Iron-Catalyzed Cross-Coupling of Imidoyl Chlorides with Grignard Reagents

Lars K. Ottesen, Fredrik Ek, and Roger Olsson*

SUPPORTING INFORMATION

Table of Contents

Supporting information file one(this file)

General experimental paragraph **S3**

Experimental details **S3-S15**

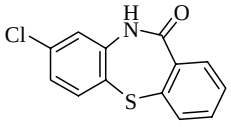
Supporting information file two

^{13}C NMR **S16-S38**

Supporting information file three

^{1}H NMR **S39-S61**

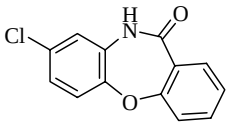
General Information. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian mercury 400 VX (^{1}H-NMR at 400 MHz and ^{13}C-NMR at 100 MHz) spectrometer with solvent resonance as the internal standard: $CDCl_3$ (δ_H: 7.26, δ_C: 77.16); DMSO-d_6: (δ_H: 2.50, δ_C: 39.52); Acetone-d_6: (δ_H: 2.05, δ_C: 29.84; 206.26) and MeOH-d_4 (δ_H: 3.31, δ_C: 49.00) ^{1}H NMR are reported as follows: chemical shifts in ppm, multiplicity (s = singlet, br s = broad singlet, d = doublet, dd = double doublet, t = triplet, tt = triple triplet, m = multiplet). The microwave-assisted reactions were carried out using a *SmithCreator*™ single mode cavity; producing continuous irradiation at 2450 MHz. Reaction temperature and pressure were determined using the build in, on-line IR- and pressure sensors. Analytical thin layer chromatography (TLC) was performed on Silica gel 60 F_{254}. Visualization was accomplished with UV light. Purification of the reaction products was carried out by column chromatography using SiO_2 (60 Å, 200 µ). Melting points were optained using SMP3 Melting Point Apparatus with an open capillary tube and are uncorrected. HRMS analyses were recorded in FAB(+) mode using direct inlet. Unless otherwise noted, all reagents were obtained from commercial sources and used without further purification.



8-chloro-10H-dibenzo[b,f][1,4]thiazepin-11-one: Cs_2CO_3 (7.43 g, 23 mmol) was added to a solution of 4-chloro-1-fluoro-2-nitrobenzene (2.00 g, 11 mmol) and methyl 2-mercaptobenzoate (3.13 ml, 23 mmol) in DMF (25 ml) and the resulting mixture was stirred for 2 hours at 40 °C. The reaction mixture was then cooled to room temperature and diluted with DCM (60 ml). The organic phase was washed with water and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave 2.6 g (73 %) of the crude product, which was sufficiently pure to be used in the next step without further purification. The crude product (2.6 g, 8.0 mmol) was dissolved in THF (15 ml) and 2 M LiOH (40 mmol) and stirred at 60 °C for 2 hours and then allowed to cool to room temperature. THF was removed at reduced pressure and the aqueous mixture was acidified with HCl (2M) until pH 2. The precipitation was filtered off, washed with 0.1 M NaOH solution and finally dried to give the crude product 2.3 g (93%). $Na_2S_2O_4$ (37 mmol) was added to a solution of the crude product (2.3 g, 7.4 mmol) in 2 M K_2CO_3 (35 mmol) and EtOH (20 ml) and the reaction was stirred at room temperature for 15 min. EtOH was removed at reduced pressure and the resulting aqueous mixture was acidified with HCl (2M) until pH 2 and poured into ethyl acetate. The organic layer was washed with water, brine, dried (Na_2SO_4), filtered and evaporated to give the crude product 1.2 g (61%). Finally, the crude product (1.2 g, 4.3 mmol), EDCI (1.24 g, 6.5 mmol), HOBt (878 mg, 6.5 mmol), DMAP (5 mg, 0.04 mmol) and TEA (19.3 mmol) in MeCN (8 ml) was heated in microwave at 140 °C for 10

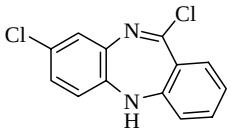
min. The reaction mixture was cooled to room temperature, diluted with water and acidified with HCl (2M) until pH 2. The precipitation was filtered off, washed with 0.1 M NaOH solution and dried to give 572 mg (51%) of the title compound as a white powder, which was sufficiently pure to be used without further purification. M.p. 295-300 °C; Litt. 290 °C (*Collect Czech. Chem. Commun*. **1959**, 24, 207-211).

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.72 (br s, 1H,), 7.68 (m, 1H), 7.51 (m, 4H), 7.28 (d, 1H, *J* = 2.4 Hz), 7.20 (dd, 1H, *J* = 8.4, 2.4 Hz); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 142.0, 138.3, 136.3, 134.6 (2C), 133.0, 132.1 (2C), 129.9, 128.4, 125.8, 123.3.



