Monatsh Chem 139, 1363–1367 (2008)
DOI 10.1007/s00706-008-0925-1
Printed in The Netherlands

Monatshefte für Chemie
Chemical Monthly

Iodine as a mild, efficient, and cost-effective catalyst for the synthesis of thiiranes from oxiranes

Jhillu S. Yadav, Basi V. Subba Reddy, Sandip Sengupta, Manoj K. Gupta, Gakul Baishya, Sukkala J. Harshavardhana, Uttam Dash

Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, India

Received 26 October 2007; Accepted 27 February 2008; Published online 9 June 2008

Abstract We developed an efficient protocol for the synthesis of thiiranes from oxiranes using a catalytic amount of molecular iodine. The notable features of this procedure are mild reaction conditions, high conversions, short reaction times, economic viability of the reagents, compatibility with various functionalities, and simple experimental/product isolation procedures which make it a useful and attractive process for the synthesis of a range of thiiranes.

Keywords Oxiranes; Thiiranes; Iodine; Ammonium thiocyanate.

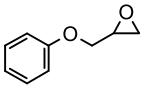
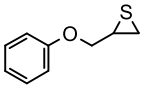
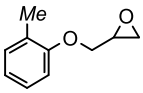
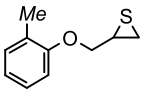
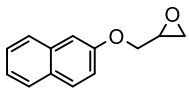
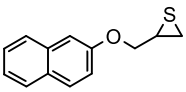
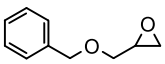
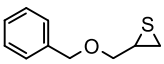
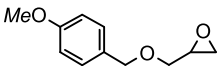
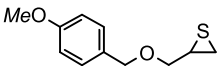
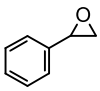
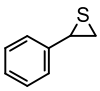
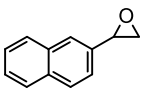
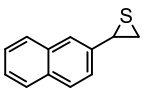
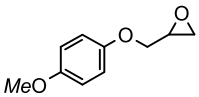
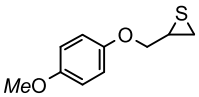
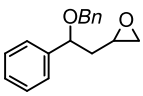
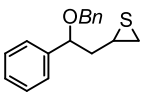
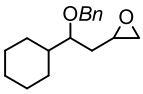
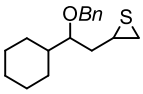
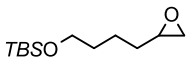
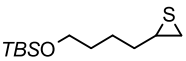
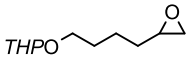
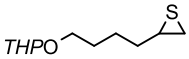
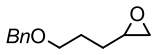
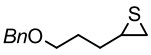
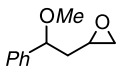
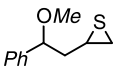
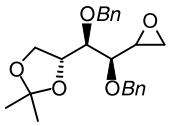
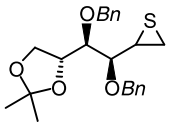
Introduction

Thiiranes are important and useful building blocks for the synthesis of polymers, pharmaceuticals, pesticides, and herbicides [1]. Since organo-sulfur compounds have become increasingly useful and important in the field of drugs and pharmaceuticals, the development of simple, convenient and efficient approaches are desirable. As a result, numerous methods have been reported to synthesize thiiranes using a variety of reagents such as β-cyclodextrin/thiourea [2], phosphine sulfide [3], *N*,*N*-dimethylthioformamide in the presence of trifluoroacetic acid [4], silica gel supported potassium thiocyanate [5], indium halides/KSCN [6] and polymeric cosolvent/NH_4SCN [7], together with solvent-free conditions [8], ionic liquids [9], and several more [10, 11]. However, many of these methods often involve the use of expensive or toxic reagents, the formation of mixtures of products resulting in low yields, and undesirable side reactions due to the rearrangement or polymerization of the starting oxiranes. In spite of a number of methods reported for the synthesis of thiiranes, there is always a great demand in developing catalytic methods for high yielding protocols using readily available and less expensive reagents. Recently, molecular iodine has received considerable attention as an inexpensive, non-toxic, and readily available reagent for various organic transformations, affording the corresponding products with high selectivity in excellent yields [12–16]. The mild *Lewis* acidity associated with iodine has led to its use in organic synthesis using catalytic to stoichiometric amounts. However, there have been no reports on the use of iodine for the synthesis of thiiranes from oxiranes and ammonium thiocyante.

