Thiol-Catalyzed Acyl Radical Cyclization of Alkenals

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General. Purification was carried out using silica gel column chromatography. NMR (500 MHz for ^1H and 125 MHz for ^{13}C) was measured in CDCl_3 , and chemical shifts and coupling constants were presented in ppm δ and Hz, respectively. The wavenumbers of maximum absorption peaks of IR spectroscopy were presented in cm^{-1} .

Preparation of the Starting Materials. Aldehydes **1a**¹, **1d**² and **1f**³ were prepared according to the reported procedure.

General Procedure for the Preparation of Aldehydes 1b, 1c, and 1g–i. Methyl (*E*)-8-oxo-2-octenoate (1b):

to a solution of 6-heptenal⁴ (784 mg, 7.0 mmol) and methyl acrylate (6.3 mL, 70 mmol) in CH_2Cl_2 (15 mL) was added 2nd generation Grubbs catalyst⁵ (119 mg, 0.14 mmol) at rt. The flask was fitted with an oil bath and the mixture was refluxed under argon for 1h. The reaction mixture was concentrated in vacuo and purified directly by column chromatography (hexane/ether 9/1) followed by distillation (140 °C/0.5 mmHg) to give the product (828 mg, 68%) as a colorless oil. The spectroscopic data were identical with those reported.⁶

1 House, H. O.; Cronin, T. H. *J. Org. Chem.* **1965**, *30*, 1061–1070.

2 Schnatter, W. F. K.; Almarsson, Ö.; Bruice, T. C. *Tetrahedron* **1991**, *47*, 8687–8700.

3 Ho, E.; Cheng, Y.-S.; Mariano, P. S. *Tetrahedron Lett.* **1988**, *29*, 4799–4802.

4 Farquhar, D.; Cherif, A.; Bakina, E.; Nelson, J. A. *J. Med. Chem.* **1998**, *41*, 965–972.

5 (a) Scholl, M.; Ding, S.; Lee, C. W.; Grubbs, R. H. *Org. Lett.* **1999**, *1*, 953–956. (b) Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360–11370.

6 Little, R. D.; Fox, D. P.; Hijfte, L. V.; Dannecker, R.; Sowell, G.; Wolin, R. L.; Moëns, L.; Baizer, M. *J. Org. Chem.* **1988**, *53*, 2287–2294.

Methyl (*E*)-6-methyl-8-oxo-2-octenoate (1c):

purified by column chromatography (hexane/acetone 25/1) followed by distillation (150 °C/0.4 mmHg). A colorless oil (40% yield): ¹H NMR: 0.99 (d, *J* = 6.7, 3H), 1.37–1.43 (m, 1H), 1.49–1.56 (m, 1H), 2.08–2.14 (m, 1H), 2.18–2.31 (m, 3H), 2.43 (ddd, *J* = 16.5, 4.0, 1.2, 1H), 3.73 (s, 3H), 5.85 (dd, *J* = 15.6, 1.2, 1H), 6.95 (dt, *J* = 15.6, 7.0, 1H), 9.77 (brs, 1H). ¹³C NMR: 19.4 (CH₃), 27.4 (CH), 29.4 (CH₂), 34.8 (CH₂), 50.7 (CH₂), 51.3 (CH₃), 121.2 (CH), 148.7 (CH), 166.9 (C), 202.3 (CH). IR (neat): 1724, 1659. EIMS (*m/z*): 184 (M⁺), 152 (M⁺–CHO). HRMS–EI: M⁺ calcd for C₁₀H₁₆O₃, 184.1099; found, 184.1104.

(*E*)-8-Phenyl-5-octenal (1g):

4 mol % of 2nd generation Grubbs catalyst was used. Purified by column chromatography (hexane/acetone 50/1) followed by distillation (140 °C/0.3 mmHg). A colorless oil (50% yield). The spectroscopic data were identical with those reported.⁷

(*E*)-9-Phenyl-6-nonenal (1h):

4 mol % of 2nd generation Grubbs catalyst was used. Purified directly by column chromatography (hexane/acetone 50/1) followed by distillation (170 °C/0.5 mmHg). A colorless oil (47% yield): ¹H NMR: 1.36 (m, 2H), 1.58 (m, 2H), 1.99 (m, 2H), 2.30 (dt, *J* = 7.5, 7.5, 2H), 2.38 (t, *J* = 7.5, 2H), 2.66 (t, *J* = 7.5, 2H), 5.34–5.48 (m, 2H), 7.16–7.28 (m, 5H), 9.73 (brs, 1H). ¹³C NMR: 21.3 (CH₂), 28.8 (CH₂), 32.1 (CH₂), 34.3 (CH₂), 35.9 (CH₂), 43.6 (CH₂), 125.7 (CH), 128.2 (CH), 128.5 (CH), 130.0 (CH), 130.3 (CH), 142.0 (C), 202.8 (CH). IR (neat): 2928, 1724. EIMS (*m/z*): 216 (M⁺), 91 (tolyl). Anal. calcd. for C₁₅H₂₀O: C, 83.28; H, 9.32. Found: C, 83.02; H, 9.17.

⁷ Chottard, J.-C.; Julia, M. *Bull. Soc. Chim. Fr.* **1968**, 9, 3700–3712.

