Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 63 (2007) 3312–3320

Synthesis of *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans

Meng-Yang Chang,[a,*] Chun-Yu Lin[b] and Ching-Yi Hung[a]

[a]*Department of Applied Chemistry, National University of Kaohsiung, No. 700, Kaohsiung University Rd., Kaohsiung 811, Taiwan*
[b]*Department of Chemistry, National Sun Yat-Sen University, Kaohsiung 804, Taiwan*

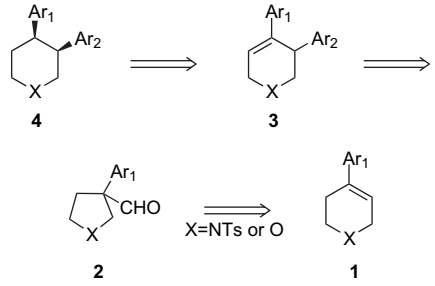
Received 18 January 2007; revised 13 February 2007; accepted 14 February 2007
Available online 20 February 2007

Abstract—Substituted *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans are synthesized in modest overall yields starting from 4-aryl-1,2,5,6-tetrahydropyridines and 4-aryl-1,2,5,6-tetrahydropyrans via the following sequence: (1) pinacol-type ring contraction having the combination of *m*-chloroperoxybenzoic acid and boron trifluoride etherate, (2) Grignard addition with arylmagnesium bromide reagents and followed by boron trifluoride etherate-mediated intramolecular ring-expanded rearrangement, and (3) hydrogenation with hydrogen on 10% palladium-activated carbon. A facile synthesis of 3,4-diarylpyridines was also described by base-induced aromatization.

1. Introduction

Depending on the substitution pattern and functionalization, different derived substitutents in the structural skeleton of piperidines[1] and tetrahydropyrans[2] with six-membered heterocyclic ring have been shown to be effective biologically active compounds. While a great number of piperidines, tetrahydropyrans, and their derivatives with this specific substitution pattern are of particular interest, more significant efforts toward the development of new methods for synthesizing different substituted piperidines[3] and tetrahydropyrans[4] are needed. In order to address this issue and continue our preliminary investigation,[5] we want to utilize this useful combination of *m*-chloroperoxybenzoic acid (MCPBA) and boron trifluoride etherate (BF_3-OEt_2) toward the frameworks of *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans.

As shown in Scheme 1, an easy synthetic approach of *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans starting from 4-aryl-1,2,5,6-tetrahydropyridine and 4-aryl-1,2,5,6-tetrahydropyran was described as the following sequence: (1) regioselective pinacol-type ring contraction with the combination of *m*-chloroperoxybenzoic acid and boron trifluoride etherate, (2) Grignard addition with different arylmagnesium bromide reagents, (3) boron trifluoride etherate-mediated regioselective rearrangement, and (4) hydrogenation with hydrogen in the presence of a catalytic amount of 10% palladium on activated carbon.



Scheme 1. Synthetic approach toward *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans.

2. Results and discussion

2.1. Synthesis of *cis*-3,4-diarylpiperidines and *cis*-3,4-diaryltetrahydropyrans

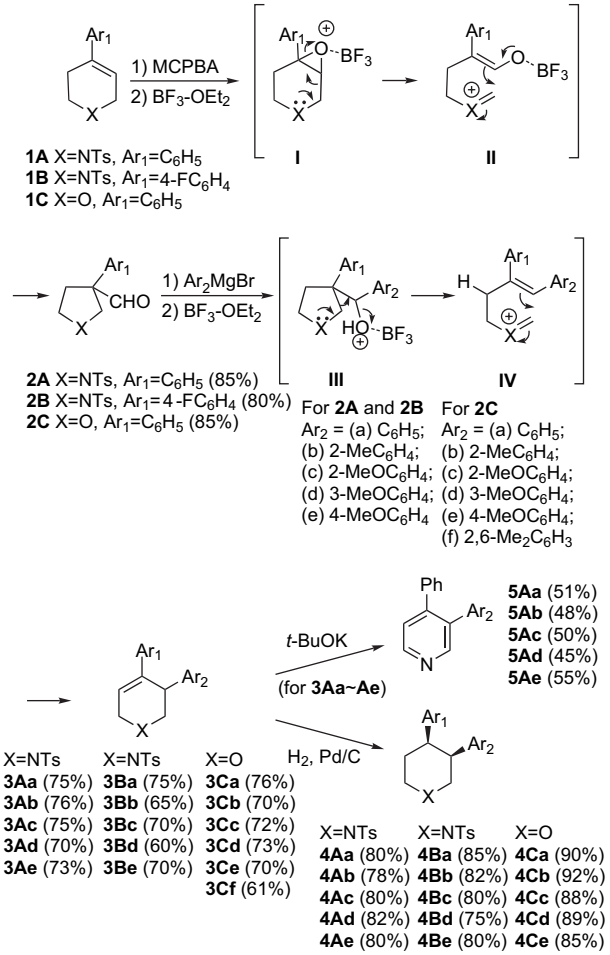
For the preparation of *cis*-3,4-diarylpiperidines **4Aa**–**4Ae** and **4Ba**–**4Be** and *cis*-3,4-diaryltetrahydropyrans **4Ca**–**4Ce**, three starting materials 4-aryl-1,2,5,6-tetrahydropyridines **1A** (Ar_1=C_6H_5) and **1B** (Ar_1=4-FC_6H_4) and 4-phenyl-1,2,5,6-tetrahydropyran **1C** were easily prepared from 1-tosylpiperidin-4-one and tetrahydro-4*H*-pyran-4-one via Grignard addition followed by dehydration. By our preliminary synthetic experiences,[5a–c] aldehydes **2A**–**2C** were first prepared by epoxidation of olefin **1A**–**1C** with

Keywords: *m*-Chloroperoxybenzoic acid; Boron trifluoride etherate; *cis*-3,4-Diarylpiperidines; *cis*-3,4-Diaryltetrahydropyrans; 3,4-Diarylpyridines.
* Corresponding author. Tel.: +886 7 5919464; fax: +886 7 5919348; e-mail: mychang@nuk.edu.tw

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.02.055

m-chloroperoxybenzoic acid at rt for 3 h followed by regioselective ring contraction of the resulting epoxides with boron trifluoride etherate at 0 °C for 15 min.

Next, Grignard addition of aldehydes **2A**–**2C** with different arylmagnesium bromide reagents (a, C_6H_5; b, 2-MeC_6H_4; c, 2-$MeOC_6H_4$; d, 3-$MeOC_6H_4$; e, 4-$MeOC_6H_4$; f, 2,6-$Me_2C_6H_3$) in tetrahydrofuran at −78 °C for 2 h yielded a pair of secondary alcohols in nearly 1:1 ratios (monitored by TLC plate) as shown in Scheme 2. Without purification, boron trifluoride etherate-mediated rearrangement of the resulting secondary alcohols afforded 4,5-diaryl-1,2,5,6-tetrahydropyridines **3Aa**–**3Ae** and **3Ba**–**3Be**, and 4,5-diaryl-1,2,5,6-tetrahydropyrans **3Ca**–**3Cf** at 0 °C for 2 h.



Scheme 2. Synthesis of *cis*-3,4-diarylpiperidines **4Aa**–**4Ae** and **4Ba**–**4Be**, *cis*-3,4-diaryltetrahydropyrans **4Ca**–**4Ce**, and 3,4-diarylpyridines **5Aa**–**5Ae**.

How is the regioselective rearrangement of ring contraction and ring expansion initiated by boron trifluoride etherate? During the ring-reconstructed structural migration of intermediate **I** with six-membered piperidine or tetrahydropyran ring and intermediate **III** with five-membered pyrrolidine or tetrahydrofuran ring, the most likely explanation would be that it is controlled by involvement of the heteroatom (nitrogen or oxygen) lone pair. We believed that heteroatom lone pair plays the important role to promote the occurrence of rearrangement reaction.[6] The resulting aldehydes **2A**–**2C** and olefins **3Aa**–**3Ae**, **3Ba**–**3Be**, and **3Ca**–**3Cf** were immediately formed as the sole products by the intramolecular rearrangement of intermediates **II** and **IV**. During two regioselective approaches, other rearranged frameworks were not observed under the boron trifluoride etherate-mediated condition.

Compounds **4Aa**–**4Ae**, **4Ba**–**4Be**, and **4Ca**–**4Ce** were easily obtained by the hydrogenation with hydrogen on 10% palladium-activated carbon at rt for 10 h (Scheme 2). The relative configuration of the structure of compound **4Cb** with two contiguous stereocenters is based on a single-crystal X-ray analysis as shown in Figure 1.[7] With the result in hand, the assignment of two diaryl functional groups on the other framework of 3,4-diarylpiperidines **4Aa**–**4Ae** and **4Ba**–**4Be**, and 3,4-diaryltetrahydropyrans **4Ca**–**4Ce** could be also arranged as the *cis* configuration.

To deserve to be mentioned, compounds **4Ad** and **4Bd** were the 4-arylpreclamol analogs. Preclamol was reported to be the first selective D_2-like dopamine autoreceptor agonist.[8] If the –CH_2O– motif was introduced into compounds **4Ba**–**Be** between 3-aryl group and piperidine skeleton during the structural modification, it would exhibit the structural characteristics of paroxetine. Paroxetine (Paxil/Seroxat) is a selective serotonin reuptake inhibitor used as an antidepressant and anti-Parkinson agent.[9]

With compounds **3Aa**–**3Ae** in hand, a facile synthesis of 3,4-diarylpyridines **5Aa**–**5Ae** via potassium *tert*-butoxide-mediated aromatization was also examined. Treatment of compounds **3Aa**–**3Ae** with potassium *tert*-butoxide in tetrahydrofuran at rt for 10 min afforded 3,4-diarylpyridines **5Aa**–**5Ae** in 45–55% yields.[10] In view of the experimental simplicity, the preparation of 3,4-diarylpiperidine **5Aa** was also conducted in a multigram scale (20 mmol) with 31% overall yield in three steps from aldehyde **2A**.