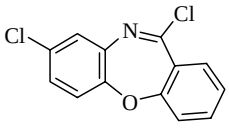
8-Chloro-10H-dibenzo[b,1][1,4]oxazepin-11-one: Cs_2CO_3 (7.43 g, 23 mmol) was added to a solution of 4-chloro-1-fluoro-2-nitrobenzene (2.00 g, 11 mmol) and methyl salicylate (2.92 ml, 23 mmol) in DMF (25 ml) and the resulting mixture was stirred for 2 hours at 60 °C. The reaction mixture was cooled to room temperature and diluted with DCM (60 ml). The organic phase was washed with water and then dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave 2.80 g (80%) of the crude product, which was sufficiently pure to be used in the next step without further purification. The crude product (2.8 g, 9.55 mmol) was then dissolved in THF (15 ml) and 2 M LiOH (40 mmol) and stirred at 60 °C for 2 h and then allowed to cool to room temperature. THF was removed at reduced pressure and the aqueous mixture was acidified with HCl (2M) until pH 2. The precipitation was filtered off, washed with 0.1 M NaOH solution and finally dried to give the crude product 2.4 g (86%). $Na_2S_2O_4$ (37 mmol) was added to a solution of the crude product (2.4 g, 8.2 mmol) in 2 M K_2CO_3 (41 mmol) and EtOH (20 ml) and the reaction was stirred at room temperature for 15 min. EtOH was then removed at reduced pressure and the resulting aqueous mixture was acidified with HCl (2M) until pH 2 and poured into ethyl acetate. The organic layer was washed with water, brine, dried (Na_2SO_4), filtered and evaporated to give the crude product 1.1 g (52%). Finally, the crude product (1.1 g, 4.2 mmol), EDCI (1.20 g, 6.3 mmol), HOBt (851 mg, 6.3 mmol), DMAP (5 mg, 0.04 mmol) and TEA (18.9 mmol) in MeCN (8 ml) was heated in microwave at 140 °C for 10 min. The reaction mixture was cooled to room temperature, diluted with water and acidified with HCl (2M) until pH 2. The precipitation was filtered off, washed with 0.1 M NaOH solution and dried (Na_2SO_4) to give 676 mg (66%) of the title compound as a white powder, which was sufficiently pure to be used without further purification. M.p. 255-258 °C (decomposition); Litt. 250-255 °C (*Applied and Environmental Microbiology* **1977**, 33 (1), 26-30).

^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.61 (br s, 1H), 7.76 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.64-7.58 (m, 1H), 7.38-7.28 (m, 3H), 7.20-7.12 (m, 2H); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 166.3, 159.2, 149.8, 135.4, 133.3, 132.2, 130.2, 126.4, 126.0, 125.4, 123.7, 121.6, 121.3.



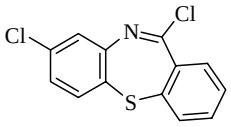
8,11-Dichloro- 5H-dibenzo[b,e][1,4]diazepine (8): A mixture of 8-Chloro-11-oxo-10,11-dihydro-5H-dibenzo-1,4-diazepine (2.90 g, 20 mmol), phosphorus oxychloride (5.6 ml, 60 mmol) and N-dimethylaniline (10.2 ml, 80 mmol) in toluene (40 ml) was heated at 95 °C for 2 hours. The reaction mixture was then cooled to room temperature and excess of phosphorus oxychloride, N-dimethylaniline and toluene was removed at reduced pressure. The resulting residue was then dissolved in dioxane (20 ml) and 2 M Na_2CO_3 (30 ml, 0.06 mol) and heated at 80 °C for 1 hour. The reaction mixture was cooled to room temperature and dioxane was removed at reduced pressure and the resulting aqueous solution was extracted with EtOAc (30 ml). The organic phase was washed with water, brine and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (EtOAc/heptane 1:4) afforded 3.76 g (72%) of the title compound as a yellow powder. M.p. 128-130 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.31 (1H, dt, *J* = 7.6, 1.6 Hz), 7.15 (d, 1H, *J* = 2.4 Hz), 7.04-7.00 (m, 2H), 6.63 (dd, 1H, *J* = 8.0, 1.2 Hz), 6.58 (d, 1H, *J* = 8.4 Hz), 4.95 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 152.1, 140.3, 138.3, 134.1, 132.0, 129.8, 128.6, 128.1, 127.1, 123.6, 121.0, 119.8; HRMS (Ion Mode: FAB$^+$) *m/z* [M] Calcd for $C_{13}H_8Cl_2N_2$, 262.0065; Found, 262.0068.



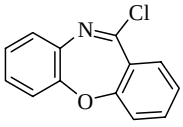
8,11-Dichlorodibenzo[b,f][1,4]oxazepine (9): 8-Chloro-10H-dibenzo [b,1] [1,4] oxazepin-11-one (490 mg, 2.0 mmol) was heated in phosphorus oxychloride (15 ml) at 95 °C for 2 hours. The reaction mixture was then cooled to room temperature and excess of phosphorus oxychloride was removed at reduced pressure. The resulting residue was dissolved in EtOAc (30 ml) and the organic phase was washed with brine and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (EtOAc/heptane 1:4) afforded 440 mg (84%) as a white powder. M.p. 101-103 °C; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{13}H_7Cl_2NO_2$, 263.9983; Found, 263.9993.

^{1}H NMR (400 MHz, acetone-d_6) δ 7.82 (dd, 1H, *J* = 7.6, 1.6 Hz), 7.72-7.67 (m, 1H) 7.43-7.39 (m, 1H), 7.36-7.29 (m, 4H); ^{13}C NMR (100 MHz, acetone-d_6) δ 160.1, 155.3, 150.5, 139.2, 135.7, 130.9, 130.6, 129.0, 127.3, 127.1, 126.3, 122.9, 121.3.



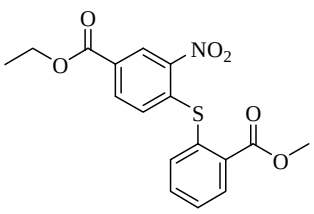
8,11-Dichloro-dibenzo [b,f] [1,4] thiazepine (10): 8-Chloro-10H-dibenzo [b,f] [1,4] thiazepin-11-one (500 mg, 1.92 mmol) was heated in phosphorus oxychloride (15 ml) at 95 °C for 2 hours. The reaction mixture was then cooled to room temperature and excess of phosphorus oxychloride was removed at reduced pressure. The resulting residue was dissolved in EtOAc (30 ml) and the organic phase was washed with brine and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (EtOAc/heptane 1:4) afforded 395 mg (74 %) of the title compound as a white powder. M.p. 120-124 °C; Litt. 118-119 °C (*Helv. Chim. Acta* **1967**, 50, 245-254).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, 1H, *J* = 8.0Hz), 7.45-7.36 (m, 4H), 7.28-7.26 (m, 1H), 7.15-7.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 147.1, 138.7, 137.9, 135.4, 133.6, 133.0, 132.2, 130.1, 129.0, 127.4, 126.4, 125.7.



11-Chloro-dibenzo[b,f][1,4]oxazepine (1): 10H-Dibenzo[b,f][1,4]oxazepine-11-one (500 mg, 2.37 mmol) was added phosphorus oxychloride (20 ml) and heated at 95 °C for 2 hours. The reaction mixture was then cooled to room temperature and excess of phosphorus oxychloride was removed at reduced pressure. The resulting residue was dissolved in EtOAc (25 ml) and the organic phase was washed with brine and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (EtOAc/Heptane 1:4) afforded 424 mg (78%) of the title compound as an oil, which solidifies on standing at 5 °C. M.p. 53-55; Litt. 53-55 °C (US 4002639).

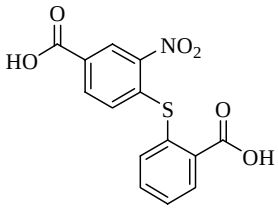
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, 1H, *J* = 2Hz), 7.54-7.50 (m, 1H), 7.35-7.32 (m, 1H), 7.27-7.23 (m, 2H), 7.21-7.16 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 154.2, 151,6, 138.2, 134.7, 130.6, 129.1, 128.2, 127.4, 126.1, 125.5, 121.3, 121.



4-(2-Methoxycarbonyl-phenylsulfanyl)-3-nitro-benzoic acid ethyl ester: Cs_2CO_3 (10.06 g, 30.9 mmol) was added to a solution of ethyl 4-flouro-3-nitrobenzoate (6.60 g, 30.9 mmol) and methyl 2-

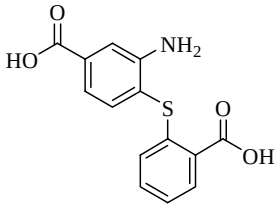
mercaptobenzoate (4.67 ml, 34 mmol) in DMF (60 ml) and the resulting mixture was stirred for 2 hours at 40 °C. The reaction mixture was cooled to room temperature and diluted with DCM (60 ml). The organic phase was washed with water and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure and column chromatography (ethyl acetate/heptane 1:4) gave a yellow crystalline residue. Recrystallization from EtOAc-heptane gave 10.3 g (92%) of the title compound as yellow crystals. M.p. 117-119 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, 1H, *J* = 1.9 Hz), 7.94 (m, 2H), 7.62-7.57 (m, 3H), 6.92 (d, 1H, *J* = 8.6 Hz), 4.38 (q, 2H, *J* = 7.2 Hz), 3.78 (s, 3H), 1.38 (t, 3H, *J* = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.8, 164.6, 145.5, 144.1, 137.6, 136.3, 133.4, 133.0, 131.5, 131.3, 130.5, 129.8, 128.1, 126.9, 61.9, 52.7, 14.5; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{17}H_{15}NO_6S$, 362.0698; Found, 362.0701.



4-(2-Carboxy-phenylsulfanyl)-3-nitro-benzoicacid: 4-(2-Methoxy carbonyl-phenylsulfanyl)-3-nitro-benzoic acid ethyl ester (9.56 g, 26.5 mmol) dissolved in THF (570 ml) and aqueous LiOH (264 ml, 1M) was stirred at 60 °C for 2 hours and then allowed to cool to room temperature. THF was removed at reduced pressure and the remaining aquerous mixture was extracted once with EtOAc. HCl (2M) was then added to the resulting solution until pH 2. The precipitation was filtered off, washed with water and finally dried, which afforded 8.7 g (99%) of the title compound as yellow crystals. M.p. 250-253 °C.

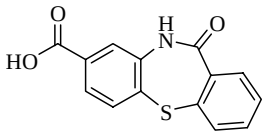
^{1}H NMR (400 MHz, methanol-d_4) δ 8.71 (d, 1H, *J* = 1.8 Hz), 7.95 (m, 2H), 7.64-7.59 (m, 3H), 7.00 (d, 1H, *J* = 8.6 Hz); ^{13}C NMR (100 MHz, methanol-d_4) δ 168.3, 166.1, 145.9, 143.3, 137.0, 136.5, 133.2, 132.6, 131.2, 131.1, 130.1, 130.0, 128.6, 126.3; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{14}H_9NO_6S$, 320.0229; Found, 320.0232.



3-Amino-4-(2-carboxy-phenylsulfanyl)-benzoic acid: Pd/C (10%, 200 mg) and PtO_2 (100 mg) were added to 4-(2-carboxy-phenylsulfanyl)-3-nitro-benzoicacid (2.9 g, 9.1 mmol) dissolved in 100 ml MeOH. A balloon containing H_2 was connected to the flask and the reaction flask was repeatedly evacuated and refilled with H_2. After 16 hours the reaction mixture was filtered through a pad of celite, which then was washed carefully with MeOH. Concentration of the filtrate at reduced pressure gave the crude product. Purification by

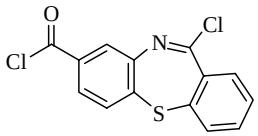
recrystallization from EtOAc/MeOH afforded 2.3g (88%) of the title compound as yellow crystals. M.p. 244-248 °C.

^{1}H NMR (400 MHz, methanol-d_4) δ 8.01 (d, 1H, *J* = 7.6 Hz), 7.51 (s, 1H), 7.44 (d, 1H, *J* = 8.0 Hz), 7.31 (d, 1H, *J* = 8.0 Hz), 7.28 (t, 1H, *J* = 8.0 Hz), 7.16 (t, 1H, *J* = 7.2 Hz), 6.74 (d, 1H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, methanol-d_4): 169.8, 151.6, 141.6, 138.6 (2C), 134.7, 133.5, 132.7, 128.8, 127.2, 125.6, 119.9, 119.6, 117.3; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{14}H_{11}NO_4S$, 290.0487; Found, 290.0487.



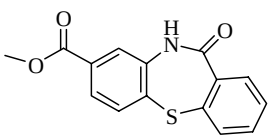
11-Oxo-10,11-dihydro-dibenzo [b,f][1,4] thiazepine-8-carboxylic acid: CDI (4.53 g, 29 mmol) was added to 3-amino-4-(2-carboxy-phenylsulfanyl)-benzoic acid (2.1 g, 7.3 mmol) dissolved in THF (30 ml). The reaction mixture was stirred for 16 hours at room temperature. Water (200 ml) was then added to the reaction and the precipitant was filtered off and dried. Recrystallization from toluene gave 1.78 g (91%) of the title compound as a white solid. M.p. 330-335 °C.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (br s, 1H), 7.77 (s, 1H), 7.67 (m, 3H), 7.55-7.42 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 166.9, 140.3, 138.3, 136.0, 134.5, 133.5, 133.0, 132.9, 132.2, 132.1, 129.9, 126.5, 124.3; MS (ES$^+$, M+1): 272.4.



11-Chloro-dihydro-dibenzo [b,f][1,4] thiazepine-8-carbonyl chloride: A solution of 11-oxo-10,11-dihydro-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid (200 mg, 0.74 mmol) and phosphorus pentachloride (756 mg, 3.68 mmol) in 4 ml toluene was heated at 110 °C for 2 hours. Toluene and excess of phosphorus pentachloride were removed at reduced pressure to give 193 mg (85%) of the title compound as a yellow solid, which was sufficiently pure to be used without further purification. M.p. 130-132 °C.

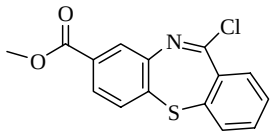
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, 1H, *J* = 2.0 Hz), 7.87 (dd, 1H, *J* = 8.4, 2.2 Hz), 7.77 (m, 1H), 7.58 (d, 1H, *J* = 8.2 Hz), 7.47-7.44 (m, 2H), 7.44-7.39 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 157.1, 146.7, 137.8, 137.4, 136.3, 134.5, 133.4, 133.3, 132.6, 130.3, 129.5, 129.1, 128.8.



