DEPT135 and two-dimensional (COSY, HMQC) NMR spectroscopy were used where appropriate to assist the assignment of signals in the \(^1\text{H}\) and \(^13\text{C}\) NMR spectra. Low resolution mass spectrometry (EI, CI) was recorded on a Fissions VG Trio 2000 quadropole mass spectrometer. High resolution mass spectra (accurate mass) were recorded on a Thermo Finnigan Mat 95XP mass spectrometer. Infrared spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer from a thin film deposited onto a sodium chloride plate, or by mean of KBr disk.

4) General procedures for synthesis of starting materials
Dimethyl propargylmalonate (12), methyl 2-(phenylsulfonyl)pent-4-ynoate (used as starting material for synthesis of 27, 28 and 29) and ethyl 2-(phenylsulfonyl)pent-4-ynoate (for 26) were all synthesized by treating dimethylmalonate or the 2-(phenylsulfonyl)pent-4-ynoate with NaH and performing the nucleophilic addition of the obtained anions to propargyl chloride in presence of KI.[S1] Dimethyl 2-(3-phenylprop-2-ynyl)malonate (30, starting material for 31) was obtained by a Sonogashira coupling[S2] of 12 with iodobenzene. Methyl substituted cycloexenones (starting materials for synthesis of 17, 18 and 19) were synthesized by t-BuOK-catalyzed annulation of appropriate β-ketoesters with conjugated enones or enals.[S3]

2. Practical experimental

2.1. General procedure for one-pot reactions.

\[
\begin{array}{c}
\text{R}_1\text{R}_2\text{O} & \overset{\text{EWG}}{\text{EWG}} & \overset{\text{ps-BEMP 10 mol\%}, \text{pyrrolidine 20 mol\%}}{\text{Cu(OTf)}_2 \ 5 \text{ mol\%}, \text{PPh}_3 \ 20 \text{ mol\%}} & \text{MeOH, RT} \\
\end{array}
\]

To a solution of the nucleophile (0.62 mmol), Cu(OTf)\textsubscript{2} (7.4 mg, 0.020 mmol) and PPh\textsubscript{3} (22 mg, 0.082 mmol) in anhydrous MeOH (1 mL) ps-BEMP (19 mg, 0.041 mmol) was suspended, then the conjugated ketone (0.41 mmol) and pyrrolidine (7 μL, 0.082 mmol) were added; the mixture was stirred at RT till complete conversion of the ketone by TLC, then diluted with CH\textsubscript{2}Cl\textsubscript{2} and filtered to eliminate ps-BEMP. Solvents were evaporated and the obtained crude was purified by chromatography.

2.2. Synthesis and characterization of compounds 16-29 and 31

2.2.1. Compound 16

5,5-Dicarboxymethyl-7-methyl-1-oxo-bicyclo[4.3.0]non-7-ene (16). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cyclohexenone (40 μL); the
mixture was stirred at RT for 3h and the obtained crude was purified by chromatography (AcOEt/petroleum ether 1:10, R\text{f} 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (93 mg, 85%): mp 97-98 °C; ^1H NMR (500 MHz, CDCl\textsubscript{3}) δ 3.76 (s, 3H), 3.73 (s, 3H), 3.70 (dd, J = 5.0, 2.5 Hz, 1H), 3.09 (d, J = 18.0 Hz, 1H), 2.77 (d, J = 18.0 Hz, 1H), 2.45 (ddd, J = 17.5, 2.0, 2.0 Hz, 1H), 2.22-2.12 (m, 2H), 2.09 (s, 3H), 2.04-2.01 (m, 1H), 1.77 (ddddd, J = 25.0, 13.5, 3.0, 3.0 Hz, 1H), 1.16 (ddddd, J = 25.0, 12.5, 12.5, 2.5 Hz, 1H); ^13C NMR (125 MHz, CDCl\textsubscript{3}) δ 199.2, 171.7, 170.7, 149.5, 131.9, 61.9, 52.7, 52.3, 51.9, 46.0, 40.6, 27.5, 23.4, 15.7; IR ν\text{max} (film)/cm\textsuperscript{-1} 3455, 2992, 2953, 2935, 2865, 1732, 1677, 1619, 1437, 1272, 1264, 1251, 1228, 1178, 1160, 1095, 1083, 1060, 1044, 952, 936; MS (ES+) m/z (rel. intensity %) 267 (M+H\textsuperscript{+}, 25), 289 (M+Na\textsuperscript{+}, 100); HRMS (ES) calcd. C\textsubscript{14}H\textsubscript{18}O\textsubscript{5}Na (M+Na\textsuperscript{+}) 289.1046, found 289.1046.

