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# Synthesis of novel spiro-β-lactams

RENU ARORA, P VENUGOPALAN and S S BARI*

Department of Chemistry and Centre of Advanced studies in chemistry, Panjab University, Chandigarh 160 014
e-mail: ssbari@pu.ac.in

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**Abstract.** A new synthetic approach for spiro-β-lactams by cyclization of *cis*-3-allyl-3-benzylthio-β-lactams is presented. The reaction involves step-wise electrophilic addition-dealkylation sequence giving stereospecific synthesis of C-3-spiro-β-lactams.

**Keywords.** β-lactams; spiro; halogen-mediated cyclization; electrophilic; episulfonium ion.

## 1. Introduction

Since β-lactam antibiotics are a group of drugs of unparallel importance in chemotherapy, considerable efforts have been made in the development of novel and biologically more active compounds. The search for improved antibiotics also includes designing of new methodology for the total synthesis as well as the semi-synthesis of β-lactam derivatives. Recently, spiro-β-lactams have become centre of attraction for many reasons. Primarily this is due to their antiviral[1] and antibacterial properties.[2] In addition, it has been reported that these spiro-β-lactams also acting as cholesterol absorption inhibitors (CAI),[3] making them potentially useful compounds for development of drugs for lowering the high level of cholesterol. More recently the enzymatic cleavage of the amyloid precursor protein responsible for the pathogenesis of Alzheimer's disease has also been shown to be coupled with cholesterol regulation.[4] Structure-activity studies have identified 3-spiro-β-lactams SCH 54016 **A** and SCH 58053 **B** as most potent cholesterol absorption inhibitors.[5]

Several approaches for the synthesis of spiro-β-lactams have been described in literature. Recently reported synthesis of spiro-β-lactams involves either intramolecular cyclization of substituted β-lactam enolates[6] or the Staudinger reaction of unsymmetrical ketenes[7] as well as halocyclization of *cis*-3-(prop-2-ynyloxy/-enyloxy)-β-lactams as reported from our laboratory.[8] Keeping in view, the importance of spiro-β-lactams, we extended our work on C-3 allylation of β-lactams[9] to the synthesis of spiro-β-lactams using halocyclization. The reaction employs intramolecular addition of nucleophilic sulphur to carbon–carbon double bond of allyl group of *cis*-3-allyl-3-phenylthio/benzylthio-azetidin-2-ones (**5/6**) in the presence of $Br_2$ or $I_2$ as electrophilic reagent.[10] The reaction proceeds through a step-wise electrophilic attack and dealkylation sequence giving C-3 spiro-β-lactams, 7-halo-5-thia-2-azaspiro[3,4]octan-1-ones. Since, such type of spiro-β-lactams are not easily accessible by classical ketene-imine cycloaddition, this reaction serves as an operationally simple, efficient and better metho-

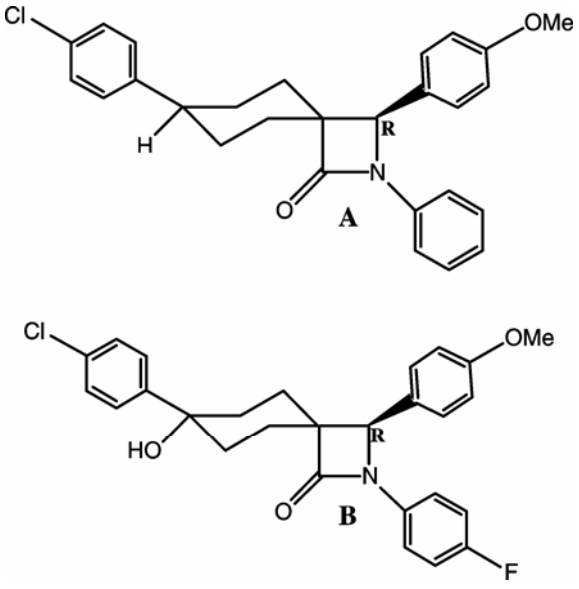



**Figure 1.** Potent cholesterol absorption inhibitors.

*For correspondence

dology for the formation of heterocyclic ring at C-3 of $\beta$-lactams under very mild conditions.

## 2. Experimental

Melting points are uncorrected. IR spectra were taken on a FTIR spectrophotometer and are reported in $cm^{-1}$. $^1H$ and $^{13}C$ NMR spectra were recorded on JEOL 300 and Bruker Avance II 400 NMR spectrometers. Chemical shifts are given in parts per million relative to tetramethylsilane as internal standard ($\delta = 0$) for $^1H$ NMR and $CDCl_3$ ($\delta = 77{\cdot}0$ ppm) for $^{13}C$ NMR spectra. Mass spectra were recorded on a Shimadzu GCMS-QT 5000 instrument and elemental analysis (C, H, and N) was carried out using a PERKIN-ELMER 2400 elemental analyzer. Column chromatography was performed using Merck Silica Gel (100–200 mesh). Thin-layer chromatography (TLC) was performed using Merck Silica Gel. For visualization, TLC plates were stained with iodine vapours. All commercially available compounds/reagents were used without further purification. Dichloromethane and carbon tetrachloride distilled over $P_2O_5$ were redistilled over $CaH_2$ before use. The melting point of compounds **11** and **12** is not reported as most of them have separated as mixture only. Crystallographic data (excluding structure factors) of compound **10e** with CCDC-642729 in CIF format have been deposited with the Cambridge Crystallographic Data Centre. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.com.ac.uk/data_request/cif.

### 2.1 *General procedure for halocyclization*

To a stirred solution of *cis*-3-allyl-3-benzylthio-$\beta$-lactams **6** (1 mmol) in 15 mL of dry methylene chloride was added bromine/iodine (1·1 mmol) at room temperature. The mixture was allowed to stir (2–3 h) at the same temperature. The progress of reaction was monitored by TLC. After completion of reaction, the reaction mixture was poured into aqueous 5% $Na_2S_2O_3/Na_2S_2O_5$ solution (15 mL) and stirred until the reddish colouration of bromine/purplish colouration of iodine dissipated. The aqueous mixture was extracted with methylene chloride (3 × 5 mL) and the combined organic extracts were washed with brine and dried over anhydrous $Na_2SO_4$. After evaporation of solvent under vacuum, the residue was purified by column chromatography on silica gel in hexanes/ethyl acetate.

2.1a *1-(4′-Methoxyphenyl)-3-benzylthio-3-(2′,3′-dibromopropyl)-4-phenyl azetidin-2-one* (**8a**): Oil; yield 9%; IR $\nu_{max}$ ($CCl_4$) 1750 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·71–7·54 (14H, *m*, Ph), 5·42 (1H, *s*, C4-H), 4·49–4·56 (1H, *m*, C2′-H), 3·98 (1H, *d*, $J = 16{\cdot}4$ Hz, $CH_2S$), 3·91 (1H, *d*, $J = 16{\cdot}4$ Hz, $CH_2S$), 3·71 (3H, *s*), 3·50 (1H, *dd*, $J = 14{\cdot}6$ Hz, 5·6 Hz, C3′-H), 3·41 (1H, *dd*, $J = 14$ Hz, 10·8 Hz, C3′-H), 2·96 (1H, *dd*, $J = 20$ Hz, 2·4 Hz, C1′-H), 2·41(1H, *dd*, $J = 20$ Hz, 13·2 Hz, C1′-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 164·9, 156·3, 137·6, 133·3, 130·8, 129·4, 128·8, 128·7, 128·6, 128·1, 127·4, 118·7, 114·4, 66·2, 63·9, 55·2, 47·7, 40·6, 37·2, 33·2· Anal. Calcd. For $C_{26}H_{25}O_2NSBr_2$: C 54·27, H 4·38, N 2·43. Found: C 54·21, H 4·29, N 2·39.

