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Imidazolium chiral ionic liquids deriving carbenes -catalyzed conjugate umpolung for synthesis of γ-butyrolactones

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Supporting information

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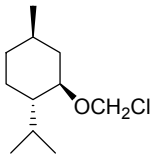
Experimental

1. General

All chemicals were used as purchased and of chemically pure or reagent grade. All solvents were purified and dried according to standard methods prior to use. All the glass vessels were dried before use. Thin layer chromatography (TLC) was conducted on glass plates coated with silica gel GF_{254}. The reaction products were analyzed by a HPLC (Waters 600 controller) equipped with an ultraviolet absorption detector and a capillary column (Venusil MP-C18, 5 μm, 4.6×250 mm) or a chiral capillary column (AD-H, 5 μm, 4.6×250 mm). ^{1}H and ^{13}C NMR spectra (500 and 125 MHz, respectively) were recorded on a Brucker AV 500 MHz spectrometer with tetramethylsilane as the standard. The melting point was determined by using an X-4A microscopic melting apparatus and uncorrected.

2. Preparation of chloromethyl (1R,2S,5R)-(-)-menthyl ether

Chloromethyl (-)-menthyl ether was prepared by following the published procedure with a slight modification. (1R,2S,5R)-(-)-menthol (98%, 9.55 g, 60 mmol), paraformaldehyde (96%, 1.88 g, 60 mmol), and toluene (50 mL) were added to a 100 mL three-neck flask equipped with a thermometer and a gas absorption device. With stirring, gaseous hydrogen chloride was introduced into the reaction mixture until the solution was saturated for about 2 h. During this process, the reaction temperature was kept at 10 °C. After the reaction, the solution was elevated to room temperature and stirred for another 1 h. Then, the filtrate was collected by filtration, and dried over anhydrous $MgSO_4$. Superfluous hydrogen chloride in the solution was stripped off with dry nitrogen. After that, the solvent was removed by atmospheric distillation and the residue was purified by fractional distillation under vacuum to afford the corresponding product as colorless oil: 106~108 °C/8 mmHg. Yield: 8.83 g, 72%. ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.56-5.61 (dd, J=20.5 Hz, 5.5 Hz, 2H), 3.52-3.54 (m, 1H), 2.14 (m, 2H), 1.66 (m, 2H), 1.40 (m, 1H), 1.22 (m, 1H), 1.01 (m, 1H), 0.86-0.95 (m, 8H), 0.80 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 81.2, 78.7, 47.7, 39.8, 34.1, 31.3, 25.0, 22.9, 22.1, 20.9, 15.8.

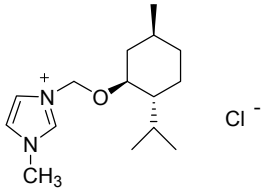


3. General procedure for quaternization

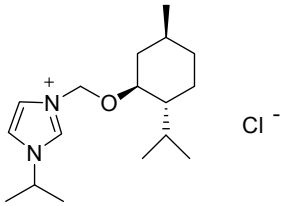
Chloromethyl (-)-menthyl ether (0.01 mol), N-substituted imidazole (0.01 mol), and 30 mL dried acetonitrile were mixed in a 100 mL round-bottomed flask with a reflux condenser (potassium hydroxide drying tube) and heated under reflux for 24 h with efficient stirring. After cooling to room temperature, the solvent was removed under atmospheric distillation to give a sticky residue. The residue was washed with 2×15 mL anhydrous diethyl ether to remove any residual materials, followed by drying in high vacuum to afford the corresponding product.

3.1. 3-methyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium chloride **1a**. Colorless solid, m.p. 104~105 ^{o}C. ^{1}H NMR (500 MHz, DMSO): δ 9.30 (s, 1H), 7.90 (s, 1H), 7.74 (s,1H), 5.59 (d, J=12.0 Hz, 1H), 5.56 (d, J=12.0 Hz, 1H), 3.88 (s, 3H), 3.24 (m, 1H), 2.04 (m, 1H), 1.87 (m, 1H),

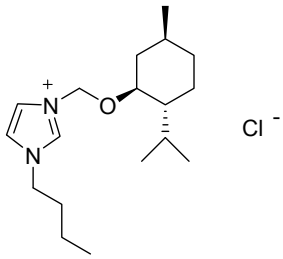
1.54-1.61 (m, 2H), 1.34 (m, 1H), 1.14 (m, 1H), 0.78-0.89 (m, 9H), 0.40 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.5, 129.0, 119.9, 78.8, 76.3, 48.3, 42.1, 40.7, 34.1, 33.0, 31.3, 25.1, 22.8,22.0, 20.9, 15.8.



