Supporting Information


Synthesis of bicyclo[4.2.0]octane ring of kingianin via [2+2] ketene cycloaddition

Mohamad Nurul Azmi\textsuperscript{1,2,*} Marc Litaudon, Khalijah Awang \textsuperscript{4} and Yvan Six\textsuperscript{2,*}

\textsuperscript{1}Natural Products and Synthesis Organic Laboratory (NPSOLab), School of Chemical Sciences, Universiti Sains Malaysia, 11800 Minden, Penang, Malaysia
\textsuperscript{2}Laboratoire de Synthèse Organique (LSO), UMR 7652 CNRS/ENSTA/École Polytechnique, Institut Polytechnique de Paris, 91128 Palaiseau Cedex, France
\textsuperscript{3}Institut de Chimie des Substances Naturelles, CNRS-ICSN UP 01, Univ. Paris-Sud 11, Av. de la Terrasse, 91198 Gif-sur-Yvette, France
\textsuperscript{4}Department of Chemistry, Faculty of Science, University of Malaya, 50603 Kuala Lumpur, Malaysia

Table of Contents

<table>
<thead>
<tr>
<th>Table of Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synthesis protocol and spectroscopic data analysis</td>
<td>3</td>
</tr>
<tr>
<td>Figure S1: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 6.</td>
<td>17</td>
</tr>
<tr>
<td>Figure S2: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 6.</td>
<td>17</td>
</tr>
<tr>
<td>Figure S3: IR spectrum. of compound 6.</td>
<td>18</td>
</tr>
<tr>
<td>Figure S4: MS spectrum (positive Cl, NH\textsubscript{3}) of compound 6.</td>
<td>18</td>
</tr>
<tr>
<td>Figure S5: HRMS spectrum (EI) of compound 6.</td>
<td>19</td>
</tr>
<tr>
<td>Figure S6: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 7.</td>
<td>19</td>
</tr>
<tr>
<td>Figure S7: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 7.</td>
<td>20</td>
</tr>
<tr>
<td>Figure S8: IR spectrum of compound 7</td>
<td>20</td>
</tr>
<tr>
<td>Figure S9: MS spectrum (positive Cl, NH\textsubscript{3}) of compound 7.</td>
<td>21</td>
</tr>
<tr>
<td>Figure S10: HRMS spectrum (EI) of compound 7.</td>
<td>21</td>
</tr>
<tr>
<td>Figure S11: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 8.</td>
<td>22</td>
</tr>
<tr>
<td>Figure S12: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 8.</td>
<td>22</td>
</tr>
<tr>
<td>Figure S13: IR spectrum of compound 8.</td>
<td>23</td>
</tr>
<tr>
<td>Figure S14: MS spectrum (positive Cl, NH\textsubscript{3}) of compound 8.</td>
<td>23</td>
</tr>
<tr>
<td>Figure S15: HRMS spectrum (EI) of compound 8.</td>
<td>24</td>
</tr>
<tr>
<td>Figure S16: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 10.</td>
<td>24</td>
</tr>
<tr>
<td>Figure S17: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 10.</td>
<td>25</td>
</tr>
<tr>
<td>Figure S18: MS spectrum (EI) of compound 10.</td>
<td>25</td>
</tr>
<tr>
<td>Figure S19: HRMS spectrum (EI) of compound 10.</td>
<td>26</td>
</tr>
<tr>
<td>Figure S20: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 11.</td>
<td>26</td>
</tr>
<tr>
<td>Figure S21: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 11.</td>
<td>27</td>
</tr>
<tr>
<td>Figure S22: HRMS spectrum (EI) of compound 11.</td>
<td>27</td>
</tr>
<tr>
<td>Figure S23: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 13.</td>
<td>28</td>
</tr>
<tr>
<td>Figure S24: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 13.</td>
<td>28</td>
</tr>
<tr>
<td>Figure S25: MS spectrum (positive Cl, NH\textsubscript{3}) of compound 13.</td>
<td>29</td>
</tr>
<tr>
<td>Figure S26: HRMS spectrum (EI) of compound 13.</td>
<td>29</td>
</tr>
<tr>
<td>Figure S27: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 19.</td>
<td>30</td>
</tr>
<tr>
<td>Figure S28: \textsuperscript{13}C NMR spectra (CDCl\textsubscript{3}, 100.6 MHz) of compound 19.</td>
<td>30</td>
</tr>
<tr>
<td>Figure S29: IR spectrum of compound 19.</td>
<td>31</td>
</tr>
<tr>
<td>Figure S30: HRMS spectrum (EI) of compound 19</td>
<td>31</td>
</tr>
<tr>
<td>Figure S31: \textsuperscript{1}H NMR spectrum (CDCl\textsubscript{3}, 400 MHz) of compound 20.</td>
<td>32</td>
</tr>
</tbody>
</table>

© 2024 ACG Publications. All rights reserved.
Figure S32: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 20.
Figure S33: IR spectrum of compound 20.
Figure S34: MS spectrum (positive CI, NH$_3$) of compound 20.
Figure S35: HRMS spectrum (EI) of compound 20.
Figure S36: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 21.
Figure S37: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 21.
Figure S38: IR spectrum of compound 21.
Figure S39: MS spectrum (positive CI, NH$_3$) of compound 21.
Figure S40: HRMS spectrum (EI) of compound 21.
Figure S41: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 25.
Figure S42: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 25.
Figure S43: IR spectrum of compound 25.
Figure S44: HRMS spectrum (EI) of compound 25.
Figure S45: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 26.
Figure S46: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 26.
Figure S47: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 29.
Figure S48: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 29.
Figure S49: IR spectrum of compound 29.
Figure S50: HRMS spectrum (EI) of compound 29.
Figure S51: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 30.
Figure S52: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 30.
Figure S53: HRMS spectrum (EI) of compound 30.
Figure S54: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 31.
Figure S55: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 31.
Figure S56: IR spectrum of compound 31.
S1: Synthesis protocol and spectroscopic data analysis

