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Synthesis of Some New Highly Functionalized C_6-Synthons

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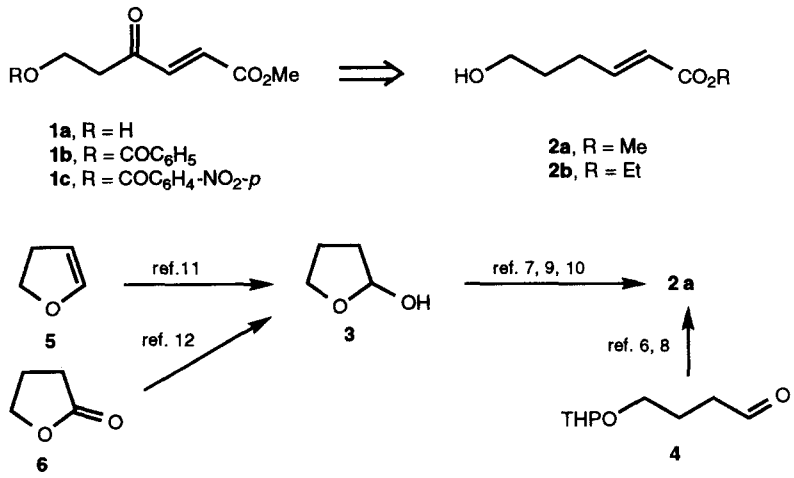
Abstract: Starting with ε–caprolactone a new synthesis of methyl 6-hydroxy-2-hexenoate, **2a**, is described. The preparation of the new highly functionalized C_6-synthons methyl 6-acyloxy-4-oxo-2-hexenoates, **1b** and **1c**, methyl 6-benzoyloxy-4-hydroxy-2-hexenoate, **13**, and methyl 6-benzoyloxy-4-oxohexanoate, **14**, is also reported.

As a part of an ongoing programme in the field of alkaloid synthesis, during the last years we have undertaken an extensive study on the stereochemical course of the 1,3-dipolar cycloaddition reaction of cyclic nitrones to polyfunctionalized α,β-unsaturated carboxylic acid derivatives with a six carbon atom skeleton.[1-3] In this context, we prepared several new α,β-unsaturated lactones[1-3] to be used as the dipolarophiles. In order to complete this study we needed also some functionalized C_6-synthons with the *E* configuration of the double bond. Most of the compounds that we required for our synthetic purposes could be considered as derivatives of methyl (*E*)-6-hydroxy-4-oxo-2-hexenoate, **1a** (Scheme 1).

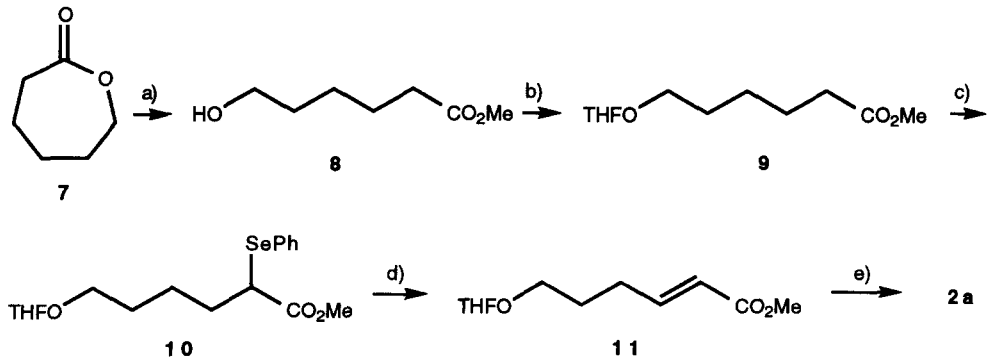


Scheme 1

To the best of our knowledge, compound **1a** was not described in the literature and methyl (*E*)-6-hydroxy-2-hexenoate, **2a**, seemed to us an appropriate precursor for its synthesis, since the allylic oxidation of

an alcohol protected derivative of **2a** could yield compounds **1b** or **1c**. The ethyl ester **2b** had been previously prepared by Dolezal,[4] although in low yield and, some years later, van der Gen and co-workers[5] obtained also this compound as a by-product. The methyl ester **2a** was reported for the first time in 1989,[6] and since then both esters **2a** and **2b** have received much attention as key intermediates in synthetic processes including the preparation of several natural products.[7-10]

