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A short stereoselective synthesis of (−)-chloramphenicol and (+)-thiamphenicol ☆

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Abstract—A common strategy for the synthesis of (−)-chloramphenicol and (+)-thiamphenicol is described. These antibiotics have been synthesized from commercially available 4-nitrobenzaldehyde and 4-(methylthio)benzaldehyde in three and four steps, respectively.
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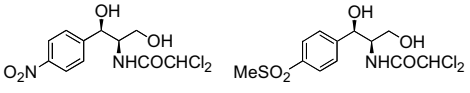
1. Introduction

Chloramphenicol **1**[1] is a well-known broad-spectrum antibiotic that was isolated from *Streptomyces venezuelae* in 1947. It is used in the treatment of typhoid, dysentery and ocular bacterial infections. It is only active in its D-*threo* configuration and perhaps the first antibiotic to be produced in optically active form by chemical synthesis rather than using fermentation techniques.[2]

Thiamphenicol **2**[3] is a synthetic analogue of chloramphenicol and is active against both gram-negative and gram-positive microorganisms. Owing to their potent biological activity, several syntheses of these molecules have been reported.[4–7]



(-)-Chloramphenicol **1** (+)-Thiamphenicol **2**

2. Result and discussion

Herein, we report short syntheses for **1** and **2**. The key features of the syntheses are a Sharpless asymmetric epoxydation under kinetic resolution and $BF_3{\cdot}OEt_2$ mediated cascade reactions involving the intramolecular opening of epoxydichloroimidates **6** and **12** and in situ oxazoline hydrolysis to give the target molecule.

Sharpless asymmetric epoxydation has previously been utilized for synthesis of **1** and **2**.[5c,d,7c,e] The reason for choosing the Sharpless epoxydation protocol is the utilization of the *Z*-cinnamyl alcohol derivative.[5c,6b] Generally *Z*-allylic alcohols are known to give low enantioselectivity during the epoxidation[9a] and in the case of *Z*-(*p*-nitro)cinnamyl alcohol take long reaction times to give better results.[5c] Although, Lou et al. synthesized[5d] chloramphenicol from *E*-cinnamyl alcohol, it took more transformations to reach the target molecule. Similarly, Wu et al. also synthesized[7c,e] **1** and **2** from *E*-cinnamyl alcohol derivatives via a Sharpless epoxydation and epoxydichloroimidate opening; but this procedure also has more transformations, which involves an inversion of configuration. Herein, we report a short synthesis of **1** and **2** starting from commercially available aldehydes **3** and **8** in just three and four steps, respectively.

Our synthesis of (−)-chloramphenicol **1** (Scheme 1) starts with the reaction of 4-nitrobenzaldehyde **3** with divinylzinc[8] (prepared in situ) to give 1-(4-nitrophenyl) allyl alcohol **4**. Allylic alcohol **4** was subjected to Sharpless asymmetric epoxydation[9] conditions (kinetic resolution) using (−)-DIPT to afford the chiral epoxyalcohol **5** in 45% chemical yield with 94.9% ee (determined by ^{1}H NMR analysis of corresponding Mosher ester). Then, **5** was directly converted to the target (−)-chloramphenicol **1** in one pot, upon treatment with dichloroacetonitrile in the presence of NaH, followed by