S1.1: Generals

All reactions were carried out in heat-dried glassware under an atmosphere of nitrogen unless otherwise stated. All liquid transfers were conducted using standard syringe or cannula techniques. THF, Et₂O, DCM, toluene and MeOH were purified by a MBraun® Solvent Purification system. DMF and cyclohexane were dried under 4 Å molecular sieves. All other reagents were obtained from Merck, Across, Alfa-Aesar or Aldrich and used as received. Column chromatography was performed on silica gel (Merck, 60 Å C. C. 40-63 μm) as the stationary phase. Thin Layer Chromatography (TLC) was performed on alumina plates pre-coated with silica gel (Merck silica gel, 60 F254), which were visualised by the quenching of UV fluorescence when applicable (λ_max = 254 nm and/or 366 nm) and/or by spraying with vanillin or anisaldehyde in acidic ethanol, followed by heating with a heat gun. HRMS was run on a JEOL JMS-GCmate II mass spectrometer. NMR spectra were recorded on a Bruker Avance (400 MHz for ¹H NMR, 100.6 MHz for ¹³C NMR) spectrometer system. Data were analysed via TopSpin software package. Spectra were referenced to TMS or residual solvent (CDCl₃ = 7.26 ppm in ¹H NMR spectroscopy and 77.0 ppm in ¹³C NMR spectroscopy).

S1.2: Synthetic sequence starting from 4-methoxy-1,4-cyclohexadiene.

![Chemical structure diagram]

7-Chloro-4-methoxy-7-methyl-bicyclo[4.2.0]oct-4-en-8-ones (6 and 7). Triethylamine (1.18 mL, 30.0 mmol) was added to a refluxing mixture of 4-methoxy-1,4-cyclohexadiene 1 (5.59 g, 50.8 mmol) and 2-chloropropanoyl chloride 5 (3.81 g, 30.0 mmol) in diethyl ether (25 mL). The reaction mixture was stirred at room temperature for 1.5 hrs and then filtered. The solid residue was rinsed with diethyl ether. The filtrate was washed with 1 M HCl, 1 M NaOH and then brine. After drying (Na₂SO₄), the organic layer was concentrated, and the crude product was distilled with a Kugelrohr apparatus at 150 °C (0.62 mbar) to give a mixture of diastereoisomers 6 (2.11 g, 35 %) and 7 (0.66 g, 11 %).

Pale yellow oil. Rᵣ = 0.30 [UV-active, EtOAc/Pet. ether 5 %, anisaldehyde (yellow spot)]. IR (neat): ν_max 2939 (m), 2855 (w), 2836 (w), 1786 (s, C=O), 1656 (m), 1443 (m), 1285 (w), 1219 (m), 1197 (m), 1174 (m), 1139 (m), 1066 (m), 1031 (m), 952 (m), 826 (m) cm⁻¹. ¹H NMR (CDCl₃) 1.48 (3H, s, H9), 1.67 (1H, m, H2a), 1.95–2.15 (3H, m, H2b, H3), 3.26 (1H, ddt, J = 10.0, 5.0, 1.0 Hz, H6), 3.55 (3H, s, H10), 4.12 (1H, dddd, J = 10.0, 6.0, 3.5, 1.5 Hz, H1), 4.73 (1H, dd, J = 5.0, 1.5 Hz, H5). ¹³C NMR (CDCl₃) 19.2 (C9), 19.4 (C3), 24.7 (C2), 40.7 (C6), 53.9 (C1), 54.1 (C10), 77.3 (C7).
Correlations not observed: H1 – H9, H6 – H9.

(1R*,6S*,7S*)-7-Chloro-4-methoxy-7-methyl-bicyclo[4.2.0]oct-4-en-8-one 7

Pale yellow oil. Rᵃ ≈ 0.20 [UV-active, EtOAc/Pet. ether 5 %, anisaldehyde (dark orange spot)]. IR (neat): νmax 3049 (m), 2984 (m), 2306 (m), 2685 (w), 1796 (m, C=O), 1723 (m), 1688 (w), 1443 (m), 1422 (m), 1263 (s), 1155 (w) 1070 (w) 1024 (w), 895 (m) cm⁻¹. ¹H NMR (CDCl₃) 1.68 (1H, m, H2a), 1.77 (3H, s, H9), 1.94 (1H, m, H3a), 2.05–2.17 (2H, m, H2b, H3b), 3.05 (1H, ddt, J = 10.0, 5.0, 1.0 Hz, H6), 3.54 (3H, s, H10), 3.67 (1H, distorted dddd, J = 10.0, 6.0, 3.0, 1.0 Hz, H1), 4.69 (1H, dd, J = 5.0, 1.5 Hz, H5). ¹³C NMR (CDCl₃) 19.8 (C3), 24.3 (C2), 26.2 (C9), 38.5 (C6), 51.6 (C1), 54.2 (C10), 77.4 (C7), 91.4 (C5), 157.6 (C4), 206.7 (C8). MS m/z (positive CI, NH₃) 110, 129, 137, 165, 167, 183, 201 (MH⁺ with ³⁵Cl), 202, 203 (MH⁺ with ³⁷Cl). MS m/z (EI) 105, 109, 110, 111, 112, 113, 125, 132, 135, 137, 150, 151, 162, 170, 182, 200 (M⁺ with ³⁵Cl), 202 (M⁺ with ³⁷Cl). HRMS m/z (EI): 200.0599 (M⁺ C₁₀H₁₃ClO₂⁺ requires 200.0599).

NOESY (CDCl₃) Observed correlations: H5 – H10 (very intense), H6 – H9 (moderate).
Correlation not observed: H5 – H9.