3.2. 3-isopropyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium chloride **1b**. Colorless solid, m.p. 54~55 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.16 (s, 1H), 7.71 (s, 1H), 7.51 (s, 1H), 5.99 (d, J=10.5 Hz, 1H), 5.69 (d, J=10.5 Hz, 1H), 4.92 (m, 1H), 3.43 (m, 1H), 2.14 (m, 1H), 1.93 (m, 1H), 1.64 (d, J=6.5 Hz, 6H), 1.59 (m, 2H), 1.53 (m, 1H), 1.23 (m, 1H), 0.76-0.96 (m, 9H), 0.46 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.8, 121.4, 120.1, 79.4, 76.7, 53.3, 47.5, 40.0, 33.9, 30.9, 25.2, 23.6, 22.7, 21.9, 20.7, 15.1.



3.3. 3-*n*-butyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium chloride **1c**. Colorless solid, m.p. 60~62 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.56 (s, 1H), 7.50 (s, 1H), 7.47 (s, 1H), 5.85 (d, J=10.5 Hz, 1H), 5.65 (d, J=10.5 Hz, 1H), 4.30 (t, J=7.0 Hz, 2H), 3.28 (m, 1H), 2.10 (m, 1H), 1.95 (m, 1H), 1.80 (m, 2H), 1.52 (m, 2H), 1.26 (m, 3H), 1.15 (m, 1H), 0.70-0.87 (m, 12H), 0.40 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.2, 122.3, 121.4, 79.4, 76.7, 49.6, 47.5, 40.0, 33.9, 31.8, 30.9, 25.2, 22.6, 21.8, 20.7, 19.1, 15.1, 13.0.



3.4. 3-benzyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium chloride **1d**. Colorless solid, m.p. 65~67 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.00 (s, 1H), 7.36-7.53 (m, 7H), 5.85 (d, J=10.5 Hz, 1H), 5.66 (d, J=10.5 Hz, 1H), 5.62 (s, 2H), 3.37 (m, 1H), 2.03 (m, 1H), 1.88 (m, 1H), 1.57-1.62 (m, 2H), 1.40 (m, 1H), 1.21 (m, 1H), 0.77-0.93 (m, 9H), 0.40 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.3, 133.0, 129.2, 128.7, 128.5, 122.1, 121.2, 116.3, 79.7, 77.0, 53.2, 47.4, 40.1, 33.7, 30.9, 25.1, 22.5, 21.9, 20.6, 15.2.

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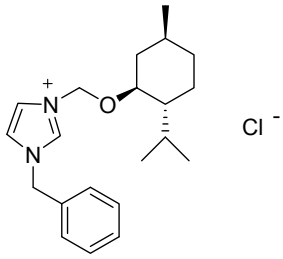
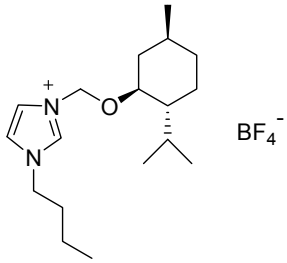


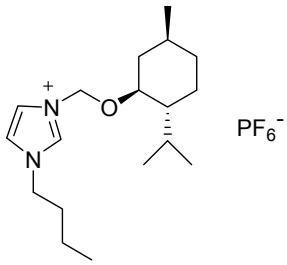
4. General procedure for ion exchange

Chiral imidazolium chloride **1** was dissolved in methanol, then an excess and saturated aqueous solution of $NaBF_4$, $NaPF_6$, CF_3COONa or CF_3SO_3Na was added. The reaction mixture was stirred at room temperature for 24 h producing a heterogeneous mixture. After completion of the reaction, the crude product was separated from the reaction mixture by filtration, and washed twice with distilled water to remove any inorganic salt. The obtained residue was dried in vacuo. In the cases of water soluble product, the water was first evaporated and the remnant was dissolved in dry acetone. The inorganic salt was precipitated and separated. Then, the solvent was evaporated to give the corresponding product.