All the recently published syntheses of **2** are based on the Wittig type reaction between tetrahydro-2-furanol, **3**,[7,9,10] or 4-(tetrahydropyranyloxy)butanal, **4**,[6,8] and a phosphorus derivative of an ester of acetic acid (Scheme 1). Hemiacetal **3** may be prepared by hydration of 2,3-dihydrofuran, **5**,[11] or by DIBAL-H reduction of γ-butyrolactone, **6**,[12] although both methods afford **3** in low yield (≈30%). Aldehyde **4** has been prepared from butane-1,4-diol in low yield also (≤30%).[8] Trying to improve the described procedures, we repeated several times the Wittig condensation over **3** (prepared either from **5** or **6**) using different experimental modifications, but our best overall yield of **2a** with this methodology was 26%, in good agreement with most literature data. Recently, Prudhomme *et al.*[10] described the preparation of **2b** in 54% yield starting from γ-butyrolactone, **6**, the experimental modification consisting apparently in the simultaneous addition of the reducing agent and the phosphorus derivative to the reaction mixture. In view of all these precedents, we decided to open a new synthetic route to ester **2a** (Scheme 2), which results are reported here.



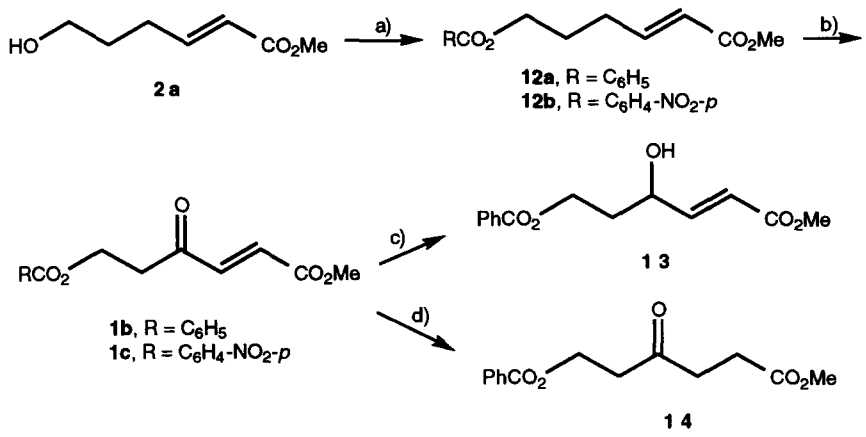
a) MeOH, H_2SO_4; b) 2,3-dihydrofuran, *p*-TsOH, CH_2Cl_2; c) LDA, PhSeBr, -78 °C; d) H_2O_2, 0 °C; e) *p*-TsOH, MeOH, reflux

Scheme 2

Methanolysis of commercial ε-caprolactone, **7**, gave methyl 6-hydroxyhexanoate, **8**, in almost quantitative yield.[13] Protection of the hydroxyl group through reaction with 2,3-dihydrofuran using conventional conditions (cat. *p*-TsOH in CH_2Cl_2) gave the new tetrahydrofuryl derivative **9** in 86% yield. The acetalization was also accomplished by irradiation of a solution of ester **8** and sulphuryl chloride in THF with a high pressure mercury lamp,[14] but this procedure did not improve the former yield. Reaction of the lithium enolate of **9** with phenylselenenyl bromide[15] afforded ester **10**, whose oxidation and subsequent elimination of PhSeOH allowed the isolation of the α,β-unsaturated ester **11** in 70% overall yield. Finally, removal of the protecting tetrahydrofuryl moiety afforded the desired ester **2a** almost quantitatively. This new preparative sequence of methyl (*E*)-6-hydroxy-2-hexenoate, **2a**, from ε-caprolactone, **7**, with an overall yield of 54%, represents a significant improvement of its synthesis compared to the other previously published methods.

