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TETRAHEDRON: *ASYMMETRY*

Synthesis of chiral sulfonamide/Schiff base ligands

Jaume Balsells,[a] Lupe Mejorado,[a] Mimi Phillips,[a] Fernando Ortega,[b] Gerardo Aguirre,[b] Ratnasamy Somanathan [b] and Patrick J. Walsh [a,b,*]

[a]*Department of Chemistry, San Diego State University, San Diego, CA 92182-1030, USA*

[b]*Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana, Apartado Postal 1166, 22000 Tijuana, B.C. Mexico*

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Abstract

We report a facile two step synthesis of chiral ligands for bonding to transition metals. The ligands are easily prepared from *trans*-1,2-diaminocyclohexane by reaction with sulfonyl chlorides to give amino-sulfonamide compounds. These intermediates are then condensed with salicylaldehyde derivatives to provide sulfonamide/Schiff base compounds which represent a new class of chiral ligands.

The preparation of new ligands is perhaps the most important step in the development of metal complexes which exhibit unique properties and novel reactivity. Changes in the electronic, steric, and geometric properties of the ligand alter the orbitals at the metal center and thus affect its properties. In catalytic asymmetric systems, small changes in the donating ability of the ligand or the size of its substituents can have a dramatic effect on the catalyst efficiency and enantioselectivity.[1–6] The work of Jacobsen et al. in the asymmetric epoxidation of olefins stands as an excellent example of the optimization of these parameters to achieve high enantioselectivities.[7] The salen ligands used in the Jacobsen epoxidation have proven to be exceptional in several asymmetric processes including aziridination[8,9] and cyclopropanation of olefins,[10] epoxide opening[11–14] and kinetic resolution of epoxides,[12,15–17] the Diels–Alder cycloaddition,[16,18] and the trimethylsilylcyanation of aldehydes.[19] Another class of ligands that is also prepared from chiral diamines is the bis(sulfonamide) complexes. These ligands have been used in the asymmetric Diels–Alder reaction,[20,21] alkylation of aldehydes,[22–29] the cyclopropanation of allylic alcohols,[29–34] and the amination of N-acyloxazolidones.[35]

The salen and bis(sulfonamide) ligands are electronically very different. The tetradentate salen ligand is a strong electron donor.[36,37] In contrast, in the deprotonated bis(sulfonamide) ligand, the electron density is delocalized into the sulfonyl group and the ligand is a poor electron donor. The resulting bis(sulfonamido) complexes exhibit enhanced Lewis acidity. Although the bis(sulfonamide) ligands bind well to early transition metals[28,38–40] and main group elements,[20] they have not been shown to coordinate to late transition metals. Because the salen and bis(sulfonamide) ligands impart different properties on the

* Corresponding author. E-mail: pwalsh@sundown.sdsu.edu

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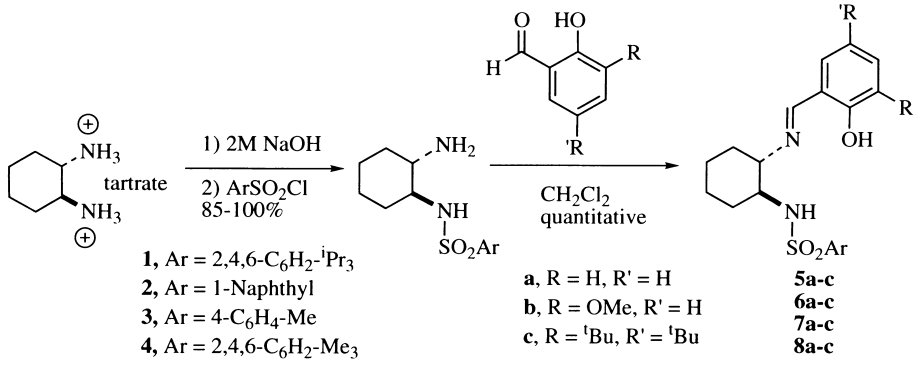
metal, we decided to prepare hybrids of these ligands and explore their use in transition metal chemistry and asymmetric catalysis. The imine and phenol groups of the salen will assure strong binding to the metal as found in tetradentate salen complexes while the deprotonated sulfonamide will increase the Lewis acidity of the metal center. Since a large number of inexpensive salicylaldehyde derivatives and sulfonyl chlorides are commercially available, a wide range of ligands are synthetically accessible in two easy steps.

