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ARTICLE

Regioselective and diastereoselective iodocyclization reaction of alkene-thioureas: an efficient approach to bicyclic β-lactams

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Bicyclic β-lactams i.e. 3-thia-1-dethiacephams were synthesized via highly regioselective and diastereoselective iodocyclization reaction of alkene-thioureas with molecular iodine. Further, the structure of 3-thia-1-dethiacepham was confirmed by chemical method, most notable by dehydrohalogenation reaction using DBU.

Introduction

β-Lactam antibiotics,[1] one of the most important contributions of science to human health, account for 50% of the world's total antibiotic market.[2] The increasing bacterial resistance inflicted to explore new β-lactams by skeletal modification of naturally occurring β-lactam antibiotics. In this regard, it is surprising to note that, few reports are available for the synthesis of 3-thia-1-dethiacephams.[3] In continuation to our ongoing project on synthesis of bicyclic β-lactams,[4] we recently decided to explore new synthetic strategy for the preparation of 3-thia-1-dethiacephams. However, during the last few years an explosive increase of interest in iodocyclization has taken place, thus becoming an extremely active and original field of carbocycles and heterocycles synthesis.[5] Whereas, few reports are available in literature for the synthesis of bicyclic β-lactam ring systems via iodocyclization reaction that have the lactam unit in different bonding arrangements compared to the classical compounds.[6] Selenium-containing bicyclic beta-lactams were synthesized via regioselective iodocyclization alkyne- and allene-selenoureas.[7] Further, Bari et al. have shown the utility of iodocyclization reaction for the synthesis of spirocyclic β-lactams.[8] Recently, we have reported the synthesis of bicyclic β-lactams *via* regioselective iodocyclization approach.[9] To the best of our knowledge, no report on iodocyclization reaction of alkene-thioureas i.e. *N*`-substituted-*N*-homoallyl-*N*-acyl-thioureas for the construction of bicyclic β-lactams.[10] In recent years, development of an asymmetric version of halogenation reaction is in continuous demand.[11] In this paper for the first time, we describe the regioselective and diastereoselective iodocyclization reaction of alkene-thioureas i.e. *N*`-substituted-*N*-homoallyl-*N*-acyl-thioureas for the synthesis of 3-thia-1-dethiacephams.

Results and discussion

Our journey in this direction started with 4-allyl-azetidinone **1**. The 4-allyl-azetidinone **1** was prepared by the selective introduction of allyl groups at the C4-position of commercially available (3R,4R)-(+)-4-acetoxy-3-[(R)-(tert-butyldimethylsilyloxy)ethyl]-azetidinone with organo-indium reagent generated from indium and allyl bromide.[12] As shown in table 1, the *N*-alkylation reaction of 4-allyl-azetidinone **1**, with substituted isothiocyanates **2**[13] under basic conditions readily resulted in the formation of alkene-thioureas **3a-3m** in good to excellent yield (entries 1-13). The structure of the alkene–thiourea **3** was confirmed by the studies of spectral analyses.

As shown in Table 2, our initial optimization studies for the iodocyclization reaction were carried out with alkene-thiourea (**3a**). First, we examined the iodocyclization reaction of alkene-thiourea (**3a**) with 1 equiv of I_2 in CH_2Cl_2 at room temperature and to our delight; the desired bicyclic β-lactam i.e. 3-thia-dethiacepham **4a** was formed in 45% yield (entry 1). Different reaction conditions were then screened to improve the yield of iodocyclization reaction (entries 2-10). The iodocyclization reaction was heavily influenced by the amount of iodine used in the reaction and the use of 1.50 equiv. of iodine in the cyclization reaction found to be best (entry 3, 76% yield).

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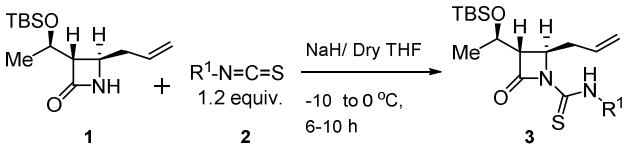
Further, when the reaction was carried out using non-polar solvents such as $CHCl_3$, THF, CH_3CN and toluene the 3-thia-dethiacepham **4a** was formed in moderate to good yield (entries 4-7). Whereas, the use of polar solvents such as DMF, DMSO and MeOH afforded 3-thia-dethiacepham **4a** in low yields (entries 8-10). Finally, we discovered that the best result can be obtained by carrying out the reaction with 1.5 equiv of I_2 in CH_2Cl_2 at room temperature (entry 3). In all reaction condition seven-membered ring product was never detected (Table 2).

Table-1: Synthesis of alkene-thioureas **3**.[a]



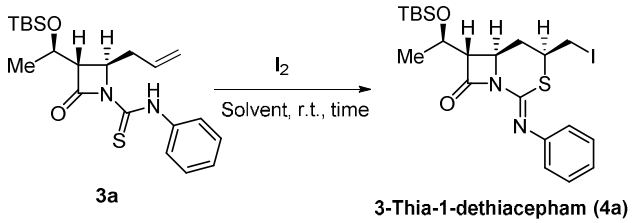
Entry	R^1	% Yield (**3**)[b]
1	C_6H_5	95 (**3a**)
2	*o*-$CH_3C_6H_4$	86 (**3b**)
3	*m*-$CH_3C_6H_4$	79 (**3c**)
4	*p*-$CH_3C_6H_4$	91 (**3d**)
5	*o*-ClC_6H_4	80 (**3e**)
6	*m*-ClC_6H_4	86 (**3f**)
7	*p*-ClC_6H_4	84 (**3g**)
8	$CH_2C_6H_5$	81 (**3h**)
9	*p*-FC_6H_5	81(**3i**)
10	*P*-$OMeC_6H_5$	85 (**3j**)
11	*P*-$NO_2C_6H_5$	78 (**3k**)
12	*P*-CNC_6H_5	75 (**3l**)
13	*P*-$CF_3C_6H_5$	74 (**3m**)

[a] All reactions were carried out using 1.0 equiv of **1**, 1.5 equiv of NaH and 1.2 equiv of isothiocyanate (**2**) in Dry THF at -10 to 0 °C unless otherwise noted.

[b] Isolated yields.