2.2.2. Compound 17

![Image of compound 17](image)

**5,5-Dicarboxymethyl-4,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (17).** The general procedure was followed, using 4-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT 18h; crude NMR showed the dr of product was 20:1. Purification was accomplished by chromatography (Et\textsubscript{2}O/petroleum ether 5:1, R\text{f} 0.48 in AcOEt/petroleum ether 1:2), affording the major diastereomer as a white solid (77 mg, 66%): mp 84-85 °C; ^1H NMR (400 MHz, CDCl\textsubscript{3}) δ 3.70 (s, 3H), 3.68 (s, 3H), 3.46-3.40 (m, 1H), 2.95 (d, J = 17.8 Hz, 1H), 2.68 (d, J = 17.8 Hz, 1H), 2.35 (d, J = 17.4 Hz, 1H), 2.26-2.15 (m, 1H), 2.05 (s, 3H), 1.86-1.80 (m, 1H), 1.56-1.45 (m, 2H), 1.04 (d, J = 5.9 Hz, 3H); ^13C NMR (100 MHz, CDCl\textsubscript{3}) δ 199.2, 172.0, 171.0, 150.4, 131.2, 62.7, 57.7, 52.7, 57.2, 47.4, 40.5, 33.9, 32.9, 20.1, 15.9; IR ν\text{max} (KBr)/cm\textsuperscript{-1} 2996, 2971, 2952, 2930, 2854, 1748, 1729, 1678, 1618, 1436, 1374, 1338, 1314, 1274, 1254, 1219, 1201, 1173, 1098, 1081, 1065, 1052, 999, 961, 940, 853, 807, 748, 722, 675, 623, 610; MS (CI) m/z (rel. intensity %)
281 (M+H\(^+\), 99), 298 (M+NH\(_4^+\), 39); HRMS (Cl) calcd. C\(_{15}\)H\(_{24}\)NO\(_5\) (M+NH\(_4^+\)) 298.1649, found 298.1645.

2.2.3. Compound 18

\[\text{5,5-Dicarboxymethyl-3,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (18).} \]

The general procedure was followed, using 3-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 16h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, R\(_f\) 0.41 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (87 mg, 74%) with a diastereomeric ratio 2:1: mp 58-60 \(^0\)C; \(\text{\textsuperscript{1}H} \text{NMR (500 MHz, CDCl}_3\) \(\delta 3.87-3.83 \) (m, 1H, major), 3.69 (s, 4H of minor and 3H of major), 3.67 (s, 3H, of minor), 3.66 (s, 3H of major), 3.02 (d, \(J = 18.2 \) Hz, 1H of major and 1H of minor), 2.74 (d, \(J = 18.1 \) Hz, 1H of major and 1H minor), 2.38 (d, \(J = 17.0 \) Hz, 1H of minor), 2.30 (dd, \(J = 5.3 \) Hz, \(J = 16.3 \) Hz, 1H of major), 2.27-2.23 (m, 1H of major), 2.16-2.12 (m, 1H of major), 2.02 (s, 3H of major and 3H of minor), 2.00-1.98 (m, 1H of minor), 1.97-1.78 (m, 1H of major and 2H of minor), 1.38 (dt, \(J = 4.3 \) Hz, \(J = 12.5 \) Hz, 1H of major), 1.00 (d, \(J = 7.1 \) Hz, 3H of major), 0.95 (d, \(J = 6.5 \) Hz, 3H of minor), 0.87-0.80 (m, 1H of minor); \(\text{\textsuperscript{13}C} \text{NMR (125 MHz, CDCl}_3\) \(\delta 198.1, 197.3, 170.2, 170.2, 169.4, 169.2, 147.9, 147.7, 130.2, 129.7, 60.7, 60.4, 51.3, 51.2, 50.8, 50.8, 49.9, 47.7, 46.1, 45.4, 44.8, 44.6, 34.5, 31.4, 29.3, 26.8, 20.5, 18.0, 14.1, 14.1; IR \(\nu_{\text{max}}\) (film)/cm\(^{-1}\) 2954, 1733, 1683, 1628, 1435, 1378, 1266, 1222, 1198, 1170, 1088, 1060, 953; MS (ES\(^+\)) m/z (rel. intensity %) 303 (M+Na\(^+\), 100); HRMS (ES) calcd. C\(_{15}\)H\(_{24}\)O\(_5\)Na (M+Na\(^+\)) 303.1203, found 303.1196.