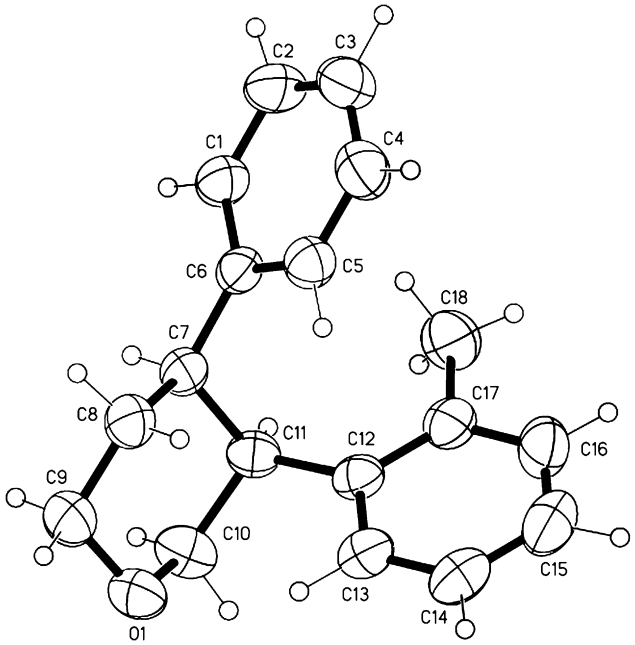
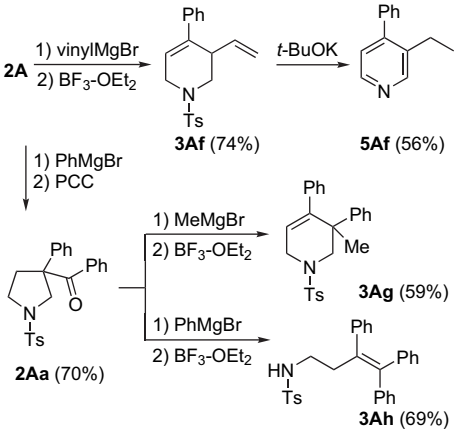


Figure 1. X-ray crystallography of compound **4Cb**.

2.2. Synthetic application toward compound 2A

When compound **2A** was treated by Grignard addition with vinylmagnesium bromide, ring-expanded rearrangement with boron trifluoride etherate, and aromatization of compound **3Af** with potassium *tert*-butoxide, the sole 3-ethyl-4-phenylpyridine **5Af** was obtained in 56% yield. The most likely explanation of reaction mechanism from compound **3Af** to compound **5Af** would be that terminal olefin isomerizes to internal olefin followed by desulfonation and aromatization under the basic condition. The aliphatic substitutent was also introduced on the skeleton of pyridine ring by our methods as shown in Scheme 3.



Scheme 3. Synthetic application of aldehyde **2A**.

In the other way, compound **2Aa** was afforded by treatment of ketone **2A** with Grignard addition of phenylmagnesium bromide and oxidation of pyridinium chlorochromate and Celite in 70% overall yields. With ketone **2Aa** in hand, the ring-expanded 3-methyl-3,4-diphenylpiperidine **3Ag** was still yielded by Grignard addition of ketone **2Aa** with methylmagnesium bromide followed by boron trifluoride etherate. Further, the ring-opening 3,4,4-triphenyl-3-buten-1-amine **3Ah** was isolated in 69% yield by Grignard addition of ketone **2Aa** with phenylmagnesium bromide followed by boron trifluoride etherate. Based on these results, we envisioned that geminal diaryl groups are the important substitutents, which easily provides a more stable benzylic cation in the overall process. It is worthy of note that compound **3Ah** is a Tamoxifen analog with interesting biological activities.[11]

3. Conclusion

In summary, we present a straightforward synthesis of *cis*-3,4-diarylpiperidines, *cis*-3,4-diaryltetrahydropyrans, and 3,4-diarylpyridines by the treatment of 4-aryl-1,2,5,6-tetrahydropyridines via the regioselective ring contraction, Grignard addition, regioselective ring expansion, and hydrogenation or aromatization sequence. The exhibited methodology provided a new approach for the preparation of substituted piperidines, tetrahydropyrans, and pyridines with potential biological activities. We are currently studying the scope of this process as well as additional applications of the method for the synthesis of 2-azatriphenylene.

4. Experimental section

4.1. General

Tetrahydrofuran (THF) was distilled prior to use. All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo.

4.2. A representative procedure for compounds 3Aa–3Ah, 3Ba–3Be, and 3Ca–3Cf

A solution of aryl- or vinyl- or methylmagnesium bromide (0.5 M in tetrahydrofuran, 1 mL) was added to a solution of compounds **2A**–**2C** (0.3 mmol) in tetrahydrofuran (5 mL) at −78 °C. The reaction mixture was stirred at rt for 2 h. The total procedure was monitored by TLC until the reaction was completed. Without further purification, boron trifluoride etherate (0.5 mL) was added to a stirred solution of the resulting reaction mixture at 0 °C. The reaction mixture was stirred at rt for 15 min. Saturated sodium bicarbonate solution (1 mL) was added to the reaction mixture and the solvent was concentrated. Water (2 mL) and ethyl acetate (10 mL) were added to the residue and the mixture was filtered through a short plug of Celite. The filtrate was concentrated. The residue was extracted with ethyl acetate (3×20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexane/ethyl acetate=10/1–6/1) afforded compounds **3Aa**–**3Ah**, **3Ba**–**3Be**, and **3Ca**–**3Cf**.

4.2.1. 1-(4-Methylphenylsulfonyl)-4,5-diphenyl-1,2,5,6-tetrahydropyridine (3Aa). Oil; IR ($CHCl_3$) 3027, 2923, 1598, 1346, 1161, 1106, 757 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J=8.0 Hz, 2H), 7.25–7.13 (m, 12H), 6.20 (t, J=3.5 Hz, 1H), 4.07 (br s, 1H), 4.03 (dd, J=3.5, 17.5 Hz, 1H), 3.75 (dt, J=2.5, 17.5 Hz, 1H), 3.49 (dd, J=4.5, 11.5 Hz, 1H), 3.34 (dd, J=4.5, 11.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.47, 140.82, 139.46, 137.74, 133.33, 129.53 (2×), 128.42 (2×), 128.40 (2×), 128.24 (2×), 127.69 (2×), 127.25, 126.77, 125.83 (2×), 121.40, 50.63, 45.29, 43.81, 21.49; HRMS (ESI) m/z calcd for $C_{24}H_{24}NO_2S$ (M^++1) 390.1528, found 390.1530; Anal. Calcd for $C_{24}H_{23}NO_2S$: C, 74.00; H, 5.95; N, 3.60. Found: C, 73.68; H, 6.15; N, 3.96.

4.2.2. 5-(2-Methylphenyl)-1-(4-methylphenylsulfonyl)-4-phenyl-1,2,5,6-tetrahydropyridine (3Ab). Oil; IR ($CHCl_3$) 3024, 2923, 1598, 1345, 1164, 1094, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J=8.0 Hz, 2H), 7.26 (d, J=8.0 Hz, 2H), 7.18–7.12 (m, 6H), 7.08–7.05 (m, 1H), 7.01–6.97 (m, 2H), 6.24 (t, J=3.5 Hz, 1H), 4.28 (br s, 1H), 3.98 (d, J=17.0 Hz, 1H), 3.84 (dt, J=2.5, 17.0 Hz, 1H), 3.40 (dd, J=4.5, 12.0 Hz, 1H), 3.30 (dd, J=4.5, 12.0 Hz, 1H), 2.43 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.44, 139.58, 138.34, 138.23, 134.95, 133.52, 130.42, 129.53 (2×), 128.43, 128.25 (2×), 127.65 (2×), 127.20, 126.67, 126.01, 125.54 (2×), 121.61, 48.88, 45.22, 39.65, 21.48, 19.51; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_2S$ (M^++1) 404.1684, found 404.1683; Anal.

Calcd for $C_{25}H_{25}NO_2S$: C, 74.41; H, 6.24; N, 3.47. Found: C, 74.59; H, 6.56; N, 3.13.

4.2.3. 5-(2-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenyl-1,2,5,6-tetrahydropyridine (3Ac). Mp=169–170 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3020, 2918, 1598, 1490, 1343, 1163, 1096, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J=8.0 Hz, 2H), 7.23–7.13 (m, 7H), 7.00 (dd, J=1.5, 7.5 Hz, 1H), 6.81 (t, J=8.0 Hz, 2H), 6.76 (d, J=7.5 Hz, 1H), 6.27 (t, J=3.5 Hz, 1H), 4.52 (br s, 1H), 4.09 (dd, J=3.5, 17.0 Hz, 1H), 3.86 (s, 3H), 3.69 (dt, J=2.5, 17.0 Hz, 1H), 3.61 (dd, J=3.5, 12.0 Hz, 1H), 3.18 (dd, J=3.5, 12.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.45, 143.23, 139.30, 137.59, 133.64, 129.56, 129.42 (2×), 128.49, 128.24 (2×), 127.80, 127.71 (2×), 127.24, 125.51 (2×), 121.33, 120.36, 110.07, 55.35, 48.60, 45.18, 36.25, 21.49; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_3S$ (M^++1) 420.1633, found 420.1635; Anal. Calcd for $C_{25}H_{25}NO_3S$: C, 71.57; H, 6.01; N, 3.34. Found: C, 71.40; H, 5.86; N, 3.66.

