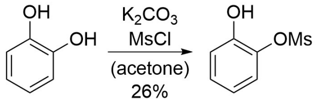
Supplementary Material on SolQ2Br

Synthesis of solQ2Br

Building block sources, solvent grades, synthetic conditions, characterisation and purification procedures, and instrumentation, were as previously described [https://doi.org/10.1021/jacs.2c01020].

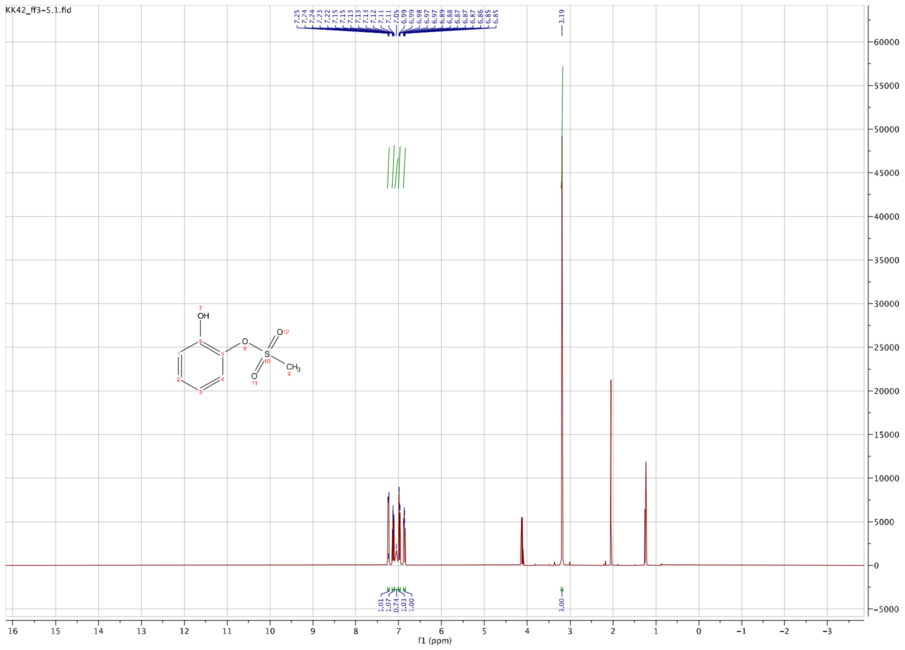
2-hydroxyphenyl methanesulfonate (1):



1

Commercially available catechol (1.0 g, 9.0 mmol, 1.0 eq.) was dissolved in dry acetone (30 mL). Finely ground K_2CO_3 (2.5 g, 18 mmol, 2.0 eq.) and methanesulfonyl chloride (MsCl, 0.78 mL, 10 mmol, 1.1 eq.) were added and the reaction mixture was heated to reflux, stirring at 50°C for 3 h until full consumption of starting material. After cooling to ambient temperature, K_2CO_3 was filtered off and the filtrate concentrated under reduced pressure. The obtained residue was taken up in dichloromethane (DCM, 20 mL), acidified to pH 1 with aqueous HCl (2 M, 200 mL) and extracted with DCM (4 x 50 mL). The combined organic phases were washed with brine (1 x 100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to give the crude product as a yellow oil. Flash column chromatography on silica (hexane:EtOAc, 5:1 → 1:1) afforded the known mono-mesylated catechol (0.44 g, 2.3 mmol, 26%) that matched literature data [https://doi.org/10.1002/chir.20055].

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.24 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.13 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 7.06 (br. s, 1H), 6.98 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.87 (ddd, *J* = 8.2, 7.4, 1.6 Hz, 1H), 3.19 (s, 3H).



