Introduction

Azetidines are four membered nitrogen containing strained heterocycles of immense biological and pharmacological importance.\(^1\) Several racemic as well as chiral azetidines exhibit a diverse range of biological activities \(\text{e.g.}\) compounds 1–2 show inhibition properties against thrombin\(^{1a,b}\) 3 possesses potent protein kinase C inhibitory activity,\(^1c\) 4–5 exert inhibitory effects against the angiotensin-converting enzyme,\(^1d\) 6 is potentially capable of introducing some functional groups at the 3’-nitrogen atom, such as a fluorescent or a chemiluminescent probe, an intercalator and DNA scissors (Fig. 1).\(^1e\) Due to the high ring strain, the synthesis of substituted azetidines and further structural modifications still remain a challenge. However, many useful strategies have been developed for the synthesis of substituted azetidines.\(^2\) Imino-aldol reaction (addition of ester enolate to imine) is one of the prominent routes for the synthesis of \(\beta\)-amino esters,\(^3\) non-proteinogenic \(\beta\)-amino acids\(^4a,b\) and \(\beta\)-lactam antibiotics\(^4c\) \(\text{via}\) the formation of carbon–carbon bonds.\(^4d\) Lewis acid promoted reaction between a silyl enol ether and an imine is another useful method for the synthesis of \(\beta\)-amino esters.\(^5\) In most of the cases effective Lewis acid-activation of the aldimines is required because of poor electrophilicity of the stable \(N\)-substituted imines.\(^6\) Some other methods are also known to generate \(\beta\)-amino esters.\(^7\) Recently, the synthesis of 2,4-disubstituted azetidines \(\text{via}\) Lewis acid catalyzed imino-aldol reaction was reported,\(^8\) however, the substrate scope of the strategy is narrow. We have developed an efficient route to various racemic and nonracemic azetidines \(\text{via}\) imino-aldol reaction of ester enolates with \(N\)-sulfonyl or \(N\)-sulfinyl aldimines as the key step and describe our results in detail in this article.

Results and discussion

We envisioned that \(N\)-sulfonyl azetidine 5 could be synthesized easily from the precursor \(\beta\)-amino ester derivative 3 which would be obtained through imino-aldol reaction of 1 and 2 (Scheme 1).\(^9a\) We further anticipated that various chiral azetidines could be synthesized from chiral \(\beta\)-amino esters 10 which could easily be obtained from the imino-aldol reaction utilizing chiral sulfinimines 9 as the source of chirality.\(^9b\)
yields by refluxing a lytic amount of BF₃·OEt₂.

γ\-corresponding Nβ-directing group.

nyle auxiliary as a C\-directing group for the synthesis of taxol C-13 side chain\(^1\) and \(\alpha\)-amino acids, \(^{14}\) employing \(N\)-sulfinyl auxiliary as well as the stereo-directing group.

Initially, for the synthesis of \(\beta\)-amino esters a number of \(N\)-sulfonyl aldimines 2a-g (Scheme 2) were prepared in excellent yields by refluxing \(N\)-sulfonyl amine 6 and the corresponding aromatic aldehydes 7 in dry benzene in the presence of a catalytic amount of BF₃·OEt₂.

Next, the ester enolate from \(t\)-butyl acetate was generated by treatment with LDA and reacted with \(N\)-tosyl phenyl aldimine 2a to afford the corresponding addition product \(N\)-tosyl-\(\beta\)-amino ester 3a in quantitative yield. 3a was reduced to the corresponding \(\gamma\)-amino alcohol 4a by treatment with LiAlH₄.\(^{15}\) After the usual work up, the crude \(\gamma\)-amino alcohol 4a was treated with TsCl in the presence of excess KOH in THF under reflux conditions to produce 2-phenyl-\(N\)-tosyl azetidine 5a in excellent yield in a short period of time (Scheme 3).\(^{16}\) The Mitsunobu protocol\(^{16}\) was also found to be equally effective in the cyclization step for the synthesis of 5a from 4a, but the byproduct Ph₂P₀ generated in this reaction made the purification process difficult.