2.1b *2-(4′-Methoxyphenyl)-3-phenyl-7α-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**9a**): White solid; yield 28%; m.p. 215–217°C; IR $\nu_{max}$ (KBr) 1743 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·73–7·56 (9H, *m*, Ph), 5·01 (1H, *s*, C3-H), 4·11–4·20 (1H, *m*, C7-H), 3·73 (3H, *s*, $OCH_3$), 3·21 (1H, *t*, $J = 14$ Hz, C6-H), 2·97–3·19 (2H, *m*, C8-H, and C6-H), 2·70 (1H, *t*, $J = 17{\cdot}2$ Hz, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 166·0, 156·0, 135·2, 130·7, 129·0, 128·8, 127·4, 124·6, 118·6, 114·4, 71·0, 70·9, 55·0, 48·0, 43·2, 41·00. Anal. Calcd. For $C_{19}H_{18}O_2NSBr$: C 56·44, H 4·48, N 3·46. Found: C 56·36, H 4·34, N 3·36.

2.1c *2-(4′-Methoxyphenyl)-3-phenyl-7β-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**10a**): Crystalline solid; yield 56%; m.p. 174–176°C; IR $\nu_{max}$ (KBr) 1740 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·72–7·55 (9H, *m*, Ph), 5·17 (1H, *s*, C3-H), 4·75–4·81 (1H, *m*, C7-H), 3·72 (3H, *s*, $OCH_3$), 3·44 (1H, *dd*, $J = 11{\cdot}8$ Hz, 5·2 Hz, 6α-H–7α-H, C6-H), 2·97–3·10 (2H, *m*, C6-H and C8-H), 2·85 (1H, *dd*, $J = 13{\cdot}5$ Hz, 5·65 Hz, 8β-H–7α-H, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 166·7, 156·3, 135·1, 130·6, 129·1, 128·8, 127·4, 118·8, 114·4, 71·9, 68·2, 55·2, 48·6, 47·8, 42·6. Anal. Calcd. For $C_{19}H_{18}O_2NSBr$: C 56·44, H 4·48, N 3·46. Found: C 56·36, H 4·34, N 3·36.

2.1d *1-(4′-Methoxyphenyl)-3-benzylthio-3-(2′,3′-dibromopropyl)-4-(4′-methoxy phenyl)azetidin-2-one* (**8b**): Oil; yield 23%; IR $\nu_{max}$ ($CCl_4$) 1748(C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·71–7·38 (13H, *m*, Ph), 5·35 (1H, *s*, C4-H), 4·48–4·60 (1H, *m*, C2′-H), 4·05 (1H, *d*, $J = 16{\cdot}4$ Hz, $CH_2S$), 3·92 (1H, *d*, $J = 16{\cdot}4$ Hz, $CH_2S$), 3·76 (3H, *s*, $OCH_3$), 3·74

(3H, *s*, $OCH_3$), 3·48 (1H, *dd*, *J* = 14·6 Hz, 5·6Hz, C3′-H), 3·38 (1H, *dd*, *J* = 14 Hz, 10·8 Hz, C3′-H), 2·97 (1H, *dd*, *J* = 20 Hz, 2·4 Hz, C1′-H), 2·44 (1H, *dd*, *J* = 20 Hz, 13·2 Hz, C1′-H)· Anal. Calcd. For $C_{27}H_{27}O_3NSBr_2$: C 53·57, H 4·49, N 2·31. Found: C 53·51, H 4·39, N 2·24.

2.1e *2,3-Di-(4′-methoxyphenyl)-7α-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**9b**): Oil; yield 36%; IR $\nu_{max}$ ($CCl_4$) 1751 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6·71–7·24 (8H, *m*, Ph), 4·93 (1H, *s*, C3-H), 4·09–4·15 (1H, *m*, C7-H), 3·79 (3H, *s*, $OCH_3$), 3·73 (3H, *s*, $OCH_3$), 3·20 (1H, *t*, *J* = 14 Hz, C6-H), 2·09–3·90 (2H, *m*, C8-H and C6-H), 2·75 (1H, *t*, *J* = 17·2 Hz, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 166·6, 160·2, 160·1, 130·7, 128·7, 126·9, 118·9, 118·7, 118·6, 114·5, 114·4, 114·2, 114·0, 70·7, 69·9, 55·3, 55·1, 47·0, 43·2, 41·0. Anal. Calcd. For $C_{20}H_{20}O_3NSBr$: C 55·30, H 4·64, N 3·22. Found: C 55·22, H 4·54, N 3·14.

2.1f *2,3-Di-(4′-Methoxyphenyl)-7β-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**10b**): Oil; yield 28%; IR $\nu_{max}$ ($CCl_4$) 1745 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6·70–7·52 (8H, *m*, Ph), 5·10 (1H, s, C3-H), 4·75–4·82 (1H, *m*, C7-H), 3·80 (3H, *s*, $OCH_3$), 3·74 (3H, *s*, $OCH_3$), 3·42 (1H, *dd*, *J* = 11·8 Hz, 5·2 Hz, C6-H), 2·92 (2H, *m*, C6-H and C8-H), 2·71 (1H, *dd*, *J* = 13·5 Hz, 5·65 Hz, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 166·6, 160·1, 130·7, 128·6, 126·9, 118·9, 118·8, 114·4, 114·3, 72·2, 68·0, 55·3, 55·1, 48·6, 48·1, 42·7. Anal. Calcd. For $C_{20}H_{20}O_3NSBr$: C 55·30, H 4·64, N 3·22. Found: C 55·22, H 4·54, N 3·14.

2.1g *1-(4′-Methylphenyl)-3-benzylthio-3-(2′,3′-dibromopropyl)-4-(4′-chlorophenyl)azetidin-2-one* (**8c**)*:* Oil; yield 20%; IR $\nu_{max}$ ($CCl_4$) 1748 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6·89–7·39 (13H, *m*, Ph), 5·34 (1H, *s*, C4-H), 4·43–4·50 (1H, *m*, C2′-H), 3·93 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·88 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·50 (1H, *dd*, *J* = 14·6 Hz, 5·6 Hz, C3′-H), 3·39 (1H, *dd*, *J* = 14 Hz, 10·8 Hz, C3′-H), 2·86 (1H, *dd*, *J* = 20 Hz, 2·4 Hz, C1′-H), 2·40 (1H, *dd*, *J* = 20 Hz, 13·2 Hz, C1′-H), 2·21 (3H, *s*, $CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 165·1, 136·7, 134·6, 133·2, 132·4, 132·0, 129·0, 128·9, 128·3, 128·2, 126·8, 119·3, 116·9, 66·2, 63·9, 48·1, 40·0, 36·0, 34·0, 21·3. Anal. Calcd. For $C_{26}H_{24}O_2NSBr_2Cl$: C 51·21, H 3·96, N 2·29. Found: C 51·11, H 3·89, N 2·24.

2.1h *2-(4′-Methylphenyl)-3-(4′-chlorophenyl)-7α-bromo-5-thia-2-azaspiro[3,4] octan-1-one* (**9c**): Oil; yield 15%; IR $\nu_{max}$ ($CCl_4$) 1751 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6·99–7·45 (8H, *m*, Ph), 4·95 (1H, *s*, C3-H), 4·00–4·10 (1H, *m*, C7-H), 3·30 (1H, *t*, *J* = 14 Hz, C6-H), 2·90–3·10 (2H, *m*, C6-H and C8-H), 2·74 (1H, *t*, *J* = 17·2 Hz, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 165·0, 136·7, 134·6, 133·4, 132·3, 132·0, 129·0, 128·2, 126·8, 119·2, 70·5, 70·0, 48·0, 43·0, 41·2, 21·0. Anal. Calcd. For $C_{19}H_{17}O_2NSBrCl$: C 51·98, H 3·90, N 3·19. Found: C 51·86, H 3·84, N 3·12.