(E)-6-Phenyl-5-hexenal (1i):

purified by column chromatography (hexane/acetone 15/1) followed by distillation (150 °C/0.4 mmHg). A colorless oil (34% yield). The spectroscopic data were identical with those reported.⁸

Methyl (E)-4-(2-formylphenyl)-2-pentenoate (1e):

to a solution of 2-formylbenzenepropanal⁹ (3.24 g, 20 mmol) in toluene (24 mL) was added methyl triphenylphosphoranylidene acetate (5.57 g, 16.7 mmol) in acetonitrile/toluene (1/3, 24 mL) at -78 °C. After stirred for 2h the mixture was concentrated in vacuo and purified directly by column chromatography (hexane/ethyl acetate 9/1) to give the product (2.34 g, 64%) as a colorless oil: ¹H NMR: 2.52 (tdd, *J* = 7.9, 7.0, 1.6, 2H), 3.20 (t, *J* = 7.9, 2H), 3.73 (s, 3H), 5.85 (dd, *J* = 15.6, 1.6, 1H), 7.03 (dt, *J* = 15.6, 7.0, 1H), 7.27 (d, *J* = 7.7, 1H), 7.43 (td, *J* = 7.7, 1.2, 1H), 7.53 (td, *J* = 7.7, 1.3, 1H), 7.82 (dd, *J* = 7.7, 1.3, 1H), 10.19 (s, 1H). ¹³C NMR: 31.5 (CH₂), 33.8 (CH₂), 51.4 (CH₃), 121.7 (CH), 127.0 (CH), 131.2 (CH), 133.7 (C), 133.80 (CH), 133.83 (CH), 143.2 (C), 147.9 (CH), 166.9 (C), 192.8 (CH). IR (neat): 2951, 1724, 1697, 1659. EIMS (*m/z*): 218 (M⁺), 186 (M⁺ - CHO). Anal. calcd. for C₁₃H₁₄O₃: C, 71.54; H, 6.47. Found: C, 71.60; H, 6.60.

⁸ Hudson, C. M.; Marzabadi, M. R.; Moeller, K. D.; New, D. G. *J. Am. Chem. Soc.* **1991**, *113*, 7372–7385.

⁹ Sieber, F.; Wentworth Jr., P.; Toker, J. D.; Wentworth, A. D.; Metz, W. A.; Reed, N. N.; Janda, K. D. *J. Org. Chem.* **1999**, *64*, 5188–5192.

Characterization Data of New Compounds

Methyl (4-methyl-2-oxocyclohexane)acetate (**5c**):

purified by column chromatography (hexane/acetone 25/1) to give a 1.2:1 mixture of the diastereomers as a colorless oil: ^1H NMR: 0.94 (d, $J = 7.0$, 1.35H), 1.04 (d, $J = 6.4$, 1.65H), 1.35–1.50 (m, 1.1H), 1.60–1.71 (m, 0.9H), 1.80–1.90 (m, 1.1H), 1.94–2.02 (m, 0.9H), 2.05–2.22 (m, 2.55H), 2.41 (ddd, $J = 13.2, 3.7, 2.4$, 0.55H), 2.41–2.47 (m, 0.45H), 2.58 (dd, $J = 13.5, 5.8$, 0.45H), 2.75 (dd, $J = 16.5, 7.3$, 0.45H), 2.76–2.89 (m, 1.55H), 3.68 (s, 3H). ^{13}C NMR: 18.6 (CH_3), 22.3 (CH_3), 28.5 (CH_2), 30.3 (CH_2), 31.8 (CH_2), 32.6 (CH_2), 33.7 (CH_2), 33.9 (CH_2), 34.1 (CH), 35.4 (CH), 46.2 (CH), 46.6 (CH), 47.8 (CH_2), 49.9 (CH_2), 51.6 (2 CH_3), 173.0 (C), 173.2 (C), 210.6 (C), 211.2 (C). IR (neat): 2955, 2923, 1740, 1713. EIMS (m/z): 184 (M^+), 152. HRMS–EI: M^+ calcd for $\text{C}_{10}\text{H}_{16}\text{O}_3$, 184.1099; found, 184.1102.

2-(3-Phenylpropyl)cyclohexanone (**5h**):

Purified by column chromatography (hexane/ether 19/1) after concentration in vacuo. A colorless oil: ^1H NMR: 1.22–1.43 (m, 2H), 1.56–1.71 (m, 4H), 1.80–1.87 (m, 2H), 2.00–2.13 (m, 2H), 2.24–2.39 (m, 3H), 2.56–2.66 (m, 2H), 7.15–7.28 (m, 5H). ^{13}C NMR: 24.8 (CH_2), 27.9 (CH_2), 29.0 (CH_2), 29.1 (CH_2), 33.8 (CH_2), 36.0 (CH_2), 41.9 (CH), 50.6 (CH_2), 125.7 (CH), 128.3 (CH), 128.4 (CH), 142.5 (C), 213.4 (C). IR (neat): 2936, 2858, 1709, 1450. EIMS (m/z): 216 (M^+), 91 (tolyl). HRMS–EI: M^+ calcd for $\text{C}_{15}\text{H}_{20}\text{O}$, 216.1514; found, 216.1507.

1b

5f

5h

No.	(ppm)	(Hz)	Height
1	24.78	3114.1	0.3469
2	27.93	3509.3	0.2787
3	28.97	3640.7	0.4826
4	29.07	3653.1	0.4497
5	33.80	4246.9	0.5306
6	36.01	4524.1	0.5576
7	41.92	5266.9	0.3453
8	50.61	6362.4	0.3265
9	76.74	9843.0	0.5385
10	77.00	9675.1	0.4904
11	77.26	9707.1	0.4682
12	125.67	15790.1	0.5292
13	128.26	16116.0	1.0000
14	128.38	16131.5	0.9274
15	142.48	17902.6	0.1911

trans 5j

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