Supporting Information

Reversal of Regioselectivity in Acetylation and Deacetylation of Aryl-Naphthalene Diols and Diacetates by Amano Lipase

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S1: Experimental procedure and spectral data of the compounds

Procedure for Garratt-Braverman cyclisation:

Synthesis of 11a:

To the solution of bis-propargylsulfone 10a (1.4mmol) in dry $CHCl_3$, Et_3N (2.8 mmol) was added and stirred for 1 h. at room temperature. The reaction mixture was partitioned between water-dichloromethane. The organic layer was washed with brine and dried over Na_2SO_4. After evaporation of the solvent the crude product was purified by column chromatography over Si gel, using petroleum ether: ethyl acetate (2:1) as eluent.

State: Sticky mass; **Yield:** 92%;δ_H (400 MHz, $CDCl_3$)8.28- 8.24 (3H, m), 8.14 (1H, d, *J* = 8.8 Hz), 7.95 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8 4Hz), 4.63 (2H, s), 4.25 (2H, s), 4.02 (3H, s), 3.89 (3H, S); δ_C (100 MHz, $CDCl_3$)166.7, 166.5, 137.3, 137.0, 134.0, 132.4, 131.3, 131.0, 130.7, 130.5, 129.9, 129.7, 129.4, 128.6, 126.7, 126.6, 126.4, 57.0, 56.4, 52.5.

Synthesis of 11b:

DBU (1.4 mmol) was added to the solution of bis-propargyltosyl amine 10b (0.7 mmol) in dry toluene, and refluxed for 48 h. After completion of the reaction, toluene was removed under vacuo. The crude was extracted with ethyl acetate and after removing the solvent, it was purified by column chromatography using petroleum ether: ethyl acetate (3:1) as eluent.

State: Sticky mass; **Yield:** 90%;δ_H (400 MHz, $CDCl_3$) 8.25-8.23(3H, m), 8.07 (1H, d, *J* = 8.4), 7.89 (1H, d, *J* = 8.4 Hz), 7.77-7.73 (3H, m), 7.38(2H, d, *J* = 8.4 Hz), 7.33 (2H, d, *J*= 8.4 Hz), 4.83 (2H, s), 4.47 (2H, s), 4.03 (3H, s), 3.88 (3H, s), 2.41 (3H, s);δ_C (100 MHz, $CDCl_3$) 167.0, 166.8, 144.0, 141.6, 137.0, 135.7, 134.8, 134.5, 133.3, 130.7, 130.3, 130.2, 130.0, 129.6, 128.4, 128.3, 128.0, 127.7, 125.7, 121.2, 53.6, 52.9, 52.5, 52.4, 21.6.

Synthesis of 11c:

To the solution of bis-propargyl ether (0.6 mmol) in toluene, potassium tert-butoxide (1.2 mmol) was added and was allowed to reflux for 6h. After completion of the reaction, toluene was removed under vacuo. The reaction mixture was partitioned between water and ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. The crude product was purified by column chromatography over Si gel, using petroleum ether: ethyl acetate (3:1) as eluent.

State: Gummy liquid; **Yield:** 90%;**δ_H** (400 MHz, $CDCl_3$)7.88 (1H, d, *J* = 8.4 Hz), 7.69 (2H, s), 7.53 (3H, d, *J* = 8.1 Hz), 7.37 (2H, d, *J* = 6.6 Hz), 5.30 (2H, s), 5.05 (2H, s), 4.94 (1H, d, *J* = 12 Hz), 4.88-4.84 (2H, m), 4.72-4.70 (1H, m), 4.64-4.57 (2H, m), 3.99-3.89 (2H, m), 3.66-3.52 (2H, m), 1.68-1.52 (12 H, m); **δ_C** (100 MHz, $CDCl_3$) 138.0, 137.8, 137.4, 137.3, 136.0, 133.4, 132.6, 131.9, 129.7, 128.5, 128.1, 126.0, 124.6, 118.8, 98.3, 98.0, 73.6, 73.2, 69.2, 68.9, 62.4, 30.8, 25.7, 20.0, 19.6.

General procedure for the reduction of diester:

To the solution of diesters 11a and 11b in THF (15 ml), finely powdered $NaBH_4$ (2 eq) was added and stirred for 15 min at 65°C. Methanol (2ml) was then added drop wise and stirred at 65°C for 5h.The reaction mixture was cooled to room temperature and quenched with saturated NH_4Cl. The organic layer was extracted with ethyl acetate (40 mL) and dried over Na_2SO_4. After evaporation of the solvent, diols 2a and 2b was purified by column chromatography over Si gel, using petroleum ether: ethyl acetate.

Synthesis of 2a: State: White solid; **Yield:**90%; **mp**: 200°C; **δ_H** (400 MHz, $CDCl_3$) 7.88 (1H, d, *J* = 8.5 Hz), 7.85 (1H, s), 7.59-7.52 (4H, m), 7.29 (2H, d, *J* = 8.0 Hz), 4.83 (2H, s), 4.73 (2H, s), 4.59 (2H, s), 4.22 (2H, s); **δ_C** (100 MHz, $CDCl_3$) 141.2, 139.8, 138.0, 136.9, 133.0, 132.3, 130.0, 128.7, 128.7, 128.6, 127.8, 127.7, 126.5, 125.0, 123.9, 65.5, 65.2.

Synthesis of 2b: State: White solid; **Yield:** 90%;**mp:** 220°C;**δ_H** (400 MHz, $CDCl_3$) 7.81 (1H, d, *J* = 8.4 Hz), 7.73 (2H, d, *J* = 8.0 Hz), 7.63 (1H, s), 7.52-7.47 (4H, m), 7.31-7.24 (4H, m), 4.83 (2H, s), 4.78 (2H, s), 4.69 (2H, s), 4.45 (2H, s), 2.39 (3H, s); **δ_C** (100 MHz, $CDCl_3$)143.7, 140.5, 138.6, 136.7, 134.3, 134.0, 133.8, 133.0, 131.7, 129.8, 129.5, 128.4, 127.6, 127.4, 125.4, 123.3, 120.5, 65.4, 65.0, 53.5, 53.1, 22.4.

Procedure for the synthesis of 2c: To the solution of 11c in ethanol PPTS and drop of water were added and allowed to stir at 50°C for 8h. Ethanol was removed under vacuo. The mixture was partitioned between water-ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. After removing the solvent, the pure product was obtained by column chromatography over Si gel, petroleum ether: ethyl acetate (1:2) as eluent.

State: Sticky mass; **Yield:** 85%; **δ_H** (400 MHz, $CDCl_3$) 7.89 (1H, d, *J* = 8.4 Hz), 7.71 (1H, s), 7.63 (1H, s), 7.51 (3H, d, *J* = 8.0 Hz), 7.34 (2H, d, *J* = 7.6 Hz), 5.31 (2H, s), 5.00 (2H, s), 4.81 (2H, s), 4.73 (2H, s); δ_C (100 MHz, $CDCl_3$)140.5, 138.5, 137.8, 137.5, 137.4, 133.4, 132.5, 131.9, 129.8, 128.8, 127.5,125.4,123.5,118.9, 73.5, 73.1, 65.7, 65.3.

General procedure for di acetylation: Et_3N (6 eq), DMAP (catalytic amount), AcCl (3eq) were added successively to the solution of diol 2a-c in CH_2Cl_2 (20 mL) at 0°C and stirred at room temperature for 1h. The reaction mixture was partitioned between water-dichloromethane. The organic layer was washed with brine, dried over Na_2SO_4. After evaporation of the solvent the pure diacetate was isolated by column chromatography.

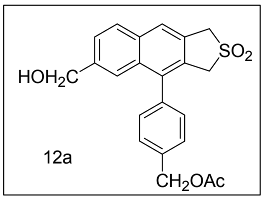
Synthesis of 1a: State: Sticky yellow mass**; Yield:**80%**;** δ_H (400 MHz, $CDCl_3$) 7.90 (1H, d, *J* = 8.4 Hz), 7.85 (1H, s), 7.57-7.54 (3H, m), 7.50 (1H, s), 7.33-7.29 (2H, m), 5.25 (2H, s), 5.15 (2H, s), 4.61 (2H, s), 4.25 (2H, s), 2.20 (3H, s), 2.08 (3H, s);δ_C (100 MHz, $CDCl_3$) 171.0, 170.8, 137.7, 137.2, 136.4, 134.8, 133.0, 131.9, 129.8, 129.1, 128.9, 128.6, 127.0, 125.6, 124.9, 66.3, 65.9, 57.2, 56.5, 21.2, 21.0.

Synthesis of 1b: State: Sticky mass**; Yield:** 70%**;** δ_H (400 MHz, $CDCl_3$) 7.84 (1H, d, *J* = 8.4 Hz), 7.77 (2H, d, *J* = 8.0 Hz), 7.66 (1H, s), 7.55-7.46 (4H, m), 7.33 (2H, d, *J* = 7.6 Hz), 7.28 (2H, d, *J* = 7.6 Hz),5.26 (2H, s), 5.13 (2H, s), 4.81 (2H, s), 4.49 (2H, s), 2.42 (3H, s), 2.23 (3H, s), 2.06 (3H, s);δ_C (100 MHz, $CDCl_3$)171.2, 171.0, 144.0, 137.4, 136.0, 135.0, 134.3, 134.1, 133.9, 133.6, 133.4, 131.7, 130.1, 129.8, 129.0, 128.7, 127.9, 126.3, 125.3, 120.9, 66.6, 66.2, 53.7, 53.3, 21.7, 21.3, 21.2.

Synthesis of 1c: State: Gummy liquid**; Yield:** 70%**;** δ_H (400 MHz, $CDCl_3$) 7.87 (1H, d, *J* = 8.4 Hz), 7.69 (1H, s), 7.61 (1H, s), 7.51-7.46 (3H, m), 7.35 (2H, d, *J* = 8.0 Hz), 5.28 (2H, s), 5.22 (2H, s), 5.14 (2H, s), 5.01 (2H, s), 2.18 (3H, s), 2.06 (3H, s);δ_C (100 MHz, $CDCl_3$) 171.1, 171.0, 138.3, 137.9, 137.6, 135.6, 133.5, 133.5, 132.3, 131.6, 129.8, 129.0, 128.8, 128.7, 126.0, 125.3, 119.0, 73.5, 73.0, 66.6, 66.2, 21.2, 21.1.