To generalize this strategy a number of \(N\)-sulfonyl aldimines 2b-g were reacted with different ester enolates leading to the formation of \(N\)-sulfonyl-\(\beta\)-amino esters 3b-k in excellent yields. Reduction of 3b-k with LAH followed by cyclization of the \(\gamma\)-amino alcohols 4b-k using TsCl and KOH in refluxing THF afforded the corresponding azetidines 5b-k in almost quantitative yields (Table 1). All the compounds 5a-k were characterized by spectroscopic data.

(Table 2) Enantiopure sulfinimines\(^{10}\) have been extensively used by the Davis group for the stereo-selective synthesis of \(\alpha\)-amino acids,\(^{11}\) \(N\)-sulfinyl-cis-aziridine-2-carboxylic acids,\(^{12}\) taxol C-13 side chain\(^1\) and \(\beta\)-amino acids\(^{14}\) employing \(N\)-sulfinyl auxiliary as well as the stereo-directing group.

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The present protocol was extended to provide azetidines with substitution both at 2- and 4-positions. For this purpose, compound 3a was converted to \(N\)-tosyl-\(\beta\)-amino aldehyde 7 by treatment with DIBAL-H. Next, compound 7 was reacted with ethylmagnesium bromide to afford the \(\gamma\)-amino alcohols 8a and 8b (dr 30:70) in 85% combined yield as a mixture of diastereomers. The pure diastereomers 8a and 8b were separated.
via flash column chromatography and they were individually reacted with tosyl chloride and KOH in THF to furnish diastereopure 2,4-disubstituted-N-tosyl azetidines 5i and 5m, respectively, in high yields (Scheme 4).

After the successful demonstration of our strategy for the synthesis of a variety of racemic azetidines 5a–m, we extended our protocol for the synthesis of chiral azetidines employing enantioselectively pure N-sulfinyl imines as the source of chirality. To optimize the reaction conditions for the imino aldol reaction, different bases (e.g. LDA, NaHMDS, and KHMDMS) and solvents were explored to generate the enolate from the methyl acetate ester. Among the bases studied, KHMDMS was found to be the best. The enolate generated from methyl acetate upon treatment with KHMDMS in THF at −78 °C was reacted with (S)-(+)N-sulfinimine10 9a (Ar = Ph) to produce the N-sulfinyl-β-amino ester 10a (de 84%) in 68% yield. The protocol was generalized with a number of (S)-(+)N-sulfinimines 9b–e to produce the corresponding imino-aldol products 10b–e in 65–93% yield and dr up to >99 : 1 (Table 2).

The addition product 10a was then converted into N-sulfinyl-γ-amino alcohol 11a by treatment with LAH. When 11a was reacted with tosyl chloride and KOH in THF under our optimized reaction conditions, (S,2R)-2-phenyl-N-sulfinyl azetidine 12a was obtained in 70% yield. Synthesis of four to six membered N-sulfinyl heterocycles via intramolecular alkylation of sulfinyl amides with alkyl halides has been reported in the literature.17 A number of enantiopure N-sulfinyl azetidines 12b–e were obtained in good yields and excellent diastereoselectivity from 11b–e following the same procedure (Table 3).

In order to ascertain the stereoselectivity (de/ee) of the products in the described imino-aldol reaction, as a representative example, β-amino ester 10a (de 84%) was converted to 2-phenyl-N-tosylazetidine (R)-5a as shown in Scheme 5. The N-sulfinyl auxiliary of 10a was removed by treatment with TFA in MeOH following a reported procedure18 (Scheme 5). The crude concentrate of the reaction mixture was treated with tosyl chloride and triethylamine in dichloromethane to produce

Table 3 Synthesis of γ-amino alcohols 11a–e and 2-aryl/alkyl-N-sulfinylazetidines 12a–e from N-sulfinyl-β-amino esters 10a–e

| Entry | Ester 10 (%) yield | Alcohol 11 (%) de | Azetidine 12 (%) yield | de e |
|-------|-------------------|------------------|----------------------|------|
| 1     | 10a               | 11a (95)          | 12a (70)             | >99% |
| 2     | 10b               | 11b (81)          | 12b (82)             | >99% |
| 3     | 10c               | 11c (75)          | 12c (85)             | >99% |
| 4     | 10d               | 11d (73)          | 12d (75)             | >99% |
| 5     | 10e               | 11e (78)          | 12e (81)             | >99% |

*12a–e were obtained as single diastereomers after column chromatography.