2.2.4. Compound 19
5,5-Dicarboxymethyl-2,7-dimethyl-1-oxo-bicyclo[4.3.0]non-7-ene (19). The general procedure was followed, using 3-methylcyclohexenone (46 mg) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, Rf 0.33 and 0.37 in AcOEt/petroleum ether 1:3), affording the pure product as a colorless oil (99 mg, 84%) with a diasteromeric ratio 3:1. Major diastereoisomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 3.77-3.75 (m, 1H), 3.74 (s, 3H), 3.72 (s, 3H), 3.10 (d, $J = 18.0$ Hz, 1H), 2.77 (d, $J = 18.0$ Hz, 1H), 2.19-2.13 (m, 1H), 2.12-2.05 (m, 2H), 2.03 (s, 3H), 160-1.52 (m, 1H), 1.32-1.20 (m, 1H), 1.11 (d, $J = 6.5$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 201.4, 171.7, 170.8, 147.6, 132.2, 61.8, 52.8, 52.7, 52.3, 46.2, 45.0, 32.6, 27.9, 15.4, 14.9; IR $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2954, 2867, 1731, 1683, 1631, 1435, 1375, 1327, 1269, 1221, 1200, 1173, 1094, 1060, 956, 899, 844, 806, 734; MS (EI) m/z (rel. intensity %) 280 (M$^+$, 37); HRMS (EI) calcd. C$_{15}$H$_{20}$O$_5$ (M$^+$) 280.1311, found 280.1320.

Minor diastereoisomer: $^1$H NMR (500 MHz, CDCl$_3$) δ 3.78-3.77 (m, 1H), 3.76 (s, 3H), 3.73 (s, 3H), 3.15 (d, $J = 16.5$ Hz, 1H), 2.81 (d, $J = 16.5$ Hz, 1H), 2.52-2.47 (m, 1H), 2.08 (s, 3H), 2.04-1.98 (m, 2H), 1.71-1.65 (m, 1H), 1.43-1.29 (m, 1H), 1.08 (d, $J = 7.5$ Hz, 3H); $^{13}$C NMR (100.6 MHz, CDCl$_3$) δ 202.7, 171.8, 170.7, 150.0, 131.2, 61.8, 52.8, 52.3, 51.2, 46.3, 42.6, 29.5, 22.5, 17.2, 15.6; IR $\nu_{\text{max}}$ (film)/cm$^{-1}$ 2954, 2871, 1734, 1682, 1629, 1435, 1374, 1326, 1268, 1173, 1121, 1092, 1059, 993, 955, 902, 846.

2.2.5. Compound 20

![Compound 20](image)

6,6-Dicarboxymethyl-8-methyl-1-oxo-bicyclo[5.3.0]dec-8-ene (20). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cycloheptenone (45 μL); the
mixture was stirred at RT for 72 h and the obtained crude was purified by chromatography (Et₂O/petroleum ether 1:5, R_f 0.24 in AcOEt/petroleum ether 1:2), affording the pure product as a colorless oil (78 mg, 66%): ¹H NMR (400 MHz, CDCl₃) δ 3.67 (s, 3H), 3.26 (d, J = 18.7 Hz, 1H), 2.76 (d, J = 18.7 Hz, 1H), 2.54-2.41 (m, 2H), 2.00 (s, 3H), 1.98-1.93 (m, 1H), 1.89-1.82 (m, 1H), 1.70 (d, J = 13.0 Hz, 1H), 1.59-1.47 (m, 1H), 1.39-1.28 (m, 1H), 1.19 (qd, J = 12.6 Hz, J = 3.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 201.6, 171.9, 170.3, 150.9, 137.2, 62.8, 52.6, 51.7, 45.4, 45.3, 31.8, 30.4, 24.6, 16.3; IR ν_max (film)/cm⁻¹ 2999, 2928, 2854, 1737, 1676, 1619, 1436, 1376, 1316, 1257, 1177, 1163, 1082, 1003, 964, 896, 860, 819, 724, 693; MS (EI) m/z (rel. intensity %) 280 (M⁺, 6), 249 (M-OMe⁺, 21); HRMS (EI) calcd. C₁₄H₁₇O₄ (M-OMe⁺) 249.1127, found 249.1124.