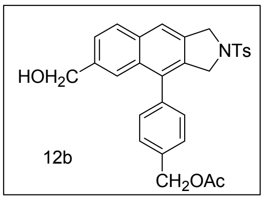
General procedure for enzymatic catalysis:

General procedure for enzymatic hydrolysis of the diacetate: To the solution of diacetates1a-c (0.14mmol)in acetone- phosphate buffer (1:3 v/v, pH 7), the enzyme Amano lipase was added and stirred at room temperature until the reaction was completed. The reaction mixture was filtered and acetone was removed under vacuo. The crude was extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. After removal of the solvent the crude was purified by column chromatography over Si gel, using petroleum ether and ethyl acetate (2:1) as eluent to get the pure monoacetates 12a-c.



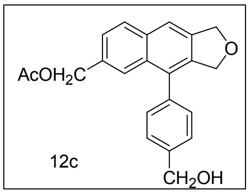
12a

State: Sticky mass; **Yield:** 75%; δ_H (400 MHz, $CDCl_3$) 7.88 (1H, d, *J* = 8.4 Hz), 7.83 (1H, s), 7.58-7.51 (4H, m), 7.31-7.29 (2H, m), 5.24 (2H, s), 4.75 (2H, s), 4.59 (2H, s), 4.23 (2H, s), 2.19 (3H, s); δ_C (100 MHz, $CDCl_3$) 171.1,139.8, 137.6, 137.4, 136.3,132.8, 132.0, 129.8, 128.9, 128.6, 128.5, 128.4, 127.6, 126.4, 124.9, 123.7, 65.9,65.3, 57.2,56.6, 21.2.



12b

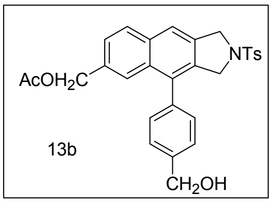
State: Semi solid; **Yield**: 68%; δ_H (400 MHz, $CDCl_3$) 7.82 (1H, d, *J* = 8.9 Hz), 7.74 (2H, d, *J* = 8.0 Hz), 7.64 (1H, s), 7.50 (4H, d, *J* = 9.4 Hz), 7.31 (4H, d, *J* = 8.1 Hz), 5.23 (2H, s), 4.78 (2H, s), 4.71 (2H, s), 4.46 (2H, s), 2.39 (3H, s), 2.21 (3H, s); δ_C (100 MHz, $CDCl_3$) 171.2, 144.0, 138.9, 137.6, 135.9, 134.5, 133.5, 134.1, 133.2, 131.8, 130.1, 129.8, 129.0, 128.7, 127.9, 125.7, 123.5, 120.9, 66.2, 65.7, 53.7, 53.3, 21.8, 21.4.



12c

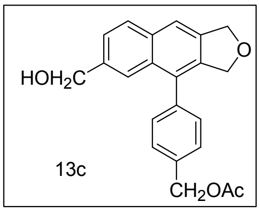
State: Sticky mass**; Yield:** 72%; δ_H (400 MHz, $CDCl_3$) 7.88 (1H, d, *J* = 8.4 Hz), 7.69 (1H, s), 7.62 (1H, s), 7.52 (2H, d, *J* = 7.8 Hz), 7.47 (1H, d, *J* = 8.4 Hz), 7.35 (2H, d, *J* = 7.7 Hz), 5.29 (2H, s), 5.14 (2H, s), 5.01 (2H, s), 4.83 (2H, s), 2.06 (3H, s); δ_C (100 MHz, $CDCl_3$) 171.1, 140.5, 138.4, 137.6, 137.4, 133.5, 132.6, 131.8, 129.9, 128.9, 127.6, 126.0, 125.6, 124.7, 124.2, 119.3, 118.9, 73.6, 73.1, 66.9, 65.4, 21.2.

General procedure for the enzymatic acetylation of the diol: vinyl acetate (0.64mmol) and the Amano lipase was added to the THF solution of diol 2a-c (0.34mmol). The reaction mixture was allowed to stir at room temperature until the reaction was completed. It was then filtered and THF was removed under vacuo. The Pure monoacetates 13a-c were isolated by column chromatography of the crude residue over Si gel, using petroleum ether and ethyl acetate (2:1) as eluent.



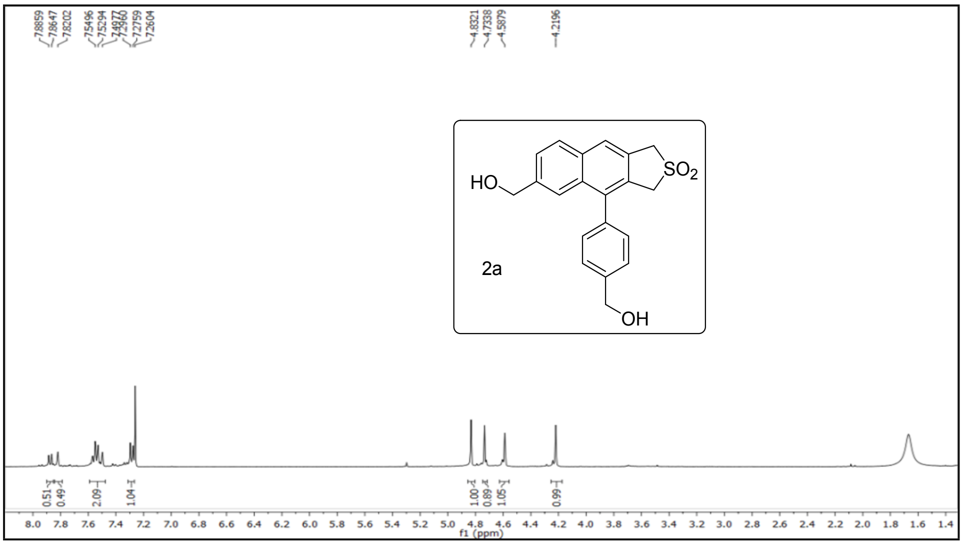
13b

State: Semi solid; **Yield:** 75%;δ_H (400 MHz, $CDCl_3$) 7.81 (1H, d, *J* = 9.6 Hz), 7.73 (2H, d, *J* = 8.0 Hz), 7.63 (1H, s), 7.53-7.49 (3H, m), 7.43 (1H, d, *J* = 8.0 Hz), 7.29 (3H, d, *J* = 8.0 Hz), 7.23 (1H, s), 5.09 (2H, s), 4.83 (2H, s), 4.78 (2H, s), 4.46 (2H, s), 2.39 (3H, s), 2.04 (3H, s); δ_C (100 MHz, $CDCl_3$) 170.8, 143.7, 140.6, 136.4, 134.7, 134.1, 134.0, 133.6, 133.4, 133.1, 131.5, 129.8, 129.5, 128.4, 127.6, 127.4, 126.0, 125.2, 120.5, 65.0, 64.4, 53.5, 53.0, 21.5, 20.9.

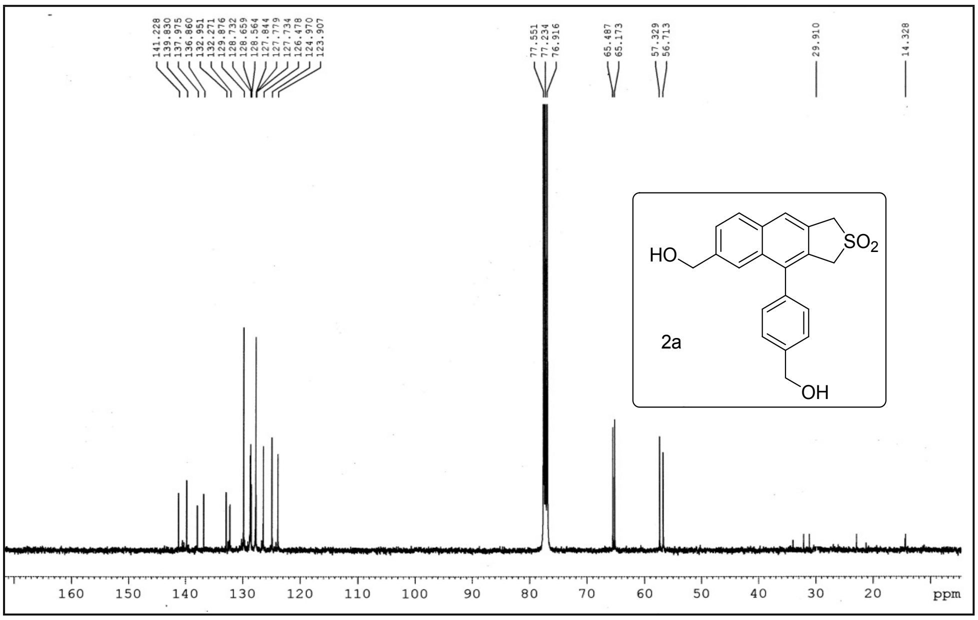


State: Sticky mass; **Yield:** 75%;δ_H (400 MHz, $CDCl_3$) 7.86 (1H, d, *J* = 8.4 Hz), 7.68 (1H, s), 7.60 (1H, s), 7.50-7.47 (3H, m), 7.35-7.33 (2H, m), 5.27 (2H, s), 5.21 (2H, s), 4.99 (2H, s), 4.73 (2H, s), 2.17 (3H, s); δ_C (100 MHz, $CDCl_3$) 171.0, 138.5, 138.0, 137.7, 137.3, 135.4, 133.2, 132.1, 131.7, 129.7, 128.6, 128.5, 125.2, 123.3, 118.8, 73.3, 72.9, 66.0, 65.5, 21.1.