To incorporate a carbonyl group at C_4 in **2a** an oxidation process was required, therefore the primary alcohol had to be conveniently protected. Using conventional methods the new benzoyl and *p*-nitrobenzoyl

derivatives, **12a** and **12b**, were prepared in high yields (Scheme 3). Allylic oxidation was successfully carried out with CrO_3 in acetic acid/acetic anhydride,[16] giving the new γ-oxo-α,β-unsaturated esters **1b** and **1c** in 82 and 73% yield respectively.



a) RCOCl, pyr, 0 °C; b) CrO_3, HOAc, Ac_2O, benzene, 0 °C; c) $NaBH_4$, MeOH, CH_2Cl_2, 0 °C; d) H_2, AcOEt, 5% Pd/C

Scheme 3

In order to prepare other C_6 derivatives, we also performed the reactions of ester **1b** with two different reducing agents. Treatment with $NaBH_4$ afforded the hydroxyester **13** in 77% yield. We have very recently described the synthesis of an analog of **13** with a benzyl ether protection of the primary hydroxyl group[17] and other authors have also dedicated much attention to the synthesis of γ-hydroxy-α,β-unsaturated esters in the last years.[18] Catalytic hydrogenation of **1b** using 5% Pd/C gave the new oxoester **14** in 91% yield.

In summary, we have developed a new and improved synthesis of methyl 6-hydroxy-2-hexenoate, **2a**, and this compound has been transformed in several new C_6-synthons, namely **1b**, **1c**, **12a**, **12b**, **13**, and **14**. The regio- and stereochemistry of the cycloadditions of compounds **1** and some of their derivatives is currently being investigated in our laboratories.

EXPERIMENTAL SECTION

Reaction mixtures were stirred magnetically. The organic extracts were dried over anhydrous sodium sulphate. Reaction solutions were concentrated using a rotary evaporator at 15-20 Torr. Flash chromatographies were performed by using silica gel (230-400 mesh). Infrared spectra were recorded on a Nicolet 5 ZDX spectrophotometer. ^1H nmr and ^{13}C nmr spectra were recorded on Bruker AC-250-WB or AM-400-WB instruments from deuterated chloroform solutions; chemical shifts are given in ppm relative to TMS (δ values). Mass spectra were performed on a Hewlett-Packard 5985B instrument at 70 eV.

Methyl 6-(2'-tetrahydrofuryloxy)hexanoate, **9**

2,3-Dihydrofuran (2.01 g, 28.7 mmol) was added to a solution of methyl 6-hydroxyhexanoate, **8**,[13] (4.00 g , 27.4 mmol) and *p*-toluenesulphonic acid (20 mg) in methylene chloride (60 mL) at 0 °C. The reaction mixture was left at this temperature for 2 h and then it was successively washed with saturated $NaHCO_3$ solution (40 mL) and water (40 mL). The organic phase was dried and the solvent was removed to afford a yellow oil (5.90 g). Flash chromatography of this crude product using hexane-ethyl acetate (2:1) as eluent gave ester **9** as a colorless oil (5.09 g, 23.6 mmol, 86% yield): ir (film) 2946, 2889, 1740, 1167, 1096, 1039 cm^{-1};

^{1}H nmr (250 MHz) 5.06 (s, 1 H, $H_{2'}$), 3.86-3.79 (m, 2 H, H_6), 3.63 (s, 3 H, OMe), 3.61 (dt, J = 9.5 Hz, J' = 6.6 Hz, 1 H, $H_{5'}$), 3.32 (dt, J = 9.5 Hz, J' = 6.6 Hz, 1 H, $H_{5'}$), 2.28 (t, $J_{2,3}$ = 7.5 Hz, 2 H, H_2), 2.00-1.30 (m, 10 H); ^{13}C nmr (63 MHz) 174.1 (CO), 103.8 ($C_{2'}$), 66.9/66.8 (C_6/$C_{5'}$), 51.4 (OMe), 34.0 (C_2), 32.3 ($C_{3'}$), 29.4 (C_5), 25.8 (C_3), 24.7 (C_4), 23.5 ($C_{4'}$); ms *m/z* 145 (M^+-71, 9), 129 (13), 97 (16), 71 (100). Anal. Calcd for $C_{11}H_{20}O_4$: C, 61.09; H, 9.32. Found: C, 60.92; H, 9.31.

