Tetrahedron 68 (2012) 846–850

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Regio-selective reduction of the C–C double bonds in α,β-unsaturated acyl 4-substituted oxazolidin-2-ones and oxazolidine-2-thiones

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ARTICLE INFO

Article history:
Received 7 October 2011
Received in revised form 4 November 2011
Accepted 15 November 2011
Available online 22 November 2011

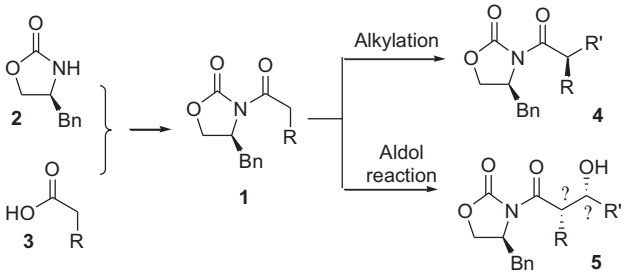
Keywords:
Reduction
Alkenes
Chiral auxiliary
Hydride
Stereochemistry

ABSTRACT

Selective saturation of the conjugated C–C double bonds in the title compounds was examined in a systematic way for the first time. Many established protocols effective for similar reduction of α,β-unsaturated ketones and esters in the literature were found to be inapplicable in the present context. The most satisfactory results were finally obtained using the DIBAL-H/MeLi/CuI/HMPA/THF conditions.

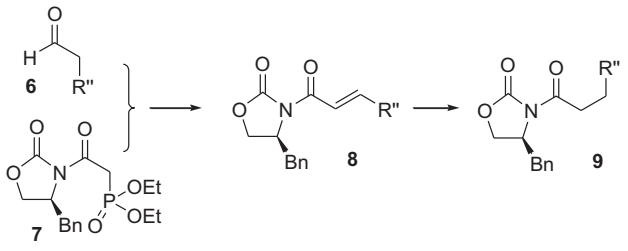
1. Introduction

N-acyl oxazolidinones (e.g., **1**) are the key precursors in Evans asymmetric alkylation and aldol reactions (Scheme 1).[1] Since their introduction in the early 1980s, these reactions have found countless successful applications in enantioselective synthesis of a diverse of optically active compounds.



Scheme 1. The most common route to *N*-acyl oxazolidinones and their applications.

In many cases so far documented in the literature the R (in **1**, Scheme 1) is a simple alkyl group. Therefore, the most straightforward access to **1** is the N-acylation[2] of the chiral auxiliary **2**[3] with the corresponding carboxylic acid **3**. However, exceptions also exist. For instance, for those *N*-acyl oxazolidinones exemplified by **9**, especially when the R″ contains multi stereogenic centers and functionalities, it is often more convenient to derive such species from **8**,[4] which in turn may be constructed from **6** and **7** (Scheme 2).



Scheme 2. An alternative route to the *N*-acyl oxazolidinones.

As the selective reduction of the conjugated C–C double bonds in species like **8** is an essential step in such an approach and to our knowledge no systematic investigations[5] on this type of reductions have ever been reported, we performed the present work in connection with some on-going total synthesis projects. The results are given below.

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doi:10.1016/j.tet.2011.11.038

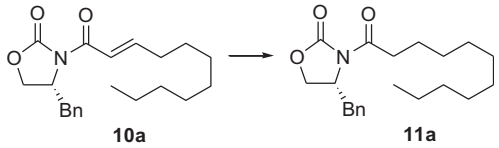
2. Results and discussion

There have been quite a few established protocols that were shown to be effective for selective reduction of the conjugate C–C double bonds in α,β-unsaturated ketones and esters. Because of the apparent structural similarity as far as the conjugate system is concerned, we first examined those conditions listed in Table 1, using the readily accessible **10a** as the substrate (Scheme 3).

Table 1
Reduction of **10a** into **11a** under different conditions

Entry	Conditions	Yield of **11a**
1	K-Selectride/THF/−78 °C	0[a]
2	Super Hydride/THF/0 °C	0[b]
3	Sm/I_2/THF/MeOH/0 °C	0[b]
4	$LiAlH_4$/CuI/THF/0 °C	57%[c]
5	CuI/MeLi/DIBAL-H/HMPA/THF/−78 °C	27%[d]
6	CuI/MeLi/DIBAL-H/HMPA/THF/−78 °C	95%[e]

[a] The chiral auxiliary **2** was completely cut off from the acyl chain.
[b] No species with an intact oxazolidinone ring could found in the product mixture.
[c] The remainder of the product mixture were side product(s) without the oxazolidinone moiety.
[d] Using 1.2 mol equiv (with respect to **10a**) of DIBAL-H with most of the starting **10a** unreacted.
[e] Using 8 mol equiv of DIBAL-H with the starting **10a** fully consumed.



Scheme 3. The model reaction used for screening the conditions.

The results are listed in Table 1. Under the K-Selectride (KBH(*sec*-Bu)$_3$) conditions, which had led to satisfactory 1,4-reduction of some cyclic enones in the literature,[6] neither the desired **11a** nor any other species with an intact oxazolidinone ring in the molecule was detected (Table 1, entry 1).

