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Synthesis of a new optically active carbamoyl azide and its use as an aminating agent

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Abstract—The synthesis of a chiral carbamoyl azide derived from Oppolzer's sultam is described. The thermal and photochemical behaviour in the presence of simple alkenes as well as of masked ketones is also reported. Diastereoselective amination reactions have been observed giving different products. © 2001 Elsevier Science Ltd. All rights reserved.

Different examples of stereoselective amination[1] of substituted alkenes have been reported in the literature either in the presence of a chiral catalyst[2–4] or starting from substrates bearing a chiral centre,[5] also by us.[6] Recently we reported a highly diastereoselective synthesis of 3,6-dioxazocan-2-one derivatives by an intramolecular cycloaddition of optically active azidoformates.[7]

In contrast, efficient methods for reagent-controlled stereoselective amination reactions are few in number. Cadogan and co-workers attempted chiral aziridination of styrene using an optically active alkoxycarbonylnitrene with no perceptible chiral induction.[8] More recently, Atkinson achieved moderate to high stereoselectivities by the oxidation of a chiral 3-acetoxyaminoquinazolinone in the presence of different kinds of prochiral substrates.[9]

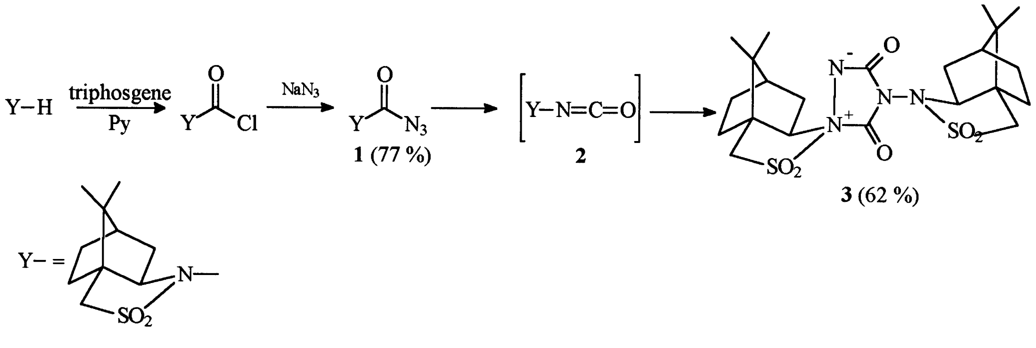
We wish to report the synthesis of a chiral aminating agent, namely the carbamoyl azide **1**, prepared in 77% overall yield from Oppolzer's sultam[10–12] via reaction with triphosgene and then sodium azide (Scheme 1).

This azide[13] is stable up to 77°C while at 140°C for 2 h gives **3**, probably by dimerisation of the unisolated aminoisocyanate **2**, derived from thermal Curtius rearrangement[14,15] of the azide.

Norbornene (**4**) does not react with **1** at room temperature.[16] Instead the corresponding aziridine **5** can be obtained either at reflux in benzene for 10 h or by a photolysis reaction in a shorter time (2 h) with a good yield (75%; Scheme 2).

Commercial prochiral alkenes **6** and **9** were also tested to study the stereoselectivity of the addition of **1**. The photolysis reaction was performed in anhydrous CH_2Cl_2, under a nitrogen atmosphere and using an equimolar amount of azide (Scheme 3).

In both cases two interesting products were obtained:[17] the substituted allylic amines **7** and **10** and the oxazolines **8** and **11**. All the amination products showed a good diastereoselectivity (d.e. >90%), as proved by ^{1}H and ^{13}C NMR spectra, which also allowed us to establish the regiochemistry of



Scheme 1.

Keywords: amination; amino ketones; asymmetric reactions; oxazolines.