Scheme 5 Synthesis of chiral 2-aryl-N-tosylazetidine from chiral β-amino ester.
**Conclusions**

In summary, we have developed a simple and efficient synthetic route to a variety of 2-aryl-N-sulfonylazetidines and 2-alkyl/aryl-N-sulfinylazetidines utilizing imino-aldol reaction of ester enolates with N-sulfonfyl/chiral N-sulfinyl aldimines as the key step.

**Experimental**

**General remarks**

Analytical thin layer chromatography (TLC) was carried out using silica gel 60 F~254~ pre-coated plates. Visualization was accomplished with a UV lamp or I~2~ stain. Silica gel with a 230–400 mesh size was used for flash column chromatography using the combination of ethyl acetate and petroleum ether as the eluent. Unless noted, all reactions were carried out in oven-dried glassware under an atmosphere of nitrogen/argon using anhydrous solvents. Where appropriate, all reagents were purified prior to use following the guidelines of Perrin and Armero. All commercial reagents were used as received. Proton nuclear magnetic resonance (~1~H~ NMR~) spectra were recorded at 400 MHz/500 MHz. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethyl silane (δ 0.00). ~1~H~ NMR~ splitting patterns are designated as singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quartet (q), multiplet (m). Carbon nuclear magnetic resonance (~13~C~ NMR~) spectra were recorded at 100 MHz/125 MHz. Mass spectra (MS) were obtained using an ESI mass spectrometer (TOF). IR spectra were recorded in KBr for solids. Melting points were determined using a hot stage apparatus and are uncorrected. Optical rotations were measured using a 2.0 mL cell with a 1.0 dm path length and are reported as [α]D~25~ (c in g per 100 mL solvent) at 25 °C. Enantiomeric excess was determined by HPLC using a Chiralpak Cellulose 1 analytical column (detection at 254 nm).

**General procedure A: the addition of Li-enolate of ester to N-sulfinoniminne (Scheme 3, Table 1).** To a solution of diisopropylamine (4.24 mmol) in anhydrous tetrahydrofuran (15 mL), n-butyliithium (2.5 M solution in hexane, 4.24 mmol) was added slowly at 0 °C and the solution was stirred for 20 min at the same temperature. Then the reaction flask was placed at −78 °C bath and ester (1-butylacetate/ethyl isobutyrate) (4.24 mmol) was added. The reaction mixture was stirred for another hour at the same temperature. A solution of N-sulfonylaldimine 2a−g (3.86 mmol) in THF (10 mL) was added dropwise and stirring was continued for 2 h at the same temperature. The reaction was quenched with saturated aqueous NH~4~Cl solution (10 mL) at −78 °C, and the mixture was allowed to warm to rt. The reaction mixture was extracted with ethyl acetate (3 × 15 mL) and the combined organic phase was washed with saturated brine (10 mL), and dried over anhydrous Na~2~SO~4~. The organic layer was concentrated to give the crude product which was purified by silica gel column chromatography (ethyl acetate/petroleum ether) to afford β-amino esters 3a−k.

