



SUPPLEMENTARY MATERIAL TO
**Microwave-assisted synthesis of 1,2,3,4-tetrahydroisoquinoline
sulfonamide derivatives and their biological evaluation**

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SPECTRAL DATA FOR THE SYNTHESIZED COMPOUNDS

*Synthesis of amine 1c*¹

Aminoacetaldehyde dimethylacetal (2 mmol) was dissolved in 1,2-dimethoxybenzene (22.47 mmol) in an open flask and polyphosphoric acid (3g) was added. The reaction mixture was stirred for 10 min at rt. After completion of the reaction, the mixture was poured over ice. The organic layer was removed and after that the water layer the solution was neutralized with sodium hydroxide, then extracted with CH₂Cl₂ (3 × 20 mL). Combined extracts were dried (Na₂SO₄) and concentrated. The products, after evaporation of the solvent, were purified by column chromatography on silica gel using Et₂O as eluent.

2-(3,4-dimethoxyphenylethyl) ethanamine (1a): Commercially available

2,2-diphenylethanamine (1b): Commercially available

2,2-bis(3,4-dimethoxyphenyl) ethanamine (1c): Known compound

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Synthesis of amides 2^{2,3}

To a solution of amine **3** (3mmol) in dichloromethane (10 ml) methanesulfochloride (3mmol) was added. The reaction mixture was stirred vigorously for 10 minutes on an electromagnetic stirrer, then triethylamine (3.2 mmol) in excess was added and stirring was continued for another 1 hour. The progress of the reaction is monitored by thin layer chromatography. After completion of the reaction, the resulting mixture was washed three times with HCl: H₂O = 1: 4, Na₂CO₃ solution and H₂O. The organic layer is dried with anhydrous Na₂SO₄, filtered through a short column packed with neutral AlCl₃ and concentrated by distillation.

N-(3,4-dimethoxyphenyl) methanesulfonamide (**2a**) Known compound

N-(2,2-diphenylethyl) methanesulfonamide (**2b**) Known compound

N- (2,2-bis (3,4-dimethoxyphenyl) ethyl) methanesulfonamide (**2c**):
Known compound

Synthesis of 2-methylsulfonyl-1,2,3,4-tetrahydroisoquinolines 3

The starting amides **2** (3mmol), paraformaldehyde (5mmol) and 0.06g PPA/SiO₂ catalyst were placed in a Teflon microwave vessel and dissolved in toluene (10 ml). The reaction mixture was irradiated in the microwave reactor at 100°C at a set microwave power of 1200 watts. Maximum conversion of the starting amides to 2-methylsulfonyl-1,2,3,4-isoquinoline compounds was achieved after 60 minutes. After completion of the reaction, the reaction mixture was cooled and filtered to separate the catalyst (PPA/SiO₂). Filtrate was transferred to a round bottom flask and removes the toluene using a rotary evaporator. The residue was washed with H₂O and extracted with dichloromethane (3x20 ml), dried over anhydrous Na₂SO₄ and the solvent were removed by distillation.

6,7-Dimethoxy-2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline (**3a**):

MP = 141-144°C; ¹H-NMR (600 MHz, CDCl₃, δ / ppm): 6.55 (1H, s), 6.49 (1H, s), 4.32 (2H, s), 3.79 (3H, s), 3.78 (3H, s), 3.49-3.47 (2H, t, J = 5.87, 5.87), 2.84 - 2.81 (2H, t, J = 6.16, 6.16 Hz), 2.76 (s, 3H); ¹³C-NMR (150.9 MHz, CDCl₃, δ / ppm): 148.1, 147.9, 125.0, 123.5, 111.6, 109.0, 56.0, 47.0, 43.5, 36.1, 28.1. IR (KBr, cm⁻¹): 3023, 3007, 2935, 1612, 1469, 1459, 1387, 1228, 750; HRMS [M+Na]⁺m/z: 430.1298.