4.2.4. 5-(3-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenyl-1,2,5,6-tetrahydropyridine (3Ad). Oil; IR ($CHCl_3$) 3027, 2916, 1598, 1488, 1344, 1164, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J=8.5 Hz, 2H), 7.25 (d, J=8.5 Hz, 2H), 7.20–7.12 (m, 6H), 6.78 (d, J=8.0 Hz, 1H), 6.70 (dd, J=2.0, 8.0 Hz, 1H), 6.69 (s, 1H), 6.19 (t, J=4.0 Hz, 1H), 4.03 (br s, 1H), 4.01 (dd, J=3.5, 17.5 Hz, 1H), 3.76 (dt, J=2.5, 17.5 Hz, 1H), 3.72 (s, 3H), 3.49 (dd, J=4.0, 12.0 Hz, 1H), 3.35 (dd, J=4.0, 12.0 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.52, 143.46, 142.46, 139.50, 137.70, 133.45, 129.55 (2×), 129.34, 128.27 (2×), 127.69 (2×), 127.28, 125.81 (2×), 121.48, 120.92, 114.27, 112.03, 55.04, 50.52, 45.22, 43.79, 21.49; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_3S$ (M^++1) 420.1633, found 420.1634.

4.2.5. 5-(4-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenyl-1,2,5,6-tetrahydropyridine (3Ae). Oil; IR ($CHCl_3$) 3014, 2915, 1510, 1345, 1246, 1164, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J=8.5 Hz, 2H), 7.26 (d, J=8.5 Hz, 2H), 7.19–7.14 (m, 5H), 7.09 (d, J=8.5 Hz, 2H), 6.74 (d, J=8.5 Hz, 2H), 6.17 (t, J=3.5 Hz, 1H), 4.03 (dd, J=3.5, 17.5 Hz, 1H), 4.01 (br s, 1H), 3.75 (s, 3H), 3.72 (dt, J=2.0, 17.5 Hz, 1H), 3.46 (dd, J=4.5, 11.5 Hz, 1H), 3.29 (dd, J=4.5, 11.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.36, 143.45, 139.56, 138.03, 133.39, 132.91, 129.53 (2×), 129.35 (2×), 128.24 (2×), 127.71 (2×), 127.24, 125.84 (2×), 121.13, 113.81 (2×), 55.10, 50.78, 45.39, 43.01, 21.49; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_3S$ (M^++1) 420.1633, found 420.1634; Anal. Calcd for $C_{25}H_{25}NO_3S$: C, 71.57; H, 6.01; N, 3.34. Found: C, 71.71; H, 6.26; N, 3.59.

4.2.6. 1-(4-Methylphenylsulfonyl)-4-phenyl-5-vinyl-1,2,5,6-tetrahydropyridine (3Af). Oil; IR ($CHCl_3$) 3026, 2920, 1598, 1457, 1345, 1164, 1093, 764, 670 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J=8.5 Hz, 2H), 7.35–7.24 (m, 7H), 5.95 (t, J=3.5 Hz, 1H), 5.82 (ddd, J=7.5, 9.5, 17.0 Hz, 1H), 5.09 (d, J=17.0 Hz, 1H), 5.08 (d, J=11.0 Hz, 1H), 4.00 (dd, J=3.5, 17.0 Hz, 1H), 3.61 (dd, J=3.5, 11.5 Hz, 1H), 3.50 (dt, J=2.5, 17.0 Hz, 1H), 3.48–3.46 (m, 1H), 2.99 (dd, J=4.0, 11.5 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.61, 139.56, 137.90, 137.35, 133.14, 129.65 (2×), 128.31 (2×), 127.75 (2×), 127.44, 126.01 (2×), 120.30, 117.54, 48.20, 45.35, 41.41, 21.52; HRMS (ESI) m/z calcd for $C_{20}H_{22}NO_2S$ (M^++1) 340.1371, found 340.1376.

4.2.7. 5-Methyl-1-(4-methylphenylsulfonyl)-4,5-diphenyl-1,2,5,6-tetrahydropyridine (3Ag). Oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J=8.0 Hz, 2H), 7.40–7.38 (m, 2H), 7.33–7.25 (m, 5H), 7.16–7.10 (m, 3H), 6.93–6.91 (m, 2H), 5.97 (t, J=3.5 Hz, 1H), 4.03 (dd, J=4.0, 17.0 Hz, 1H), 3.69 (dd, J=3.0, 17.0 Hz, 1H), 3.41 (d, J=11.5 Hz, 1H), 2.92 (d, J=11.5 Hz, 1H), 2.42 (s, 3H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.05, 143.66, 143.39, 139.94, 133.48, 129.55 (2×), 128.21 (2×), 127.82 (2×), 127.68 (2×), 127.67 (2×), 127.25 (2×), 127.00, 126.65, 122.13, 57.76, 45.38, 43.57, 23.73, 21.51; HRMS (ESI) m/z calcd for $C_{25}H_{26}NO_2S$ (M^++1) 404.1684, found 404.1688.

4.2.8. 3,4,5-Triphenyl-3-butenyl-1-benzasulfonamide (3Ah). Oil; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J=8.5 Hz, 2H), 7.37–7.28 (m, 3H), 7.23–7.20 (m, 4H), 7.15–7.11 (m, 3H), 7.03–6.98 (m, 5H), 6.86–6.84 (m, 2H), 4.18 (t, J=6.0 Hz, 1H), 2.93 (q, J=7.0 Hz, 2H), 6.62 (t, J=7.0 Hz, 2H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.20, 142.49, 142.38, 142.09, 140.77, 136.73, 135.89, 130.40 (2×), 129.58 (2×), 129.33 (2×), 129.20 (2×), 128.45 (2×), 128.20 (2×), 127.48 (2×), 127.02, 127.00 (2×), 126.71, 126.17, 41.90, 35.52, 21.50; HRMS (ESI) m/z calcd for $C_{29}H_{28}NO_2S$ (M^++1) 454.1841, found 454.1840.

4.2.9. 4-(4-Fluorophenyl)-1-(4-methylphenylsulfonyl)-5-phenyl-1,2,5,6-tetrahydropyridine (3Ba). Oil; IR ($CHCl_3$) 3028, 2920, 1600, 1510, 1344, 1224, 1163, 1106, 970, 816, 758 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J=8.0 Hz, 2H), 7.26–7.13 (m, 9H), 6.86 (dd, J=8.5, 8.5 Hz, 2H), 6.14 (t, J=3.5 Hz, 1H), 4.01 (br s, 1H), 3.99 (d, J=3.0, 17.0 Hz, 1H), 3.75 (dt, J=3.0, 17.0 Hz, 1H), 3.45 (dd, J=4.5, 11.5 Hz, 1H), 3.36 (dd, J=4.5, 11.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.94, 160.97, 143.54, 140.56, 136.93, 135.61, 135.58, 133.29, 129.58 (2×), 128.48, 128.39, 127.69 (2×), 127.49, 127.43, 126.90, 121.39, 115.20, 115.03, 50.58, 45.24, 44.00, 21.49; HRMS (ESI) m/z calcd for $C_{24}H_{23}FNO_2S$ (M^++1) 408.1434, found 408.1437; Anal. Calcd for $C_{24}H_{22}FNO_2S$: C, 70.74; H, 5.44; N, 3.44. Found: C, 70.50; H, 5.63; N, 3.20.

4.2.10. 4-(4-Fluorophenyl)-5-(2-methylphenyl)-1-(4-methylphenylsulfonyl)-1,2,5,6-tetrahydropyridine (3Bb). Mp=150–151 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3024, 2923, 1600, 1510, 1344, 1164, 1094, 970, 817, 757, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, J=8.0 Hz, 2H), 7.26 (d, J=8.0 Hz, 2H), 7.12 (d, J=7.5 Hz, 1H), 7.08–7.06 (m, 3H), 7.01–6.96 (m, 2H), 6.85 (t, J=7.5 Hz, 2H), 6.17 (t, J=3.5 Hz, 1H), 4.23 (br s, 1H), 3.97 (d, J=17.0 Hz, 1H), 3.83 (dt, J=2.5, 17.0 Hz, 1H), 3.41 (dd, J=4.5, 12.0 Hz, 1H), 3.29 (dd, J=4.5, 12.0 Hz, 1H), 2.42 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.90, 160.94, 143.51, 138.09, 137.43, 135.75, 135.02, 130.52, 129.56 (2×), 128.39, 127.67 (2×), 127.21, 127.14, 126.81, 126.09, 121.62, 115.23, 115.06, 48.89, 45.19, 39.81, 21.49, 19.51; HRMS

(ESI) *m/z* calcd for $C_{25}H_{25}FNO_2S$ (M^++1) 422.2590, found 422.2593; Anal. Calcd for $C_{25}H_{24}FNO_2S$: C, 71.23; H, 5.74; N, 3.32. Found: C, 71.09; H, 5.46; N, 3.61.