The synthesis of the ligands is outlined in Eq. 1. The first step involves derivatization of *trans*-1,2-diaminocyclohexane with the sulfonyl chloride to give the amino-sulfonamide. Using a 1:1 ratio of diamine to sulfonyl chloride is problematic because the amino-sulfonamide initially formed competes effectively with the diamine for the remaining sulfonyl chloride. As a result, substantial amounts of the bis(sulfonamide) product can be formed. Surprisingly, even with the bulky 2,4,6-triisopropylbenzene sulfonyl chloride, a 1.2:1 ratio of amino-sulfonamide to bis(sulfonamide) was obtained. As reported by Xu and coworkers, the addition of one equivalent of ethyl trifluoroacetate, a highly selective reagent for the differentiating of amino groups,[41] and *trans*-1,2-diaminocyclohexane, caused the ratio of the mono-amide to the bis(amide) to increase to 1.8:1. This is in sharp contrast with *cis*-1,2-diaminocyclohexane which gives the monoamide and bis(amide) in a ratio of 68:1.[41] To circumvent the need for separation of the amino-sulfonamide from the bis(sulfonamide), Neumann and coworkers employed a three fold excess of the diamine relative to the sulfonyl chloride.[42] In our synthesis, we started with the tartrate salt of the diamine, which is the product obtained in the resolution of the diamine. The tartrate salt was added to 2 M NaOH to generate the free diamine, then dichloromethane was added and the solution cooled in an ice bath. Next, the sulfonyl chloride was added slowly as a solution in dichloromethane. The isolated amino-sulfonamide products were very clean and no bis(sulfonamide) product was detected for **1**–**3** (500 MHz NMR). However, in the case of **4**, the product was chromatographed to remove traces of the bis(sulfonamide). We have made a sterically diverse group of amino-sulfonamides and anticipate that this methodology should be applicable using a range of sulfonyl chlorides.



(1)

We were able to crystallize **4** and performed an X-ray diffraction study. Two molecules were found in the unit cell which differed in their conformations. The structure of one of these is illustrated in Fig. 1.

In the second step, the amino-sulfonamide was allowed to react with the salicylaldehyde derivatives in dichloromethane at room temperature. The product sulfonamide-Schiff bases were isolated by removing the solvent and drying under high vacuum. The reactions were very clean and proceeded readily, even in the case of the bulky amino-sulfonamide **1** reacting with the di-*tert*-butyl substituted aldehyde **c** (Eq. 1 and Table 1). We were able to grow X-ray quality crystals of **5b**. The results of the X-ray structure determination are shown in Fig. 1.

In related work, Bu and coworkers reported complementary methodology which may be suitable

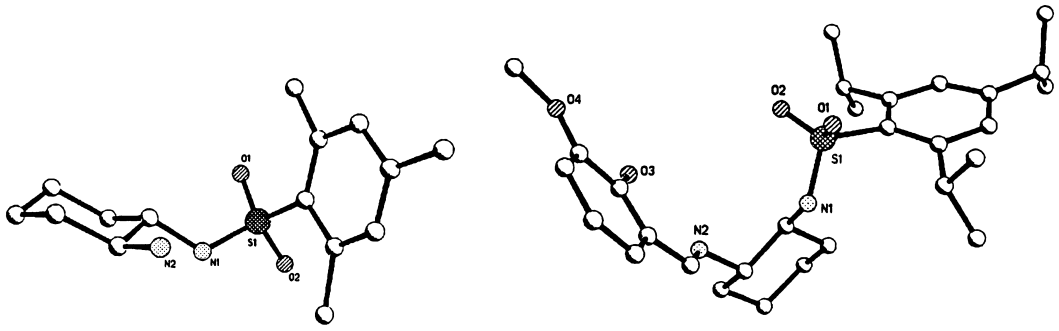


Figure 1. X-Ray crystal structures of **4** (left) and **5b** (right)

Table 1
Chiral sulfonamide/Schiff base ligands

Entry	Ar	R	R'
5a	2,4,6-C_6H_2-^{i}Pr$_3$	H	H
5b	2,4,6-C_6H_2-^{i}Pr$_3$	OMe	H
5c	2,4,6-C_6H_2-^{i}Pr$_3$	*t*Bu	*t*Bu
6a	1-naphthyl	H	H
6b	1-naphthyl	OMe	H
6c	1-naphthyl	*t*Bu	*t*Bu
7a	4-C_6H_4-Me	H	H
7b	4-C_6H_4-Me	OMe	H
7c	4-C_6H_4-Me	*t*Bu	*t*Bu
8a	2,4,6-C_6H_2-Me$_3$	H	H
8b	2,4,6-C_6H_2-Me$_3$	OMe	H
8c	2,4,6-C_6H_2-Me$_3$	*t*Bu	*t*Bu

for the synthesis of sulfonamide-Schiff base ligands.[43] They derivatized *trans*-1,2-diaminocyclohexane with one equivalent of salicylaldehyde to provide the unsymmetrical amino-Schiff base. Apparently this reaction proceeds without formation of the tetradentate salen ligand (although mention is made of use of up to 1.5 equivalents of diamine). Reaction of this intermediate with different salicylaldehyde derivatives gave the unsymmetrical tetradentate salen ligands. It is likely that the unsymmetrical amino-Schiff base compound would react with sulfonyl chlorides to provide the sulfonamide-Schiff base ligands.

