Lewis acid promoted radical annulation reaction of 2-bromopentenoyl-2-oxazolidinones with 1-hexene

Ivanka K. Kavrakova*

Institute of Organic Chemistry with Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria

Radical Lewis acid promoted annulation reaction of 2-bromopentenoyl-2-oxazolidinones with 1-hexene proceeded smoothly under mild conditions to give functionalised cyclopentane derivatives in good yield but with modest diastereoselectivity. Reductive debromination with tris(trimethylsilyl)silane, LiOOH hydrolysis and esterification provided cleanly the corresponding cyclopentaneacetic acid and its methyl ester.

Keywords: radical annulation, stereoselection, oxazolidinones, Lewis acids, alkenes

Much attention has been devoted to the synthesis of cyclopentane derivatives from alkenes,[1] owing to their usefulness in organic chemistry and the need for an efficient preparation of highly substituted cyclopentanes. Radical annulation reactions[2] provide a powerful one-step synthesis of cyclopentanoids. Thus, Curran has demonstrated successful annulations of mono- and 1,1-disubstituted alkenes with allyl and propargyl iodomalonates.[3] It was subsequently shown[4] that iodomalononitriles significantly extend the scope of the annulation of electrophilic radicals with mono-, di- and trisubstituted alkenes. However, light-sensitive iodides were used as the starting material, and these reactions proceeded at prolonged heating in the dark. Cyclopentanedicarboxylic acid derivatives were thus obtained in good yields but with modest diastereoselectivity.

Porter and co-workers[5] have shown that Lewis acids promote the stereoselective atom-transfer addition of 3-bromoacetyl-2-oxazolidinones to terminal and internal alkenes at room temperature and below. The Lewis acid complexation enhanced both the rate of the addition of the α-carbonyl radical to the alkene and the halogen abstraction by the resulting nucleophilic carbon radical.[5]

We reported recently the stereoselective Lewis acid promoted Kharasch-type addition of 3-bromoacetyl-2-oxazolidinones to cycloalkenes.[6,7] We report here experiments that explore the opportunity to apply this approach to the bromine atom-transfer radical annulation of 1-hexene using the readily prepared 3-(2-bromopentenoyl)-2-oxazolidinones **2a–c** as radical precursors (Scheme 1).

In the presence of $Yb(OTf)_3$ as the Lewis acid, the reaction of 1-hexene with **2a** proceeded cleanly at 25 °C in dichloroethane and at –78 °C in dichloromethane/tetrahydrofuran (9:1) co-solvent system. The desired annulation product **3a** was obtained with improved yield and diastereoselectivity compared with the reaction in the absence of Lewis acid (Scheme 1, Table 1).

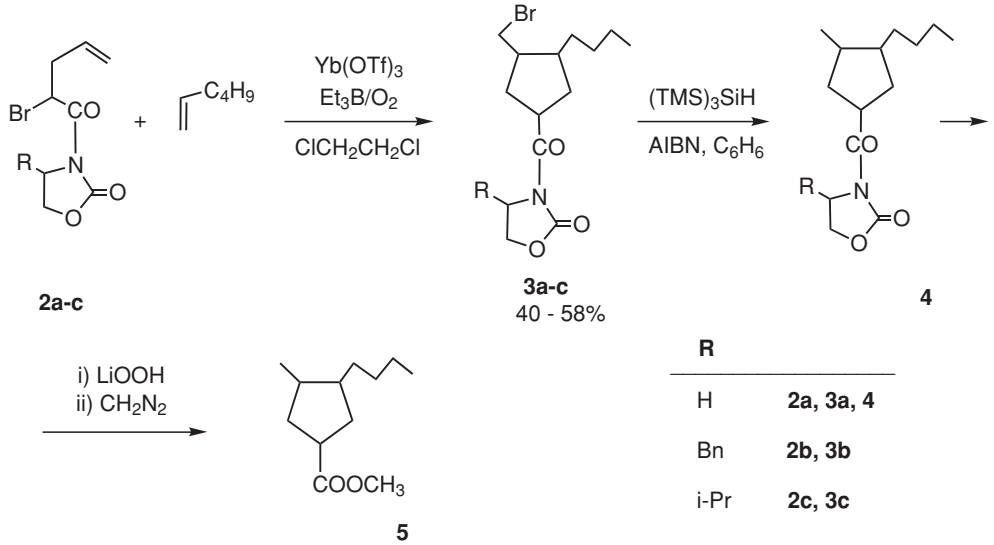
Product of 5-*exo* cyclisation was formed exclusively. Only small amounts of reductive debromination product were detected.