S2: ^{1}H and ^{13}C NMR spectra of compounds (All are recorded in $CDCl_3$)



^{1}H NMR in 400 MHz



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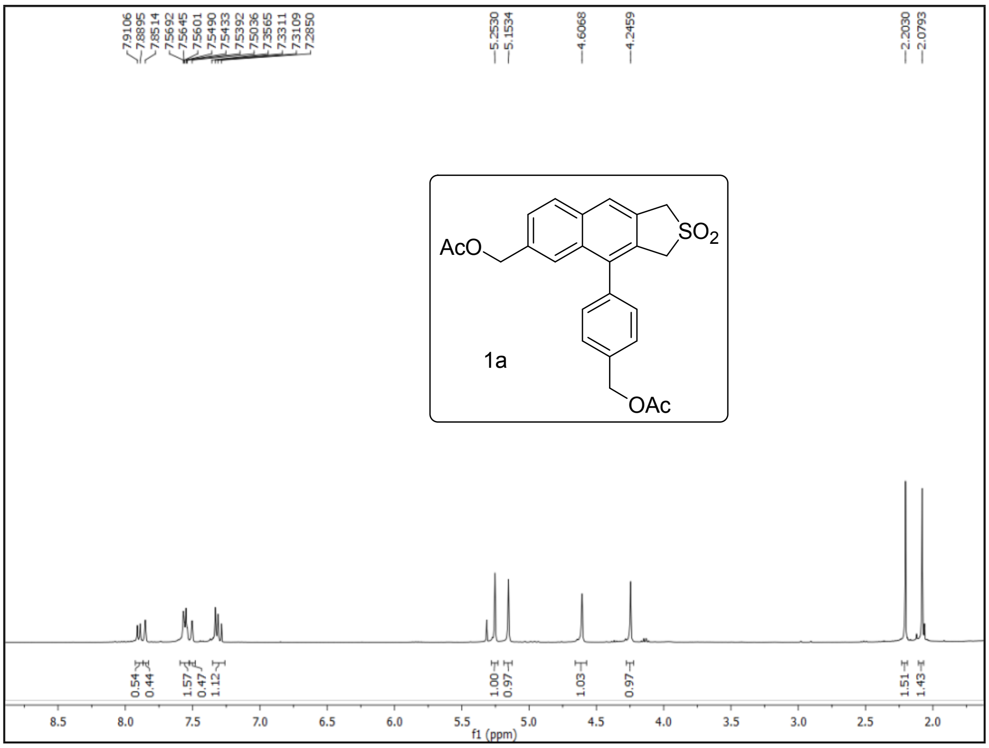

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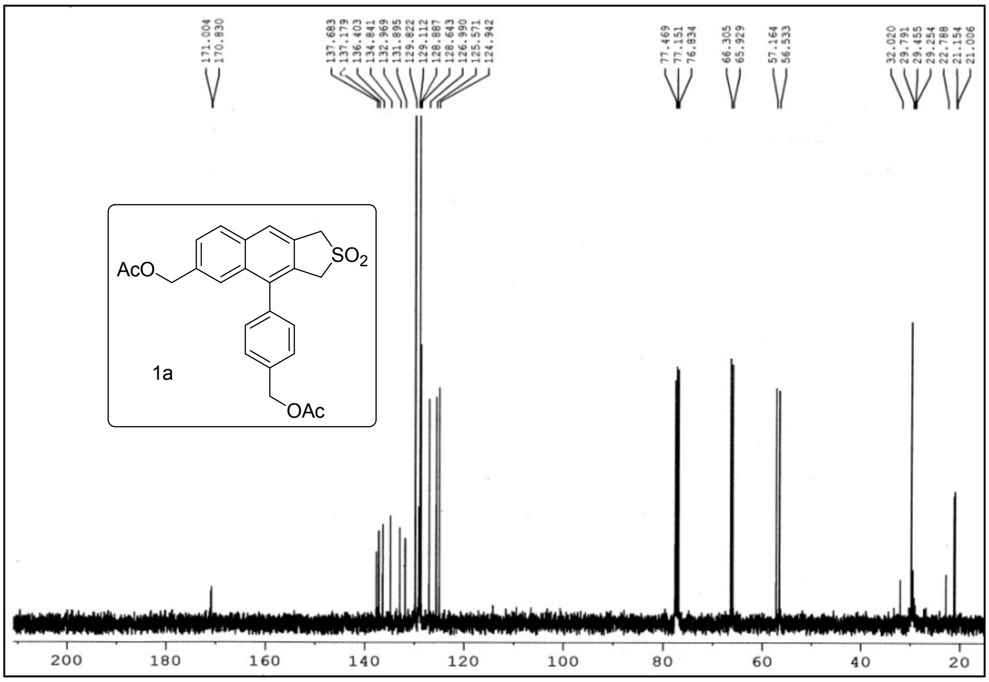

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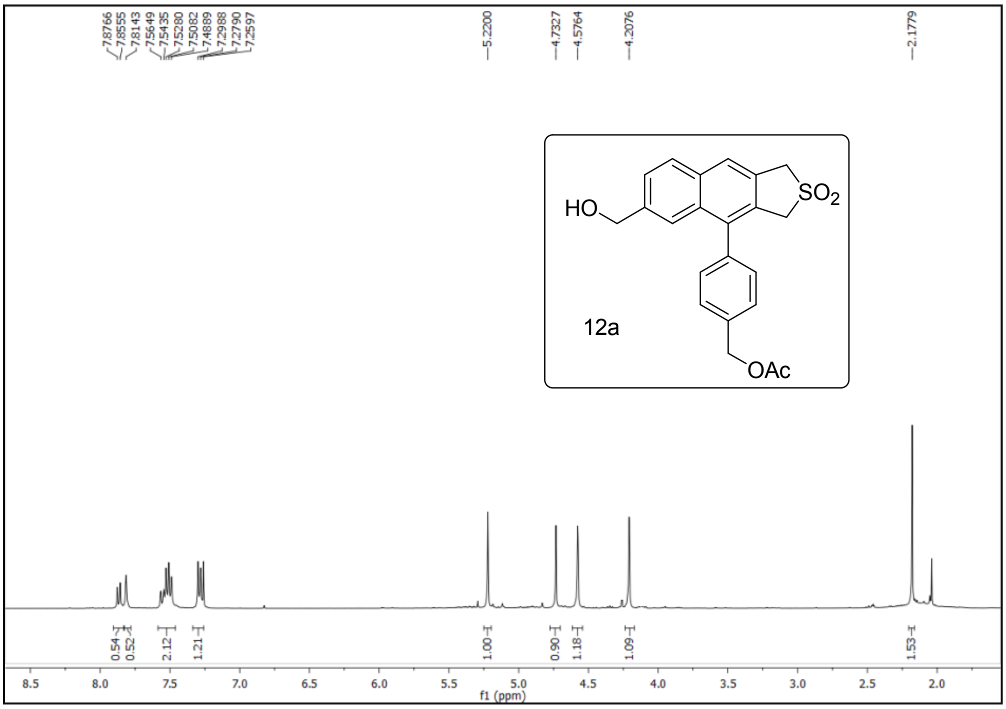

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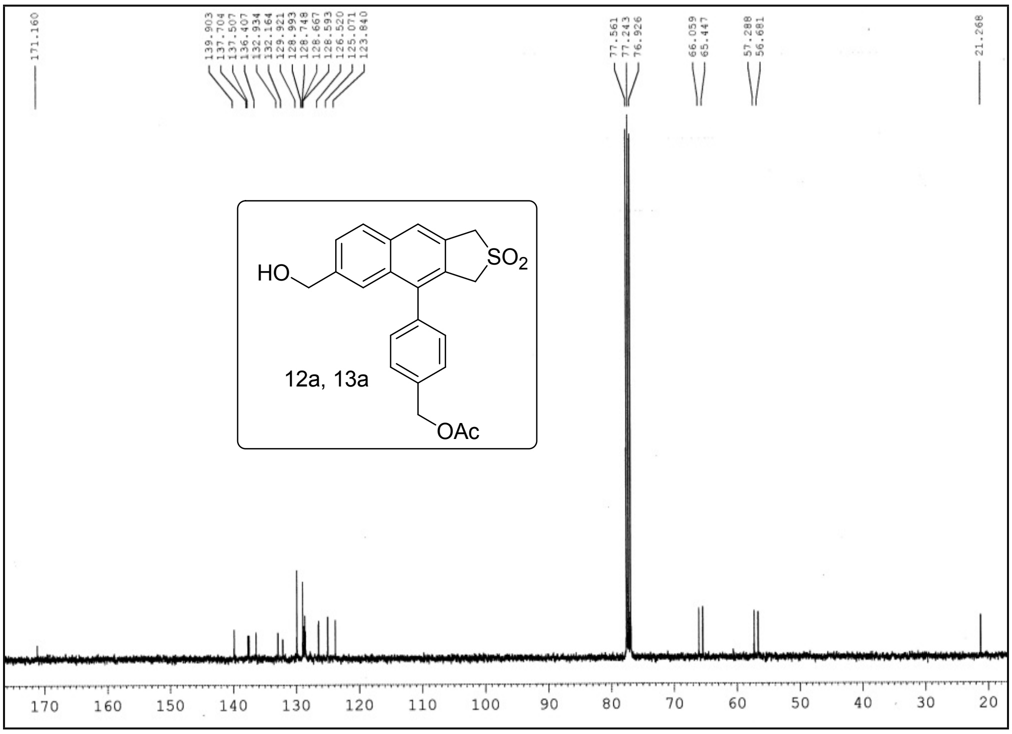

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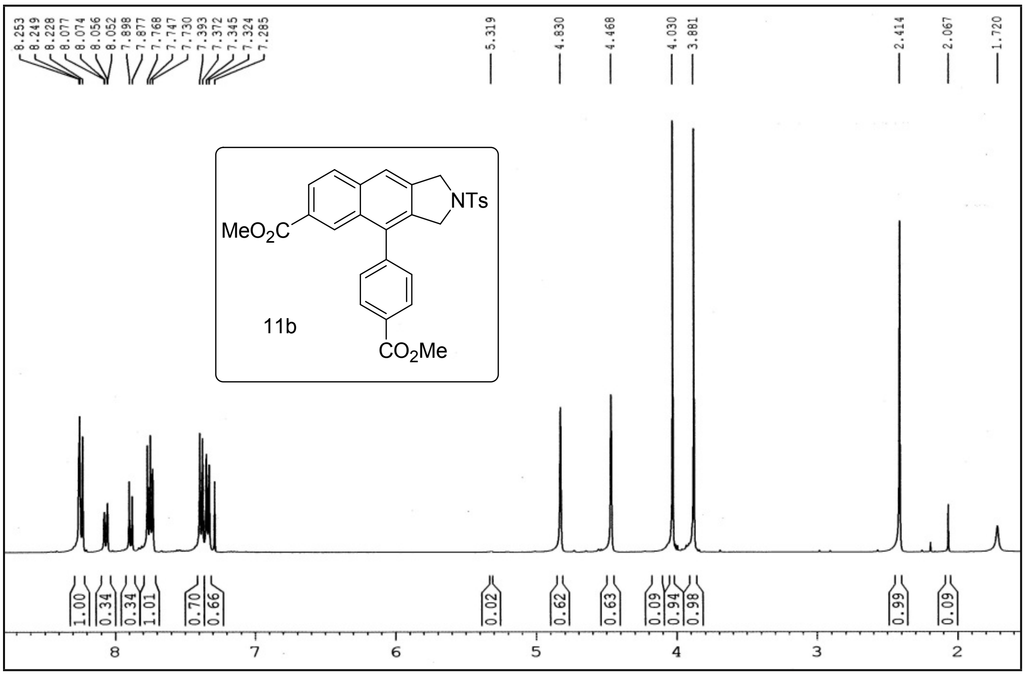