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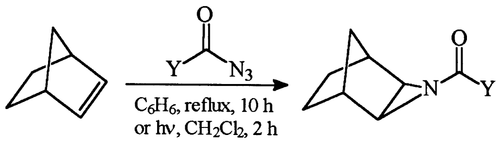


4 **5** (75%)

Scheme 2.

the oxazolines. Starting from **9** it was possible to isolate the aziridine **12**, as an additional minor product.

In order to expand the utility of the chiral azide, we tested the reaction of **1** with two different kinds of masked ketones found by us in the past to be prone to stereoselective substrate-controlled amination.[17,18]

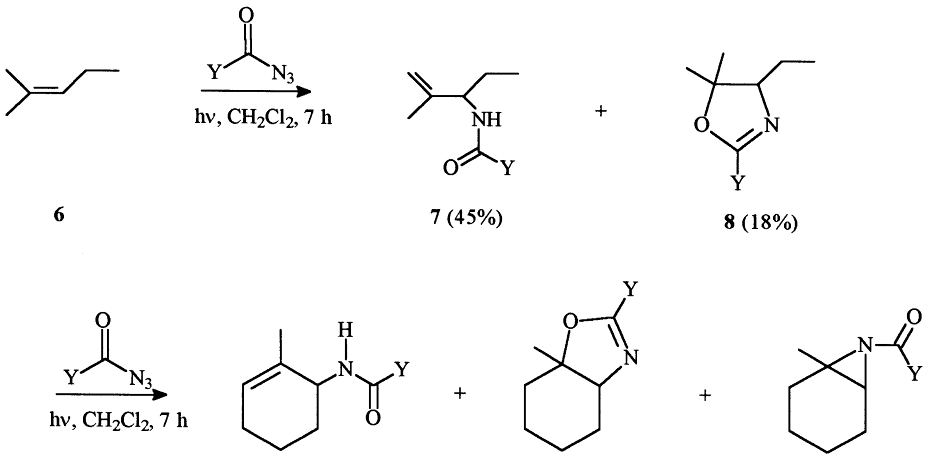
The amination of enamine **13** was carried out simply by mixing the two reagents in CH_2Cl_2 solution at room temperature and a fast nitrogen evolution was observed. After flash chromatography on silica gel, the products **14–16** were obtained, all probably arising from a common undetected intermediate triazoline[17] (Scheme 4). The substituted imine **15** is an interesting new product, obtained with a very high diastereoselectivity (d.e. $>$95%, evaluated by HPLC analysis and ^{13}C NMR spectra) by a rare 1,2-shift of the pyrrolidinyl residue recalling those already observed in other triazolines for the migration of morpholinyl[19] or sulfur-containing[20] groups during nitrogen expulsion.

The α-amino ketone **14** was isolated in low yield and only 45% d.e.,[21] together with the product of ring opening **16**.[17]

To circumvent these problems and to obtain optically active α-amino ketones, the amination of the silyl enol ether **17** and of the enol ether **18** was attempted. After 7 h of photolysis at room temperature starting from **17** and at 0°C starting from **18**, an 80:20 mixture of **19** and **20**[21] was obtained in 61% and 53% yield, respectively (Scheme 5), as detected by HPLC analysis and NMR spectra. Also in these cases, the diastereomeric ratios could be lowered during the spontaneous hydrolysis of the unisolated intermediate aziridines.[17]

Nevertheless the substituted α-amino cyclohexanones were easily obtained as pure diastereomers by flash chromatography on silica gel. We underline that to the best of our knowledge, there are only a few examples of direct asymmetric amination of similar substrates using chiral reagents.[22–25]

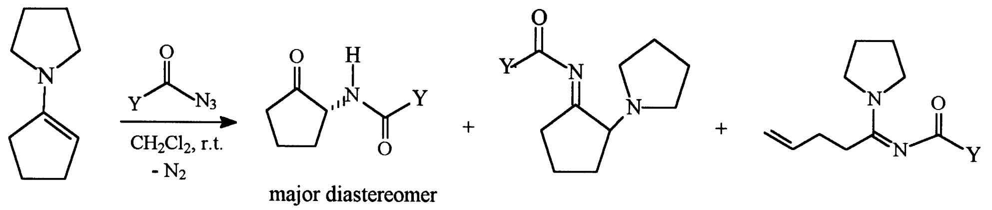
In conclusion, the synthesis of a new optically active carbamoyl azide was proposed and several examples of its use were presented. Further experiments aimed at the asymmetric C—N bond construction by the use of this reagent will be reported in due course.