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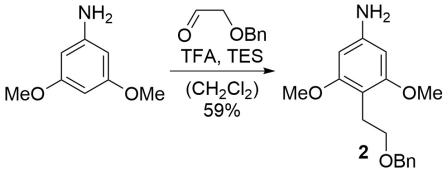
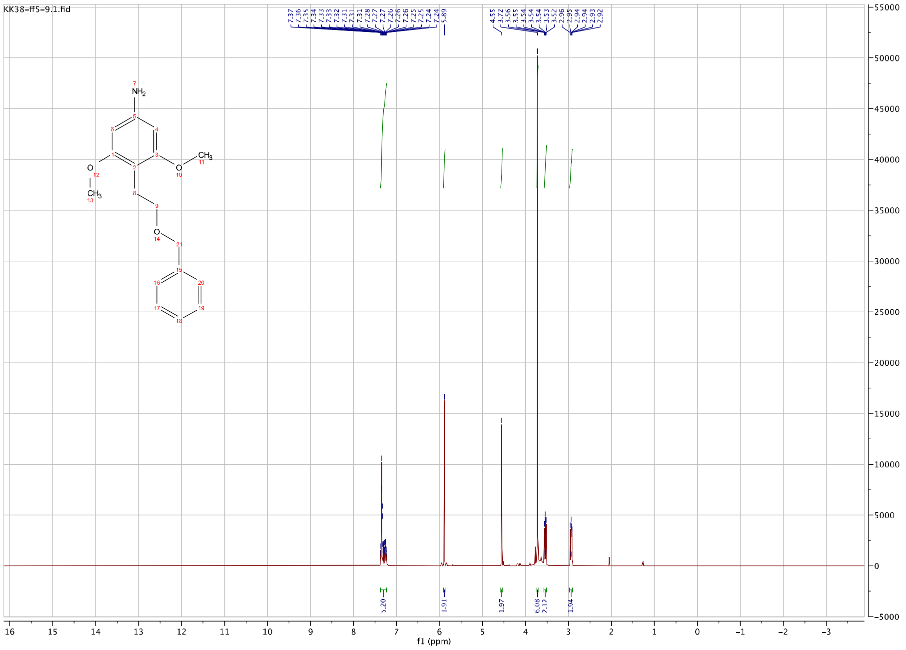
4-(2-(benzyloxy)ethyl)-3,5-dimethoxyaniline (2):

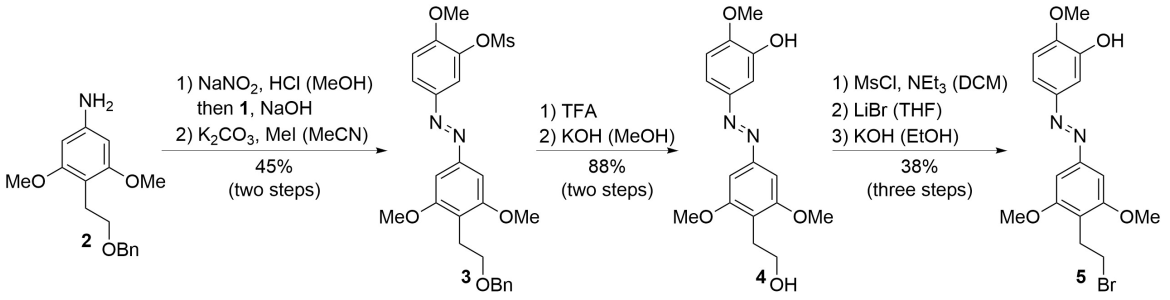


Analogously to the elegant *para*-alkylation procedure for electron rich anilines optimised by Augustine [https://doi.org/10.1055/s-2008-1078207], to a solution of commercially available 3,5-dimethoxyaniline (1.0 g, 6.7 mmol, 1.0 eq.) and benzyloxyacetaldehyde (1.0 g, 6.7 mmol, 1.0 eq.) in DCM (25 mL) was added trifluoracetic acid (TFA, 1.0 mL, 13 mmol, 2.0 eq.). The mixture was stirred at room temperature for 10 min before being cooled in an ice bath. To this cooled solution triethylsilane (1.8 mL, 11 mmol, 1.7 eq.) was added dropwise. The reaction mixture was allowed to warm to ambient temperature and left stirring for 3 h. The crude mixture was then diluted with KH_2PO_4/K_2HPO_4-buffer (50 mL) and extracted with DCM (4 x 50 mL). The combined organic phases were washed with brine (1 x 100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. Flash column chromatography on silica (hexane:EtOAc, 5:1 → 1:1 + 1% MeOH) gave aniline **2** as a beige solid (1.1 g, 3.8 mmol, 57%).