2.2.6. Compound 21

4,4-Dicarboxymethyl-6-methyl-1-oxo-bicyclo[3.3.0]octene (21a-c, mixture of isomers). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and cyclohexenone (35 μL); the mixture was stirred at RT for 2 d and the obtained crude was purified by chromatography (AcOEt/petroleum ether 1:10, R_f 0.30 and 0.27 in AcOEt/petroleum ether 1:2), affording pure isomer 21a and a mixture of 21b with traces of 21c both as colorless oils (89 mg, 86%). Compound 21a: ¹H NMR (500 MHz, CDCl₃) δ 4.15-4.10 (m, 1H), 3.71 (s, 3H), 3.67 (s, 3H), 3.34 (d, J = 18.0 Hz, 1H), 3.03 (d, J = 18.0 Hz, 1H), 2.45-2.42 (m, 2H), 2.16-2.11 (m, 1H), 1.98 (s, 3H), 1.30-1.22 (m, 1H); ¹³C NMR (125 MHz, CDCl₃) δ 201.0, 171.5, 170.2, 146.2, 137.1, 62.6, 54.0, 52.9, 52.5, 50.7, 43.8, 26.1, 14.6; IR ν_max (film)/cm⁻¹ 3464, 2956, 1734, 1665, 1435, 1376, 1264, 1175, 1138, 1083, 1018, 952, 867; MS (Cl) m/z (rel. intensity %) 253 (M+H⁺, 90), 270 (M+NH₄⁺, 100); HRMS (ES) calcd. C₁₃H₂₉NO₅ (M+NH₄⁺) 270.1336, found 270.1330. Compound 21b: ¹H NMR (500 MHz, CDCl₃) δ 5.48 (dd, J = 1.5 Hz, J = 2.5 Hz, 1H), 3.70 (s, 3H), 3.66 (s, 3H), 3.59 (td, J =
7.5 Hz, $J = 10.0$ Hz, 1H), 3.27 (d, $J = 7.0$ Hz, 1H), 2.25-2.13 (m, 2H), 2.00 (ddt, $J = 3.5$ Hz, $J = 7.0$ Hz, $J = 7.5$ Hz, 1H), 1.75 (t, $J = 1.5$ Hz, 3H), 1.51-1.43 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) δc 215.2, 170.6, 170.1, 142.3, 124.2, 69.2, 61.3, 52.9, 52.5, 44.9, 38.5, 23.9, 14.7; IR: $\nu_{\text{max}}$ (film)/cm$^{-1}$ 3463, 2955, 2917, 2847, 1739, 1729, 1648, 1435, 1410, 1382, 1275, 1221, 1176, 1117, 1066, 1028, 1025, 856, 837; MS (CI) m/z (rel. intensity %) 253 (M+H$^+$, 40), 270 (M+NH$_4^+$, 100); HRMS (ES) calcd. C$_{13}$H$_{20}$NO$_5$ (M+NH$_4^+$) 270.1336, found 270.1329.

2.2.7. Compound 22

![3-Acetyl-1,1-dicarboxymethyl-4-methyl-cyclopent-3-ene (22)](image)

3-Acetyl-1,1-dicarboxymethyl-4-methyl-cyclopent-3-ene (22). The general procedure was followed, using dimethyl propargylmalonate (106 mg) and methyl vinyl ketone (35 μL) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:10, R$_f$ 0.30 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (71 mg, 71%): $^1$H NMR (500 MHz, CDCl$_3$) δ 3.74 (s, 6H), 3.32 (d, $J = 2.0$ Hz, 2H), 3.17 (s, 2H), 2.25 (s, 3H), 2.07 (t, $J = 2.0$ Hz, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 196.7, 171.9 (2C), 149.9, 132.6, 56.4, 53.0 (2C), 47.8, 41.9, 30.4, 16.3; IR $\nu_{\text{max}}$ (film)/cm$^{-1}$ 3002, 2956, 1735, 1684, 1655, 1621, 1435, 1362, 1269, 1254, 1201, 1168, 1073; MS (CI) m/z (rel. intensity %) 241 (M+H$^+$, 77), 258 (M+NH$_4^+$, 98); HRMS (CI) calcd. C$_{12}$H$_{20}$NO$_5$ (M+NH$_4^+$) 258.1336, found 258.1333.

2.2.8. Compound 23

![1,1-Dicarboxymethyl-4-methyl-3-propionyl-cyclopent-3-ene (23)](image)

1,1-Dicarboxymethyl-4-methyl-3-propionyl-cyclopent-3-ene (23). The general procedure was followed, using ethyl vinyl ketone (40 μL) and dimethyl propargylmalonate (106 mg) and stirring the mixture at RT for 84h; purification was accomplished by chromatography
(Et₂O/petroleum ether 1:5, R₇ 0.33 in AcOEt/petroleum ether 1:2), affording the pure product as a colorless oil (96 mg, 94%): ¹H NMR (400 MHz, CDCl₃) δ 3.68 (s, 6H), 3.37 (dd, J = 3.8 Hz, J = 1.9 Hz, 2H), 3.10 (s, 2H), 2.47 (q, J = 7.2 Hz, 2H), 2.02 (s, 3H), 1.01 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 199.5, 172.0 (2C), 149.5, 132.0, 56.7, 53.1 (2C), 47.6, 41.6, 35.5, 16.3, 7.5; IR νₘₐₓ (film)/cm⁻¹ 3473, 3280, 2849, 2367, 2343, 1995, 1739, 1684, 1657, 1623, 1436, 1376, 1267, 1201, 1169, 1075, 963, 893, 806; MS (Cl) m/z (rel. intensity %) 255 (M+H⁺, 32), 272 (M+NH₄⁺, 100); HRMS (Cl) calcd. C₁₃H₂₂NO₅ (M+NH₄⁺) 272.1492, found 258.1496.