Scheme 1

Correspondence: Jhillu S. Yadav, Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad 500 007, India. E-mail: yadavpub@iict.res.in

Table 1 Iodine catalyzed synthesis of thiiranes from oxiranes

Entry	Oxiiranes	Thiiranes[a]	Time/h	Yield/%[b]
a			2.5	94
b			3.5	96
c			3.5	96
d			2.5	95
e			3.5	90
f			4.0	90
g			5.0	80
h			3.0	93
i			2.5	93
j			3.5	96
k			3.5	96
l			3.0	80
m			3.5	82
n			3.5	82
o			7.5	85
P			7.0	75

[a] All products were characterized by IR, ^{1}H NMR spectra and mass spectrometry
[b] Isolated and unoptimized yields after column chromatography

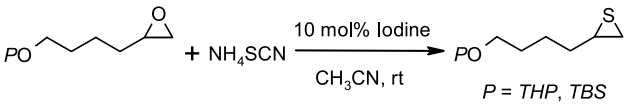
Results and discussion

In continuation of our interest in the catalytic application of elemental iodine [17–19], we disclose herein a mild, efficient, and practical methodology for the synthesis of thiiranes from oxiranes and ammonium thiocyanate using molecular iodine as a catalyst. Initially, we attempted the reaction of 2-(phenoxymethyl)oxirane (**1**, 1 eq.) with ammonium thiocyante (**2**, 1.5 eq.) in the presence of 10 mol% of elemental iodine in acetonitrile at room temperature. The reaction went to completion in 2.5 h affording thiirane **3a** in 94% yield (Scheme 1).

The remarkable catalytic activity of molecular iodine provided the incentive for further study of reactions with other epoxides. Interestingly, a variety of epoxides reacted efficiently with ammonium thiocyanate to furnish the corresponding thiiranes in good yields (entries b–p, Table 1). In addition, functionalized oxiranes also worked well under these reaction conditions without affecting the protecting groups (entries e, i–p, Table 1, Scheme 2).

This method is compatible with substrates bearing acid sensitive protecting groups such as *THP*, *TBDMS*, benzyl, and methyl ethers (entries e, i–p, Table 1). This procedure is also useful for the selective conversion of an epoxide into a thiirane without affecting an acid labile primary acetonide (entry p, Table 1).

The reaction may proceed *via* the activation of oxirane by I_2 followed by nucleophilic ring opening with $^-$SCN and a subsequent formation of oxathiolanium intermediate, which eventually undergoes a rearrangement to thiirane (Scheme 3) [20]. However, most of the existing methods failed to produce thiiranes from oxiranes without the cleavage of *THP*, *TBDMS* ethers, and acetonide [1]. The products thus obtained were



Scheme 2

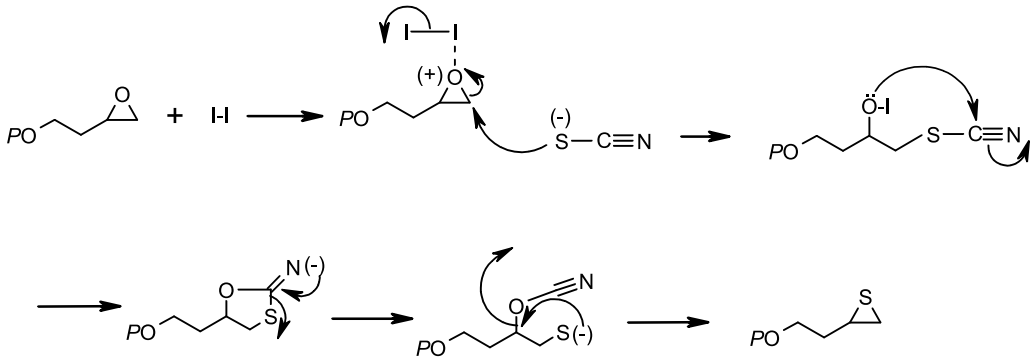
characterized by ^{1}H NMR, IR, and mass spectrometry. In all cases, the reactions proceeded well in refluxing acetonitrile and the products were obtained in relatively high yields. To know the efficiency of elemental iodine, we have carried out the experiments with some reported catalysts and the comparative results are summarized in Table 2. The scope and generality of this process is illustrated in Table 1.