6 **7** (45%) **8** (18%)

9 **10** (25%) **11** (21%) **12** (15%)

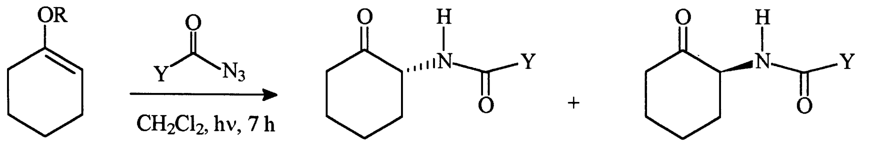
Scheme 3.



major diastereomer

13 **14** (5%, d.e. 45%) **15** (22%, d.e. > 95%) **16** (17%)

Scheme 4.



17 (R = SiMe$_3$)
18 (R = Me)

19 (major)

20

Scheme 5.

1. Experimental

1.1. General

GC analyses were performed on an HP 5890 Series II gas chromatograph with a capillary column (methyl silicone, 12.5 m×0.2 mm). GC–MS was carried out on an HP G1800A GCD System with a capillary column (phenyl methyl silicone, 30 m×0.25 mm). ESI-MS analyses were performed using a commercial API 365 triple–quadrupole mass spectrometer from Perkin–Elmer Sciex Instruments, equipped with an ESI source and a syringe pump. The experiments were conducted in the positive ion mode. The separations by HPLC were performed with a Varian 9001 instrument equipped with a Varian RI-4 differential refractometer. Solvents were HPLC grade. Optical rotations were obtained by a Perkin–Elmer 241 polarimeter (10 mm, 1 mL) at room temperature. IR spectra were recorded on a Perkin–Elmer 1600 Series FTIR spectrophotometer. NMR spectra were recorded by a Varian Gemini 200, using CDCl$_3$ as solvent and CHCl$_3$ as internal standard. Microanalyses were carried out on a Carlo Erba Instruments EA1110.

1.1.1. (1*R*,5*S*)-10,10-Dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carbonyl azide (1). To a solution of triphosgene (1.7 g, 5.8 mmol) in 25 mL of toluene, the Oppolzer's sultam (2.5 g, 12 mmol) and pyridine (0.95 mL, 12 mmol) in 33 mL of toluene were added during 40 min at 0°C. The mixture was allowed to come up to room temperature and heated gently (40°C) for 2 h. After cooling, filtration of pyridinium chloride and evaporation of the solvent, the residue was dissolved in 10 mL of CH$_2$Cl$_2$ and was added dropwise at 0°C to a solution of NaN$_3$ (1.7 g, 26 mmol) in 26 mL of H$_2$O. After 25 h at room temperature, the mixture was extracted with CH$_2$Cl$_2$ and the solvent was evaporated to give **1** (1.3 g, 4.5 mmol, 77% overall) as a white solid; $[\alpha]_D=-110$ (*c* 1.0, CHCl$_3$); IR (CHCl$_3$) 2156, 1704 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.95 (s, 3H, CH$_3$), 1.14 (s, 3H, CH$_3$), 1.32–1.45 (m, 2H, CH$_2$), 1.84–2.07 (m, 4H, 2 CH$_2$), 2.17–2.30 (m, 1H, CH), 3.39 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.51 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.82 (dd, *J*=7.3 and 5.1 Hz, 1H, CHN); ^{13}C NMR (CDCl$_3$) δ 19.7, 20.6, 26.3, 32.6, 38.0, 44.6, 47.7, 50.3, 52.6, 65.1, 153.3; Calcd for C$_{11}$H$_{16}$N$_4$O$_3$S: C, 46.47; H, 5.67; N, 19.70; S, 11.28%. Found: C, 46.64; H, 5.65; N, 19.63; S, 11.11%.