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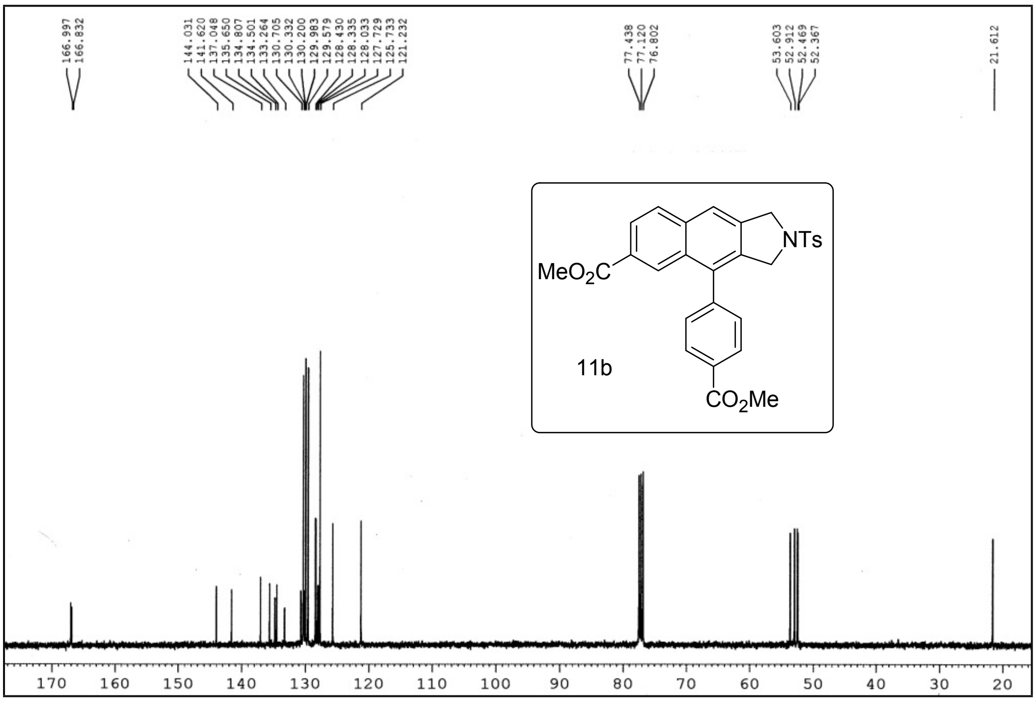

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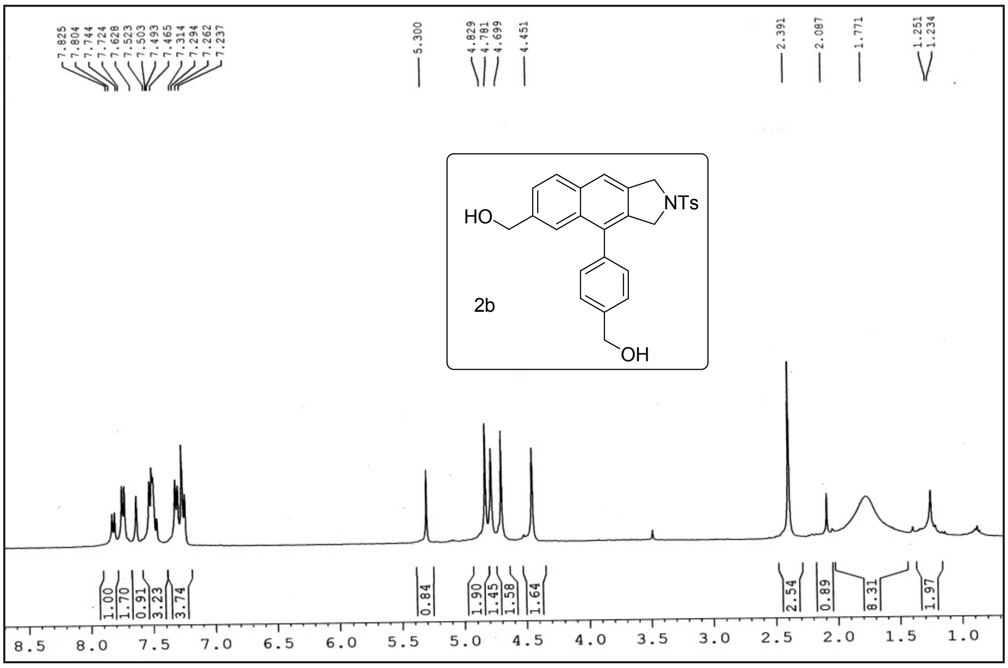

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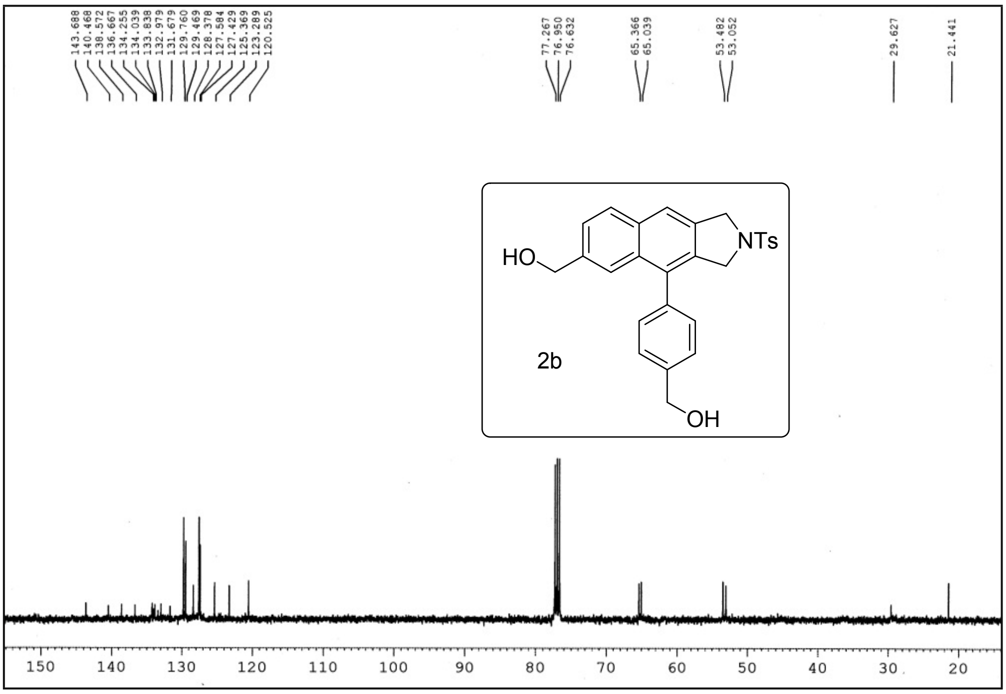

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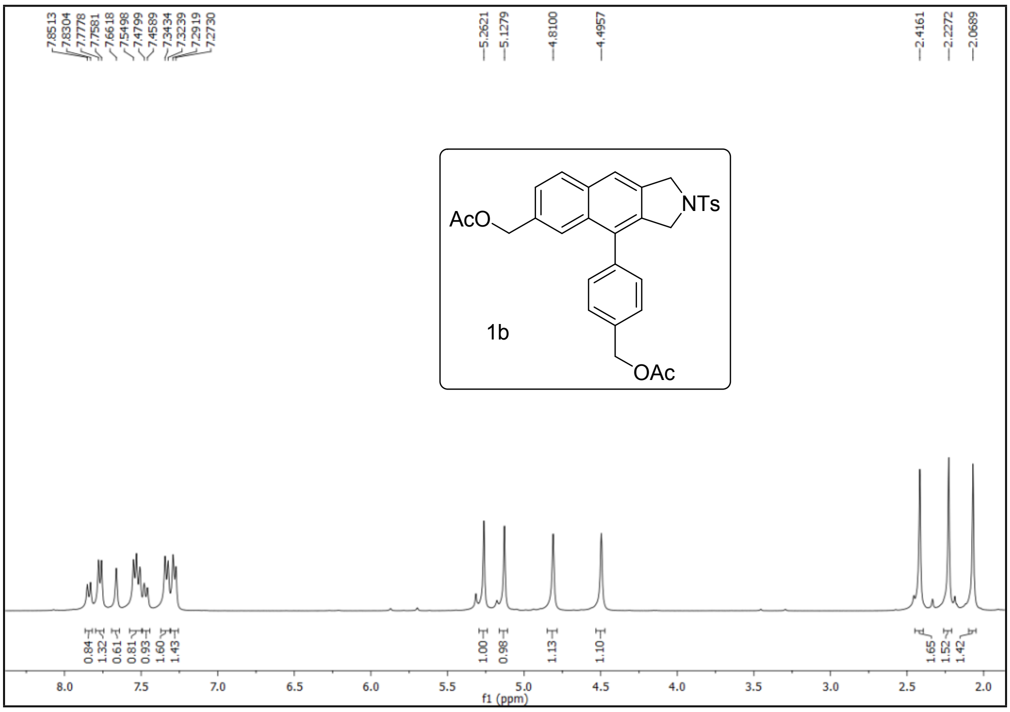