4.2.11. 4-(4-Fluorophenyl)-5-(2-methoxyphenyl)-1-(4-methylphenylsulfonyl)-1,2,5,6-tetrahydropyridine (3Bc). Mp=155–156 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 1917, 1599, 1509, 1490, 1342, 1242, 1158, 1096, 816, 754, 666 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J*=8.0 Hz, 2H), 7.23 (d, *J*=8.0 Hz, 2H), 7.19–7.14 (m, 3H), 6.98 (dd, *J*=1.5, 8.0 Hz, 1H), 6.86 (t, *J*=8.5 Hz, 2H), 6.82 (d, *J*=8.0 Hz, 1H), 6.76 (t, *J*=8.0 Hz, 1H), 6.19 (t, *J*=3.5 Hz, 1H), 4.47 (br s, 1H), 4.06 (dd, *J*=3.0, 16.5 Hz, 1H), 3.86 (s, 3H), 3.68 (dt, *J*=3.0, 16.5 Hz, 1H), 3.57 (dd, *J*=3.5, 12.0 Hz, 1H), 3.19 (dd, *J*=3.5, 12.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.99, 161.04, 156.44, 143.30, 136.79, 135.43, 133.57, 129.45 (2×), 128.22, 127.94, 127.71 (2×), 127.14, 127.08, 121.20, 120.39, 115.17, 115.00, 110.12, 55.35, 48.60, 45.14, 36.34, 21.50; HRMS (ESI) *m/z* calcd for $C_{25}H_{25}FNO_3S$ (M^++1) 438.1539, found 438.1537; Anal. Calcd for $C_{25}H_{24}FNO_3S$: C, 68.63; H, 5.53; N, 3.20. Found: C, 68.78; H, 5.36; N, 3.59.

4.2.12. 4-(4-Fluorophenyl)-5-(3-methoxyphenyl)-1-(4-methylphenylsulfonyl)-1,2,5,6-tetrahydropyridine (3Bd). Oil; IR ($CHCl_3$) 3019, 2917, 1599, 1509, 1217, 1163, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J*=8.0 Hz, 2H), 7.26 (d, *J*=8.0 Hz, 2H), 7.16–7.12 (m, 3H), 6.86 (t, *J*=8.5 Hz, 2H), 6.75 (d, *J*=8.0 Hz, 1H), 6.71 (dd, *J*=2.5, 8.5 Hz, 1H), 6.67 (br s, 1H), 6.13 (t, *J*=3.5 Hz, 1H), 3.99–3.96 (m, 2H), 3.80–3.72 (m, 1H), 3.72 (s, 3H), 3.45 (dd, *J*=4.0, 11.5 Hz, 1H), 3.36 (dd, *J*=4.0, 11.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.01, 159.57, 143.51, 142.20, 136.89, 135.60, 133.40, 129.58 (2×), 129.44, 127.69 (2×), 127.47, 127.40, 121.46, 120.88, 115.24, 115.06, 114.35, 112.03, 55.07, 50.49, 45.18, 43.97, 21.51; HRMS (ESI) *m/z* calcd for $C_{25}H_{25}FNO_3S$ (M^++1) 438.1539, found 438.1539; Anal. Calcd for $C_{25}H_{24}FNO_3S$: C, 68.63; H, 5.53; N, 3.20. Found: C, 68.50; H, 5.90; N, 3.43.

4.2.13. 4-(4-Fluorophenyl)-5-(4-methoxyphenyl)-1-(4-methylphenylsulfonyl)-1,2,5,6-tetrahydropyridine (3Be). Oil; IR ($CHCl_3$) 2907, 1509, 1339, 1162, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J*=8.5 Hz, 2H), 7.26 (d, *J*=5.0 Hz, 2H), 7.14 (dd, *J*=5.0, 8.5 Hz, 2H), 7.06 (d, *J*=8.5 Hz, 2H), 6.86 (t, *J*=8.5 Hz, 2H), 6.75 (d, *J*=8.5 Hz, 2H), 6.11 (t, *J*=3.5 Hz, 1H), 4.00 (d, *J*=17.0 Hz, 1H), 3.95 (br s, 1H), 3.76 (s, 3H), 3.72 (dt, *J*=2.5, 17.0 Hz, 1H), 3.42 (dd, *J*=4.0, 11.5 Hz, 1H), 3.30 (dd, *J*=4.0, 11.5 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.45, 143.51, 137.23, 133.34, 132.62, 135.70, 135.68, 129.56 (2×), 129.34 (2×), 127.71 (2×), 127.50, 127.43, 121.11, 115.21, 115.03, 113.87 (2×), 55.12, 50.73, 45.25, 43.20, 21.51; HRMS (ESI) *m/z* calcd for $C_{25}H_{25}FNO_3S$ (M^++1) 438.1539, found 438.1540; Anal. Calcd for $C_{25}H_{24}FNO_3S$: C, 68.63; H, 5.53; N, 3.20. Found: C, 68.88; H, 5.72; N, 3.44.

4.2.14. 3,4-Diphenyl-3,6-dihydro-2*H*-pyran (3Ca). Mp=75–76 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3025, 2916, 1600, 1493, 1445, 1127, 749, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.31–7.14 (m, 10H), 6.36 (t, *J*=2.5 Hz, 1H), 4.51 (dt, *J*=2.5, 17.5 Hz, 1H), 4.43 (dt, *J*=2.5, 17.5 Hz, 1H), 4.05 (dd, *J*=4.0, 11.0 Hz, 1H), 3.92 (dd, *J*=4.0, 11.0 Hz, 1H), 3.87 (br s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.03, 139.53, 136.32, 128.40 (2×), 128.38 (2×), 128.26 (2×), 127.09, 126.48, 125.55 (2×), 124.44, 71.47, 66.21, 43.21; HRMS (ESI) *m/z* calcd for $C_{17}H_{17}O$ (M^++1) 237.1280, found 237.1282; Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.65; H, 6.68.

4.2.15. 3-(2-Methylphenyl)-4-phenyl-3,6-dihydro-2*H*-pyran (3Cb). Oil; IR ($CHCl_3$) 3022, 2923, 1601, 1492, 1459, 1127, 1077, 760, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25–7.13 (m, 7H), 7.09–7.04 (m, 2H), 6.40 (t, *J*=2.5 Hz, 1H), 4.52 (dt, *J*=2.5, 17.0 Hz, 1H), 4.43 (dt, *J*=2.5, 17.0 Hz, 1H), 4.12 (br s, 1H), 4.04 (dd, *J*=4.0, 11.0 Hz, 1H), 3.83 (dd, *J*=4.0, 11.0 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.63, 139.40, 136.72, 134.96, 130.36, 128.43, 128.30 (2×), 127.06, 126.41, 126.03, 125.30 (2×), 124.67, 69.85, 66.24, 39.02, 19.64; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}O$ (M^++1) 251.1436, found 251.1434; Anal. Calcd for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found: C, 86.58; H, 7.06.

4.2.16. 3-(2-Methoxyphenyl)-4-phenyl-3,6-dihydro-2*H*-pyran (3Cc). Oil; IR ($CHCl_3$) 2913, 1489, 1457, 1241, 1130, 1028, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J*=7.5 Hz, 2H), 7.21 (t, *J*=7.5 Hz, 2H), 7.16–7.13 (m, 3H), 6.86 (d, *J*=8.5 Hz, 1H), 6.81 (t, *J*=7.5 Hz, 1H), 6.42 (t, *J*=2.5 Hz, 1H), 4.49 (dd, *J*=2.5, 17.0 Hz, 1H), 4.43 (dt, *J*=2.5, 17.0 Hz, 1H), 4.37 (br s, 1H), 3.97 (dd, *J*=3.5, 11.0 Hz, 1H), 3.93 (dd, *J*=3.5, 11.0 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.58, 139.34, 136.22, 129.72, 129.51, 128.24 (2×), 127.46, 127.04, 125.23 (2×), 124.51, 120.40, 110.09, 69.89, 66.23, 55.37, 35.38; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}O_2$ (M^++1) 267.1385, found 267.1385; Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.29; H, 7.03.

4.2.17. 3-(3-Methoxyphenyl)-4-phenyl-3,6-dihydro-2*H*-pyran (3Cd). Oil; IR 2916, 1600, 1488, 1261, 1151, 1045, 755, 699 ($CHCl_3$) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J*=7.0 Hz, 2H), 7.24–7.14 (m, 4H), 6.87 (d, *J*=7.5 Hz, 1H), 6.82 (br s, 1H), 6.71 (dd, *J*=3.0, 8.0 Hz, 1H), 6.35 (t, *J*=2.5 Hz, 1H), 4.50 (dd, *J*=2.5, 17.5 Hz, 1H), 4.41 (dt, *J*=2.5, 17.5 Hz, 1H), 4.04 (dd, *J*=4.0, 11.0 Hz, 1H), 3.93 (dd, *J*=4.0, 11.0 Hz, 1H), 3.80 (br s, 1H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.56, 143.70, 139.54, 136.25, 129.31, 128.29 (2×), 127.10, 125.53 (2×), 124.47, 120.92, 114.54, 111.47, 71.37, 66.18, 55.07, 43.19; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}O_2$ (M^++1) 267.1385, found 267.1388; Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.95; H, 6.98.

4.2.18. 3-(4-Methoxyphenyl)-4-phenyl-3,6-dihydro-2*H*-pyran (3Ce). Oil; IR ($CHCl_3$) 2914, 1610, 1510, 1302, 1247, 1032, 828, 748 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J*=8.0 Hz, 2H), 7.24–7.14 (m, 5H), 6.79 (d, *J*=8.5 Hz, 2H), 6.33 (t, *J*=2.5 Hz, 1H), 4.49 (dd, *J*=2.5, 17.0 Hz, 1H), 4.41 (dt, *J*=2.5, 17.0 Hz, 1H), 4.02 (dd, *J*=4.0, 11.0 Hz, 1H), 3.89 (dd, *J*=2.5, 11.0 Hz, 1H), 3.82 (br s, 1H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$)

δ 158.19, 139.61, 136.61, 134.13, 129.31 (2×), 128.26 (2×), 127.06, 125.56 (2×), 124.24, 113.81 (2×), 71.63, 66.19, 55.15, 42.35; HRMS (ESI) *m/z* calcd for $C_{18}H_{19}O_2$ (M^++1) 267.1385, found 267.1388; Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.29; H, 6.70.