Although both our method and that of Bu et al. are simple, they each have minor shortcomings. In our methodology, an excess of the chiral diamine must be used. However, based on the results of Xu et al., excess diamine is not likely to be necessary in the synthesis of amino-sulfonamides with other diamines.[41] In the procedure of Bu et al., it is necessary to use the diamine as starting material because of the anhydrous conditions needed for imine formation. Liberation of the diamine from the tartrate salt is a two step procedure which must be done carefully because of the water solubility and air sensitivity of the diamine.[44]

In conclusion, we have developed an efficient method to synthesize modular sulfonamide-Schiff base ligands. Compounds containing the Schiff base moiety have an extensive and well documented coordination chemistry while the transition metal chemistry of sulfonamides is just beginning to be addressed. We are currently exploring the structure of complexes derived from these hybrid ligands and will evaluate their use in asymmetric catalysis in due course.

1. Experimental

1.1. Synthesis and characterization of *1*–*4*

The procedures for the preparation of compounds **1**–**4** were identical, and details are given for the synthesis of **1**.

To a stirred solution of the L-tartrate salt of (*R*,*R*)-1,2-diaminocyclohexane (1.98 g, 7.5 mmol) in 8 ml of a 2 N NaOH solution, were added 20 ml of dichloromethane. The mixture was cooled to 0°C and a solution of 2,4,6-triisopropylbenzene sulfonyl chloride (757 mg, 2.5 mmol) in 20 ml of dichloromethane was added dropwise over 20 min. After the addition was complete, the mixture was allowed to warm to room temperature and stirred overnight. The resulting solution was washed with water (3×50 ml) and the solvent removed at reduced pressure. In this manner, **1** was isolated in 99% yield (950 mg, 2.49 mmol). Data for **1**: m.p. 199°C; $[\alpha]_D$ −26.2 (c 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.0–1.23 (m, 3H), 1.25 (d, J=7.0 Hz, 6H), 1.27 (d, J=7.0 Hz, 6H), 1.28 (d, J=7.0 Hz, 6H), 1.3–1.6 (m, 3H), 1.6–1.7 (m, 2H), 1.9–2.0 (m, 2H), 2.33 (td, J_1=3.0 Hz, J_2=10.0 Hz, 1H), 2.84 (td, J_1=3.5 Hz, J_2=10.5 Hz, 1H), 2.89 (hept, J=7.0 Hz, 1H), 4.16 (hept, J=7.0 Hz, 2H), 4.90 (b, 1H), 7.15 (s, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 23.55 (CH_3), 23.56 (CH_3), 24.8 ($2CH_3$), 24.95 (CH_2+CH_2), 24.97 ($2CH_3$), 29.8 (2CH), 33.0 (CH_2), 34.1 (CH), 36.1 (CH_2), 55.0 (CH), 60.1 (CH), 123.8 (2CH), 133.9 (C), 149.9 (2C), 152.6 (C) ppm; IR (KBr) 3348, 3287, 2957, 2863, 1604, 1568, 1461, 1425, 1364, 1313, 1154, 1118, 1082, 1037, 944, 914, 878, 847 cm^{-1}; ME (EI, 70 eV) m/z: 381 (M^+, 5%), 113 (95%), 96 (100%).

Data for **2**: The yield was 100%. M.p. 63°C; $[\alpha]_D$ −32.3 (c 0.51, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.8–1.2 (m, 3H), 1.2–1.4 (m, 1H), 1.45–1.52 (m, 1H), 1.52–1.6 (m, 1H), 1.6–1.7 (m, 1H), 1.8–1.9 (m, 1H), 2.33 (td, J_1=4.0 Hz, J_2=10.0 Hz, 1H), 2.60 (td, J_1=4.0 Hz, J_2=10.5 Hz, 2H), 7.54 (dd, J_1=7.5 Hz, J_2=8.0 Hz, 1H), 7.59 (m, 1H), 7.67 (m, 1H), 7.94 (d, J=8.0 Hz, 1H), 8.06 (d, J=8.5 Hz, 1H), 8.31 (dd, J_1=1.0 Hz, J_2=7.0 Hz, 1H), 8.68 (dd, J_1=0.5 Hz, J_2=8.5 Hz, 1H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 24.7 (CH_2), 24.8 (CH_2), 32.5 (CH_2), 35.3 (CH_2), 54.7 (CH), 60.7 (CH), 124.1 (CH), 124.5 (CH), 126.8 (CH), 128.1 (C), 128.2 (CH), 129.1 (CH), 129.6 (CH), 134.1 (CH), 135.4 (C), 145.7 (C) ppm; IR (KBr) 3288, 3057, 2934, 2857, 1555, 1499, 1448, 1320, 1161, 1134, 1069, 986, 913, 805, 771, 676, 598 cm^{-1}; ME (EI, 70 eV) m/z: 304 (M^+, 4%), 113 (70%), 96 (100%).