4-Methoxy-7-methyl-bicyclo[4.2.0]oct-4-en-8-one (8). To mixture of 2.00 g (30.7 mmol) of Zn dust and 4.5 mL of TMEDA (29.0 mmol) in 10 mL of absolute EtOH at 0 °C was added 2.00 mL (33.0 mmol) of AcOH. The reaction mixture was maintained at 0 °C while a solution of enol ether 6 (1.10 g, 5.0 mmol) in 2.0 mL of EtOH was added over 10 min period. After an additional 15 min at 0 °C the reaction mixture was allowed to warm to room temperature and stirred for 15 min. The resulting grey mixture was filtered, and the solid residue was rinsed with diethyl ether. The filtrate was washed with ice cold 1 M HCl (10 mL), H₂O (10 mL), sat. NaHCO₃ (10 mL) and sat. NaCl (10 mL). The resulting material was dried over MgSO₄ and concentrated under reduced pressure to afford 0.37 g (45 %) of desired enol ether 8 which was of sufficient purity for subsequent transformation.
Colourless oil. $R_f \approx 0.30$ [UV-active, EtOAc/Pet. ether 5 %, anisaldehyde (yellow spot)]. IR (neat):

$\nu_{max}$ 3020 (s), 2985 (m), 2401 (w), 1771 (s, C=O), 1713 (s), 1553 (m), 1422 (m), 1264 (s), 1216 (s), 1017 (m), 890 (s) cm$^{-1}$. $^1$H NMR (CDCl$_3$) 0.91 (3H, d, $J = 8.4$ Hz, H9), 1.65 (1H, m, H2a), 1.87 (1H, m, H3a), 1.98–2.12 (2H, m, H2b, H3b), 3.07 (1H, d, $J = 8.4$, 4.6 Hz, H7), 3.31 (1H, dd, $J = 9.1$, 4.6 Hz, H6), 3.47 (3H, s, H10), 3.52 (1H, m, H1), 4.55 (1H, dd, $J = 4.6$, 2.0 Hz, H5).

$^{13}$C NMR (CDCl$_3$)

8.8 (C9), 19.2 (C2), 24.6 (C3), 27.6 (C7), 53.9 (C10), 54.5 (C1), 56.0 (C6), 91.0 (C5), 157.4 (C4), 213.9 (C8).

MS m/z (positive CI, NH$_3$) 165, 167 (M$^+$), 171, 172, 183, 200. MS m/z (EI) 109, 114, 121, 124, 135, 137, 151, 152, 161, 166 (M$^+$). HRMS m/z (EI): 166.0993 (M$^+$ C$_{10}$H$_{14}$O$_2$ requires 166.0989).

7-Methyl-4-oxobicyclo[4.2.0]octan-8-ylidene)butanoic acid (10). To a stirred slurry of (3-carboxypropyl)-triphenylphosphonium bromide (9) (2.11 g, 4.9 mmol) in dry THF (10 mL) under nitrogen at −75 °C was added potassium tert-butoxide (1.38 g, 12.3 mmol). After 15 min at −75 °C, a solution of enol ether 8 (0.68 g, 4.1 mmol) in dry THF (5.0 mL) was added to a mixture and stirred at −75 °C for 10 min. The mixture was continuously stirred at room temperature overnight. The mixture was pouring into 5 % Na$_2$CO$_3$ solution (30 mL), washed with ethyl acetate (30 mL mL), and then acidified with conc. HCl. The aqueous layer was extracted with ether (3 x 50 mL) and the combined extracts were concentrated to 20 mL and kept at −20 °C for 2 hrs. The resulting precipitate was filtered off and discarded. Evaporation of the filtrate gave a yellowish oil (0.79 g) which was purified by column chromatography on silica gel, eluted with petroleum ether/ethyl acetate (7:3) to give the desired product 10 as a mixture of the two geometrical isomers (1:1) (0.46 g, 51 %).
(1R*,6S*,7R*)-7-Methyl-4-oxobicyclo[4.2.0]octan-8-ylidene)butanoic acid 10

Yellowish oil. \( R_t \approx 0.20 \) [UV-active, EtOAc/Pet. ether 50 %, anisaldehyde (violet spot)]. IR (neat): \( \nu_{\text{max}} \) 2950 (m), 2362 (w), 1736 (m, C=O), 1708 (m, C=O), 1438 (w), 1170 (m), 923 (w), 634 (w) cm\(^{-1}\). 1H NMR (CDCl\(_3\)) 1.13 (3H, d, \( J = 7.7 \) Hz, H9), 1.90 (1H, m, H2a), 2.02 (1H, m, H2b), 2.24 (1H, m, H3b), 2.31 – 2.47 (5H, m, H5, H11, H12a), 2.51 (1H, m, H3b), 2.55 (1H, m, H12b), 2.61 (1H, m, H6), 3.22 (1H, m, H1), 3.34 (1H, m, H7), 5.22 (1H, t, \( J = 7.7 \) Hz, H10). 13C NMR (CDCl\(_3\)) 13.5 (C9), 23.2 (C2), 23.5 (C11), 31.7 (C6), 34.5 (C12), 36.8 (C3), 37.8 (C1), 38.2 (C5), 38.5 (C7), 121.5 (C10), 148.4 (C8), 178.5 (C13), 214.5 (C4). MS \( m/z \) (EI) 167, 177, 195, 205, 221, 223 (MH\(^+\)), 240, 241, 256. HRMS \( m/z \) (EI): 222.1252 (M\(^+\)C\(_{13}\)H\(_{18}\)O\(_3\)+ requires 222.1251).

Methyl-((7-methyl-4-oxobicyclo[4.2.0]octan-8-yl)butanoate (11). To a solution of the bicycloalkene 10 (0.24 g, 1.1 mmol) in MeOH (5.0 mL) was added 10 % Pd/C (10 % w/w, 0.02 g), and the resulting mixture was hydrogenated at 1 atm for 12 hrs. Filtration through Celite and evaporation of the filtrate in vacuo afforded 11 as a yellowish oil (0.21 g, 80 %).