4.2.19. 3-(2,6-Dimethylphenyl)-4-phenyl-3,6-dihydro-2*H*-pyran (3Cf). Oil; IR ($CHCl_3$) 2907, 1238, 1457, 1216, 754, 696 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.20–7.05 (m, 5H), 6.99 (d, *J*=7.5 Hz, 1H), 6.93 (d, *J*=7.5 Hz, 1H), 6.74 (d, *J*=7.5 Hz, 1H), 6.14 (dd, *J*=3.0, 5.5 Hz, 1H), 4.64–4.61 (m, 1H), 4.47 (t, *J*=3.0 Hz, 2H), 4.09 (dd, *J*=6.0, 12.0 Hz, 1H), 3.84 (dd, *J*=9.5, 12.0 Hz, 1H), 2.53 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.77, 139.42, 137.11, 136.85, 136.01, 130.18, 128.35, 127.98 (2×), 126.92, 126.43, 125.33 (2×), 123.09, 67.65, 66.04, 38.92, 21.41, 20.29; HRMS (ESI) *m/z* calcd for $C_{19}H_{21}O$ (M^++1) 265.1592, found 265.1597.

4.3. A representative procedure for compounds 4Aa–4Ae, 4Ba–4Be, and 4Ca–4Ce

Palladium (10%) on activated carbon (5 mg) was added to a stirring solution of compounds **3Aa**–**3Ae** or **3Ba**–**3Be** or **3Ca**–**3Ce** (0.2 mmol) in methanol (10 mL). Then hydrogen was bubbled into the mixture for 10 min and the reaction mixture was continued to stir at rt for 10 h. The catalyst was filtered through a short plug of Celite and washed with methanol (2×10 mL). The combined organic layers were evaporated to afford crude product. Purification on silica gel (hexane/ethyl acetate=10/1) afforded compounds **4Aa**–**4Ae**, **4Ba**–**4Be**, and **4Ca**–**4Ce**.

4.3.1. *cis*-1-(4-Methylphenylsulfonyl)-3,4-diphenylpiperidine (4Aa). Mp=142–143 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3027, 2918, 1493, 1452, 1352, 1339, 1165, 1095, 755, 717 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J*=8.0 Hz, 2H), 7.38 (d, *J*=8.0 Hz, 2H), 7.14–7.07 (m, 8H), 6.71–6.69 (m, 2H), 4.18–4.12 (m, 2H), 3.12 (br s, 1H), 2.91 (ddd, *J*=3.5, 4.5, 13.0 Hz, 1H), 2.82 (dd, *J*=4.0, 11.5 Hz, 1H), 2.50 (dt, *J*=2.5, 11.5 Hz, 1H), 2.48 (s, 3H), 2.30 (dq, *J*=4.0, 13.0 Hz, 1H), 1.71 (dd, *J*=3.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.64, 142.48, 139.26, 132.32, 130.01 (2×), 129.66 (2×), 127.96 (2×), 127.88 (2×), 127.79 (2×), 127.40 (2×), 126.42, 126.40, 50.88, 47.15, 45.88, 44.90, 24.88, 21.57; HRMS (ESI) *m/z* calcd for $C_{24}H_{26}NO_2S$ (M^++1) 392.1684, found 392.1687; Anal. Calcd for $C_{24}H_{25}NO_2S$: C, 73.62; H, 6.44; N, 3.58. Found: C, 73.82; H, 6.56; N, 3.70.

4.3.2. *cis*-3-(2-Methylphenyl)-1-(4-methylphenylsulfonyl)-4-phenylpiperidine (4Ab). Oil; IR ($CHCl_3$) 3026, 2926, 1492, 1351, 1341, 1168, 1094, 920, 760, 715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J*=8.0 Hz, 1H), 7.70 (d, *J*=8.0 Hz, 2H), 7.37 (d, *J*=8.0 Hz, 2H), 7.21 (t, *J*=8.0 Hz, 1H), 7.11–7.01 (m, 4H), 6.85 (d, *J*=7.5 Hz, 1H), 6.60 (d, *J*=7.5 Hz, 2H), 4.12–4.09 (m, 1H), 3.98 (d, *J*=12.0 Hz, 1H), 3.43 (br s, 1H), 2.93 (dt, *J*=4.0, 12.5 Hz, 1H), 2.86 (dd, *J*=4.0, 11.5 Hz, 1H), 2.58 (dt, *J*=2.5, 11.5 Hz, 1H), 2.48 (s, 3H), 2.43 (dt, *J*=4.0, 12.5 Hz, 1H), 1.69 (dd, *J*=4.0, 11.5 Hz, 1H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.58, 142.29, 138.52, 137.32, 132.42, 129.73, 129.62 (2×), 129.30, 128.15 (2×), 127.94 (2×), 127.70 (2×), 126.56, 126.46, 125.80, 50.93, 47.02, 46.06, 38.46, 26.19, 21.55, 19.38; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_2S$ (M^++1) 406.1841, found 406.1843; Anal. Calcd for $C_{25}H_{27}NO_2S$: C, 74.04; H, 6.71; N, 3.45. Found: C, 74.23; H, 6.91; N, 3.26.

4.3.3. *cis*-3-(2-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenylpiperidine (4Ac). Mp=170–171 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 2918, 1491, 1352, 1245, 1164, 1094, 758, 715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, *J*=1.5, 8.0 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 2H), 7.37 (d, *J*=8.0 Hz, 2H), 7.14 (dt, *J*=1.5, 8.0 Hz, 1H), 7.04–7.03 (m, 3H), 6.95 (dt, *J*=1.0, 7.5 Hz, 1H), 6.67–6.65 (m, 2H), 6.48 (d, *J*=1.0, 7.5 Hz, 1H), 4.10–4.06 (m, 1H), 3.99 (dt, *J*=2.0, 11.5 Hz, 1H), 3.82–3.80 (m, 1H), 3.01 (s, 3H), 2.91 (ddd, *J*=3.5, 4.5, 12.5 Hz, 1H), 2.82 (dd, *J*=4.0, 11.5 Hz, 1H), 2.51 (dt, *J*=2.5, 11.5 Hz, 1H), 2.47 (s, 3H), 2.35 (dt, *J*=4.5, 13.0 Hz, 1H), 1.67 (dd, *J*=3.5, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.88, 143.54, 142.93, 132.39, 130.01, 129.61 (2×), 128.70, 127.96 (2×), 127.83 (2×), 127.47, 127.22 (2×), 126.01, 120.19, 109.55, 54.49, 50.86, 47.11, 45.45, 34.85, 25.70, 21.56; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_3S$ (M^++1) 422.1790, found 422.1787; Anal. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46; N, 3.32. Found: C, 71.46; H, 6.32; N, 3.58.

4.3.4. *cis*-3-(3-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenylpiperidine (4Ad). Mp=199–200 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 2913, 1597, 1337, 1165, 754, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J*=8.5 Hz, 2H), 7.38 (d, *J*=8.5 Hz, 2H), 7.15–7.12 (m, 3H), 7.00 (d, *J*=8.0 Hz, 2H), 6.76–6.72 (m, 2H), 6.69 (dd, *J*=2.5, 8.5 Hz, 1H), 6.63 (br s, 1H), 4.18 (d, *J*=11.0 Hz, 1H), 4.15–4.11 (m, 1H), 3.60 (s, 3H), 3.11 (br s, 1H), 2.93 (dt, *J*=4.0, 12.5 Hz, 1H), 2.81 (dd, *J*=4.0, 12.0 Hz, 1H), 2.50 (d, *J*=2.5, 11.0 Hz, 1H), 2.47 (s, 3H), 2.30 (dt, *J*=4.0, 12.5 Hz, 1H), 1.73 (dq, *J*=2.5, 12.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.56, 143.62, 142.54, 140.64, 132.43, 129.66 (2×), 128.28, 127.93 (4×), 127.83 (2×), 126.45, 122.46, 114.94, 112.88, 55.03, 50.81, 47.11, 45.87, 44.80, 24.96, 21.56; HRMS (ESI) *m/z* calcd for $C_{25}H_{28}NO_3S$ (M^++1) 422.1790, found 422.1792; Anal. Calcd for $C_{25}H_{27}NO_3S$: C, 71.23; H, 6.46; N, 3.32. Found: C, 71.50; H, 6.68; N, 3.44.

4.3.5. *cis*-3-(4-Methoxyphenyl)-1-(4-methylphenylsulfonyl)-4-phenylpiperidine (4Ae). Mp=185–186 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3027, 2952, 1610, 1596, 1463, 1338, 1250, 1182, 1163, 1034, 954, 755, 713 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J*=8.5 Hz, 2H), 7.38 (d, *J*=8.5 Hz, 2H), 7.14–7.11 (m, 3H), 7.03 (d, *J*=8.5 Hz, 2H), 6.73–6.71 (m, 2H), 6.64 (d, *J*=8.5 Hz, 2H), 4.14 (d, *J*=11.5 Hz, 2H), 3.75 (s, 3H), 3.08 (br s, 1H), 2.89 (dt, *J*=4.0, 14.0 Hz, 1H), 2.79 (dd, *J*=4.0, 11.5 Hz, 1H), 2.50–2.45 (m, 1H), 2.47 (s, 3H), 2.29 (dt, *J*=4.0, 13.0 Hz, 1H), 1.70 (dd, *J*=2.5, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.00, 143.62, 142.61, 131.36, 130.96 (2×), 129.63 (2×), 127.90 (2×), 127.86 (2×), 127.80 (3×), 126.34, 112.72 (2×), 55.05, 51.16, 47.16, 45.92, 44.06, 24.79, 21.53; HRMS (ESI)

m/z calcd for $C_{25}H_{28}NO_3S$ (M^++1) 422.1790, found 422.1791.

