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Stereoselective Addition of 2-Phenyloxazol-4-yl Trifluoromethanesulfonate to *N*-Sulfinyl Imines: Application to the Synthesis of the HCV Protease Inhibitor Boceprevir

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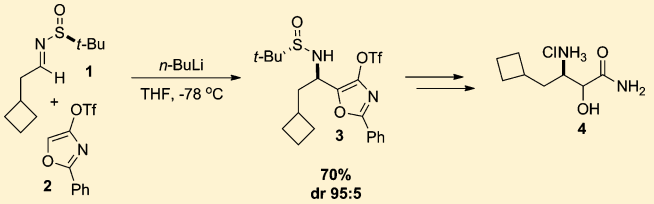
Supporting Information

ABSTRACT: The stereoselective addition of 2-phenyloxazol-4-yl trifluoromethanesulfonate to *N*-sulfinylimines is described. Vinyl anions derived from enol triflate **2** undergo 1,2-addition with a variety of aldimines to afford the corresponding secondary sulfonamides as single diastereomers. The absolute stereochemistry was confirmed by X-ray crystallography which provides support that the reaction proceeds through an open, nonchelate transition state. This methodology has been applied to the synthesis of the ketoamide fragment of the protease inhibitor boceprevir.



Hepatitis C is an infectious disease of the liver caused by the hepatitis C virus (HCV). Once established, hepatitis C can lead to chronic liver disease including cirrhosis, liver cancer, or liver failure. Approximately 3% of the world's population is infected with the HCV including over 4 million Americans.[1] Of those infected, up to 80% develop chronic infection. The standard of care for hepatitis C has been a combination therapy of pegylated interferon in conjunction with ribavirin. Many patients experience undesirable side effects in response to this therapy including anemia, depression, fatigue, insomnia, and anxiety. Perhaps of greater significance is that this combination therapy provides sustained virological response in approximately 50% of patients with the genotype 1.[2] This limited response rate, in combination with the side effects, has provided the impetus for pharmaceutical companies to develop alternative therapies for the treatment of hepatitis C. Two products of these efforts, telaprevir and boceprevir (Figure 1), have recently garnered approval from the US Food and

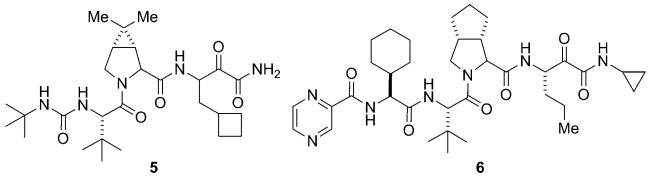


Figure 1. Boceprevir (**5**) and telaprevir (**6**).

Drug administration. These two HCV NS3 protease inhibitors, which prevent a critical step in HCV genome replication, represent a significant advancement in the care for patients infected with HCV.

Each of these protease inhibitors contain a β-amino-α-ketoamide that binds to the NS3 protease at the S1 pocket and forms a covalent and reversible complex with Ser139.[3] In the case of boceprevir (**5**), the amino stereocenter of the β-amino-α-ketoamide undergoes rapid equilibration under cellular conditions. Consequently, **5** is prepared commercially as a mixture of diastereomers at this amino stereocenter. Although this simplifies the synthesis of **5**, preparing a mixture of diastereomers can introduce problems with respect to process development as the isolation and characterization of these diastereomeric mixtures becomes more complex. It is for these reasons that we sought an alternative approach[4] aimed at maintaining control of the amino stereocenter throughout the synthesis of hydroxy amide **4**.

Our synthetic approach to **4** is shown in Figure 2. In order to control the outcome at the amino stereocenter, we chose to employ *N*-sulfinylimine[5] **1** as an electrophile and couple it with enol triflate **2**. The product of this addition reaction can be further converted to hydroxy amide **4** under basic conditions.