Methyl-((1R*,6S*,7R*)-7-methyl-4-oxobicyclo[4.2.0] octan-8-yl)butanoate 11

Yellowish oil. \( R_t \approx 0.40 \) [non UV-active, EtOAc/Pet. ether 50 %, anisaldehyde (red-violet spot)]. IR (neat): \( \nu_{\text{max}} \) 2933 (m), 1738 (s, C=O), 1714 (s, C=O), 1455 (w), 1438 (w), 1377 (w), 1197 (m), 1170 (m), 1112 (w), 1015 (w), 883 (w) cm\(^{-1}\). 1H NMR (CDCl\(_3\)) 1.05 (3H, d, \( J = 7.4 \) Hz, H9), 1.46 (2H, m, H10), 1.56 (2H, m, H11), 1.87 (1H, m, H2a), 1.97 – 2.06 (2H, m, H2b, H3a), 2.19 (1H, m, H5a), 2.34 (2H, t, \( J = 7.2 \) Hz, H12), 2.40 – 2.62 (4H, m, H1, H3b, H5b, H8), 2.72 (1H, qd, \( J = 8.1, 2.0 \) Hz, H7), 2.79 (1H, q, \( J = 8.1 \) Hz, H6), 3.69 (3H, s, H14). 13C NMR (CDCl\(_3\)) 12.3 (C9), 22.1 (C2), 23.2 (C3), 26.0 (C10), 31.3 (C6), 34.2 (C12), 32.7 (C7), 34.4 (C1), 37.2 (C8), 37.4 (C5), 38.4 (C3), 51.5 (C14), 173.8 (C13), 214.4 (C4). MS \( m/z \) (EI) 110, 123, 135, 151, 162, 182, 195, 206, 224, 236, 238 (M\(^+\)). HRMS \( m/z \) (EI): 238.1562 (M\(^+\)C\(_{14}\)H\(_{22}\)O\(_3\)+ requires 238.1563).
Methyl-\{5-bromo-7-methyl-4-oxobicyclo[4.2.0]octan-8-yl\}butanoate (13). To a stirred solution of the bicyclic ketone 11 (0.19 g, 0.8 mmol) in dry THF (10 mL) at \(-75 \degree C\) under argon was added phenyltrimethylammonium tribromide (298 mg, 0.79 mmol). The mixture was stirred at \(-75 \degree C\) for 20 min and then allowed to slowly warm to room temperature over 30 min. Brine (10 mL) was added, and then the resulting mixture was extracted with ether (2 \(\times\) 20 mL). The combined extracts were dried (MgSO\(_4\)) and concentrated to give an orange oil (0.23 g). Analysis by \(^1H\) and \(^13C\) NMR spectroscopy revealed that this crude product contained mostly the bromoketone 13.

Orange oil. \(R_f \approx 0.15\) [non UV-active, EtOAc/Pet. ether 30 %, anisaldehyde (red-violet spot)]. \(\text{IR (neat): } \nu_{\text{max}} 2937 (m), 1738 (s, C=O), 1731 (s, C=O), 1455 (w), 1436 (w), 1379 (w), 1246 (w), 1170 (w), 1066 (w), 1030 (w), 884 (w), 755 (w) \text{cm}^{-1}\). \(^1H\) NMR (CDCl\(_3\)) 1.24 (3H, d, \(J = 8.2\) Hz, H9), 1.49 (2H, m, H10), 1.58 (2H, m, H11), 1.97 (1H, m, H2a), 2.15 (1H, dd, \(J = 8.2, 5.4\) Hz, H2b), 2.37 (2H, m, H12), 2.49 (1H, dd, \(J = 8.2, 5.4\) Hz, H3a), 2.62 – 2.68 (4H, m, H1, H3b, H8), 2.89 (1H, qd, \(J = 8.2, 2.9\) Hz, H7), 3.04 (1H, q, \(J = 8.2\) Hz, H6), 3.71 (3H, s, H14), 4.86 (1H, d, \(J = 8.2\) Hz, H5). \(^13C\) NMR (CDCl\(_3\)) 11.5 (C9), 22.4 (C2), 23.7 (C11), 25.3 (C10), 33.1 (C7), 34.1 (C12), 36.2 (C8), 37.0 (C1), 37.6 (C3), 41.9 (C6), 51.6 (C14), 53.5 (C5), 174.0 (C13), 203.6 (C4). MS \(m/z\) (positive CI, NH\(_3\)) 223, 237, 239, 255, 271, 287, 317 (MH\(^+\)), 333, 334 (MH\(^+\)‥NH\(_3\)), 335, 336. MS \(m/z\) (EI) 110, 123, 142, 151, 177, 187, 205, 237, 259, 287, 299, 316 (M\(^+\) with \(^79\)Br), 318 (M\(^+\) with \(^81\)Br). HRMS \(m/z\) (EI): 316.0670 (M\(^+\) C\(_{14}\)H\(_{21}\)^{79}BrO\(_4\)^{13} requires 316.0669).
3.0 Synthetic sequence involving cycloaddition with 1,3-cyclohexadiene.

\[
\begin{array}{c}
\text{O} & \text{O} \\
\text{H} & \\
\end{array}
\xrightarrow{\text{SOCl}_2, \text{TEA, PHCH}_3}
\begin{array}{c}
\text{O} & \text{Cl} \\
\end{array}
\]

Piperonyl chloride (20). Piperonyl alcohol (22) (10.0 g, 65.7 mmol) was dissolved in dry toluene (100 mL). Triethylamine (7.98 g, 78.9 mmol) and thionyl chloride (15.6 g, 131 mmol) were added. The reaction mixture was stirred for 24 hrs at 0 °C and then washed with saturated NaHCO₃ (2 × 100 mL) and extracted with ethyl acetate. The combined organic layers were dried over MgSO₄ and concentrated under vacuum to give the desired product 20 as a brown oil (10.9 g, 98 %) which was of sufficient purity for subsequent transformation.

Piperonyl chloride 20

Pale yellow oil. \( R_f \approx 0.30 \) [UV-active, EtOAc/Pet. ether 5 %, anisaldehyde (dark blue spot)]. IR (neat): \( \nu_{\text{max}} \) 2962 (w), 2886 (m, C-H aromatic), 2777 (w), 1504 (s), 1497 (s), 1436 (s), 1363 (s), 1251 (s), 1194 (m), 1100 (m), 1043 (s, O-CH₂-O), 947 (m), 932 (s, O-CH₂-O) cm⁻¹. \(^1\)H NMR (CDCl₃) 4.41 (2H, s, H1), 5.84 (2H, s, H8), 6.64-6.77 (3H, m, H3, H6, H7). \(^{13}\)C NMR (CDCl₃) 46.5 (C1), 101.2 (C8), 108.1 (C6), 109.0 (C3), 122.2 (C7), 131.2 (C2), 147.7 (C4), 147.8 (C5). MS m/z (positive CI, NH₃) 118, 136, 148, 152, 161, 171 (MH⁺), 172, 180, 208, 225. MS m/z (EI) 105, 117, 121, 135, 136, 170 (M⁺ with \(^{35}\)Cl), 171, 172 (M⁺ with \(^{37}\)Cl). HRMS m/z (EI): 170.0137 (M⁺C₈H₇\(^{35}\)ClO₂⁺ requires 170.0129).