1.1.2. Spiro[(4-((1*R*,5*S*)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]dec-4-yl)-3,5-dioxo-1,2,4-triazolidin-2-ium-1-ide)-2,4′-((1′*R*,5′*S*)-10′,10′-dimethyl-3′,3′-dioxo-3′λ^6-thia-4′-azoniatricyclo[5.2.1.0^{1,5}]decane)] (3). A solution of **1** (1.2 g, 4 mmol) in 10 mL of anhydrous CH$_2$Cl$_2$ was heated at 140°C for 2 h in a sealed tube. After evaporation of solvent, the crude mixture was separated by flash chromatography on silica gel (hexane/ethyl acetate, 80:20) to give **3** (1.28 g, 2.5 mmol, 62%) as a white solid; IR (CHCl$_3$) 1812, 1765 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.00 (s, 3H, CH$_3$), 1.03 (s, 3H, CH$_3$), 1.36 (s, 3H, CH$_3$), 1.38 (s, 3H, CH$_3$), 1.48–2.19 (m, 14H), 3.38 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.42 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.47 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.59 (d, *J*=13.9 Hz, 1H, CH$_A$H$_B$S), 3.89 (m, 1H, CHN), 4.35 (m, 1H, CHN); ^{13}C NMR (CDCl$_3$) δ 19.8, 20.1, 20.6, 20.9, 25.9, 26.7, 32.8, 33.3, 34.5, 36.4, 45.0, 46.2, 47.6, 47.8, 48.8, 49.2, 51.0, 53.2, 63.3, 65.9, 145.8, 150.6.

1.2. Photolysis reactions. General procedure

A solution of the alkene (1 mmol) and **1** (1 mmol) in 2 mL of anhydrous CH$_2$Cl$_2$ was photolysed in a quartz vessel under a N$_2$ atmosphere at room temperature, using a medium pressure Hanovia PCR lamp (100 W) or a high pressure Helios Italquartz lamp (125 W). When the azide band disappeared in the IR spectrum (2 h for **4**, 7 h for **6**, **9**, **17** and **18**) the solvent was evaporated in vacuo. The products were separated by flash chromatography on silica gel (hexane/ethyl acetate, 60:40 for **5**, **7**, **8**, **19** and **20**; 80:20 for **10**–**12**).

1.2.1. (1*R*,5*S*)-4-[(3-Azatricyclo[3.2.1.0^{2,4}]oct-3-yl)carbonyl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide (5). Oil (0.26 g, 0.75 mmol, 75%); IR (CHCl$_3$) 1684 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.96 (s, 3H, CH$_3$), 1.15 (s, 3H, CH$_3$), 1.18–1.53 (m, 6 H), 1.75–2.14 (m, 7 H), 2.49–2.53 (br, 1H CH), 2.55–2.60 (br, 1H, CH), 2.70 (d, *J*=5.1 Hz, 1H, CHN), 2.90 (d, *J*=5.1 Hz, 1H, CHN), 3.38 (d, *J*=13.9 Hz, 1H, CH$_A$CH$_B$S), 3.44 (d, *J*=13.9 Hz, 1H, CH$_A$CH$_B$S), 3.82 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS); ^{13}C NMR (CDCl$_3$) δ 19.8, 20.7, 25.3, 25.6, 26.5, 28.9, 32.5, 36.1, 38.1, 40.0, 43.6, 44.5, 47.6, 48.4, 52.6, 64.9, 158.4; GC–MS *m/z* 350 (M$^+$, 11), 332 (34), 321 (52), 136 (16), 135 (91), 110 (13), 109 (38), 108 (53), 107 (26), 93 (49), 91 (29), 82 (17), 81 (100), 80 (52), 79 (49), 77 (25), 67 (32), 55 (14), 53 (21), 43 (12), 42 (34), 41 (35).