2.1i *2-(4′-Methylphenyl)-3-(4′-chlorophenyl)-7β-bromo-5-thia-2-azaspiro[3,4] octan-1-one* (**10c**): Crystalline solid; yield 35%; m.p. 211–214°C; IR $\nu_{max}$ (KBr) 1740 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7·01–7·37 (8H, *m*, Ph), 5·19 (1H, *s*, C3-H), 4·79–4·81 (1H, *m*, C7-H), 3·48 (1H, *dd*, *J* = 11·72 Hz, 5·1 Hz, 8βH–7αH, C6-H), 2·97–3·03 (2H, *m*, C6-H and C8-H), 2·82 (1H, *dd*, *J* = 13·8 Hz, 5·6 Hz, 8βH–7αH, C8-H), 2·29 (3H, *s*, $CH_3$); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 166·0, 136·7, 134·2, 133·2, 133·1, 129·0, 128·9, 128·3, 118·7, 72·0, 68·2, 48·4, 47·8, 42·7, 20·5· Anal. Calcd. For $C_{19}H_{17}O_2NSBrCl$: C 51·98, H 3·90, N 3·19. Found: C 51·86, H 3·84, N 3·12.

2.1j *1-Phenyl-3-benzylthio-3-(2′,3′-dibromopropyl)-4-phenylazetidin-2-one* (**8d**): Oil; yield 5%; IR $\nu_{max}$ ($CCl_4$) 1750 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 6·98–7·39 (15H, *m*, Ph), 5·37 (1H, *s*, C4-H), 4·47–4·56 (1H, *m*, C2′-H), 3·98 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·91 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·51 (1H, *dd*, *J* = 14·6 Hz, 5·6 Hz, C3′-H), 3·40 (1H, *dd*, *J* = 14 Hz, 10·8 Hz, C3′-H), 2·96 (1H, *dd*, *J* = 20 Hz, 2·4 Hz, C1′-H), 2·41 (1H, *dd*, *J* = 20 Hz, *J* = 13·2 Hz, C1′-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 164·9, 137·7, 133·3, 130·8, 129·4, 128·8, 128·7, 128·6, 128·1, 127·3, 118·7, 114·4, 63·9, 66·2, 47·8, 40·6, 37·2, 33·2. Anal. Calcd. For $C_{25}H_{23}ONSBr_2$: C 55·06, H 4·25, N 2·56. Found: C 55·01, H 4·19, N 2·49.

2.1k *2,3-Diphenyl-7α-bromo-5-thia-2-azaspiro[3,4] octan-1-one* (**9d**): White solid; yield 28%; m.p. 225–227°C; IR $\nu_{max}$ (KBr) 1747·8 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7·06–7·43 (10H, *m*, Ph), 5·03 (1H, *s*, C3-H), 4·06–4·17 (1H, *m*, C7-H), 3·25 (1H, *t*, *J* = 14 Hz, C6-H), 2·98–3·10 (2H, *m*, C6-H and C8-H), 2·71 (1H, *t*, *J* = 17·2 Hz, C8-H); $^{13}C$

NMR (100 MHz, $CDCl_3$) $\delta$ 166·4, 136·9, 135·2, 132·2, 129·1, 129·0, 126·9, 124·5, 119·1, 117·5, 70·8, 70·1, 48·0, 43·5, 41·2. Anal. Calcd. For $C_{18}H_{16}ONSBr$: C 57·76, H 4·31, N 3·74. Found: C 57·66, H 4·24, N 3·62.

2.1l *2,3-Diphenyl-7β-bromo-5-thia-2-azaspiro[3,4] octan-1-one* (**10d**): Crystalline solid; yield 66%; m.p. 142–145°C; IR $\nu_{max}$ (KBr) 1745·9 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·03–7·42 (10H, *m*, Ph), 5·27 (1H, *s*, C3-H), 4·76–4·80 (1H, *m*, C7-H), 3·44 (1H, *dd*, *J* = 11·4 Hz, 5·1 Hz, 6α-H–7α-H, C6-H), 2·97–3·10 (2H, *m*, C6-H and C8-H), 2·80 (1H, *dd*, *J* = 13·8 Hz, 5·7 Hz, 8β-H-7α-H, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 167·5, 135·9, 134·5, 132·2, 129·2, 129·1, 128·8, 127·3, 119·1, 72·2, 68·2, 48·6, 47·9, 42·7; $^{13}C$ NMR (DEPT 135) $\delta$ 129·2 (+), 129·1 (+), 128·8 (+), 127·3 (+), 119·1 (+), 68·2 (+), 48·6 (–), 47·9 (+), 42·7 (–). Anal. Calcd. For $C_{18}H_{16}ONSBr$: C 57·76, H 4·31, N 3·74. Found: C 57·66, H 4·24, N, 3·62.

2.1m *1-(4′-Chlorophenyl)-3-benzylthio-3-(2′,3′-di-bromopropyl)-4-phenyl azetidin-2-one* (**8e**): Oil; yield 26%; IR $\nu_{max}$ ($CCl_4$) 1751 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·00–7·40 (14H, *m*, Ph), 5·38 (1H, *s*, C4-H), 4·48–4·56 (1H, *m*, C2′-H), 3·99 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·92 (1H, *d*, *J* = 16·4 Hz, $CH_2S$), 3·50 (1H, *dd*, *J* = 14·6 Hz, 5·6 Hz, C3′-H), 3·40 (1H, *dd*, *J* = 14 Hz, 10·8 Hz, C3′-H), 2·95 (1H, *dd*, *J* = 20 Hz, 2·4 Hz, C1′-H), 2·41 (1H, *dd*, *J* = 20 Hz, 13·2 Hz, C1′-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 166·1, 135·6, 134·6, 129·6, 129·4, 129·3, 129·2, 129·0, 128·9, 127·9, 127·6, 127·3, 118·0, 65·1, 63·2, 47·1, 40·0, 36·5, 33·6. Anal. Calcd. For $C_{25}H_{22}ONSClBr_2$: C 51·78, H 3·82, N 2·41. Found: C 51·70, H 3·70, N, 2·29.

2.1n *2-(4′-Chlorophenyl)-3-phenyl-7α-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**9e**): White solid; yield 16%; m.p. 220–223°C; IR $\nu_{max}$ (KBr) 1747·8 (C=O), $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·10–7·72 (9H, *m*, Ph), 5·29 (1H, *s*, C3-H), 4·10–4·20 (1H, *m*, C7-H), 3·22 (1H, *t*, *J* = 14 Hz, C6-H), 2·95–3·10 (2H, *m*, C6-H and C8-H), 2·79 (1H, *t*, *J* = 17·2 Hz, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 167·4, 135·2, 134·7, 129·6, 129·4, 129·3, 128·62 127·2, 118·8, 71·0, 70·6, 48·2, 44·4, 41·2. Anal. Calcd. For $C_{18}H_{15}ONSBrCl$: C 52·89, H 3·70, N 3·42. Found: C 52·80, H 3·66, N 3·35.