Bromide **3a**, which was isolated as an inseparable mixture of stereoisomers by silica gel chromatography, was stable on storage at ambient temperature. Its reduction with tris

Table 1 Diastereoselectivity and yields of **3a–c**

Entry	**2** (R)	T/°C	**3a–c**	
			Dr[a]	Yield/%
1	**2a** (H)[b]	25	20 : 12 : 58 : 10	43
2	**2a** (H)	25	17 : 7 : 75 : 0	58
3	**2a** (H)	–78	13 : 1 : 86 : 0	40
4	**2b** (*4R*-Bn)	25	22 : 4 : 7 : 58 : 9	44
5	**2c** (*4S*-iPr)	25	20 : 6 : 67 : 7 : 4	45

[a]Ratio of peaks in the order eluted from the GLC column.
[b]Without $Yb(OTf)_3$.
All reactions with 1 eq. $Yb(OTf)_3$, 5 eq.1-hexene, 0.5 eq. Et_3B.



Scheme 1

* Correspondent. E-mail: ivkav@orgchm.bas.bg

(trimethylsilyl)silane at 75 °C in benzene with AIBN initiation produced the corresponding cyclopentaneacetic acid derivative **4**. Standard hydrolysis[5a] of **4** and esterification provided the methyl ester of 3-methyl-4-butyl-cyclopentanecarboxylic acid **5** (Scheme 1).

Disappointingly, 1,1- and 1,2-disubstituted alkenes (*cis* and *trans*-3-hexene, *trans*-4-octene, 2-ethyl-1-butene) failed to react, presumably due to insufficiently rapid initial radical addition to these disubstituted alkenes.

The reaction of 1-hexene with the (4*R*)-benzyl and (4*S*)-isopropyl-2-oxazolidinone auxiliaries **2b** and **2c** led to products **3** with modest diastereoselectivity (Table 1). Very low degrees of conversion were observed with **2b** and **2c** at –78 °C.

The annulation reaction exhibited moderate stereocontrol, which could be expected considering its complexity as well as literature precedent for this type of reactions.[3] Various other Lewis acids ($MgBr_2$, $Mg(OTf)_2$, $Zn(OTf)_2$, $La(OTf)_3$, $Eu(OTf)_3$, $Sc(OTf)_3$) and solvents tested did not substantially affect the diastereoselectivity. Our tentative assignment of all-*cis* configuration for the major stereoisomer obtained is based on Beckwith's guidelines[8] for hex-5-enyl radical cyclisations, assuming a chair-like transition state with all three substituents in pseudoequatorial positions.

Experimental

α-Bromoacyl-1,3-oxazolinones **2a–c** were prepared in analogy to the reported method.[9] All other reagents were obtained from commercial suppliers and used without further purifucation. Diastereomeric ratios were determined by GC (column HP-5-30m × 0.25mm × 0.25μm; gas, N_2, 25 cm/s., injector temp. 280°C, detector temp. 280°C; oven temp. 100–250@150°C/min, 250–280@50°C/min. NMR spectra were recorded at 250 MHz in $CDCl_3$ relative to TMS as internal standard.

3-(Pent-4-enoyl)-1,3-oxazolidin-2-one (**1a**): Oil, 69% yield; ^{1}H NMR: 5.64–5.78 (m, 1H), 4.84–4.99 (m, 2H), 4.24–4.33 (m, 2H), 3.88–3.92 (m, 2H), 2.86–3.85 (m, 2H), 2.22–2.31 (m, 2H); ^{13}C NMR: 171.2, 152.7, 136.1, 114.0, 61.3, 41.3, 33.0, 26,8. Anal. Calcd. for $C_8H_{11}NO_3$: C, 56.80; H, 6.55; N, 8.28; Found: C, 56.71; H, 6.29; N, 8.52.