2.2.9. Compound 24

![Compound 24](image)

1,1-Dicarboxymethyl-4-methyl-3-(4-(thiophen-2-yl)butanoyl)-cyclopent-3-ene (24). The general procedure was followed, using dimethyl propargylmalonate (102 mg) and 6-(thiophen-2-yl)hex-1-en-3-one (72 µL) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (Et₂O/toluene 1:50, R₇ 0.49 in AcOEt/petroleum ether 1:2), affording the pure product as a colourless oil (105 mg, 75%): ¹H NMR (500 MHz, CDCl₃) δ 7.12 (d, J = 5.0 Hz, 1H), 6.92 (dd, J = 5.0, 3.5 Hz, 1H), 6.79 (d, J = 3.5 Hz, 1H), 3.75 (s, 6H), 3.30 (s, 2H), 3.15 (s, 2H), 2.87 (t, J = 7.0 Hz, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.06 (s, 3H), 1.98 (m, 2H); ¹³C NMR (125.8 MHz, CDCl₃) δ 198.3, 171.8, 149.8, 144.4, 131.9, 126.7, 124.3, 123.0, 56.5, 53.0, 47.5, 41.5, 41.0, 29.0, 25.2, 16.2; IR νₘₐₓ (film)/cm⁻¹ 2953, 2851, 1996, 1737, 1682, 1656, 1622, 1555, 1435, 1371, 1265, 1200, 1168, 1073, 965, 849, 824; MS (Cl) m/z (rel. intensity %) 373 (M+Na⁺, 100); HRMS (Cl) calcd. C₁₈H₂₂NaO₅S (M+Na⁺) 373.1080, found 373.1094.
2.2.10. Compound 25

![Chemical Structure of Compound 25](image.png)

**1,1-Dicarboxymethyl-4-methyl-3-(4-(3,4-dimethoxyphenyl)butanoyl)-cyclopent-3-ene (25).** The general procedure was followed, using dimethyl propargylmalonate (105 mg) and 6-(3,4-dimethoxyphenyl)hex-1-en-3-one (97 mg) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8, →1:2, R_f 0.31 in AcOEt/petroleum ether 1:2), affording the pure product as a colourless oil (135 mg, 79%): ^1H NMR (500 MHz, CDCl_3) δ 6.79 (d, J = 8.5 Hz, 1H), 6.71-6.70 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 3.74 (s, 3H), 3.29 (s, 2H), 3.15 (s, 2H), 2.58 (t, J = 7.5 Hz, 1H), 2.50 (t, J = 7.0 Hz, 1H), 2.05 (s, 3H), 1.94-1.88 (m, 2H); ^13C NMR (125.8 MHz, CDCl_3) δ 198.7, 171.8, 149.6, 148.7, 141.0, 134.2, 132.0, 120.1, 111.5, 111.0, 56.5, 55.8, 55.6, 52.9, 47.5, 41.5, 41.3, 34.6, 25.0, 16.2; IR ν_max (film)/cm⁻¹: 2952, 2837, 1995, 1737, 1681, 1654, 1621, 1516, 1436, 1370, 1261, 1200, 1157, 1072, 1029, 868, 809, 763; MS (CI) m/z (rel. intensity %) 405 (M+H⁺, 100); HRMS (CI) calcd. C_{22}H_{32}NO_7 (M+NH₄⁺) 422.2173, found 422.2163.

2.2.11. Compound 26

![Chemical Structure of Compound 26](image.png)