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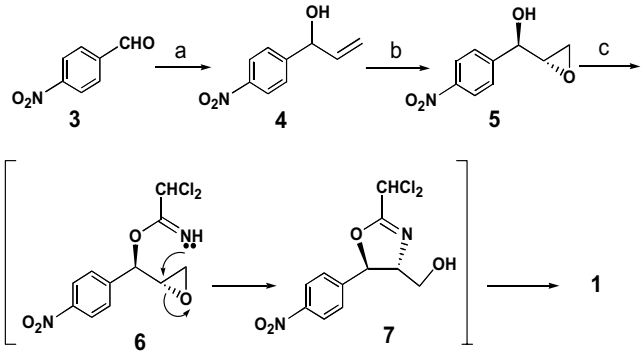
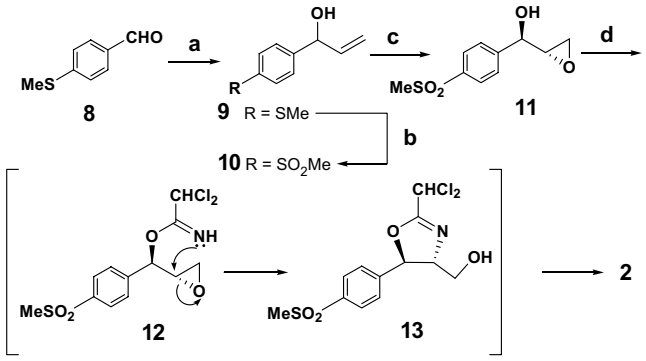


Scheme 1. Reagents and conditions: (a) Divinyl zinc, THF, Et_2O, −78 °C–rt, 10 h, 72%; (b) (−)-DIPT, $Ti(O^iPr)_4$, TBHP, CH_2Cl_2, −20 °C, 14 h, 45%; (c) NaH, dichloro acetonitrile, CH_2Cl_2, 0 °C–rt, 1 h, then $BF_3{\cdot}OEt_2$, −78 °C–rt, 3 h, 71%.



Scheme 2. Reagents and conditions: (a) Vinyl magnesium bromide, THF, 0 °C–rt, 2 h, 88%; (b) Oxone, MeOH–H_2O–THF (1:1:2), 0 °C–rt, 6 h, 87%. (c) (−)-DIPT, $Ti(O^iPr)_4$, TBHP, CH_2Cl_2, −20 °C, 24 h, 42%. (d) NaH, dichloroacetonitrile, CH_2Cl_2, 0 °C–rt, 4 h, then $BF_3{\cdot}OEt_2$, −78 °C–rt, 4 h, 64%.

an in situ epoxide opening reaction of the resulting epoxy dichloroimidate **6** with 2 equiv of $BF_3{\cdot}OEt_2$. It is known that trichloroimidates of some epoxyalcohols undergo opening with Lewis acids to give oxazolines.[10] Interestingly in our case, the excess $BF_3{\cdot}OEt_2$ complexed with oxazoline **7** and hydrolyzed the resulting ring to give (−)-chloramphenicol **1**, whose spectroscopic data was in agreement with the reported values.[1b]

This strategy was extended to the synthesis of (+)-thiamphenicol **2** (Scheme 2). Commercially available 4-(methylthio)benzadehyde **8** was converted to the allyl alcohol **9** using vinylmagnesium bromide, which was oxidized to sulphone **10** using oxone.[11] The allylic alcohol **10** was subjected to Sharpless asymmetric epoxydation[9] under kinetic resolution conditions using (−)-DIPT to give the chiral epoxyalcohol **11** in 42% chemical yield with 95.1% ee (determined by ^1H NMR analysis of corresponding Mosher ester), which was subsequently converted to (+)-thiamphenicol **2** using the same protocol as mentioned above (Scheme 1), whose ^{13}C NMR spectrum data was in agreement with the reported values.[12]

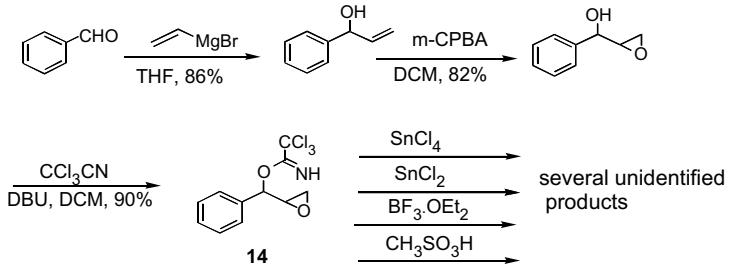
Although it is known that some of the epoxy trichloimidates in the presence of Lewis acids give oxazolines, to the best of our knowledge, this reaction has not been reported on aryl epoxyimidate of type **6** and **12**. In our earlier attempts, we observed that the reaction of phenyl epoxyimidate **14** with a range of Lewis acids gave a mixture of inseparable products (Scheme 3). This can be attributed to the formation of a stable benzylic carbocation via benzylic imidate cleavage, followed by secondary reactions, whilst the presence of an electron withdrawing group on the phenyl ring of **6** and **12** prevented the formation of a benzylic carbocation and resulted in regioselective epoxide opening.