After having established the optimized conditions for the present reaction, various alkene-thiourea derivatives were subjected to the above conditions and the results are shown in Table 3. The aryl-substitution at alkene-thiourea **3a-m** was also well accommodated and afforded the iodocyclized products **4a-m** in excellent yields (entries 1-8). Electron donating as well as electron withdrawing functional groups at the aromatic ring such as methyl, methoxy, chloro, fluoro, nitro and cyano were well tolerated under the reaction condition (entries 1-13). When alkyl-substituted thiourea **3h** was used in the reaction, the required product **4h** was formed in traces as confirmed by ^{1}H NMR (table 3, entry 8). The structure of the 3-thia-1-dethicepham **4c** was confirmed by the studies of IR, ^{1}H-NMR, ^{13}C-NMR, COSY, HMQC and HRMS spectral analyses. As shown in Figure 1, the absolute configuration of 3-thia-dethiacephams **4c** was determined by the study of NOESY GPPH spectral analysis (for detail see supporting information). The H_6 proton showed the NOE with H_{5b}, H_4 and H_{7b} protons. Thus, confirming the stereochemistry of H_6-proton which is back-side of the plane. Moreover, H_{5a}-proton showed the NOE with H_{5b}, H_3 and H_{7a} protons (figure 1). Finally, the structures of other bicyclic β-lactams were confirmed by comparing with 3-thia-dethiacephams **4c**.

Table 2. Optimal conditions for the iodocyclization reaction of **4a**.[a]

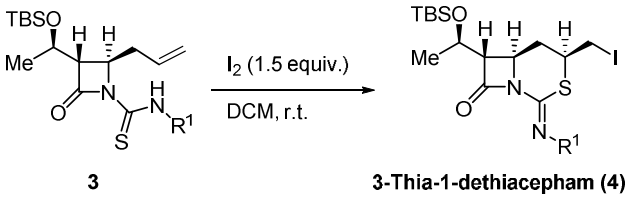


Entry	Solvent	Iodine (equiv.)	Time (h)	Yield (%)[b]
1	CH_2Cl_2	1.00	36.0	45
2	CH_2Cl_2	1.25	28.0	59
3	**CH_2Cl_2**	**1.50**	**8.0**	**76**
4	$CHCl_3$	1.5	8.0	44
5	THF	1.5	9.5	46
6	CH_3CN	1.5	9.0	62
7	Toluene	1.5	14.0	66
8	DMF	1.5	26.0	15
9	DMSO	1.5	6.5	21
10	CH_3OH	1.5	24.0	9

[a] All iodocyclization reactions were carried out at r.t. on 0.115 mmol of **3a**.

[b] Isolated yields.

Table 3. Synthesis of 3-Thia-1-dethiacephem **4** *via* Iodocyclization.[a]



3 **3-Thia-1-dethiacepham (4)**

Entry	R^1	Time (hr)	Product	Yield (%)[b]
1	C_6H_5	8	**4a**	76
2	*o*-$CH_3C_6H_4$	9	**4b**	71
3	*m*-$CH_3C_6H_4$	9	**4c**	68
4	*p*-$CH_3C_6H_4$	12	**4d**	75
5	*o*-ClC_6H_4	12	**4e**	74
6	*m*-ClC_6H_4	11	**4f**	81
7	*p*-ClC_6H_4	9	**4g**	79
8	$CH_2C_6H_5$	12	**4h**	traces
9	*p*-FC_6H_5	9	**4i**	81
10	*P*-$OMeC_6H_5$	12	**4j**	85
11	*P*-$NO_2C_6H_5$	11	**4k**	78
12	*P*-CNC_6H_5	9	**4l**	75
13	*P*-$CF_3C_6H_5$	8	**4m**	74

[a] All iodocyclization reactions were conducted at r.t. with 1.50 equiv. of I_2 in CH_2Cl_2 under nitrogen atmosphere.

[b] Isolated yields.

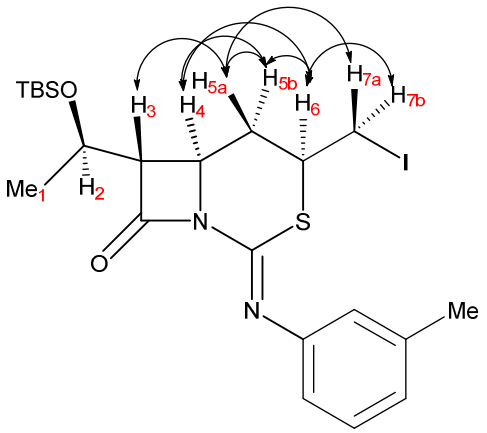
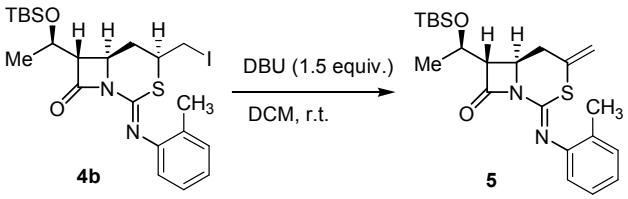


Figure 1. NOESY GPPH correlations observed in NMR of Compound **4c**.

Further, the structure of 3-thia-1-dethiacepham **4** was confirmed by chemical method, most notable by dehydrohalogenation reaction using DBU. As shown in scheme 1, when compound **4b** was treated with 1.5 equiv of DBU in DCM at room temperature, the corresponding 3-thia-1-dethaicepham **5** was isolated in 79% yield (Scheme 1). The structure of the 3-thia-1-dethaicepham **5** was confirmed by the studies of IR, ^{1}H-NMR, ^{13}C-NMR, DEPT and HRMS spectral analyses.



Scheme 1. Dehydrohalogenation reaction of **4b** using DBU.

Plausible mechanism

A plausible mechanism for the above iodocyclization reactions is depicted in Figure 2. The reaction is initiated by the coordination of **3** with I^+, thereby enhancing the electrophilicity of the alkene moiety to generate iodonium intermediate **A** and released an iodine anion at the same time. The iodonium intermediate can be formed in two different ways **B** and **C**. With the assistance of iodine anion, intramolecular nucleophilic attack of sulphur in the thiourea group on the internal carbon of iodonium intermediate **B** in the favored 6-exo mode affords the corresponding cyclization product 3-thia-1-dethiacepham **4**. The -OTBS group of alkene-thioureas **3** is curled in such a way that making steric hindrance with iodonium intermediate **C** from below side thus attack of sulphur in thiourea group on the internal carbon of iodonium intermediate **C** in the favored 6-exo mode was not observed. The iodocyclization reaction is highly regioselective and diastereoselective.