**3-Acetyl-1-carboxyethyl-4-methyl-1-(phenylsulphonyl)-cyclopent-3-ene (26).** The general procedure was followed, using methyl vinyl ketone (35 μL) and ethyl 2-(phenylsulfonyl)pent-4-ynoate (156 mg) and stirring the mixture at RT for 72h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8, R_f 0.35 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish solid (94 mg, 71%): mp 71-72 °C; ^1H NMR (500 MHz, CDCl_3) δ 7.86 (d, J = 7.5 Hz, 2H), 7.70 (t, J = 7.5 Hz,
1H), 7.57 (dd, J = 7.5, 7.5 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H), 3.56 (d, J = 17.0 Hz, 1H), 3.49 (J = 19.0 Hz, 1H), 3.37 (d, J = 17.0 Hz, 1H), 3.33 (J = 19.0 Hz, 1H), 2.26 (s, 3H), 2.07 (s, 3H), 1.17 (t, J = 7.0 Hz, 3H); 13C NMR (125.8 MHz, CDCl3) δ 196.0, 167.8, 149.3, 136.1, 134.3, 132.5, 129.8 (2C), 128.9 (2C), 75.2, 62.9, 45.3, 39.8, 30.3, 16.3, 13.7; IR νmax (KBr)/cm⁻¹ 3069, 2988, 2915, 1378, 1909, 1737, 1690, 1625, 1584, 1471, 1450, 1430, 1358, 1306, 1279, 1241, 1222, 1209, 1144, 1085, 1066, 1028, 997, 962, 864, 763, 726, 691, 590, 580, 524; MS (CI) m/z (rel. intensity %) 354 (M+NH₄⁺, 28); HRMS (CI) calcd. C₁₇H₂₄NO₅S (M+NH₄⁺) 354.1370, found 354.1362.

2.2.12. Compound 27

![Chemical Structure](image)

3-Acetyl-1-carboxymethyl-4-methyl-1-(phenylsulphonyl)-cyclopent-3-ene (27). The general procedure was followed, using methyl vinyl ketone (35 μL) and methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8→1:2, Rf 0.20 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (95 mg, 70%); 1H NMR (500 MHz, CDCl₃) δ 7.81 (d, J = 6.5 Hz, 2H), 7.67 (t, J = 7.5 Hz, 1H), 7.54 (dd, J = 7.5, 6.5 Hz, 2H), 3.65 (s, 3H), 3.53 (d, J = 17.0 Hz, 1H), 3.45 (d, J = 19.5 Hz, 1H), 3.35 (d, J = 17.0 Hz, 1H), 3.29 (d, J = 19.5 Hz, 1H), 2.21 (s, 3H), 2.03 (s, 3H); 13C NMR (125.8 MHz, CDCl₃) δ 195.9, 168.3, 149.2, 135.9, 134.4, 132.5, 129.7 (2C), 128.9 (2C), 75.2, 53.4, 45.3, 39.7, 30.2, 14.1; IR νmax (film)/cm⁻¹ 3066, 1001, 2954, 2924, 1995, 1737, 1685, 1655, 1623, 1583, 1447, 1434, 1365, 1310, 1258, 1213, 1163, 1083, 1023, 948, 844, 761, 723, 692; MS (CI) m/z (rel. intensity %) 323 (M+H⁺, 3), 340 (M+NH₄⁺, 100); HRMS (CI) calcd. C₁₆H₂₂NO₅S (M+NH₄⁺) 340.1213, found 340.1224.
2.2.13. Compound 28

![Chemical Structure of 1-Carboxymethyl-4-methyl-1-(phenylsulphonyl)-3-propionyl-cyclopent-3-ene (28)]

**1-Carboxymethyl-4-methyl-1-(phenylsulphonyl)-3-propionyl-cyclopent-3-ene (28).** The general procedure was followed, using ethyl vinyl ketone (40 μL) and methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:8→1:2, Rf 0.21 in AcOEt/petroleum ether 1:2), affording the pure product as a yellowish oil (93 mg, 66%):

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.69 (t, J = 7.5 Hz, 1H), 7.56 (dd, J = 8.0, 7.5 Hz, 2H), 3.68 (s, 3H), 3.57 (d, J = 17.0 Hz, 1H), 3.44 (d, J = 19.5 Hz, 1H), 3.39 (d, J = 17.0 Hz, 1H), 3.27 (d, J = 19.5 Hz, 1H), 2.50 (q, J = 7.0 Hz, 2H), 2.05 (s, 3H), 1.05 (t, J = 7.0 Hz, 3H); $^{13}$C NMR (125.8 MHz, CDCl$_3$) δ 198.8, 168.5, 148.7, 136.1, 134.4, 131.8, 129.8 (2C), 129.0 (2C), 75.5, 53.6, 45.2, 39.5, 35.5, 16.3, 7.4; IR $\nu_{\text{max}}$ (film)/cm$^{-1}$ 3066, 2982, 2938, 2367, 1995, 1737, 1685, 1655, 1628, 1447, 1376, 1310, 1262, 1214, 1157, 1083, 951, 893, 761, 723, 691; MS (CI) m/z (rel. intensity %) 336 (M$^+$, 9); HRMS (CI) calcd. C$_{17}$H$_{24}$NO$_5$S (M+NH$_4^+$) 354.1370, found 354.1364.