Data for **3**: The reaction mixture was extracted with a 2 N HCl solution (3×50 ml). The organic layer was rejected and the aqueous phase was basified with 2 N NaOH, and extracted with CH_2Cl_2 (3×50 ml). Removal of the solvent at reduced pressure yielded 634 mg (2.36 mmol, 94%) of compound **3** as a white solid. M.p. 104°C; $[\alpha]_D$ −42.7 (c 0.52, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.0–1.3 (m, 4H), 1.45–1.95 (m, 4H), 2.34 (m, 1H), 2.42 (s, 3H), 2.77 (m, 1H), 7.30 (d, J=8.0 Hz, 2H), 7.78 (d, J=8.0 Hz, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 21.5 (CH_3), 24.2 (CH_2), 24.8 (CH_2), 32.6 (CH_2), 35.5 (CH_2), 54.8 (CH), 60.5 (CH), 127.0 (2CH), 129.6 (2CH), 137.9 (C), 143.2 (C) ppm; IR (KBr) 3338, 3281, 3055, 2920, 1594, 1491, 1448, 1327, 1160, 1091, 949, 812, 709, 662 cm^{-1}; ME (EI, 70 eV) m/z: 269 (M^+, 12%), 113 (72%), 96 (100%).

Data for **4**: The white solid obtained from the reaction was purified by column chromatography using SiO_2. Traces of bis-sulfonamide were eluted using ethyl acetate, while pure **4** was eluted using CH_2Cl_2:$CHCl_3$ (10% v/v). The yield was 85% (627 mg, 2.11 mmol). M.p. 127°C; $[\alpha]_D$ −44.8 (c 0.50, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.0–1.25 (m, 4H), 1.6–1.7 (m, 2H), 1.85–1.95 (m, 2H), 2.29 (s, 3H), 2.34 (m, 1H), 2.58 (m, 1H), 2.66 (s, 6H), 6.94 (s, 2H) ppm; ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz) δ 21.8 (CH_3), 23.0 ($2CH_3$), 24.8 (CH_2), 24.9 (CH_2), 32.5 (CH_2), 35.8 (CH_2), 54.7 (CH), 60.2 (CH), 131.9 (2CH), 134.6 (C), 138.7 (2C), 141.9 (C) ppm; IR (KBr) 3360, 3300, 2922, 1606, 1583, 1458, 1405, 1315,

1145, 1112, 1076, 963, 934, 847, 653, 578, 539 cm^{-1}; ME (EI, 70 eV) m/z: 297 (M^+, 3%), 113 (68%), 96 (100%).

*1.2. Synthesis and characterization of **5a–8c***

The procedures for the preparation of compounds **5a–8c** were identical, and details are given for the synthesis of **5a**.

To a stirred solution of **5a** (190 mg, 0.5 mmol) in 6 ml of CH_2Cl_2 were added at room temperature 61 mg (0.5 mmol) of salicylaldehyde in 4 ml of CH_2Cl_2. The mixture was stirred at room temperature overnight. Anhydrous sodium sulfate was added, the solution filtered and the solvent removed at reduced pressure to obtain 244 mg (0.5 mmol, 100%) of **5a** as a yellow solid. M.p. 150°C; $[\alpha]_D$ −59.2 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.0–1.4 (m, 4H), 1.20 (d, J=7.0 Hz, 6H), 1.22 (d, J=7.0 Hz, 6H), 1.23 (d, J=7.0 Hz, 6H), 1.6–1.7 (m, 2H), 1.7–1.8 (m, 1H), 1.8–1.9 (m, 1H), 2.0–2.1 (m, 1H), 2.9 (hept, J=7.0 Hz, 1H), 3.1–3.2 (m, 1H), 3.4–3.5 (m, 1H), 4.1 (hept, J=7.0 Hz, 2H), 4.35–4.45 (m, 1H), 6.84 (t, J=7.5 Hz, 1H), 6.91 (d, J=8.0 Hz, 1H), 7.10 (s, 2H), 7.20 (dd, J_1=7.5 Hz, J_2=2.0 Hz, 1H), 7.28 (td, J_1=8.0 Hz, J_2=2.0 Hz, 1H), 8.33 (s, 1H), 12.9 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 23.2 (CH_2), 23.4 (CH_3), 23.5 (CH_3), 23.8 (CH_2), 24.7 ($2CH_3$), 24.8 ($2CH_3$), 29.7 (2CH), 31.2 (CH_2), 33.0 (CH_2), 34.0 (CH), 56.7 (CH), 71.3 (CH), 117.0 (CH), 118.5 (CH), 123.7 (2CH), 131.4 (CH), 132.3 (CH), 133.9 (C), 149.7 (2C), 152.6 (C), 161.0 (C), 165.2 (CH) ppm; IR (KBr) 3216, 2931, 2861, 1636, 1565, 1458, 1284, 1156, 1040, 943, 884, 766, 679, 569, 517 cm^{-1}; ME (EI, 70 eV) m/z: 484 (M^+, 48%), 217 (100%), 122 (62%), 96 (67%).