Conclusion

In conclusion, we have described the highly regioselective and diastereoselective iodocyclization reaction alkene-thioureas i.e. *N*'-substituted-*N*-homoallyl-*N*-acyl-thioureas for the construction of bicyclic β-lactams such as 3-thia-1-dethaicephams **4**. Further, the structure of 3-thia-1-dethiacepham **4** was confirmed by chemical method by a dehydrohalogenation reaction using DBU. Expansion of current strategies is underway in our laboratory.

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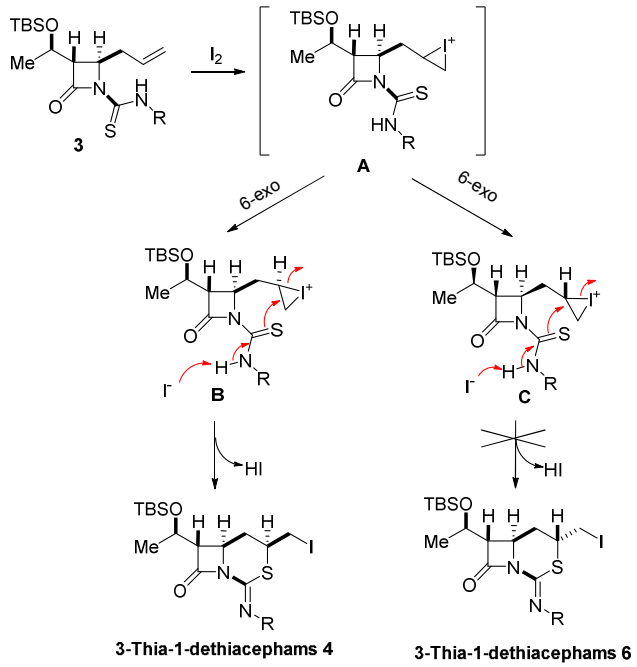

Figure 2. Mechanism for the iodocyclization reaction of alkene-thiourea.

Experimental

General Information:

Commercially available chemicals were used without prior purification. The reactions were monitored by thin-layer chromatography (TLC) on silica plated aluminium sheets (Silica gel 60 F_{254}, E. Merck). Column chromatography was performed on silica gel 60-120 mesh. Melting point was recorded on Buchi instrument. IR spectra were measured on SHIMADZU FT-IR8400 or JASCO FT/IR-410 Fourier Transform Infrared Spectrometer. ^{1}H and ^{13}C NMR spectroscopy measurements were carried out on JEOL:JNM ECX-400 P or Bruker Advance II-400 spectrometers in $CDCl_3$, and TMS was used as an internal standard. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm downfield from chloroform-d (δ = 7.27) or TMS and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and brs = broad. The multiplicity of ^{13}C NMR signals was assigned with the help of DEPT spectra. HRMS mass spectra were on a JEOL JMS-700 or Thermo Scientific Q-Exactive, Accela 1250 pump.

General procedure for the synthesis of Alkene-thioureas (3)

To a suspension of NaH (1.113 mmol, 60% in mineral oil) in 5 mL of THF at -10 °C was added (3*S*,4*R*)-3-[(*R*)-*tert*-butyldimethylsilyloxyethyl]-4-(2-allyl)-2-azetidinone, **1** (0.742 mmol, 200 mg) in 4 mL THF over 5 minutes under nitrogen. The mixture was stirred at -10 °C for an additional 15 minutes and isothiocyanate (0.891 mmol) was added dropwise. The reaction mixture was stirred at -10 to 0 °C for 6-10 hours under nitrogen and the excess of NaH was quenched with 2N HCl. The organic layer was washed with water. The aqueous layer was extracted 3 times with 15 mL of ethyl acetate each. The combined organic layers were dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (SiO_2: hexane / ethyl acetate = 30/1) to give the corresponding alkene-thioureas **3a-h**.

The isolated yield and the spectral data for **4a-m** are as follows:

Alkene-thiourea (3a)

Yield: 95%; semi-solid; IR: 664, 771, 839, 1001, 1089, 1105, 1134, 1201, 1280, 1305, 1390, 1480, 1597, 1755, 2851, 2941, 3023, 3280 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.57 (s, 3H), 2.64-2.74 (m, 1H), 2.97 (t, *J* = 3.1 Hz, 1H), 3.16 (m, 1H), 4.29-4.37 (m, 1H), 4.46-4.54 (m, 1H), 5.17-5.26 (m, 2H), 5.74-5.89 (m, 1H), 7.25 (d, *J* = 6.3 Hz, 1H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.57 (d, *J* = 7.5 Hz, 2H), 10.25 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.17, -3.97, 17.8, 22.6, 25.7, 35.7, 55.6, 60.8, 64.9, 119.5, 124.2, 126.6, 128.9, 132.2, 137.4, 167.7, 176.3; HRMS: *m/z* = 427.1846, calcd. for $C_{21}H_{32}N_2O_2NaSSi$, found 418.1846 [M+ Na]$^{+}$.

Alkene-thiourea (3b)

Yield: 86%; semi-solid; IR (Neat): 668, 762, 836, 933, 1008, 1056, 1138, 1219, 1318, 1381, 1460, 1520, 1597, 1752, 2358, 2404, 2862, 2943, 3021, 3297 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.10 (s, 3H), 0.12 (s, 3H), 0.90 (s, 9H), 1.24 (d, *J* = 6.5 Hz, 3H), 2.32 (s, 3H), 2.70-2.80 (m, 1H), 3.01 (t, *J* = 2.8 Hz, 1H), 3.10-3.21 (m, 1H), 4.30-4.40 (m, 1H), 4.51-4.55 (m, 1H), 5.20-5.27 (m, 2H), 5.79-5.88 (m, 1H), 7.23-7.28 (m, 3H), 7.66 (d, *J* = 7.5 Hz, 1H), 10.03 (brs, 1H); ^{13}C NMR: -5.2, -4.15, 17.8, 17.9, 22.6, 25.6, 35.5, 55.3, 60.7, 64.7, 119.5, 126.4, 127.4, 130.7, 132.1, 133.4, 135.8, 167.4, 176.9; HRMS: *m/z* = 419.2183, calcd. For $C_{22}H_{35}O_2N_2SSi$, found 419.2185 [M+H]$^{+}$.