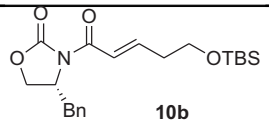
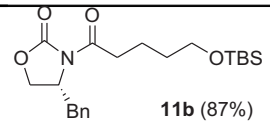
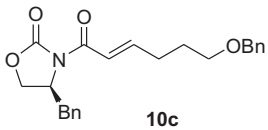
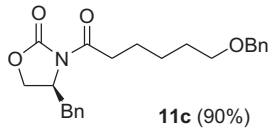
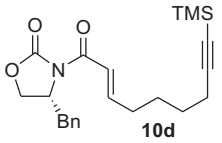
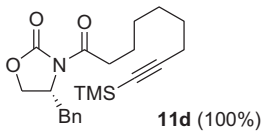
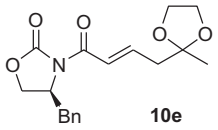
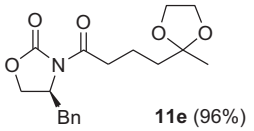
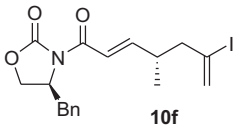
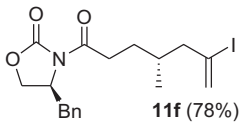
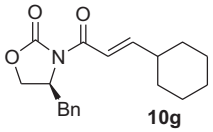
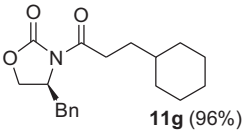
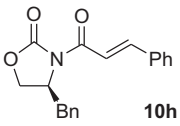
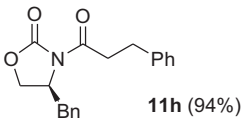
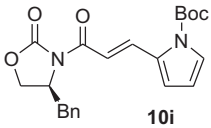
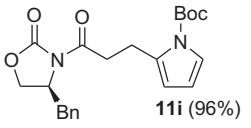
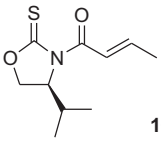
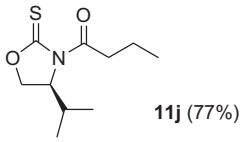
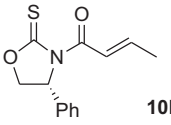
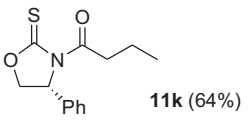
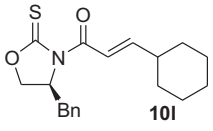
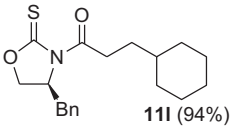
Super Hydride ($LiBHEt_3$) is also one of the reducing agents that may result in 1,4-reductions. Using this reagent Nagamitsu and Omura[7] recently achieved regioselective 1,4-reduction of a cyclic amide. Unfortunately, when applied to the reduction of **10a** only reductive ring-opening of the oxazolidinone occurred (Table 1, entry 2). Similar results were also observed with SmI_2, which was quite successful with Nagata's[8] substrate but appeared incompatible with the oxazolidinone rings (Table 1, entry 3).

The outcome with $LiAlH_4$/CuI[9] was much better (Table 1, entry 4). Under such conditions the desired **11a** could be isolated in 57% yield. Nevertheless, all the remaining components in the product mixture did not have the oxazolidinone moiety, making this protocol less attractive for further studying.

The yield of **11a** was only 27% when performing the reduction under the DIBAL-H (1.2 equiv)/MeLi/CuI/HMPA[10] conditions (Table 1, entry 5). However, as the remainder of the product mixture was the unreacted starting **10a** rather than undesired side products. Further improvements were thus still possible. Indeed, when we increased the amount of the added DIBAL-H from 1.2 to 8 mol equiv (with respect to substrate **10a**), all starting **10a** was reduced, affording the anticipated **11a** in 95% isolated yield (Table 1, entry 6).

With such a satisfactory set of mild conditions in hand, we next set out to examine the 1,4-reduction with a range of other substrates. The main results are summarized in Table 2. Generally speaking, the reduction with the DIBAL-H/MeLi/CuI/HMPA

Table 2
Outline for the conjugate reduction of **10b–l**[a]

Entry	Substrate	Product (yield)
1	 **10b**	 **11b** (87%)
2	 **10c**	 **11c** (90%)
3	 **10d**	 **11d** (100%)
4	 **10e**	 **11e** (96%)
5	 **10f**	 **11f** (78%)
6	 **10g**	 **11g** (96%)
7	 **10h**	 **11h** (94%)
8	 **10i**	 **11i** (96%)
9	 **10j**	 **11j** (77%)
10	 **10k**	 **11k** (64%)
11	 **10l**	 **11l** (94%)

[a] All reductions were performed in THF at −78 °C for 70 min in the presence of DIBAL-H (8 mol equiv, with respect to **10**)/MeLi (0.5 mol equiv)/CuI (0.5 mol equiv)/HMPA (10 mol equiv).

proceeded very well, with the chiral auxiliary in the substrates remained intact while the C–C double bonds in conjugation with the *N*-acyl carbonyl group were cleanly saturated. Quite a few different functional groups and protecting groups, such as a Me_3Si protected triple bond, an isolated double bond with an iodine and a cyclic ketal, were all well-tolerated (Table 2, entries 1–5).

The DIBAL-H derived reducing species are bound to being sterically bulky. Therefore, whether the steric crowding at the reducing sites would affect the efficiency of the desired conjugate reduction deserves particular attention. It is interesting to note that several substrates with a substituent at the allylic position, such as **10f** and **10g**, still gave rather high yields of the 1,4-reduction products (Table 2, entries 5 and 6).

Additional conjugation is apparently present in substrates **10h** and **10i** (Table 2, entries 7 and 8). In a sense, these compounds are also similar to those allylic substituted substrates and consequently may suffer substantially increased steric crowding at the C–C double bond compared with those linear substrates (Table 2, entries 1–4). Interestingly, the yields for the corresponding 1,4-reduction products turned out to be very good. It is also noteworthy that the Boc (*tert*-butoxycabonyl) protecting group on the pyrrole (**10i**) survived the reduction.