4.3.6. *cis*-4-(4-Fluorophenyl)-1-(4-methylphenylsulfonyl)-3-phenylpiperidine (4Ba). Mp=165–166 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3028, 2925, 1600, 1510, 1339, 1224, 1168, 1096, 954, 759 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J*=8.0 Hz, 2H), 7.37 (d, *J*=8.0 Hz, 2H), 7.16–7.10 (m, 5H), 6.80 (dd, *J*=8.5, 8.5 Hz, 2H), 6.63 (dd, *J*=8.5, 8.5 Hz, 2H), 4.14 (d, *J*=12.0 Hz, 2H), 3.07 (br s, 1H), 2.91 (dt, *J*=4.0, 13.0 Hz, 1H), 2.80 (dd, *J*=4.0, 12.0 Hz, 1H), 2.48 (dt, *J*=2.5, 11.5 Hz, 1H), 2.47 (s, 3H), 2.26 (dq, *J*=4.0, 13.0 Hz, 1H) 1.68 (dq, *J*=4.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.40, 160.45, 143.68, 139.05, 138.21, 132.27, 130.01 (2×), 129.66 (2×), 129.16, 127.93 (2×), 127.52 (2×), 126.53, 114.73, 114.56, 50.77, 47.08, 45.17, 44.90, 25.16, 21.55; HRMS (ESI) *m/z* calcd for $C_{24}H_{25}FNO_2S$ (M^++1) 410.1590, found 410.1593; Anal. Calcd for $C_{24}H_{24}FNO_2S$: C, 70.39; H, 5.91; N, 3.42. Found: C, 70.61; H, 5.83; N, 3.60.

4.3.7. *cis*-4-(4-Fluorophenyl)-3-(2-methylphenyl)-1-(4-methylphenylsulfonyl)piperidine (4Bb). Oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J*=7.5 Hz, 1H), 7.69 (d, *J*=8.0 Hz, 2H), 7.37 (d, *J*=8.0 Hz, 2H), 7.22 (t, *J*=7.5 Hz, 1H), 7.10 (t, *J*=7.5 Hz, 1H), 6.87 (d, *J*=7.5 Hz, 1H), 6.72 (dd, *J*=8.5, 9.0 Hz, 2H), 6.54 (dd, *J*=8.5, 9.0 Hz, 2H), 4.10 (d, *J*=9.5 Hz, 1H), 3.97 (d, *J*=11.5 Hz, 1H), 3.39 (br s, 1H), 2.92 (dt, *J*=4.5, 12.5 Hz, 1H), 2.84 (dd, *J*=4.5, 11.5 Hz, 1H), 2.56 (dt, *J*=3.0, 11.5 Hz, 1H), 2.47 (s, 3H), 2.38 (dq, *J*=3.0, 12.0 Hz, 1H), 1.66 (dq, *J*=3.0, 12.0 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.56, 160.62, 143.64, 138.29, 137.17, 132.39, 129.87, 129.64 (2×), 129.45, 129.30, 127.96 (2×), 126.63, 125.95, 114.57, 114.41, 109.46, 50.86, 47.00, 45.30, 38.36, 26.47, 21.57, 19.50; HRMS (ESI) *m/z* calcd for $C_{25}H_{27}FNO_2S$ (M^++1) 424.1747, found 424.1750; Anal. Calcd for $C_{25}H_{26}FNO_2S$: C, 70.89; H, 6.19; N, 3.31. Found: C, 71.02; H, 6.33; N, 3.52.

4.3.8. *cis*-4-(4-Fluorophenyl)-3-(2-methoxyphenyl)-1-(4-methylphenylsulfonyl)piperidine (4Bc). Oil; IR ($CHCl_3$) 2917, 1597, 1509, 1338, 1244, 1162, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, *J*=1.5, 7.5 Hz, 1H), 7.79 (d, *J*=8.0 Hz, 2H), 7.47 (d, *J*=8.0 Hz, 2H), 7.25 (dt, *J*=1.5, 7.5 Hz, 1H), 7.06 (t, *J*=7.5 Hz, 1H), 6.83 (dd, *J*=8.5, 9.0 Hz, 2H), 6.71 (dd, *J*=5.5, 8.5 Hz, 2H), 6.60 (d, *J*=8.5 Hz, 1H), 4.21–4.17 (m, 1H), 4.09 (d, *J*=11.5 Hz, 1H), 3.88–3.85 (m, 1H), 3.20 (s, 3H), 2.99 (dt, *J*=4.0, 12.5 Hz, 1H), 2.89 (dd, *J*=4.0, 11.5 Hz, 1H), 2.60 (dd, *J*=3.5, 12.0 Hz, 1H), 2.57 (s, 3H), 2.40 (dq, *J*=3.5, 13.0 Hz, 1H), 1.74 (dq, *J*=3.5, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.30, 156.72, 143.60, 138.63, 132.33, 130.03, 129.63 (2×), 129.18, 129.12, 128.37, 127.96 (2×), 127.64, 120.27, 113.95, 113.79, 109.46, 54.45, 50.80, 47.08, 44.71, 34.72, 25.87, 21.57; HRMS (ESI) *m/z* calcd for $C_{25}H_{27}FNO_3S$ (M^++1) 440.1696, found 440.1701; Anal. Calcd for $C_{25}H_{26}FNO_3S$: C, 68.31; H, 5.96; N, 3.19. Found: C, 68.65; H, 6.11; N, 3.42.

4.3.9. *cis*-4-(4-Fluorophenyl)-3-(3-methoxyphenyl)-1-(4-methylphenylsulfonyl)piperidine (4Bd). Mp=152–153 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 2917, 1659, 1509, 1338, 1195, 923, 717 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, *J*=8.5 Hz, 2H), 7.38 (d, *J*=8.0 Hz, 2H), 7.01 (t, *J*=8.5 Hz, 1H), 6.82 (t, *J*=8.5 Hz, 2H), 6.72 (br s, 1H), 6.69–6.66 (m, 4H), 4.16 (d, *J*=11.5 Hz, 1H), 4.13 (d, *J*=11.5 Hz, 1H), 3.66 (s, 3H), 3.05 (br s, 1H), 2.91 (dt, *J*=4.0, 12.0 Hz, 1H), 2.79 (dd, *J*=4.0, 12.0 Hz, 1H), 2.50–2.46 (m, 1H), 2.47 (s, 3H), 2.26 (dq, *J*=4.0, 13.0 Hz, 1H), 1.69 (dq, *J*=4.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.45, 160.51, 158.72, 143.67, 140.48, 132.42, 129.69 (2×), 129.21, 129.15, 128.39, 127.91 (2×), 122.55, 115.10, 114.78, 114.61, 112.79, 55.08, 50.74, 47.07, 45.19, 44.84, 25.31, 21.57; HRMS (ESI) *m/z* calcd for $C_{25}H_{27}FNO_3S$ (M^++1) 440.1696, found 440.1698; Anal. Calcd for $C_{25}H_{26}FNO_3S$: C, 68.31; H, 5.96; N, 3.19. Found: C, 68.50; H, 6.23; N, 3.45.

4.3.10. *cis*-4-(4-Fluorophenyl)-3-(4-methoxyphenyl)-1-(4-methylphenylsulfonyl)piperidine (4Be). Oil; IR ($CHCl_3$) 2916, 1510, 1334, 1250, 1163, 548 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J*=8.0 Hz, 2H), 7.37 (d, *J*=8.0 Hz, 2H), 7.02 (d, *J*=8.5 Hz, 2H), 6.81 (t, *J*=8.5 Hz, 2H), 6.67–6.63 (m, 4H), 4.12 (d, *J*=11.0 Hz, 2H), 3.75 (s, 3H), 3.02 (br s, 1H), 2.85 (dd, *J*=4.0, 13.0 Hz, 1H), 2.77 (dd, *J*=4.0, 12.0 Hz, 1H), 2.47 (s, 3H), 2.43 (dd, *J*=3.0, 15.0 Hz, 1H), 2.22 (dq, *J*=4.0, 13.0 Hz, 1H), 1.67–1.65 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.54, 158.13, 143.66, 138.36, 132.27, 131.12, 131.01 (2×), 129.66 (2×), 129.20, 129.15, 127.93 (2×), 114.76, 114.59, 112.86 (2×), 55.10, 51.09, 47.15, 44.13, 30.94, 25.11, 21.57; HRMS (ESI) *m/z* calcd for $C_{25}H_{27}FNO_3S$ (M^++1) 440.1696, found 440.1697.

4.3.11. *cis*-3,4-Diphenyltetrahydropyran (4Ca). Oil; IR ($CHCl_3$) 3085, 3061, 3027, 2951, 1602, 1493, 1452, 1190, 1126, 1095, 1013, 765 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.17–7.07 (m, 8H), 6.81–6.79 (m, 2H), 4.36 (dd, *J*=11.5 Hz, 1H), 4.31 (dd, *J*=3.0, 11.5 Hz, 1H), 4.04 (dd, *J*=3.0, 11.5 Hz, 1H), 3.72 (dt, *J*=2.5, 11.5 Hz, 1H), 3.32 (dt, *J*=4.5, 13.0 Hz, 1H), 2.98 (br s, 1H), 2.28 (dq, *J*=4.5, 13.0 Hz, 1H), 1.55 (dd, *J*=2.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.25, 140.67, 130.19 (2×), 127.82 (4×), 127.18 (2×), 126.17, 125.97, 72.53, 68.71, 46.55, 45.56, 26.04; HRMS (ESI) *m/z* calcd for $C_{17}H_{19}O$ (M^++1) 239.1436, found 239.1441; Anal. Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.86; H, 7.76.