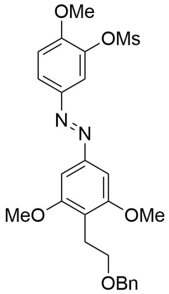
TLC (hexane:EtOAc 1:1): R_f = 0.40 [UV, CAM]. **^{1}H NMR** (400 MHz, $CDCl_3$, 300 K): δ[ppm] = 7.38 – 7.20 (m, 5H), 5.89 (s, 2H), 4.55 (s, 2H), 3.72 (s, 6H), 3.54 (dd, *J* = 8.8, 7.0 Hz, 2H), 2.94 (dd, *J* = 8.8, 7.0 Hz, 2H). **HRMS-ESI (m/z):** calc. for $[C_{17}H_{22}NO_3]^+$ ($[M+H]^+$): 288.15942; found: 288.15941.



Supplementary Material on SolQ2Br



5-((4-(2-(benzyloxy)ethyl)-3,5-dimethoxyphenyl)diazenyl)-2-methoxyphenyl methanesulfonate (3):



To the aniline **2** (0.56 g, 1.95 mmol, 1.0 eq.) were added methanol (MeOH, 5 mL) and conc. HCl (1 mL), while cooling the mixture in an ice bath. An aqueous solution of $NaNO_2$ (2.3 M, 0.80 mL, 1.95 mmol, 1.2 eq.) was added dropwise and the mixture was left stirring for 15 min in the cold. This diazonium solution was then transferred dropwise into a well-stirred cold solution of phenol **1** (0.44 g, 2.34 mmol, 1.2 eq.) in aqueous NaOH (2.0 M, 1.2 mL, 1.2 eq.). During and after the addition, the pH was maintained at $9<pH<12$ by adjusting when necessary. The mixture was left stirring overnight until complete consumption. MeOH was removed under reduced pressure and the crude aqueous mixture was extracted with ethyl acetate (EtOAc, 3 x 20 mL). The combined organic layers were then washed with water (2 x 20 mL), brine (2 x 20 mL), dried over Na_2SO_4 and filtered. The crude *para*-phenolic intermediate was concentrated and used without further purification.

To a solution of the crude intermediate in acetonitrile (MeCN, 5 mL) were added an excess of finely ground K_2CO_3 and methyl iodide (0.15 mL, 2.41 mmol, 1.2 eq.). The reaction mixture was heated to 80°C for 1h until full conversion was observed via TLC. The crude mixture was then diluted with water (30 mL) and extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with water (2 x 10 mL), brine (1 x 10 mL), dried over Na_2SO_4 and filtered. The crude was concentrated *in vacuo* and purified by flash column chromatography on silica (hexane:EtOAc, 5:1 → 1:1) to yield the azobenzene **3** as an orange solid (0.44 g, 0.88 mmol, 45%).

TLC (hexane:EtOAc 1:1): $R_f = 0.47$ [UV, CAM]. **^{1}H NMR** (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.95 – 7.92 (m, 2H), 7.36 – 7.24 (m, 5H), 7.15 (s, 2H), 7.13 (d, *J* = 8.0 Hz, 1H), 4.57 (s, 2H), 3.98 (s, 3H), 3.90 (s, 6H), 3.64 dd, *J* = 8.3, 7.1 Hz, 2H), 3.24 (s, 2H), 3.11 (dd, *J* = 8.3, 7.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 158.95 (s, 2C), 153.64 (s, 1C), 152.08 (s, 1C), 146.58 (s, 1C), 138.88 (s, 1C), 138.81 (s, 1C), 128.33 (s, 2C), 127.65 (s, 2C), 127.42 (s, 1C), 125.14 (s, 1C), 118.45 (s, 1C), 117.31 (s, 1C), 112.48 (s, 1C), 98.81 (s, 2C), 72.56 (s, 1C), 68.89 (s, 1C), 56.45 (s, 1C), 55.92 (s, 2C), 38.60 (s, 1C), 24.04 (s, 1C). **HRMS-EI (m/z):** calc. for $[C_{25}H_{28}N_2O_7S]^+$ ($[M+H]^+$): 500.16117; found: 500.1612.