Apart from the above mentioned *N*-acyl oxazolidinones, we also briefly examined the corresponding oxazolidinethiones, which are often more labile to reductive cleavage (a main advantage for introducing such sulfur-containing chiral auxiliaries) than the similar oxazolidinone auxiliaries. Indeed, when the chiral auxiliary in the substrate is an oxazolidinethione, reductive cleavage of the auxiliary became more significant. However, as the last three entries in Table 2 show, it is still possible to acquire the desired 1,4-reduction products in reasonably good yields.

3. Conclusions

Regio-selective reduction of the C–C double bonds in conjugation with the *N*-acyl carbonyl groups in a series of oxazolidinones and oxazolidinethiones was examined systematically for the first time. Several sets of conditions that were shown to be effective for conjugate reduction of α,β-unsaturated ketones, esters or amides were checked in the present context. Because of the presence of the chiral auxiliary, the 1,4-reduction of the *N*-acyl oxazolidinones and oxazolidenethiones was apparently more complicated than the corresponding reduction of α,β-unsaturated ketones, esters or amides. Cleavage (cutting-off) and/or ring-opening of the chiral auxiliaries were observed with several sets of conditions. However, the DIBAL-H/MeLi/CuI/HMPA combination gave good to excellent yields of the desired products. Because this reduction protocol has the functional group compatibility apparently different from that for hydrogenation[4a] or catecholborane reduction,[4b] it may greatly complement the existing methodologies and provide more facile access to the *N*-acyl oxazolidinones and oxazolidinethiones containing multi stereogenic centers and functionalities.

4. Experimental

4.1. General

THF was distilled over Na/Ph_2CO under N_2 prior to use. HMPA was stirred with CaH_2 for several days (using a flat balloon to collect the gas evolved) before being distilled under vacuum prior to use. Addition of air/moisture sensitive reagents was done using syringe techniques. PE (for chromatography) stands for petroleum ether (bp 60–90 °C). Column chromatography was performed on silica gel (300–400 mesh) under slightly positive pressure. NMR spectra were recorded on a Bruker Avance 400 NMR spectrometer operating at 400 MHz for proton. IR spectra were measured on a Nicolet 380 Infrared Spectrometer. ESI-MS data were acquired on a Shimadzu LCMS-2010EV mass spectrometer. MALDI-HRMS data were obtained with a Bruker APEXIII 7.0 Tesla FT-MS or an Agilent 6538 UHD Accurate-Mass Q-TOF spectrometer. Optical rotations were measured on a Jasco P-1030 Polarimeter. Melting points (uncorrected) were measured on a hotstage melting point apparatus equipped with a microscope.

4.2. Synthesis

*4.2.1. General procedure for the preparation of the reduction substrates **10** (Wittig–Horner reaction).* *i*-Pr_2NEt (3.0 mmol) was added to a solution of **7**[11] (or a similar Horner reagent as required, 1.0 mmol), LiCl (4.0 mmol), and the aldehyde (1.3 mmol) in MeCN (5 mL) stirred in an ice-water bath. The mixture was stirred at the same temperature for 4 h before being partitioned between water (10 mL) and Et_2O (70 mL). The phases were separated. The aqueous layer was back extracted with Et_2O (10 mL×2). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (EtOAc/PE) on silica gel gave the condensation product **10**.

Data for **10a** (a white solid, 58% yield): mp 69–69 °C (very sharp). $[\alpha]_D^{25}$ −55.0 (*c* 1.00, $CHCl_3$). ^1H NMR: (400 MHz, $CDCl_3$) δ 7.37–7.15 (m, 7H), 4.77–4.67 (m, 1H), 4.25–4.12 (m, 2H), 3.33 (dd, *J*=13.3, 3.0 Hz, 1H), 2.79 (dd, *J*=13.3, 7.3 Hz, 1H), 2.30 (dt, *J*=6.0, 7.3 Hz, 2H), 1.57–1.45 (m, 2H), 1.40–1.21 (m, 10H), 0.88 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 153.4, 152.0, 135.4, 129.4, 128.9, 127.3, 120.3, 66.0, 55.3, 37.9, 32.7, 31.8, 29.3, 29.17, 29.15, 28.1, 22.6, 14.0; FT-IR (KBr) 2956, 2924, 2854, 1783, 1681, 1355, 1205, 1054, 1002, 988, 732, 713 cm^{-1}. ESI-MS *m*/*z* 366.1 ($[M+Na]^+$); ESI-HRMS calcd for $C_{21}H_{29}NO_3Na$ ($[M+Na]^+$) 366.2040, found 366.2045.

Data for **10b** (a colorless oil, 58% yield): $[\alpha]_D^{24}$ −42.65 (*c* 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.17 (m, 7H), 4.77–4.69 (m, 1H), 4.24–4.13 (m, 2H), 3.77 (t, *J*=6.2 Hz, 1H), 3.33 (dd, *J*=13.5, 2.8 Hz, 1H), 2.80 (dd, *J*=13.5, 8.5 Hz, 1H), 2.52 (dt, *J*=6.2, 12.9 Hz, 1H), 0.90 (s, 9H), 0.07 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 153.4, 148.4, 135.3, 129.4, 128.9, 127.3, 121.8, 66.1, 61.6, 55.2, 37.8, 36.2, 25.9, 18.3, −5.4; FT-IR (film) 2954, 2928, 2857, 1782, 1683, 1637, 1100, 837, 777, 701 cm^{-1}. ESI-MS *m*/*z* 412.3 ($[M+Na]^+$); ESI-HRMS calcd for $C_{21}H_{31}NO_4SiNa$ ($[M+Na]^+$) 412.1915, found 412.1914.