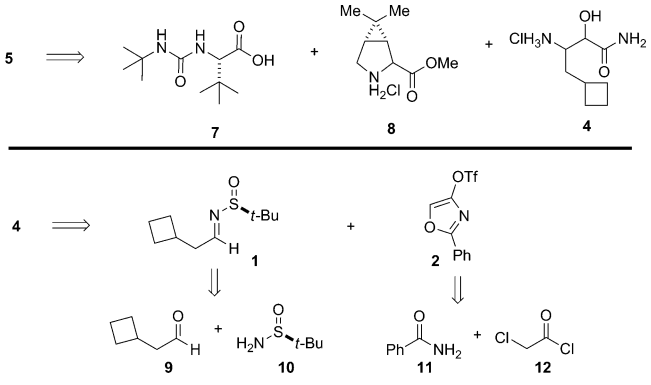


Figure 2. Retrosynthetic analysis.

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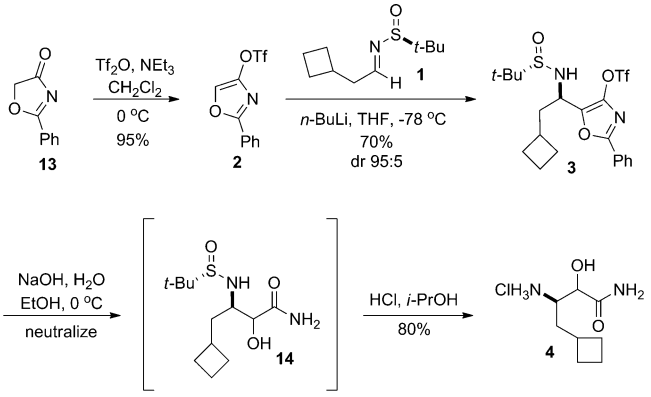
The synthesis of hydroxy amide **4** is shown in Scheme 1. Oxazolone **13** was prepared via known procedures and

Scheme 1. Synthesis of Hydroxyamide 4

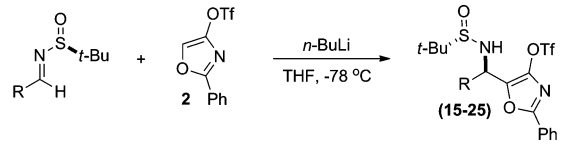


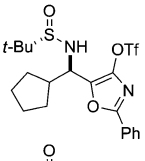
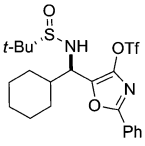
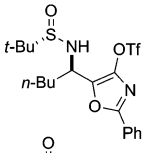
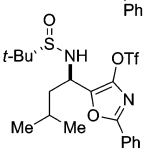
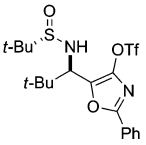
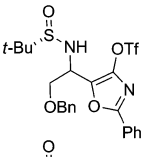
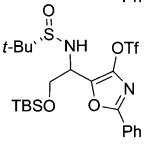
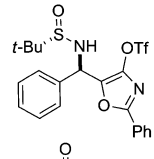
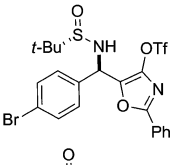
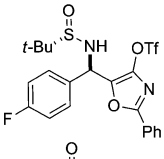
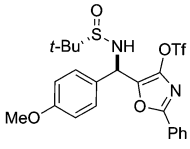
converted to enol triflate **2**.[6] Enol triflate **2** was treated with *n*-BuLi[7] at −78 °C followed by addition of the *N*-sulfinylimine **1**. Following an aqueous workup, a single diastereomer was observed by ^{1}H NMR and was isolated in 70% yield. Exposure to aqueous NaOH resulted in hydrolysis of the triflate with concomitant cleavage of the 2-phenyloxazol-4-yl intermediate **3** resulting in the formation of a mixture of diastereomers at the secondary carbinol stereocenter.[8] The sulfinyl group was removed under acidic conditions furnishing the HCl salt of hydroxyamide **4**.[9]

