Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

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

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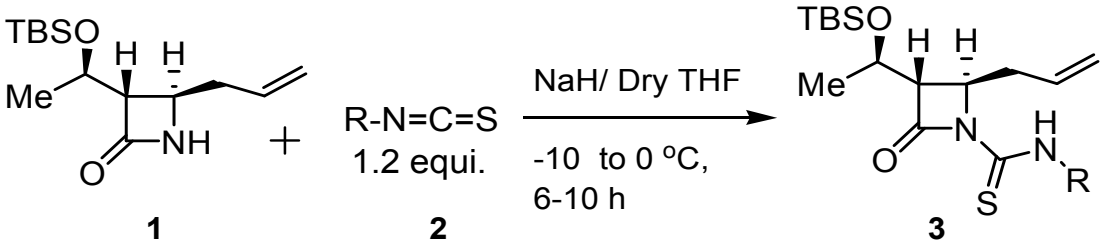
EXPERIMENTAL

General

All reactions were performed in round-bottom flask fitted with balloon filled with nitrogen, otherwise specified. TLC analysis was performed on Merck TLC (silica gel $60F_{254}$ on glass plate). Evaporation and condensation were carried out *in vacuo*. Silica gel (60-120 mesh) manufactured by Fisher Scientific was used for column chromatography. Visualization of TLC was carried out by using Iodine or by charring solutions such as molybdenum, anisaldehyde, and ninhydrin. Dichloromethane (DCM) distilled from CaO_2 prior to use. Commercially available chemicals were used without prior purification.

Column chromatographic purifications were carried out on flash silica-gel (240-400 mesh) using petroleum ether and ethyl acetate as eluents. IR spectra were measured on SHIMADZU FT-IR8400. The ^{1}H, ^{13}C, NMR spectra were recorded on 200/400/500 MHz, 50/100/125 MHz NMR spectrometer respectively in $CDCl_3$. Chemical shifts of protons are reported in δ values referred to TMS as an internal standard, and the following abbreviation were used as follows: s: singlet, d: doublet, t: triplet, m: multiplet. Melting point was recorded on Buchi instrument. Mass spectra were taken on LC-MS (ESI) mass spectrometer. HRMS were scanned at NCL, Pune.

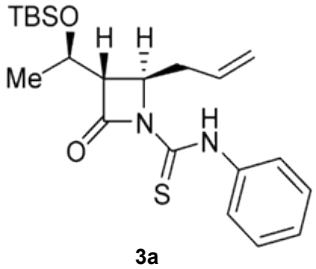
Synthesis of β-Alkene Thioureas (3)



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-m**.

The isolated yield and the spectral data for **3a-m** are as follows:

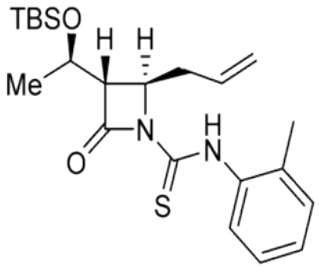
Alkene-thiourea (3a)



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}; ^1H 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 $[M+ Na]^+$.

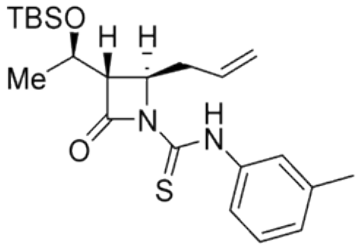
Alkene-thiourea (3b)



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}; ^1H 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 $[M+H]^+$.

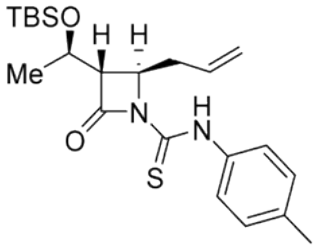
Alkene-thiourea (3c)



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 $[M+H]^+$.

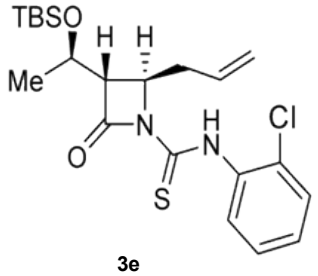
Alkene-thiourea 3d:



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 $[M+H]^+$.