Data for **10c** (a yellowish oil, 76% yield): $[\alpha]_D^{24}$ +46.7 (*c* 1.00, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.19 (m, 12H), 4.77–4.67 (m, 1H), 4.51 (s, 2H), 4.24–4.13 (m, 2H), 3.52 (t, *J*=6.1 Hz, 2H), 3.33 (dd, *J*=13.3, 3.3 Hz, 1H), 2.79 (dd, *J*=13.3, 9.6 Hz, 1H), 2.42 (dt, *J*=7.4, 7.7 Hz, 2H), 1.83 (tt, *J*=7.7, 6.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0, 153.4, 151.0, 138.4, 135.4, 129.4, 128.9, 128.4, 127.6, 127.5, 127.3, 120.6, 72.9, 69.3, 66.1, 55.3, 37.8, 29.4, 28.2; FT-IR (film) 3065, 3022, 2924, 2848, 1770, 1681, 1489, 1451, 1092, 913, 745, 696 cm^{-1}. ESI-MS *m*/*z* 402.2 ($[M+Na]^+$); ESI-HRMS calcd for $C_{23}H_{25}NO_4Na$ ($[M+Na]^+$) 402.1676, found 402.1675.

Data for **10d** (a white solid, 78% yield): mp 64–65 °C $[\alpha]_D^{24}$ −27.1 (*c* 0.28, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.15 (m, 7H), 4.78–4.67 (m, 1H), 4.25–4.14 (m, 2H), 3.34 (dd, *J*=13.3, 3.0 Hz, 1H), 2.80 (dd, *J*=13.3, 10.4 Hz, 1H), 2.33 (dt, *J*=6.9, 6.4 Hz, 2H), 2.25 (t, *J*=6.8 Hz, 2H), 1.67–1.55 (m, 4H). 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 153.4, 151.3, 135.4, 129.4, 129.0, 127.3, 120.6, 106.9, 84.1, 66.1, 55.3, 37.9, 32.2, 28.0, 27.2, 19.6, 0.1; FT-IR (KBr) 2939, 2173, 1781, 1638, 1635, 1355, 842, 760, 700 cm^{-1}. ESI-MS *m*/*z* 406.2 ($[M+Na]^+$); MALDI-HRMS calcd for $C_{22}H_{29}NO_3SiNa$ ($[M+Na]^+$) 406.1809, found 406.1811.

Data for **10e** (a white solid, 98% yield): mp 71–72 °C $[\alpha]_D^{24}$ +52.4 (*c* 1.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.15 (m, 7H), 4.76–4.69 (m, 1H), 4.24–4.15 (m, 2H), 4.02–3.94 (m, 4H), 3.35 (dd,

J=13.5, 3.2 Hz, 1H), 2.79 (dd, J=13.5, 9.8 Hz, 1H), 2.66 (d, J=7.1 Hz, 2H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 153.3, 145.6, 135.3, 129.4, 128.9, 127.3, 123.2, 108.9, 66.1, 64.8, 55.3, 42.4, 37.8, 24.3; FT-IR (KBr) 2983, 2921, 1780, 1704, 1682, 1638, 1488, 1361, 1288, 1211, 1143, 1051, 761, 702 cm^{-1}. ESI-MS m/z 354.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{18}H_{21}NO_5Na$ ([M+Na]$^+$) 354.1312, found 354.1324.

Data for **10f** (a yellowish oil, 46% yield): $[\alpha]_D^{28}$ −22.2 (c 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.07 (m, 7H), 6.10 (s, 1H), 5.79 (s, 1H), 4.78–4.68 (m, 1H), 4.25–4.14 (m, 2H), 3.33 (dd, J=13.2, 3.8 Hz, 1H), 2.87–2.75 (m, 2H), 2.54 (dd, J=14.3, 7.0 Hz, 1H), 2.39 (dd, J=14.3, 7.0 Hz, 1H), 1.12 (d, J=6.7 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9, 154.1, 153.3, 135.3, 129.4, 128.9, 127.6, 127.3, 119.5, 109.1, 66.1, 55.2, 50.8, 37.8, 35.9, 18.1; FT-IR (film) 2963, 2923, 1775, 1680, 1632, 1354, 1210, 895, 701 cm^{-1}. ESI-MS m/z 426.0 ([M+H]$^+$); ESI-HRMS calcd for $C_{18}H_{21}NO_3I$ ([M+H]$^+$) 426.0566, found 426.0573.

Data for **10g** (a white solid, 84% yield): mp 114–114 °C (very sharp). $[\alpha]_D^{24}$ +58.4 (c 1.03, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.11 (m, 7H), 4.77–4.67 (m, 1H), 4.23–4.13 (m, 2H), 3.34 (dd, J=13.3, 3.3 Hz, 1H), 2.78 (dd, J=13.3, 9.7 Hz, 1H), 2.30–2.20 (m, 1H), 1.87–1.72 (m, 4H), 1.72–1.63 (m, 1H), 1.39–1.13 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 156.6, 154.4, 135.4, 129.4, 128.9, 127.2, 118.1, 66.0, 55.3, 40.9, 37.9, 31.7, 31.6, 25.8, 25.6; FT-IR (KBr) 2922, 2851, 1782, 1679, 1633, 1386, 1353, 1201, 1052, 764, 734, 703 cm^{-1}. ESI-MS m/z 336.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{19}H_{23}NO_3Na$ ([M+Na]$^+$) 336.1570, found 336.1577.