2.1o *2-(4′-Chlorophenyl)-3-phenyl-7β-bromo-5-thia-2-azaspiro[3,4]octan-1-one* (**10e**): Crystalline solid; yield 33%; m.p. 133–135°C; IR $\nu_{max.}$(KBr) 1739·7 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·16–7·44 (9H, *m*, Ph), 5·27 (1H, *s*, C3-H), 4·76–4·82 (1H, *m*, C7-H), 3·42 (1H, *dd*, *J* = 11·72 Hz, 5·1 Hz, 6α-H–7α-H, C6-H), 3·10–2·80 (2H, *m*, C6-H and C8-H), 2·40 (1H, *dd*, *J* = 13·8 Hz, 5·6 Hz, 8β-H-7α-H, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 167·4, 135·6, 134·6, 129·6, 129·3, 129·2, 128·9, 127·3, 118·7, 72·2, 68·3, 48·7, 47·8, 42·7; MS (EI) *m/z* 409 ($M^+$), 215 ($M^+$-$C_5H_5OSBr$), 193 ($M^+$-$C_{13}H_{10}NCl$). Anal. Calcd. For $C_{18}H_{15}ONSBrCl$: C 52·89, H 3·70, N 3·40. Found: C 52·80, H 3·66, N 3·35.

2.1p *2-(4′-Methoxyphenyl)-3-phenyl-7(α,β)-iodo-5-thia-2-azaspiro[3,4]octan-1-one* (**11a**, **12a**): White solid; yield 80%; IR $\nu_{max}$ (KBr) 1749, (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·69–7·34 (18H, *m*, Ph, both isomers), 5·06 (1H, *s*, for one isomer, C3-H), 4·96 (1H, *s*, for one isomer, C3-H), 4·52–4·62 (1H, *m*, for one isomer, C7-H), 3·80–4·10 (1H, *m*, for one isomer, C7-H), 3·67 (6H, *s*, both isomers, $OCH_3$), 3·23–3·32 (2H, *m*, both isomers, C6-H), 3·03–3·09 (4H, *m*, both isomers, C6-H and C8-H), 2·66–2·78 (2H, *m*, both isomers, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 165·5, 156·4, 135·5, 130·5, 129·0, 128·8, 127·0, 118·8, 114·4, 72·7, 70·3, 66·7, 55·4, 50·8, 50·2, 43·7, 16·6. Anal. Calcd. For $C_{19}H_{18}O_2NSI$: C 50·56, H 4·02, N 3·10. Found: C 50·47, H 4·01, N 3·04.

2.1q *2,3-Di-(4′-methoxyphenyl)-7(α,β)-iodo-5-thia-2-azaspiro[3,4]octan-1-one* (**11b**, **12b**): White solid; yield 80%; IR $\nu_{max}$ (KBr) 1747·6, (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·95–7·40 (16H, *m*, Ph, both isomers), 5·01(1H, *s*, for one isomer, C3-H), 4·91 (1H, *s*, for one isomer, C3-H), 4·51–4·60 (1H, *m*, for one isomer, C7-H), 3·80–4·10 (1H, *m*, for one isomer, C7-H), 3·72 (12H, *s*, both isomers, $OCH_3$), 3·20–3·32 (2H, *m*, both isomers, C6-H), 2·88–3·10 (4H, *m*, both isomers, C6-H and C8-H), 2·75–2·83 (2H, *m*, both isomers, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 160·1, 156·2, 135·4, 130·5, 128·4, 128·3, 118·8, 114·6, 114·4, 114·3, 72·0, 70·1, 67·2, 55·3, 55·1, 50·8, 49·1, 43·7, 16·7. Anal. Calcd. For $C_{20}H_{20}O_3NSI$: C 49·90, H 4·18, N 2·90. Found: C 49·87, H 4·12, N 2·81.

2.1r *2,3-Di-(4′-Methoxyphenyl)-7α-iodo-5-thia-2-azaspiro[3,4]octan-1-one* (**11b**): White solid; yield

62%; m.p. 174–175°C; IR $\nu_{max}$ (KBr) 1748, (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·68–7·18 (8H, *m*, Ph), 4·84 (1H, *s*, C3-H), 3·90–3·94 (1H, *m*, C7-H), 3·75 (3H, *s*, $OCH_3$), 3·70 (3H, *s*, $OCH_3$), 3·25–3·30 (1H, *m*, C6-H), 3·10–3·20 (1H, *m*, C6-H), 2·95–2·99 (1H, *m*, C8-H), 2·71–2·77 (1H, *m*, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 165·7, 160·0, 156·3, 130·6, 128·3, 127·3, 118·8, 114·37, 96·1, 72·8, 70·0, 55·4, 55·2, 50·7, 43·7, 16·7.

2.1s *2-(4′-Methylphenyl)-3-(4′-chlorophenyl)-7(α,β)-iodo-5-thia-2-azaspiro[3,4] octan-1-one* (**11c**, **12c**): Solid; yield 62%; IR $\nu_{max}$ (KBr) 1746·8, 1707·5 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·95–7·30 (16H, *m*, Ph, both isomers), 5·05 (1H, *s*, for one isomer, C3-H), 4·88 (1H, *s*, for one isomer, C3-H), 4·50–4·61 (1H, *m*, for one isomer, C7-H), 3·82–4·00 (1H, *m*, for one isomer, C7-H), 3·19–3·32 (2H, *m*, both isomers, C6-H), 2·90–3·15 (4H, *m*, both isomers, C6-H and C8-H), 2·61–2·80 (2H, *m*, both isomers, C8-H), 2·17 (6H, *s* both isomers); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 165·7, 165·4, 134·9, 134·8, 134·4, 134·3, 134·0, 133·6, 129·7, 129·3, 129·1, 128·5, 128·3, 117·4, 72·6, 72·3, 69·5, 66·3, 50·8, 50·3, 44·1, 43·7, 29·6, 20·9, 26·0, 16·31. Anal. Calcd. For $C_{19}H_{17}O_2NSICl$: C 46·98, H 3·52, N 2·88. Found: C 46·88, H 3·43, N 2·81.

2.1t *2,3-Diphenyl-7(α,β)-iodo-5-thia-2-azaspiro [3,4]octan-1-one* (**11d**, **12d**): Solid; yield 71%; IR $\nu_{max}$ (KBr) 1747, (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·03–7·40 (20H, *m*, Ph, both isomers), 5·15 (1H, s, for one isomer, C3-H), 5·06 (1H, s, for one isomer, C3-H), 4·52–4·60 (1H, *m*, for one isomer, C7-H), 3·82–4·00 (1H, *m*, for one isomer, C7-H), 3·19–3·31 (2H, *m*, both isomers, C6-H), 2·90–3·10 (4H, *m*, both isomers, C6-H and C8-H), 2·70–2·85 (2H, *m*, both isomers, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 160·0, 133·4, 127·1, 126·9, 126·8, 124·8, 124·7, 116·4, 70·4, 68·1, 64·5, 48·8, 48·1, 41·4. Anal. Calcd. For $C_{18}H_{16}ONSI$: C 51·31, H 3·82, N 3·32. Found: C 51·24, H 3·79, N 3·24.