4.1. 3-*n*-butyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium tetrafluoroborate **2a**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.38 (s, 1H), 7.46 (s, 1H), 7.43 (s,1H), 5.66 (d, J=11.0 Hz, 1H), 5.54 (d, J=11.0 Hz, 1H), 4.24 (t, J=7.0 Hz, 2H), 3.25 (m, 1H), 1.85 (m, 4H), 1.60 (m, 2H), 1.32 (m, 3H), 1.24 (m, 1H), 0.83-0.95 (m, 12H), 0.45 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 135.6, 122.8, 121.6, 79.7, 76.7, 49.7, 47.5, 40.0, 33.9, 31.7, 30.9, 25.2, 22.7, 21.8, 20.6, 19.1, 15.4, 13.0.



4.2. 3- *n*-butyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium hexafluorophosphate **2b**. Colorless solid, m.p. 40~42 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.94 (s, 1H), 7.45 (s, 1H), 7.38 (s,1H), 5.59 (d, J=10.5 Hz, 1H), 5.52 (d, J=10.5 Hz, 1H), 4.21 (t, J=7.0 Hz, 2H), 3.28 (m, 1H), 1.90 (m, 2H), 1.83 (m, 2H), 1.61 (m, 2H), 1.35 (m, 3H), 1.22 (m, 1H), 0.74-0.96 (m, 12H), 0.45 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 138.1, 121.9, 120.9, 79.8, 76.7, 49.9, 47.6, 40.3, 33.9, 32.0, 31.0, 25.4, 22.7, 22.0, 20.9, 19.4, 15.5, 13.3.



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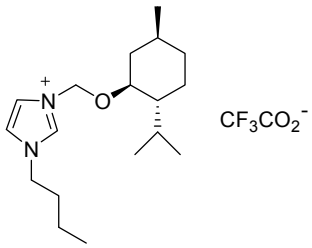
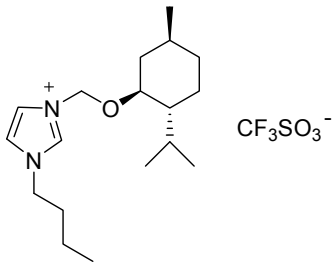
4.3. 3-*n*-butyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium trifluoacetate **2c**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.03 (s, 1H), 7.41 (s, 1H), 7.36 (s,1H), 5.68 (d, J=11.0 Hz, 1H), 5.52 (d, J=11.0 Hz, 1H), 4.20 (t, J=6.5 Hz, 2H), 3.24 (m, 1H), 1.94 (m, 2H), 1.79 (m, 2H), 1.58 (m, 2H), 1.29 (m, 3H), 1.19 (m, 1H), 0.80-0.91 (m, 12H), 0.42 (d, J=7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.1, 120.9, 119.4, 79.8, 76.7, 50.7, 48.0, 40.8, 33.5, 31.9, 30.9, 26.0, 23.3, 22.7, 21.6, 20.0, 16.1, 13.9.



4.4. 3-*n*-butyl-1-(1R,2S,5R)-(-)-menthoxymethyl imidazolium trifluomethanesulfonate **2d**. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.57 (s, 1H), 7.65 (s, 1H), 7.43 (s,1H), 5.75 (d, J=11.0 Hz, 1H), 5.53 (d, J=11.0 Hz, 1H), 4.23 (t, J=6.5 Hz, 2H), 3.23 (m, 1H), 1.91 (m, 2H), 1.87 (m, 2H), 1.44 (m, 2H), 1.21 (m, 3H), 1.07 (m, 1H), 0.87-0.98 (m, 12H), 0.50 (d, J=6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 136.3, 122.7, 121.5, 79.8, 76.7, 49.9, 47.6, 40.1, 33.9, 31.9, 30.9, 25.3, 22.7, 21.9, 20.8, 19.2, 15.3, 13.2.

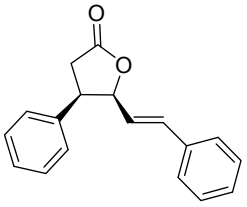


5. General procedure for synthesis of γ-butyrolactones

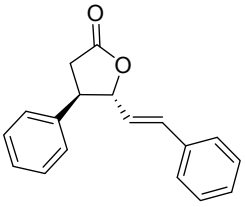
Under an atmosphere of nitrogen, the ionic liquids catalyst **1** or **2** (0.1 mmol) and potassium *tert*-butoxide (0.2 mmol) were dissolved in THF (5 mL) and stirred for 30 min at room temperature. Freshly distilled *trans*-cinnamaldehyde (1 mmol) and the corresponding aromatic aldehyde (2 mmol) were added to the above solution. Then, the mixture was stirred at room temperature. After the reaction time indicated, the solvent was evaporated in vacuo. The remnants were extracted with ethyl acetate for several times. The lower ionic liquids catalyst could be recovered and reused. The upper extract was combined and dried over anhydrous sodium sulfate. After the evaporation of volatile solvent, the crude products were purified by silica gel column chromatography. Alternatively, the products were analysed by the HPLC.