4.3.12. *cis*-3-(2-Methylphenyl)-4-phenyltetrahydropyran (4Cb). Mp=126–127 °C (recrystallized from hexane and ethyl acetate); ^1H NMR (500 MHz, $CDCl_3$) δ 8.19 (dd, *J*=1.0, 7.5 Hz, 1H), 7.22 (t, *J*=7.5 Hz, 1H), 7.15–7.06 (m, 4H), 6.87 (d, *J*=7.5 Hz, 1H), 6.71 (d, *J*=8.5 Hz, 2H), 4.33 (ddd, *J*=2.0, 4.0, 11.0 Hz, 1H), 4.26 (d, *J*=11.5 Hz, 1H), 4.04 (dd, *J*=2.5, 12.5 Hz, 1H), 3.75 (dt, *J*=2.5, 11.5 Hz, 1H), 3.32 (dt, *J*=4.5, 12.5 Hz, 1H), 3.25 (br s, 1H), 2.42 (dq, *J*=4.5, 13.5 Hz, 1H), 1.52 (dd, *J*=2.5, 13.5 Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.10, 139.90, 137.67, 129.80, 129.59, 128.19 (2×), 127.67 (2×), 126.35, 126.17, 125.44, 72.80, 68.72, 46.05, 40.18, 27.31, 19.39; HRMS (ESI) *m/z* calcd for $C_{18}H_{21}O$ (M^++1) 253.1592, found 253.1596; Anal. Calcd for $C_{18}H_{20}O$: C, 85.67; H, 7.99. Found: C, 85.93; H, 8.22. Single-crystal X-ray diagram: crystal of compound **4Cb** was grown by slow diffusion of ethyl acetate into a solution of compound

4Cb in dichloromethane to yield colorless prism. The compound crystallizes in the monoclinic crystal system. Space group $P2(1)/c$, a=9.8430(19) Å, b=5.8261(11) Å, c=24.461(5) Å, V=1401.3(5) Å^3, Z=4, d_{calcd}=1.196 mg/m^3, absorption coefficient=0.072 mm^{-1}, R indices (all data) R_1=0.0706, wR_2=0.1333, $F(000)$=544, 2θ range (1.67–28.35°).

4.3.13. *cis*-3-(2-Methoxyphenyl)-4-phenyltetrahydropyran (4Cc). Mp=81–82 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 2913, 1577, 1488, 1261, 1093, 774, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (dd, J=1.5, 8.0 Hz, 1H), 7.14 (dt, J=1.5, 7.5 Hz, 1H), 7.10–7.05 (m, 3H), 6.94 (dt, J=1.0, 7.5 Hz, 1H), 6.77–6.75 (m, 2H), 6.49 (dd, J=1.0, 8.5 Hz, 1H), 4.29 (ddd, J=2.0, 4.5, 11.0 Hz, 1H), 4.24 (d, J=11.5 Hz, 1H), 4.01 (dd, J=3.5, 12.0 Hz, 1H), 3.70 (dt, J=2.5, 11.5 Hz, 1H), 3.60 (t, J=4.0 Hz, 1H), 3.28 (dt, J=3.5, 13.0 Hz, 1H), 3.00 (s, 3H), 2.32 (dq, J=4.5, 13.0 Hz, 1H), 1.49 (dd, J=2.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.13, 143.75, 130.49, 130.05, 127.87 (2×), 127.16 (3×), 125.78, 119.81, 109.50, 72.74, 68.76, 54.41, 45.35, 36.83, 26.78; HRMS (ESI) m/z calcd for $C_{18}H_{21}O_2$ (M^++1) 269.1542, found 269.1545; Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.72; H, 7.35.

4.3.14. *cis*-3-(3-Methoxyphenyl)-4-phenyltetrahydropyran (4Cd). Mp=102–103 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 2960, 1608, 1510, 1455, 1259, 1093, 802 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18–7.13 (m, 3H), 7.01 (t, J=8.0 Hz, 1H), 6.84–6.82 (m, 2H), 6.75 (d, J=7.5 Hz, 1H), 6.67 (dd, J=2.0, 8.0 Hz, 1H), 6.56 (t, J=2.0 Hz, 1H), 4.35 (d, J=11.5 Hz, 1H), 4.29 (dd, J=2.5, 11.5 Hz, 1H), 4.01 (dd, J=3.0, 11.5 Hz, 1H), 3.70 (dt, J=2.0, 11.5 Hz, 1H), 3.57 (s, 3H), 3.31 (dt, J=4.5, 13.0 Hz, 1H), 2.95 (br s, 1H), 2.27 (dq, J=4.5, 13.0 Hz, 1H), 1.56–1.54 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.47, 143.30, 142.13, 128.04, 127.87 (2×), 127.84 (2×), 126.19, 122.69, 115.57, 112.01, 72.41, 68.68, 54.96, 46.57, 45.53, 26.03; HRMS (ESI) m/z calcd for $C_{18}H_{21}O_2$ (M^++1) 269.1542, found 269.1544; Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.74; H, 7.80.

4.3.15. *cis*-3-(4-Methoxyphenyl)-4-phenyltetrahydropyran (4Ce). Oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18–7.12 (m, 3H), 7.50 (d, J=9.0 Hz, 2H), 6.81–6.79 (m, 2H), 6.63 (d, J=9.0 Hz, 2H), 4.32 (d, J=11.5 Hz, 1H), 4.30–4.28 (m, 1H), 4.01 (dd, J=3.0, 11.5 Hz, 1H), 3.74 (s, 3H), 3.69 (dt, J=2.0, 11.5 Hz, 1H), 3.27 (dt, J=4.0, 12.5 Hz, 1H), 2.92 (br s, 1H), 2.25 (dq, J=4.0, 13.0 Hz, 1H), 1.53 (dd, J=2.0, 13.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.81, 54.42, 143.78, 142.14 (2×), 138.87 (2×), 138.83 (2×), 137.12, 123.54 (2×), 83.80, 79.73, 66.07, 56.74, 56.64, 37.03; HRMS (ESI) m/z calcd for $C_{18}H_{21}O_2$ (M^++1) 269.1542, found 269.1546; Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.42; H, 7.67.

4.4. A representative procedure for compounds 5Aa–5Af

Potassium *tert*-butoxide (50 mg, 0.45 mmol) was added to a stirring solution of olefins **3Aa–3Af** (0.1 mmol) in tetrahydrofuran (10 mL). The reaction mixture was stirred at rt for 20 min. Water (1 mL) was added to the residue and the reaction mixture was concentrated. The residue was extracted with ethyl acetate (3×20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexane/ethyl acetate=20/1) afforded compounds **5Aa–5Af**.

4.4.1. 3,4-Diphenylpyridine (5Aa).[12a] Mp=116–117 °C (recrystallized from hexane and ethyl acetate) (lit.[12a] mp=113–114 °C); IR ($CHCl_3$) 3058, 3025, 1585, 1473, 1445, 1399, 1074, 761, 577 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (s, 1H), 8.64 (d, J=5.0 Hz, 1H), 7.39 (d, J=5.0 Hz, 1H), 7.31–7.26 (m, 6H), 7.18–7.15 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.33, 148.37, 147.97, 138.37, 137.39, 136.05, 129.77 (2×), 129.29 (2×), 128.31 (4×), 128.00, 127.45, 124.79; HRMS (ESI) m/z calcd for $C_{17}H_{14}N$ (M^++1) 232.1126, found 232.1130; Anal. Calcd for $C_{17}H_{13}N$: C, 88.28; H, 5.67; N, 6.06. Found: C, 88.43; H, 5.82; N, 6.35.

4.4.2. 3-(2-Methylphenyl)-4-phenylpyridine (5Ab). Oil; IR ($CHCl_3$) 3059, 3024, 1584, 1472, 1443, 1398, 1076, 1003, 840, 728, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, J=5.0 Hz, 1H), 8.54 (s, 1H), 7.40 (d, J=5.0 Hz, 1H), 7.25–7.10 (m, 9H), 1.88 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.06, 148.61, 148.30, 138.52, 137.23, 136.15, 135.64, 130.60, 130.06, 128.84 (2×), 128.14 (2×), 127.94, 127.88, 125.68, 124.01, 19.91; HRMS (ESI) m/z calcd for $C_{18}H_{16}N$ (M^++1) 246.1283, found 246.1288; Anal. Calcd for $C_{18}H_{15}N$: C, 88.13; H, 6.16; N, 5.71. Found: C, 88.40; H, 6.35; N, 5.42.

4.4.3. 3-(2-Methoxyphenyl)-4-phenylpyridine (5Ac). Oil; IR ($CHCl_3$) 3027, 2934, 1584, 1493, 1461, 1251, 1026, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (d, J=5.0 Hz, 1H), 8.59 (s, 1H), 7.36 (d, J=5.0 Hz, 1H), 7.29 (dt, J=1.5, 8.0 Hz, 2H), 7.25–7.22 (m, 2H), 7.19 (dd, J=1.5, 7.5 Hz, 1H), 7.16–7.14 (m, 2H), 6.97 (t, J=7.0 Hz, 1H), 6.74 (d, J=8.0 Hz, 1H), 3.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.37, 151.11, 149.08, 148.39, 139.43, 132.83, 131.40, 129.42, 128.27 (2×), 127.87 (2×), 127.61, 126.71, 123.89, 120.66, 110.86, 54.83; HRMS (ESI) m/z calcd for $C_{18}H_{16}NO$ (M^++1) 262.1232, found 262.1232; Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.98; H, 5.61; N, 5.20.