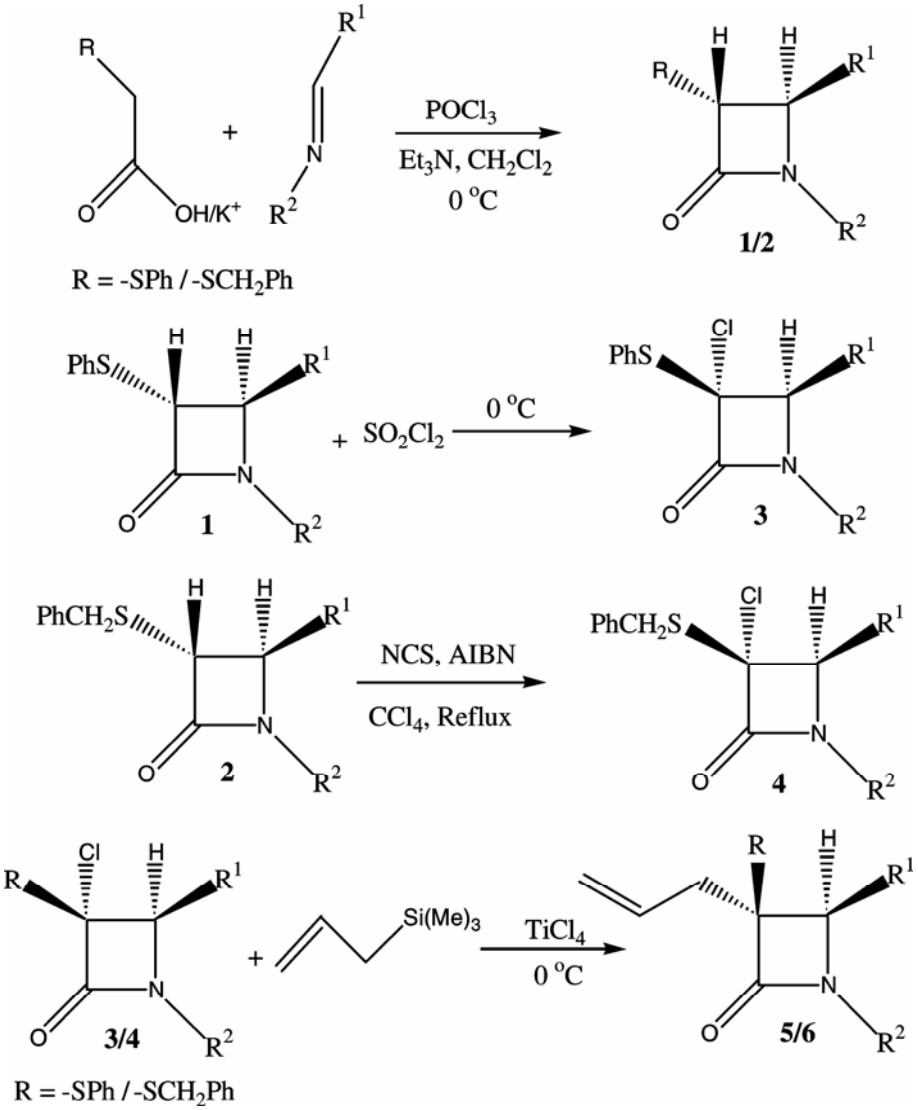
2.1u *2-(4′-Chlorophenyl)-3-phenyl-7(α,β)-iodo-5-thia-2-azaspiro[3,4]octan-1-one* (**11e**, **12e**): White solid; yield 48%; IR $\nu_{max}$ (KBr) 1747·5, (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·12–7·43 (18H, *m*, Ph, both isomers), 5·15 (1H, *s*, for one isomer, C3-H), 5·05 (1H, *s*, for one isomer, C3-H), 4·56–4·62 (1H, *m*, for one isomer, C7-H), 3·86–4·10 (1H, *m*, for one isomer, C7-H), 3·20–3·34 (2H, *m*, both isomers, C6-H), 2·85–3·14 (4H, *m*, both isomers, C6-H and C8-H), 2·77–2·90 (2H, *m*, both isomers, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 168·0, 166·3, 135·4, 134·8, 134·5, 129·6, 129·4, 129·2, 129·0, 128·0, 127·0, 126·9, 118·8, 118·7, 73·0, 72·6, 70·3, 66·8, 50·8, 50·2, 43·8, 43·7, 19·32, 16·3. Anal. Calcd. For $C_{18}H_{15}ONSICl$: C 47·44, H 3·31, N 3·07. Found: C 47·37, H 3·23, N 3·01.

## 2.2 *General procedure for desulphurization*

To a stirred solution of spiro-β-lactams **9** + **10/11** + **12** (1mmol) and catalytic amount of AIBN in 5mL of dry benzene was added *n*-$Bu_3SnH$ (1·1 mmol) under nitrogen atmosphere. The reaction mixture was refluxed for 40 min and progress was monitored by TLC. Upon completion of the reaction, the solvent was removed under reduced pressure. The residue was dissolved in methylene chloride and was washed with water, brine, and dried over anhydrous $Na_2SO_4$ and filtered. After evaporation of solvent under vacuum, the residue was purified by column chromatography on silica gel in hexanes/ethyl acetate.

2.2a *2-(4′-Methoxyphenyl)-3-phenyl-5-thia-2-aza-spiro[3,4]octan-1-one* (**13a**): White flakes; yield 75%; m.p. 185–187°C; IR $\nu_{max}$ (KBr) 1736 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 6·72–7·39 (9H, *m*, Ph), 4·97 (1H, *s*, C4-H), 3·74 (3H, *s*, $OCH_3$), 2·90–3·00 (1H, *m*, C6-H), 2·75–2·85 (1H, *m*, C6-H), 2·45–2·58 (2H, *m*, C7-H), 2·25–2·40 (1H, *m*, C8-H), 1·95–2·01 (1H, *m*, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 168·0, 156·1, 136·5, 131·3, 128·6, 128·3, 127·0, 118·6, 114·4, 74·1, 68·5, 55·2, 39·7, 33·8, 30·4; $^{13}C$ NMR (DEPT 135) $\delta$ 128·6 (+), 128·3 (+), 127·0 (+), 118·6 (+), 114·4 (+), 68·5 (+), 55·2 (+), 39·7 (–), 33·8 (–), 30·4 (–); MS (EI) *m/z* 325 ($M^+$), 219, 176, 147 ($M^+ - C_{11}H_{12}S$), 115 ($M^+ - C_{14}H_{13}NO$). Anal. Calcd. For $C_{19}H_{19}O_2NS$: C 70·12, H 5·88, N 4·30. Found: C 70·04, H 5·73, N 4·21.

2.2b *2,3-Diphenyl-5-thia-2-azaspiro[3,4]octan-1-one* (**13d**): White solid; yield 80%; m.p. 200–202°C; IR $\nu_{max}$ (KBr) 1733 (C=O) $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7·04–7·51 (10H, *m*, Ph), 5·02 (1H, *s*, C4-H), 2·92–3·00 (1H, *m*, C6-H), 2·71–2·81 (1H, *m*, C6-H), 2·40–2·50 (2H, *m*, C7-H), 2·28–2·40 (1H, *m*, C8-H), 2·00–2·10 (1H, *m*, C8-H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 168·8, 135·6, 132·0, 129·0, 127·7, 126·8, 124·0, 118·9, 117·4, 74·2, 68·5, 39·7,