5.1. 3-phenyl-4-[(E)-styryl]-γ-butyrolactone **3**. Prepared according to the general procedure only using *trans*-cinnamaldehyde. The products were isolated by column chromatography (4:1 hexane/EtOAc). c*is*-**3**: colorless needle crystal, m.p. 75-76 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34-7.36 (m, 2H), 7.31 (m, 1H), 7.21-7.24 (m, 3H), 7.13-7.17 (m, 4H), 6.61 (d, J=11.0 Hz, 1H), 5.63 (dd, J=6.5 Hz, 6.5 Hz, 1H), 5.38 (m, 1H), 3.94 (m, 1H), 2.95 (dd, J=17.0 Hz, 7.2 Hz, 1H), 2.92 (dd, J=17.0 Hz, 7.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.2, 136.9, 135.8, 133.4,

126.6-129.3, 123.8, 83.5, 45.6, 34.2. *trans*-**3**: colorless solid, m.p. 62-64 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27-7.40 (m, 10H), 6.60 (d, J=11.0 Hz, 1H), 6.23 (dd, J=16.5 Hz, 7.0 Hz, 1H), 5.03-5.06 (m, 1H), 3.52-3.55 (m, 1H), 3.03 (dd, J=17.5 Hz, 8.5 Hz, 1H), 2.87 (dd, J=17.5 Hz, 10.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 175.2, 137.9, 135.6, 133.4, 132.3, 126.3-129.1, 124.7, 86.7, 48.3, 36.6.

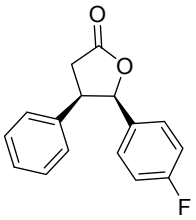


cis-**3**

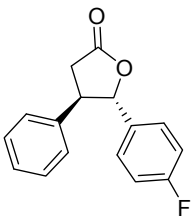


trans-**3**

5.2. 3-phenyl-4-(*p*-fluorophenyl)-γ-butyrolactone **4**. Prepared according to the general procedure using *trans*-cinnamaldehyde and *p*-fluorobenzaldehyde. The products were isolated by column chromatography (4:1 hexane/EtOAc). *cis*-**4**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13-7.26 (m, 3H), 6.80-6.87 (m, 6H), 5.81 (d, J=7.0 Hz, 1H), 4.03 (m, 1H), 3.07 (dd, J=17.5 Hz, 8.5 Hz, 1H), 2.95 (dd, J=17.5 Hz, 6.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.8, 137.4, 133.4, 126.7-129.1, 115.5, 86.7, 50.7, 37.1. *trans*-**4**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31-7.38 (m, 5H), 7.22 (m, 2H), 7.07 (m, 2H), 5.43 (d, J=8.5 Hz, 1H), 3.58 (m, 1H), 3.10 (dd, J=17.5 Hz, 8.5 Hz, 1H), 3.03 (dd, J=17.5 Hz, 11.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.38, 140.0, 136.0, 129.2-132.4, 118.0, 89.3, 53.3, 39.6.



cis-**4**



trans-**4**

5.3. 3-phenyl-4-(*p*-bromophenyl)-γ-butyrolactone **5**. Prepared according to the general procedure using *trans*-cinnamaldehyde and *p*-bromobenzaldehyde. The products were isolated by column chromatography (6:1 hexane/EtOAc). *cis*-**5**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12-7.14 (m, 3H), 6.79-6.87 (m, 6H), 5.80 (d, J=7.0 Hz, 1H), 4.03 (m, 1H), 3.06 (dd, J=17.5 Hz, 8.5 Hz, 1H), 2.93 (dd, J=17.5 Hz, 6.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 137.1, 133.2, 129.1, 128.6, 128.4, 128.0, 127.9, 127.6, 127.5, 127.3, 118.1, 84.6, 47.0, 36.8. *trans*-**5**: light yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.36 (m, 5H), 7.18 (m, 2H), 7.01-7.05 (m, 2H), 5.40 (d, J=8.5 Hz, 1H), 3.56 (m, 1H), 3.07 (dd, J=17.5 Hz, 8.0 Hz, 1H), 2.95 (dd, J=17.5 Hz, 11.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.8, 139.7, 135.8, 131.4, 130.7, 130.3, 130.1, 129.9, 129.8, 129.6, 129.5, 129.1, 117.2, 88.3, 50.7, 38.5.