Following the successful application of this directed metalation[10] reaction to the synthesis of hydroxy amide **4**, we chose to evaluate the scope of this addition reaction. Sulfinyl imines[11] derived from aliphatic aldehydes provided addition products as single diastereomers in moderate to good yields (Table 1, entries 1−5). Imines with α-alkoxy substitution resulted in no stereocontrol (Table 1, entries 6 and 7) likely due to the interruption of the transition state by coordination of the ethereal oxygen to the aryl lithium reagent.[12] It is noteworthy that α-alkyl substitution of the aldehydes can be tolerated with minimal loss of conversion and no impact on stereoselectivity (entries 1, 2, and 5). Imines derived from aromatic aldehydes also were competent substrates for this reaction. The imine derived from benzaldehyde provided the addition adduct as a single diastereomer (entry 8) as did 4-substutituted benzaldehydes when the substitution was an electron-withdrawing group (entries 9 and 10). Imines from aromatic aldehydes with electron-donating substituents at the *para* position failed to react with the aryllithium nucleophile (entry 11). This lack of reactivity is possibly due to a combination of factors including the reduced electrophilicity of 4-OMe-substituted sulfinyl imines in conjunction with the attenuated nucleophilicity of an aryllithium reagent possessing an electron-withdrawing triflate substituent and a σ-withdrawing oxygen atom adjacent to the reactive carbanion. Efforts were made to improve these results by employing additives such as TMEDA, HMPA, and Lewis acids such as $BF_3{\cdot}OEt_2$ and $AlMe_3$ without any success.[13]

The stereochemistry of this addition reaction was confirmed through X-ray crystallography.[14] The stereochemical outcome observed for the addition is consistent with open transition state **I** (Figure 3), which is consistent with previous reports when employing organolithium reagents in coordinating solvents such as THF.[15]

Table 1. Reaction Scope[a]



Entry	No.	Product	Yield (% isolated)	dr[b]
1	**15**		65	95:5
2	**16**		57	95:5
3	**17**		64	95:5
4	**18**		68	95:5
5	**19**		40	95:5
6	**20**		30	1:1
7	**21**		28	1:1
8	**22**		56	95:5
9	**23**		38	95:5
10	**24**		59	95:5
11	**25**		0	na

[a]See the Supporting Information for experimental details. [b]Determined by analysis of unpurified ^{1}H NMR.

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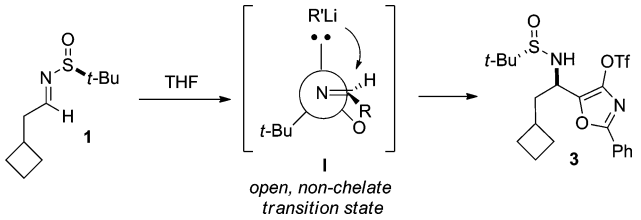

Figure 3. Model for stereochemical induction.

In summary, the reaction between the vinyllithium reagent derived from **2** and *N*-sulfinyl imines provides 1,2-addition products in moderate to good yield. In most cases, the addition products are formed as a single diastereomer. X-ray crystallography provides support that the reaction proceeds via an open, nonchelated transition state. This methodology has been applied to the synthesis of the *β*-amino-*α*-hydroxy (**4**) fragment of the NS3 protease inhibitor Boceprevir and is being evaluated as a potential route for commercial manufacturing.