Ethyl-2-chloro-3-oxobutanoate (21). Sulfuryl chloride (11.4 g, 84.5 mmol) was added dropwise by dropping funnel to ethyl acetoacetate 23 (10.0 g, 76.8 mmol) in CH₂Cl₂ (65 mL) and maintained at 0 °C. The mixture was stirred overnight at room temperature. The mixture was washed with H₂O (2 × 100 mL), dried over MgSO₄ and concentrated under vacuum to give the desired product 21 as a yellowish oil (12.3 g, 98 %) which was of sufficient purity for subsequent transformation.
Ethyl-2-chloro-3-oxobutanoate 21

Pale yellow oil. IR (neat): \( \nu_{\text{max}} \) 2985 (m), 2941 (w), 1735 (s, C=O), 1645 (w), 1616 (w), 1369 (m), 1255 (s), 1163 (s), 1096 (w), 1070 (w), 1034 (m) cm\(^{-1}\). \(^{1}\)H NMR (CDCl\(_3\)) 1.23-1.31 (3H, m, H6), 2.32 (3H, s, H1), 4.20-4.34 (2H, m, H5), 4.71 (1H, s, H3). \(^{13}\)C NMR (CDCl\(_3\)) 13.5 (C6), 25.9 (C1), 61.0 (C3), 62.7 (C5), 164.6 (C4), 196.1 (C2). MS \( m/z \) (positive CI, NH\(_3\)) 103, 135, 137, 148, 152, 162, 165 (MH\(^+\)), 170, 182, 184. MS \( m/z \) (EI) 118, 120, 121, 122, 124, 136, 164 (M\(^+\) with \(^{35}\)Cl), 166 (M\(^+\) with \(^{37}\)Cl). HRMS \( m/z \) (EI): 164.0245 (M\(^+\)\(\text{C}_{6}\text{H}_{9}\text{ClO}_{3}\text{Cl}^{+}\) requires 164.0235).

2-Chloro-3-(3,4-methylenedioxyphenyl)propanoic acid (19). A solution of ethyl 2-chloroacetooacetate (21) (2.47 g, 15.0 mmol) in DMF (25 mL) was treated with 60 % NaH in oil (0.60 g, 15.0 mmol) at room temperature for 20 min. A solution of 3,4-methylenedioxybenzyl chloride (20) (2.56 g, 15.0 mmol) in DMF (5.0 mL) was added thereto, and the mixture was stirred at 80 °C for 2 hrs, poured into ice-H\(_2\)O and extracted with EtOAc (3×50 mL). The combined organic layers were dried (MgSO\(_4\)) and concentrated at reduced pressure to give solid 19 (3.10 g, 90%).
Ethyl 2-acetyl-2-chloro-3-(3,4-methylenedioxyphenyl) propionate 24

Brown liquid. $^1$H NMR (CDCl$_3$) 1.20 (3H, t, $J = 7.0$ Hz, H12), 2.22 (3H, s, H14), 3.33 (2H, AB system, $\delta_a$ 3.26, $\delta_b$ 3.38, $J_{AB} = 16.1$ Hz, H3), 4.17 (2H, q, $J = 7.0$ Hz, H11), 5.89 (2H, s, H10), 6.57 – 6.66 (3H, m, H5, H6, H9). $^{13}$C NMR (CDCl$_3$) 13.8 (C12), 26.3 (C14), 41.8 (C3), 63.0 (C11), 75.4 (C2), 101.0 (C10), 107.9 (C6), 110.1 (C9), 123.8 (C5), 127.4 (C4), 147.0 (C7), 147.4 (C8), 166.8 (C1), 198.4 (C13).

2-chloro-3-(3,4-methylenedioxyphenyl)propanoic acid 19

Amorphous white solid. $R_t \approx 0.15$ [non UV-active, EtOAc/Pet. ether 50 %, anisaldehyde (red-violet spot)]. IR (neat): $\nu_{\max}$ 3155 (w), 2895 (w), 2902 (w), 2253 (s, C=O), 1795 (w), 1728 (w), 1490 (w), 1469 (m), 1447 (w), 1384 (m), 1166 (w), 1097 (m), 1044 (w, O-CH$_2$-O) cm$^{-1}$. $^1$H NMR (CDCl$_3$) 3.21 (2H, AB part of an ABX system, $\delta_a$ 3.12, $\delta_b$ 3.31, $J_{AB} = 14.1$, $J_{AX} = 7.7$, $J_{BX} = 7.7$ Hz, H3), 4.44 (1H, t, $J = 7.7$ Hz, H2), 5.95 (2H, s, H10), 6.70 (1H, dd, $J = 7.3$, 1.6 Hz, H9), 6.73 (1H, d, $J = 1.6$ Hz, H-5), 6.76 (1H, d, $J = 7.3$ Hz, H-8). $^{13}$C NMR (CDCl$_3$) 40.6 (C3), 57.2 (C2), 101.1 (C10), 108.5 (C8), 109.7 (C5), 122.7 (C9), 129.1 (C4), 147.0 (C7), 147.9 (C6), 173.3 (C1). MS m/z (positive CI, NH$_3$) 135, 137, 152, 175, 192, 195, 210, 229 (MH$^+$ with $^{35}$Cl), 230, 246, 248. MS m/z (EI) 117, 120, 122, 135, 136, 152, 170, 175, 192, 220, 228 (M$^+$ with $^{35}$Cl), 230 (M$^+$ with $^{37}$Cl). HRMS m/z (EI): 228.0186 (M$^+$ C$_{10}$H$_9$O$_2$Cl requires 228.0184).
7-Chloro-7-(3,4-methylenedioxyphenyl)bicyclo[4.2.0]oct-4-en-8-one (25). The 2-chlorocarboxylic acid 19 (0.46 g, 2.0 mmol) was added to 2.0 mL (28.0 mmol) of SOCl₂, and the reaction solution was heated under reflux condition for 3 hrs. The reaction solution was cooled, and the solvent was removed in vacuo. The residue was then dissolved in cyclohexane (5.0 mL).