**General procedure B: the reduction of β-amino ester (3a−k) to γ-aminoalcohol (4a−k) (Scheme 3, Table 1).** To a suspension of lithium aluminium hydride (4.64 mmol) and dry THF (5.0 mL), a solution of β-amino ester 3a−k (2.32 mmol) dissolved in dry THF (10 mL) was slowly added at 0 °C and the mixture was stirred at rt for 1−1.5 h. Then it was quenched with ethyl acetate (5.0 mL) at 0 °C and the reaction mixture was filtered through a sintered funnel. Further, water (10 mL) was added to the filtrate resulting in the formation of a white precipitate which was separated again by filtration and washed with ethyl acetate 2−3 times. In the filtrate, the organic layer was separated and the aqueous layer was extracted with ethyl acetate (2 × 10 mL). The ethyl acetate layer was washed with brine solution (10 mL), and dried over anhydrous Na~2~SO~4~. The organic layer was concentrated to give the crude product which was purified by silica gel column chromatography (ethyl acetate/petroleum ether) to afford γ-amino alcohols 4a−k.

**General procedure C: the cyclization of γ-amino alcohols (4a−k) to 2-aryl-N-sulfonylazetidines (5a−k) (Scheme 3, Table 1).** To a suspension of powdered KOH (21.3 mmol) in dry THF (10 mL), a solution of 4a−k (7.1 mmol) in 25 mL dry THF was added. Then TsCl (7.81 mmol) was added portionwise at rt and the reaction mixture was refluxed for 30 min (for 1 h, as in Scheme 5 and Table 3). After completion of the reaction, cold water was added and the reaction mixture was extracted with ethyl acetate twice. The combined organic layer was washed with brine, dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The crude azetidines 5a−k were purified by column chromatography on silica gel using ethyl acetate and petroleum ether as the eluent.

**General procedure D: the addition of K-enolate of methyl acetate to N-(aryl/alkyl)idene-p-toluenesulfinamide (9a−e) (Table 2).** In a 25 mL dry two-necked round bottom flask fitted with a magnetic stir bar, a nitrogen balloon, and a rubber septum were placed 1.0 mL of anhydrous tetrahydrofuran (THF) and 1.64 M KH~2~MS (1.5 M solution in toluene) (0.45 mmol), and the solution was cooled to −78 °C. Then 0.07 mL (0.45 mmol) of methyl acetate was added slowly into the reaction vessel at the same temperature. The reaction mixture was stirred for another hour and a solution of 0.1 g (0.30 mmol) of aryl/alkyl-N-sulfinyl imine 9a−e in 1.0 mL of THF was added dropwise at −78 °C and the mixture was stirred for 8.5−10 h. Then the reaction was quenched with saturated NH~4~Cl solution (2.0 mL) at −78 °C, and the mixture was allowed to warm to rt. The mixture was extracted with ethyl acetate (3 × 4.0 mL) and the combined layer was washed with saturated brine (5.0 mL) and dried over anhydrous Na~2~SO~4~. The organic layer was concentrated to give the crude product.
which was purified by silica gel column chromatography (15% ethyl acetate/petroleum ether) to afford β-amino esters 10a-e.

2-Phenyl-1-tosylazetidine (5a). The general method C described above was followed when 4a (100 mg, 0.32 mmol) was reacted with KOH (54 mg, 0.96 mmol) and TSCl (67 mg, 0.35 mmol) under reflux in THF for 30 min to afford 92 mg of 5a as a white solid in 98% yield; mp 104–108 °C; Rf 0.52 (40% ethyl acetate/petroleum ether); IR \( \nu_{\text{max}} \) (KBr, cm\(^{-1}\)) 3062, 2982, 2936, 2934, 1595, 1466, 1394, 1354, 1430, 1302, 1280, 1246, 1217, 1174, 1121, 1088, 1087, 1018, 974, 930, 842; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 2.08–2.18 (m, 1H), 2.20–2.28 (m, 1H), 2.36 (s, 3H); 3.64–3.75 (m, 2H), 4.80 (t, \( J = 8.3 \) Hz, 1H), 7.19–7.35 (m, 7H), 7.61 (d, \( J = 8.0 \) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 21.6, 25.8, 47.2, 65.4, 126.3, 127.9, 128.4, 128.5, 129.6, 132.1, 140.5, 143.9; HRMS (ESI-TOF) calcld for C\(_{16}\)H\(_{18}\)NO\(_2\)S (M\(^+\) + H): 288.1058, found: 288.1056.