2-(Methylsulfonyl)-4-phenyl-1,2,3,4-tetrahydroisoquinoline (**3b**): MP =

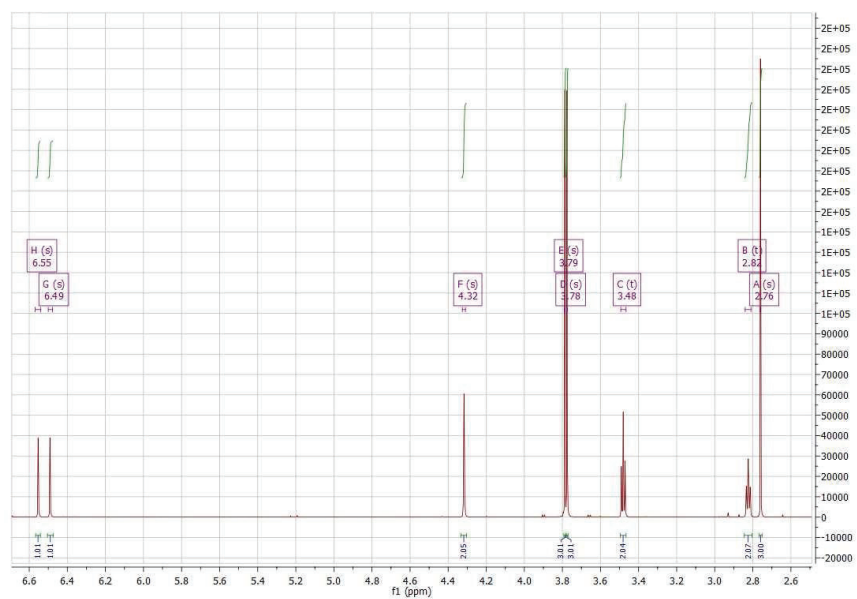
152-154°C; ¹H-NMR (600 MHz, CDCl₃, δ / ppm): 7.31–7.21 (4H, m), 7.18–7.11 (4H, m), 6.98–6.94 (1H, m), 4.57 (2H, q, J = 15.4, 15.38 Hz), 4.33 (1H, t, J = 6.3 Hz), 3.86 (1H, ddd, J = 1.0, 5.0, 12.4 Hz), 3.47 (1H, dd, J = 7.4, 12.5 Hz); ¹³C-NMR (150.9 MHz, CDCl₃, δ / ppm): 142.5, 136.2, 132.2, 129.9, 128.9, 128.6, 127.2, 127.0, 126.3, 50.9, 47.9, 45.1, 36.4; IR (KBr, cm⁻¹): 3058, 3024, 2927, 1600, 1495, 1473, 1452, 1388, 1320, 1150, 701, 750. HRMS [M+Na]⁺m/z: 294.0768.

4-(3,4-Dimethoxyphenyl)-6,7-dimethoxy-2-(methylsulfonyl)-1,2,3,4-tetra-

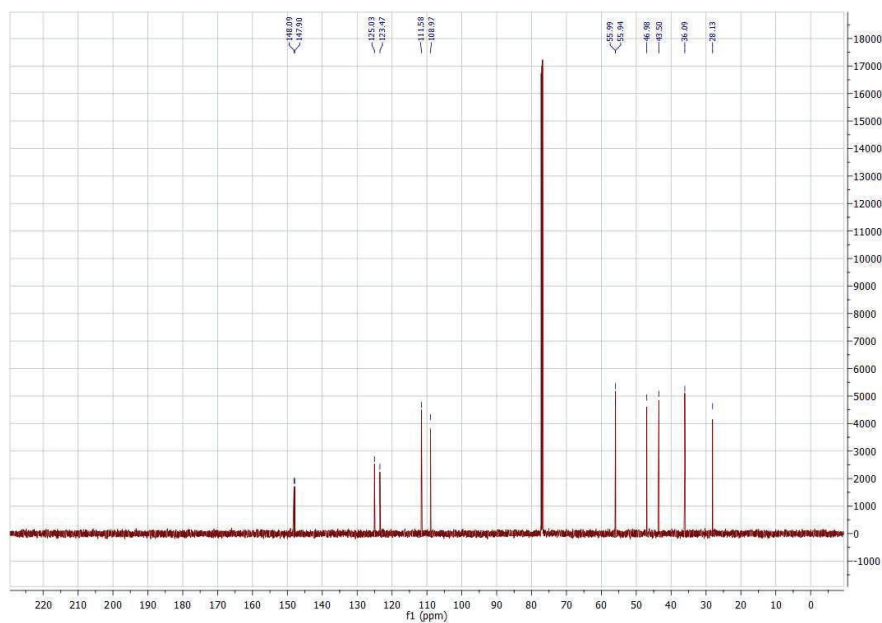
hydroisoquinoline (**3c**): MP = 178-180°C; ¹H-NMR(600 MHz, CDCl₃, δ / ppm): 6.85–6.81 (1H, m), 6.71–6.67 (2H, m), 6.64 (1H, s), 6.46 (1H, s), 4.51 (2H, q, J = 6.25, 15.0 Hz), 4.21 (1H, dd, J = 5.58, 6.24 Hz), 3.90 (3H, s), 3.89 (3H, s), broad with 3.84 (3H, s), 3.86–3.81 (1H, m), 3.72 (3H, s), 3.41 (1H, dd, J = 7.42, 12.37 Hz), 2.72 (3H, s); ¹³C-NMR (150.9 MHz, CDCl₃, δ / ppm): 149.0, 148.2, 148.1, 135.0, 128.2, 124.1, 121.0, 112.1, 111.9, 111.2, 108.5, 56.0, 55.9, 51.1, 47.3, 44.3, 36.3. IR (KBr, cm⁻¹): 2997, 2935, 2895, 2845, 1612, 1588, 1520, 1470, 1364, 1235, 1159, 860, 841, 826, 809, 751. HRMS [M+Na]⁺m/z: 310.0876.