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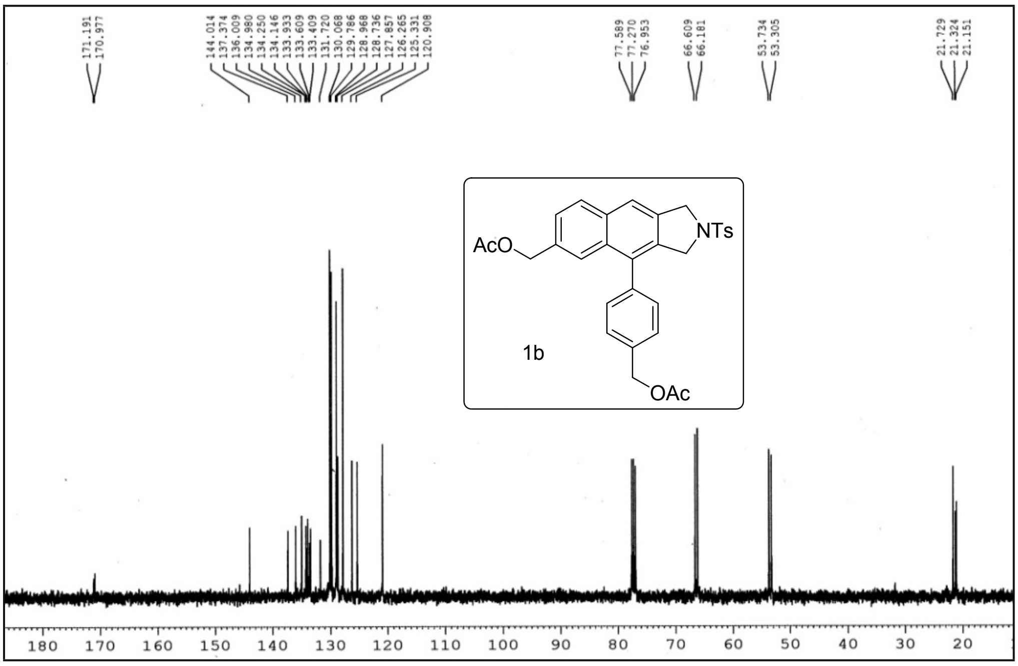

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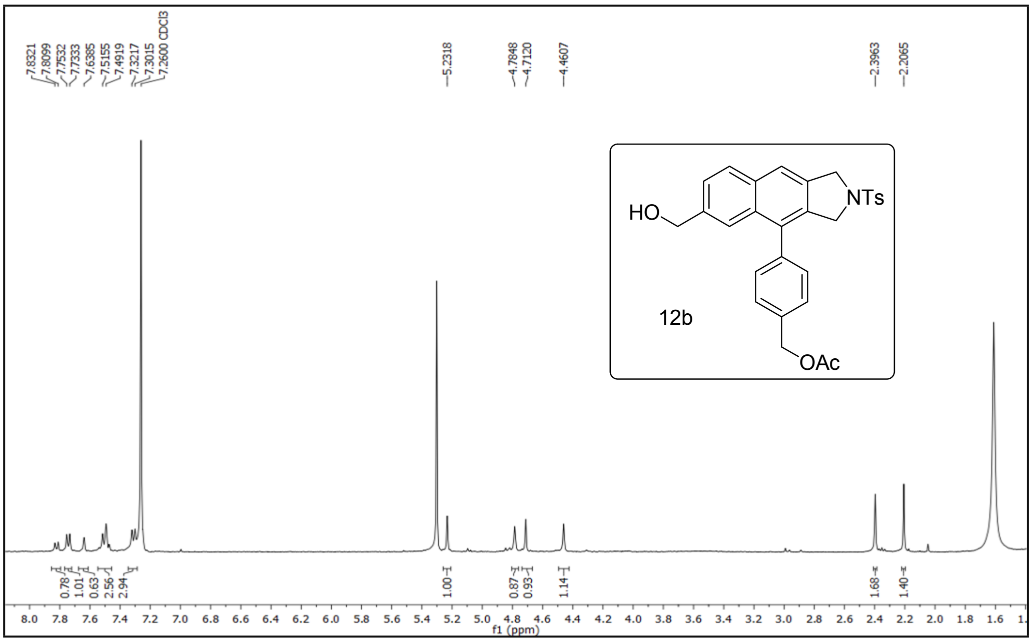

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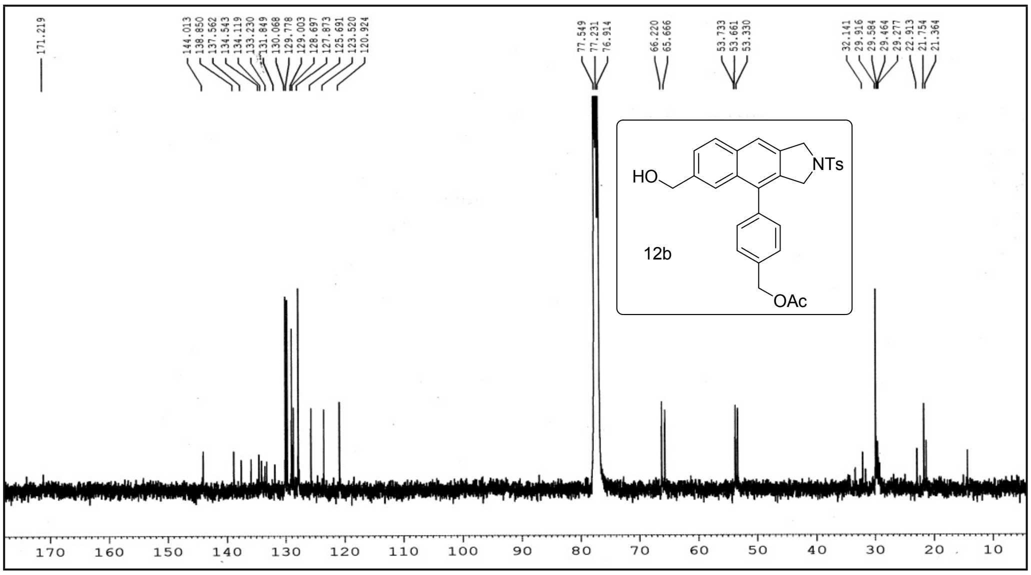

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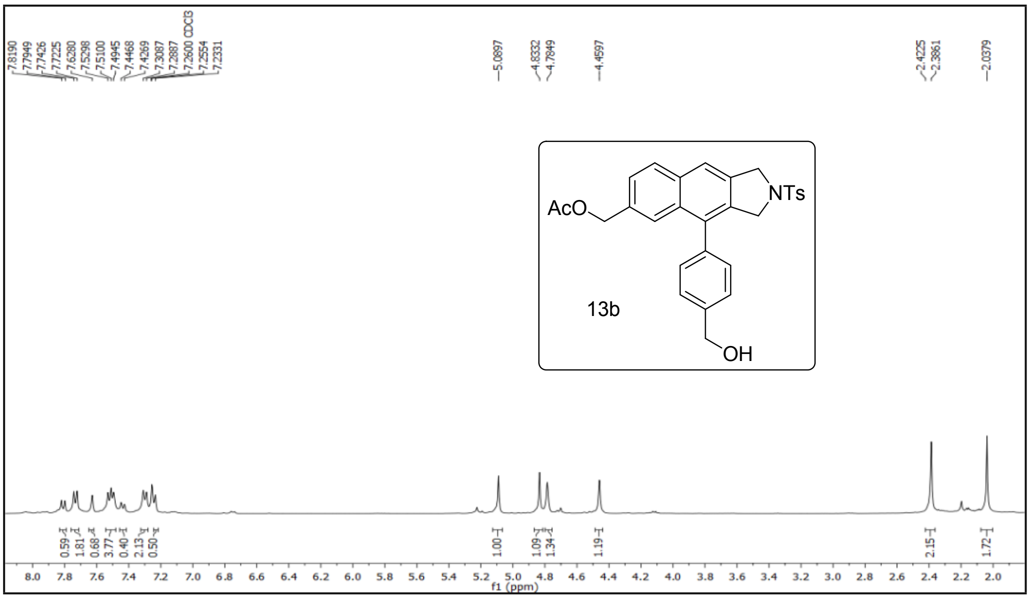

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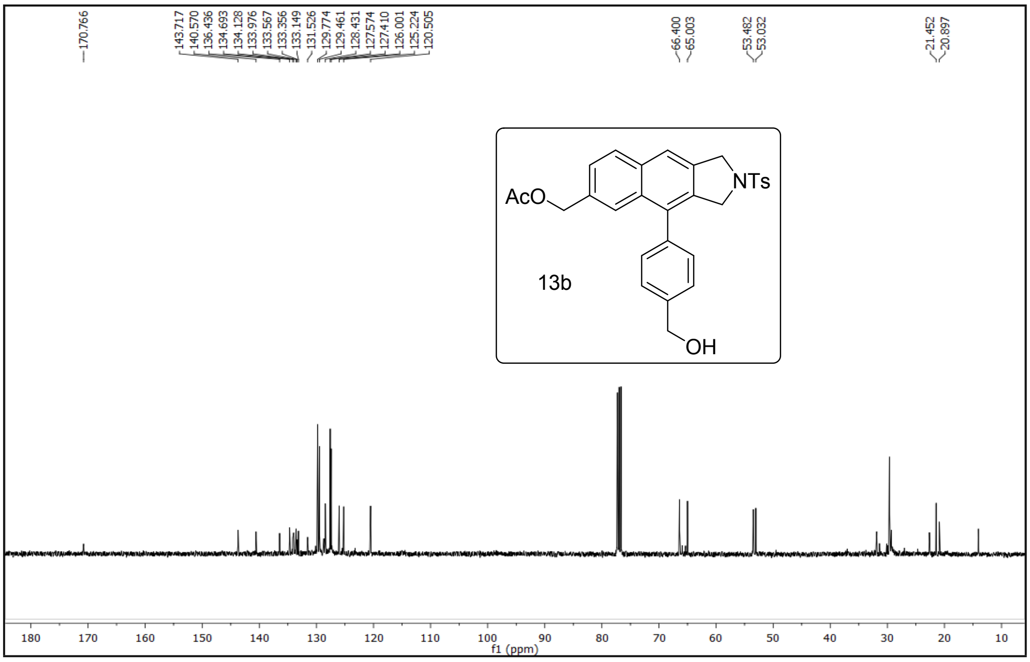