Data for **5b**: The yield was 100% (258 mg, 0.50 mmol). M.p. 139°C; $[\alpha]_D$ −54.9 (c 0.51, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.20–1.25 (m, 18H), 1.2–1.44 (M, 3H), 1.54–1.64 (m, 2H), 1.68–1.76 (m, 1H), 1.8–1.9 (m, 1H), 1.95–2.20 (m, 1H), 2.86 (hept, J=7.0 Hz, 1H), 3.26–3.33 (m, 1H), 3.38–3.45 (m, 1H), 3.88 (s, 3H), 4.12 (hept, J=7.0 Hz, 2H), 4.55–4.65 (m, 1H), 6.79 (t, J=8.0 Hz, 1H), 6.82 (dd, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 6.91 (dd, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 7.10 (s, 2H), 8.33 (s, 1H), 13.55 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 22.6 (CH_2), 23.2 (CH_2), 23.40 (CH_3), 23.41 (CH_3), 24.7 ($2CH_3$), 24.8 ($2CH_3$), 29.6 (2CH), 30.2 (CH_2), 32.0 (CH_2), 33.9 (CH), 56.0 (CH_3), 56.1 (CH), 70.3 (CH), 114.3 (CH), 117.8 (CH), 118.5 (C), 123.1 (CH), 123.7 (2CH), 133.7 (C), 148.4 (C), 149.7 (2C), 151.7 (C), 152.5 (C), 165.1 (CH) ppm; IR (KBr) 3240, 2932, 2863, 1636, 1601, 1465, 1255, 1163, 1087, 1031, 973, 942, 884, 789, 731, 680, 571 cm^{-1}; ME (EI, 70 eV) m/z: 514 (M^+, 100%), 247 (63%), 152 (75%), 96 (40%).

Data for **5c**: The yield was 100% (300 mg, 0.50 mmol). M.p. 118°C; $[\alpha]_D$ −43.0 (c 0.53, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.20 (d, J=7.0 Hz, 6H), 1.23 (d, J=7.0 Hz, 6H), 1.25 (d, J=7.0 Hz, 6H), 1.30 (s, 9H), 1.0–1.4 (m, 4H), 1.44 (s, 9H), 1.6–1.7 (m, 2H), 1.7–1.8 (m, 1H), 1.78–1.87 (m, 1H), 2.1–2.2 (m, 1H), 2.86 (hept, J=7.0 Hz, 1H), 3.1–3.2 (m, 1H), 3.4–3.5 (m, 1H), 3.7–3.8 (m, 1H), 4.12 (hept, J=7.0 Hz, 2H), 4.38–4.42 (m, 1H), 7.06 (d, J=2.5 Hz, 1H), 7.12 (s, 2H), 7.37 (d, J=2.5 Hz, 1H), 8.36 (s, 1H), 13.2 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 23.3 (CH_2), 23.5 (CH_3+CH_3), 23.7 (CH_2), 24.7 ($2CH_3$), 24.8 ($2CH_3$), 29.4 ($3CH_3$), 29.7 (2CH), 30.7 (CH_2), 31.5 ($3CH_3$), 33.0 (CH_2), 34.0 (CH), 34.1 (C), 35.0 (C), 56.9 (CH), 71.5 (CH), 117.7 (C), 123.7 (2CH), 126.1 (CH), 127.2 (CH), 133.7 (C), 136.6 (C), 140.1 (C), 149.7 (2C), 152.6 (C), 157.9 (C), 166.6 (CH) ppm; IR (KBr) 3281, 2958, 2865, 1628, 1600, 1458, 1437, 1362, 1314, 1275, 1253, 1152, 1060, 941, 881, 827, 773, 660, 575 cm^{-1}; ME (EI, 70 eV) m/z: 596 (M^+, 100%), 581 (24%).