11-Oxo-10,11-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methyl ester: Na_2CO_3 (1.39 g, 13.05 mmol) was added to a solution of 11-oxo-

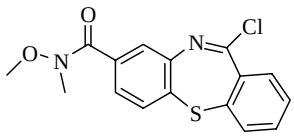
10,11-dihydro-dibenzo [b,f][1,4] thiazepine-8-carboxylic acid (715 mg, 2.61 mmol) in DMF (20 ml) and the reaction mixture was stirred for 30 min at room temperature. CH_3I (0.81 ml, 13.05 mmol) was added and the two-phase mixture was stirred for 30 min. DMF was then removed at reduced pressure using an oil pump and the resulting residue was dissolved in EtOAc (25 ml). The organic phase was washed with saturated aqueous $NaHCO_3$, brine and then dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by recrystallization from toluene afforded 640 mg (86%) of the title compound as a white solid. M.p. 245-250 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (br s, 1H), 7.88-7.86 (m, 2H), 7.79-7.77 (m, 1H), 7.64 (d, 1H, *J* = 8.0Hz), 7.52-7.50 (m, 1H), 7.45-7.38 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 165.9, 139.6, 136.8, 136.4, 135.8, 133.3, 132.7, 132.3, 132.2, 131.8, 129.3, 127.0, 123.7, 52.7; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{14}H_{11}NO_3S$, 286.0538; Found, 286.0534.



11-chloro-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methyl ester (14): A solution of 11-oxo-10,11-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methyl ester (540 mg, 1.89 mmol) and phosphorus pentachloride (1.97 g, 9.45 mmol) in 15 ml toluene was heated at 110 °C for 2 hours. Toluene and excess of phosphorus pentachloride were removed at reduced pressure. The resulting residue was dissolved in EtOAc (70 ml) and the organic phase was washed with water, brine and then dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (EtOAc/heptane 1:4) afforded 410 mg (71 %) of the title compound as a yellow oil.

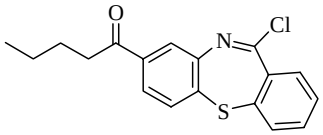
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, 1H, *J* = 2.0, 0.4Hz), 7.75 (dd, 1H, *J* = 8.0, 1.6 Hz), 7.69-7.67 (m, 1H), 7.45 (dd, 1H, *J* = 8.4, 0.4Hz), 7.40-7.32 (m, 3H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 156.1, 146.3, 138.1, 137.9, 133.2, 133.1, 132.9, 132.4, 131.7, 130.2, 129.2, 128.1, 127.1, 52.6; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{15}H_{10}ClNO_2S$, 304.0199; Found, 304.0197.



11-Chloro-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methoxy-methyl-amide (16): A flame dried 10 ml flask under argon was charged with 8,11-dichloro-dibenzo[b,f][1,4]thiazepine (622 mg, 2.0 mmol) in dry DCM (4 ml) and the resulting solution was then slowly added to a mixture of N,O-

dimethylhydroxylamine hydrochloride (388 mg, 4.0 mmol) and TEA (0.83 ml, 6.0 mmol) in dry DCM (6 ml). The resulting reaction mixture was stirred at room temperature for 30 min and then diluted with DCM (20 ml). The organic phase was washed with water, brine and dried (Na_2SO_4). Filtration and removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 518 mg (78 %) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76-7.73 (m, 1H), 7.57-7.56 (m, 1H), 7.50-7.83 (m, 5H), 3.54 (s, 3H), 3.33 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 168.5, 156.0, 146.0, 138.4, 137.9, 135.7, 133.1, 132.6, 132.3, 130.4, 130.2, 129.1, 127.2, 125.7, 61.5, 33.8; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{16}H_{13}ClN_2O_2S$, 333.0464; Found, 333.0467.



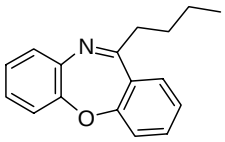
1-(11-Chloro-dibenzo [b,f][1,4] thiazepine-8-yl)-pentan-1-one (19): Butylmagnesium chloride (0.10 ml, 0.2 mmol) was added to a solution of 11-chloro-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methoxy-methyl-amide (34 mg, 0.10 mmol) in dry THF (2 ml). The resulting reaction mixture was stirred at room temperature for 1 hour and then quenched with saturated aqueous NH_4Cl (0.2 ml) and diluted with Et_2O (15 ml). The organic phase was washed with water, brine and dried (Na_2SO_4). Filtration and removal of the solvent at reduced pressure gave the crude product. Purification by column chromatography (ethyl acetate/heptane 1:5) afforded 26 mg (81 %) of the title compound as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, 1H, *J* = 1.6Hz), 7.77-7.74 (m, 2H), 7.53 (d, 1H, *J* = 8.4Hz), 7.47-7.39 (m, 3H), 2.90 (t, 2H, *J* = 7.2Hz), 1.68 (quintet , 2H, *J* = 7.2Hz), 1.37 (sextet , 2H, *J* = 7.2Hz), 0.93 (t, 3H, J = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 156.2, 146.4, 138.3, 138.1, 137.8, 133.2, 133.1(2), 132,5, 1302, 129.2, 126.6, 125.8, 38.7, 26.5, 22.6, 14.1.; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{18}H_{16}ClNOS$, 330.0719; Found, 330.0718.