1.2.2. (1*R*,5*S*)-*N*-(1-Ethyl-2-methylprop-2-enyl)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carboxamide (7). Viscous oil (0.15 g, 0.45 mmol, 45%); $[\alpha]_D=-74.8$ (*c* 0.37, CHCl$_3$); IR (CHCl$_3$) 1711, 1630 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 0.85–0.92 (t+s, 6 H, 2 CH$_3$), 1.13 (s, 3H, CH$_3$), 1.22–2.22 (m, 9 H), 1.72 (s, 3H, CH$_3$), 3.34 (d, *J*=13.9 Hz, 1H, CH$_A$CH$_B$S), 3.40 (d, *J*=13.9 Hz, 1H, CH$_A$CH$_B$S), 3.82 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS), 4.15 (m, 1H, C*H*NH), 4.88 (br, 2H, CH$_2$=C), 5.91–6.04 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 10.1, 19.3, 19.9, 20.2, 26.1, 26.7, 32.0, 37.6, 44.2, 47.9, 48.4, 51.8, 57.1, 64.2, 111.3, 144.2, 150.4; ESI-MS *m/z* 341 (M^++1); Calcd for $C_{17}H_{28}N_2O_3S$: C, 59.97; H, 8.29; N, 8.23; S, 9.41%. Found: C, 59.78; H, 8.31; N, 8.20; S, 9.29%.

1.2.3. (1*R*,5*S*)-[(4-Ethyl-5,5-dimethyl)-4,5-dihydrooxazol-2-yl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-3,3-dioxide (8). Viscous oil (61 mg, 0.18 mmol, 18%); $[\alpha]_D=-57.2$ (*c* 0.11, $CHCl_3$); IR ($CHCl_3$) 1719, 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.92 (s, 3H, CH_3), 1.02 (t, *J*=7 Hz, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.25–2.20 (m, 9 H), 1.39 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 3.31–3.49 (m, 3H, CH_2S, CHN=C), 3.82 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS); ^{13}C NMR ($CDCl_3$) δ 11.1, 19.9, 20.7, 21.3, 25.2, 26.6, 28.1, 32.5, 37.6, 44.5, 47.8, 49.4, 52.2, 65.7, 73.0, 88.9, 152.7; ESI-MS *m/z* 341 (M^++1); Calcd for $C_{17}H_{28}N_2O_3S$: C, 59.97; H, 8.29; N, 8.23; S, 9.41%. Found: C, 60.15; H, 8.02; N, 8.12; S, 9.26%.

1.2.4. (1*R*,5*S*)-*N*-(2-Methylcyclohex-2-enyl)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carboxamide (10). Oil (88 mg, 0.25 mmol, 25%); $[\alpha]_D=-39.6$ (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) 3400, 1706 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.12–2.10 (m, 13H), 1.66 (s, 3H, CH_3), 3.30 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.36 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.79 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS), 4.20–4.22 (m, 1H, C*H*NH), 5.55 (br, 1H, C=CH), 5.83–5.86 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 18.3, 19.9, 20.3, 20.9, 25.1, 26.7, 29.7, 32.1, 37.7, 44.3, 47.9, 48.6, 48.9, 51.8, 64.2, 126.8, 132.4, 150.7; GC–MS *m/z* 352 (M^+, 1), 288 (18), 259 (27), 152 (100), 136 (24), 135 (64), 110 (83), 109 (32), 108 (17), 107 (16), 96 (13), 95 (71), 94 (36), 93 (34), 91 (19), 82 (12), 81 (14), 80 (12), 79 (36), 77 (17), 67 (41), 55 (27), 53 (14), 44 (11), 43 (16), 41 (31); Calcd for $C_{18}H_{28}N_2O_3S$: C, 61.33; H, 8.01; N, 7.95; S, 9.10%. Found: C, 61.51; H, 7.96; N, 7.85; S, 8.96%.