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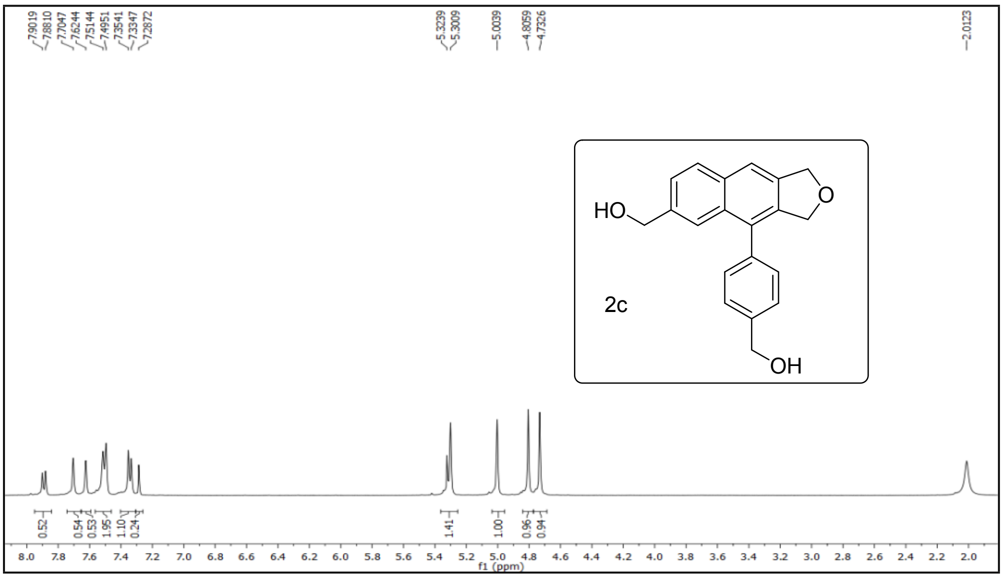

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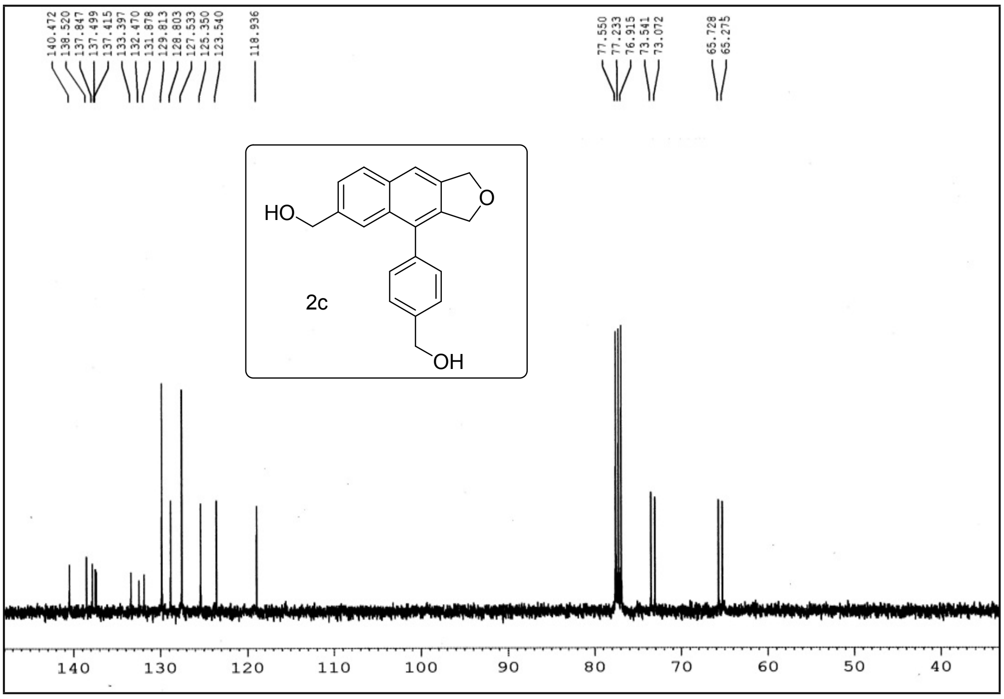

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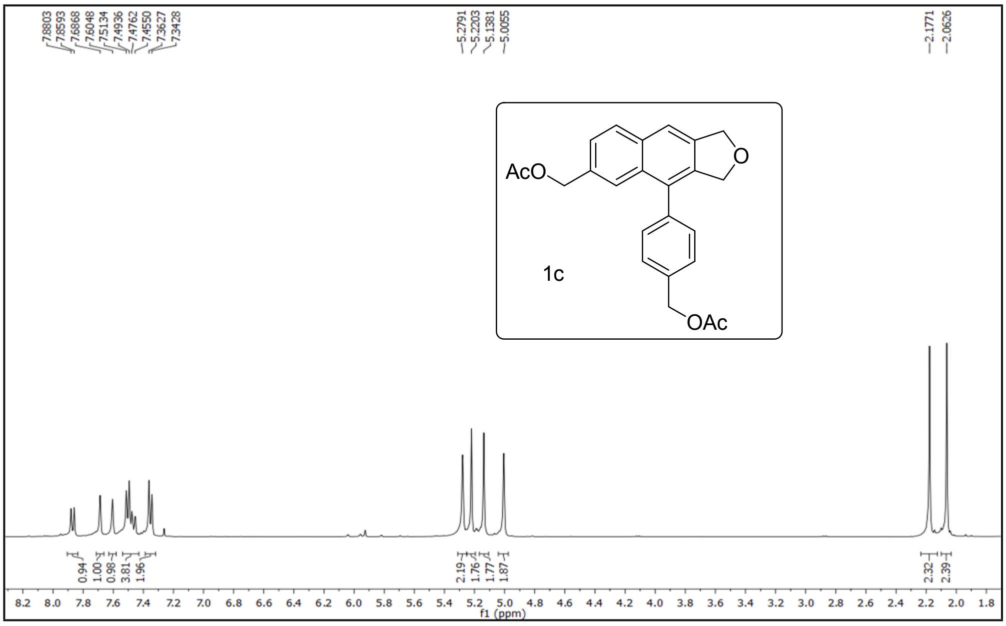

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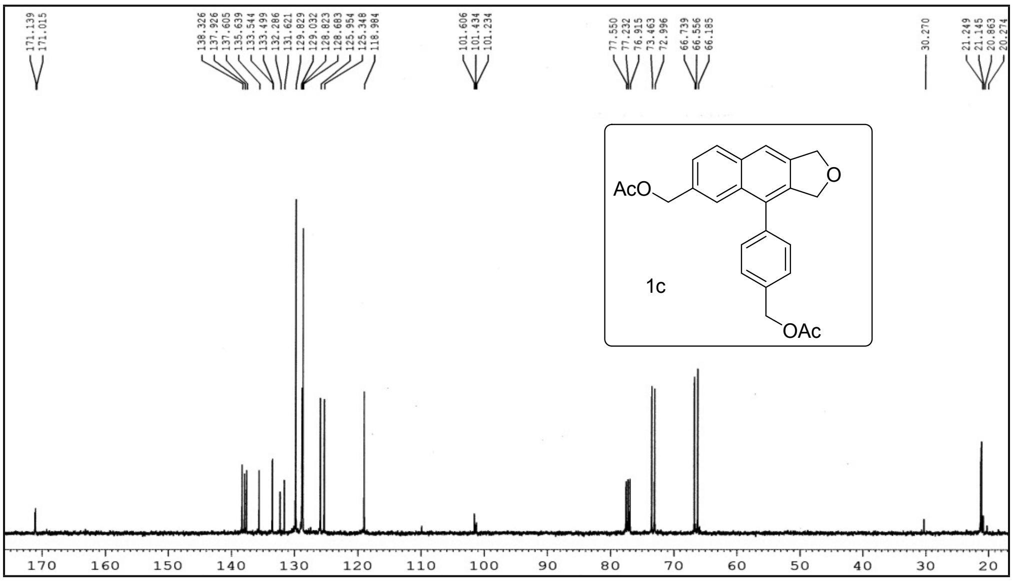

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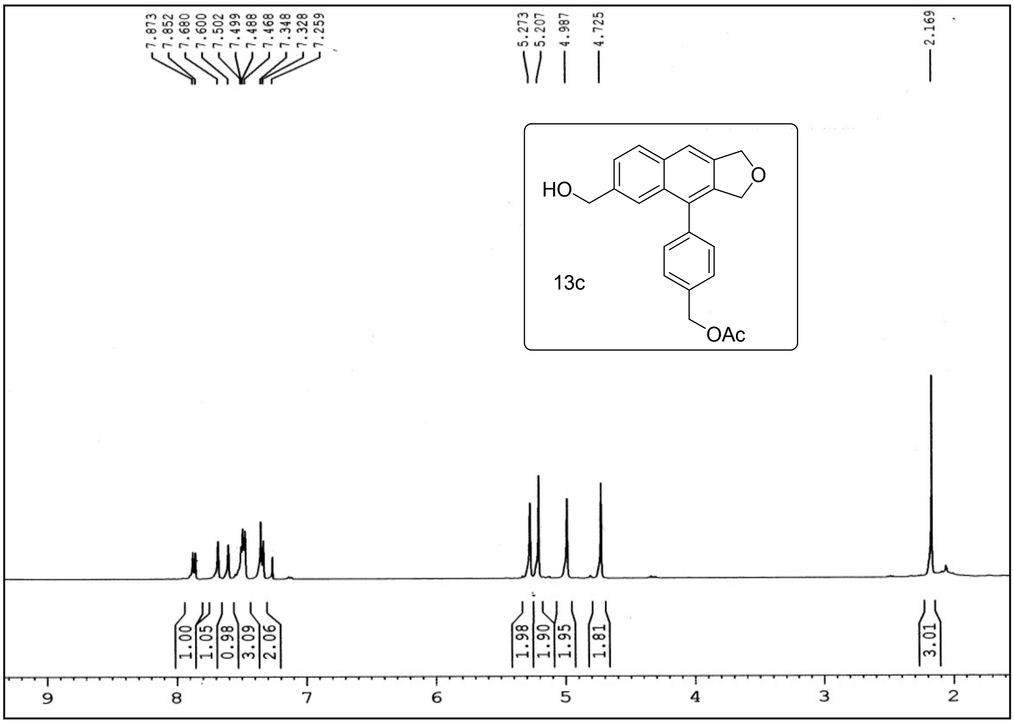