Alkene-thiourea (3c)

Yield: 79%; semi-solid; IR (Neat): 659, 711, 806, 991, 1001, 1086, 1118, 1201, 1389, 1421, 1459, 1492, 1561, 1683, 2273, 2391, 2782, 2898, 3061, 3305 cm^{-1}; 1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 1.21 (t, *J* = 6.4 Hz, 3H), 2.37 (s, 1H), 2.64-2.72 (m, 1H), 2.96 (t, *J* = 2.8 Hz, 1H), 3.12-3.18 (m, 1H), 4.30-4.35 (m, 1H), 4.47-4.51 (m, 1H), 5.18-5.25 (m, 2H), 5.77–5.88 (m, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 7.8 Hz, 1H), 7.37 (s, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 10.22 (brs, 1H); ^{13}C NMR: -5.28, -4.10, 17.7, 21.4, 22.5, 25.6, 35.6, 55.5, 60.7, 64.8, 119.4, 121.2, 124.6, 127.3, 128.6, 132.1, 137.2, 138.8, 167.5, 176.1; HRMS: *m/z* = 419.2183, calcd. for $C_{22}H_{35}O_2N_2SSi$, found 419.2182 [M+H]$^{+}$.

Alkene-thiourea (3d)

Yield: 91%; semi-solid; IR (Neat): 667, 762, 829, 919, 1006, 1055, 1136, 1223, 1315, 1377, 1459, 1528, 1604, 1752, 2862, 2891,

2941, 3291 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.08 (s, 3H), 0.09 (s, 3H), 0.87 (s, 9H), 1.21 (d, *J* = 6.2 Hz, 3H), 2.36 (s, 3H), 2.65-2.69 (m, 1H), 2.97 (t, *J* = 2.7 Hz, 1H), 3.13-3.19 (m, 1H), 4.29-4.35 (m, 1H), 4.48-4.51 (m, 1H), 5.17-5.27 (m, 2H), 5.75-5.86 (m, 1H), 7.19 (d, *J* = 8.6 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 10.18 (brs, 1H); ^{13}C NMR: -5.3, -4.08, 17.7, 21.1, 22.5, 25.6, 35.7, 55.4, 60.7, 64.9, 119.4, 124.3, 129.4, 132.2, 134.7, 136.5, 167.5, 176.4; HRMS: *m/z* = 419.2183, calcd. for $C_{22}H_{35}O_2N_2SSi$, found 419.2184 $[M+H]^+$.

Alkene-thiourea (3e)

Yield: 80%; semi-solid; IR (Neat): 670, 763, 835, 936, 1003, 1053, 1136, 1221, 1259, 1367, 1460, 1542, 1597, 1757, 2861, 2891, 2942, 3075, 3257 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 1.22 (d, *J* = 5.9 Hz, 3H), 2.69-2.75 (m, 1H), 2.99 (t, *J* = 2.9 Hz, 1H), 3.11-3.18 (m, 1H), 4.31-4.34 (m, 1H), 4.50-4.53 (m, 1H), 5.19-5.26 (m, 2H), 5.75-5.86 (m, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.45 (dd, *J* = 8.1 & 1.5 Hz, 1H), 8.37 (d, *J* = 8.3 Hz, 1H), 10.48 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.21,-4.16, 17.7, 22.6, 25.6, 35.4, 55.5, 60.7, 64.7, 119.5, 125.8, 126.8, 127.0, 129.5, 132.0, 134.6, 167.2, 175.9; HRMS: *m/z* = 439.1637, calcd. For $C_{21}H_{32}O_2N_2ClSSi$, found 439.1640 $[M+H]^+$.

Alkene-thiourea (3f)

Yield: 86%; semi-solid; IR (Neat): 751, 830, 1055, 1083, 1190, 1350, 1354, 1570, 1660, 1692, 2860, 2898, 3034, 3260 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 3H), 0.07 (s, 3H), 0.84 (s, 9H), 1.21 (t, *J* = 6.2 Hz, 3H), 2.64-2.7 (m, 1H), 2.97 (t, *J* = 3.2 Hz, 1H), 3.0-3.11 (m, 1H), 4.29-4.30 (m, 1H), 4.47-4.50 (m, 1H), 5.17-5.24 (m, 2H), 5.71-5.84 (m, 1H), 7.24 (d, *J* = 8.1 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.29 (t, *J* = 8.1 Hz, 1H), 7.71 (d, *J* = 2.2 Hz, 1H), 10.27 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.17,-3.96, 17.8, 22.6, 25.6, 35.6, 55.7, 60.9, 64.9, 119.6, 122.1, 123.99, 126.5, 129.9, 132.1, 134.4, 138.6, 167.7, 176.1; HRMS: *m/z* = 439.1637, calcd. For $C_{21}H_{32}O_2N_2ClSSi$, found 439.1660 $[M+H]^+$.

Alkene-thiourea (3g)

Yield: 84%; semi-solid; IR (Neat): 762, 835, 1056, 1099, 1218, 1317, 1370, 1535, 1606, 1752, 2860, 2934, 3021, 3296 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.06 (s, 3H), 0.08 (s, 3H), 0.85 (s, 9H), 1.21 (d, *J* = 7.1 Hz, 3H), 2.62-2.70 (m, 1H), 2.98 (t, *J* = 2.9 Hz, 1H), 3.11-3.17 (m, 1H), 4.30-4.33 (m, 1H), 4.44-4.52 (m, 1H), 5.18-5.25 (m, 2H), 5.74-5.83 (m, 1H), 7.35 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.6 Hz, 2H), 10.24 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.33, -4.07, 17.7, 22.4, 25.5, 35.6, 55.5, 60.8, 64.7, 119.5, 125.3, 128.9, 131.99, 135.8, 167.7, 176.1; HRMS: *m/z* = 439.1637, calcd. For $C_{21}H_{32}O_2N_2ClSSi$, found 439.1640 $[M+H]^+$.