EXPERIMENTAL SECTION

Synthesis of Hydroxyl Amide 4 from 3: (2*R*)-4-Amino-1-cyclobutyl-3-hydroxy-4-oxobutan-2-aminium Chloride. To a round-bottom flask containing **3** (500 mg, 1.01 mmol) was added EtOH (5 mL). The solution was cooled to 0 °C and treated with aqueous 1 M NaOH (3 mL, 3.03 mmol) for 4 h. The reaction was neutralized (pH 7) at 0 °C with aqueous 1 M HCl and diluted with a 1:1 mixture of CH_2Cl_2/H_2O (40 mL). The aqueous layer was split and extracted with CH_2Cl_2 (3 × 20 mL). The combined organics were concentrated to ∼20 mL at which time 2-propanol was added (40 mL). The solution was again concentrated to ∼10 mL at which time another 40 mL of 2-propanol was added. The mixture was reduced to a volume of ∼10 mL and treated with 5 M HCl in 2-propanol (1 mL, 5.1 mmol) at room temperature. The mixture was allowed to stir at room temperature for 3 h. MTBE (10 mL) was added to the mixture and stirred at room temperature for 30 min. The solid hydrochloride salt was filtered and washed with MTBE (20 mL). The collected solid was dissolved in 2-propanol/H_2O (9:1, 10 mL) and heated to 80 °C for 1 h (homogeneous solution). The mixture was cooled to 0−5 °C over 3 h and held at 0−5 °C for 1 h. The solid was collected by filtration to afford 168 mg of **4** (80%) as a 1:1 mixture of diastereomers as a white solid: ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 4.36−4.31 (m, 1H), 4.22−4.17 (m, 1H), 3.53−3.48 (m, 2H), 3.37−3.33 (O*H*, 1H), 2.57−2.49 (m, 2H), 2.13−1.99 (m, 4H), 1.89−1.58 (m, 12H), ^{13}C NMR (400 MHz, $CDCl_3$) 175.0, 174.7, 70.5, 69.1, 51.9, 51.7, 36.1, 34.1, 31.6, 31.5, 27.6, 27.2, 17.8, 17.6; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_8H_{16}N_2O_2$ [M + H], 173.1290, found 173.1287.

General Procedure for Addition of 2-Phenyloxazol-4-yl Trifluoromethanesulfonate to *N*-Sulfinylimines. To a three-necked round-bottomed flask was added triflate followed by 10 volumes of THF. The mixture was cooled to −78 °C, and *n*-BuLi (2.5 M in hexanes, 1.2 equiv) was added at a rate such that the internal temperature did not exceed −70 °C. After 10 min, the sulfinyl imine was added as a solution in THF (2 volumes of THF) over 3−5 min. The reaction was stirred for 10 min at −78 °C. The reaction was quenched with 15 volumes of 10% aqueous NH_4Cl, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were concentrated and purified by flash column chromatography with EtOAc/hexanes.

*5-[1-[(tert-Butylsulfinyl)amino]-2-cyclobutylethyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**3**).* Purified with 30% ethyl acetate/hexanes, yielding 1.09g (70%) as yellow oil: IR (KBr, cm^{-1}) 3110, 2948, 2868, 2323, 1713, 1638, 1553, 1474, 1450, 1362, 1317, 1289, 1212, 1128, 1070, 1045, 943, 859, 779, 748, 724, 690, 662; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.99−8.01 (dd, *J* = 1.5 Hz, 1.96 Hz, 2H), 7.47−7.57 (m, 3H), 4.55−4.6 (m, 1H), 3.53 (d, *J* = 5 Hz, 1H), 2.32−2.38 (m, 1H), 2.12−2.19 (m, 1H), 2.09−2.12 (m, 1H), 1.98−2.04 (m, 1H), 1.85−1.91 (m, 1H), 1.79−1.83 (m, 1H), 1.70−1.75 (m, 1H), 1.61−1.68 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.1, 141.6, 139.8, 135.4, 130.2, 126.4, 126.1, 69.7, 56.3, 49.6, 41.9, 32.6, 28.1, 22.3, 18.6; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{20}H_{25}F_3N_2O_5S_2$ [M + H], 495.1235, found 495.1240.