Experimental

Melting points were recorded on a Büchi R-535 apparatus. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr optics. ^{1}H NMR spectra were recorded on a Varian-unity 300 spectrometer in $CDCl_3$ using *TMS* as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV.

General procedure for the synthesis of thiiranes

A mixture of 1 mmol oxiranes, 1.5 mmol ammonium thiocyanate, and 25 mg iodine (10 mol%) in 5 cm^3 dry acetonitrile was stirred for a specified time (see Table 1). After completion of the reaction as indicated by TLC, the solvent was evaporated under vacuum and reaction mass was quenched with 2 cm^3 sat. ammonium thiosulphate and extracted with 2×10 cm^3 ethyl acetate. The combined organic layers were dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate:*n*-hexane, 1:9) to afford pure thiiranes. The products thus obtained were characterized by their TLC, IR, NMR spectroscopy,



Scheme 3

Table 2 A Comparative study for the synthesis of benzyloxymethylthiirane from benzyloxymethyloxirane

S. No.	Catalyst	Conversion %	Time h	Yield[a] %
1	Oxalic acid (0.2 eq)	91	2.0	85
2	$RuCl_3$ (0.05 eq)	95	0.5	90
3	SiO_2–$AlCl_3$ (0.1 eq)	90	2.0	89
4	$Al(DS)_3 \cdot 3H_2O$ (0.1 eq)	92	2.5	90
5	*PVA* and *PAA*/NaOH	92	1.0	90
6	$TiO(TFA)_2$ or $TiCl_3(OTf)$	98	0.5	95
7	Iodine (0.1 eq)	96	2.5	94

[a] Yield refers to pure products after chromatography

and mass spectrometry. Data for **3e**, **3g**, **3h**, and **3i** are identical with these in Refs. [2, 6, 21, 22].

2-(Phenoxymethyl)thiirane (**3a**, $C_9H_{10}OS$)
Colorless liquid; IR (KBr): $\bar{\nu}_{max} = 3034$, 2925, 2860, 1599, 1495, 1241, 1036, 753 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.26$–7.19 (m, 2H), 6.93–6.82 (m, 3H), 4.23 (dd, $J =$ 11.3, 6.4 Hz, 1H), 3.77 (dd, $J = 9.8$, 7.5 Hz, 1H), 3.25–3.17 (m, 1H), 2.57 (dd, $J = 6.0$, 1.5 Hz, 1H), 2.27 (d, $J = 6.0$ Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.9$, 31.3, 72.5, 114.6, 121.1, 129.5, 158.3 ppm; ESI/MS: $m/z = 189.9$ $[M^+ + Na]$, 117.2; HRMS (ESI): calcd for $C_9H_{10}ONaS$ 189.0350, found 189.0359.

2-[(2-Methylphenoxy)methyl]thiirane (**3b**, $C_{10}H_{12}OS$)
Colorless liquid; IR (KBr): $\bar{\nu}_{max} = 2922$, 2858, 1494, 1460, 1242, 1120, 1047, 1011, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.07$ (t, $J = 7.5$ Hz, 2H), 6.81 (t, $J = 7.5$ Hz, 1H), 6.72 (d, $J = 8.3$ Hz, 1H), 4.21 (dd, $J = 10.5$, 5.2 Hz, 1H), 3.82 (dd, $J = 10.5$, 7.5 Hz, 1H), 3.27–3.19 (m, 1H), 2.55 (d, $J = 6.0$ Hz, 1H), 2.28 (dd, $J = 5.2$, 1.5 Hz, 1H), 2.23 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 16.1$, 23.7, 31.5, 72.5, 111.4, 120.8, 126.6, 126.9, 130.7, 156.4 ppm; ESI/MS: $m/z = 181$ $[M^+ + H]$, 179; HRMS (ESI): calcd for $C_{10}H_{12}ONaS$ 203.0506, found 203.0510.