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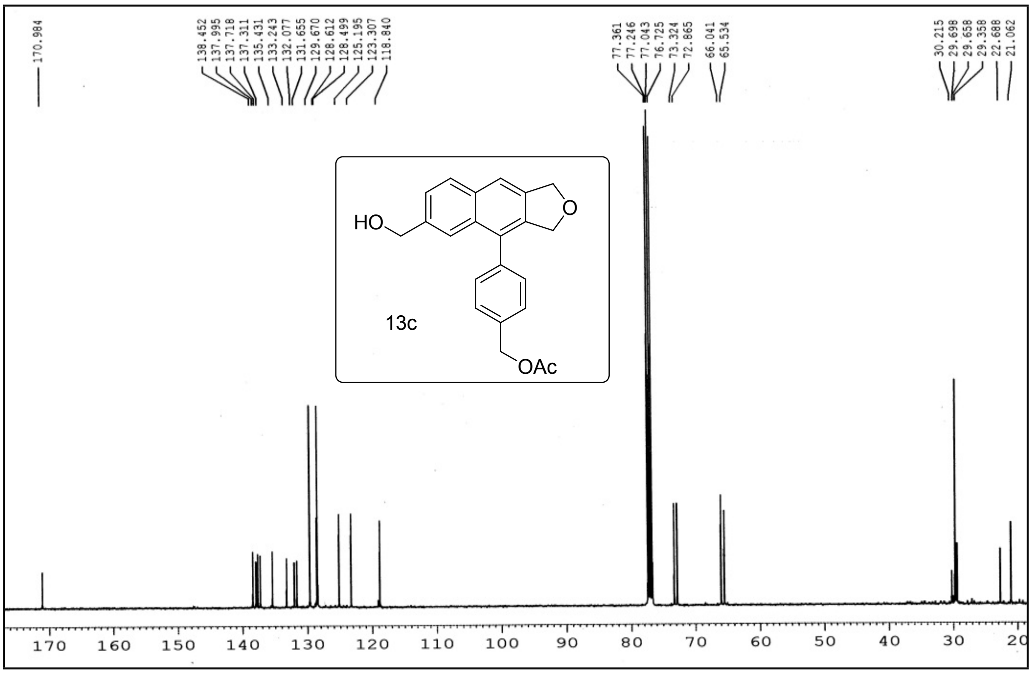

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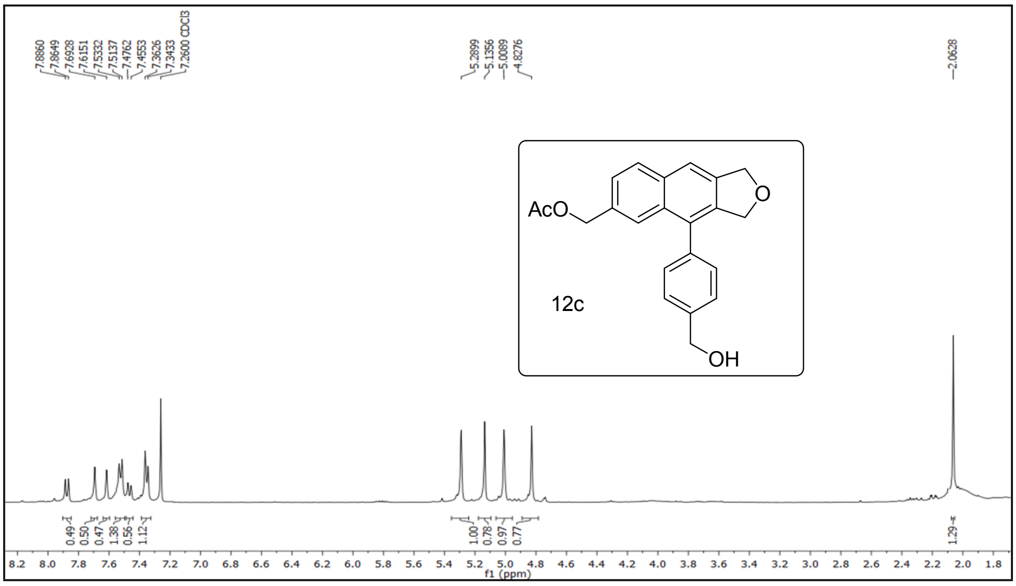

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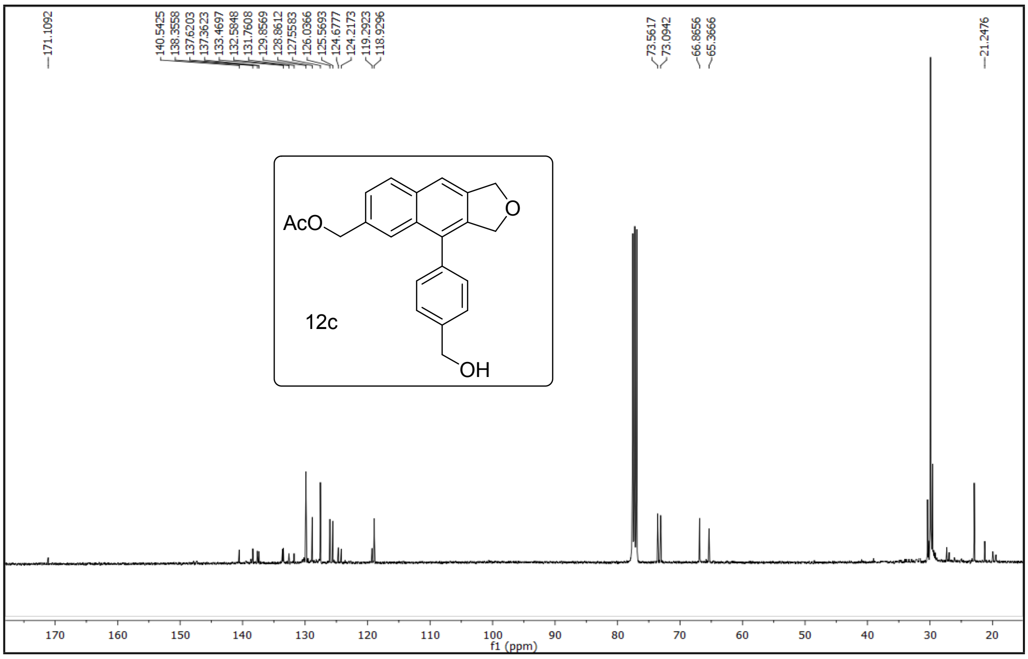
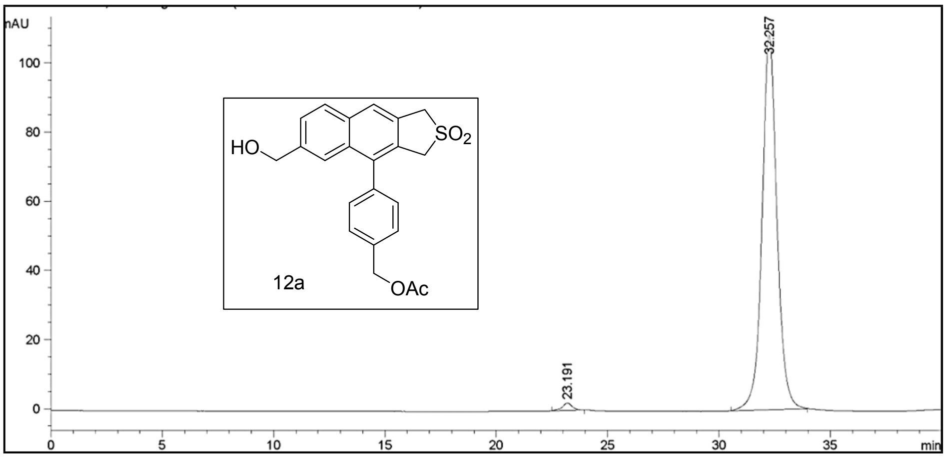
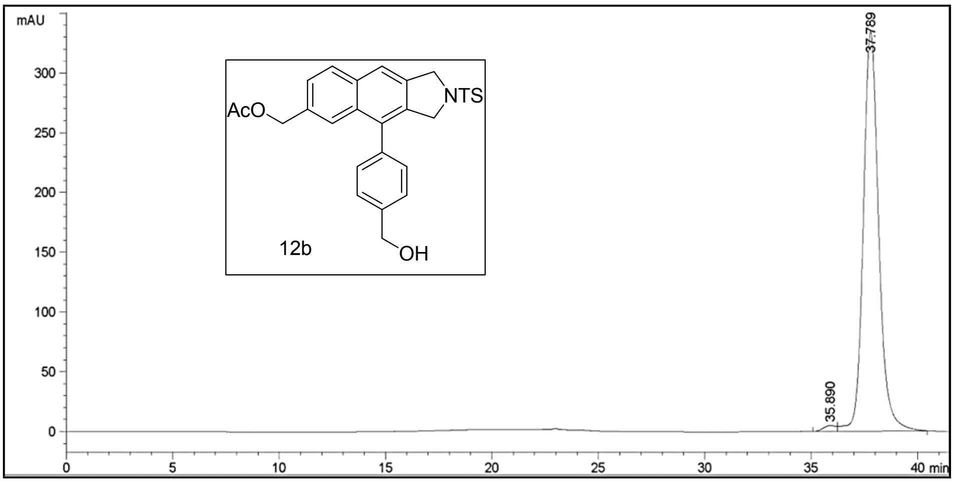
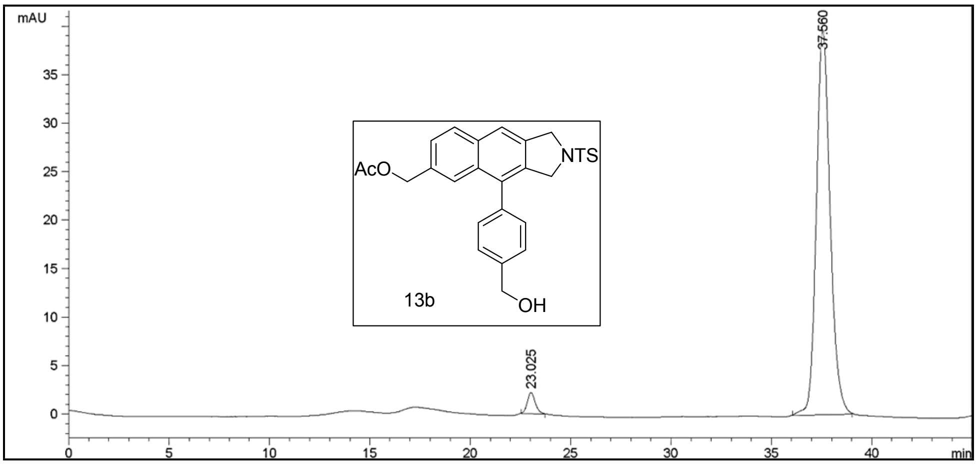