2.2.14. Compound 29

![Chemical Structure of 5-Carboxymethyl-7-methyl-1-oxo-5-(phenylsulphonyl)-bicyclo[4.3.0]non-7-ene (29)]

**5-Carboxymethyl-7-methyl-1-oxo-5-(phenylsulphonyl)-bicyclo[4.3.0]non-7-ene (29).** The general procedure was followed, using methyl 2-(phenylsulfonyl)pent-4-ynoate (159 mg) and cyclohexenone (40 μL) and stirring the mixture at RT for 48h; purification was accomplished by chromatography (Et$_2$O/petroleum ether 1:4→1:1, Rf 0.26 in AcOEt/petroleum ether 1:3), affording the pure product as a white solid (61 mg, 42%). Alternatively, the same procedure
was followed using NMP as solvent instead of MeOH, after purification affording the product with a 63% yield as a mixture of inseparable diasteromers (5:1 dr): mp 135-136 °C; $^1$H NMR (400 MHz, CDCl$_3$) δ 7.88 (d, $J = 7.5$ Hz, 2H of major), 7.72 (d, $J = 7.5$ Hz, 2H of minor), 7.62 (t, $J = 7.5$ Hz, 1H of major and minor), 7.50 (t, $J = 7.5$ Hz, 2H of major and minor), 3.82-3.76 (m, 1H of major), 3.70 (s, 3H of minor), 3.62 (s, 3H of major and 1H of minor), 3.47 (d, $J = 18.0$ Hz, 1H of major), 3.06 (d, $J = 18.0$ Hz, 1H of major), 3.02 (d, $J = 19.6$ Hz, 1H of minor), 2.87 (d, $J = 19.6$ Hz, 1H of minor), 2.60-2.55 (m, 1H of minor), 2.46-2.23 (m, 1H of major and 3H of minor), 2.11-2.00 (m, 4H of major and 4H of minor), 1.93-1.86 (m, 1H of major), 1.83-1.77 (m, 1H of major), 1.69-1.57 (m, 1H of major and 1H of minor), 1.04 (qd, $J = 12.7$, 3.1 Hz, 1H of major); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 199.0 (minor), 198.2 (major), 168.8 (minor), 167.2 (major), 150.0 (major), 147.2 (minor), 137.7 (major), 136.5 (minor), 134.4 (minor), 134.3 (major), 132.9 (minor), 130.6 (major), 130.2 (2C, major), 130.1 (2C, minor), 128.8 (2C, major and minor), 80.2 (major), 79.0 (minor), 53.9 (minor), 53.4 (minor), 52.7 (major), 51.8 (major), 45.2 (major), 44.0 (major), 40.8 (minor), 40.2 (major), 28.3 (major), 26.8 (minor), 24.1 (minor), 23.1 (major), 15.8 (major), 15.8 (minor); IR ν$_{max}$ (KBr)/cm$^{-1}$ 3068, 2962, 2877, 1734, 1682, 1618, 1448, 1440, 1415, 1322, 1299, 1241, 1208, 1189, 1143, 1082, 954, 922, 890, 836, 811, 756, 735, 714, 689, 594, 548, 512; MS (Cl) m/z (rel. intensity %) 349 (M+H$^+$, 8), 366 (M+NH$_4^+$, 41); HRMS (Cl) calcd. C$_{18}$H$_{24}$NO$_5$S (M+NH$_4^+$) 366.1370, found 366.1366.

2.2.15. Compound 31

![Diagram of Compound 31](image)

**5,5-Dicarboxymethyl-7-benzyl-1-oxo-bicyclo[4.3.0]non-7-ene (31).** The general procedure was followed, using cyclohexenone (40 μL) and dimethyl 2-(3-phenylprop-2-ynyl)malonate 30 (150 mg) and stirring the mixture at reflux for 16h; purification was accomplished by chromatography (AcOEt/petroleum ether 1:20, R$_f$ 0.30 in AcOEt/petroleum ether 1:4),
affording the pure product as a colorless oil (94 mg, 69%): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.29-7.18 (m, 5H), 4.08 (d, \(J = 14.0\) Hz, 1H), 3.76 (d, \(J = 14.0\) Hz, 1H), 3.73-3.71 (m, 1H), 3.69 (s, 3H), 3.68 (s, 3H), 3.02 (d, \(J = 18.5\) Hz, 1H), 2.63 (d, \(J = 18.5\) Hz, 1H), 2.52 (ddd, \(J = 17.5, 2.0, 2.0\) Hz, 1H), 2.25 (ddd, \(J = 19.5, 13.0, 6.0\) Hz, 1H), 2.16-2.13 (m, 1H), 2.08-2.04 (m, 1H), 1.84-1.75 (m, 1H), 1.25-1.20 (m, 1H); \(^{13}\)C NMR (125.8 MHz, CDCl\(_3\)) \(\delta\) 198.9, 171.5, 170.6, 150.9, 138.1, 132.3, 129.0 (2C), 128.4 (2C), 126.3, 62.0, 52.7, 52.2, 52.0, 43.5, 40.9, 35.6, 27.5, 23.4; IR \(\nu_{\text{max}}\) (film)/cm\(^{-1}\) 3027, 2952, 2867, 2360, 1735, 1681, 1623, 1494, 1435, 1326, 1269, 1221, 1198, 1172, 1090, 1034, 960, 934, 844, 803; MS (APCI) m/z (rel. intensity %) 343 (M+H\(^+\), 100), 360 (M+NH\(_4^+\), 11); HRMS (CI) calcd. C\(_{20}\)H\(_{22}\)NO\(_5\) (M+H\(^+\)) 343.1545, found 343.1549.