(4R)-4-Benzyl-3-(pent-4-enoyl)-1,3-oxazolidin-2-one (**1b**): Oil, 91% yield; $[\propto]_D$ –73.83° (c, 1.13 in CH_2Cl_2). ^{1}H NMR: 7.19–7.31 (m, 5H), 5.80–5.96 (m, 1H), 5.00–5.15 (m, 2H), 4.15–4.28 (m, 2H), 4.63–4.72 (m, 1H), 3.29 (dd, 1H, *J* = 3.9, 15.9), 2.93–3.17 (m, 2H), 2.75 (dd, 1H, *J* = 11.5, 15.9), 2.17–2.50 (m, 2H); ^{13}C NMR: 172.3, 153.3, 145.6, 136.5, 135.1, 129.2, 128.7, 128.4, 127.1, 115.5, 66.0, 54.9, 37.6, 34.6, 28.0. Anal. Calcd. for $C_{15}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40; Found: C, 69.37; H, 6.61; N, 5.46.

(4S)-4-Isopropyl-3-(pent-4-enoyl)-1,3-oxazolidin-2-one (**1c**): Oil, 81% yield; $[\propto]_D$ +76.47° (c, 1.13 in CH_2Cl_2). ^{1}H NMR: 5.75–5.91 (m, 1H), 4.96–5.28 (m, 2H), 4.38–4.44 (m, 1H), 4.16–4.28 (m, 2H), 2.87–3.15 (m, 2H), 2.23–2.43 (m, 3H), 0.83–0.90 (m, 6H); ^{13}C NMR: 171.7, 153.5, 136.3, 114.9, 62.9, 57.8, 34.1, 27.9, 27.8, 17.3, 14.1. Anal. Calcd. for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11; N, 6.72; Found: C, 62.77; H, 8.20; N, 6.72.

3-(2-Bromopent-4-enoyl)-1,3-oxazolidin-2-one (**2a**): Oil, 57% yield; ^{1}H NMR: 5.66–5.88 (m, 1H), 5.61 (t, *J* = 8.8, 1H), 5.11–5.19 (m, 2H), 4.41–4.52 (m, 2H), 4.02–4.11 (m, 2H), 2.61–2.96 (m, 2H); ^{13}C NMR: 168.8, 152.6, 133.0, 112.2, 62.1, 42.7, 41.6, 38.0. Anal. Calcd. for $C_8H_{10}BrNO_3$: C, 38.73; H, 4.06; N, 5.65; Found: C, 38.98; H, 3.89; N, 5.79.

(4R)-4-Benzyl-3-(2-bromopent-4-enoyl)-1,3-oxazolidin-2-one (**2b**): Oil, 75% yield; $[\propto]_D$ –67.67° (c, 0.72 in CH_2Cl_2). ^{1}H NMR: 7.99–7.69 (m, 5H), 5.71–5.90 (m, 1H), 5.66 (t, *J* = 8.9, 1H), 5.14–5.26 (m, 2H), 4.63–4.77 (m, 1H), 4.14–4.27 (m, 2H), 3.31 (dd, *J* = 3.8, 15.3, 1H), 2.91–3.12 (m, 1H), 2.72–2.86 (m, 2H); ^{13}C NMR: 168.5, 152.3, 134.7, 133.0, 129.4, 128.9, 127.3, 119.2, 66.0, 55.0, 42.1, 37.8, 36.8. Anal. Calcd. for $C_{15}H_{16}BrNO_3$: C, 53.27; H, 4.77; N, 4.14; Found: C, 53.13; H, 4.71; N, 4.21.

(4S)-3-(2-Bromopent-4-enoyl)-4-isopropyl-1,3-oxazolidin-2-one (**2c**): Oil, 54% yield; $[\propto]_D$ +59.49° (c, 0.97 in CH_2Cl_2). ^{1}H NMR: 5.73–5.85 (m, 1H), 5.69 (t, *J* = 9.7, 1H), 5.11–5.22 (m, 2H), 4.42–4.53 (m, 1H),4.22–4.35 (m, 2H), 2.47–3.37(m, 1H), 2.88–3.01 (m, 1H), 2.70–2.80 (m, 1H), 0.96 (d, *J* = 3.5, 3H), 0.93 (d, *J* = 3.5, 3H); ^{13}C NMR: 168.6, 152.9, 133.2, 119.1, 63.4, 58.2, 42.0, 37.6, 27.8, 17.7, 14.7. Anal. Calcd. for $C_{11}H_{16}BrNO_3$: C, 45.53; H, 5.56; N, 4.83; Found: C, 45.40; H, 5.51; N, 4.85.