Data for **6a**: The yield was 100% (203 mg, 0.50 mmol). M.p. 179°C; $[\alpha]_D$ −127.6 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 2.2–2.3 (m, 1H), 2.8–2.9 (m, 1H), 3.25–3.35 (m, 1H), 5.33 (d, J=8.0 Hz, 1H), 6.58 (td, J_1=7.5 Hz, J_2=1.5 Hz, 1H), 6.60–6–64 (m, 2H), 7.16 (td, J_1=7.7 Hz, J_2=2.0

Hz, 1H), 7.19 (td, J_1=8.0 Hz, J_2=1.0 Hz, 1H), 7.26 (td, J_1=7.0 Hz, J_2=1.5 Hz, 1H), 7.40 (t, J=8.0 Hz, 1H), 7.56 (d, J=8.5 Hz, 1H), 7.80 (s, 1H), 8.22 (dd, J_1=7.0 Hz, J_2=1.0 Hz, 1H), 8.41 (d, J=8.5 Hz, 1H), 12.2 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 23.6 (CH_2), 24.6 (CH_2), 33.7 (CH_2), 33.8 (CH_2), 57.7 (CH), 72.4 (CH), 116.6 (CH), 118.0 (C), 118.1 (CH), 123.8 (CH), 1, 127.7 (CH), 128.9 (CH), 129.0 (CH), 131.3 (CH), 131.7 (CH), 134.0 (C), 134.1 (CH), 135.1 (C), 160.5 (C), 164.4 (CH) ppm; IR (KBr) 3277, 3052, 2934, 2858, 1629, 1577, 1496, 1458, 1419, 1320, 1279, 1199, 1158, 1132, 1093, 1067, 984, 949, 914, 841, 811, 773, 754, 675, 599, 516 cm^{-1}; ME (EI, 70 eV) m/z: 408 (M^+, 75%), 217 (77%), 127 (53%), 96 (100%).

Data for **6b**: The yield was 100% (219 mg, 0.50 mmol). M.p. 88°C; $[\alpha]_D$ −106.4 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 2.2–2.3 (m, 1H), 2.8–2.9 (m, 1H), 3.25–3.35 (m, 1H), 3.88 (s, 3H), 5.36 (d, J=8.5 Hz, 1H), 6.22 (dd, J_1=8.0 Hz, J_2=1.0 Hz, 1H), 6.56 (t, J=8.0 Hz, 1H), 6.78 (dd, J_1=8.0 Hz, J_2=1.5 Hz, 1H), 7.17 (td, J_1=7.0 Hz, J_2=1.0 Hz, 1H), 7.27 (td, J_1=7.7 Hz, J_2=1.5 Hz, 1H), 7.42 (t, J=7.7 Hz, 1H), 7.53 (d, J=8.0 Hz, 1H), 7.78 (s, 1H), 7.80 (d, J=8.5 Hz, 1H), 8.21 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 1H), 8.40 (d, J=8.5 Hz, 1H), 12.6 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 23.4 (CH_2), 24.4 (CH_2), 33.4 (CH_2), 33.5 (CH_2), 56.0 (CH_3), 57.6 (CH), 72.0 (CH), 113.6 (CH), 117.4 (CH), 117.8 (C), 123.0 (CH), 123.7 (CH), 123.8 (CH), 126.0 (CH), 127.5 (C), 127.6 (CH), 128.7 (CH), 129.0 (CH), 134.0 (CH+C), 135.0 (C), 148.0 (C), 151.0 (C), 164.3 (CH) ppm; IR (KBr) 3299, 3058, 2928, 2857, 1628, 1464, 1320, 1254, 1161, 1131, 1080, 974, 900, 839, 800, 769, 736, 677, 595, 517 cm^{-1}; ME (EI, 70 eV) m/z: 438 (M^+, 100%), 247 (30%), 152 (70%), 127 (72%), 96 (63%).

Data for **6c**: The yield was 100% (260 mg, 0.50 mmol). M.p. 159°C; $[\alpha]_D$ −56.3 (c 0.54, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 1.26 (s, 9H), 1.39 (s, 9H), 2.24–2.34 (m, 1H), 2.8–2.9 (m, 1H), 3.3–3.4 (m, 1H), 5.32 (d, J=8.0 Hz, 1H), 6.57 (d, J=2.5 Hz, 1H), 7.24 (t, J=7.5 Hz, 1H), 7.28 (d, J=2.5 Hz, 1H), 7.36 (t, J=8.5 Hz, 2H), 7.58 (d, J=8.5 Hz, 1H), 7.78 (t, J=8.5 Hz, 1H), 7.87 (s, 1H), 8.23 (dd, J_1=7.0 Hz, J_2=1.0 Hz, 1H), 8.50 (d, J=8.5 Hz, 1H), 12.8 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 23.5 (CH_2), 24.4 (CH_2), 29.5 ($3CH_3$), 31.4 ($3CH_3$), 33.1 (CH_2), 33.7 (CH_2), 33.9 (C), 34.9 (C), 57.6 (CH), 72.3 (CH), 117.2 (C), 123.9 (CH), 124.1 (CH), 126.0 (CH), 126.2 (CH), 126.8 (CH), 127.7 (C), 127.8 (CH), 128.7 (CH), 129.0 (CH), 133.8 (C), 133.9 (CH), 135.3 (C), 136.0 (C), 139.4 (C), 157.6 (C), 165.7 (CH) ppm; IR (KBr) 3257, 3057, 2953, 2860, 1629, 1595, 1440, 1361, 1320, 1274, 1242, 1201, 1160, 1133, 1092, 1067, 984, 900, 856, 827, 799, 769, 677, 633, 596, 518 cm^{-1}; ME (EI, 70 eV) m/z: 520 (M^+, 100%), 505 (55%), 477 (24%), 127 (43%).