**Scheme 1.** Synthesis of *cis*-3-allyl-3-phenylthio/benzylthio *β*-lactams **5/6**.

**Table 1.** 3-Allyl-3-phenylthio/benzylthioazetidin-2-ones **5** and **6**.

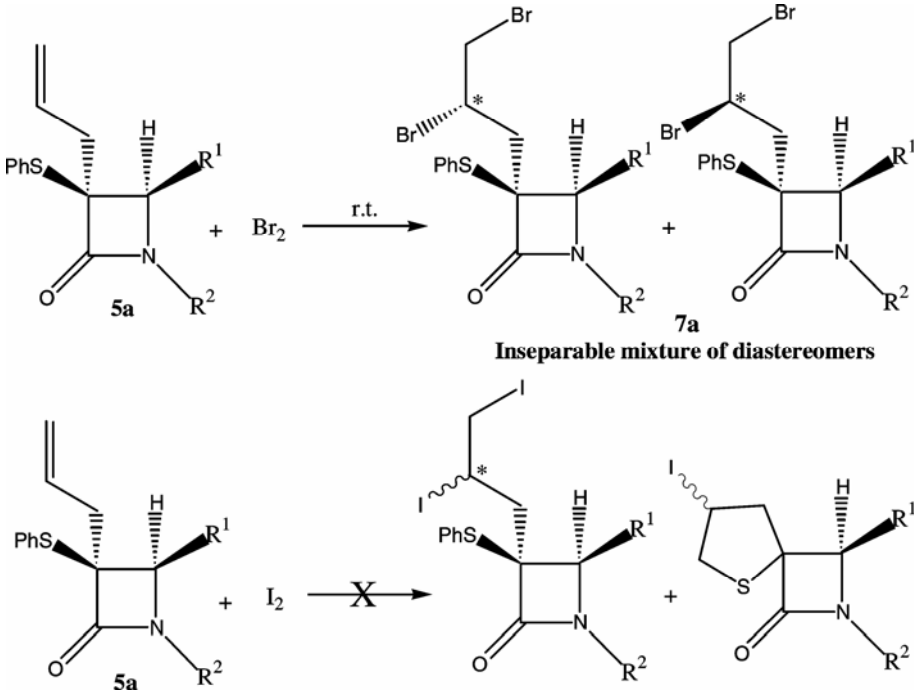
| Entry | $R^1$ | $R^2$ | Substrate (% yield)[a] | |
|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_4$·OMe (4) | **5a** (86) | **6a** (90) |
| 2 | $C_6H_4$·OMe (4) | $C_6H_4$·OMe (4) | **5b** (85) | **6b** (99) |
| 3 | $C_6H_4$·Cl (4) | $C_6H_4.CH_3$ (4) | **5c** (88) | **6c** (69) |
| 4 | $C_6H_5$ | $C_6H_4$Br (4) | **5d** (85) | – |
| 5 | $C_6H_5$ | $C_6H_5$ | – | **6d** (99) |
| 6 | $C_6H_5$ | $C_6H_4$Cl (4) | – | **6e** (95) |

[a]Isolated yield

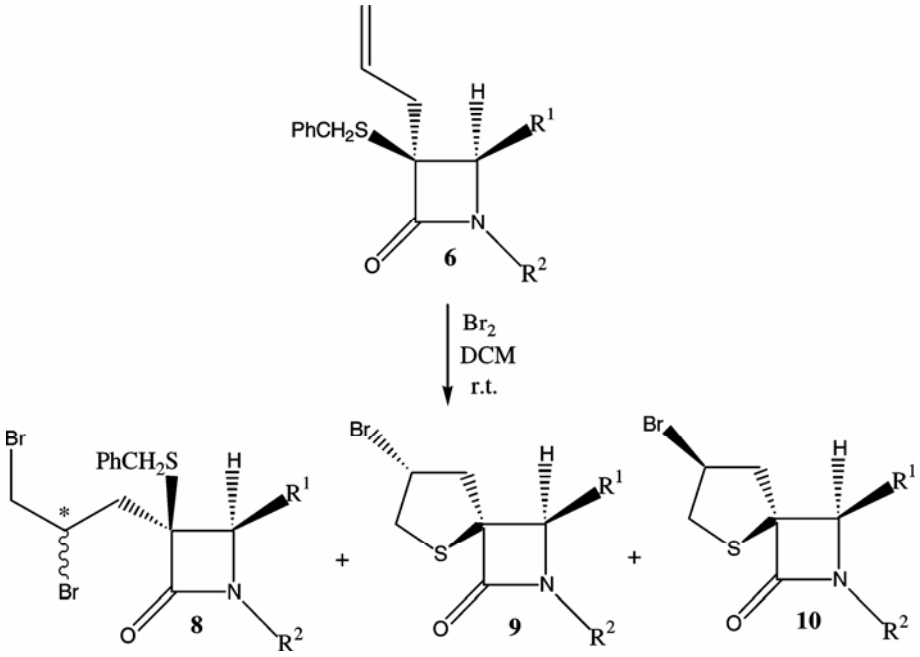
34·0, 30·3; $^{13}$C NMR (DEPT 135) $\delta$ 132·0 (+), 129·0 (+), 127·7 (+), 126·8 (+), 118·9 (+), 117·4 (+), 68·5 (+), 39·7 (–), 34·0 (–), 30·3 (–). Anal. Calcd. For $C_{18}H_{17}ONS$: C 73·18, H 5·80, N 4·74. Found: C 73·09, H 5·73, N 4·61.

## 3. Results and discussion

The studies start with the preparation of *trans*-3-phenylthio/benzylthio-*β*-lactams (**1/2**) by reacting Schiff base and phenylthio/benzylthioacetic acid




**Scheme 2.** Cyclization studies of substrate **5** with $Br_2$ and $I_2$.




**Scheme 3.** Synthesis of spiro-β-lactams **9a–e** and **10a–e**.

using reported procedure.[11,12] These were transformed into their 3-chloro derivatives using $SO_2Cl_2$ as chlorinating agent.[12,13] The conversion of 3-benzylthio-β-lactams into 3-chloro-3-benzylthio-β-lactams **(4)** was done with NCS in the presence of AIBN. These *trans*-3-chloro-β-lactams **(3/4)** on treatment with allylsilane in the presence of $TiCl_4$ afforded *cis*-3-allyl-3-phenyl/benzylthio-β-lactams **(5/6)** in good yield.[9] The structures of these products were established spectroscopically. However, the stereochemistry was assigned on the basis of X-ray crystallographic studies (scheme 1 and table 1).[9]

The halocyclization studies were initially carried out using substrate **5a**. Treatment of β-lactam **5a**

**Table 2.** 7-Bromo-5-thia-2-azaspiro[3,4]octan-1-ones **9a–e** and **10a–e**.

| Entry | $R^1$ | $R^2$ | Addition product (% yield)[a,b] | $\alpha$-Bromoisomer (% yield) [a,b] | $\beta$-Bromoisomer (% yield)[a,b] |
|---|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_4OCH_3$ (4) | **8a** (9) | **9a** (28) | **10a** (27) |
| 2 | $C_6H_4OCH_3$ (4) | $C_6H_4OCH_3$ (4) | **8b** (23) | **9b** (26) | **10b** (28) |
| 3 | $C_6H_4Cl$ (4) | $C_6H_4CH_3$ (4) | **8c** (20) | **9c** (15) | **10c** (35) |
| 4 | $C_6H_5$ | $C_6H_5$ | **8d** (5) | **9d** (28) | **10d** (66) |
| 5 | $C_6H_5$ | $C_6H_4Cl$ (4) | **8e** (27) | **9e** (16) | **10e** (33) |

[a]All new compounds gave satisfactory CHN analysis
[b]Yields quoted are for the isolated products characterized by IR, $^1$H NMR, $^{13}$C NMR