3. Conclusion

In conclusion, an efficient and common strategy for the asymmetric synthesis of (−)-chloramphenicol **1** and (+)-thiamphenicol **2** has been developed. This strategy can be adoptable for synthesizing analogues of more therapeutic value.

4. Experimental

TLC was performed on Merck Kiesel gel 60, F_{254} plates (layer thickness 0.25 mm). Column chromatography was performed on silica gel (60–120 mesh) using ethyl acetate and petroleum ether mixture as eluent. Melting points were determined on a Fisher John's melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer RX-1 FT-IR system as KBr pellets. ^1H NMR (200 MHz) and ^{13}C NMR (50 MHz) spectra were recorded on a Varian Gemini-200 MHz spectrometer. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on Bruker Avance-



Scheme 3.

300 MHz spectrometer. Optical rotations were measured with a Horiba-SEPA-300 digital polarimeter. The mass spectra were recorded on a VG MICROMASS-7070H at 70 eV using a direct inlet system. FABMS were recorded on a VG AUTOSPEC at 70 eV using a direct inlet system.

4.1. 1-(4-Nitrophenyl)-2-propen-1-ol 4

To a stirred solution of vinyl magnesium bromide [prepared from vinyl bromide (8.49 g, 79.41 mmol) and magnesium (1.93 g, 79.41 mmol)] in THF (90 mL), freshly fused $ZnCl_2$ (5.40 g, 39.70 mmol) dissolved in THF (30 mL) was added at 0 °C under nitrogen atmosphere. This solution was maintained at 55 °C for 18 h with stirring, after which it was cooled to 10 °C and dry ether (150 mL) added and stirred for 10 min. The reaction mixture was allowed to settle for 30 min. The supernatant liquid was transferred through a canula to another flask. This solution was allowed to cool to −78 °C, then 4-nitrobenzaldehyde **3** (1.5 g, 9.92 mmol) in THF (20 mL) slowly added over a period of 15 min. The reaction mixture was allowed to warm to room temperature and stirring continued for 10 h. The reaction mixture was then quenched at −20 °C by the addition of aqueous ammonium chloride. The aqueous layer was extracted with ethyl acetate (3 × 100 mL) and the combined organic fractions collected and washed with water and brine solution, then dried over Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using ethyl acetate–petroleum ether (2:8) to afford compound **4** (1.27 g, 72%) as a pale yellow solid. mp: 48–49 °C; IR (KBr, cm^{-1}): 3415, 2364, 1518, 1345, 767; ^1H NMR (300 MHz, $CDCl_3$): δ 2.04 (br s, 1H), 5.25 (dt, 1H, $J = 1.5$, 10.5 Hz), 5.29 (m, 1H), 5.38 (dt, 1H, $J = 1.5$, 17.1 Hz), 5.96 (ddd, 1H, $J = 6.4$, 10.5, 17.1 Hz), 7.53 (d, 2H, $J = 8.7$ Hz), 8.19 (d, 2H, $J = 8.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, proton decoupled): δ 74.47, 116.74, 123.63, 126.89, 139.05, 147.20, 149.61; MS (EI): m/z (% relative intensity): 179(M^+) (19),150 (35), 137 (28), 132 (73), 115 (36), 105 (31), 91 (29), 77 (100), 55 (83), 50 (44); Anal. Calcd for $C_9H_9NO_3$: C, 60.33; H, 5.06; N, 7.82. Found: C, 60.48; H, 4.89; N, 7.34.

4.2. (α*S*,2*R*)-α-(4-Nitrophenyl)oxiranemethanol 5

To a stirred suspension of 4 Å molecular sieves powder (1.5 g) in dry CH_2Cl_2 (25 mL), $Ti(O^iPr)_4$ (1.27 g, 4.47 mmol) was added under nitrogen atmosphere. The reaction mixture was cooled to −20 °C and (−) diisopropyl tartate (1.25 g, 5.36 mmol) added and stirred for 10 min, after which allyl alcohol **4** (0.8 g, 4.47 mmol) dissolved in CH_2Cl_2 (20 mL) was added and stirred at −20 °C for about 30 min. To the above solution *tert*-butyl hydroperoxide (0.2 g, 2.23 mmol) dissolved in toluene was added and stirred at −20 °C for about 14 h. After completion of half of the reaction (monitored by TLC), the reaction mixture was quenched with 10% aqueous solution of tartaric acid (25 mL), after which stirring was continued for 1 h at −20 °C and 2 h at room temperature. The organic layer was separated, washed with water, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was diluted with ether (75 mL) and stirred with 1 M NaOH (25 mL) for about 1 h at 0 °C. The organic layer was then separated, washed with brine solution, dried over Na_2SO_4 and then concentrated under reduced pressure. The crude compound was purified by column chromatography using ethyl acetate–petroleum ether (3:7) to afford epoxy alcohol **5** (0.39 g, 45%) as a white solid with 94.9% ee and unreacted allylic alcohol *R*-**4** (0.34 g, 42%). mp: 74–75 °C; $[\alpha]_D^{25} = -60.8$ (*c* 1.0, $CHCl_3$); IR (KBr, cm^{-1}): 3441, 1605, 1519, 1350, 856, 808, 744; ^1H NMR (300 MHz, $CDCl_3$): δ 2.45 (br s, 1H), 2.72 (dd, 1H, $J = 4.2$, 4.9 Hz), 2.88 (dd, 1H, $J = 2.6$, 4.9 Hz), 3.20 (ddd, 1H, $J = 2.6$, 3.0, 4.2 Hz), 5.01 (br d, 1H, $J = 3.0$ Hz), 7.57 (d, 2H, $J = 9.0$ Hz), 8.23 (d, 2H, $J = 9.0$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, proton decoupled): δ 43.48, 54.59, 70.11, 123.67, 126.93, 146.71, 147.60; MS (EI): m/z (% relative intensity): 195 (M^+) (13), 152 ($M-C_2H_3O$) (100), 106 (19), 91 (8), 77 (29), 51 (18), 43 (13); Anal. Calcd for $C_9H_9NO_4$: C, 55.38; H, 4.65; N, 7.18. Found: C, 54.83; H, 4.51; N, 6.41.