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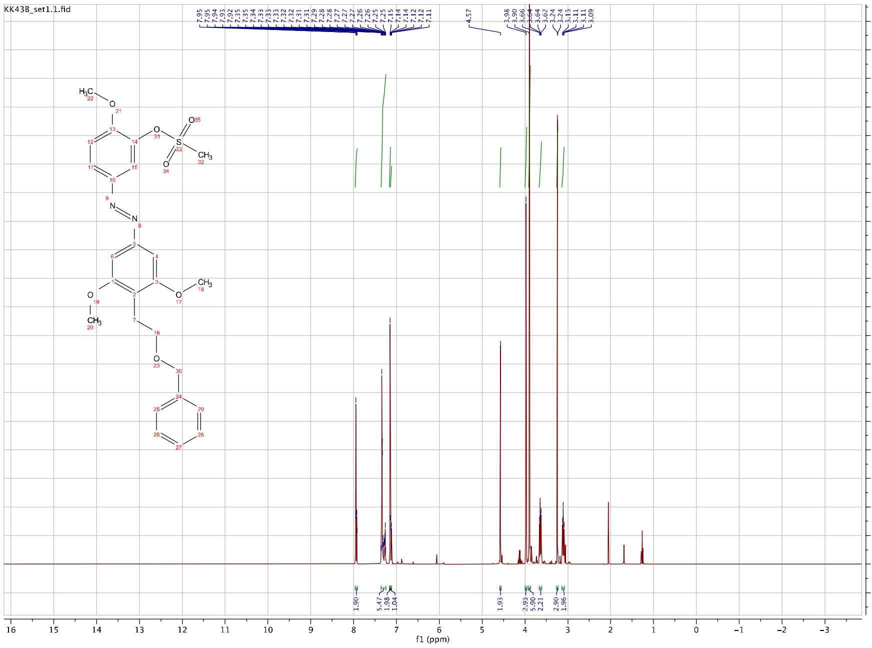
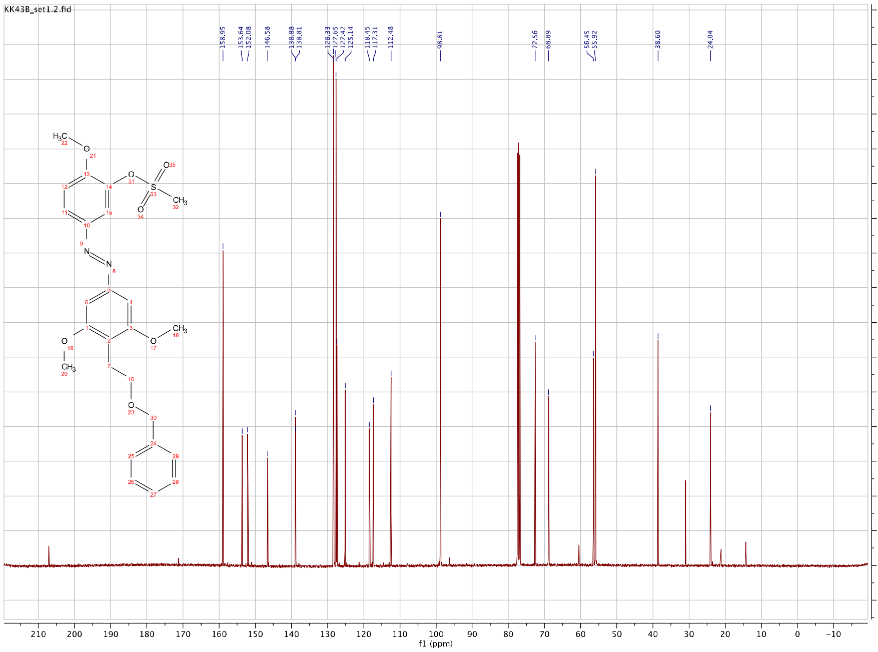
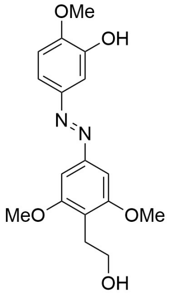