Methyl 2-phenylseleno-6-(2'-tetrahydrofuryloxy)hexanoate, **10**

To a THF (40 mL) solution of LDA, prepared from 2.01 mL of diisopropylamine and 9.0 mL of 1.6 M *n*-BuLi in hexane, at -78 °C under argon atmosphere, a solution of ester **9** (2.60 g, 12.0 mmol) in THF (10 mL) was added. After 15 min a freshly prepared solution of phenylselenenyl bromide (14.4 mmol, obtained from 2.24 g of diphenyl diselenide and 0.39 mL of bromine) in THF (10 mL) was added and the mixture was stirred 20 min at the same temperature. Water (3 mL) was added, the THF was removed under vacuum, and the residue was diluted with methylene chloride (30 mL). The solution was successively washed with 5% HCl (25 mL), saturated $NaHCO_3$ solution (25 mL), and water (25 mL), dried, and the solvent was removed to afford a yellow oil (4.21 g). Purification of this product by flash chromatography using hexane-ethyl acetate (4:1) as eluent gave a colorless oil identified as **10** (3.43 g, 9.2 mmol, 77% yield): ir (film) 2943, 2857, 1732, 1437, 1038, 741 cm^{-1}; ^{1}H nmr (250 MHz) 7.48 (m, 2 H, Ph), 7.20 (m, 3H, Ph), 4.97 (br s, 1 H, $H_{2'}$), 3.75 (m, 2 H, H_6), 3.52 (s, 3 H, OMe), 3.56-3.48 (m, 2 H, H_2, $H_{5'}$), 3.24 (m, 1 H, $H_{5'}$), 1.93-1.22 (m, 10 H); ^{13}C nmr (63 MHz) 173.3 (CO), 135.6/128.9/128.4/127.8 (Ph), 103.7 ($C_{2'}$), 66.7/66.6 (C_6/$C_{5'}$), 51.9 (OMe), 43.3 (C_2), 32.2 ($C_{3'}$), 31.5 (C_3), 29.1 (C_5), 24.8 (C_4), 23.4 ($C_{4'}$); ms *m/z* 372-370 (M^+, 1, 1), 312 (1), 310 (1), 157 (9), 155 (5), 71 (100), 43 (25). Anal. Calcd for $C_{17}H_{24}O_4Se$: C, 54.99; H, 6.51. Found: C, 54.99; H, 6.59.