4.3. (−)-Chloramphenicol 1

To a stirred solution of epoxy alcohol **5** (0.11 g, 0.56 mmol) in CH_2Cl_2 (5 mL), dichloroacetonitrile (0.19 g, 1.69 mmol) was added at 0 °C under nitrogen atmosphere. Then NaH (34 mg, 60% suspension in mineral oil, 0.85 mmol) was added, the reaction mixture allowed to return to room temperature, and stirred for 1 h. The resulting brown solution was cooled to −78 °C $BF_3{\cdot}OEt_2$ (0.14 mL, 1.13 mmol) then added and the reaction mixture allowed to room temperature. After 3 h stirring, the reaction was quenched with saturated $NaHCO_3$ (15 mL) at 0 °C. The solvent was removed under reduced pressure and then extracted with ethyl acetate (3 × 75 mL). The combined organic layers were collected and dried over Na_2SO_4. The solvent was evaporated and the crude product purified by column chromatography using ethyl acetate–petroleum ether (7:3) to afford **1** (0.13 g, 71%) as a white solid. mp: 148–149 °C lit.[13] 149.7–150.7 °C); $[\alpha]_D^{25} = -25.4$ (*c* 0.57, EtOAc) {lit.[13] $[\alpha]_D^{23} = -25.5$ (*c* 1, EtOAc)}; IR (KBr, cm^{-1}): 3261, 3078, 1686, 1564, 1521, 1350, 1065,844, 815, 653; ^1H NMR (200 MHz, DMSO-d_6): δ 3.37 (m, 1H), 3.59 (m, 1H), 3.94 (m, 1H), 5.01 (t, 1H, $J = 5.9$ Hz), 5.06 (m, 1H), 6.05 (d, 1H, $J = 4.5$ Hz), 6.47 (s, 1H), 7.59 (d, 2H, $J = 8.9$ Hz), 8.16 (d, 2H, $J = 8.9$ Hz), 8.32 (d, 1H, $J = 8.9$ Hz); ^{13}C NMR (75 MHz, DMSO-d_6, proton decoupled): δ 56.86, 60.34, 66.50, 69.06, 122.98, 127.39, 146.48, 151.33, 163.47; MS (EI): m/z (% relative intensity): 170 ($M-NO_2C_6H_4CH_2O^+$) (40), 153 ($M-NO_2C_6H_4CHO$, $-H_2O$) (100), 136 (23), 118 (18), 106 (20), 83 (11), 77 (18), 70 (32), 60 (38), 51 (10), for mass spectra see Ref. 1b; Anal. Calcd for $C_{11}H_{12}Cl_2N_2O_5$: C, 40.89; H, 3.74; N, 8.67. Found: C, 40.70; H, 3.59; N, 8.42.

4.4. 1-(4-Methylsulfanylphenyl)-2-propen-1-ol 9

To a stirred suspension of Mg (2.39 g, 98.54 mmol) in THF (25 mL), vinyl bromide (5.27 g, 49.27 mmol) in

THF (15 mL) was added at 0 °C under nitrogen atmosphere over a period of 15 min and the continued stirring at room temperature for a further 30 min. The reaction mixture was cooled to 0 °C and 4-(methylthio)benzaldehyde **8** (2.5 g, 16.42 mmol) dissolved in THF (25 mL) added over a period of 10 min. After the addition was completed, the reaction mixture was allowed to return to room temperature and stirring continued for another 2 h. The reaction mixture was quenched by the addition of aqueous ammonium chloride and extracted with ethyl acetate (3×100 mL). The combined organic fractions were collected and washed with water and brine solution, then dried over Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using ethyl acetate–petroleum ether (2:8) to afford compound **9** (2.6 g, 88%) as a thick syrup. IR (KBr, cm^{-1}): 3414, 2921, 1598, 1493, 1404, 1219, 1093, 989, 927, 815, 771, 530; ^1H NMR (300 MHz, $CDCl_3$): δ 1.88 (br s, 1H), 2.46 (s, 3H), 5.11 (m, 1H), 5.16 (dt, 1H, $J = 1.5$, 10.5 Hz), 5.31 (dt, 1H, $J = 1.5$, 17.1 Hz), 5.98 (ddd, 1H, $J = 6.0$, 10.5, 17.1 Hz), 7.19 (d, 2H, $J = 8.7$ Hz), 7.24 (d, 2H, $J = 8.7$ Hz); ^{13}C NMR (50 MHz, $CDCl_3$, proton decoupled): δ 15.90, 74.82, 115.08, 126.77, 137.78, 139.50, 140.06; MS (EI): *m/z* (% relative intensity): 180 (M^+) (100), 154 (31), 138 (28), 134 (66), 110 (50), 106 (11), 92 (11), 78 (35), 55 (88), 45 (25). Anal. Calcd for $C_{10}H_{12}SO$: C, 66.63; H, 6.71; S, 17.79. Found: C, 66.16; H, 6.38; S, 17.75.