1.2.5. (1*R*,5*S*)-10,10-Dimethyl-4-(7a-methyl-3a,4,5,6,7,7a-hexahydrobenzooxazol-2-yl)-3-thia-4-azatricyclo[5.2.1.0^{1,5}]-decane-3,3-dioxide (11). Oil (74 mg, 0.21 mmol, 21%); $[\alpha]_D=-57.3$ (*c* 0.3, $CHCl_3$); IR ($CHCl_3$) 1736, 1706, 1648 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.94 (s, 3H, CH_3), 1.18–2.05 (m, 15 H), 1.20 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 3.31 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.43 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.57 (t, *J*=5.9 Hz, 1H, CHN=C), 3.81 (dd, *J*= 7.3 and 5.1 Hz, 1H, CHNS); ^{13}C NMR ($CDCl_3$) δ 18.6, 19.2, 20.0, 20.9, 26.4, 26.8, 28.2, 31.8, 32.6, 37.9, 44.7, 47.9, 49.6, 52.3, 65.8, 67.1, 88.2, 153.8; GC–MS *m/z* 352 (M^+, 1), 288 (21), 259 (20), 153 (12), 152 (100), 136 (22), 135 (59), 110 (78), 109 (30), 108 (14), 107 (15), 96 (13), 95 (68), 94 (34), 93 (33), 91 (16), 81 (12), 79 (33), 77 (16), 67 (37), 55 (24), 53 (12), 43 (12), 41 (27); Calcd for $C_{18}H_{28}N_2O_3S$: C, 61.33; H, 8.01; N, 7.95; S, 9.10%. Found: C, 61.24; H, 8.07; N, 8.04; S, 9.02%.

1.2.6. (1*R*,5*S*)-4-[(1-Methyl-7-azabicyclo[4.1.0]hept-7-yl)-carbonyl]-10,10-dimethyl-3-thia-4-azatricyclo[5.2.1.0^{1,5}]-decane-3,3-dioxide (12). Oil (53 mg, 0.15 mmol, 15%); $[\alpha]_D=-64.0$ (*c* 0.6, $CHCl_3$); IR ($CHCl_3$) 1681 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (s, 3H, CH_3), 1.09–2.30 (m, 15 H), 1.14 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 2.72 (dd, *J*=4.4 and 2.2 Hz; 1H, CHNCO), 3.37 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.43 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.87 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS); ^{13}C NMR ($CDCl_3$) δ 19.8, 20.3, 20.5, 20.9, 21.2, 26.4, 29.6, 30.1, 32.9, 38.5, 41.6, 44.7, 47.6, 47.9, 50.6, 52.9, 65.6, 159.8; GC–MS *m/z* 352 (M^+, 30), 273 (10), 259 (18), 178 (11), 152 (84), 151 (13), 137 (15), 136 (31), 135 (85), 134 (15), 112 (10), 111 (25), 110 (80), 109 (40), 108 (30), 107 (29), 96 (23), 95 (100), 94 (44), 93 (59), 91 (31), 83 (15), 82 (23), 81 (27), 80 (19), 79 (53), 77 (25), 69 (20), 68 (16), 67 (69), 65 (12), 56 (12), 55 (46), 54 (11), 53 (24), 44 (12), 43 (25), 41 (55); Calcd for $C_{18}H_{28}N_2O_3S$: C, 61.33; H, 8.01; N, 7.95; S, 9.10%. Found: C, 61.49; H, 7.93; N, 7.86; S, 8.93%.