2-[(2-Napthyloxy)methyl]thiirane (**3c**, $C_{13}H_{12}OS$)
White solid; mp 72°C; IR (KBr): $\bar{\nu}_{max} = 2923$, 2854, 1627, 1595, 1463, 1389, 1256, 1216, 1182, 1045, 1005, 839, 813, 741 cm^{-1}; ^1H NMR ($CDCl_3$ 300 MHz): $\delta = 7.71$–7.62 (m, 3H), 7.38 (t, $J = 7.5$ Hz, 1H), 7.28 (t, $J = 8.3$ Hz, 1H), 7.09 (dd, $J = 9.0$, 2.2 Hz, 1H), 7.05 (d, $J = 2.2$ Hz, 1H), 4.33 (dd, $J = 9.8$, 5.2 Hz, 1H), 3.88 (dd, $J = 9.8$, 7.5 Hz, 1H), 3.30–3.22 (m, 1H), 2.58 (d, $J = 6.0$ Hz, 1H), 2.30 (dd, $J = 5.2$, 1.5 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.9$, 31.2, 72.4, 76.9, 106.8, 118.6, 123.7, 127.5, 129.0, 129.5, 134.3, 156.2 ppm; ESI/MS: $m/z = 217$ $[M^+ + H]$, 197; HRMS (ESI): calcd for $C_{13}H_{12}ONaS$ 239.0506, found 239.0512.

2-[(Benzyloxy)methyl]thiirane (**3d**, $C_{10}H_{12}OS$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 3028$, 2923, 2855, 1452, 1368, 1249, 1092, 739, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.31$–7.20 (m, 5H), 4.53 (d, $J = 0.9$ Hz, 2H), 3.67 (ddd, $J = 10.3$, 5.4, 0.7 Hz, 1H), 3.38 (dd, $J = 10.3$, 6.7 Hz, 1H), 3.06–2.98 (m, 1H), 2.45 (td, $J = 6.2$, 2.0, 0.9 Hz, 1H), 2.15 (dd, $J = 5.2$, 1.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 32.5$, 42.8, 71.8, 73.5, 127.9, 128.6, 130.1, 140.6 ppm; ESI/MS: $m/z = 181.0$ $[M^+ + H]$, 102.1; HRMS (ESI): calcd for $C_{10}H_{12}ONaS$ 203.0506, found 203.0509.

2-Phenylthiirane (**3f**, C_8H_8S)
Colorless liquid; IR (KBr): $\bar{\nu}_{max} = 3061$, 3029, 2924, 2852, 1492, 1453, 1071, 1040, 760, 695, 613 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.27$–7.18 (m, 5H), 3.81 (t, $J =$ 6.5 Hz, 1H), 2.80 (d, $J = 6.5$ Hz, 1H), 2.56 (dd, $J = 5.0$, 1.4 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 35.2$, 42.4, 125.1, 128.3, 130.2, 139.8 ppm; FAB Mass: $m/z = 137$ $[M^+ + H]$, 136.0; HRMS (ESI): calcd for C_8H_8NaS 159.0245, found 159.0252.

2-[2-(Benzyloxy)-2-phenylethyl]thiirane (**3j**, $C_{17}H_{18}OS$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 3061$, 3028, 2861, 1493, 1451, 1091, 783, 699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta =$ 7.36–7.14 (m, 10H), 4.53–4.39 (m, 2H), 4.31–4.21 (dd, $J = 11.7$, 8.8 Hz, 1H), 3.21–2.93 (m, 1H), 2.50–2.31 (m, 2H), 2.12–1.96 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 25.6$, 31.9, 70.3, 81.2, 126.8, 127.6, 127.7, 127.9, 128.3, 128.5, 141.1, 141.6 ppm; ESI/MS: $m/z = 271$ $[M^+ + H]$, 179.1; HRMS (ESI): calcd for $C_{17}H_{18}ONaS$ 293.0976, found 293.0971.