*4-[[(tert-Butylsulfinyl)amino](cyclopentyl)methyl]-2-phenyl-1,3-oxazol-5-yl Trifluoromethanesulfonate (**15**).* Purified with 30% ethyl acetate/hexanes, yielding 1.09g (65%) as yellow oil: IR (KBr, cm^{-1}) 2956, 2869, 1633, 1426, 1451, 1363, 1344, 1205, 1132, 1111, 1047, 943, 869, 798, 778, 718, 690, 697; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.97−7.99 (dd, *J* = 1.5 Hz, 1.96 Hz, 2H), 7.45−7.51 (m, 3H), 4.40−4.44 (dd, *J* = 3.9 Hz, 1H), 3.53(d, J = 3.8 Hz, 1H), 2.48−2.53 (m, 1H), 1.97−2.04 (m, 1H),1.47−1.73 (m,5H), 1.21−1.34 (m,2H), 1.18 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.1, 141.8, 139.9, 131.4, 128.9, 126.4, 126.1, 56.2, 54.9, 43.9, 30.3, 29.6, 25.2, 22.3; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{20}H_{25}F_3N_2O_5S_2$ [M + H] 495.1235, found 495.1232.

*5-[[(tert-Butylsulfinyl)amino](cyclohexyl)methyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**16**).* Purified with 30% ethyl acetate/hexanes, yielding 989 mg (57%) as yellow oil: IR (KBr, cm^{-1}) 3128, 2930, 2856, 2323, 1634, 1553, 1487, 1474, 1450, 1419, 1348, 1331, 1317, 1306, 1280, 1214, 1129, 1115, 1077, 1041, 943, 898, 861, 800, 778, 760, 745, 722, 690, 638; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.97−7.99 (dd, *J* = 1.5 Hz, 2.0 Hz, 2H), 7.45−7.51 (m, 3H), 4.39−4.43 (q, *J* = 5 Hz, 1H), 3.51 (d, *J* = 5 Hz, 1H), 1.99−2.02 (m, 1H), 1.86−1.93 (m, 1H), 1.70−1.85 (m, 2H), 1.61−1.69 (m, 1H), 1.20−1.35 (m, 3H), 1.19 (s, 9H), 1.05−1.13 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.2, 142.3, 139.3, 131.4, 129.9, 126.4, 126.1, 56.3, 55.9, 42.4, 30.3, 29.3, 26.1, 25.7, 22.4; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{21}H_{27}F_3N_2O_5S_2$ [M + H], 509.1392, found 509.1392

*5-[1-[(tert-Butylsulfinyl)amino]pentyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**17**).* Purified with 30% ethyl acetate/hexanes, yielding 1.05g (64%) as yellow oil: IR (KBr, cm^{-1}) 3133, 2961, 2871, 2324, 1639, 1554, 1451, 1425, 1363, 1348, 1318, 1212, 1128, 1098, 1077, 1046, 944, 927, 861, 779, 724, 690, 663, 612; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.97−7.99 (dd, *J* = 1.48 Hz, 1.88 Hz, 2H), 7.45−7.52 (m, 3H), 4.61−4.65 (m, 1H), 3.48 (d, *J* = 5.32 Hz, 1H), 2.01−2.06 (m, 2H), 1.30−1.48 (m, 4H), 1.20 (s, 9H), 0.89 (t, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.2, 141.7, 139.9, 131.4, 128.9, 126.8, 126.4, 120.1, 116.9, 56.3, 51.1, 34.5, 27.9, 22.2, 13.8; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{19}H_{25}F_3N_2O_5S_2$ [M + H] 483.1235, found 483.1229.

*5-[1-[(tert-Butylsulfinyl)amino]-3-methylbutyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**18**).* Purified with 30% ethyl acetate/hexanes, yielding 1.12g (68%) as yellow solid: IR (KBr, cm^{-1}) 3075, 2964, 2876, 2323, 2051, 1640, 1554, 1473, 1451, 1422, 1361, 1347, 1318, 1286, 1213, 1124, 1099, 1080, 1044, 1009, 943, 927, 887, 585, 781, 727, 709, 691, 664, 614; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.97−7.99 (dd, *J* = 1.3 Hz, 1.84 Hz, 2H), 7.45−7.51 (m, 3H), 4.68−4.72 (m, 1H), 3.43 (d, *J* = 5 Hz, 1H), 1.89−1.94 (m, 2H), 1.59−1.65 (m, 1H), 1.19 (s, 9H), 0.96−1.03 (m, 6H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.2, 140.1, 131.5, 128.9, 126.4, 126.1, 120.1, 116.9, 56.3, 49.3, 43.7, 24.9, 22.2, 21.9; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{19}H_{25}F_3N_2O_5S_2$ [M + H], 483.1235, found 483.1240.

