A New Synthesis of Methyl 3-Oxo-2-pentyl-1-cyclopentene-1-acetate

Khushrav Crawford,*[a] Valentin Rautenstrauch,[b] Arnold Uijttewaal[b]

[a]Firmenich Chemical Manufacturing Center, 150 Firmenich Way, Newark, NJ 07114 USA

[b]Firmenich SA, 1, route des Jeunes, 1211 Geneva 8, Switzerland

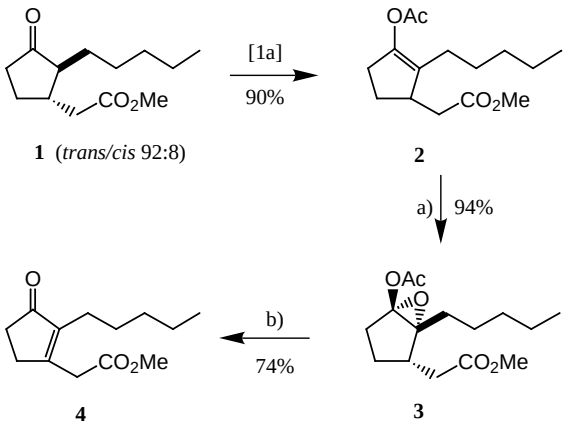
Fax +1 973 344 29 99; E-mail: khushrav.crawford@firmenich.com

Received 9 April 2001

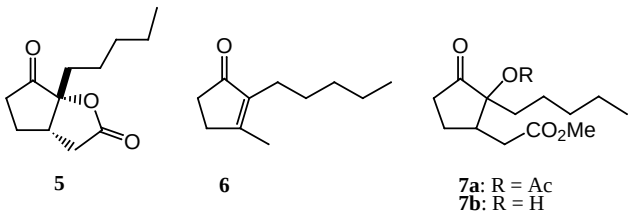
Abstract: The 92:8 equilibrium mixture of (±)-*trans*-methyl dihydrojasmonate (**1**) and its *cis*-isomer is transformed in 63% overall yield into the title compound **4** by epoxidation of the derived enol acetate **2** with peracetic acid/Na_2CO_3 in toluene and heating the resulting α-acetoxy epoxide **3** in MeOH in the presence of catalytic amounts of methanesulfonic acid.

Key words: jasmonoids, enol esters, epoxidations, cyclopentenones, indirect dehydrogenations

This communication describes a new synthetic approach (see Scheme) to methyl 3-oxo-2-pentyl-1-cyclopentene-1-acetate (**4**),[1] a direct precursor of (+)-*cis*-methyl dihydrojasmonate,[2] an important perfumery ingredient.[3]



a) AcO_2H, [Na_2CO_3], toluene, 25° C;
b) [MsOH], MeOH, reflux.



Scheme

Our starting material, the commercially available 92:8 mixture of racemic *trans*-methyl dihydrojasmonate (**1**)[4] and its *cis*-isomer, was first converted to the known enol acetate **2** in 90% yield following the reported procedure.[1d] Optimum conditions for epoxidation were found to involve treatment of a toluene solution of **2** with peracetic acid (1.1 equiv) in the presence of catalytic amounts of Na_2CO_3, leading to formation of the unstable α-acetoxy epoxide **3** in 94% yield.[5] Within the limits of the ^1H NMR analysis (structure assignment by 2D ^1H NMR), only the *cis*-isomer **3** was formed, which is consistent with related work.[6]

Although the acid-catalysed rearrangement of α-acetoxy epoxides to α-acetoxy ketones is well precedented in the literature,[7] we were more interested in finding reaction conditions in which **3** was converted directly to **4**. Indeed, after screening a variety of Brønsted and Lewis acids in protic and aprotic solvents, it was found that catalytic amounts of methanesulfonic acid in refluxing MeOH gave satisfactory results, converting **3** to **4** in 74% yield;[8] bicyclic lactone **5** (3% (GC)), and dihydrojasmone **6** (4%), were formed as minor side-products.[9] Under these conditions rearrangement of **3** to the α-acetoxy ketone **7a** is believed to be the first step.[10] Lactone **5** is presumed to originate from lactonisation of the α-hydroxy ketone **7b**, and dihydrojasmone **6** by decarboxylation of the acid corresponding to **4**, a vinylogous β-keto acid.