2-[2-(Benzyloxy)-2-cyclohexylethyl]thiirane (**3k**, $C_{17}H_{24}OS$)
Colorless liquid; IR (KBr): $\bar{\nu}_{max} = 2925$, 2852, 1449, 1098, 1068, 737, 697 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.42$–7.17 (m, 5H), 4.57 (d, $J = 3.6$ Hz, 1H), 4.48 (s, 1H), 3.39–3.21 (m, 1H), 3.08–2.82 (m, 1H), 2.52 (d, $J = 6.6$ Hz, 1H), 2.40 (d, $J = 5.8$ Hz, 1H), 2.20–1.88 (m, 2H), 1.83–1.55 (m, 6H), 1.42–0.93 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 26.3$, 26.8, 28.6, 28.9, 34.0, 38.6, 41.4, 72.7, 83.3, 127.7, 127.8, 128.2, 138.8 ppm; ESI/MS: $m/z = 277$ $[M^+ + H]$, 278.1; HRMS (ESI): calcd for $C_{17}H_{24}ONaS$ 299.1445, found 299.1454.

tert-Butyldimethyl(4-(thiiran-2-yl)butoxy)silane
(**3l**, $C_{12}H_{26}OSiS$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 2932$, 2858, 2363, 1731, 1467, 1388, 1361, 1253, 1102, 1007, 837, 776, 662 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 3.63$–3.59 (m, 2H), 2.81–2.77 (m, 1H), 2.43 (d, $J = 6.0$ Hz, 1H), 2.08 (d, $J = 6.0$ Hz, 1H), 1.86–1.82 (m, 2H), 1.60–1.51 (m, 4H), 0.88 (s, 9H), 0.33 (s, 6H) ppm. ESI/MS: $m/z = 247$ $[M^+ + H]$.

2-(4-(Thiiran-2-yl)butoxy)-tetrahydro-2H-pyran
(**3m**, $C_{11}H_{20}O_2S$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 2925$, 2853, 2366, 1742, 1458, 1370, 1167, 1121, 1026 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 4.56$–4.51 (m, 1H), 3.84–3.77 (m, 1H), 3.73–3.67 (m, 1H), 3.50–3.41 (m, 1H), 3.38–331 (m, 1H), 2.88–2.81 (m, 1H), 2.46 (d, $J = 6.7$ Hz, 1H), 2.11 (d, $J = 5.2$ Hz, 1H), 1.92–1.76

(m, 2H), 1.77–1.48 (m, 10H) ppm; ESI/MS: $m/z = 217$ $[M^+ + H]$.

2-[3-(Benzyloxy)propyl]thiirane (**3n**, $C_{12}H_{16}OS$)
Colorless liquid; IR (KBr): $\bar{\nu}_{max} = 2927, 2855, 1449, 1362, 1102, 740\,cm^{-1}$; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.31–7.18$ (m, 5H), 4.43 (s, 2H), 3.46 (dt, $J = 8.0, 5.8, 2.1$ Hz, 2H), 2.86–2.74 (dt, $J = 7.3, 5.8, 2.1$ Hz, 1H), 2.39 (d, $J = 6.5$ Hz, 1H), 2.05 (d, $J = 6.5$ Hz, 1H), 2.01–1.88 (m, 1H), 1.84–1.70 (m, 2H), 1.53–1.39 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 35.6, 25.8, 29.3, 33.2, 69.4, 72.8, 128.2, 127.5, 127.4, 138.3$ ppm; ESI/MS: $m/z = 231$ $[M^+ + Na]$, 184.1; HRMS (ESI): calcd for $C_{12}H_{16}ONaS$ 231.0819, found 231.0826.