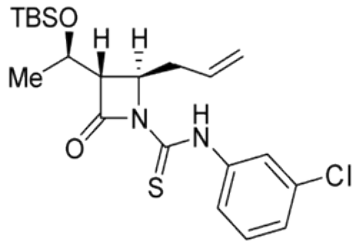
Alkene-thiourea (3e)



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 $[M+H]^+$.

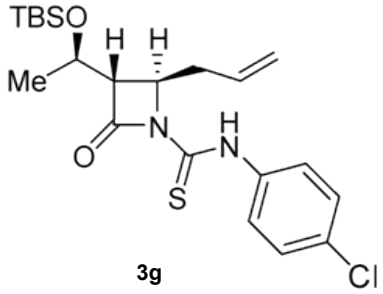
Alkene-thiourea (3f)



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 $[M+H]^+$.

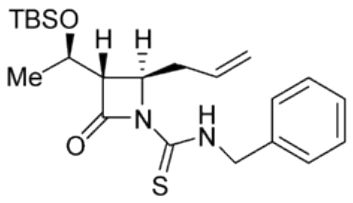
Alkene-thiourea (3g)



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 $[M+H]^+$.

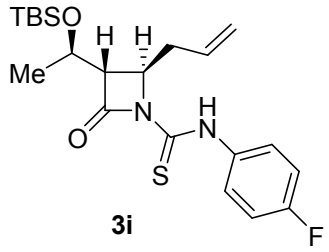
Alkene-thiourea (3h)



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 $[M+H]^+$.

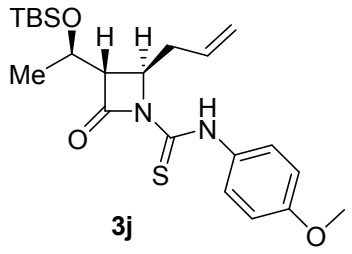
Alkene-thiourea (3i)



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 $[M+H]^+$.

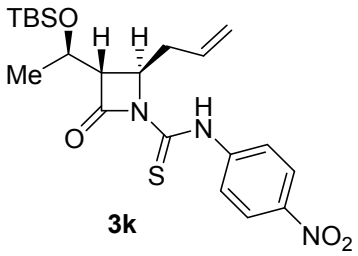
Alkene-thiourea (3j)



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 $[M+H]^+$.

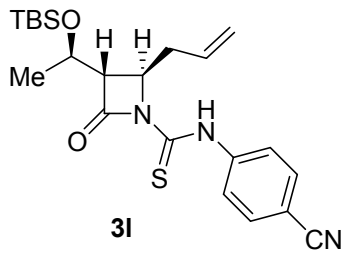
Alkene-thiourea (3k)



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 $[M+H]^+$.

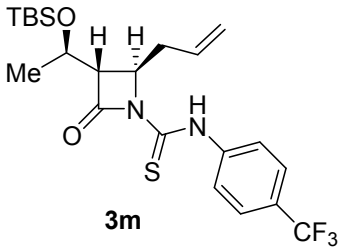
Alkene-thiourea (3l)



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 $[M+H]^+$.

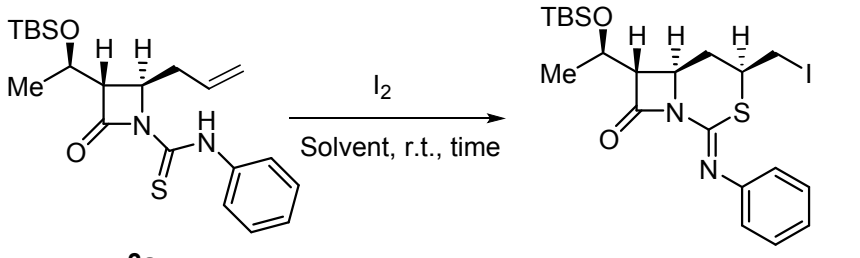
Alkene-thiourea (3m)



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}; ^1H 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, $^3J_{C\text{-}F}$ = 3.9 Hz), 127.9 (q, $^2J_{C\text{-}F}$ = 33.2 Hz), 131.9, 140.5, 167.7, 175.8; HRMS: m/z = 495.1720, calcd. for $C_{22}H_{31}F_3N_2ONaSSi$, found 495.1720 $[M+Na]^+$.