Acknowledgement

We are much indebted to Dr. Roger Snowden (*Firmenich SA*) for his contributions to the preparation of this letter.

References and Notes

(1) Previous syntheses: (a) Oberhänsli P., DO 2008878 **1969** (Givaudan SA) *Chem. Abstr*. **1970**, *73*, P109363d. (b) Dubs P.; Stüssi R., *Helv. Chim. Acta* **1978**, 998. (c) Ravid, U.; Ikan, R., *J. Org. Chem*. **1974**, *39*, 2637. (d) Shono, T.; Okawa; M.; Nishiguichi, I., *J. Am. Chem. Soc*. **1975**, *97*, 6144.

(2) Fehr, C.; Galindo, J., *Angew. Chem. Int. Ed.* **2000**, *39*, 569. Dobbs, D.A.; Vanhessche, K.P.M.; Brazi, E.; Rautenstrauch, V.; Lenoir, J.-Y.; Genêt, J.-P.; Wiles, J.A.; Bergens, S.H., *Angew. Chem. Int. Ed*. **2000**, *39*, 1992. Bergens, S.H.; Wiles, J.A.; Vanhessche, K.P.M.; Dobbs, D.A.; Rautenstrauch, V., *Angew. Chem. Int. Ed.* **2001**, *40*, 914.

(3) Kraft, P.; Bajgrowicz, J.; Denis, C.; Fráter, G., *Angew. Chem. Int. Ed.* **2000**, *39*, 2981.

(4) Trade name: Hedione® (*Firmenich SA*).

(5) Preparation of (±)-methyl t-3-acetoxy-c-2,3-epoxy-2-pentyl-r-1-cyclopentaneacetate (**3**):[1a] A 40% solution of AcO_2H in AcOH (5.10 g, 27 mmol) was added dropwise during 1 h to a stirred mixture of **2** (6.45 g, 24 mmol) and Na_2CO_3 (0.22 g, 20 mmol) in toluene (6 mL) at r.t. under N_2. After a further 2 h stirring at r.t., H_2O (5 mL) was added and the organic phase

was separated. Repeated washing of the organic phase with H_2O was followed by concentration in vacuo to afford crude **3** (purity 93% (GC), 7.75 g, 94%). Spectral data of **3**: ^{1}H NMR (ppm, $CDCl_3$, 360 MHz) δ 0.90 (br *t*, *J* = 6.7 Hz, 3H); 1.02-1.17 (*m*, 1H), 1.20-1.56 (overlapping *m*, 7H); 1.78-2.68 (*m*, 7H); 2.11 (*s*, 3H); ^{13}C NMR (ppm, $CDCl_3$, 90 MHz): δ 13.9 (CH_3), 21.0 ($MeCO_2$), 22.4, 24.5, 26.3, 27.2, 28.2, 31.9, 34.4 (CH_2), 36.0 (CH), 51.7 (MeO), 71.2, 91.8 (C), 169.5, 172.9 (CO_2); MS (electrospray ionisation): $(M+H)^+$ = 285. Attempted purification of **3** either by distillation or chromatography led to extensive decomposition. Crude **3** was therefore employed for transformation to **4**.

(6) Fehr C., *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 2407.