2-(2-Chlorophenyl)-1-tosylazetidine (5b). The general method C described above was followed when 4b (100 mg, 0.29 mmol) was reacted with KOH (48 mg, 0.87 mmol) and TSCl (61 mg, 0.32 mmol) under reflux in THF for 30 min to afford 90 mg of 5b as a white solid in 95% yield; mp 160–165 °C; Rf 0.35 (40% ethyl acetate/petroleum ether); IR \( \nu_{\text{max}} \) (KBr, cm\(^{-1}\)) 3064, 3030, 2985, 2928, 2876, 1596, 1574, 1490, 1460, 1408, 1386, 1342, 1298, 1265, 1234, 1180, 1129, 1088, 1065, 1042, 1014, 976, 912, 868, 835; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 1.95–1.99 (m, 1H), 2.37–2.42 (m, 1H), 2.42 (s, 3H), 3.63–3.70 (m, 1H), 3.74–3.79 (m, 1H), 5.14 (t, \( J = 8.3 \) Hz, 1H), 7.15–7.34 (m, 5H), 7.69 (d, \( J = 8.3 \) Hz, 2H), 7.85 (dd, \( J = 7.8, 1.8 \) Hz, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 21.6, 24.9, 47.5, 62.9, 127.1, 127.9, 128.6, 128.7, 128.9, 129.8, 131.0, 131.2, 138.3, 144.2; HRMS (ESI-TOF) calcld for C\(_{10}\)H\(_{14}\)CHO\(_2\)N\(_2\)O\(_3\)S (M\(^+\) + H): 322.0669, found: 322.0666.

2-(4-Nitrophenyl)-1-tosylazetidine (5e). The general method C described above was followed when 4e (100 mg, 0.28 mmol) was reacted with KOH (54 mg, 0.96 mmol) and TSCl (67 mg, 0.35 mmol) under reflux in THF for 30 min to afford 88 mg of 5f as a white solid in 93% yield; mp 126–128 °C; Rf 0.32 (20% ethyl acetate/petroleum ether); IR \( \nu_{\text{max}} \) (KBr, cm\(^{-1}\)) 3068, 2947, 2925, 2833, 1589, 1491, 1454, 1405, 1343, 1291, 1229, 1157, 1091, 1018, 956, 926, 841, 817; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 2.10–2.22 (m, 2H), 2.26–2.35 (m, 1H), 3.70–3.79 (m, 2H), 4.87 (t, \( J = 8.3 \) Hz, 1H), 7.08–7.34 (m, 7H), 7.70–7.73 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 25.7, 47.1, 65.8, 116.1, 126.2, 128.5, 130.9, 132.1, 146.1, 166.6; HRMS (ESI-TOF) calcld for C\(_{13}\)H\(_{16}\)FNO\(_3\)S (M\(^+\) + H): 290.0651, found: 290.0650.

1-(4-Methoxyphenylsulfonyl)-2-phenylazetidine (5g). The general method C described above was followed when 4g (100 mg, 0.31 mmol) was reacted with KOH (52 mg, 0.93 mmol) and TSCl (65 mg, 0.34 mmol) under reflux in THF for 30 min to afford 86 mg of 5g as a white solid in 91% yield; mp 116–118 °C; Rf 0.32 (35% ethyl acetate/petroleum ether); IR \( \nu_{\text{max}} \) (KBr, cm\(^{-1}\)) 3071, 3032, 3004, 2980, 2956, 2885, 2840, 1596, 1496, 1453, 1419, 1364, 1338, 1310, 1300, 1258, 1234, 1188, 1154, 1095, 1061, 1023, 956, 927, 832, 803; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 2.09–2.18 (m, 1H), 2.12–2.29 (m, 1H), 3.64–3.83 (m, 5H), 4.80 (t, \( J = 8.3 \) Hz, 1H), 6.90 (d, \( J = 8.0 \) Hz, 2H), 7.18–7.34 (m, 5H), 7.66 (d, \( J = 8.0 \) Hz, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 25.8, 47.0, 55.6, 65.3, 114.1, 126.3, 127.1, 127.9, 128.4, 130.5, 140.6, 163.3; HRMS (ESI-TOF) calcld for C\(_{17}\)H\(_{18}\)NO\(_3\)S (M\(^+\) + H): 304.1007, found: 304.1007.