Data for **10h** (a white solid, 49% yield): mp 126–126 °C (very sharp). $[\alpha]_D^{26}$ +60.3 (c 1.38, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.87 (m, 2H), 6.68–6.60, (m, 2H), 7.45–7.38 (m, 3H), 7.38–7.31 (m, 2H), 7.31–7.21 (m, 3H), 4.85–4.75 (m, 1H), 4.29–4.17 (m, 2H), 3.37 (dd, J=13.4, 3.0 Hz, 1H), 2.85 (dd, J=13.4, 9.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 153.5, 146.4, 135.3, 134.5, 130.7, 129.4, 128.93, 128.87, 128.6, 127.3, 116.9, 66.1, 55.4, 37.9; FT-IR (KBr) 3058, 3059, 3028, 2914, 1776, 1677, 1619, 1389, 1211, 764, 730, 701 cm^{-1}. ESI-MS m/z 330.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{19}H_{17}NO_3Na$ ([M+Na]$^+$) 330.1101, found 330.1108.

Data for **10i** (a gray-brown oil, 60% yield): mp 114–114 °C (very sharp). $[\alpha]_D^{23}$ +42.1 (c 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J=15.9 Hz, 1H), 7.68 (d, J=15.9 Hz, 1H), 7.44–7.40 (m, 1H), 7.39–7.18 (m, 5H), 6.92–6.87 (m, 1H), 6.28–6.21 (m, 1H), 4.84–4.73 (m, 1H), 4.28–4.13 (m, 2H), 3.41–3.31 (m, 1H), 2.83 (dd, J=13.3, 9.8 Hz, 1H), 1.64 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 153.5, 148.8, 136.4, 135.4, 131.5, 129.4, 128.8, 127.2, 125.4, 116.1, 114.8, 111.6, 84.8, 66.0, 55.3, 37.8, 27.9; FT-IR (film) 2978, 2931, 2860, 1778, 1744, 1673, 1601, 1454, 1360, 1277, 1211, 1071, 846, 740, 680 cm^{-1}. ESI-MS m/z 419.2 ([M+Na]$^+$); ESI-HRMS calcd for $C_{22}H_{24}N_2O_5Na$ ([M+Na]$^+$) 419.1577, found 419.1592.

Data for **10j** (a colorless oil, 71% yield): $[\alpha]_D^{26}$ +139.1 (c 1.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J=15.2 Hz, 1H), 7.02–6.90 (m, 1H), 4.61 (ddd, J=7.8, 3.9, 3.7 Hz, 1H), 4.38–4.27 (m, 2H), 2.38–2.22 (m, 1H), 1.87 (d, J=6.9 Hz, 3H), 0.83 (d, J=7.0 Hz, 3H), 0.78 (d, J=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.0, 165.8, 145.7, 123.2, 67.6, 63.1, 28.6, 18.2, 17.9, 14.6; FT-IR (film) 2965, 1780, 1682, 1635, 1481, 1361, 1394, 1199, 1164, 1108, 958, 922, 823 cm^{-1}. ESI-MS m/z 236.0 ([M+Na]$^+$); ESI-HRMS calcd for $C_{10}H_{15}NO_2SNa$ ([M+Na]$^+$) 236.0716, found 236.0727.

Data for **10k** (a yellowish wax, 96% yield): $[\alpha]_D^{26}$ −184.0 (c 0.50, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.65 (m, 1H), 7.43–7.25 (m, 5H), 7.08–6.96 (m, 1H), 5.68 (dd, J=8.7, 4.4 Hz, 1H), 4.81 (dd, J=9.0, 8.7 Hz, 1H), 4.43 (dd, J=9.0, 4.4 Hz, 1H), 1.95 (dd, J=7.0, 1.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 165.7, 146.8, 138.3, 129.2, 128.8, 126.0, 123.3, 74.1, 62.3, 18.5; FT-IR (film) 3065, 3030, 2967, 2914, 1687, 1634, 1367, 1346, 1321, 1298, 1280, 1194, 1161, 1068, 1018, 956, 919, 762, 699, 603, 572 cm^{-1}. ESI-MS m/z 270.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{13}H_{13}NO_2SNa$ ([M+Na]$^+$) 270.0559, found 270.0570.

Data for **10l** (a white solid, 60% yield): mp 93–94 °C $[\alpha]_D^{23}$ +72.2 (c 1.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=5.4 Hz, 1H), 7.38–7.16 (m, 5H), 7.09 (dd, J=15.5, 6.4 Hz, 1H), 4.98–4.84 (m, 1H), 4.38–4.23 (m, 2H), 3.43 (d, J=11.8 Hz, 1H), 2.79 (dd, J=13.0, 10.5 Hz, 1H), 3.32–2.18 (m, 1H), 1.93–1.61 (m, 5H), 1.43–1.10 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.5, 166.5, 155.9, 135.2, 129.3, 128.8, 127.2, 119.5, 70.4, 60.0, 40.7, 37.4, 31.4, 31.3, 25.8, 25.5; FT-IR (KBr) 3062, 3027, 2926, 2852, 1681, 1632, 1474, 1343, 1228, 1193, 1008, 966, 966 cm^{-1}. ESI-MS m/z 330.2 ([M+H]$^+$); MALDI-HRMS calcd for $C_{19}H_{24}NO_2S$ ([M+H]$^+$) 330.1522, found 330.1527.

4.2.2. General procedure for reduction of the C–C double bond in conjugation with the acyl carbonyl group in N-acyl oxazolidinones and oxazolidinethione. MeLi (1.6 M, in Et_2O, 0.8 mL, 0.5 mmol) was added to a mixture of CuI (95 mg, 0.5 mmol) in dry THF (12 mL) stirred under N_2 (balloon) in an ice-water bath. Stirring was continued at the same temperature for 15 min. The ice-water bath was replaced by a −78 °C one. With stirring, dry HMPA (1.7 mL, 10 mmol) was added, followed by DIBAL-H (1 M, in cyclohexane, 8.0 mL, 8 mmol). The mixture was stirred at the same temperature for 70 min. Substrate **10** (1.0 mmol) was added. Stirring was continued at −78 °C for another 70 min. MeOH (5 mL) was added. The bath was allowed to warm to ambient temperature naturally. Aq satd potassium sodium tartrate (20 mL) was added, followed by Et_2O (30 mL). The mixture stirred at ambient temperature over night. The phases were separated. The aqueous layer was back extracted with Et_2O (20 mL×2). The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. Removal of the solvent by rotary evaporation and column chromatography (EtOAc/PE) on silica gel gave the reduction product **11**.