A typical procedure for the cross-coupling reactions (table 1).

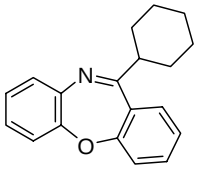
A flame-dried 10 ml flask was charged under argon with the imidoyl chloride (0.20 mmol), $Fe(acac)_3$ (0.01 mmol) in dry THF (2 ml) and NMP (0.2 ml). A solution of butylmagnesium chloride (0.40 mmol) was then slowly added to the resulting red solution, causing an immediate color change to dark brown. The resulting mixture was stirred for 5 min at room temperature and

the reaction was then quenched upon the addition of saturated aqueous NH_4Cl (0.2 ml) and diluted with Et_2O (25 ml). The organic phase was washed with water, brine and dried (Na_2SO_4). Filtration, removal of the solvent at reduced pressure gave the crude product.



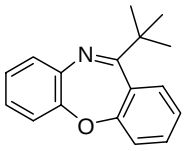
11-Butyl-dibenzo[b,f][1,4]oxazepine (2): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol). Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 48 mg (96%) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.41 (m, 2H), 7.30-7.26 (m, 1H), 7.22-7.18 (m, 2H), 7.16-7.13 (m, 3H), 2.93 (t, 2H, *J* = 7.2Hz), 1.71 (quintet, 2H, *J* = 7.6Hz), 1.46 (m, 2H), 0.99 (t, 3H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 161.7, 152.8, 141.0, 132.7, 128.7, 128.4, 127.9, 127.2, 125.7, 125.3, 121.1, 120.8, 40.2, 29.9, 22.7, 14.2; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{17}H_{17}NO$, 252.1388; Found: 252.1387.



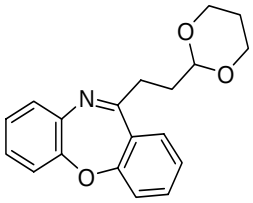
11-Cyclohexyl-dibenzo[b,f][1,4]oxazepine (3): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol) except cyclohexylmagnesium chloride (0.20 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 52 mg (93 %) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.37 (m, 2H), 7.28-7.25 (m, 1H), 7.20-7.09 (m, 5H), 2.91 (tt, 1H, *J* = 14.8, 3.2Hz), 2.00-1.97 (m, 2H), 1.89-1.85 (m, 2H), 1.75-1.71 (m, 1H), 1.67-1.55 (m, 2H), 1.45-1.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 162.0, 152.7, 141.2, 132.3, 128.9, 127.9 (2C), 126.9, 125.6, 125.2, 120.9, 120.6, 47.0, 31.6, 26.6, 26.4; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{19}H_{19}NO$, 278.1545; Found: 278.1554.



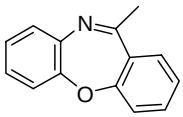
11-Tertbutyl-dibenzo[b,f][1,4]oxazepine (4): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol), except *tert*-butylmagnesium chloride (2 M in Et_2O, 0.20 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 14 mg (27%) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (dd, 1H, *J* = 7.6, 1.6Hz), 7.38-7.33 (m, 1H), 7.23-7.20 (m, 2H), 7.18-7.06 (m, 4H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.0,162.2, 152.5, 141.1, 131.5, 128.1, 127.2, 126.8, 126.4, 125.5, 124.3, 121.0, 120.2,41.5, 30.5; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{17}H_{17}NO$, 252.1388; Found, 252.1402.



11-(2-[1,3]Dioxane-2-yl-ethyl)-dibenzo[b,f][1,4]oxazepine (5): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol) except 1,3-dioxane-2-yl-ethyl magnesium bromide (0.5 M in Et_2O, 0.80 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 59 mg (95 %) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, 1H, *J* = 7.6, 1.2 Hz), 7.40 (dt, 1H, *J* = 8.0, 1.6Hz), 7.28-7.25 (m, 1H), 7.20-7.12 (m, 5H), 4.69 (t, 1H, *J* = 5.2Hz), 4.10 (dd, 2H, *J* = 11.6, 4.8Hz), 3.75 (dt, 2H, *J* = 12.0, 1,6Hz), 3.03 (t, 2H, *J* = 4.8Hz), 2.13-2.02 (m, 3H), 1.35-1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.76, 161.5, 152.7, 141.0, 132.7, 128.9, 128.4, 128.0, 127.2, 125.6, 125.3, 120.9, 120.7, 101.6, 67.1, 34.1, 32.6, 26.0; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{19}H_{19}NO_3$: 310.1443; Found: 310.1433.