*5-[1-[(tert-Butylsulfinyl)amino]-2,2-dimethylpropyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**19**).* Purified with 30% ethyl acetate/hexanes, yielding 650 mg (40%) as yellow solid: IR (KBr, cm^{-1}) 3328, 2960, 1689, 1631, 1557, 1475, 1427, 1367, 1343, 1322, 1290, 1225, 12121, 1133, 1060, 1025, 943, 911, 868, 802, 779, 725, 692, 659, 604; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.95−7.98 (dd, *J* = 1.2 Hz, 1.64 Hz, 2H), 7.48−7.51 (m, 3H), 4.41 (d, *J* = 4.6 Hz, 1H), 3.62 (d, *J* = 4.5 Hz, 1H), 1.18 (s, 9H), 1.11 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.3, 143.2, 138.3, 131.5, 129.1, 126.4, 126.1, 116.9, 59.2, 56.4, 36.3, 26.7, 22.3; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{19}H_{25}F_3N_2O_5S_2$ [M + H], 483.1235, found 483.1232.

*5-[2-(Benzyloxy)-1-[(tert-butylsulfinyl)amino]ethyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**20**).* Purified with 30% ethyl acetate/hexanes, yielding 559 mg (30%) of **20** as an inseparable1:1 mixture of diastereomers (yellow oil): IR (KBr, cm^{-1}) 3213, 3064, 3031, 2957, 2866, 1737, 1633, 1555, 1452, 1428, 1390, 1363, 1211,

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1132, 1068, 863, 777, 734, 695, 607; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 6.6 Hz, 2H), 7.44−7.51 (m, 4H), 7.27−7.37 (m, 13H), 4.89−4.92 (q, J = 5.4 Hz, 1H), 4.53−4.66 (m, 6H), 4.4 (d, J = 8.5 Hz, 1H), 4.15−4.18 (m,1H), 3.86−3.95 (m, 3H), 3.67−3.71(m, 1H), 3.59−3.61 (m, 1H), 3.54−3.56 (m, 1H), 3.41−3.48 (m, 1H), 3.36−3.39 (m, 1H), 1.18−1.25 (m 18H); ^{13}C NMR (400 MHz, $CDCl_3$) 165.9, 159.8, 138.9, 138.4, 131.7, 130.1, 129.1, 127.1, 125.7, 125.1, 87.5, 86.1, 73.4, 72.1, 70.3, 58.3, 57.1, 57.8, 50.6, 22.7, 22.3; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{23}H_{25}F_3N_2O_6S_2$ [M + H], 547.1184, found 547.1187.

*5-(2,2,9,9,10,10-Hexamethyl-3-oxido-7-oxa-3^4-thia-4-aza-9-silaundecan-5-yl)-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**21**).* Purified with 30% ethyl acetate/hexanes, yielding 558 mg (28%) of **21** as an inseparable 1:1 mixture of diastereomers (yellow oil): IR (KBr, cm^{-1}) 3191, 2954, 2928, 2857, 1636, 1605, 1555, 1471, 1430, 1389, 1362, 1345, 1226, 1068, 1006, 937, 833, 776, 719, 689; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.98 (dd, J = 1.4 Hz,1.84 Hz, 2H), 7.45−7.51 (m, 3H), 4.78−4.79 (q, J = 1.1 Hz, 1H), 4.55 (d, J = 3 Hz, 1H) ; 4.42−4.46 (m, 1H), 4.2 (d, J = 5.1 Hz, 1H), 4.02 (m, 1H), 3.85−3.92 (m, 2H), 3.76−3.77 (m, 1H), 3.63- 3.69 (m, 3H), 3.42−3.45 (m, 1H), 1.24 (s, 9H), 1.22 (s, 9H), 0.89 (m, 18H), 0.11−0.19 (m, 12H); ^{13}C NMR (400 MHz, $CDCl_3$)158.3, 142.7, 137.7, 131.9, 129.1, 126.4, 88.9, 87.4, 68.1, 66.3, 64.3, 56.7, 51.9, 31.9, 25.1, 22.9, 22.4, 18.7, 13.7; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{23}H_{35}F_3N_2O_6S_2Si$ [M + H] 571.1580, found 571.1587.