*Methyl (*E*)-6-(2'-tetrahydrofuryloxy)-2-hexenoate,* **11**

To a solution of the seleno derivative **10** (2.91 g, 7.8 mmol) in THF (25 mL) at 0 °C, 3 drops of glacial acetic acid were added. The solution was carefully treated with 30% H_2O_2 (2.48 mL, 23.4 mmol) and stirred at 0 °C for 1 h. Then, the mixture was neutralized with saturated $NaHCO_3$ solution and extracted with ether (3 x 30 mL). The organic phase was dried and the solvent removed to afford pure unsaturated ester **11** as a colorless oil (1.53 g, 7.1 mmol, 91% yield). An analytical sample was obtained by flash chromatography using hexane-ether (1:1) as eluent. **11**: ir (film) 2947, 2927, 1725, 1656, 1438, 1272, 1095, 1040 cm^{-1}; ^{1}H nmr (250 MHz) 6.81 (dt, $J_{3,2}$ = 15.3 Hz, $J_{3,4}$ = 7.3 Hz, 1 H, H_3), 5.67 (d, $J_{2,3}$ = 15.3 Hz, 1 H, H_2), 4.92 (br s, 1 H, $H_{2'}$), 3.69 (t, $J_{6,5}$ = 6.6 Hz, 2 H, H_6), 3.55 (s, 3 H, OMe), 3.49 (dt, J = 9.5 Hz, J = 6.6 Hz, 1 H, $H_{5'}$), 3.22 (dt, J = 9.5 Hz, J = 6.6 Hz, 1 H, $H_{5'}$), 2.11 (q, $J_{4,3}$ = $J_{4,5}$ = 7.3 Hz, 2 H, H_4), 1.88-1.50 (m, 6 H); ^{13}C nmr (63 MHz) 166.7 (CO), 148.8 (C_3), 120.9 (C_2), 103.6 ($C_{2'}$), 66.6/65.9 (C_6/$C_{5'}$), 51.1 (OMe), 32.1 ($C_{3'}$), 28.8 (C_5), 28.0 (C_4), 23.3 ($C_{4'}$); ms *m/z* 127 (M^+-87, 9), 71 (100), 43 (22). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.70; H, 8.44.

*Methyl (*E*)-6-hydroxy-2-hexenoate,* **2a**

A solution of tetrahydrofuryl derivative **11** (3.20 g, 14.9 mmol) and *p*-toluenesulphonic acid (20 mg) in methanol (60 mL) was heated at the reflux temperature for 2 h. The solvent was removed, the residue was dissolved in methylene chloride (50 mL), and the solution successively washed with saturated $NaHCO_3$ solution (40 mL) and water (40 mL). The organic phase was dried and the solvent removed to give pure ester **2a** (2.02 g, 14.0 mmol, 94% yield): ^{1}H nmr (400 MHz) 6.99 (dt, $J_{3,2}$ = 15.9 Hz, $J_{3,4}$ = 7.3 Hz, 1 H, H_3), 5.86 (dt, $J_{2,3}$ = 15.9 Hz, $J_{2,4}$ = 1.8 Hz, 1 H, H_2), 3.72 (s, 3 H, OMe), 3.63 (t, $J_{6,5}$ = 6.4 Hz, 2 H, H_6), 2.30 (dq, $J_{4,3}$ = $J_{4,5}$ = 7.3 Hz, $J_{4,2}$= 1.8 Hz, 2 H, H_4), 1.71 (m, 2 H, H_5); ^{13}C nmr (63 MHz) 167.0 (CO), 148.9 (C_3), 120.8 (C_2), 61.1 (C_6), 51.1 (OMe), 30.5 (C_5), 28.2 (C_4).

*Methyl (*E*)-6-benzoyloxy-2-hexenoate,* **12a**

Benzoyl chloride (7.03 g, 50.0 mmol) was slowly added to a methylene chloride solution (100 mL) of compound **2a** (6.00 g, 41.7 mmol) and pyridine (10.1 mL, 125 mmol) at 0 °C. The mixture was stirred at room temperature for 18 h and afterwords it was successively washed with 5% HCl (3 x 80 mL), saturated $NaHCO_3$ solution (2 x 60 mL), and water (60 mL). The organic layer was dried, the solvent removed, and the yellow oily residue (9.5 g) was purified by flash chromatography using hexane-ethyl acetate (2:1) as eluent