Alkene-thiourea (3h)

Yield: 81%; semi-solid; IR (Neat): 761, 835, 938, 997, 1060, 1103, 1142, 1221, 1250, 1349, 1404, 1454, 1533, 1753, 2862, 2891, 2941, 3021, 3322 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.02 (s, 3H), 0.07 (s, 3H), 0.84 (s, 9H), 1.20 (d, *J* = 6.2 Hz, 3H), 2.63-2.74 (m, 1H), 2.92 (t, *J* = 3.2 Hz, 1H), 3.08-3.17 (m, 1H), 4.24-4.29 (m, 1H), 4.43-4.46 (m, 1H), 4.78-4.82 (m, 1H), 4.84-4.88 (m, 1H), 5.17-5.26 (m, 2H), 5.74-5.85 (m, 1H), 7.26-7.38 (m, 5H), 8.81 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.27, -4.16, 17.7, 22.5, 25.5, 35.7, 48.2, 55.4, 60.7, 64.8, 119.3, 127.9, 128.7, 132.1, 136.5, 167.2, 178.0; HRMS: *m/z* = 419.2183, calcd. For $C_{22}H_{35}N_2O_2SSi$, found 419.2184 $[M+H]^+$.

Alkene-thiourea (3i)

Yield: 81%; semi-solid; IR (Neat): 667, 763, 836, 919, 936, 1006, 1056, 1106, 1141, 1222, 1317, 1375, 1460, 1519, 1616, 1754, 2862, 2892, 2942, 3278 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.86 (s, 9H), 1.20 (d, *J* = 6.3 Hz, 3H), 2.65-2.70 (m, 1H), 2.98 (t, *J* = 2.9 Hz, 1H), 3.13-3.17 (m, 1H), 4.30-4.35 (m, 1H), 4.49-4.51 (m, 1H), 5.18-5.25 (m, 2H), 5.75-5.85 (m, 1H), 7.08 (t, *J* = 8.8 Hz, 2H), 7.50 (dd, *J* = 8.8 & 4.1 Hz, 2H), 10.17 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ -5.31, -4.06, 17.7, 22.5, 25.5, 35.6, 55.5, 60.8, 64.8, 115.7 (d, $^2J_{C\text{-}F}$ = 22.4 Hz), 119.5, 126.34 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 132.1, 133.20 (d, $^4J_{C\text{-}F}$ = 2.3 Hz), 160.78 ($^1J_{C\text{-}F}$ = 247 Hz), 167.7, 176.7; HRMS: *m/z* = 423.1932, calcd. For $C_{21}H_{32}O_2N_2FSSi$, found 423.1935 $[M+H]^+$.

Alkene-thiourea (3j)

Yield: 85%; semi-solid; IR (Neat): 667, 763, 834, 917, 1047, 1136, 1180, 1247, 1314, 1380, 1431, 1458, 1522, 1608, 1752, 2857, 2894, 2943, 3077, 3290 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.08 (s, 3H), 0.09 (s, 3H), 0.87 (s, 9H), 1.20 (d, *J* = 6.2 Hz, 3H), 2.65-2.70 (m, 1H), 2.98 (t, *J* = 2.6 Hz, 1H), 3.12-3.19 (m, 1H), 3.81 (s, 3H), 4.30-4.35 (m, 1H), 4.48-4.50 (m, 1H), 5.17-5.25 (m, 2H), 5.75-5.85 (m, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.42 (d, *J* = 8.8 Hz, 2H), 10.10 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.34, -4.10, 17.7, 22.4, 25.5, 35.6, 55.4, 60.7, 64.7, 113.98, 119.3, 126.1, 130.1, 132.2, 158.0, 167.5, 176.7; HRMS: *m/z* = 435.2132, calcd. For $C_{22}H_{35}O_3N_2SSi$, found 435.2136 $[M+H]^+$.

Alkene-thiourea (3k)

Yield: 78%; semi-solid; IR (Neat): 763, 842, 919, 937, 1004, 1056, 1111, 1186, 1233, 1302, 1423, 1460, 1515, 1583, 1756, 2861, 2891, 2942, 3084, 3270 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.05 (s, 3H), 0.08 (s, 3H), 0.81 (s, 9H), 1.20 (d, *J* = 6.1 Hz, 3H), 2.64-2.70 (m, 1H), 3.02 (t, *J* = 3.0 Hz, 1H), 3.06-3.12 (m, 1H), 4.31-4.35 (m, 1H), 4.47-4.52 (m, 1H), 5.19-5.25 (m, 2H), 5.74-5.82 (m, 1H), 7.93 (d, *J* = 9.1 Hz, 2H), 8.24 (d, *J* = 9.1 Hz, 2H), 10.62 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.40, -4.10, 17.6, 22.4, 25.4, 35.3, 55.6, 60.8, 64.7, 119.7, 122.4, 124.5, 131.7, 143.2, 144.6, 167.8, 175.3; HRMS: *m/z* = 450.1877, calcd. For $C_{21}H_{32}O_4N_3SSi$, found 450.1879 $[M+H]^+$.

Alkene-thiourea (3l)

Yield: 75%; mp 83-85 °C; IR (KBr): 763, 836, 914, 1006, 1056, 1134, 1182, 1228, 1308, 1361, 1425, 1458, 1539, 1603, 1754, 2229, 2862, 2892, 2942, 3268 cm^{-1}; ^1H NMR ($CDCl_3$): δ 0.04 (s,

3H), 0.07 (s, 3H), 0.81 (s, 9H), 1.20 (d, *J* = 6.3 Hz, 3H), 2.61-2.69 (m, 1H), 3.00 (t, *J* = 2.9 Hz, 1H), 3.05-3.10 (m, 1H), 4.30-4.33 (m, 1H), 4.49-4.51 (m, 1H), 5.17-5.24 (m, 2H), 5.72-5.82 (m, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.85 (d, *J* = 8.6 Hz, 2H), 10.50 (brs, 1H); ^{13}C NMR ($CDCl_3$): -5.43, -4.14, 17.6, 22.3, 25.4, 35.3, 55.5, 60.7, 64.6, 108.9, 118.4, 119.6, 122.9, 131.7, 132.8, 141.4, 167.7, 175.3; HRMS: *m/z* = 430.1979, calcd. For $C_{22}H_{32}O_2N_3SSi$, found 430.1984 $[M+H]^+$.