Annulation reaction: The ∝-bromoacyl-1,3-oxazolinone **2a–c** (0.25 mmols) was dissolved in 1,2-dichloroethane (5 ml), ytterbium trifluoromethanesulfonate (0.155g, 0.25 mmols) were added and stirred for 15 min. The mixture was purged with dry air for 5 min and 1-hexene (0.16 ml, 5 equiv.) and triethylborane (1M in hexanes, 125 μl, 0.5 equiv.) were added sequentially. Stirring was continued for 2 h. The mixture was diluted with ether (100 ml), washed with saturated ammonium chloride solution (75 ml), dried over anhydrous magnesium sulfate and volatiles were removed by rotary evaporation.

For the low temperature experiments 10% solution of tetrahydrofuran in methylenechloride was used as a solvent and the reaction mixture was cooled to –78°C before 1-hexene addition and initiation with Et_3B.

3-(3-Bromomethyl-4-butylcyclopentanecarbonyl)-1,3-oxazolidin-2-one (**3a**): ^{1}H NMR: 4.45–4.48 (m, 2H), 3.93–4.10 (m, 3H), 3.40–3.60 (m, 1H), 3.32 (t, *J* = 11.9, 1H), 2.02–2.47 (m, 4H), 1.83–1.98 (m, 1H), 1.61–1.79 (m, 1H), 1.24–1.43 (m, 6H), 0.84–1.05 (m, 3H); ^{13}C NMR: 176.2, 153.1, 61.9, 48.0, 44.9, 42.8, 41.0, 35.5, 34.2, 34.0, 30.5, 29.0, 22.7, 14.0. Anal. Calcd. for $C_{14}H_{22}BrNO_3$: C, 50.61; H, 6.67; N, 4.22; Found: C, 50.66; H, 6.38; N, 4.31.

(4R)-4-Benzyl-3-(3-bromomethyl-4-butylcyclopentanecarbonyl)-1,3-oxazolidin-2-one (**3b**): $[\propto]_D$ –56.25° (c, 0.30 in CH_2Cl_2). ^{1}H NMR: 7.20–7.37 (m, 5H), 4.62–4.73 (m, 1H), 4.09–4.29 (m, 2H), 3.88–4.06 (m, 1H), 3.50–3.56 (m, 1H), 3.35 (t, *J* = 10.0, 1H), 3.24–3.60 (m, 1H), 2.71–2.82 (m, 1H), 2.35–2.53 (m, 1H), 1.63–2.32 (m, 5H), 1.14–1.47 (m, 6H), 0.82–1.00 (m, 3H); ^{13}C NMR: 175.8,153.1, 135.3, 129.4, 128.9, 127.3, 66.2, 55.4, 48.0, 43.4, 42.9, 41.4, 40.9, 37.5, 35.1, 33.9, 33.6, 30.3, 29.1, 22.8, 14.1. Anal. Calcd. for $C_{21}H_{28}BrNO_3$: C, 59.72; H, 6.68; N, 3.32; Found: C, 61.06; H, 6.76; N, 3.37.

(4S)-3-(3-Bromomethyl-4-butylcyclopentanecarbonyl)-4-isopropyl-1,3-oxazolidin-2-one (**3c**): $[\propto]_D$ +50.50° (c, 0.50 in CH_2Cl_2). ^{1}H NMR: 4.35–4.50 (m, 1H), 4.11–4.32 (m, 2H), 3.80–4.08 (m, 1H), 3.41–3.62 (m, 1H), 3.32 (t, *J* = 10.0, 1H), 1.59–2.07 (m, 7H), 1.20–1.30 (m, 6H), 0.88 (dd, *J* = 6.9, 9.9, 9H); ^{13}C NMR: 175.7, 153.7, 63.2, 58.6, 45.0, 42.9, 40.9, 36.3, 35.5, 34.8, 33.3, 30.5, 28.3, 22.8, 17.9, 14.6, 14.0. Anal. Calcd. for $C_{17}H_{28}BrNO_3$: C, 54.55; H, 7.54; N, 3.74; Found: C, 54.77; H, 7.56; N, 3.87.