Data for **11a** (a white solid, 95% yield): mp 44–45 °C $[\alpha]_D^{24}$ −41.8 (c 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.18 (m, 5H), 4.71–4.63 (m, 1H), 4.22–4.13 (m, 2H), 3.29 (dd, J=13.3, 3.5 Hz, 1H), 3.02–2.84 (m, 2H), 2.76 (dd, J=13.3, 9.5 Hz, 1H), 1.74–1.62 (m, 2H), 1.43–1.19 (m, 14H), 0.88 (t, J=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 153.3, 135.3, 129.4, 128.9, 127.3, 66.1, 55.1, 37.9, 35.5, 31.8, 29.5, 29.45, 29.36, 29.27, 29.1, 24.3, 22.6, 14.1; FT-IR (KBr) 3029, 2926, 2854, 1789, 1704, 1398, 1454, 1385, 1352, 1210, 1099, 1076, 1051, 762, 746, 702 cm^{-1}. ESI-MS m/z 368.2 ([M+Na]$^+$); ESI-HRMS calcd for $C_{21}H_{31}NO_3Na$ ([M+Na]$^+$) 368.2196, found 368.2193.

Data for **11b** (a colorless oil, 87% yield): $[\alpha]_D^{24}$ −41.33 (c 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37–7.18 (m, 5H), 4.73–4.63 (m, 1H), 4.23–4.13 (m, 2H), 3.66 (t, J=6.2 Hz, 2H), 3.30 (dd, J=13.4, 3.3 Hz, 1H), 3.07–2.86 (m, 2H), 2.76 (dd, J=13.4, 9.6 Hz, 1H), 1.84–1.70 (m, 2H), 1.67–1.55 (m, 2H), 0.90 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 153.4, 135.3, 129.4, 128.9, 127.3, 66.1, 62.7, 55.1, 37.9, 35.3, 32.1, 25.9, 20.6, 18.3, −5.3; FT-IR (film) 2954, 2929, 2857, 1789, 1704, 1698, 1386, 1253, 1210, 1100, 836, 744, 702 cm^{-1}. ESI-MS m/z 414.3 ([M+Na]$^+$); ESI-HRMS calcd for $C_{21}H_{33}NO_4SiNa$ ([M+Na]$^+$) 414.2071, found 414.2069.

Data for **11c** (a colorless oil, 90% yield): $[\alpha]_D^{24}$ +40.2 (c 0.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39–7.16 (m, 10H), 4.72–4.61 (m, 1H), 4.51 (s, 2H), 4.23–4.12 (m, 2H), 3.49 (t, J=6.7 Hz, 2H), 3.29 (dd, J=13.3, 3.5 Hz, 1H), 3.05–2.84 (m, 2H), 2.76 (dd, J=13.3, 9.6 Hz, 1H), 1.78–1.61 (m, 4H), 1.54–1.44 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 153.4, 138.6, 135.3, 129.4, 128.9, 128.3, 127.6, 127.4, 127.3, 72.9, 70.1, 66.1, 55.1, 37.9, 35.4, 29.5, 25.7, 24.0; FT-IR (film) 3062, 2934, 2860, 1783, 1698, 1386, 1329, 1209, 1097, 738 cm^{-1}. ESI-MS m/z 404.3 ([M+Na]$^+$); ESI-HRMS calcd for $C_{23}H_{27}NO_4Na$ ([M+Na]$^+$) 404.1832, found 404.1836.

Data for **11d** (a white solid, 100% yield): mp 41–41 °C $[\alpha]_D^{26}$ −42.1 (c 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.18 (m, 5H), 4.72–4.62 (m, 1H), 4.24–4.13 (m, 2H), 3.29 (dd, J=13.4, 3.1 Hz, 1H), 3.03–2.84 (m, 2H), 2.76 (dd, J=13.4, 9.7 Hz, 1H), 2.23 (t, J=7.2 Hz,

2H), 1.76–1.65 (m 2H), 1.59–1.49 (m, 2H), 1.49–1.34 (m, 4H), 0.15 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 153.4, 135.3, 129.4, 128.9, 127.3, 107.5, 84.4, 66.1, 55.1, 37.9, 35.4, 28.6, 28.5, 28.4, 24.1, 19.8, 0.1; FT-IR (KBr) 2925, 2854, 2171, 1789, 1704, 1455, 1378, 1248, 1211, 842 cm^{-1}. ESI-MS *m*/*z* 408.4 ([M+Na]$^+$); ESI-HRMS calcd for $C_{22}H_{31}NO_3SiNa$ ([M+Na]$^+$) 408.1965, found 408.1971.

Data for **11e** (a white solid, 96% yield): mp 63–64 °C $[\alpha]_D^{23}$ +41.9 (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.17 (m, 5H), 4.71–4.62 (m, 1H), 4.24–4.13 (m, 2H), 3.95 (s, 4H), 3.29 (dd, *J*=13.3, 2.6 Hz, 1H), 3.07–2.88 (m, 2H), 2.76 (dd, *J*=13.3, 9.8 Hz, 1H), 1.87–1.70 (m, 4H), 1.33 (s, 3H); ^{13}C NMR: (100 MHz, $CDCl_3$) δ 173.0, 153.4, 135.2, 129.3, 128.9, 127.3, 109.7, 66.1, 64.6, 55.0, 38.1, 37.8, 35.3, 23.8, 18.7; FT-IR (KBr) 2980, 2952, 1781, 1698, 1479, 1387, 1351, 1211, 1099, 1062, 762, 703 cm^{-1}. ESI-MS *m*/*z* 356.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{18}H_{23}NO_5Na$ ([M+Na]$^+$) 356.1468, found 356.1455.