4.4.4. 3-(3-Methoxyphenyl)-4-phenylpyridine (5Ad). Oil; IR ($CHCl_3$) 3028, 2936, 1588, 1471, 1322, 1221, 1045, 779, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.63 (d, J=5.0 Hz, 1H), 7.37 (d, J=5.0 Hz, 1H), 7.30–7.27 (m, 3H), 7.19–7.17 (m, 3H), 6.82 (dd, J=2.5, 8.5 Hz, 1H), 6.76 (d, J=7.5 Hz, 1H), 6.67 (t, J=2.5 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.33, 150.35, 148.20, 138.75, 138.47, 135.83, 129.33, 129.20 (2×), 128.31 (3×), 127.96, 124.70, 122.20, 115.15, 113.40, 55.10; HRMS (ESI) m/z calcd for $C_{18}H_{16}NO$ (M^++1) 262.1232, found 262.1234.

4.4.5. 3-(4-Methoxyphenyl)-4-phenylpyridine (5Ae).[12b] Mp=133–134 °C (recrystallized from hexane and ethyl acetate); IR ($CHCl_3$) 3030, 2957, 1609, 1514, 1474, 1293, 1223, 1178, 1036, 831, 751, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.59 (d, J=5.0 Hz, 1H), 7.33 (d,

J=5.0 Hz, 1H), 7.29–7.27 (m, 3H), 7.18–7.16 (m, 2H), 7.07 (d, J=9.0 Hz, 2H), 6.81 (d, J=9.0 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.93, 150.76, 148.06, 147.70, 138.73, 135.44, 130.87 (2×), 129.81, 129.24 (2×), 128.28 (2×), 127.77, 124.63, 113.76 (2×), 55.17; HRMS (ESI) m/z calcd for $C_{18}H_{16}NO$ (M^++1) 262.1232, found 262.1234; Anal. Calcd for $C_{18}H_{15}NO$: C, 82.73; H, 5.79; N, 5.36. Found: C, 82.92; H, 5.92; N, 5.53.

4.4.6. 3-Ethyl-4-phenylpyridine (5Af).[12c] Oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (br s, 1H), 8.51 (d, J=5.0 Hz, 1H), 7.52–7.46 (m, 3H), 7.36 (d, J=5.0 Hz, 1H), 7.34–7.32 (m, 2H), 2.73 (q, J=7.5 Hz, 2H), 1.16 (t, J=7.5 Hz, 3H); HRMS (ESI) m/z calcd for $C_{13}H_{14}N$ (M^++1) 184.1126, found 184.1132.

Acknowledgements

The authors would like to thank the National Science Council (NSC 95-2113-M-390-003-MY2) of the Republic of China for financial support.

References and notes

1. (a) Baliah, V.; Jeyraman, R.; Chandrasekaran, L. *Chem. Rev.* **1983**, *83*, 379; (b) Buffat, M. G. P. *Tetrahedron* **2004**, *60*, 1701; (c) Weintraub, P. M.; Sabol, J. S.; Kane, J. M.; Borcherding, D. R. *Tetrahedron* **2003**, *59*, 2953; (d) Henry, G. D. *Tetrahedron* **2004**, *60*, 6043.
2. (a) Tamaruya, Y.; Suzuki, M.; Kamura, G.; Kanai, M.; Hama, K.; Shimizu, K.; Aoki, J.; Arai, H.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2004**, *21*, 2834; (b) Kuehne, M. E.; Bornmann, W. G.; Marko, I.; Qin, Y.; LeBoulluec, K. L.; Frasier, D. A.; Xu, F.; Mulamba, T.; Ensinger, C. L.; Borman, L. S.; Huot, A. E.; Exon, C.; Bizzarro, F. T.; Cheung, J. B.; Bane, S. L. *Org. Biomol. Chem.* **2003**, *1*, 2120; (c) Yokomatsu, T.; Hayakawa, Y.; Kihara, T.; Koyanagi, S.; Soeda, S.; Shimeno, H.; Shibuya, S. *Bioorg. Med. Chem.* **2000**, *8*, 2571; (d) Suto, M. J.; Stier, M. A.; Werbel, L. M.; Arundel-Suto, C. M.; Leopold, W. R.; Elliott, W. E.; Sebolt-Leopold, J. S. *J. Med. Chem.* **1991**, *34*, 2484.
3. (a) Johnson, T. A.; Jang, D. O.; Slafer, B. W.; Curtis, M. D.; Beak, P. *J. Am. Chem. Soc.* **2002**, *124*, 11689; (b) Lee, S. J.; Beak, P. *J. Am. Chem. Soc.* **2006**, *128*, 2178; (c) Sicre, C.; Alonso-Gomez, J. L.; Cid, M. M. *Tetrahedron* **2006**, *62*, 11063.
4. (a) Bernardi, A.; Dotti, P.; Poli, G.; Scolastico, C. *Tetrahedron* **1992**, *48*, 5597; (b) Cakir, S. P.; Mead, K. T.; Smith, L. T.; Zakharova, I. S.; Lyssenko, K. A.; Kuleshova, L. N.; Antipin, M. Y. *Tetrahedron Lett.* **2003**, *44*, 6355; (c) Minowa, N.; Mukaiyama, T. *Chem. Lett.* **1987**, 1719; (d) Funk, R. L.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1980**, *102*, 5245; (e) Yamaguchi, M.; Tsukamoto, M.; Tanaka, S.; Hirao, I. *Tetrahedron Lett.* **1984**, *25*, 5661; (f) Rosiak, A.; Frey, W.; Christoffers, J. *Eur. J. Org. Chem.* **2006**, 4044; (g) Harkat, H.; Weibel, J.-M.; Pale, P. *Tetrahedron Lett.* **2007**, *48*, 1439.
5. (a) Chang, M. Y.; Pai, C. L.; Kung, Y. H. *Tetrahedron Lett.* **2005**, *46*, 8463; (b) Chang, M. Y.; Pai, C. L.; Kung, Y. H. *Tetrahedron Lett.* **2006**, *47*, 855; (c) Chang, M. Y.; Pai, C. L.; Lin, C. Y. *Tetrahedron Lett.* **2006**, *47*, 3641; (d) Chang, M. Y.; Lin, C. Y.; Pai, C. L. *Heterocycles* **2006**, *68*, 1941; (e) Chang, M. Y.; Kung, Y. H.; Ma, C. C.; Chen, S. T. *Tetrahedron Lett.* **2007**, *48*, 199.
6. (a) Chang, M. Y.; Wang, S. Y.; Pai, C. L. *Tetrahedron Lett.* **2006**, *47*, 6389; (b) Chang, M. Y.; Kung, Y. H.; Chen, S. T. *Tetrahedron Lett.* **2006**, *47*, 4865 and cited references therein.
7. CCDC 624867 (**4Cb**) contains the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: 44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).
8. (a) Astra, P. *Drugs Future* **1987**, *12*, 88; (b) Wikstrom, H.; Sanchez, D.; Lindberg, P.; Hacksell, U.; Arvidsson, L.-E.; Johansson, A. M.; Thorberg, S.-O.; Nilsson, J. L. G.; Svensson, K.; Hjorth, S.; Clark, D.; Carlsson, A. *J. Med. Chem.* **1984**, *27*, 1030; (c) Liljefors, T.; Wikstrom, H. *J. Med. Chem.* **1986**, *29*, 1896.
9. (a) Dechant, K. L.; Clissold, S. P. *Drugs* **1991**, *41*, 225; (b) Chen, C. Y.; Chang, B. R.; Tasi, M. R.; Chang, M. Y.; Chang, N. C. *Tetrahedron* **2003**, *59*, 9383; (c) Brandau, S.; Landa, A.; Franzen, J.; Marigo, M.; Jorgensen, K. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4305 and cited references therein.
10. (a) Karig, G.; Spencer, J. A.; Gallagher, T. *Org. Lett.* **2001**, *6*, 835 and cited references therein; (b) Tu, S.; Jiang, B.; Zhang, Y.; Jia, R.; Zhang, J.; Yao, C.; Shi, F. *Org. Biomol. Chem.* **2007**, *5*, 355; (c) Anabha, E. R.; Nirmala, K. N.; Thomas, A.; Asokan, C. V. *Synthesis* **2007**, 428.
11. (a) Yus, M.; Ramon, D. J.; Gomes, I. *Tetrahedron* **2003**, *59*, 3219; (b) Itami, K.; Kamei, T.; Yoshida, J.-i. *J. Am. Chem. Soc.* **2003**, *125*, 14670; (c) Tessier, P. E.; Penwell, A. J.; Souza, F. E. S.; Fallis, A. G. *Org. Lett.* **2003**, *5*, 2989; (d) Chen, J.; Halls, S. C.; Alfaro, J. F.; Zhou, Z.; Hu, M. *Pharm. Res.* **2004**, *21*, 2095; (e) Kaku, T.; Ogura, K.; Nishiyama, T.; Ohnuma, T.; Muro, K.; Hiratsuka, A. *Biochem. Pharmacol.* **2004**, *67*, 2093; (f) Seo, J. W.; Comninos, J. S.; Chi, D. Y.; Kim, D. W.; Carlson, K. E.; Katzenellenbogen, J. A. *J. Med. Chem.* **2006**, *49*, 2496.
12. (a) Yamamoto, K.; Yamazaki, S.; Murata, I.; Fukazawa, Y. *J. Org. Chem.* **1987**, *52*, 5239; (b) Karig, G.; Thasana, N.; Gallagher, T. *Synlett* **2002**, 808; (c) Weller, D. D.; Luellen, G. R.; Weller, D. L. *J. Org. Chem.* **1982**, *47*, 4803.