3-(3-Methyl-4-butylcyclopentanecarbonyl)-1,3-oxazolidin-2-one (**4**): Under argon, **3a** (0.25 mmols) was dissolved in degassed benzene (5 ml), tris(trimethylsilyl)silane (0.10 ml, 1.3 equiv.) were added and the mixture was warmed to 75 °C.

AIBN (15 mg) dissolved in benzene (0.5 ml) were added and the mixture heated for 2 h. The reaction was quenched with saturated ammonium chloride solution (50 ml) and extracted with ether (50 ml), dried over anhydrous magnesium sulfate, filtered and concentrated. Product **4** was isolated as an oil in 73% yield by column chromatography on silica gel, using 20% ethyl acetate in hexanes.

^{1}H NMR: 4.35–4.43 (m, 2H), 3.95–4.06 (m, 2H), 3.78–3.93 (m, 1H), 1.80–2.30 (m, 3H), 1.44–1.77 (m, 3H), 1.05–1.40 (m, 6H), 0.70–0.97 (m, 6H); ^{13}C NMR: 176.8, 153.2, 61.8, 43.3, 42.9, 41.6, 27.2, 35.7, 33.9, 30.8, 29.8, 23.0, 15.5, 14.1. Anal. Calcd. for $C_{14}H_{23}NO_3$: C, 66.37; H, 9.15; N, 5.53; Found: C, 66.21; H, 9.17; N, 5.29.

Methyl 3-methyl-4-butylcyclopentane-1-carboxylate (**5**): 41% yield; ^{1}H NMR: 3.65 (s, 3H), 2.71–2.77 (m, 1H), 2.07–2.08 (m, 3H), 1.30–1.62 (m, 3H), 1.25–1.27 (m, 6H), 0.83–0.91 (m, 6H); ^{13}C NMR: 117.3, 51.6, 43.2, 42.3, 37.2, 34.3, 30.8, 29.8, 22.9, 15.5. 14.1. Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18; Found: C, 72.81; H, 11.34.

The author thanks Dr Ned A. Porter, Vanderbilt University, Nashville, USA, for his support of this work.

Received 17 March 2005; accepted 2 June 2005
paper 05/3134

References

1 Reviews on cyclopentannulation: (a) L.A. Paquette and A.M. Doherty, *Polyquinane Chemistry*, Springer-Verlag; NY, 1987; (b) M. Ramaiah, *Synthesis*, 1984, 529.

2 R.L. Danheiser, S.K. Gee and H. Sard, *J. Am. Chem. Soc*., 1982, **104**, 7670.

3 D.P. Curran, M.H. Chen, E. Spletzer, C.M. Seong and C.T. Chang, *J. Am. Chem. Soc.*, 1989, **111**, 8872; (b) D.P. Curran and C.T. Chang, *J. Org. Chem*., 1989, **54**, 3140.

4 (a) D.P. Curran and C.M. Seong, *Tetrahedron*, 1992, **48**, 2157; (b) 2175.

5 (a) C.L. Merro and N.A. Porter, *J. Am. Chem. Soc*., 1999, **121**, 5155; (b) H. Feng, I.K. Kavrakova, D.A. Pratt, J. Tellinghuisen and N.A. Porter, *J. Org. Chem*., 2002, **67**, 6050.

6 I.K. Kavrakova and J.H. Mills, *J. Chem. Res*., 2005, **1**, 59.

7 I.K. Kavrakova, P.S. Denkova and R.P. Nikolova, *Tetrahedron: Asymmetry*, 2005, **16**, 1085.

8 A.L.J. Beckwith and C. Schiesser, *Tetrahedron*, 1985, **41**, 3925.

9 D.A. Evans, T.C. Britton, A.E. Jonathan and R.L. Dorow, *J. Am. Chem. Soc*., 1990, **112**, 4011.