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



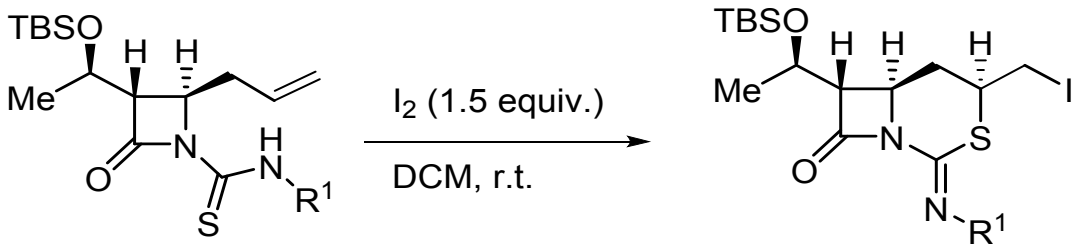
3a **3-Thia-1-dethiacepham (4a)**

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

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

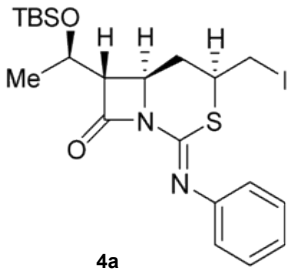


3 **3-Thia-1-dethiacepham (4)**

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-l** are as follows:

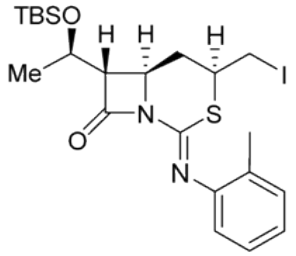
3-Thia-1-dethiacepham (4a)



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}; ^1H 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 $[M+Na]^+$.

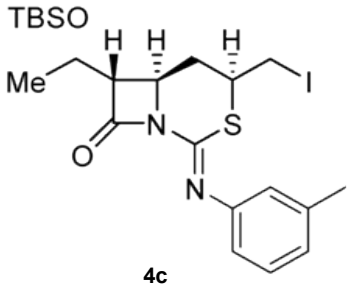
3-Thia-1-dethiacepham (4b)



4b

Yield: 71%; semi-solid; IR (Neat): 668, 761, 835, 1137, 1216, 1335, 1620, 1783, 2402, 2860, 2942, 3019 cm^{-1}; ^1H 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 $[M+H]^+$.

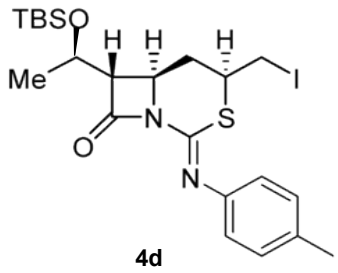
3-Thia-1-dethiacepham (4c)



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}; ^1H 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 $[M+H]^+$.

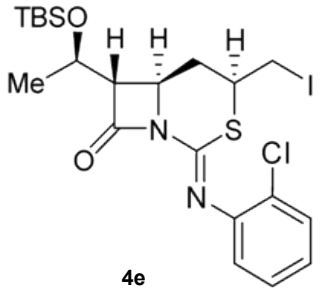
3-Thia-1-dethiacepham (4d)



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 $[M+H]^+$.

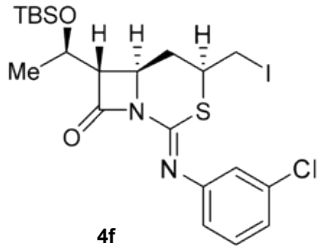
3-Thia-1-dethiacepham (4e)



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 $[M+H]^+$.

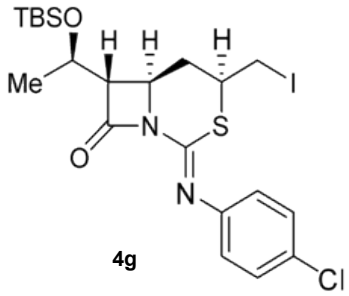
3-Thia-1-dethiacepham (4f)



4f

Yield: 81%; semi-solid; IR: 669, 760, 834, 1035, 1138, 1212, 1252, 1359, 1466, 1614, 1786, 2859, 2942, 3012 cm^{-1}; ^1H 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 $[M+ H]^+$.