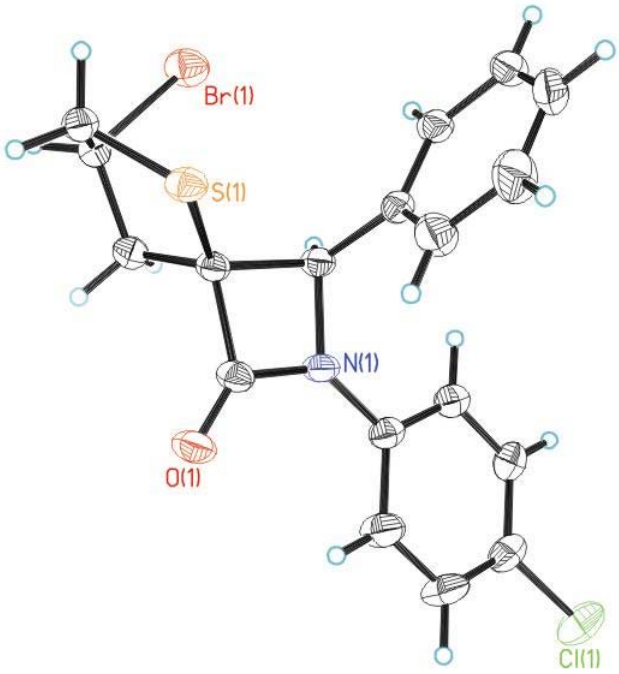
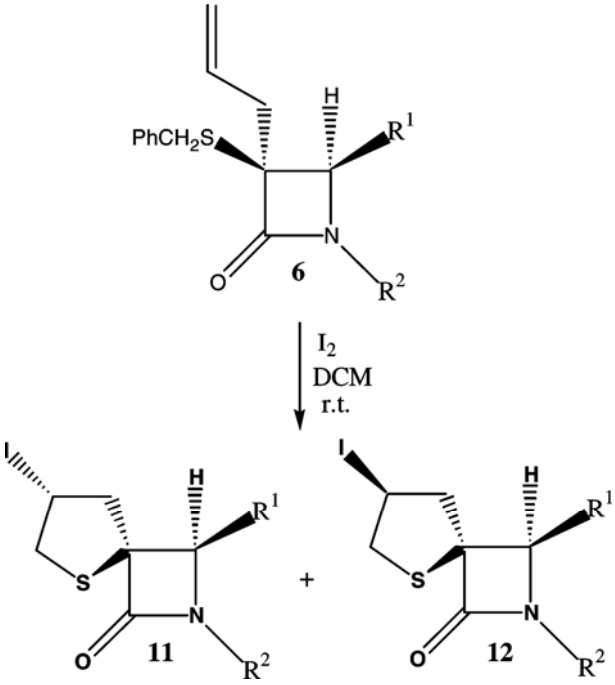



**Figure 2.** An ORTEP diagram of compound **10e**.




**Scheme 4.** Synthesis of spiro-$\beta$-lactams **11a–e** and **12a–e**.

with $Br_2$ in methylene dichloride at room temperature did not provide the anticipated spiro-$\beta$-lactam, rather it produced product **7a** from addition of $Br_2$ across the double bond as a mixture of inseparable diastereomers. However, the reaction when carried with $I_2$ neither gave spiro nor addition product, as was evident from the $^1$H NMR spectra of reaction mixture.

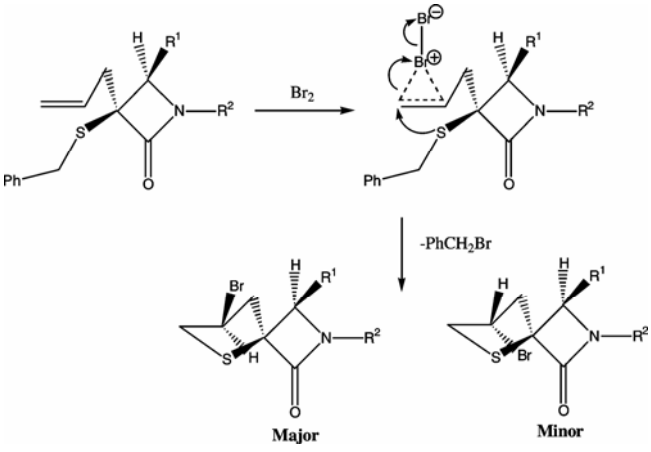
These results showed that **5a** was not suitable substrate for halocyclization. This might be ascribed to poor leaving ability of phenyl group. The lone pair on sulphur might not be fully available for cyclization due to resonance with phenyl group (scheme 2).

Continuing further, these studies were repeated using substrate **6a**. It was envisaged that since compound **6a** has a methylene inserted between sulphur and phenyl group, this might be having different reactivity and might prove to be a suitable substrate for this reaction. Thus addition of $Br_2$ (1 equiv.) to $\beta$-lactam substrate **6a** in methylene dichloride at room temperature initially showed no change in TLC profile. However, after stirring for 3 h, the TLC profile showed two new spots having $R_f$ lower than that of the substrate. Of these three spots, first one having same $R_f$ as substrate was identified as acyclic dibromide i.e. 1-(4′-methoxyphenyl)-3-benzylthio-3-(2′,3′-dibromopropyl)-4-phenylazetidin-2-one

**Table 3.** 7-Iodo-5-thia-2-azaspiro[3,4]octan-1-ones **11a–e** and **12a–e**.

| Entry | $R^1$ | $R^2$ | α-Iodoisomer (% yield)[a,b] | β-Iodoisomer (% yield)[a,b] |
|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_4OCH_3$ (4) | **11a** (63) | **12a** (19) |
| 2 | $C_6H_4OCH_3$ (4) | $C_6H_4OCH_3$ (4) | **11b** (62) | **12b** (19) |
| 3 | $C_6H_4Cl$ (4) | $C_6H_4CH_3$ (4) | **11c** (47) | **12c** (16) |
| 4 | $C_6H_5$ | $C_6H_5$ | **11d** (51) | **12d** (20) |
| 5 | $C_6H_5$ | $C_6H_4Cl$ (4) | **11e** (34) | **12e** (14) |

[a]All new compounds gave satisfactory CHN analysis
[b]Yields quoted are for the isolated products characterized by IR, $^1$H NMR, $^{13}$C NMR




**Scheme 5.** Plausible mechanism for the formation of spiro-β-lactams **9** and **10**.

**(8a)** formed by addition of $Br_2$ across the double bond. Its structure was assigned on the basis of spectroscopic data. A shift in the position of allylic protons from their original value was indicative of the formation of additional product.

The second product was identified as spiro compound 2-(4′-methoxyphenyl)-3-phenyl-7α-bromo-5-thia-2-azaspiro[3,4]octan-1-one **(9a)** containing five-membered ring, formed by halocyclization. The third compound was identified as the second diastereomer of the above product **(9a)** i.e. 2-(4′-methoxyphenyl)-3-phenyl-7β-bromo-5-thia-2-azaspiro [3,4]octan-1-one **(10a)**. This reaction was tried with many substrates and was found to be general (scheme 3 and table 2).

The structures of these products were established by spectroscopic studies such as IR, $^1$H NMR, $^{13}$C NMR, DEPT-135, $^1$H–$^1$H COSY, $^1$H–$^{13}$C COSY and MS. These results were further substantiated by double irradiation studies of spiro-β-lactam **10e**. The stereochemistry was established through single crystal X-ray analysis of major isomer **10e** (figure 2).[14]

It is clear that substrate **6** cyclize to give exclusively the five-membered ring *via* a 5-*endo* ring closure process, instead of 4-*exo* ring closure. The regiospecificity of these ring closure reactions may be due to kinetic preference for forming the less strained five membered ring compared to four-membered ring.

In continuation to these studies, this reaction was also studied using $I_2$ as halogenating agent. Thus, treatment of **6a** with $I_2$ (1 equiv.) under similar conditions though did not show any significant change in TLC profile, but the residue after work up and purification did show the formation of spiro product 2-(4′-methoxyphenyl)-3-phenyl-7-iodo-5-thia-2-azaspiro[3,4]octan-1-one. The product was found to be a mixture of diastereomers **11a** and **12a** formed in the ratio 3:1 as evident from $^1$H NMR of the crude product (scheme 4). In one compound, the major α-iodo isomer got separated in pure form from ethyl acetate-hexanes. The other isomeric cyclized product, i.e. β-iodo isomer did not crystallize in pure form. The reaction was carried out with number of substrates as given in table 3.