3. Mechanism study

3.1. Identification of Cu-PPh\(_3\) complex

Two reactions were performed in the NMR tube:

Reaction A, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 \(\mu\)L) in 0.7 ml of methanol-d\(_4\); \(^{31}\)P NMR was taken when the reaction finished: \(^{31}\)P NMR (162 MHz, CD\(_3\)OD) \(\delta\) 32.2 (s, P(O)Ph\(_3\)), -1.7 (br s, complex of Cu-PPh\(_3\)).

Reaction B, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 \(\mu\)L) in 0.7 ml of methanol-d\(_4\), (CuOTf)\(_2\).C\(_6\)H\(_6\) (3 mg) was used
instead of Cu(OTf)$_2$; $^{31}$P NMR was taken when the reaction finished: $^{31}$P NMR (162 MHz, CD$_3$OD) δ 32.2 (s, P(O)Ph$_3$), -1.1 (br s, complex of Cu-PPh$_3$).

$^{31}$P NMR of a 1:1 mixture of reaction A and reaction B showed the same catalyst complex in the two reactions: $^{31}$P NMR (162 MHz, CD$_3$OD) δ 32.2 (s, P(O)Ph$_3$), -1.2 (br s, complex of Cu-PPh$_3$).

3.2. Reactions in CD$_3$OD

Two reactions were performed in the NMR tube:

Reaction C, the general procedure was followed, using dimethyl propargylmalonate (51 mg) and cyclohexenone (20 μL) in 0.7 ml of methanol-d$_4$. The reaction was followed by $^1$H NMR. Cyclohexenone was consumed after 3.5h. Solvent was removed. The obtained crude was immediately purified by chromatography (Et$_2$O/petroleum ether 1:4 to 1:2, R$_f$ 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (46 mg, 87%).

Reaction D, the general procedure was followed, compound 16 (53 mg) was added in 0.7 ml of methanol-d$_4$ instead of dimethyl propargylmalonate and cyclohexenone. Reaction was put on and worked up at the same as reaction C. The obtained crude was immediately purified by chromatography (Et$_2$O/petroleum ether 1:4 to 1:2, R$_f$ 0.29 in AcOEt/petroleum ether 1:2), affording the pure product as a white solid (50 mg, 94%).
4. References


5. Spectra

5.1. Spectra for reaction scope:

5.1.1. Compound 16

![1H NMR spectrum of compound 16](image)

![13C NMR spectrum of compound 16](image)
5.1.2. Compound 17

$^1$H NMR

$^{13}$C NMR

ppm (t1)
5.1.3. Compound 18

$\text{1H NMR}$

$\text{13C NMR}$
5.1.4. Compound 19 (major isomer)
5.1.5. Compound 19 (minor isomer)
5.1.6. Compound 20
5.1.7. Compound 21a

**1H NMR**

![1H NMR Spectrogram](image)

**13C NMR**

![13C NMR Spectrogram](image)
5.1.8. Compound 21b

$^1$H NMR

$^{13}$C NMR
5.1.9. Compound 22

\[ \text{MeOOC} \quad \text{COOMe} \]

\[ \text{MeOOC} \quad \text{COOMe} \]

Supplementary Material (ESI) for Chemical Communications
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5.1.10. Compound 23
5.1.11. Compound 24

$^{1}$H NMR

$^{13}$C NMR

Supplementary Material (ESI) for Chemical Communications
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5.1.12. Compound 25
5.1.13. Compound 26
5.1.14. Compound 27
5.1.15. Compound 28
5.1.16. Compound 29

![1H NMR spectrum of compound 29](image1)

![13C NMR spectrum of compound 29](image2)
5.1.17. Compound 31
5.2. Mechanism study

5.2.1. $^{31}$P NMR of reaction A

$^{31}$P CPD NMR

5.2.2. $^{31}$P NMR of reaction B

$^{31}$P CPD NMR
5.2.3. $^{31}$P NMR of a mixture of reaction A and reaction B