Alkene-thiourea (3m)

Yield: 74%; semi-solid; IR (Neat): 733, 774, 836, 918, 1006, 1056, 1106, 1141, 1222, 1315, 1374, 1460, 1519, 1617, 1755, 2862, 2891, 2942, 3080, 3277 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.07 (s, 3H), 0.09 (s, 3H), 0.84 (s, 9H), 1.22 (d, *J* = 6.4 Hz, 3H), 2.64-2.72 (m, 1H), 3.00 (t, *J* = 2.7 Hz, 1H), 3.11–3.16 (m, 1H), 4.30–3.36 (m, 1H), 4.51–4.53 (m, 1H), 5.19-5.26 (m, 2H), 5.75-5.85 (m, 1H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.80 (d, *J* = 8.5 Hz, 2H), 10.44 (brs, 1H); ^{13}C NMR ($CDCl_3$): δ -5.34, -4.07, 17.7, 22.4, 25.5, 35.5, 53.6, 55.6, 60.8, 64.7, 119.6, 123.3, 123.85 (q, $^1J_{CF3}$ = 272 Hz), 125.0 (d, $^3J_{C-F}$ = 3.9 Hz), 127.9 (q, $^2J_{C-F}$ = 33.2 Hz), 131.9, 140.5, 167.7, 175.8; HRMS: m/z = 495.1720, calcd. for $C_{22}H_{31}F_3N_2O_2NaSSi$, found 495.1720 $[M+Na]^+$.

Synthesis of 3-Thia-1-Dethiacephams *via* Iodocyclization

4 (a-m):

To a solution of **3** (0.115 mmol, 1 equiv.) in CH_2Cl_2 (2 mL) was added I_2 (1.5 equiv.) at room temperature. After stirring at this temperature (8 to 12 h), the reaction mixture was extracted with CH_2Cl_2 and washed with saturated $Na_2S_2O_3$ and $NaHCO_3$. The organic phase was washed with brine, dried over Na_2SO_4, filtered and evaporated in vacuo. The residue was chromatographed on silica gel using ether/hexane (1.5:8.5) as eluent to give corresponding product 3-Thia-1-dethiacepham **4**.

The isolated yield and the spectral data for **4a-m** are as follows:

3-Thia-1-Dethiacepham (4a)

Yield: 76%; semi-solid; IR (Neat): 661, 783, 824, 905, 949, 1004, 1089, 1142, 1209, 1359, 1392, 1455, 1517, 1601, 1689, 2740, 2792, 2843, 2987 cm^{-1}; ^{1}H NMR: δ 0.09 (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.49-1.55 (m, 1H), 2.79-2.83 (m, 1H), 3.08-3.12 (m, 2H), 3.26-3.29 (m, 1H), 3.53-3.57 (m, 1H), 3.91-3.94 (m, 1H), 4.28-4.32 (m, 1H), 6.87 (d, *J* = 7.2 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 1H), 7.27 (m, 2H); ^{13}C NMR ($CDCl_3$): δ -5.03, -4.21, 7.4, 17.9, 22.6, 25.7, 35.5, 44.9, 52.9, 65.2, 65.9, 121.1, 124.3, 128.8, 141.3, 147.2, 163.5; HRMS: *m/z* = 553.0812, calcd. For $C_{21}H_{31}O_2N_2INaSSi$, found 553.0827 $[M+Na]^+$.

3-Thia-1-Dethiacepham (4b)

Yield: 71%; semi-solid; IR (Neat): 668, 761, 835, 1137, 1216, 1335, 1620, 1783, 2402, 2860, 2942, 3019 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.12 (s, 3H), 0.14 (s, 3H), 0.92 (s, 9H), 1.29 (d, *J* = 6.8 Hz, 3H), 1.51-1.57 (m, 1H), 2.15 (s, 3H), 2.82-2.87 (m, 1H), 3.09-3.15 (m, 2H), 3.29-3.31 (m, 1H), 3.57-3.59 (m, 1H), 3.97-4.00 (m, 1H), 4.34-4.37 (m, 1H), 6.77 (d, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.3 Hz, 1H), 7.12-7.15 (m, 2H); ^{13}C NMR ($CDCl_3$): δ -5.12, -4.17, 7.8, 17.8, 22.6, 25.7, 35.5, 44.8, 52.4, 64.95, 65.9, 120.2, 124.3, 126.1, 128.9, 130.3, 140.7, 145.9, 163.6; HRMS: *m/z* = 545.1149, calcd. For $C_{22}H_{34}O_2N_2ISSi$, found 545.1155 $[M+H]^+$.

3-Thia-1-Dethiacepham (4c)

Yield: 68%; semi-solid; IR (Neat): 669, 764, 824, 876, 889, 1009, 1081, 1147, 1280, 1374, 1482, 1647, 1688, 2289, 2754, 2845, 2901, 2991 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.12 (s, 3H), 0.13 (s, 3H), 0.92 (s, 9H), 1.29 (d, *J* = 6.5 Hz, 3H), 1.51-1.57 (m, 1H), 2.32 (s, 3H), 2.82-2.86 (m, 1H), 3.11-3.16 (m, 2H), 3.30-3.33 (m, 1H), 3.56-3.62 (m, 1H), 3.92-3.96 (m, 1H), 4.28- 4.33 (m, 1H), 6.68-6.78 (m, 2H), 6.91 (d, *J* = 7.4 Hz, 1H), 7.18 (t, *J* = 7.6 Hz, 1H); ^{13}C-NMR: δ -5.01, -4.21, 7.4, 17.9, 21.4, 22.6, 25.7, 35.6, 44.9, 52.9, 65.2, 65.9, 117.95, 121.7, 125.0, 128.5, 138.5, 140.9, 147.1, 163.4; HRMS: *m/z* = 545.1149, calcd. For $C_{22}H_{34}O_2N_2ISSi$, found 545.1161 $[M+H]^+$.

3-Thia-1-Dethiacepham (4d)

Yield: 75%; semi-solid; IR (Neat): 666, 760, 830, 1139, 1212, 1249, 1333, 1461, 1508, 1611, 1781, 2860, 2941, 3012 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.11 (s, 3H), 0.12 (s, 3H), 0.91 (s, 9H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.51-1.58 (m, 1H), 2.32 (s, 3H), 2.83 (d, *J* = 12.6 Hz, 1H), 3.10-3.15 (m, 2H), 3.29-3.32 (m, 1H), 3.58-3.62 (m, 1H), 3.94 (d, *J* = 11.9 Hz, 1H), 4.28-4.34 (m, 1H), 6.80 (d, *J* = 7.7 Hz, 2H), 7.10 (d, *J* = 7.7 Hz, 2H); ^{13}C NMR: δ -5.03, -4.2, 7.5, 17.9, 20.9, 22.6, 25.7, 35.5, 44.8, 52.9, 65.2, 65.8, 120.9, 129.3, 133.7, 140.97, 144.6, 163.4; HRMS: *m/z* = 545.1149, calcd. For $C_{22}H_{34}O_2N_2ISSi$, found 545.1156 $[M+H]^+$.