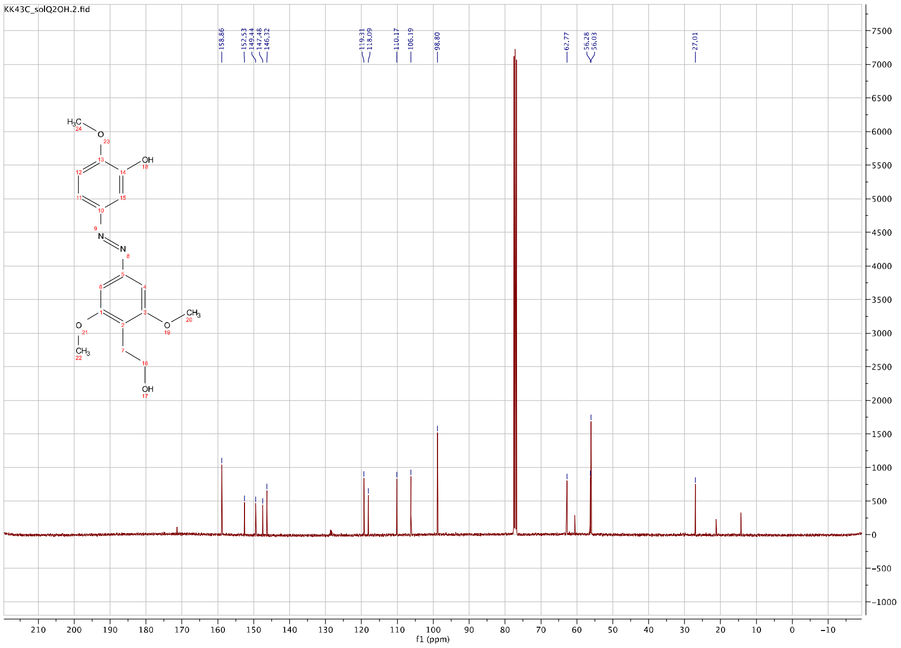
Supplementary Material on SolQ2Br

5-((4-(2-hydroxyethyl)-3,5-dimethoxyphenyl)diazenyl)-2-methoxyphenol (4):

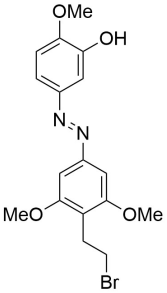


The azobenzene **3** (400 mg, 0.8 mmol, 1.0 eq.) was dissolved in neat trifluoroacetic acid (5 mL) and heated to 50°C. Reaction progress was checked via TLC and the mixture stirred at 50°C overnight until complete consumption of the starting material. The crude mixture was then concentrated under reduced pressure and redissolved in MeOH (3 mL). Solid KOH was added in excess and the reaction mixture quickly heated to reflux using a heat gun until full hydrolysis of the trifluoroacetic acid ester was observed via LC-MS. The crude mixture was acidified using aqueous HCl (2 M, 20 mL) and extracted with EtOAc (3 x 10 mL). The combined organic phases were washed with water (2 x 10 mL), brine (1 x 10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by flash column chromatography on silica (hexane:EtOAc, 2.5:1 → 1:1 + 1% MeOH) afforded the azobenzene **4** as an orange solid (232 mg, 0.7 mmol, 88%).