The residue and cyclohexadiene 15 (504 mg, 6.3 mmol) was treated with triethylamine (0.44 g, 4.3 mmol) within 10 min. The reaction mixture was stirred at reflux for 3 hrs and then filtered. The solid residue was rinsed with cyclohexane (5.0 mL). The filtrate was washed with 1 M HCl (10 mL), 1 M NaHCO₃ (10 mL) and brine (20 mL). After drying over MgSO₄, the organic layer was concentrated and the crude product was purified by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (95:5) to afford 25 (0.15 g, 25 %).

Yellowish oil. 

IR (neat): νmax 3030 (w), 2932 (m), 2775 (s), 1744 (s), 1490 (s), 1249 (s), 1239 (s), 1191 (w), 1120 (w), 1045 (s) cm⁻¹. 1H NMR (CDCl₃) 1.47 (1H, m, H2a), 1.91–2.01 (3H, m, H2b, H3), 2.96 (2H, dd, J = 6.0, 4.4 Hz, H9), 3.11 (1H, m, H6), 4.01 (1H, m, H1), 5.81 (2H, s, H16), 5.84 (1H, m, H5), 5.96 (1H, m, H4), 6.64 (2H, d, J = 8.0, H11, H12), 6.74 (1H, s, H15). 13C NMR (CDCl₃) 18.5 (C2), 21.1(C3), 37.0 (C9), 40.6 (C6), 54.4 (C1), 80.2 (C7), 100.7 (C16), 107.7 (C12), 110.4 (C15), 123.1 (C5), 124.1 (C4), 128.7 (C10), 132.1 (C11), 146.2 (C13), 147.2 (C14), 204.6 (C8). MS m/z (positive CI, NH₃) 108, 136, 170, 255, 274, 291 (MH⁺ with 35Cl), 293 (MH⁺ with 37Cl), 308 (MH⁺.NH₃ with 35Cl), 310 (MH⁺.NH₃ with 37Cl), 342. MS m/z (EI) 105, 135, 136, 149, 170, 179, 210, 235, 255, 267, 290 (M⁺ with 35Cl). HRMS m/z (EI): 290.0711 (M⁺·C₁₆H₁₅ClO₃⁺ requires 290.0704).
7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-en-8-one (26). To a mixture of Zn dust (43.3 mmol, 1.30 g) and TMEDA (20.1 mmol, 3.00 mL) in absolute EtOH (7.0 mL) at 0 °C was added AcOH (30.9 mmol, 1.50 mL). The reaction mixture was maintained at 0 °C while a solution of cyclobutanone 25 (1.00 g, 3.44 mmol) in EtOH (3.0 mL) was added over a 10 min period. After an additional 15 min at 0 °C, the reaction mixture was allowed to warm to room temperature and further stirred for 2 hrs. The resulting grey mixture was filtered, and the solid residue was rinsed with diethyl ether. The filtrate was washed with 1 M HCl (10 mL), H₂O (10 mL), sat. NaHCO₃ (10 mL) and sat NaCl (10 mL). The resulting material was dried over MgSO₄ and concentrated under reduced pressure to afford 0.78 g (88 %) of desired cyclobutanone 26 which was of sufficient purity for subsequent transformation.

(1R*,6S*,7S*)-7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-en-8-one 26

Yellowish oil. Rᵋ ≈ 0.35 [UV-active, EtOAc/Pet. ether 15 %, anisaldehyde (violet spot)]. IR (neat): \( \nu \max \) 3025 (m), 2931 (s), 2653 (m), 2774 (m), 1773 (s, C=O), 1645 (w), 1610 (w), 1505 (s), 1489 (s), 1445 (s), 1413 (w), 1366 (w), 1293 (w), 1247 (s), 1189 (m), 1099 (m), 1043 (s), 942 (m) cm⁻¹. \(^1\)H NMR (CDCl₃) 1.43 (1H, m, H₂a), 1.87-2.02 (3H, m, H₂b, H₃), 2.60 (2H, AB part of an ABX system, \( \delta_A = 2.73, \delta_B = 2.49, J_{AB} = 15.0, J_{AX} = 5.7, J_{BX} = 9.7 \) Hz, H₉), 3.00 (1H, m, H₆), 3.50-3.55 (2H, m, H₁, H₇), 5.70 (1H, m, H₅), 5.84 (2H, s, H₁₆), 5.91 (1H, m, H₄), 6.55-6.66 (3H, m, H₁₁, H₁₂, H₁₅). \(^13\)C NMR (CDCl₃) 18.5 (C₂), 21.3 (C₃), 27.7 (C₆), 30.3 (C₉), 55.0 (C₇), 61.9 (C₁), 100.8 (C₁₆), 108.1 (C₁₂), 108.7 (C₁₅), 121.0 (C₁₁), 125.8 (C₄), 130.4 (C₅), 133.5 (C₁₀), 145.7 (C₁₃), 147.5 (C₁₄), 212.3 (C₈). MS m/z (positive CI, NH₃) 136, 149, 157, 177, 183, 202, 211, 228, 240, 257 (MH⁺), 274 (MH⁺-NH₃), 275. MS m/z (EI) 105, 122, 135, 148, 175, 176, 186, 210, 220, 236, 256 (M⁺), 258. HRMS m/z (EI): 256.1097 (M⁺ C₁₆H₁₆O₃⁺ requires 256.1094).
7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-ene-8-carbaldehyde (29). To a stirred slurry of (methoxymethyl)-triphenylphosphonium chloride 27 (0.58 g, 1.7 mmol) in dry THF (7.0 mL) at −75 °C was added potassium tert-butoxide (0.14 g, 1.3 mmol). After 15 min at −75 °C, a solution of bicyclo[4.2.0]oct-4-ene-8-one 26 (0.22 g, 0.86 mmol) in dry THF (3.0 mL) was added to the mixture, which was further stirred at −75 °C for 10 min, and then at room temperature overnight. The mixture was diluted with water (20 mL) and extracted with ether (30.00 mL). The organic extract was washed with brine (2 × 20 mL), dried over MgSO₄ and concentrated under reduced pressure to give 28 as a yellowish oil, which was used as such in the next transformation.

The crude bicyclo[4.2.0]oct-4-ene 28 was stirred with 90 % formic acid (10 mL) at room temperature for 1 h. The mixture was poured into a saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford a yellowish oil. Purification by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (95:5), gave the desired product 29 as a yellowish oil (94 mg, 41 %, dr 1:2).

(1R*,6S*,7S*)-8-(Methoxymethylene)-7-(3,4-methylenedioxyphenyl)bicyclo[4.2.0]oct-4-ene 28

Yellowish oil. Rf ≈ 0.50 [UV-active, EtOAc/Pet. ether 10 %. anisaldehyde (violet spot)]. ¹H NMR (CDCl₃) 1.90 – 1.45 (3H, m, H2, H3), 2.39 – 2.78 (3H, m, H6, H9), 3.32 – 3.60 (2H, m, H1, H7), 4.07 (3H, s, H18), 5.10 (1H, s, H17), 5.52 – 5.82 (2H, m, H4, H5), 5.85 (2H, s, H16), 6.49 – 6.68 (3H, m, H11, H12, H15). ¹³C NMR (CDCl₃) 20.7 (C3), 21.9 (C2), 34.2 (C6), 35.2 (C9), 37.4 (C7), 44.8 (C1), 59.7 (C18), 100.6 (C16), 108.0 (C12), 108.9 (C15), 121.2 (C11), 126.8 (C4), 128.8 (C8), 131.4 (C5), 133.7 (C10), 139.6 (C17), 145.4 (C13), 147.6 (C14).

© 2024 ACG Publications. All rights reserved.
(1R*,6S*,7S*)-7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-ene-8-carbaldehyde 29

Yellowish oil. \textbf{IR (neat)}: $\nu_{\text{max}}$ 2928 (m), 1717 (s, C=O), 1504 (m), 1484 (s), 1444 (w), 1372 (w), 1226 (m), 1179 (m), 1039 (m, O-CH$_2$-O), 1096 (w), 939 (m, O-CH$_2$-O), 8669 (w) cm$^{-1}$. \textbf{\textsuperscript{1}H NMR (CDCl$_3$)} 0.75 – 2.45 (10H, m, H1, H2, H3, H6, H7, H8, H9), 5.68 (1H, m, H5), 5.82 (2H, s, H16), 5.95 (1H, m, H5), 6.47 – 6.74 (3H, m, H11, H12, H15), 9.33 (1H, s, H17). \textbf{\textsuperscript{13}C NMR (CDCl$_3$)} 21.2 (C3), 29.8 (C2), 31.2 (C9), 34.4 (C6), 36.7 (C1), 41.1 (C7), 51.8 (C8), 100.7 (C16), 108.3 (C12), 109.7 (C15), 121.2 (C11), 126.4 (C5), 129.5 (C4), 130.6 (C10), 145.8 (C13), 146.7 (C14), 202.6 (C17). \textbf{MS m/z (EI)} 115, 135, 173, 190, 224, 252, 270 (M$^+$), 298, 304. \textbf{HRMS m/z (EI)}: 270.1262 (M$^+$C$_{17}$H$_{18}$O$_3$ requires 270.1250).

\begin{center}
\begin{tabular}{c}
\includegraphics[width=0.5\textwidth]{reaction_diagram}
\end{tabular}
\end{center}

\textbf{4-[7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-en-8-ylidene]butanoic acid (30).} To a stirred slurry of (3-carboxypropyl)-triphenylphosphonium bromide 9 (0.77 g, 1.8 mmol) in dry THF (7.0 mL) at $-75^\circ$C was added potassium tert-butoxide (0.35 g, 3.1 mmol). After 15 min at $-75^\circ$C, a solution of cyclobutanone 26 (0.21 g, 0.8 mmol) in dry THF (3.0 mL) was added to the mixture, which was further stirred at $-75^\circ$C for 10 min, and then at room temperature overnight. The mixture was poured into 5 % Na$_2$CO$_3$ solution (20 mL), washed with ethyl acetate (20 mL), and then acidified with conc. HCl. The aqueous layer was extracted with ether (3 x 20 mL) and the combined extract was concentrated to 20 mL, then kept at $-20^\circ$C for 2 hrs. The resulting precipitate was filtered off and discarded. Evaporation the filtrate gave a yellowish oil (0.66 g) which was purified by column chromatography on silica gel, eluting with petroleum ether/ethyl acetate (7:3), to give the desired product 30 in \textit{Z/E} isomer ratio of 2:1, as a yellowish oil (0.26 g, 32%).

\copyright 2024 ACG Publications. All rights reserved.
4-[(1R*,6S*,7S*)-7-(3,4-Methylenedioxyphenyl)bicyclo[4.2.0]oct-4-en-8-ylidene]butanoic acid 30

Yellowish oil. $R_l \approx 0.30$ [UV-active, EtOAc/Pet. ether 60 %, anisaldehyde (blue spot)]. **IR (neat):** $\nu_{\text{max}}$ 2928 (s), 2863 (m), 1738 (s, C=O), 1504 (m), 1490 (m), 1246 (s), 1188 (m), 1040 (m, O-CH$_2$O), 927 (m, O-CH$_2$O), 859 (w), 810 (w) cm$^{-1}$. **$^1$H NMR (CDCl$_3$) 1.44 (1H, m, H$_2$a), 1.86 – 1.97 (3H, m, H$_{2b}$, H$_3$), 2.20 – 2.36 (4H, m, H$_{18}$, H$_{19}$), 2.53 (2H, dd, $J = 6.0, 4.4$ Hz, H$_9$), 2.79 (1H, m, H$_6$), 3.22 (2H, m, H$_1$, H$_7$), 4.97 (1H, t, $J = 7.2$ Hz, H$_{17}$), 5.57 (1H, m, H$_5$), 5.84 (2H, s, H$_{16}$), 5.92 (1H, m, H$_4$), 6.54 (1H, dd, $J = 8.1, 2.0$ Hz, H$_{11}$), 6.60 (1H, d, $J = 2.0$ Hz, H$_{15}$), 6.63 (1H, d, $J = 8.1$ Hz, H$_{12}$). **$^{13}$C NMR (CDCl$_3$) 21.9 (C$_3$), 23.1 (C$_2$), 23.7 (C$_{18}$), 33.6 (C$_6$), 34.2 (C$_{19}$), 34.9 (C$_9$), 39.2 (C$_7$), 46.6 (C$_1$), 100.7 (C$_{16}$), 108.0 (C$_{12}$), 109 (C$_{15}$), 118.0 (C$_{17}$), 121.2 (C$_{11}$), 126.8 (C$_5$), 129.9 (C$_4$), 135.0 (C$_{10}$), 145.4 (C$_{13}$), 146.6 (C$_8$), 147.4 (C$_{14}$), 179.0 (C$_{20}$). **MS $m/z$ (EI) 106, 132, 135, 136, 137, 148, 149, 174, 185, 239, 272, 274, 298, 326 (M$^+$). **HRMS $m/z$ (EI): 326.1515 (M$^+$). C$_{20}$H$_{22}$O$_4$ requires 326.1513.