3-Thia-1-Dethiacepham (4e)

Yield: 74%; semi-solid; IR (Neat): 669, 762, 833, 887, 949, 1064, 1138, 1212, 1255, 1359, 1432, 1466, 1521, 1616, 1786, 2860, 2892, 2942, 3012 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.12 (s, 3H), 0.13 (s, 3H), 0.92 (s, 9H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.53-1.59 (m, 1H), 2.85-2.88 (m, 1H), 3.13-3.18 (m, 2H), 3.29-3.32 (m, 1H), 3.63-3.65 (m, 1H), 3.99-4.02 (m, 1H), 4.34-4.37 (m, 1H), 6.90 (dd, *J* = 7.8 & 1.5 Hz, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 7.10 (t, *J* = 7.8 Hz, 1H), 7.36 (dd, *J* = 7.8 & 1.5 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ -5.08, -4.18, 7.3, 17.9, 22.6, 25.7, 35.5, 45.0, 52.6, 65.0, 66.0, 122.4, 125.1, 127.1, 129.8, 143.2, 144.5, 163.5; HRMS: *m/z* = 565.0603, calcd. For $C_{21}H_{31}O_2N_2ClISSi$, found 565.0605 $[M+H]^+$.

3-Thia-1-Dethiacepham (4f)

Yield: 81%; semi-solid; IR: 669, 760, 834, 1035, 1138, 1212, 1252, 1359, 1466, 1614, 1786, 2859, 2942, 3012 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.09 (s, 3H), 0.10 (s, 3H), 0.89 (s, 9H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.45-1.57 (m, 1H), 2.80-2.84 (m, 1H), 3.08-3.18 (m, 2H),

3.27-3.31 (m, 1H), 3.58-3.62 (m, 1H), 3.91-3.96 (m, 1H), 4.27-4.32 (m, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.89 (s, 1H), 7.05 (d, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ -5.07, -4.24, 7.2, 17.9, 22.5, 25.7, 29.6, 35.4, 45.0, 52.7, 65.0, 65.9, 119.4, 121.3, 124.2, 129.8, 134.2, 142.3, 148.4, 163.5; HRMS: *m/z* = 565.0603, calcd. For $C_{21}H_{31}O_2N_2ClISSi$, found 565.0605 $[M+ H]^+$.

3-Thia-1-Dethiacepham (4g)

Yield: 79%; semi-solid; IR (Neat): 667, 760, 834, 1011, 1091, 1139, 1212, 1248, 1336, 1477, 1613, 1784, 2859, 2941, 3015 cm^{-1}; ^{1}H-NMR ($CDCl_3$): δ 0.11 (s, 3H), 0.12 (s, 3H), 0.91 (s, 9H), 1.29 (d, *J* = 6.2 Hz, 3H), 1.52-1.59 (m, 1H), 2.82-2.85 (m, 1H), 3.13-3.15 (m, 2H), 3.30-3.33 (m, 1H), 3.61-3.64 (m, 1H), 3.95-3.98 (m, 1H), 4.31-4.35 (m, 1H), 6.84 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ -5.04, -4.2, 7.2, 17.9, 22.6, 25.7, 35.5, 45.0, 52.8, 65.1, 65.9, 122.5, 128.9, 129.5, 141.99, 145.8, 163.5; HRMS: *m/z* = 565.0603, calcd. For $C_{21}H_{31}O_2N_2ClISSi$, found 565.0612 $[M+H]^+$.

3-Thia-1-dethiacepham (4i)

Yield: 81%; semi-solid; IR (Neat): 667, 761, 835, 897, 953, 1011, 1093, 1145, 1209, 1336, 1429, 1463, 1502, 1613, 1784, 2860, 2893, 2943, 3010 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.10 (s, 3H), 0.11 (s, 3H), 0.90 (s, 9H), 1.27 (d, *J* = 6.1 Hz, 3H), 1.48-1.58 (m, 1H), 2.80-2.83 (m, 1H), 3.12-3.17 (m, 2H), 3.29 (dd, *J* = 4.1 & 10.0 Hz, 1H), 3.55-3.65 (m, 1H), 3.93-3.96 (m, 1H), 4.28-4.34 (m,1H), 6.85 (dd, *J* = 4.9 & 8.5 Hz, 2H), 6.98 (t, *J* = 8.5 Hz, 2H). ^{13}C NMR ($CDCl_3$): δ -5.09, -4.26, 7.3, 17.8, 22.5, 25.6, 35.5, 44.4, 52.7, 65.1, 65.8, 115.45 (d, $^2J_{C\text{-}F}$ = 23 Hz), 122.40 (d, $^3J_{C\text{-}F}$ = 8.5 Hz), 141.96, 143.2 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 159.71($^1J_{C\text{-}F}$ = 272 Hz), 163.4 ; HRMS: m/z = 549.0899, calcd. for $C_{21}H_{31}FIN_2O_2SSi$, found 549.0899 $[M+H]^+$.

3-Thia-1-dethiacepham (4j)

Yield: 85%; mp 108-109˚C; IR (KBr): 667, 761, 833, 886, 953, 1040, 1101, 1145, 1245, 1333, 1460, 1505, 1613, 1669, 1782, 2058, 2407, 2856, 2943 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.11 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 1.29 (d, *J* = 6.1 Hz, 3H), 1.50-1.57 (m, 1H), 2.80-2.84 (m, 1H), 3.11-3.16 (m, 2H), 3.28-3.32 (m, 1H), 3.54-3.61 (m, 1H), 3.78 (s, 3H), 3.93 (d, *J* = 11.7 Hz, 1H), 4.27-4.33 (m, 1H), 6.84 (s, 4H); ^{13}C NMR: δ -5.05, -4.24, 7.5, 17.8, 22.6, 25.7, 35.5, 44.8, 52.9, 55.3, 65.2, 65.8, 113.9, 122.1, 140.3, 141.1, 156.4, 163.4; HRMS: *m/z* = 561.1099, calcd. For $C_{22}H_{34}O_3N_2ISSi$, found 561.1099 $[M+ H]^+$.