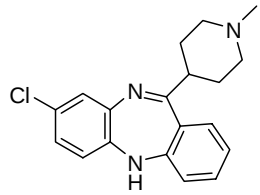


11-Methyl-dibenzo[b,f][1,4]oxazepine (6): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol) except trimethylsilylmethylmagnesium chloride (2 M in Et_2O, 0.20 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 30 mg (72 %) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.40 (m, 2H), 7.29-7.26 (m, 1H), 7.22-7.14 (m, 5H), 2.65 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 161.1, 152.7, 140.9, 132.9, 129.3, 128.7, 127.9, 127.4, 125.7, 125.2, 121.0, 120.8, 27.8; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{14}H_{11}NO$, 210.0919; Found: 210.0925.

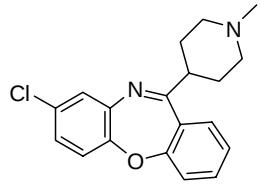
11-Methyl-dibenzo [b,f] [1,4] oxazepine (6): The reaction was performed according to the typical procedure using 11-chloro-dibenzo [b,f][1,4] oxazepine (46 mg, 0.20 mmol) except methylmagnesium chloride (1 M in THF, 0.40 ml, 0.40 mmol) was used in this reaction. ^{1}H-NMR

yield based on toluen as an internal standard showed 11-methyl-dibenzo[b,f][1,4]oxazepine in 17% yield.



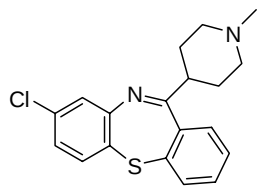
8-Chloro-11-(1-methyl-piperidine-4-yl)-5H-dibenzo [b,e][1,4] diazepine (11): The reaction was performed according to the typical procedure using 8,11-dichloro- 5H-dibenzo[b,e]-1,4-diazepine (53 mg, 0.2 mmol) except that 4-methylpiperidinemagnesium chloride (1 M in THF, 0.40 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane/MeOH/Et_3N 2:1:5%:1%) afforded 53 mg (82%) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, methanol-d_4) δ 7.32 (dd, 1H, *J* = 7.6, 1.2Hz), 7.24-7.22 (m, 1H), 7.00-6.96 (m, 2H), 6.93 (dd, 1H, *J* = 8.4, 2.4Hz), 6.83 (dd, 1H, *J* = 8.0, 1.2Hz), 6.75 (d, 1H, *J* = 8.4Hz), 6.64 (br s, 1H), 2.96-2.92 (m, 2H), 2.87-2.81 (m, 1H), 2.28 (s, 3H),2.18-2.11 (m, 2H), 1.91-1.83 (m, 4H); ^{13}C NMR (100 MHz, methanol-d_4) δ 176.7, 155.6, 143.0, 142.2, 131.6, 128.3, 128.3, 128.1, 127.0, 125.7, 122.8, 120.6, 119.5, 55.3, 45.1, 44.2, 30.0; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{19}H_{20}ClN_3$, 326.1424; Found, 326.1424.



8-Chloro-11-(1-methyl-piperidine-4-yl)-5H-dibenzo [b,f][1,4] oxazepine (12): The reaction was performed according to the typical procedure using 8,11-dichlorodibenzo [b,f][1,4] oxazepine (53 mg, 0.20 mmol) except that 4-methylpiperidinemagnesium chloride (1 M THF, 0.40 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane/MeOH/Et_3N 2:1:5%:1%) afforded 46 mg (71%) of the title compound as a yellow oil.

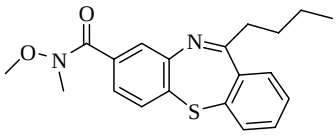
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44-7.41 (m, 2H), 7.25-7.15 (m, 2H), 7.17-7.15 (m, 1H), 7.08-7.02 (m, 2H), 2.97-2.94 (m, 2H), 2.90-2.87 (m, 1H), 2.31 (s, 3H), 2.10-2.04 (m, 2H), 1.95-1.91 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.5, 161,5, 151,0, 141.8, 132.5, 130.4, 128.0, 127.6, 127.5, 126.5, 125.3, 121.4, 120.8, 55.8, 46.5, 44.1, 30.5; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{19}H_{19}ClN_2O$, 327.1264; Found, 327.1273.