4.5. 1-(4-Methylsulfonylphenyl)-2-propen-1-ol 10

To a stirred solution of sulfide **9** (2 g, 11.11 mmol) in a mixture of MeOH–H_2O–THF (1:1:2, 50 mL), oxone (15 g, 24.44 mmol) was added portionwise at 0 °C. The reaction mixture was allowed to room temperature, then stirred for 6 h. Filtered and extracted with ethyl acetate (3×100 mL). The combined organic fractions were collected and washed with water and brine solution and dried over Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using ethyl acetate–petroleum ether (4:6) to afford sulfone **10** (2.05 g, 87%) as a white solid. mp: 56–57 °C; IR (KBr, cm^{-1}): 3431, 3023, 1601, 1410, 1308, 1155, 955, 766, 549; ^1H NMR (300 MHz, $CDCl_3$): δ 2.40 (d, 1H, $J = 3.0$ Hz), 2.99 (s, 3H), 5.23 (dt, 1H, $J = 1.5$, 10.5 Hz), 5.26 (m, 1H), 5.37 (dt, 1H, $J = 1.5$, 16.9 Hz), 5.96 (ddd, 1H, $J = 6.4$, 10.5, 16.9 Hz), 7.54 (d, 2H, $J = 8.7$ Hz), 7.84 (d, 2H, $J = 8.7$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, proton decoupled): δ 44.42, 74.37, 116.31, 127.06, 127.36, 139.13, 139.23, 148.94; MS (EI): *m/z* (% relative intensity): 212 (M^+) (18), 197 (11), 183 (66), 170 (15), 157 (34), 141 (59), 132 (70), 115 (43), 105 (49), 91 (100), 77 (88), 55 (88), 40 (44); Anal. Calcd for $C_{10}H_{12}SO_3$: C, 56.58; H, 5.70; S, 15.11. Found: C, 56.51; H, 5.57; S, 14.51.

4.6. (α*S*,2*R*)-α-(4-Methylsulfonylphenyl)oxiranemethanol 11

To a stirred suspension of 4 Å molecular sieves powder (1 g) in dry CH_2Cl_2 (20 mL), $Ti(O^iPr)_4$ (0.80 g, 2.83 mmol) was added under nitrogen atmosphere. The reaction mixture was cooled to −20 °C where (−)-diisopropyl tartate (0.79 g, 3.40 mmol) was added and stirred for 10 min. Allyl alcohol **10** (0.6 g, 2.83 mmol) dissolved in CH_2Cl_2 (15 mL) was added and stirred at −20 °C for 30 min. *tert*-Butyl hydroperoxide (0.13 g, 1.41 mmol) dissolved in toluene was then added and stirred at −20 °C for 24 h. After completion of half of the reaction (monitored by TLC), the reaction mixture was quenched with 10% aqueous solution of tartaric acid (20 mL) and stirring continued for 1 h at −20 °C and for 2 h at room temperature. The organic layer was separated, washed with water, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was diluted with ether (75 mL) and stirred with 1 M NaOH (25 mL) for 1 h at 0 °C. The organic layer was then separated, washed with brine solution, dried over Na_2SO_4 and concentrated under reduced pressure. The crude compound was purified by column chromatography using ethyl acetate–petroleum ether (6:4) to afford epoxy alcohol **11** (0.27 g, 42%) as a thick syrup with 95.1% ee and unreacted allylic alcohol (*R*)-**10** (0.26 g, 43%). $[\alpha]_D^{25} = -47.4$ (*c* 0.95, $CHCl_3$); IR (KBr, cm^{-1}): 3456, 1768, 1405, 1299, 1220, 1148, 959, 771, 545; ^1H NMR (300 MHz, $CDCl_3$): δ 2.50 (br s, 1H), 2.73 (dd, 1H, $J = 3.7$, 5.2 Hz), 2.88 (dd, 1H, $J = 3.0$, 5.2 Hz), 3.02 (s, 3H), 3.19 (m, 1H), 4.96 (br d, 1H, $J = 3.0$ Hz), 7.59 (d, 2H, $J = 8.3$ Hz), 7.91 (d, 2H, $J = 8.3$ Hz); ^{13}C NMR (75 MHz, $CDCl_3$, proton decoupled): δ 43.56, 44.48, 54.67, 70.29, 127.14, 127.64, 140.10, 145.81; MS (EI): *m/z* (% relative intensity): 228 (M^+) (2.5), 185 ($M-C_2H_3O$) (100), 123 (14), 105 (9), 77 (28), 51 (12).