^1H , ^{13}C NMR and HRMS spectra of compounds **3 a-c**

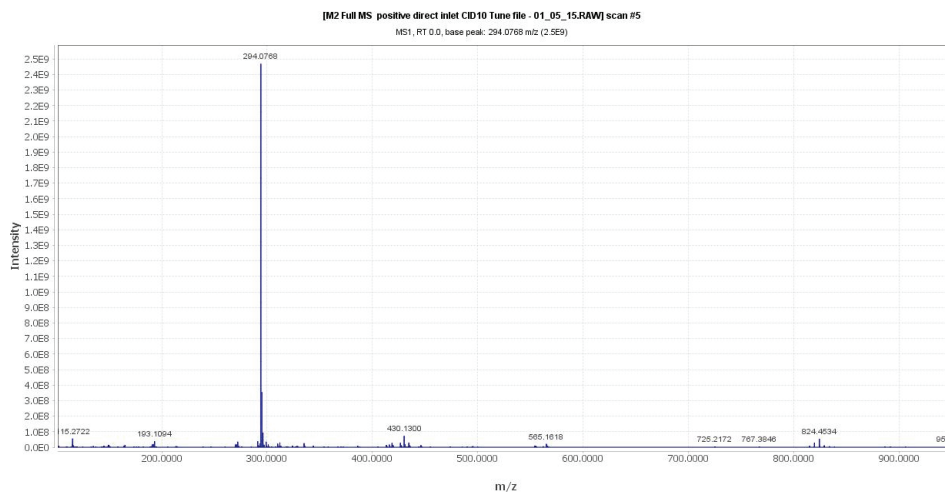
3a ^1H -NMR spectra



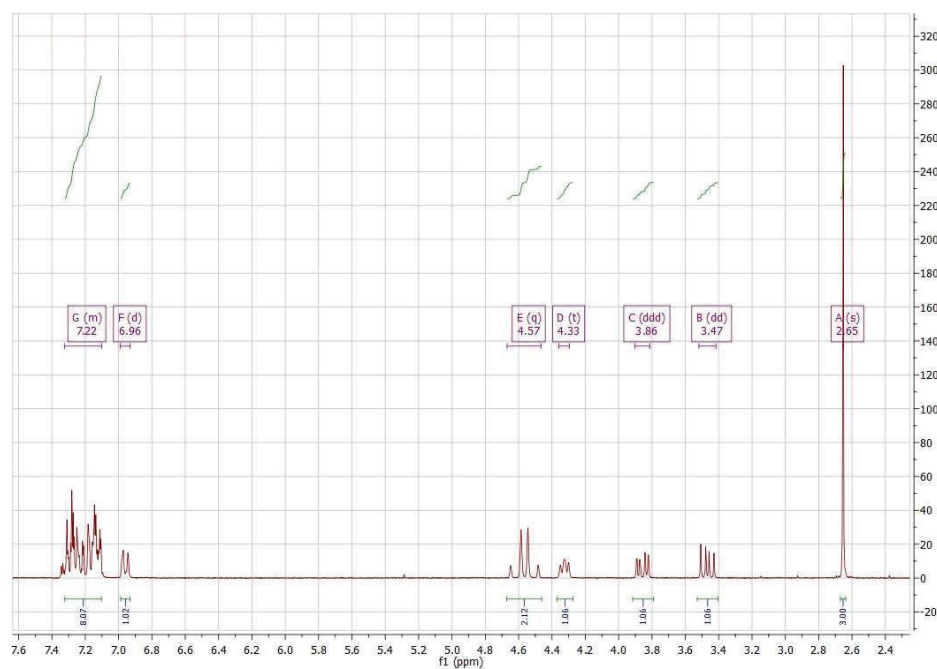
3a ^{13}C -NMR spectra