1-(4-Tert-Butylphenylsulfonyl)-2-phenylazetidine (5h). The general method C described above was followed when 4h (100 mg, 0.28 mmol) was reacted with KOH (47 mg, 0.84 mmol) and TSCl (59 mg, 0.31 mmol) under reflux in THF for 30 min to afford 85 mg of 5h as a white solid in 90% yield; mp 122–124 °C; Rf 0.38 (20% ethyl acetate/petroleum ether); IR \( \nu_{\text{max}} \) (KBr, cm\(^{-1}\)) 3063, 3032, 2951, 1596, 1476, 1401, 1361, 1340, 1311, 1293, 1269, 1230, 1202, 1160, 1114, 1090, 1066.
3,3-Dimethyl-2-phenyl-1-tosylazetidine (5i). The general method C described above was followed when 4i (100 mg, 0.30 mmol) was reacted with KOH (50 mg, 0.90 mmol) and TsCl (63 mg, 0.33 mmol) under reflux in THF for 30 min to afford 90 mg of 5i as a white solid in 95% yield; mp 132–134 °C; Rf 0.38 (20% ethyl acetate/petroleum ether); IR ν_max (KBr, cm⁻¹) 3087, 3062, 3033, 2966, 2924, 2876, 1596, 1492, 1458, 1391, 1376, 1342, 1298, 1275, 1322, 1180, 1157, 1088, 1052, 1029, 1017, 975, 909, 869, 816, 802, 763; ¹H NMR (400 MHz, CDCl₃) δ 1.27 (s, 9H), 2.10–2.27 (m, 2H), 3.70–3.74 (m, 2H), 4.84 (t, J = 8.3 Hz, 1H), 7.18–7.24 (m, 5H), 7.43 (d, J = 8.3 Hz, 2H), 7.63 (d, J = 8.3 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 25.8, 31.1, 35.2, 47.0, 65.6, 125.9, 126.3, 127.9, 128.3, 128.4, 140.5, 156.8; HRMS (ESI-TOF) calc’d for C₁₉H₂₄NO₃S (M⁺ + H): 330.1528, found: 330.1526.

2-(2-Chlorophenyl)-3,3-dimethyl-1-tosylazetidine (5j). The general method C described above was followed when 4j (100 mg, 0.27 mmol) was reacted with KOH (46 mg, 0.81 mmol) and TsCl (57 mg, 0.30 mmol) under reflux in THF for 30 min to afford 90 mg of 5j as a white solid in 95% yield; mp 137–139 °C; Rf 0.47 (25% ethyl acetate/petroleum ether); IR ν_max (KBr, cm⁻¹) 3065, 3026, 2987, 2961, 2927, 2881, 1595, 1571, 1493, 1461, 1438, 1371, 1343, 1304, 1290, 1270, 1235, 1203, 1168, 1138, 1087, 1064, 1047, 1016, 976, 955, 905, 864, 849, 819, 763; ¹H NMR (400 MHz, CDCl₃) δ 0.71 (s, 3H), 0.96 (s, 3H), 2.40 (s, 3H), 3.34 (d, J = 7.6 Hz, 1H), 3.45 (d, J = 7.6 Hz, 1H), 4.89 (s, 1H), 7.13–7.27 (m, 3H), 7.32 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.0 Hz, 2H), 7.79 (d, J = 7.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 22.9, 27.6, 36.3, 60.7, 71.6, 126.7, 128.5, 128.6, 128.9, 129.5, 129.7, 131.9, 135.4, 144.1; HRMS (ESI-TOF) calc’d for C₁₉H₂₃ClNO₂S (M⁺ + H): 350.0982, found: 350.0982.

