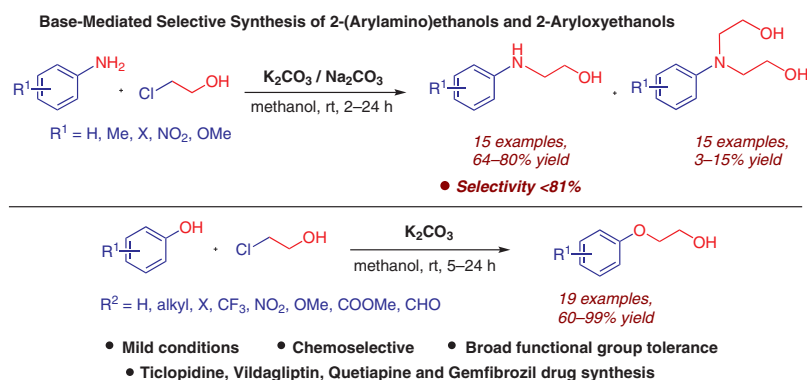


Room-Temperature, Base-Mediated Selective Synthesis of 2-(Arylamino)ethanols and 2-Aryloxyethanols

Rahul B. Sonawane¹
 Swapnali R. Sonawane
 Nishant K. Rasal
 Sangeeta V. Jagtap*¹

Department of Chemistry, Baburaoji Gholap College, Sangvi,
 Pune 411027, India (Affiliated to Savitribai Phule Pune
 University, Pune, India)
 sangeetajagtap@rediffmail.com



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Abstract A simple and efficient protocol for base-mediated selective synthesis of 2-(arylamino)ethanols from primary aromatic amines and 2-aryloxyethanols from phenols, promoted by K_2CO_3 has been achieved under mild conditions. Even in presence of excess alkyl halide, selective mono-*N*-alkylation has been achieved. Tolerance of a variety of functional groups is demonstrated by 15 examples of selective *N*-alkylation of aromatic amines and 19 examples of *O*-alkylation of phenols. The efficacy of the protocol is demonstrated by the formal synthesis of Ticlopidine®, Vildagliptin®, Quetiapine®, and Gemfibrozil®.

Key words selective *N*-alkylation, 2-(arylamino)ethanols, amines, 2-aryloxyethanols, phenols, K_2CO_3 promoted, Na_2CO_3 controlled

N-Alkylation of amines is central to the synthesis of synthetic intermediates,¹ fine chemicals,² pharmaceuticals,³ agrochemicals,⁴ dyes,⁵ rubbers,⁶ and polymers.⁷ Likewise, *O*-alkyl phenols are applied in paints, varnishes, printing inks, foaming agents, synthetic resins, and perfumes.⁸ Moreover, many important drug molecules have *N*-alkyl moieties, including Metronidazole®, Fluphenazine®, Quetiapine®, Vildagliptin®, Ticlopidine®, and Ditzazole® (Figure 1).

Under standard conditions, amines commonly undergo over-alkylation,⁹ which leads to mixtures of secondary and tertiary amines and quaternary ammonium salts instead of the desired mono-*N*-alkylation products. Methods for preparing *N*-alkyl amines include direct *N*-alkylation of primary amines with alkyl halides,¹⁰ reduction of amides,¹¹ re-

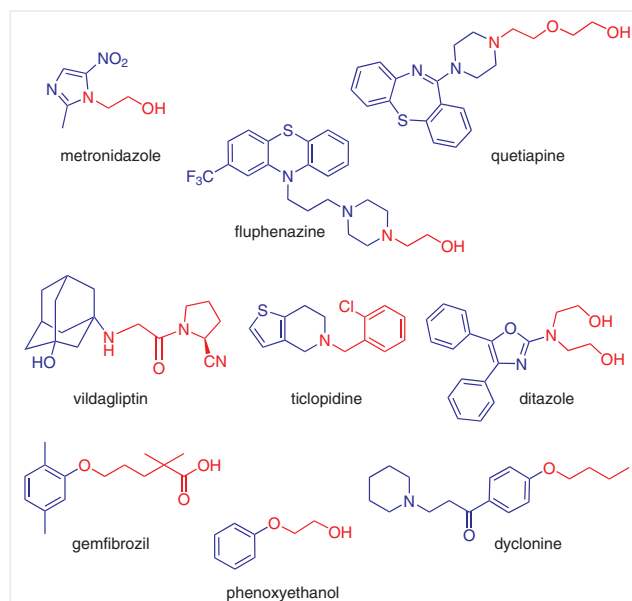


Figure 1 Drug molecules having *N*-alkyl and *O*-alkyl moieties

ductive amination of aldehydes with primary amines in the presence of reducing agents,¹² *N*-dealkylation of tertiary amines,¹³ C–N bond-coupling reactions,¹⁴ and transition-metal-catalyzed direct alkylation of amines with alcohols by the borrowing hydrogen strategy.^{3,15} *N*-Alkylation of amines can be achieved by using various alkyl sources such as alkyl halides,¹⁶ alcohols,^{3,17} dimethyl carbonate,^{17f,18} ethylene glycol,¹⁹ epoxides,²⁰ 2-chloroethanol,²¹ CO_2 ,²² and ZnEt_2 .²³ In addition, various inorganic bases have been employed, such as K_2CO_3 ,²⁴ NaHCO_3 ,²⁵ NaH ,²⁶ $\text{CsOH}\cdot\text{H}_2\text{O}$,²⁷ and Cs_2CO_3 .²⁸ In addition methods have been described using ionic liquids²⁹ and *N*-sulfonamides^{8,30} with alkyl halides.

Recently, N-alkylation of anilines with alcohols has been performed efficiently by using Mn,³¹ Ni,³² and Ru³³ metal catalysts and alkyl halides on silica.³⁴

Similarly, O-alkylation of phenols is commonly carried out by Williamson's ether synthesis³⁵ and C–O bond-coupling reactions³⁶ with alkyl halides. For O-alkylation of phenols the alkylating agents include alkyl halides,³⁷ alcohols,³⁸ dimethyl carbonate,³⁹ allylic carboxylates,⁴⁰ ethylene carbonate,⁴¹ methyl formate,^{35b} 2-chloroethanol,⁴² and epoxides.⁴³ Equally, various inorganic bases have been employed, including NaOH,⁴⁴ NaH,⁴⁵ K₂CO₃,^{24a,42,43b,46} and Cs₂CO₃,⁴⁷ and ionic liquids have also been used.⁴⁸

Nevertheless, the development of new methodologies for selective mono-N-alkylation and O-alkylation protocols continues to be a major challenge. Therefore, the development of effective methods for such conversions continues to be a focus of attention. In particular, most traditional methods for the synthesis of aryl ethers require harsh conditions, such as strong bases and high temperatures,^{35a,49} and are incompatible with a range of functional groups.

Herein, we report a selective and simple protocol to synthesize 2-(arylamino)ethanols from a range of primary aromatic amines and 2-aryloxyethanols from several phenols with 2-chloroethanol, promoted by K₂CO₃ in methanol (Table 1 and Schemes 1–2). The corresponding mono-N-alkylated 2-(phenylamino)ethanol products are isolated with high selectivity (81–96%) and moderate to excellent yields (64–80%). Similarly, O-alkylated 2-phenoxyethanol products can also be synthesized with moderate to excellent yields (60–99%). A wide range of functional groups is tolerated due to the mild reaction conditions for both N- and O-alkylation.

In preliminary reactions, 4-methylaniline (**1c**) was treated with 2-chloroethanol (**2a**) in the presence of an organic base (1 equiv) such as triethylamine or *N,N*-diisopropylethylamine (DIPEA) with methanol as solvent at ambient temperature, when 27–34% yield of the desired mono-N-alkylated product **3c** and 35–38% of di-N-alkylated product **4c** were isolated (Table 1, entries 1 and 2). By using inorganic bases such as Na₂CO₃, NaHCO₃ and KHCO₃, the reactions were unsuccessful, with negligible yields of **3c** and **4c** being observed (entries 3–5). Other bases, such as K₂CO₃, Cs₂CO₃, K₃PO₄, NaOH, KOH, and NaOMe, were found to be effective, but did not selectively furnish mono-N-alkylated product **3c** (entries 6–11). While some selectivity was observed towards mono-N-alkylated product **3c** with K₂CO₃ and, being aware of the relative solubility of K₂CO₃ in methanol,⁵⁰ to control the over-alkylation, the reaction was carried out without any solvent, but satisfactory results were still not observed (entry 12).

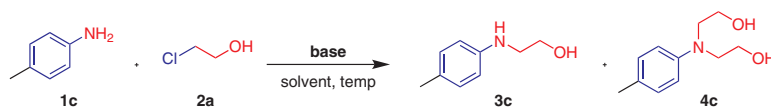
After a reevaluation of all the trials, it was clear that 1 equivalent of Na₂CO₃, NaHCO₃ and KHCO₃ showed low conversions but the selectivity was high; whereas 1 equivalent

of K₂CO₃ promoted the reaction with a **3c/4c** selectivity up to 58:42. Hence, the decision was made to use a mixture of 1 equivalent of K₂CO₃ and 1–3 equivalents of Na₂CO₃; whereupon, dramatic improvements in both selectivity and conversion were obtained (entries 13–15). Among these conditions, 3 equiv of Na₂CO₃ was most effective; under these conditions improvements in both selectivity (**3c/4c**, 84:16) and conversion (91%) were obtained, with 76% isolated yield of desired product **3c** and only 15% yield of product **4c** (entry 15). To examine the effect of Na₂CO₃ on this conversion, the reaction was carried out by replacing the Na₂CO₃ with NaHCO₃ and KHCO₃; in these cases slight decreases in selectivity and conversion were observed (entries 16 and 17). Changing K₂CO₃ with triethylamine, Cs₂CO₃ and K₃PO₄ led to a decrease in selectivity (entries 18–20).

Subsequently, various solvents such as acetonitrile, acetone, dichloromethane, THF, toluene, 1,4-dioxane, DMF, DMSO and NMP were screened, but none were successful (Table 1, entries 21–29), indicating that methanol is the most efficient solvent for this reaction. To examine the effect of alcoholic solvents on conversion and selectivity, reactions were carried out with ethanol and isopropanol, but decreases in selectivity were observed (entries 30–31). To examine the effect of the concentration of 2-chloroethanol on the reaction, experiments were performed using 1 and 2 equivalent of 2-chloroethanol **2a**, whereupon a notable decrease in both selectivity and conversion was observed (entries 32 and 33). At the end of this study, one experiment was performed by varying the temperature from ambient temperature up to 40 °C and then at reflux, but decreased selectivity at the higher temperature was observed (entry 34).

It was therefore concluded that the reaction is efficient and selective for mono-N-alkylation using 1 equiv of **1a**, 3 equiv of **2a**, 1 equiv of K₂CO₃, 3 equiv of Na₂CO₃ and 2.5 mL of methanol at room temperature.

With the optimized conditions established, mono-N-alkylation of a range of aromatic amines with **2a** was performed (Table 2). It was observed that anilines containing electron-donating groups such as Me, and OMe underwent conversion smoothly with excellent selectivity for mono-N-alkylated products with good yields. Electron-withdrawing groups such as NO₂ and COOH at *ortho*- and *para*-positions did not show any conversion, presumably due to decreased nucleophilicity of the amino group. However, a nitro group at the *meta*-position gave high selectivity and moderate yield of **3g**. For halogen-substituted anilines, better conversions were seen at all *ortho*, *meta* and *para* positions to give **3h–o** with an increase in the selectivity for mono-N-alkylated products.

Table 1 Selected Reaction Optimisation Observations^a

Entry	Base (equiv)	Additive (equiv)	Solvent (volume, mL)	Time (h)	Conv. (%) ^b	Yield ^b (selectivity) ^c (%)		Ratio of 3/4
						3	4	
1	triethylamine (1)	–	methanol (2.5)	12	72	34 (47)	38 (53)	47:53
2	DIPEA (1)	–	methanol (2.5)	12	62	27 (44)	35 (56)	44:56
3	Na ₂ CO ₃ (1)	–	methanol (2.5)	12	1	1 (100)	ND	100:0
4	NaHCO ₃ (1)	–	methanol (2.5)	12	1	1 (100)	ND	100:0
5	KHCO ₃ (1)	–	methanol (2.5)	12	1	1 (100)	ND	100:0
6	K ₂ CO ₃ (1)	–	methanol (2.5)	12	78	45 (58)	33 (42)	58:42
7	Cs ₂ CO ₃ (1)	–	methanol (2.5)	12	72	20 (28)	52 (72)	28:72
8	K ₃ PO ₄ (1)	–	methanol (2.5)	12	75	25 (33)	50 (67)	33:67
9	NaOH (1)	–	methanol (2.5)	12	85	27 (32)	58 (68)	32:68
10	KOH (1)	–	methanol (2.5)	12	87	25 (29)	62 (71)	29:71
11	NaOMe (1)	–	methanol (2.5)	12	95	30 (32)	65 (68)	32:68
12	K ₂ CO ₃ (1)	–	–	12	75	32 (43)	43 (57)	43:57
13	K ₂ CO ₃ (1)	Na ₂ CO ₃ (1)	methanol (2.5)	12	80	49 (61)	31 (39)	61:39
14	K ₂ CO ₃ (1)	Na ₂ CO ₃ (2)	methanol (2.5)	12	85	64 (74)	20 (26)	74:26
15	K₂CO₃ (1)	Na₂CO₃ (3)	methanol (2.5)	6	91	76 (84)	15 (16)	84:16
16	K ₂ CO ₃ (1)	NaHCO ₃ (3)	methanol (2.5)	12	80	65 (81)	15 (19)	81:19
17	K ₂ CO ₃ (1)	KHCO ₃ (3)	methanol (2.5)	12	83	68 (82)	15 (18)	82:18
18	triethylamine (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	75	33 (44)	42 (56)	44:56
19	Cs ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	88	55 (63)	33 (38)	63:38
20	K ₃ PO ₄ (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	90	36 (40)	54 (60)	40:60
21	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	acetonitrile (2.5)	24	3	3 (100)	ND	100:0
22	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	acetone (2.5)	24	3	3 (100)	ND	100:0
23	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	dichloromethane (2.5)	24	1	1 (100)	ND	100:0
24	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	THF (2.5)	24	2	2 (100)	ND	100:0
25	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	toluene (2.5)	24	3	3 (100)	ND	100:0
26	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	1,4-dioxane (2.5)	24	ND	ND	ND	100:0
27	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	DMF (2.5)	24	10	10 (100)	ND	100:0
28	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	DMSO (2.5)	24	7	7 (100)	ND	100:0
29	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	NMP (2.5)	24	5	5 (100)	ND	100:0
30	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	ethanol (2.5)	12	89	69 (78)	20 (22)	78:22
31	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	isopropyl alcohol (2.5)	12	87	62 (71)	25 (29)	71:29
32 ^d	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	55	50 (91)	5 (9)	91:9
33 ^e	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	76	67 (88)	9 (12)	88:12
34 ^f	K ₂ CO ₃ (1)	Na ₂ CO ₃ (3)	methanol (2.5)	12	99	70 (71)	29 (29)	71:29

^a Reaction conditions (0.5 g scale): **1c** (4.67 mmol, 1 equiv), **2a** (3 equiv), base (1–3 equiv), additives (1–3 equiv), solvent (2.5 mL) at room temperature. All reagent and substrate addition was carried out at room temperature (25 °C).

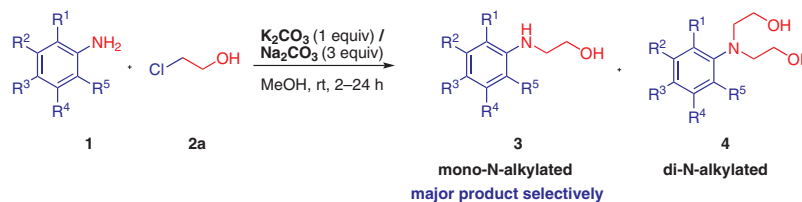
^b Isolated yields.

^c Selectivities are given in parentheses.

^d 2-Chloroethanol (**2a**) (1 equiv).

^e 2-Chloroethanol (**2a**) (2 equiv).

^f Reaction temperature initially at ambient temperature then increased to 40 °C and then heated to reflux.

Table 2 Scope of Selective Mono-N-alkylation of Aromatic Amines with 2-Chloroethanol Promoted by K_2CO_3 - Na_2CO_3 ^a

Entry	R ¹	R ²	R ³	R ⁴	R ⁵	Prod.	Conv. (%)	Yield ^b (selectivity) ^c (%)		Ratio of 3/4
								3	4	
1	H	H	H	H	H	3a/4a	88	73 (83)	15 (17)	83:17
2	Me	H	H	H	H	3b/4b	85	75 (88)	10 (12)	88:12
3	H	H	Me	H	H	3c/4c	91	76 (84)	15 (16)	84:16
4	Me	H	Me	H	H	3d/4d	89	77 (87)	12 (13)	87:13
5	OMe	H	H	H	H	3e/4e	85	66 (81)	15 (19)	81:19
6	H	H	OMe	H	H	3f/4f	81	80 (94)	5 (6)	94:6
7	H	NO ₂	H	H	H	3g/4g	69	64 (93)	5 (7)	93:7
8	Cl	H	H	H	H	3h/4h	80	72 (90)	8 (10)	90:10
9	H	Cl	H	H	H	3i/4i	82	69 (84)	13 (16)	84:16
10	H	H	Cl	H	H	3j/4j	83	71 (86)	12 (14)	86:14
11	H	H	Br	H	H	3k/4k	80	74 (93)	6 (8)	93:8
12	H	F	H	H	H	3l/4l	91	76 (84)	15 (16)	84:16
13	Cl	Cl	H	H	H	3m/4m	82	79 (96)	3 (4)	96:4
14	Me	H	Br	H	H	3n/4n	84	72 (86)	12 (14)	86:14
15	Me	F	H	H	H	3o/4o	79	72 (91)	7 (9)	91:9

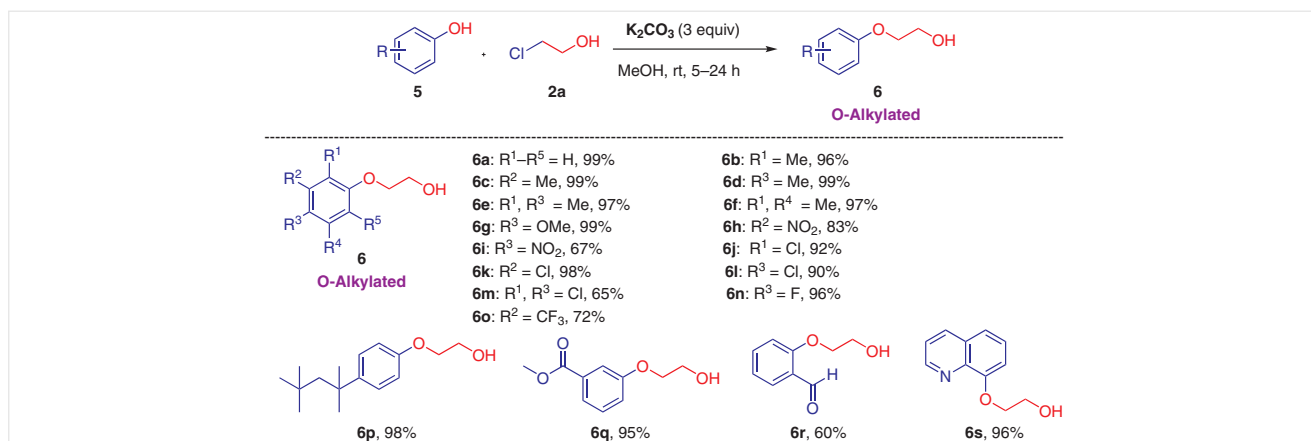
^a Reaction conditions: Amine **1** (0.5 g, 1 equiv), **2a** (3 equiv), K_2CO_3 (1 equiv), Na_2CO_3 (3 equiv), MeOH (2.5 mL, 5 volume), at room temperature stirring for 2–24 h.

^b Isolated yields are given.

^c Selectivities are given in parentheses.

The strategy was further extended towards O-alkylation of various substituted phenols **5** with **2a** to give moderate to excellent yields (Scheme 1, **6a–s**). These reactions also demonstrated similar effects on conversion for substrates with substituents having electron-donating or electron-

withdrawing groups and steric hindrance at the *ortho*, *meta* and *para* positions. The conditions were also compatible with a range of functional groups, such as alkyl, methoxy, nitro, halide, ester, and aldehyde.

**Scheme 1** Scope of O-alkylation of phenols with 2-chloroethanol promoted by K_2CO_3 . Reagents and conditions: Phenol **5** (0.5 g, 1 equiv), **2a** (3 equiv), K_2CO_3 (3 equiv), MeOH (2.5 mL, 5 volume), at room temperature stirring for 5–24 h. Isolated yields are given.

Finally, to demonstrate the synthetic potential of the developed protocol toward the synthesis of commercially important drugs, the formal synthesis of Ticlopidine[®],⁵¹ Vildagliptin[®],⁵² Quetiapine[®],⁵³ and Gemfibrozil[®]⁵⁴ (Scheme 2) was explored.

The formal synthesis of these four drug molecules was achieved by using the developed protocol with modifications of the reaction conditions as given in Scheme 2. The products formed are in good agreement with those obtained by using the previously reported methods and they were obtained in competitive yields.^{51–54} This protocol will help to improve industrial processes that can be applied in the synthesis of such drugs.

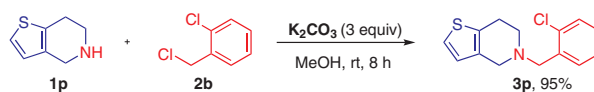
In conclusion, a simple method to attain selective mono-N-alkylation of aromatic and aliphatic primary amines with high selectivity and O-alkylation of phenols with excellent conversion, promoted by K₂CO₃ and controlled by Na₂CO₃ in methanol at room temperature is presented herein. The mild conditions allow broad functional group tolerance for both amines and phenols. Simple operational and workup procedures make this process applicable for scale-up.

All chemicals were obtained from Sigma–Aldrich, Alfa Aesar, