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SUPPORTING INFORMATION

Title: α-Haloenol Acetates: Versatile Reactants for Oxetan-2-one, Azetidin-2-one and Isoxazolidin-5-one Synthesis
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Triethylaluminum (25 % in toluene) was purchased from Aldrich, diethylaluminum ethoxide (25% in toluene) was purchased from Acros. Tetrahydrofuran (THF) was distilled over Na/benzophenone ketyl.
GC/MS analyses were carried out using a Shimadzu GCMS-QP5050A with a SGE silica capillary 25 m x 0.22 mm BPX5 column (5% phenyl polysilphenylene-siloxane / 95% methylpolysiloxane), helium carrier gas (29 mL/min; 113 kPa), 260 °C interface, 80 °C column temp., 320 °C detector, programmed for 2 min at 80 °C, then heating.

4-Phenylbutanoic acid

A solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate **1a** (50 µL, 0.25 mmol) and lithium hydroxide (24 mg, 1.0 mmol) in THF (1.0 mL) and water (1.0 mL) was stirred for 3 h at RT. The reaction mixture was acidified with 5% aqueous HCl (2.0 mL) and diluted with Et_2O. The layers were separated and the aqueous phase was extracted twice with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4. Concentration under vacuum afforded 4-Phenylbutanoic acid in quantitative yield (41 mg).

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.36-7.18 (m, 5H), 2.70 (t, *J* = 7.3 Hz, 2H), 2.40 (t, *J* = 7.3 Hz, 2H), 1.99 ppm (quint, *J* = 7.3 Hz, 2H).

***N*-Benzyl-4-phenylbutanamide and *N*-Acetyl-4-phenylbutanamide**

To a solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate **1a** (50 µL, 0.25 mmol) in anhydrous THF (2.5 mL), at RT under argon, was added benzylamine (82 µL, 0.75 mmol). The reaction mixture was stirred 5 min at RT until the appearance of a white solid. Then, aqueous ammonia was added until dissolution of the white precipitate. Concentration under vacuum and purification by column chromatography on silica gel (AcOEt/*c*-hexane = 3:7 to 1:1) afforded white needles of *N*-Benzyl-4-phenylbutanamide (53 mg, 83%) and white needles of *N*-Acetyl-4-phenylbutanamide (29 mg, 77%).

N-Benzyl-4-phenylbutanamide: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.16 (m, 10H), 5.89 (brs, 1H), 4.43 (d, *J* = 4.4 Hz, 2H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.25-2.19 (m, 2H), 2.04-1.98 ppm (m, 2H) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.8, 141.5, 138.4, 128.8, 128.6, 128.5, 127.6, 126.0, 43.6, 36.0, 35.3, 27.2 ppm ; mp 82-83 °C.

N-Acetyl-4-phenylbutanamide: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.25 (m, 5H), 6.11 (brs, 1H), 4.41 (d, *J* = 3.1 Hz, 2H), 2.00 ppm (s, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.4, 138.4, 128.8, 127.9, 127.6, 43.8, 23.4 ppm ; mp 62-63 °C.

2-Acetyl-3-methyl-4-(2-phenylethyl)isoxazol-5(2*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.13 (m, 5H), 2.89-2.78 (m, 2H), 2.55 (t, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 2.17 ppm (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.1, 165.0, 154.0, 140.6, 128.8, 128.6, 126.5, 105.9, 34.2, 27.0, 24.0, 13.2 ppm; IR : ν 1767, 1717 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{14}H_{15}N_1Na_1O_3$ (M^+) *m/z* 268.0950, found 268.0941.

Ethyl 3-oxo-6-phenyl-2-(2-phenylethyl)hexanoate: To a solution of triethylaluminum (25 % in toluene, 0.75 mL) was carefully added anhydrous ethanol (73 µL, 1.25 mmol) at -78 °C under argon. The solution was warmed to RT and diluted with anhydrous THF (2.0 mL). Then, (*Z*)-1-chloro-4-phenylbut-1-enyl acetate (50 µL, 0.25 mmol) and DMSO (36 µL, 0.5 mmol) were added to the solution of diethylaluminum ethoxide, at 0 °C under argon. After the reaction mixture was stirred for 15 h from 0 °C to RT, saturated aqueous potassium, sodium tartrate and ethyl acetate were added and the mixture was stirred for an additional 30 min at RT. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were washed with brine, then dried over Na_2SO_4. After concentration under vacuum, the crude product was purified by chromatography on silica gel to afford 16 mg of ethyl 3-oxo-6-phenyl-2-(2-phenylethyl)hexanoate (38 %) as a colourless oil.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33-7.14 (m, 10H), 4.18 (q, *J* = 7.1 Hz, 2H), 3.42 (t, *J* = 7.1 Hz, 1H), 2.66-2.44 (m, 6H), 2.23-2.10 (m, 2H), 1.92 (quint, *J* = 7.1 Hz, 2H), 1.25 ppm (t, *J* = 7.1 Hz, 3H) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ 205.0, 169.8, 141.6, 140.9, 128.62, 128.56, 126.3, 126.1, 61.5, 58.3, 41.2, 35.0, 33.5, 29.7, 25.0, 14.2 ppm ; IR : ν 1742, 1714 cm^{-1}; GC (heating at 25 °C/min) t_R = 11.22 min ; MS (CI, NH_3) *m/z* 339 ($[M+H]^+$) ; HRMS (IE) calcd for $C_{22}H_{26}O_3$ ($[M]^+$) *m/z* 331,1882, found 338.1871.

Isopropyl 2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate

To a solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate (50 µL, 0.25 mmol) and *p*-tolualdehyde (36 µL, 0,3 mmol) in anhydrous THF (2.5 mL) was added a solution of titanium isopropoxide (150 µL, 0.5 mmol), at 0 °C under argon. After the reaction mixture was stirred for 15 h from 0 °C to RT, brine and ethyl acetate were added. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were washed with brine and dried over Na_2SO_4. After concentration under vacuum, the crude product was purified by chromatography (diethyl ether / *c*-hexane 3:7) on silica gel to give 60 mg (74 %) of isopropyl 2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate.

Isopropyl *syn*-2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.09 (d, *J* = 6.4 Hz, 3H), 1.21 (d, *J* = 6.4 Hz, 3H), 1.96-2.10 (m, 2H), 2.34 (s, 3H), 2.44-2.55 (m, 1H), 2.61-2.90 (m, 3H), 4.91 (d, *J* = 5.7 Hz, 1H), 4.97 (sep, *J* = 6.4 Hz, 1H), 7.09-7.34 ppm (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 21.7, 21.9, 29.2, 33.8, 52.7, 68.2, 74.3, 126.0, 126.3, 128.5, 129.1, 137.5, 138.6, 141.7, 174.3 ppm.

Isopropyl *anti*-2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.4 Hz, 3H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.66-1.74 (m, 2H), 1.95-2.00 (m, 1H), 2.34 (s, 3H), 2.48-2.70 (m, 2H), 2.74-2.82 (m, 1H), 4.80 (d, *J* = 7.9 Hz, 1H), 5.09 (sep, *J* = 6.4 Hz, 1H), 7.09-7.34 ppm (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 21.9, 22.0, 31.3, 33.4, 52.7, 68.3, 75.2, 126.1, 126.5, 128.5, 129.3, 137.8, 139.0, 141.4, 174.8 ppm.

Isopropyl 2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate (*syn*/*anti* ≈ 1:1): IR (neat): ν 3500, 1726 cm^{-1}; MS (CI, NH_3) *m/z* (%): 309 (100) $[M\text{-}OH]^+$, 326 (15) $[M]^+$.

Ethyl 4-phenylbutanoate

A solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate (50 µL, 0.25 mmol) and diethylaluminum ethoxide (180 µL, 0.3 mmol) in anhydrous THF (2.5 mL) was refluxed for 1 h under argon. The reaction mixture was cooled to RT, quenched with K,Na tartrate and diluted with AcOEt. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were dried over Na_2SO_4. After concentration under vacuum, the crude product was purified by chromatography (diethyl ether / *c*-hexane 2:8) on silica gel to give 44 mg (92 %) of ethyl 4-phenylbutanoate as colourless oil.

Reactivity with commercial Et_2AlOEt

To a solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate **1a** (50 µL, 0.25 mmol) and *p*-tolualdehyde (60 µL, 0.5 mmol) in anhydrous THF (2.0 mL) was added a commercial solution of diethylaluminum ethoxide (25% in toluene, 190 µL, 0.3 mmol), at 0 °C under argon. After the reaction mixture was stirred for 15 h from 0 °C to RT, saturated aqueous potassium, sodium tartrate and ethyl acetate were added and the mixture was stirred for an additional 30 min at RT. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were washed with brine, then dried over Na_2SO_4 to afford a mixture of β-lactone and β-hydroxyester.

Reactivity with commercial Ti(O*i*Pr)$_3$Cl

To a solution of (*Z*)-1-chloro-4-phenylbut-1-enyl acetate (50 µL, 0.25 mmol) and *p*-tolualdehyde (35 µL, 0.3 mmol) in anhydrous THF (2.5 mL), was added Ti(O*i*Pr)$_3$Cl (75 µL, 0.3 mmol) at 0 °C, under argon. After stirring overnight from 0 °C to RT, the mixture was quenched with water and extracted thrice with AcOEt. The combined organic extracts were washed with brine, then dried over Na_2SO_4. After concentration under vacuum, trace of β-lactone could be detected by 1H NMR of the crude material, with starting materials. We could not obtain reproducible results.

***syn*-2-(Hydroxy-*p*-tolylmethyl)-4-phenylbutanoic acid 4h**

A solution of ethyl *syn*-2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoate **5h** (29 mg, 0.09 mmol) and KOH (15 mg, 0.3 mmol) in ethanol (0.2 mL) and water (0.2 mL) was stirred overnight at RT. Then, the mixture was quenched with aqueous 5% HCl and extracted thrice with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4. After concentration under vacuum, 26 mg (quantitative) of *syn*-2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoic acid **4h** was obtained.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25-7.14 (m, 9H), 5.05 (d, J = 4.9 Hz, 1H), 2.82-2.35 (m, 3H), 2.37 (s, 3H), 2.22-1.96 ppm (m, 2H).

***cis*-4-*p*-Tolyl-3-(2-phenylethyl)oxetan-2-one 4h and 4-phenyl-1-*p*-tolyl-but-1-ene 6h**

To a solution of *syn*-2-(hydroxy-*p*-tolylmethyl)-4-phenylbutanoic acid (26 mg, 0.09 mmol) in anhydrous pyridine (0.5 mL) was added benzenesulfonyl chloride (17 µL, 0.13 mmol) at 0 °C under argon. The mixture was stirred for 1 h at 0 °C, then let for standing overnight at 0 °C. The mixture was poured over ice, then extracted thrice with Et_2O. The combined organic extracts were washed with aqueous $NaHCO_3$, brine and dried over Na_2SO_4. After concentration under vacuum, analysis by ^{1}H NMR of the crude material indicated a complete conversion to *cis*-4-*p*-tolyl-3-(2-phenylethyl)oxetan-2-one **4h**. Purification by chromatography on silica gel (diethyl ether/c-hexane 5:95) furnished (*Z*)-4-phenyl-1-*p*-tolyl-but-1-ene **6h** (17.8 mg, 89%).

***cis*-4h:** Characteristic peaks: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.59 (d, J = 6.5 Hz, 1H), 3.89 (q, J = 6.5 Hz, 1H), 2.39 ppm (s, 3H).

(*Z*)-6h: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31-7.15 (m, 9H), 6.43 (d, J = 11.7 Hz, 1H), 5.67 (dt, J_1 = 11.7 Hz, J_2 = 6.6 Hz, 1H), 2.84-2.64 (m, 4H), 2.36 ppm (s, 3H) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.9, 136.4, 134.8, 131.3, 129.4, 129.0, 128.8, 128.6, 128.5 126.0, 36.3, 30.6, 21.3 ppm.

***syn*-2-Benzyl-3-hydroxy-3-*p*-tolylpropanoic acid**

To a solution of diisopropylamine (7.0 mL, 50 mmol) in anhydrous THF (100 mL) was added a solution of n-BuLi (1.6 M in n-hexane, 31 mL, 50 mmol) dropwise at -78 °C under an argon atmosphere. The mixture was warmed to RT for 1 h, then cooled to -45 °C. 3-Phenylpropionaldehyde (3.0 g, 20 mmol) in anhydrous THF (50 mL), then *p*-tolualdehyde were added into the solution of lithium diisopropylamide at -45 °C under argon. The mixture was stirred from -45 °C to RT for 4 h, then quenched with water and extracted thrice with AcOEt. The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and evaporated to dryness under reduced pressure. Recrystallization from isopropyl alcohol furnished 2.52 g (47%) of *syn*-2-benzyl-3-hydroxy-3-*p*-tolylpropanoic acid as a white solid.

***cis*-3-Benzyl-4-*p*-tolyl-oxetan-2-one 4k**

To a solution of *syn*-2-benzyl-3-hydroxy-3-*p*-tolylpropanoic acid (2.5 g, 9.2 mmol) in anhydrous pyridine (50 mL) was added benzenesulfonyl chloride (1.65 mL, 13 mmol) at 0 °C under argon. The mixture was stirred for 1 h at 0 °C, then let for standing overnight at 0 °C. The mixture was poured over ice, then extracted thrice with Et_2O. The combined organic extracts were washed with aqueous $NaHCO_3$, brine and dried over Na_2SO_4. After concentration under vacuum, recrystallization from *n*-hexane (2 crops) furnished 744 mg (32%) of *cis*-3-benzyl-4-*p*-tolyl-oxetan-2-one **4k** as a white solid.

^{1}H NMR (200 MHz, $CDCl_3$) δ 7.26-7.15 (m, 7H), 6.89-6.83 (m,2H), 5.63 (d, J = 6.6 Hz, 1H), 4.24 (ddd, J_1 = 8.8 Hz, J_2 = 7.1 Hz, J_3 = 6.6 Hz, 1H), 2.89 (dd, J_1 = 14.8 Hz, J_2 = 7.1 Hz, 1H), 2.51 (dd, J_1 = 14.8 Hz, J_2 = 8.8 Hz, 1H), 2.41 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.3, 139.1, 137.3, 131.5, 129.4, 128.6, 128.6, 126.8, 126.5, 75.7, 56.6, 31.0, 21.4 ppm; IR : ν 1721 cm^{-1}.

Decarboxylation

To a solution of *cis*-3-benzyl-4-*p*-tolyl-oxetan-2-one **4k** (64 mg, 0.25 mmol) in anhydrous THF (2.5 mL) was added a commercial solution of diethylaluminum ethoxide (25% in toluene, 300 µL, 0.5 mmol), at 0 °C under argon. After the reaction mixture was stirred for 15 h from 0 °C to RT, saturated aqueous potassium, sodium tartrate and ethyl acetate were added and the mixture was stirred for an additional 30 min at RT. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were washed with brine, then dried over Na_2SO_4 to afford a mixture of β-lactone **4k** (56%), β-hydroxyester **5k** (27%) and olefin **6k** (16% *E*/*Z* = 70:30).

To a solution of *cis*-3-benzyl-4-*p*-tolyl-oxetan-2-one **4k** (64 mg, 0.25 mmol) in anhydrous THF (2.5 mL) was added a solution of dimethylaluminum chloride (1.0 M in *n*-hexane, 250 µL, 0.5 mmol), at 0 °C under argon. After the reaction mixture was stirred for 15 h from 0 °C to RT, saturated aqueous potassium, sodium tartrate and ethyl acetate were added and the mixture was stirred for an additional 30 min at RT. The layers were separated and the aqueous phase was extracted twice with AcOEt. The combined organic extracts were washed with brine, then dried over Na_2SO_4 το αφφορδ α μιξτυρε οφ β-lactone **4k** (4%), β-hydroxyester **5k** (20%) and olefin **6k** (75% *E*/*Z* = 80:20).