2-(4-Methoxyphenyl)-3,3-dimethyl-1-tosylazetidine (5k). The general method C described above was followed when 4k (100 mg, 0.27 mmol) was reacted with KOH (46 mg, 0.82 mmol) and TsCl (57 mg, 0.30 mmol) under reflux in THF for 30 min to afford 90 mg of 5k as a white solid in 94% yield; mp 141–143 °C; Rf 0.32 (25% ethyl acetate/petroleum ether); IR ν_max (KBr, cm⁻¹) 3069, 2968, 2873, 2836, 1594, 1515, 1452, 1392, 1372, 1335, 1235, 1177, 1157, 1109, 1089, 1065, 1037, 982, 933, 898, 873, 840, 812, 765; ¹H NMR (400 MHz, CDCl₃) δ 0.68 (s, 3H), 0.94 (s, 3H), 2.47 (s, 3H), 3.39 (d, J = 7.3 Hz, 1H), 4.19 (d, J = 7.3 Hz, 1H), 7.13–7.27 (m, 1H), 7.32 (m, 1H), 7.62–7.66 (m, 1H), 7.79 (d, J = 7.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 131.2, 131.6, 134.8, 156.8; HRMS (ESI-TOF) calc’d for C₁₉H₂₄NO₃S (M⁺ + H): 346.1477, found: 346.1474.

**Note:** The provided text appears to be a continuation of the previous page, discussing the NMR and IR spectra for various compounds, along with their physical properties and reaction conditions. The text is structured in a scientific manner, typical of a research paper, detailing the experimental procedures and results. The compounds are identified by their chemical structures and purity levels, with relevant physical and spectral data mentioned. The compounds are synthesized through various reactions, and their properties are measured using NMR and IR spectroscopy. The text reflects the systematic and methodical approach typical of chemical research publications. The focus is on the synthesis and characterization of these compounds, with specific emphasis on their spectral data and reaction conditions.
(S<sub>α</sub>,2R)<sup>α</sup>-(+)-2-(3-Bromophenyl)-1-(p-tolylsulfinyl)azetidine (12c). The general method C described above was followed when 11c (100 mg, 0.27 mmol) was reacted with KOH (46 mg, 0.81 mmol) and TsCl (57 mg, 0.30 mmol) under reflux in THF for 1 h to afford 81 mg of 12c as a white solid in 85% yield; mp 89−92 °C; R<sub>f</sub> 0.35 (30% ethyl acetate in petroleum ether); [α]<sup>D</sup> = +135.5 (c 0.62 in CH<sub>2</sub>Cl<sub>2</sub>) ([α]<sup>D</sup> = +135.5 (c 0.62 in CH<sub>2</sub>Cl<sub>2</sub>) IR ν<sub>max</sub> (KBr, cm<sup>−1</sup>) 2921, 2852, 1593, 1426, 1359, 1092, 1030, 810; 1<sup>H</sup> NMR (400 MHz, CDCl<sub>3</sub>, ppm): δ 2.13−2.19 (m, 1H), 2.36 (s, 3H), 2.65−2.68 (m, 1H), 3.89−3.96 (m, 1H), 5.19 (t, J = 8.0 Hz, 1H), 7.24−7.46 (m, 5H); 7.58 (d, J = 6.7 Hz, 1H), 8.07 (s, 1H); 13<sup>C</sup> NMR (100 MHz, CDCl<sub>3</sub>): δ 21.4, 26.4, 37.5, 60.8, 122.8, 125.3, 125.8, 126.8, 129.6, 130.2, 131.0, 139.3, 141.3, 143.9; HRMS (ESI-TOF) calcd for C<sub>16</sub>H<sub>18</sub>NO<sub>2</sub>S (M + H)<sup>+</sup> 288.1058, found: 288.1056; ee 84%. The enantiomeric excess was determined by chiral HPLC analysis (Cellulose 1, n-hexane/i-propanol = 90 : 10, flow rate = 1.0 mL min<sup>−1</sup>, t<sub>R</sub> (2) = 11.35 min (major).

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