affording methyl (*E*)-6-benzoyloxy-2-hexenoate, **12a** (8.8 g, 35.4 mmol, 85% yield): ir (film) 2953, 1722, 1658, 1444, 1273, 1171, 1114, 713 cm^{-1}; ^1H nmr (250 MHz) 7.98 (d, J = 7.3 Hz, 2 H, H_o-Ph), 7.52 (t, J = 7.3 Hz, 1 H, H_p-Ph), 7.40 (t, J = 7.3 Hz, 2 H, H_m-Ph), 6.97 (dt, $J_{3,2}$ = 15.3 Hz, $J_{3,4}$ = 6.6 Hz, 1 H, H_3), 5.84 (d, $J_{2,3}$ = 15.3 Hz, 1 H, H_2), 4.31 (t, $J_{6,5}$ = 6.6 Hz, 2 H, H_6), 3.67 (s, 3 H, OMe), 2.35 (q, $J_{4,3}$ = $J_{4,5}$ = 6.6 Hz, 2 H, H_4), 1.92 (qn, $J_{5,6}$ = $J_{5,4}$ = 6.6 Hz, 2 H, H_5); ^{13}C nmr (63 MHz) 166.7/166.3 (C_1/PhCO), 147.8 (C_3), 132.8 (C_p-Ph), 130.0 (C_i-Ph), 129.4 (C_o-Ph), 128.2 (C_m-Ph), 121.5 (C_2), 63.8 (C_6), 51.3 (OMe), 28.7/27.0 (C_4/C_5); ms *m/z* 248 (M^+, 0.2), 217 (1), 127 (1), 105 (100), 77 (35). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.81; H, 6.53.

*Methyl (*E*)-6-(4'-nitrobenzoyloxy)-2-hexenoate,* **12b**

The same procedure described for the synthesis of compound **12a** was used to prepare **12b** starting from **2a** and *p*-nitrobenzoyl chloride. Derivative **12b** was isolated as a solid in 78% yield. Mp 34-35 °C; ir (KBr) 3118, 2953, 1718, 1659, 1605, 1527, 1350, 1327, 1284, 1111, 716 cm^{-1}; ^1H nmr (400 MHz) 8.26 (d, J = 8.6 Hz, 2 H, $H_{3'}$-Ph), 8.17 (d, J = 8.6 Hz, 2 H, $H_{2'}$-Ph), 6.98 (dt, $J_{3,2}$ = 15.5 Hz, $J_{3,4}$ = 6.7 Hz, 1 H, H_3), 5.86 (dt, $J_{2,3}$ = 15.5 Hz, $J_{2,4}$ = 1.5 Hz, 1 H, H_2), 4.38 (t, $J_{6,5}$ = 6.7 Hz, 2 H, H_6), 3.70 (s, 3 H, OMe), 2.37 (dq, $J_{4,3}$ = $J_{4,5}$ = 6.7 Hz, $J_{4,2}$ = 1.5 Hz, 2 H, H_4), 1.96 (qn, $J_{5,6}$ = $J_{5,4}$ = 6.7 Hz, 2 H, H_5); ^{13}C nmr (100 MHz) 166.6 (C_1), 164.4 (PhCO), 150.4 ($C_{4'}$-Ph), 147.5 (C_3), 135.3 ($C_{1'}$-Ph), 130.5 ($C_{2'}$-Ph), 123.4 ($C_{3'}$-Ph), 121.7 (C_2), 64.9 (C_6), 51.3 (OMe), 28.6/26.9 (C_4/C_5); ms *m/z* 293 (M^+, 0.3), 262 (0.6), 150 (100), 126 (27), 111 (32), 104 (33), 98 (55), 94 (88), 76 (26), 67 (41). Anal. Calcd for $C_{14}H_{15}NO_6$: C, 57.34; H, 5.16; N, 4.78. Found: C, 57.26; H, 5.12; N, 4.77.