**Methyl 4-[7-(3,4-methylenedioxyphenyl)bicyclo[4.2.0]octan-8-yl]butanoate (31).** To a solution of the bicycloalkene 30 (55 mg, 0.2 mmol) in MeOH (2.0 mL) was added 10 % Pd/C (10 % w/w, 5.5 mg), and the resulting mixture was hydrogenated at 1 atm for 12 hrs. Filtration through Celite and evaporation of the filtrate in vacuo afforded pure 31 ($dr$ 3:1) as yellowish oil (47 mg, 80 %).

© 2024 ACG Publications. All rights reserved.
Yellowish oil. \( R_f \approx 0.35 \) [UV-active, EtOAc/Pet. ether 60 %, anisaldehyde (blue spot)]. **IR (neat):** \( \nu_{\text{max}} \) 2929 (s), 2863 (m), 1739 (s, C=O), 1504 (s), 1490 (s), 1442 (m), 1246 (s), 1188 (m), 1122 (w), 1096 (w), 1040 (m, O-CH2-O), 927 (m, O-CH2-O), 861 (w), 811 (w) cm\(^{-1}\). **\(^1\)H NMR (CDCl\(_3\))** 1.14 – 1.23 (4H, m, H3, H4), 1.39 – 1.59 (H8, m, H2, H5, H17, H18), 2.15 – 2.24 (3H, m, H8, H19), 2.30 – 2.40 (2H, H1, H6), 2.62 – 2.74 (3H, m, H7, H9), 3.58 (3H, s, H21), 5.82 (2H, s, H16), 6.55 (1H, dd, \( J = 8.1, 1.7 \) Hz, H11), 6.60 (1H, d, \( J = 1.7 \) Hz, H15), 6.62 (1H, d, \( J = 8.1 \) Hz, H12). **\(^13\)C NMR (CDCl\(_3\))** 22.6 (C3), 22.7 (C4), 23.1 (C2), 23.2 (C5), 24.8 (C18), 27.6 (C17), 32.9 (C9), 33.8 (C6), 34.1 (C8), 34.4 (C19), 40.2 (C1), 40.3 (C7), 51.6 (C21), 100.6 (C16), 108.1 (C12), 108.9 (C15), 121.2 (C11), 136.2 (C10), 145.2 (C13), 147.4 (C14), 174.3 (C20). **MS \( m/z \) (EI)** 102, 145, 158, 167, 194, 214, 239, 279, 295, 313, 325, 331, 344 (M\(^+\)), 362, 380. **HRMS \( m/z \) (EI):** 344.1992 (M\(^+\) \( \text{C}_{21}\text{H}_{28}\text{O}_4 \) requires 344.1982).
Figure S1: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 6.

Figure S2: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 6.
Figure S3: IR spectrum of compound 6.

Figure S4: MS spectrum (positive Cl, NH3) of compound 6.
Figure S5: HRMS spectrum (EI) of compound 6.

Figure S6: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 7.
Figure S7: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 7.

Figure S8: IR spectrum of compound 7.
Figure S9: MS spectrum (positive Cl, NH₃) of compound 7.

Figure S10: HRMS spectrum (EI) of compound 7.
Figure S11: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 8.

Figure S12: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 8.

© 2024 ACG Publications. All rights reserved.
Figure S13: IR spectrum of compound 8.

Figure S14: MS spectrum (positive Cl, NH₃) of compound 8.
Figure S15: HRMS spectrum (EI) of compound 8.

Figure S16: 'H NMR spectrum (CDCl₃, 400 MHz) of compound 10.
Figure S17: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 10.

Figure S18: MS spectrum (EI) of compound 10.
Figure S19: HRMS spectrum (EI) of compound 10.

Figure S20: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 11.
Figure S21: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 11.

Figure S22: HRMS spectrum (EI) of compound 11.
Figure S23: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 13.

Figure S24: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 13.
Figure S25: MS spectrum (positive CI, NH$_3$) of compound 13.

Figure S26: HRMS spectrum (EI) of compound 13.
**Figure S27**: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 19.

**Figure S28**: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 19.
Figure S29: IR spectrum of compound 19.

Figure S30: HRMS spectrum (EI) of compound 19.

© 2024 ACG Publications. All rights reserved.
Figure S31: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 20.

Figure S32: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 20.
Figure S33: IR spectrum of compound 20.

Figure S34: MS spectrum (positive CI, NH₃) of compound 20.
Figure S35: HRMS spectrum (EI) of compound 20.

Figure S36: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 21.
Figure S37: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 21.

Figure S38: IR spectrum of compound 21.
Figure S39: MS spectrum (positive Cl, NH₃) of compound 21.

Figure S40: HRMS spectrum (EI) of compound 21.
Figure S41: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 25.

Figure S42: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 25.
Figure S43: IR spectrum of compound 25.

Figure S44: HRMS spectrum (EI) of compound 25.
Figure S45: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 26.

Figure S46: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 26.
Figure S47: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 29.

Figure S48: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 29.
Figure S49: IR spectrum of compound 29.

Figure S50: HRMS spectrum (EI) of compound 29.
Figure S51: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 30.

Figure S52: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 30.
**Figure S53**: HRMS spectrum (EI) of compound 30.

**Figure S54**: $^1$H NMR spectrum (CDCl$_3$, 400 MHz) of compound 31.
Figure S55: $^{13}$C NMR spectra (CDCl$_3$, 100.6 MHz) of compound 31.

Figure S56: IR spectrum of compound 31.