2-[2-(Methoxy)-2-phenylethyl]thiirane (**3o**, $C_{11}H_{14}OS$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 3061, 3027, 2983, 2930, 2856, 2821, 1453, 1356, 1237, 1191, 1100, 1048, 758, 701, 612, 561\,cm^{-1}$; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.35–7.21$ (m, 5H), 4.27–4.18 (m, 1H), 3.23 (d, $J = 18.8$ Hz, 3H), 3.14–3.05 (m, 1H), 2.64–2.48 (m, 1H), 2.37–2.26 (m, 1H), 2.10–2.01 (m, 2H) ppm; ESI/MS: $m/z = 217$ $[M^+ + Na]$, 172, 74.1.

4-(1,2-bis(benzyloxy)-2-(thiiran-2-yl)ethyl)-2,2-dimethyl-1,3-dioxolane (**3p**, $C_{23}H_{28}O_4S$)
Liquid; IR (KBr): $\bar{\nu}_{max} = 3064, 3030, 2985, 2927, 1631, 1495, 1454, 1384, 1254, 1212, 1070, 856, 736, 698\,cm^{-1}$; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 7.30–7.23$ (m, 10H), 4.82–4.74 (m, 2H), 4.63–4.57 (m, 2H), 4.17 (dt, $J = 6.8, 4.5$ Hz 1H), 3.97 (dt, $J = 12.8, 8.3$ Hz, 2H), 3.76–3.69 (m, 1H), 3.02 (dd, $J = 8.3, 3.0$ Hz, 1H), 2.95–2.88 (m, 1H), 2.09 (dd, $J = 6.0, 1.5$ Hz, 1H), 1.95 (dd, $J = 5.2, 1.5$ Hz, 1H), 1.39 (s, 3H), 1.29 (s, 3H) ppm; ESI/MS: $m/z = 423$ $[M^+ + Na]$, 407.

Acknowledgements

SS, *MKG*, *GB*, *SJH*, and *UD* thank CSIR, New Delhi, for the award of fellowships.

References

1. Ditter DC, Katritzky AR, Rees CW (eds) (1984) Thiiranes and Thiiranes in Comprehensive Heterocyclic Chemistry, Vol. 7. Pergamon, Elmsford, NY, p 132
2. Surendra K, Krishnaveni NS, Rao KR (2004) Tetrahedron Lett 45:6523
3. Chan TR, Finkenbine JR (1972) J Am Chem Soc 94:2880
4. Takido T, Kobayashi Y, Itabashi K (1986) Synthesis:779
5. Brimeyer MO, Mehrota A, Quici S, Nigam A, Regan SL (1980) J Org Chem 45:4254
6. Yadav JS, Reddy BVS, Baishya G (2002) Synlett:396
7. Tamami B, Kolahdoozan M (2004) Tetrahedron Lett 45:1535
8. Kaboudin B, Norouzi H (2004) Tetrahedron Lett 45:1283
9. Yadav JS, Reddy BVS, Reddy ChS, Rajsekhar K (2003) J Org Chem 68:2525
10. Bandgar BP, Joshi NS, Kamble VT (2006) Tetrahedron Lett 47:4775
11. Bhosale SV (2007) Synlett:175
12. Togo H, Iida S (2006) Synlett:2159
13. Bhosale RS, Bhosale SV, Wang T, Zubaidha PK (2004) Tetrahedron Lett 45:7187
14. Lipshut BH, Keith J (1998) Tetrahedron Lett 39:2495
15. Deka N, Kalita DJ, Borah R, Sharma JC (1997) J Org Chem 62:1563
16. Vaino AR, Szarek WA (1995) Synlett:1157
17. Yadav JS, Reddy BVS, Reddy UVS, Krishna AD (2007) Tetrahedron Lett 48:5243 and references cited therein.
18. Yadav JS, Reddy BVS, Premalatha K, Swamy T (2005) Tetrahedron Lett 46:2687
19. Yadav JS, Reddy BVS, Reddy PMK, Gupta MK (2005) Tetrahedron Lett 46:8493
20. Bellomo A, Gonzalez D (2007) Tetrahedron Lett 48:3047
21. Yamada N, Mizuochi M, Morita H (2007) Tetrahedron 63:3408
22. Das B, Reddy S, Krishnaiah M (2006) Tetrahedron Lett 47:8471