Data for **7a**: The yield was 100% (184 mg, 0.50 mmol). M.p. 137°C; $[\alpha]_D$ −16.4 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 2.2–2.3 (m, 1H), 2.25 (s, 3H), 2.88–2.98 (m, 1H), 3.18–3.26 (m, 1H), 5.2 (b, 1H), 6.76 (td, J_1=7.5 Hz, J_2=1.0 Hz, 1H), 6.83 (d, J=8.5 Hz, 1H), 6.93 (d, J=8.5 Hz, 2H), 7.01 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 1H), 7.2–7.3 (m, 1H), 7.53 (d, J=8.5 Hz, 2H), 8.14 (s, 1H), 12.5 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 21.5 (CH_3), 23.6 (CH_2), 24.5 (CH_2), 33.5 (CH_2), 33.6 (CH_2), 57.2 (CH), 72.0 (CH), 116.6 (CH), 118.3 (C), 118.5 (C), 126.5 (2CH), 129.3 (2CH), 131.4 (CH), 132.0 (CH), 137.5 (C), 142.9 (C), 160.9 (C), 165.1 (CH) ppm; IR (KBr) 3260, 2946, 2861, 1631, 1577, 1495, 1456, 1406, 1315, 1280, 1211, 1150, 1089, 953, 904, 812, 765, 666, 566, 546 cm^{-1}; ME (EI, 70 eV) m/z: 372 (M^+, 62%), 217 (57%), 134 (30%), 122 (38%), 96 (100%).

Data for **7b**: The yield was 100% (202 mg, 0.50 mmol). M.p. 159°C; $[\alpha]_D$ −44.4 (c 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 2.2–2.3 (m, 1H), 2.23 (s, 3H), 2.9–3.0 (m, 1H), 3.18–3.26 (m, 1H), 3.89 (s, 3H), 5.2 (b, 1H), 6.64–6.76 (m, 2H), 6.88 (d, J=7.5 Hz, 1H), 6.94 (d, J=7.5 Hz, 2H), 7.53 (d, J=7.5 Hz, 2H), 8.13 (s, 1H), 13.1 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 21.3 (CH_3), 23.4 (CH_2), 24.3 (CH_2), 33.2 (CH_2+CH_2), 55.9 (CH_3), 57.1 (CH), 71.5 (CH), 113.9 (CH), 117.6 (C), 118.3 (C), 123.1 (CH), 126.5 (2CH), 129.3 (2CH), 137.5 (C), 142.9 (C), 148.2 (C), 151.5 (C), 165.0

(CH) ppm; IR (KBr) 3299, 2938, 2861, 1636, 1565, 1465, 1437, 1325, 1253, 1157, 1080, 969, 901, 810, 741, 665, 570, 548 cm^{-1}; ME (EI, 70 eV) m/z: 402 (M^+, 100%), 247 (28%), 152 (72%), 96 (59%).

Data for **7c**: The yield was 100% (243 mg, 0.50 mmol). M.p. 91°C; $[\alpha]_D$ −4.7 (c 0.51, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 1.28 (s, 9H), 1.45 (s, 9H), 2.3–2.4 (m, 1H), 2.23 (s, 3H), 2.96–3.04 (m, 1H), 3.20–3.27 (m, 1H), 4.9 (b, 1H), 6.95 (d, J=2 Hz, 1H), 7.05 (d, J=8.0 Hz, 2H), 7.36 (d, J=2.0 Hz, 1H), 7.61 (d, J=8.0 Hz, 2H), 8.24 (s, 1H), 13.0 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 21.4 (CH_3), 23.7 (CH_2), 24.2 (CH_2), 29.5 ($3CH_3$), 31.4 ($3CH_3$), 32.8 (CH_2), 33.6 (CH_2), 34.0 (C), 35.0 (C), 57.5 (CH), 71.7 (CH), 117.6 (C), 126.1 (CH), 126.7 (2CH), 127.0 (CH), 129.5 (2CH), 136.3 (C), 137.4 (C), 140.0 (C), 142.8 (C), 157.7 (C), 166.6 (CH) ppm; IR (KBr) 3277, 2948, 2862, 1629, 1598, 1440, 1362, 1322, 1274, 1157, 1092, 1066, 899, 811, 772, 713, 665, 573, 549 cm^{-1}; ME (EI, 70 eV) m/z: 484 (M^+, 100%), 469 (65%), 441 (28%).

Data for **8a**: The yield was 100% (200 mg, 0.50 mmol). M.p. 133°C; $[\alpha]_D$ −49.8 (c 0.49, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 2.12 (s, 3H), 2.3–2.4 (m, 1H), 2.25 (s, 6H), 2.88–2.98 (m, 1H), 3.18–3.26 (m, 1H), 5.17 (d, J=8.5 Hz, 1H), 6.59 (s, 2H), 6.78–6.86 (m, 2H), 7.07 (d, J=7.5 Hz, 1H), 7.24–7.30 (m, 1H), 8.12 (s, 1H), 12.4 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 20.9 (CH_3), 23.0 ($2CH_3$), 23.6 (CH_2), 24.7 (CH_2), 33.6 (CH_2), 33.7 (CH_2), 57.5 (CH), 72.5 (CH), 116.6 (CH), 118.2 (CH), 118.4 (C), 131.2 (CH), 131.7 (2CH), 131.9 (CH), 134.2 (C), 138.0 (2C), 141.7 (C), 161.0 (C), 164.4 (CH) ppm; IR (KBr) 3292, 2936, 2858, 1628, 1577, 1496, 1457, 1324, 1279, 1152, 1093, 1060, 953, 911, 853, 765, 659, 585, 538, 425 cm^{-1}; ME (EI, 70 eV) m/z: 400 (M^+, 29%), 217 (100%), 96 (77%).

Data for **8b**: The yield was 100% (215 mg, 0.50 mmol). M.p. 114°C; $[\alpha]_D$ −67.0 (c 0.51, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.3–1.8 (m, 7H), 2.09 (s, 3H), 2.25–2.35 (m, 1H), 2.48 (s, 6H), 2.9–3.0 (m, 1H), 3.15–3.25 (m, 1H), 3.88 (s, 3H), 4.97 (d, J=8.5 Hz, 1H), 6.58 (s, 2H), 6.71 (dd, J_1=7.5 Hz, J_2=1.5 Hz 1H), 6.76 (t, J=7.5 Hz, 1H), 6.88 (dd, J_1=7.5 Hz, J_2=1.5 Hz, 1H), 8.11 (s, 1H), 12.9 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 20.7 (CH_3), 23.0 ($2CH_3$), 23.4 (CH_2), 24.6 (CH_2), 33.4 (CH_2+CH_2), 55.9 (CH_3), 57.4 (CH), 72.1 (CH), 113.7 (CH), 117.5 (CH), 118.3 (C), 123.0 (CH), 131.7 (2CH), 134.2 (C), 138.0 (2C), 141.7 (C), 148.1 (C), 151.5 (C), 164.4 (CH) ppm; IR (KBr) 3290, 2934, 2858, 1630, 1604, 1559, 1462, 1322, 1255, 1154, 1085, 974, 901, 852, 782, 729, 662, 584, 537, 448 cm^{-1}; ME (EI, 70 eV) m/z: 430 (M^+, 97%), 247 (100%), 152 (93%), 96 (71%).

Data for **8c**: The yield was 100% (255 mg, 0.50 mmol). M.p. 111°C; $[\alpha]_D$ −2.0 (c 0.53, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz) δ 1.2–1.8 (m, 7H), 1.30 (s, 9H), 1.43 (s, 9H), 2.09 (s, 3H), 2.3–2.4 (m, 1H), 2.52 (s, 6H), 2.94–3.02 (m, 1H), 3.14–3.22 (m, 1H), 4.8 (b, 1H), 6.73 (s, 2H), 6.94 (d, J=2.5 Hz, 1H), 7.34 (d, J=2.5 Hz, 1H), 8.20 (s, 1H), 12.9 (b, 1H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz) δ 20.8 (CH_3), 23.0 ($2CH_3$), 23.7 (CH_2), 24.4 (CH_2), 29.4 ($3CH_3$), 31.5 ($3CH_3$), 32.8 (CH_2), 33.7 (CH_2), 34.0 (C), 34.9 (C), 57.5 (CH), 72.3 (CH), 117.5 (C), 126.0 (CH), 127.0 (CH), 131.9 (2CH), 134.1 (C), 136.1 (C), 138.4 (2C), 139.8 (C), 141.5 (C), 157.8 (C), 166.3 (CH) ppm; IR (KBr) 3281, 2952, 2860, 1628, 1603, 1473, 1437, 1320, 1274, 1153, 1063, 896, 848, 772, 713, 659, 583, 539 cm^{-1}; ME (EI, 70 eV) m/z: 512 (M^+, 100%), 497 (49%), 469 (21%), 119 (37%).

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