*Methyl (*E*)-6-benzoyloxy-4-oxo-2-hexenoate,* **1b**

Chromic anhydride (4.03 g, 40.3 mmol) was added in small portions to a mixture of acetic acid (40 mL) and acetic anhydride (20 mL) at 0 °C.[16] The mixture was diluted with benzene (40 mL) and a solution of compound **12a** (2.00 g, 8.1 mmol) in benzene (10 mL) was added dropwise. After 1 h stirring at 0 °C water (100 mL) was added , the mixture was neutralized with 20% NaOH, and extracted with ether (3 x 200 mL). The organic phase was dried and the solvent removed to afford **1b** as a solid (1.73 g, 6.6 mmol, 82% yield). For larger amounts of material a minor modification is useful: direct extraction with ether of the reaction mixture without previous neutralization, followed by distillation of the acetic acid or neutralization with solid $NaHCO_3$. **1b**: mp 56-57 °C (hexane); ir (KBr) 3078, 3057, 2960, 2912, 1722, 1694, 1338, 1276, 1122, 714 cm^{-1}; ^1H nmr (250 MHz) 7.95 (d, J = 7.3 Hz, 2 H, H_o-Ph), 7.52 (t, J = 7.3 Hz, 1 H, H_p-Ph), 7.38 (t, J = 7.3 Hz, 2 H, H_m-Ph), 7.08 (d, $J_{3,2}$ = 15.9 Hz, 1 H, H_3), 6.70 (d, $J_{2,3}$ = 15.9 Hz, 1 H, H_2), 4.62 (t, $J_{6,5}$ = 6.2 Hz, 2 H, H_6), 3.78 (s, 3 H, OMe), 3.09 (t, $J_{5,6}$ = 6.2 Hz, 2 H, H_5); ^{13}C nmr (63 MHz) 195.8 (C_4), 165.7/165.0 (C_1/PhCO), 138.4 (C_3), 132.5 (C_p-Ph), 130.5 (C_2), 129.1 (C_i-Ph), 128.9 (C_o-Ph), 127.7 (C_m-Ph), 58.8 (C_6), 51.8 (OMe), 39.5 (C_5); ms *m/z* 157 (M^+-105, 7), 140 (10), 113 (44), 105 (100), 77 (38), 55 (20). Anal. Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.23; H, 5.40.

*Methyl (*E*)-6-(4'-nitrobenzoyloxy)-4-oxo-2-hexenoate,* **1c**

The same procedure described for the synthesis of compound **1b** was used for the preparation of the nitro derivative **1c** (73% yield) starting from **12b**. **1c**: mp 82-83 °C (hexane); ir (KBr) 3124, 2958, 1722, 1696, 1525, 1335, 1270, 1105 cm^{-1}; ^1H nmr (400 MHz) 8.24 (d, J = 8.5 Hz, 2 H, $H_{3'}$-Ph), 8.14 (d, J = 8.5 Hz, 2 H, $H_{2'}$-Ph), 7.10 (d, $J_{3,2}$ = 16.1 Hz, 1 H, H_3), 6.73 (d, $J_{2,3}$ = 16.1 Hz, 1 H, H_2), 4.69 (t, $J_{6,5}$ = 6.1 Hz, 2 H, H_6), 3.81 (s, 3 H, OMe), 3.15 (t, $J_{5,6}$ = 6.1 Hz, 2 H, H_5); ^{13}C nmr (63 MHz) 196.0 (C_4), 165.6 (C_1), 164.4 (PhCO), 150.5 ($C_{4'}$), 138.8 (C_2), 135.1 ($C_{1'}$), 131.3/130.7 (C_3/$C_{2'}$), 123.5 ($C_{3'}$), 60.2 (C_6), 52.4 (OMe), 39.9 (C_5); ms *m/z* 194 (M^+-113, 2), 167 (100), 151 (25), 150 (28), 140 (23), 137 (50), 121 (58), 120 (38), 113 (100), 109 (50), 85 (23), 81 (46), 76 (25), 75 (25), 65 (89), 55 (39), 50 (30). Anal. Calcd for $C_{14}H_{13}NO_7$: C, 54.73; H, 4.26; N, 4.56. Found: C, 54.54; H, 4.28; N, 4.45.