^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.55 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.53 (d, *J* = 2.3 Hz, 1H), 7.16 (s, 2H), 6.98 (d, *J* = 8.5 Hz, 1H), 3.98 (s, 3H), 3.92 (s, 6H), 3.80 (t, *J* = 6.5 Hz, 2H), 3.03 (t, *J* = 6.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 158.86 (s, 2C), 152.53 (s, 1C), 149.44 (s, 1C), 147.48 (s, 1C), 146.32 (s, 1C), 119.31 (s, 1C), 118.09 (s, 1C), 110.17 (s, 1C), 106.19 (s, 1C), 98.80 (s, 2C), 62.77 (s, 1C), 56.28 (s, 1C), 56.03 (s, 2C), 27.01 (s, 1C). **HRMS-ESI (m/z):** calc. for $[C_{17}H_{21}N_2O_5]^+$ ($[M+H]^+$): 333.14450; found: 333.14409.



5-((4-(2-bromoethyl)-3,5-dimethoxyphenyl)diazenyl)-2-methoxyphenol (5, solQ2Br):



The conversion of **4** to **5** was carried out similar to literature procedures. [10.1002/adsc.201100736]

To the azobenzene **4** (27 mg, 0.08 mmol, 1.0 eq.) was added anhydrous DCM (2 mL) under an atmosphere of nitrogen while cooling the mixture in an ice bath. To this cooled solution triethylamine (30 µL, 0.22 mmol, 2.8 eq.) and MsCl (20 µL, 0.26 mmol, 3.3 eq) were added. The reaction mixture was then allowed to warm to ambient temperature and left stirring overnight until consumption of the starting material was observed by LC-MS. The crude mixture was diluted with water (10 mL) and extracted with DCM (3 x 5 mL). The combined organic phases were washed with water (2 x 5 mL), brine (1 x 5 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure.

To this crude bismesylated azobenzene in THF (3 mL) was added solid LiBr in excess. The reaction mixture was heated to 75°C for 24 h and reaction progress was monitored via LC-MS. Following completion of the reaction after additionally stirring at room temperature for 60 h, the mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 5 mL). The combined organic layers were washed with water (2 x 5 mL), brine (1 x 5 mL), dried over Na_2SO_4 and filtered. The crude was concentrated *in vacuo* and used without further purification.

The crude was dissolved in 1% KOH in ethanol (2 mL). The reaction mixture was stirred at room temperature for 15 min and the amount of KOH was adjusted to 5% until full conversion was observed via TLC. The mixture was then diluted with water (15 mL) and extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with water (2 x 10 mL), brine (1 x 10 mL), dried over Na_2SO_4 and filtered. The crude was concentrated under reduced pressure and purified by column chromatography (hexane:EtOAc, 5:1 → 1:1) to yield **solQ2Br** (**5**) as an orange solid (12 mg, 0.03 mmol, 38%).

TLC (hexane:EtOAc 1:1): R_f = 0.59 [UV, CAM]. **^{1}H NMR** (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.56 (dd, *J* = 8.4, 2.3 Hz, 1H), 7.53 (d, *J* = 2.3 Hz, 1H), 7.13 (s, 2H), 6.99 (d, *J* = 8.4 Hz, 1H), 5.72 (br. s, 1H), 3.99 (s, 3H), 3.92 (s, 6H), 3.48 (dd, *J* = 9.3, 7.1 Hz, 1H), 3.28 (dd, *J* = 9.3, 7.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 158.78 (s, 2C), 152.83 (s, 1C), 149.47 (s, 1C), 147.48 (s, 1C), 146.32 (s, 1C), 119.44 (s, 1C), 117.96 (s, 1C), 110.16 (s, 1C), 106.14 (s, 1C), 98.66 (s, 2C), 56.30 (s, 1C), 56.00 (s, 2C), 31.07 (s, 1C), 27.53 (s, 1C). **HRMS-ESI (m/z):** calc. for $[C_{17}H_{20}BrN_2O_4]^+$ ($[M+H]^+$): 395.06010; found: 395.06013.