3-Thia-1-dethiacepham (4k)

Yield: 78%; mp 205 ˚C; IR (KBr): 665, 760, 842, 903, 952, 1109, 1154, 1208, 1246, 1336, 1430, 1467, 1513, 1585, 1617, 1788, 2859, 2892, 2942, 3014 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.10 (s, 6H), 0.89 (s, 9H), 1.26 (d, *J* = 6.4 Hz, 3H), 1.54-1.62 (m, 1H), 2.82-2.84 (m, 1H), 3.16-3.20 (m, 2H), 3.29-3.32 (m, 1H), 3.63-3.69 (m, 1H), 4.02 (d, *J* = 11.5 Hz, 1H), 4.31-4.34 (m, 1H), 6.99 (d, *J* = 8.8 Hz, 2H), 8.16 (d, *J* = 8.8 Hz, 2H); ^{13}C-NMR: δ -5.14, -4.29, 7.0, 17.8, 22.4, 25.6, 35.3, 45.2, 52.5, 64.8, 66.0, 121.7, 124.8, 142.8, 144.2, 153.3, 163.5; HRMS: *m/z* = 576.0844, calcd. For $C_{21}H_{31}O_4N_3ISSi$, found 576.0848 $[M+ H]^+$.

3-Thia-1-dethiacepham (4l)

Yield: 75%; semi-solid; IR (Neat): 668, 760, 838, 911, 1156, 1216, 1363, 1429, 1595, 1788, 2227, 2404, 2860, 2933, 3020 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.11 (s, 6H), 0.90 (s, 9H), 1.28 (d, *J* = 6.3 Hz, 3H), 1.52-1.61 (m, 1H), 2.82-2.85 (m, 1H), 3.15-3.19 (m, 2H), 3.29-3.31 (m, 1H), 3.62-3.65 (m, 1H), 4.00 (d, *J* = 11.9 Hz, 1H), 4.30-4.35 (m, 1H), 6.97 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H) ; ^{13}C NMR: δ -5.10, -4.24, 7.0, 17.9, 22.5, 25.7, 35.4, 45.2, 52.6, 64.9, 66.0, 107.5, 119.2, 122.0, 133.1, 142.8, 142.6, 151.4, 163.5; HRMS: *m/z* = 556.0945, calcd. For $C_{22}H_{31}O_2N_3ISSi$, found 556.0945 $[M+ H]^+$.

3-Thia-1-dethiacephem (4m)

Yield: 74%; mp 213 °C; IR (KBr): 667, 761, 835, 897, 953, 1011, 1093, 1145, 1209, 1336, 1429, 1463, 1502, 1613, 1784, 2860, 2893, 2943, 3010 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.11 (s, 6H), 0.91 (s, 9H), 1.28 (d, *J* = 6.1 Hz, 3H), 1.54-1.60 (m, 1H), 2.81-2.86 (m, 1H), 3.13-3.18 (m, 2H), 3.27-3.32 (m, 1H), 3.59-3.66 (m, 1H), 3.96-4.01 (m, 1H), 4.30-4.36 (m, 1H), 6.98 (d, *J* = 8.3 Hz, 2H), 7.54 (d, *J* = 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ -5.08, -4.25, 17.9, 22.5, 25.7, 35.5, 45.04, 52.7, 65.0, 65.97, 121.3, 124.3 (q, $^1J_{C\text{-}F}$ = 272 Hz), 126.01 (d, $^3J_{CF3}$ = 3.1 Hz), 126.0 (q, $^2J_{CF3}$ = 33.2 Hz), 128.3, 142.3, 150.3, 163.5 ; HRMS: m/z = 599.0867, calcd. for $C_{22}H_{31}F_3IN_2O_2SSi$, found 599.0867 $[M+H]^+$.

Dehydrohalogenation reaction using DBU (5)

To a stirred solution of compound **4b** (50 mg, 0.091 mmol) in 10 ml DCM was added was DBU (1.5 equiv) at room temperature. The stirring was continued for 2 h and the reaction was quenched with sodium thio sulphate and extracted with diethyl ether. The organic phase was washed with brine, dried over Na_2SO_4, filtered and evaporated in vacuo. The residue was chromatographed on silica gel using ether/hexane (1.5:8.5) as eluent to give corresponding product 3-Thia-1-dethiacepham **5**.

Yield: 79%; mp 164 °C; IR (KBr): 666, 761, 834, 886, 947, 1038, 1103, 1144, 1220, 1356, 1471, 1620, 1784, 2357, 2861, 2893, 2943, 3012 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.12 (s, 3H), 0.14 (s, 3H), 0.92 (s, 9H), 1.28 (d, *J* = 8.8 Hz, 3H), 2.16 (s, 3H), 2.53-2.56 (m, 1H), 3.00-3.04 (m, 1H), 3.13-3.14 (m, 1H), 3.98-4.01 (m, 1H), 3.33-3.39 (m, 1H), 5.08 (s, 1H), 5.17 (s, 1H), 6.79 (d, *J* = 7.2 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 1H), 7.13-7.15 (m, 2H); ^{13}C NMR ($CDCl_3$): δ -5.12, -4.19, 17.6, 17.9, 22.5, 25.7, 37.3, 52.2, 65.0, 66.2, 112.7, 120.2, 124.3, 126.1, 128.9, 130.3, 136.1, 140.7, 146.1,

163.7; HRMS: *m/z* = 417.2027, calcd. For $C_{22}H_{33}O_2N_2SSi$, found 417.2031 $[M + H]^+$.

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Supplementary data:

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/.

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ARTICLE

Regioselective and diastereoselective iodocyclization reaction of alkene-thioureas: an efficient approach to bicyclic β-lactams

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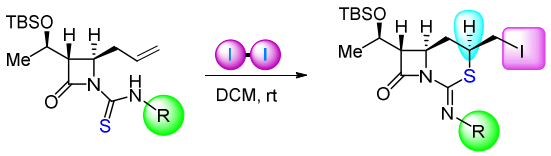

Bicyclic β-lactams i.e. 3-thia-1-dethiacephams were synthesized via highly regioselective and diastereoselective iodocyclization reaction of alkene-thioureas with molecular iodine. Further, the structure of 3-thia-1-dethiacepham was confirmed by chemical method, most notable by dehydrohalogenation reaction using DBU.

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