1.2.7. (1*R*,5*S*)-*N*-[(1*R*)-2-Oxocyclohexenyl)]-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carboxamide (19). Oil (starting from **17**, 0.17 g, 0.49 mmol, 49%; starting from **18**, 0.15 g, 0.42 mmol, 42%); $[\alpha]_D=-100$ (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) 3365, 1734, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 3H, CH_3), 1.14 (s, 3H, CH_3), 1.23–2.70 (m, 15 H), 3.35 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.43 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.80 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS), 4.33–4.49 (m, 1H, CHCO), 6.75–6.90 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 19.9, 20.3, 23.9, 26.3, 27.7, 32.1, 34.9, 37.6, 40.9, 44.2, 47.9, 48.7, 51.8, 58.9, 64.0, 150.5, 206.4; GC–MS *m/z* 354 (M^+, 20), 215 (12), 152 (18), 151 (100), 150 (16), 139 (18), 136 (59), 135 (38), 134 (58), 132 (12), 122 (14), 119 (27), 112 (11), 110 (11), 109 (24), 108 (68), 107 (23), 96 (21), 95 (36), 94 (25), 93 (45), 91 (26), 84 (25), 83 (32), 82 (25), 81 (19), 80 (11), 79 (38), 77 (17), 70 (10), 69 (47), 68 (16), 67 (38), 56 (24), 55 (32), 53 (13), 44 (21), 43 (46), 42 (14), 41 (60); Calcd for $C_{17}H_{26}N_2O_4S$: C, 57.60; H, 7.39; N, 7.90; S, 9.05%. Found: C, 57.65; H, 7.38; N, 7.90; S, 8.97%.

1.2.8. (1*R*,5*S*)-*N*-[(1*S*)-2-Oxocyclohexenyl)]-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carboxamide (20). Oil (starting from **17**, 0.04 g, 0.12 mmol, 12%; starting from **18**, 0.03 g, 0.11 mmol, 11%); $[\alpha]_D=-65.86$ (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.95 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.20–2.77 (m, 15 H), 3.34 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.42 (d, *J*=13.9 Hz, 1H, CH_ACH_BS), 3.78 (dd, *J*=7.3 and 5.1 Hz, 1H, CHNS), 4.27–4.40 (m, 1H, CHCO), 6.86–6.99 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 19.9, 20.3, 26.6, 27.9, 32.1, 35.5, 37.6, 40.8, 44.3, 47.9, 48.7, 51.7, 59.4, 64.1, 150.4, 206.0; Calcd for $C_{17}H_{26}N_2O_4S$: C, 57.60; H, 7.39; N, 7.90; S, 9.05%. Found: C, 57.70; H, 7.35; N, 7.88; S, 8.95%.

1.3. Reaction of 13 with 1

To a stirred solution of the enamine **13** (0.27 g, 2 mmol) in 2 mL of anhydrous CH_2Cl_2 at room temperature, azide **1** (0.6 g, 2.1 mmol) was added slowly. After 30 min of stirring, the azide band disappeared in the IR spectrum and the crude mixture was concentrated in vacuo. The products were separated by flash chromatography on silica gel (hexane/ethyl acetate, 55:45).

1.3.1. (1*R*,5*S*)-*N*-[2-Oxocyclopentyl]-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]decane-4-carboxamide (14). Viscous oil (34 mg, 0.1 mmol, 5%); IR ($CHCl_3$) 3394, 1752, 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (major, s, 3H, CH_3), 0.98 (minor, s, 3H, CH_3), 1.15 (major, s, 3H,

CH_3), 1.17 (minor, s, 3H, CH_3), 1.21–2.72 (m, 13H), 3.39 (d, J=13.9, 1H, CH_AH_BS), 3.42 (d, J=13.9, 1H, CH_AH_BS), 3.78–3.86 (m, 2H, CHNS, C*H*NH), 6.26–6.35 (minor, br, 1H, NH), 6.37–6.46 (major, br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 17.9, 18.2, 19.9, 20.3, 26.7, 29.4, 30.0, 32.2, 34.8, 35.0, 37.6, 44.2, 47.9, 48.7, 48.8, 51.6, 58.7, 58.7, 64.2, 150.7, 151.2, 213.5, 213.9; GC–MS *m/z* 340 (M^+, 15), 284 (39), 151 (32), 136 (22), 135 (60), 134 (21), 109 (22), 108 (31), 107 (30), 106 (31), 94 (20), 93 (45), 91 (34), 82 (20), 81 (29), 80 (20), 79 (34), 77 (23), 70 (22), 69 (36), 67 (42), 56 (22), 55 (100), 54 (21), 53 (32).