*Methyl (*E*)-6-benzoyloxy-4-hydroxy-2-hexenoate,* **13**

$NaBH_4$ (31 mg, 0.8 mmol) was added in small portions to a solution of compound **1b** (0.80 g, 3.1 mmol) in CH_2Cl_2 (50 mL) and methanol (20 mL) at 0 °C. The mixture was stirred for 30 min, the solvent was removed, and water (25 mL) was added to the residue. The solution was acidified to pH 5 with 5% HCl and

was extracted with CH_2Cl_2 (3 x 40 mL). The organic layer was dried and the solvent removed to afford 0.81 g of an oily residue. Flash chromatography using hexane-ethyl acetate (2:1) as eluent yielded a colorless oil identified as **13** (0.62 g, 2.4 mmol, 77% yield): ir (film) 3483, 2954, 1720, 1660, 1276, 1116, 713 cm^{-1}; ^1H nmr (400 MHz) 7.97 (d, J = 7.3 Hz, 2 H, H_o-Ph), 7.51 (t, J = 7.3 Hz, 1 H, H_p-Ph), 7.40 (t, J = 7.3 Hz, 2 H, H_m-Ph), 6.95 (dd, $J_{3,2}$ = 15.6 Hz, $J_{3,4}$ = 4.6 Hz, 1 H, H_3), 6.07 (dd, $J_{2,3}$ = 15.6 Hz, $J_{2,4}$ = 1.5 Hz, 1 H, H_2), 4.56 (ddd, $J_{6,6}$ = 11.6 Hz, $J_{6,5}$ = 8.6 Hz, $J'_{6,5}$ = 4.9 Hz, 1 H, H_6), 4.47 (m, 1H, H_4), 4.39 (dt, $J_{6,6}$ = 11.6 Hz, $J_{6,5}$ = $J'_{6,5}$ = 5.5 Hz, 1 H, H_6), 3.67 (s, 3 H, OMe), 2.90 (br s, 1 H, OH), 2.05 (m, 1 H, H_5), 1.92 (m, 1 H, H_5); ^{13}C nmr (63 MHz) 166.9/166.8 (C_1/PhCO), 149.5 (C_3), 133.1 (C_p-Ph), 129.7/129.6 (C_i-Ph/C_o-Ph), 128.4 (C_m-Ph), 120.0 (C_2), 67.8 (C_4), 61.2 (C_6), 51.6 (OMe), 35.6 (C_5); ms *m/z* 264 (M^+, 0.2), 233 (0.1), 122 (29), 105 (100), 77 (34). Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.62; H, 6.13.

Methyl 6-benzoyloxy-4-oxohexanoate, **14**

A solution of olefin **1b** (0.30 g, 1.1 mmol) in ethyl acetate (10 mL) was submitted to catalytic hydrogenation (30 mg of 5% Pd/C) at atmospheric pressure during 3 h at room temperature. The catalyst was filtered off using *Celite* and the solvent was removed to afford pure methyl 6-benzoyloxy-4-oxohexanoate, **14** (250 mg, 1.0 mmol, 91% yield): ir (film) 2956, 2918, 1719, 1602, 1279, 1111, 715 cm^{-1}; ^1H nmr (250 MHz) 7.95 (d, J = 6.9 Hz, 2 H, H_o-Ph), 7.50 (t, J = 6.9 Hz, 1 H, H_p-Ph), 7.37 (t, J = 6.9 Hz, 2 H, H_m-Ph), 4.55 (t, $J_{6,5}$ = 6.6 Hz, 2 H, H_6), 3.61 (s, 3 H, OMe), 2.89 (t, $J_{5,6}$ = 6.6 Hz, 2 H, H_5), 2.75 (t, $J_{3,2}$= 6.6 Hz, 2 H, H_3), 2.57 (t, $J_{2,3}$ = 6.6 Hz, 2 H, H_2) ; ^{13}C nmr (63 MHz) 205.8 (C_4), 172.9 (C_1), 166.3 (PhCO), 133.0 (C_p-Ph), 129.9 (C_i-Ph), 129.5 (C_o-Ph), 128.3 (C_m-Ph), 59.6 (C_6), 51.7 (OMe), 41.5/37.4 (C_3/C_5), 27.5 (C_2); ms *m/z* 264 (M^+, 0.2), 205 (0.1), 177 (16), 115 (59), 105 (100), 77 (37), 55 (56). Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.66; H, 6.01.

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