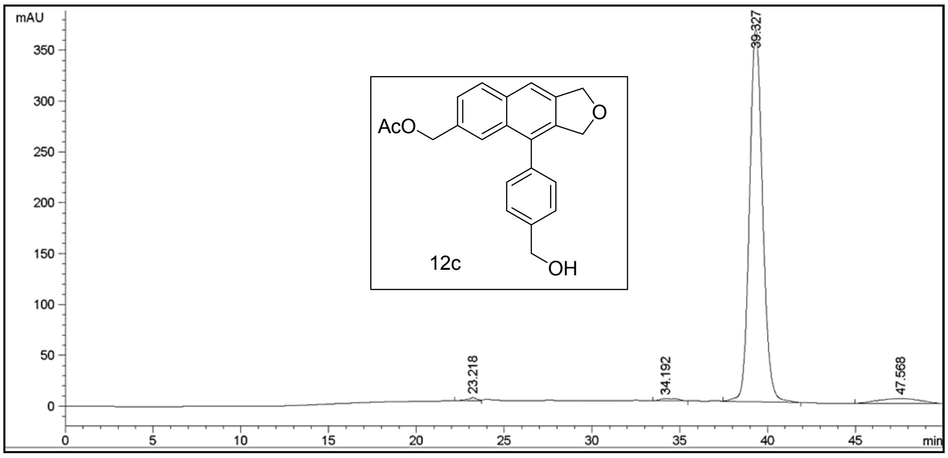
^{13}C NMR in 100 MHz

S3: HPLC profiles, 100% Methanol, 0.3 mL/min





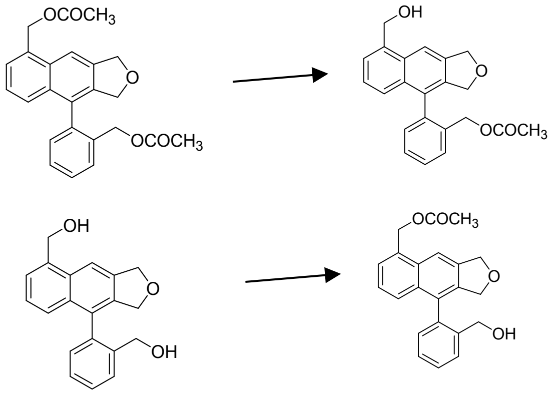




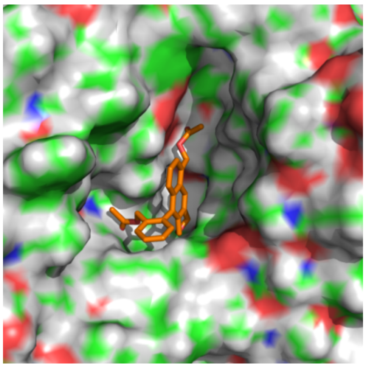
S4: Docking studies

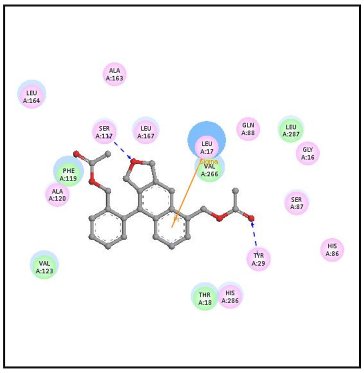
Model docking studies with previously reported aryl-napthalenes

A. Model study for furan:

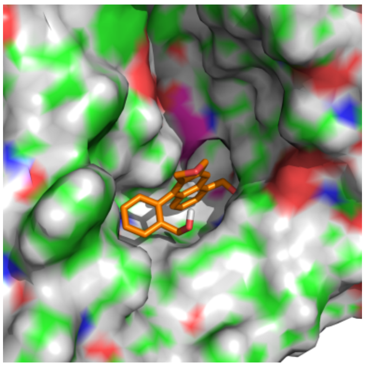


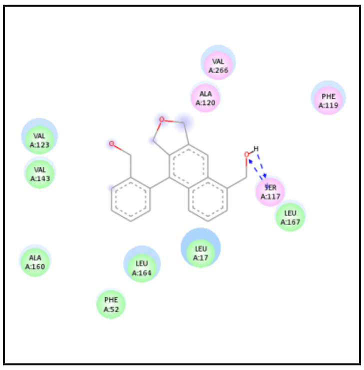
Hydrolysis reaction:





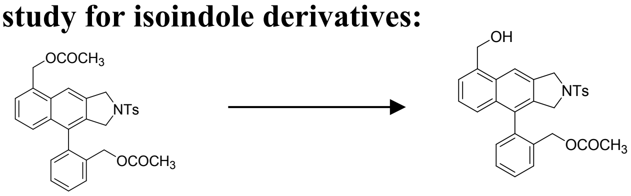
Transacetylation reaction:



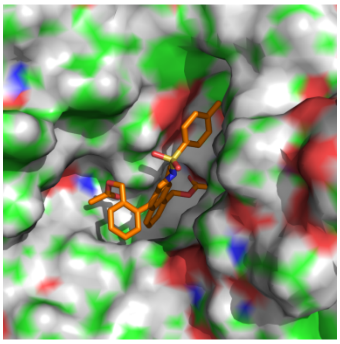


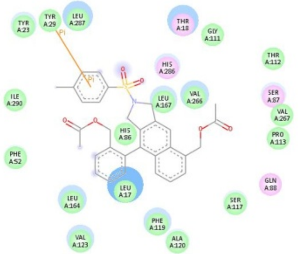
Acetate/alcohol linked C-5 of naphthalene ring is more exposed and interacts with lipase residues. The interaction between substituent and lipase has been the driving force behind selectivity.

B. Model study for isoindole derivatives:

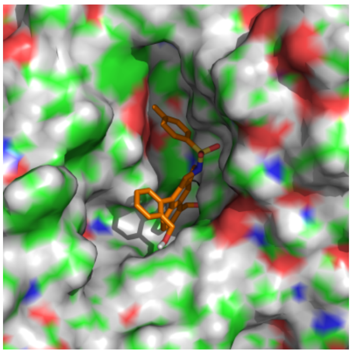


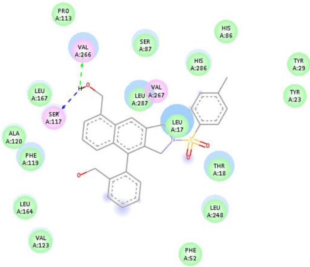
Hydrolysis Reaction:





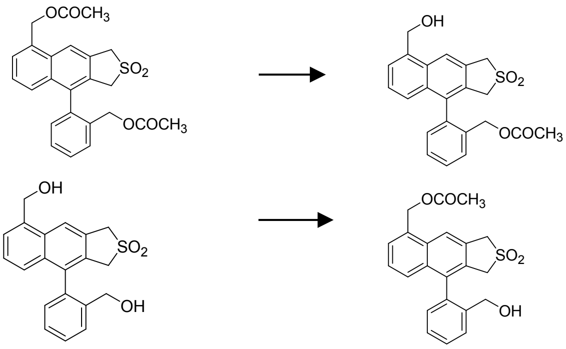
Trnasacetylation Reaction:



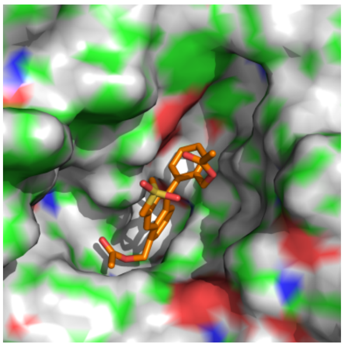


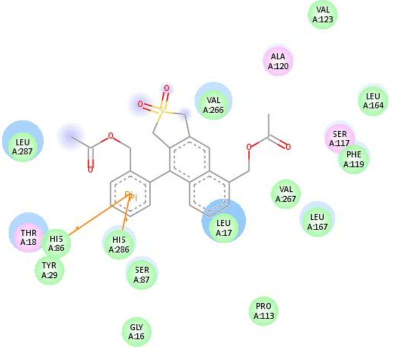
Bulky and hydrophobic N-tosyl group always acquires another binding cavity and force naphthalene ring to point towards active site cavity. Hence always the reaction takes place at naphthalene end. Positioning of tosyl group has been the driving force behind selectivity.

C. Model study for sulfone derivatives:

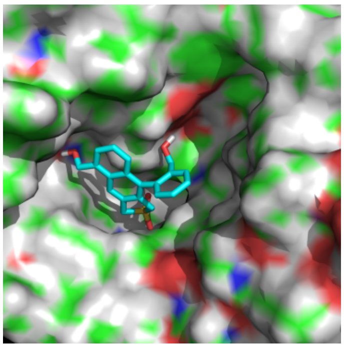


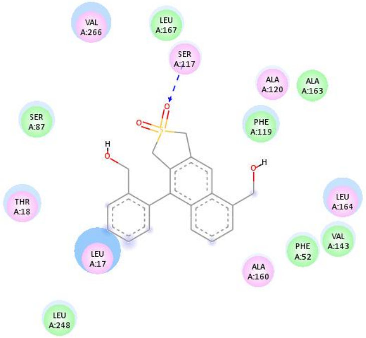
Hydrolysis reaction:





Trnasacetylation reaction:





Combined interaction of sulfone and substituent play crucial role in the selectivity of sulfone derivatives. In hydrolysis reaction, substituent plays crucial interaction; while transacetylation reaction, sulfone makes interaction. Combined effect of sulfone and substituent is the driving force.