1.3.2. (1*R*,5*S*)-*N*-[2-Pyrrolidin-1-ylcyclopentylidene)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]-decane-4-carboxamide (15). Viscous oil (0.17 g, 0.44 mmol, 22%); $[\alpha]_D$=−88.3 (c 2.1, $CHCl_3$); IR ($CHCl_3$) 1647 cm^{-1}; ^{1}H NMR (C_6D_6) δ 0.54 (s, 3H, CH_3), 0.63–1.80 (m, 12H), 1.30 (s, 3H, CH_3), 2.12 (dd, J=14.5 and 7.3 Hz, 1H, CH), 2.41–2.67 (m, 4H), 2.93 (d, J=13.9 Hz, 1H, CH_ACH_BS), 2.99 (d, J=13.9 Hz, 1H, CH_ACH_BS), 3.21 (t, J=7.2 Hz, 2H, CH_2N), 3.56–3.82 (m, 3H), 3.88 (dd, J=7.3 and 5.1 Hz, 1H, CHN); ^{13}C NMR (C_6D_6) δ 20.2, 21.8, 24.3, 26.0, 27.2, 31.0, 33.0, 33.2, 39.9, 45.0, 45.5, 46.8, 48.0, 49.4, 53.6, 65.5, 158.7, 167.5; ESI-MS *m/z* 394 (M^++1); Calcd for $C_{20}H_{31}N_3O_3S$: C, 61.04; H, 7.94; N, 10.68; S, 8.15%. Found: C, 61.15; H, 7.96; N, 10.62; S, 8.09%.

1.3.3. (1*R*,5*S*)-*N*-(1-Pyrrolidin-1-ylpent-4-enylidene)-10,10-dimethyl-3,3-dioxo-3λ^6-thia-4-azatricyclo[5.2.1.0^{1,5}]-decane-4-carboxamide (16). Viscous oil (0.13 g, 0.34 mmol, 17%); IR ($CHCl_3$) 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.96 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.83–2.10 (m, 10 H), 2.22–2.50 (m, 3H), 2.73–3.01 (m, 2H, CH_2C=N), 3.35 (d, J=13.9 Hz, 2H, CH_ACH_BS), 3.43 (d, J=13.9 Hz, 2H, CH_ACH_BS), 3.54 (t, J=7.2 Hz, 2H, CH_2N), 3.74 (t, J=7.2 Hz, 2H, CH_2N), 3.84 (dd, J=7.3 and 5.1 Hz, 1H, CHNS), 4.98–5.15 (m, 2H, CH_2=C), 5.78–6.00 (m, 1H, CH=C); ^{13}C NMR ($CDCl_3$) δ 19.9, 21.1, 24.2, 25.7, 26.6, 30.2, 31.2, 32.8, 38.8, 44.8, 47.2, 47.5, 47.6, 49.0, 53.0, 64.9, 115.5, 139.9, 157.3, 167.9; GC–MS *m/z* 393 (M^+, 9), 220 (13), 192 (33), 179 (23), 152 (17), 151 (100), 149 (11), 123 (19), 110 (12), 93 (10), 82 (27), 80 (10), 79 (10), 70 (21), 67 (14), 55 (34), 54 (22), 53 (12); Calcd for $C_{20}H_{31}N_3O_3S$: C, 61.04; H, 7.94; N, 10.68; S, 8.15%. Found: C, 61.08; H, 7.97; N, 10.61; S, 8.13%.

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