Data for **11f** (a yellowish oil, 78% yield): $[\alpha]_D^{23}$ −25.3 (*c* 1.20, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H), 6.06 (s, 1H), 5.75 (s, 1H), 4.72–4.63 (m, 1H), 4.25–4.14 (m, 2H), 3.31 (dd, *J*=13.1, 3.2 Hz, 1H), 3.03–2.94 (m, 2H), 2.78 (dd, *J*=13.1, 9.8 Hz, 1H), 2.40 (dd, *J*=13.8, 5.8 Hz, 1H), 2.20 (dd, *J*=13.8, 7.7 Hz, 1H), 1.95–1.74 (m, 2H), 1.58–1.44 (m, 1H), 0.94 (d, *J*=6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 153.4, 135.2, 129.4, 128.9, 127.3, 126.8, 111.3, 66.2, 55.2, 52.2, 37.9, 33.1, 31.8, 30.0, 18.4; FT-IR (film) 2956, 2921, 1781, 1699, 1386, 1352, 1211, 896, 702 cm^{-1}. ESI-MS *m*/*z* 450.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{18}H_{22}NO_3INa$ ([M+Na]$^+$) 450.0534, found 450.0544.

Data for **11g** (a white solid, 94% yield): mp 84–85 °C (lit.[12] mp 86–88 °C). $[\alpha]_D^{23}$ +41.2 (*c* 1.00, $CHCl_3$) (lit.[11] $[\alpha]_D^{20}$ +92 (no concentration/solvent information)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H), 4.71–4.63 (m, 1H), 4.24–4.12 (m, 2H), 3.29 (dd, *J*=13.3, 3.0 Hz, 1H), 3.04–2.86 (m, 2H), 2.78 (dd, *J*=13.3, 9.7 Hz, 1H), 1.80–1.54 (m, 7H), 1.35–1.10 (m, 4H), 1.00–0.86 (m, 2H); FT-IR (KBr) 3059, 3027, 2921, 2850, 1782, 1699, 1386, 1352, 1211, 1107, 740, 702 cm^{-1}.

Data for **11h** (a white solid, 94% yield): mp 101–102 °C $[\alpha]_D^{25}$ +67.4 (*c* 0.98, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.13 (m, 10H), 4.70–4.60 (m, 1H), 4.20–4.10 (m, 2H), 3.37–3.17 (m, 3H), 3.09–2.95 (m, 2H), 2.74 (dd, *J*=13.3, 9.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 153.4, 140.4, 135.2, 129.4, 128.9, 128.5, 128.4, 127.3, 126.2, 66.1, 55.0, 37.7, 37.1, 30.2; FT-IR (KBr) 3083, 3063, 2956, 2930, 1779, 1698, 1496, 1454, 1389, 1376, 1353, 1210, 1113, 762, 747, 700 cm^{-1}. ESI-MS *m*/*z* 332.2 ([M+Na]$^+$); MALDI-HRMS calcd for $C_{19}H_{19}NO_3Na$ ([M+Na]$^+$) 332.1257, found 333.1259.

Data for **11i** (a gray-brownish oil, 94% yield): $[\alpha]_D^{25}$ +38.4 (*c* 0.65, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.17 (m, 6H), 6.07 (dd, *J*=3.3, 3.3 Hz, 1H), 6.03–6.00 (m, 1H), 4.71–4.63 (m, 1H), 4.23–4.13 (m, 2H), 3.34–3.21 (m, 5H), 2.75 (dd, *J*=13.3, 7.6 Hz, 1H), 1.60 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 153.4, 149.3, 135.3, 133.8, 129.4, 128.9, 127.3, 121.3, 111.8, 109.9, 83.5, 66.1, 55.1, 37.9, 35.1, 28.0, 23.6; FT-IR (film) 2979, 2932, 1783, 1738, 1699, 1371, 1335, 1212, 1125, 1064, 847, 808, 734, 703 cm^{-1}. ESI-MS *m*/*z* 421.2 ([M+Na]$^+$); ESI-HRMS calcd for $C_{22}H_{26}N_2O_5Na$ ([M+Na]$^+$) 421.1734, found 421.1729.

Data for **11j** (a white solid, 77% yield): mp 39–41 °C $[\alpha]_D^{26}$ +125.3 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.73–4.76 (m,1H), 4.40–4.34 (m, 2H), 3.36 (ddd, *J*=17.0, 7.9, 6.1 Hz, 1H), 3.18 (ddd, *J*=17.0, 8.5, 6.5 Hz, 1H), 2.40–2.27 (m, 1H), 1.80–1.63 (m, 2H), 0.98 (t, *J*=7.3 Hz, 3H), 0.92 (t, *J*=7.0 Hz, 3H), 0.87 (t, *J*=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.1, 174.0, 67.5, 63.2, 39.3, 28.9, 18.2, 18.0, 14.9, 13.5; FT-IR (KBr) 2964, 2932, 2875, 1702, 1481, 1464, 1401, 1306, 1197, 1159, 1010, 957 cm^{-1}. ESI-MS *m*/*z* 238.1 ([M+Na]$^+$); ESI-HRMS calcd for $C_{10}H_{17}NO_2SNa$ ([M+Na]$^+$) 238.0872, found 238.0883.