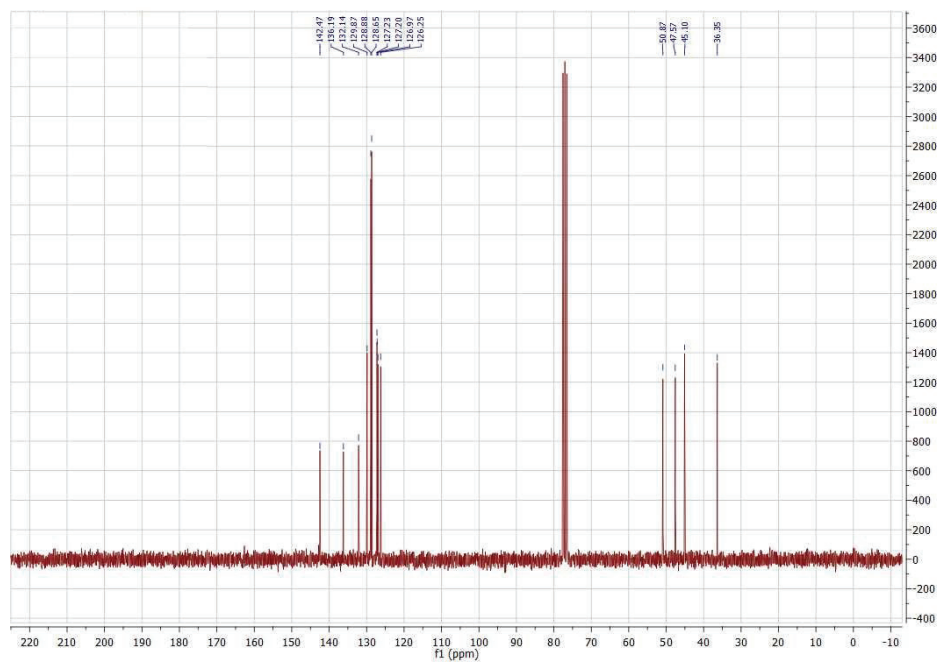
3a HRMS spectra



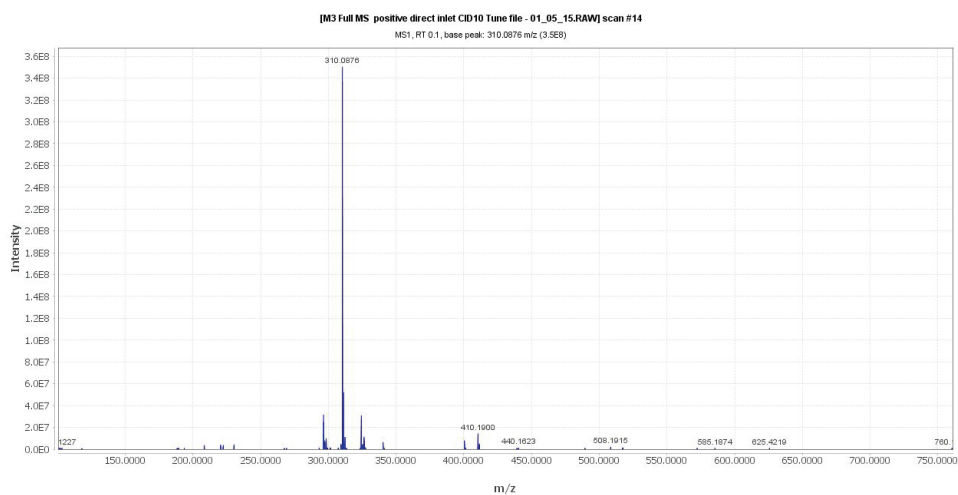
3b ¹H NMR spectra



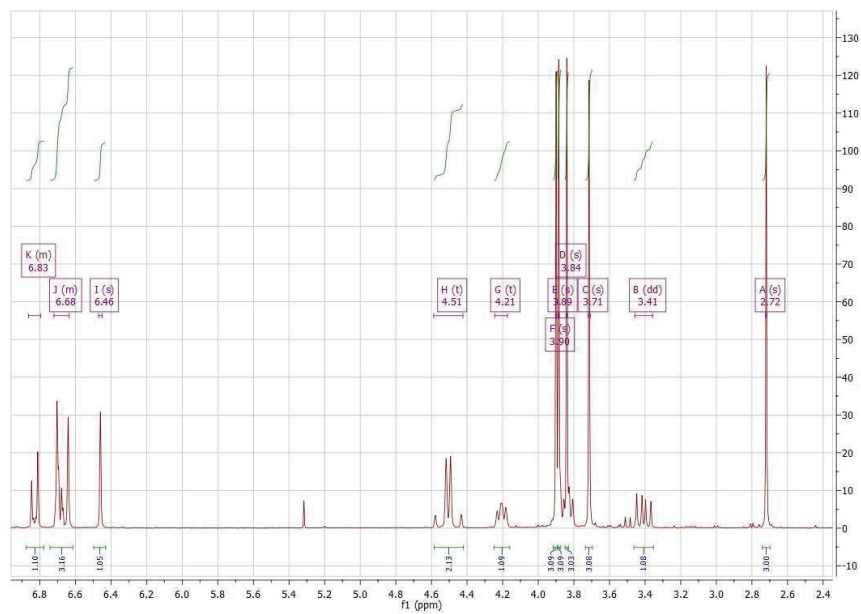
3b ¹³C NMR spectra



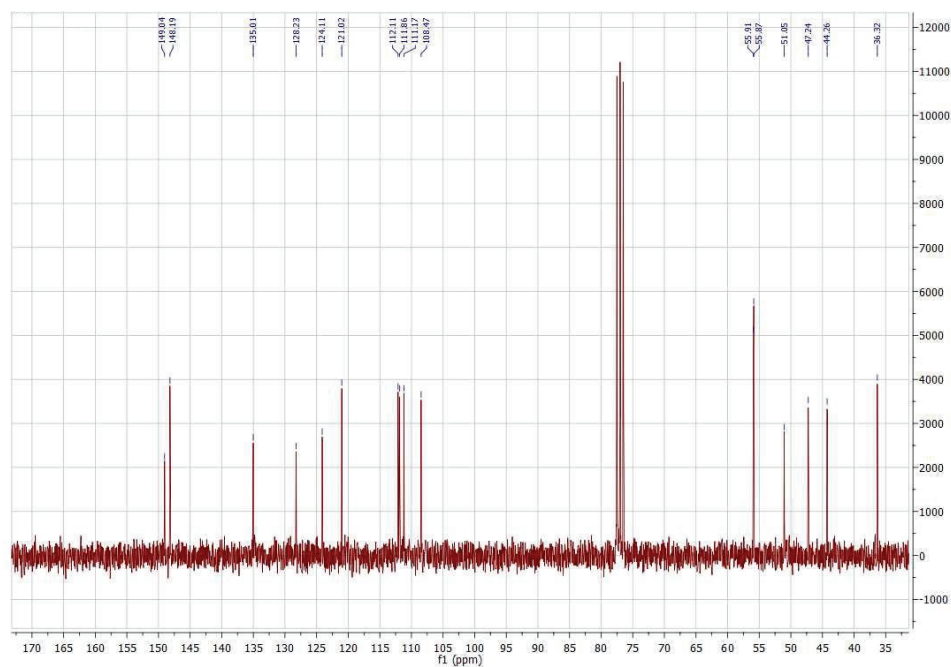