8-Chloro-11-(1-methyl-piperidine-4-yl)-5H-dibenzo [b,f] [1,4] thiazepine (13): The reaction was performed according to the typical

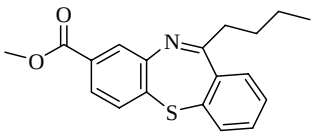
procedure using 8,11-dichloro-dibenzo[b,f][1,4]thiazepine (56 mg, 0.20 mmol) except that 4-methylpiperidinemagnesium chloride (1 M in THF, 0.40 ml, 0.40 mmol) was used in this reaction. Purification by column chromatography (ethyl acetate/heptane/MeOH/Et_3N 2:1:5%:1%) afforded 59 mg (86%) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44-7.42 (m, 1H), 7.35-7.30 (m, 4H), 7.16 (d, 1H, *J* = 2.4Hz), 6.97 (dd, 1H, *J* = 8.4, 2.4Hz), 3.02-2.99 (m, 1H), 2.86-2.83 (m, 2H), 2.29 (s, 3H), 2.11-2.09 (m, 3H), 2.03-1.96 (m, 1H), 1.71-1.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.3, 149.9, 140.8, 138.7, 134.9, 133.3, 132,0, 130.6, 128.8, 127.4, 127.3, 125.2 (2C), 56.2, 55.6, 46.6, 46.3, 31.6, 29.2; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{19}H_{19}ClN_2S$, 343.1036; Found, 343.1037.



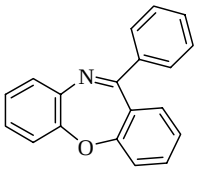
11-butyl-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methoxy-methyl-amide (17): The reaction was performed according to the typical procedure using 11-chloro-dibenzo [b,f][1,4] thiazepine-8-carboxylic acid methoxy-methyl-amide (62 mg, 0.19 mmol). Purification by column chromatography (ethyl acetate/heptane 1:1) afforded 47 mg (70 %) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45-7.42 (m, 3H), 7.39-7.29 (m, 4H), 3.54 (s, 3H), 3.32 (s, 3H), 3.01-2.82 (m, 2H), 1.69-1.59 (m, 2H), 1.51-1.41 (m, 2H), 0.92 (t, 3H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.4, 169.2, 148.7, 140.0, 139.0, 135.2, 132.2, 132.1, 131.6, 130.8, 128.7, 127.9, 125.1, 124.9, 61.4, 42.2, 34.1, 29.6, 22.7, 14.1; HRMS (Ion Mode: FAB$^+$) *m/z* [M+H$^+$] Calcd for $C_{20}H_{22}N_2O_2S$, 355,1480; Found, 355.77.



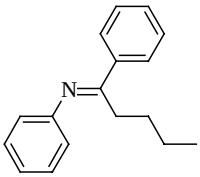
11-Butyl-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methyl ester (15): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]thiazepine-8-carboxylic acid methyl ester (152 mg, 0.50 mmol). Purification by column chromatography (ethyl acetate/heptane 1:5) afforded 144 mg (89%) of the title compound as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, 1H, *J* = 1.6Hz), 7.68 (dd, 1H, *J* = 8.0, 1.6Hz), 7.74-7.43 (m, 2H), 7.40-7.31 (m, 3H), 3.87 (s, 3H), 3.02-2.85 (m, 2H), 1.74-1.58 (m, 2H), 1.55-1.41 (m, 2H), 0.93 (t, 3H, *J* = 7.2Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 166.7, 148.8, 139.7, 139.0, 134.4, 132.5, 132.3, 131.1, 130.9, 128.9, 127.9, 126.6, 126.1, 52.4, 42.2, 29.5, 22.7, 14.2; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{19}H_{19}NO_2S$, 325.1136; Found: 325.1136.



11-Phenyl-dibenzo[b,f][1,4]oxazepine (7): The reaction was performed according to the typical procedure using 11-chloro-dibenzo[b,f][1,4]oxazepine (46 mg, 0.20 mmol) except that an excess (6 equivalents) of phenylmagnesium chloride (0.60 ml, 1.2 mmol) was used and the reaction time (30 min) was extended. Purification by column chromatography (ethyl acetate/heptane 1:4) afforded 30 mg (55%) of the title compound as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84-7.81 (m, 2H), 7.51-7.42 (m, 5H), 7.28-7.27 (m, 1H), 7.23-7.13 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 162.2, 152.6, 141.0, 140.3, 133.1, 131.4, 130.5, 129.8, 128.4, 128.3, 127.7, 127.6, 125.7, 124.6, 121.1, 120.8; HRMS (Ion Mode: FAB^+) *m/z* [$M+H^+$] Calcd for $C_{19}H_{13}NO$: 272.1075; Found: 272.1067.



Phenyl-[1-phenyl-pent-(E/Z)-ylidene]-amine (21): A mixture of Benzanilide (50 mg, 0.25 mmol) and $SOCl_2$ (5 ml) was heated at 80 °C for 1 hour. The excess of $SOCl_2$ was removed at reduced pressure and the obtained imidoyl chloride was used in the next step without purification. The cross-coupling reaction was performed according to the typical procedure. Purification by column chromatography (ethyl acetate/heptane 1:10) afforded 43 mg (72%) of the title compound (E:Z;7:1) as a colourless oil.