The structures of these products were established by IR, $^1$H NMR, $^{13}$C NMR, DEPT-135, $^1$H–$^1$H COSY, $^1$H–$^{13}$C COSY and MS. The stereochemistry at C-4 junction was also assigned on the basis of correlation of $^1$H NMR and $^{13}$C NMR data of these products with those of bromo derivatives.

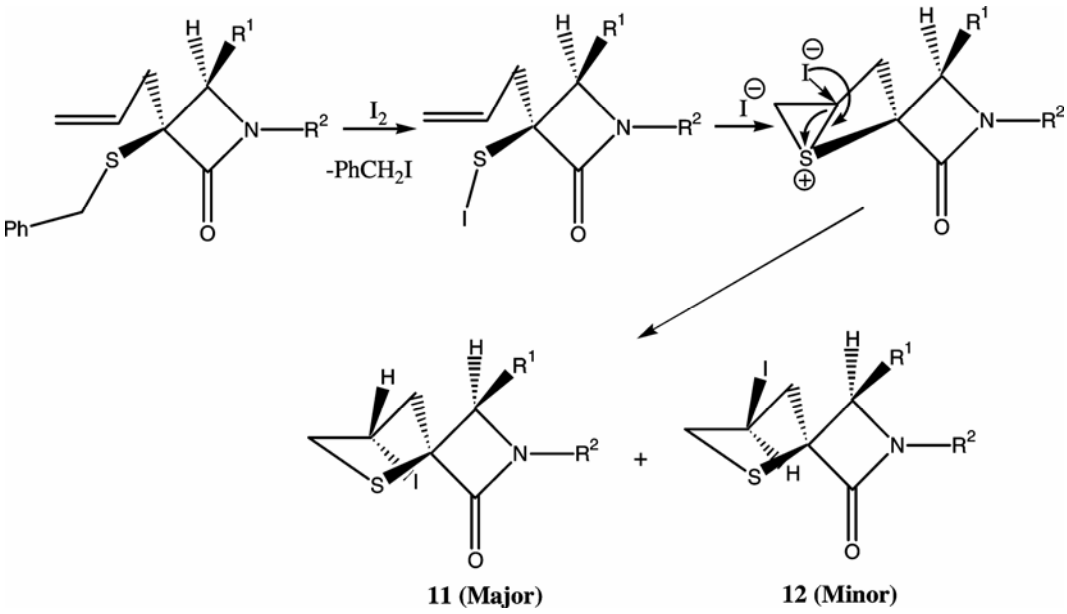
Thus, halocyclisation reaction of β-lactams of type **6** leads to the formation of both α- and β-epimers at C-7 of spiro system. The reaction employing bromine favours the formation of β-epimer, where as reaction using iodine strongly favours the formation of α-epimer as indicated by $^1$H-NMR analysis.

The favoured formation of β-bromo-spiro-β-lactam during this reaction indicates that bromocyclization occurs by the pathway in which $Br_2$ adds across the

**Table 4.** 5-Thia-2-azaspiro[3,4]octan-1-one **13a,d**.

| Entry | $R^1$ | $R^2$ | Reagent | Product (% yield)[a,b] |
|---|---|---|---|---|
| 1 | $C_6H_5$ | $C_6H_4OCH_3$ (4) | *n*-$Bu_3SnH$ | **13a** (75) |
| 2 | $C_6H_5$ | $C_6H_5$ | *n*-$Bu_3SnH$ | **13d** (70) |
| 3 | $C_6H_5$ | $C_6H_4OCH_3$ (4) | $NaBH_4$–DMSO | **13a** (40) |

[a]All new compounds gave satisfactory CHN analysis
[b]Yields quoted are for the isolated products characterized by IR, $^1$H NMR, $^{13}$C NMR




**Scheme 6.** Plausible mechanism for the formation of spiro-$\beta$-lactams **11** and **12**.

double bond. The complete mechanism involves co-ordination by halogen to form $\pi$-complex followed by nucleophilic attack of the sulphide centre as shown in scheme 5.

The bromide retains more stable pseudoequatorial position during the nucleophilic attack of sulphur on the carbon of olefin–halogen complex.

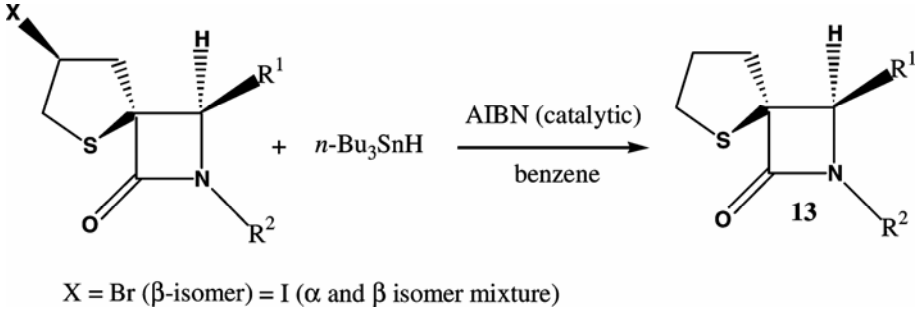
However, in case of iodocyclization the sulphur atom is transformed to an electrophilic species first, which then interacts with olefin followed by nucleophilic attack of halide anion to form the five-membered spiro ring. The iodide being bigger in size perhaps avoids the steric repulsion from phenyl group on C-4 while approaching the cyclopropane ring carbon to open it and hence attacks from $\alpha$-side (scheme 6).

Further, the halospiro-$\beta$-lactams were also subjected to dehalogenation studies. Treatment of these halospiro-$\beta$-lactams with *n*-$Bu_3SnH$ (1·2 equiv.) in the presence of catalytic amount of AIBN in refluxing benzene clearly afforded the dehalogenated product **13** in good yield (scheme 7 and table 4).

Increasing the amount of *n*-$Bu_3SnH$ afforded debromination along with desulphurization, via ring opening producing *cis*-3-propyl-$\beta$-lactam. The use of $NaBH_4$ and DMSO for dehalogenation was found to be unsatisfactory because of low yield.

## 4. Conclusion

In conclusion, a simple and efficient methodology for the synthesis of spiro $\beta$-lactams employing halocyclization of *cis*-3-allyl-3-benzylthio-$\beta$-lactams has been developed. The ring closure using $Br_2$ results in the formation of spiro-$\beta$-lactams along with a minor addition product. However, this reaction favours the formation of $\beta$-bromo epimer. In contrast, the ring closure using $I_2$ leads to the exclusive formation




**Scheme 7.** Dehalogenation reaction of spiro-*β*-lactams.

of spiro-*β*-lactams as well as favours the formation of *α*-epimer.

## Supporting Information

Crystallographic data of compound **10e** can be seen in website (www.ccdc.comac.uk/data_request).

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14. Crystal data for **10e**: triclinic, *P1*, lattice parameters: $a$ – 6·454(1), $b$ – 10·991(1), $c$ – 12·881(1) Å, $\alpha$ – 85·37(1), $\beta$ – 75·95(1), $\gamma$ – 81·90(1)°, $V$ – 876·52(10) Å$^3$, $Z$ – 2, $D_c$ = 1·549 mg/m$^3$, $\mu$(MoK$\alpha$) – 2·619 mm$^{-1}$, full matrix least square on $F^2$, $R_1$ = 0·0315, $wR_2$ = 0·0741 for 2391 reflections [$I > 2\sigma(I)$]. Crystallographic data (excluding structure factors) for the structure **10e** in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-642729