3b HRMS spectra



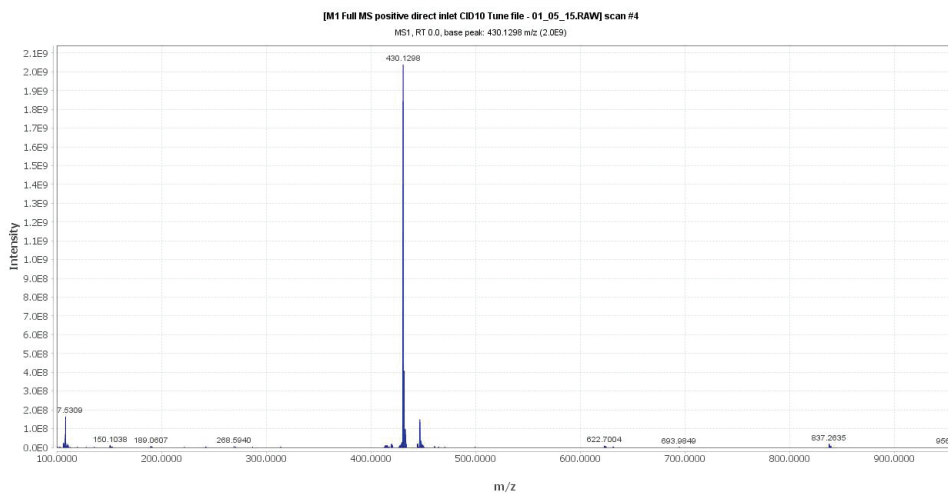
3c ^1H NMR spectra



3c ^{13}C NMR spectra



3c HRMS spectra



REFERENCES

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