*5-[[(tert-Butylsulfinyl)amino](phenyl)methyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**22**).* Purified with 30% ethyl acetate/hexanes, yielding 959 mg (56%) as yellow oil: IR (KBr, cm^{-1}) 3176, 2959, 1633, 1554, 1486, 1450, 1427, 1347, 1316, 1209, 1131, 1115, 1065, 1026, 923, 864, 795, 777, 728, 714, 688, 663; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.99 (dd, J = 1.32 Hz, 1.76 Hz, 2H), 7.37−7.53 (m, 8H), 5.86 (d J = 3.7 Hz, 1H), 3.81 (d, J = 3.6 Hz, 1H), 1.26 (s, 9H), ^{13}C NMR (400 MHz, $CDCl_3$) 158.7, 142.2, 138.3, 137.3, 131.6, 129.4, 129.1, 128.9, 127.5, 126.5, 126.1, 120.1, 56.5, 53.8, 22.4; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{21}H_{21}F_3N_2O_5S_2$ [M + H] 503.0922, found 503.0924.

*5-[(4-bromophenyl)[(tert-butylsulfinyl)amino]methyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**23**).* Purified with 30% ethyl acetate/hexanes, yielding 753 mg (38%) as yellow oil: IR (KBr, cm^{-1}) 3174, 2960, 1735, 1633, 1590, 1554, 1487, 1450, 1428, 1346, 1316, 1210, 1131, 1116, 1068, 1009, 944, 865, 841, 78, 765, 716, 688, 640; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.99 (dd, J = 1.4 Hz, 1.68 Hz, 2H), 7.39−7.56 (m, 7H), 5.82 (d, J = 4.2 Hz, 1H), 3.79 (d, J = 4.2 Hz, 1H), 1.25 (s, 9H); ^{13}C NMR (400 MHz, $CDCl_3$) 158.9, 142.2, 137.7, 136.3, 132.4, 131.7, 129.7, 129.2, 126.5, 125.9, 123.4, 120.1, 56.7, 53.5, 22.4; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{21}H_{20}BrF_3N_2O_5S_2$ [M + H] 581.0027, found 581.0034.

*5-[[(tert-Butylsulfinyl)amino](4-fluorophenyl)methyl]-2-phenyl-1,3-oxazol-4-yl Trifluoromethanesulfonate (**24**).* Purified with 30% ethyl acetate/hexanes, yielding 1.05g (59%) as brownish red oil: IR (KBr, cm^{-1}) 3177, 2962, 2324, 1734, 1633, 1605, 1555, 1509, 1486, 1428, 1347, 1317, 1210, 1160, 1131, 1116, 1064, 944, 843, 779, 767, 730, 689; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95−7.97 (dd, J = 1.28 Hz, 1.76 Hz, 2H), 7.47−7.53 (m, 5H), 7.08−7.13 (t, J = 8.6 Hz, 2H), 5.85 (d, J = 4 Hz, 1H), 3.8 (d, J = 4 Hz, 1H), 1.26 (s, 9H), ^{13}C NMR (400 MHz, $CDCl_3$) 164.2, 161.7, 158.8, 142.2, 138.1, 134.4, 131.7, 129.1, 128.1, 126.5, 125.9, 120.1, 56.5, 53.3, 22.4; HRMS (Micromass Q-Tof Ultima API) mass calcd for $C_{21}H_{20}F_4N_2O_5S_2$ [M + H] 521.0828, found 521.0830

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra and X-ray data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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