(7) Shine, H.J.; Hunt, G.E., *J. Am. Chem. Soc.* **1954**, *80*, 2434. Draper, A.L.; Heilman, W.J.; Schaeffer, W.E.; Shine, H.J.; Shoolery, J.N., *J. Org. Chem.* **1962**, *27*, 2727. Williamson, K.L.; Coburn, J.I.; Herr, M.F., *J. Org Chem.* **1967**, *32*, 3934. House, H.O. *Modern Synthetic Reactions*, 2nd ed., W. A. Benjamin: Menlo Park, 1972, pp 315-317. Jones, A.B. In *Comprehensive Organic Synthesis*, Trost, B.M., Ed. *Pergamon*: New York, 1999; vol. 7, pp 167-168. Zhu, Y.; Manske, K.J.; Shi, Y., *J. Am. Chem. Soc.* **1999**, *121*, 4080. Feng, X.; Shu, L.; Shi, Y., *J. Am. Chem. Soc.* **1999**, *121*, 11003.

(8) Preparation of methyl 3-oxo-2-pentyl-1-cyclopentene-1-acetate (**4**): A solution of crude **3** (ref. 5, 4.10 g, 13.4 mmol) in MeOH (5 mL) was added dropwise during 1 h to a stirred solution of MsOH (70 mg) in MeOH (10 mL) at reflux under N_2. After a further 2 h at reflux the mixture was cooled to r.t. and concentrated in vacuo. The residual oil was dissolved in cyclohexane (10 mL) and washed with 10% aq NaOAc. Work-up and fractional distillation afforded **1** (2.40 g, purity 93%[9] (GC), 74%), bp 98-109 °C/0.05 Torr, spectra identical with those reported previously.[1]

(9) Preparative GC allowed the isolation of (±)-*cis*-1-pentyl-2-oxabicyclo[3.3.0]octane-3,8-dione (**5**, 3%), and 3-methyl-2-pentylcyclopent-2-en-1-one (dihydrojasmone, **6**, 4%), whose spectra were identical with an authentic sample.[11] Spectroscopic data of **5**: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (br. *t*, *J* = 6.7 Hz, 3H); 1.15-1.45 (*m*, 6H); 1.67-1.87 (*m*, 3H); 2.14-2.63 (*m*, 4H); 2.84-2.97 (*m*, 2H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 13.9 (CH_3), 22.4, 22.6, 25.0, 31.9, 33.0, 35.7; 35.8 (CH_2), 38.6 (CH), 89.0 (C), 175.0 (CO_2), 210.9 (CO); MS 210 (M^+), 154, 139, 112, 111, 99, 98, 83, 71, 55, 43. Compounds **5** and **6** were also found as by-products during the screening experiments where their yields were dependent on the nature of both the acid and solvent used.

(10) (±)-Methyl t-2-acetoxy-3-oxo-2-pentyl-r-1-cyclopentane-acetate (**7a**) was detected at the initial stages of the reaction and disappeared during the course of the reaction. Isolation of (±)-*trans*-**7a** was effected by work-up at low conversion and preparative GC. Spectroscopic data of **7a**: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.88 (br. *t*, *J* = 6.7 Hz, CH_3); 1.17-1.56 (*m*, 8H); 1.59-1.74 (*m*, 1H); 2.04 (*s*, $MeCO_2$), 2.14-2.69 (*m*, 5H); 3.29-3.42 (1H, *m*); 3.70 (*s*, MeO); ^{13}C NMR (90 MHz, $CDCl_3$) δ 14.0 (CH_3), 20.9 ($MeCO_2$), 21.7, 22.4, 29.9, 32.3, 34.3, 34.6 (CH_2), 38.7 (CH), 51.7 (MeO), 85.2 (C), 169.7, 172.2 (CO_2), 211.9 (CO); MS 209, 151, 130, 111, 99, 98, 71, 55, 43.

(11) Bellina, F.; Ciuci, D.; Rossi, R.; Vergamini, P., *Tetrahedron* **1999**, *55*, 2103.

Article Identifier:
1437-2096,E;2001,0,07,1127,1128,ftx,en;G07001ST.pdf