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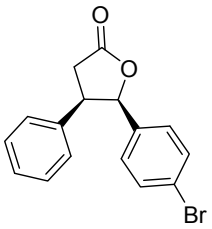
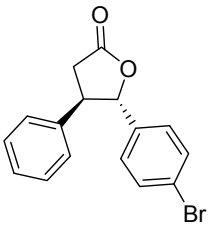
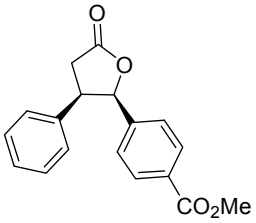


cis-**5**

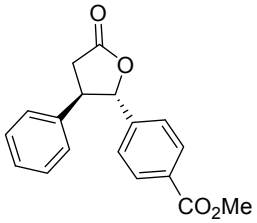


trans-**5**

5.4. 3-phenyl-4-(*p*-methoxycarbonyl)phenyl-γ-butyrolactone **6**. Prepared according to the general procedure using *trans*-cinnamaldehyde and *p*-methoxycarbonyl benzaldehyde. The products were isolated by column chromatography (5:1 hexane/EtOAc). *cis*-**6**: colorless solid, m.p. 157-160 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J=6.5 Hz, 2H), 7.11 (m, 3H), 7.00 (d, J=8.0 Hz, 2H), 6.82 (m, 2H), 5.87 (d, J=7.0 Hz, 1H), 4.10 (m, 1H), 3.87 (s, 3H), 3.10 (dd, J=17.0 Hz, 8.0 Hz, 1H), 2.95 (dd, J=17.0 Hz, 5.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 166.6, 140.7, 136.4, 129.7, 129.3, 128.6, 127.8, 127.6, 125.7, 84.1, 52.1, 46.8, 35.2. *trans*-**6**: colorless solid, m.p. 116-118 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J=8.0 Hz, 2H), 7.37-7.43 (m, 3H), 7.29 (m, 2H), 7.21 (m, 2H), 5.51 (d, J=9.0 Hz, 1H), 3.96 (s, 3H), 3.57 (m, 1H), 3.12 (dd, J=17.5 Hz, 8.5 Hz, 1H), 3.00 (dd, J=17.5 Hz, 11.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2, 165.6, 140.2, 135.6, 129.8, 129.7, 128.7, 128.0, 127.8, 126.2, 85.2, 52.5, 47.2, 37.0.

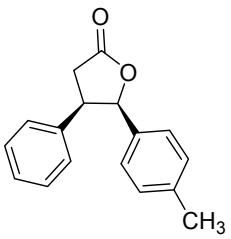


cis-**6**

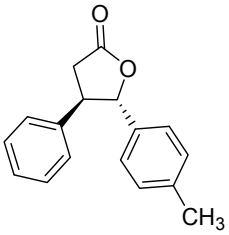


trans-**6**

5.5. 3-phenyl-4-(*p*-tolyl)-γ-butyrolactone **7**. Prepared according to the general procedure using *trans*-cinnamaldehyde and *p*-methylbenzaldehyde. The products were isolated by column chromatography (5:1 hexane/EtOAc). *cis*-**7**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09-7.17 (m, 3H), 6.83-6.91 (m, 2H), 6.82 (m, 2H), 6.76 (m, 2H), 5.79 (d, J=7.0 Hz, 1H), 4.03 (m, 1H), 3.02 (dd, J=17.5Hz, 8.0 Hz, 1H), 2.93 (dd, J=17.5 Hz, 6.5 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 137.5, 136.6, 132.3, 128.6, 128.2, 128.0, 127.8, 127.3, 125.6, 84.7, 46.9, 34.8, 21.0. *trans*-**7**: colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23-7.31 (m, 5H), 7.18 (m, 2H), 7.04 (m, 2H), 5.47 (d, J=8.5 Hz, 1H), 3.53 (m, 1H), 3.06 (dd, J=17.5 Hz, 8.5 Hz, 1H), 2.98 (dd, J=17.5 Hz, 11.5 Hz, 1H), 2.26 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 138.7, 137.5, 132.9, 129.7, 129.1, 128.7, 128.1, 127.9, 126.6, 85.8, 47.5, 35.2, 21.2.



cis-**7**



trans-**7**