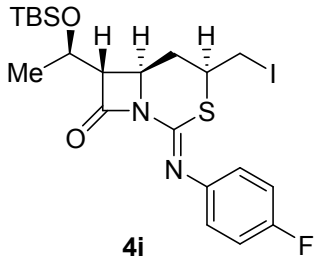
3-Thia-1-dethiacepham (4g)



4g

Yield: 79%; semi-solid; IR (Neat): 667, 760, 834, 1011, 1091, 1139, 1212, 1248, 1336, 1477, 1613, 1784, 2859, 2941, 3015 cm^{-1}; ^1H-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 $[M+H]^+$.

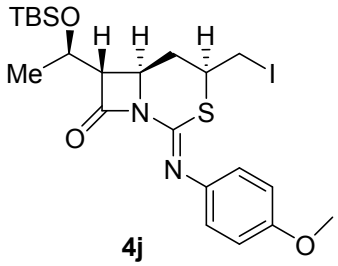
3-Thia-1-dethiacepham (4i)



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}; ^1H 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 & 10.02 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 $[M+H]^+$.

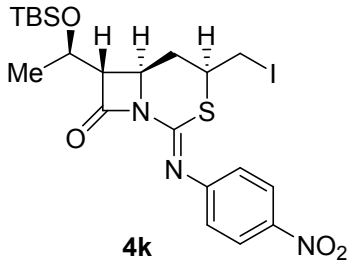
3-Thia-1-dethiacepham (4j)



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}; ^1H 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 $[M+ H]^+$.

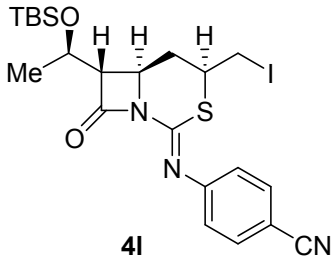
3-Thia-1-dethiacepham (4k)



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}; ^1H 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 $[M+ H]^+$.

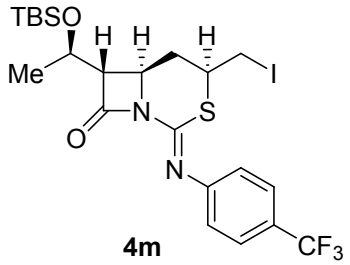
3-Thia-1-dethiacepham (4l)



4l

Yield: 75%; semi-solid; IR (Neat): 668, 760, 838, 911, 1156, 1216, 1363, 1429, 1595, 1788, 2227, 2404, 2860, 2933, 3020 cm^{-1}; ^1H 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 $[M+ H]^+$.

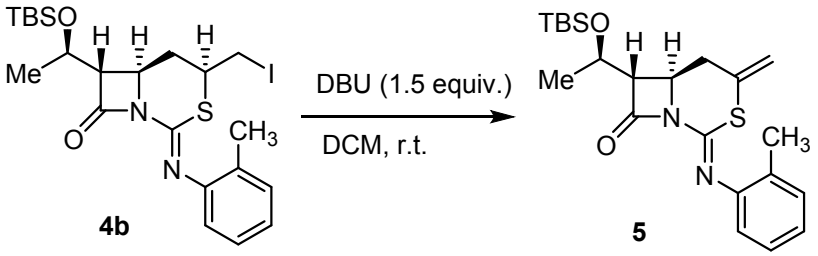
3-Thia-1-dethiacephem (4m)



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, $^{1}J_{C\text{-}F}$ = 272 Hz), 126.01 (d, $^{3}J_{CF3}$ = 3.1 Hz), 126.0 (q, $^{2}J_{CF3}$ = 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 of 3-Thia-1-dethiacepham 4b using DBU (5)



To a stirred solution of compound **4b** (50 mg, 0.091 mmol) in 10 ml DCM was added 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}; ^1H 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 $[M + H]^+$.