Data for **11k** (a white solid, 64% yield): mp 74–76 °C $[\alpha]_D^{26}$ −82.4 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.22 (m, 5H), 5.69 (dd, *J*=8.5, 2.1 Hz, 1H), 4.78 (dd, *J*=9.0, 8.5 Hz, 1H), 4.44 (dd, *J*=9.0, 2.1 Hz, 1H), 3.37–3.16 (m, 2H), 1.74–1.55 (m, 2H), 0.92 (t, *J*=7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 173.5, 138.8, 129.2, 128.8, 126.0, 74.0, 62.1, 39.4, 17.8, 13.5; FT-IR (KBr) 2962, 2927, 2874, 1705, 1455, 1366, 1339, 1311, 1189, 1152, 946, 762, 698 cm^{-1}. ESI-MS *m*/*z* 271.9 ([M+Na]$^+$); ESI-HRMS calcd for $C_{13}H_{15}NO_2SNa$ ([M+Na]$^+$) 272.0716, found 272.0716.

Data for **11l** (a white solid, 94% yield): mp 105–105 °C (very sharp). $[\alpha]_D^{25}$ +79.5 (*c* 1.10, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38–7.18 (m, 5H), 4.98–4.88 (m, 1H), 4.37–4.23 (m, 2H), 3.47–3.34 (m, 1H), 3.34–3.20 (m, 2H), 2.76 (dd, *J*=14.1, 10.0 Hz, 1H), 1.84–1.53 (m, 7H), 1.41–1.09 (m, 4H), 1.04–0.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.4, 174.5, 135.3, 129.4, 129.0, 127.4, 70.2, 59.9, 37.6, 37.1, 35.1, 33.1, 33.0, 31.5, 26.5, 26.2; FT-IR (KBr) 3027, 2919, 2849, 1698, 1450, 1400, 1367, 1352, 1319, 1287, 1270, 1195, 1155, 1017, 964, 740, 701 cm^{-1}. ESI-MS *m*/*z* 354.0 ([M+Na]$^+$); ESI-HRMS calcd for $C_{19}H_{25}NO_2SNa$ ([M+Na]$^+$) 354.1498, found 354.1507.

Acknowledgements

This work was supported by the National Basic Research Program of China (the 973 Program, 2010CB833200), the National Natural Science Foundation of China (21172247, 21032002, 20921091, 20672129, 20621062, 20772143), and the Chinese Academy of Sciences.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.11.038. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) Evans, D. A.; Bartoli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127–2129; (b) For a review, see: Ager, D. J. I.; Schaad, D. R. *Chem. Rev.* **1996**, *96*, 835–875.
2. (a) Schindler, C. S.; Forster, P. M.; Carreira, E. M. *Org. Lett.* **2010**, *12*, 4103–4105; (b) Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 83–91; (c) Gage, J. R.; Evans, D. A. *Org. Synth.* **1990**, *68*, 77–82; (d) Ho, G.-J.; Mathre, D. J. *J. Org. Chem.* **1995**, *60*, 2271–2273; (e) Andrade, C. K. Z.; Rocha, R. O.; Vercillo, O. E.; Silva, W. A.; Matos, R. A. F. *Synlett* **2003**, 2351–2352; (f) Ager, D. J.; Allen, D. R.; Schaad, D. R. *Synthesis* **1996**, 1283–1285; (g) Davies, S. G.; Doisneau, G. J.-M. *Tetrahedron: Asymmetry* **1993**, *4*, 2513–2516; (h) Gaul, C.; Schweizer, B. W.; Seiler, P.; Seebach, D. *Helv. Chim. Acta* **2002**, *85*, 1546–1566; (i) Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 9434–9453; (j) Evans, D. A.; Gage, J. R. *J. Org. Chem.* **1992**, *57*, 1958–1961.
3. For a convenient synthesis of such chiral auxiliaries, see Wu, Y.-K.; Shen, X. *Tetrahedron: Asymmetry* **2000**, *11*, 4359–4363.
4. For syntheses involving such species as **8**, see (a) Shapiro, G.; Cai, C. *Tetrahedron Lett.* **1992**, *33*, 2447–2450; (b) Evans, D. A.; Black, W. C. *J. Am. Chem. Soc.* **1992**, *114*, 2260–2262 For an example for use of **9** (derived through saturation of the double bond in **8** by hydrogenation), cf Ref. 5a below.
5. For previous reports on 1,4-reduction of individual *N*-acyl oxazolidinones, see: (a) Roush, W. R.; Brown, B. B. *J. Org. Chem.* **1993**, *58*, 2162–2172; (b) Evans, D. A.; Fu, G. C. *J. Org. Chem.* **1990**, *55*, 5678–5680.
6. Fortunato, J. M.; Ganem, B. *J. Org. Chem.* **1976**, *41*, 2194–2200.
7. Fukuda, T.; Sugiyama, K.; Arima, S.; Harigaya, Y.; Nagamitsu, T.; Omura, S. *Org. Lett.* **2008**, *10*, 4239–4242.
8. Katayama, S.; Ae, N.; Nagata, R. *J. Org. Chem.* **2001**, *66*, 3474–3483.
9. Ashby, E. C.; Lin, J. J.; Kovar, R. *J. Org. Chem.* **1976**, *41*, 1939–1943.
10. Tsuda, T.; Hayashi, T.; Satomi, H.; Kawamoto, T.; Saegusa, T. *J. Org. Chem.* **1986**, *51*, 537–540.
11. Dias, L. C.; Melgar, G. Z.; Jardim, L. S. A. *Tetrahedron Lett.* **2005**, *46*, 4427–4432.
12. Edmonds, M. K.; Graichen, F. H. M.; Gardiner, J.; Abell, A. D. *Org. Lett.* **2008**, *10*, 885–887.