4.7. (+)-Thiamphenicol 2

To a stirred solution of epoxy alcohol **11** (0.1 g, 0.44 mmol) in CH_2Cl_2 (5 mL), dichloroacetonitrile (0.14 g, 1.31 mmol) was added at 0 °C under nitrogen atmosphere. NaH (26 mg, 60% suspension in mineral oil, 0.66 mmol) was then added and the reaction mixture allowed to return to room temperature and stirred for 4 h. The resulting brown solution was cooled to −78 °C, $BF_3{\cdot}OEt_2$ (0.11 mL, 0.88 mmol) added and the reaction mixture allowed to return to room temperature. After 4 h stirring, the reaction was quenched with saturated $NaHCO_3$ (15 mL) at 0 °C. The solvent was removed under reduced pressure and then extracted with ethyl acetate (3×75 mL). The combined organic layers were collected and dried over Na_2SO_4. The solvent was evaporated and the crude product purified by column chromatography using ethyl acetate–petroleum ether (9:1) to afford **2** (0.1 g, 64%) as a white solid. mp: 163–164 °C (lit.[3] 164.3–166.3 °C); $[\alpha]_D^{25} = +12.6$ (*c* 0.65, EtOH) {lit.[3] $[\alpha]_D^{25} = +12.9$ (*c* 1, EtOH)}; IR (KBr, cm^{-1}): 3452, 3260, 2920, 1691, 1560, 1407, 1281, 1144, 1067, 1033, 769, 545; ^1H NMR (300 MHz, acetone-d_6): δ 3.07 (s, 3H), 3.68 (m, 1H), 3.78 (m, 1H), 4.14 (dddd, 1H, $J = 2.6$, 5.3, 7.6, 8.3, Hz), 4.25 (t, 1H, $J = 4.7$ Hz), 5.18 (d, 1H, $J = 4.1$ Hz), 5.29 (m, 1H), 6.37 (s, 1H), 7.53 (d, 1H, $J = 8.3$ Hz), 7.68 (d, 2H, $J = 8.3$ Hz), 7.88 (d, 2H, $J = 8.3$ Hz); ^1H NMR (300 MHz, DMSO-d_6): δ 3.15 (s, 3H), 3.39 (m, 1H), 3.56 (m, 1H), 3.91 (m, 1H), 4.96 (t,

1H, $J = 5.5$ Hz), 5.01 (m, 1H), 5.95 (d, 1H, $J = 4.5$ Hz), 6.49 (s, 1H), 7.57 (d, 2H, $J = 8.2$ Hz), 7.83 (d, 2H, $J = 8.2$ Hz), 8.27 (d, 1H, $J = 9.1$ Hz); ^{13}C NMR (75 MHz, acetone-d_6 proton decoupled): δ 44.34, 57.99, 62.08, 67.51, 71.21, 127.77, 127.85, 140.95, 149.59. 164.42, for data of ^{13}C spectrum see Ref. 12; ^{13}C NMR (75 MHz, DMSO-d_6, proton decoupled): δ 43.68, 56.96, 60.31, 66.55, 69.17, 126.55, 127.13, 139.25, 149.26, 163.57; MS (FAB): m/z 356 (M^++1); Anal. Calcd for $C_{12}H_{15}Cl_2NSO_5$: C, 40.46; H, 4.24; N, 3.93; S, 9.00. Found: C, 40.02; H, 4.07; N, 3.58; S, 8.67.

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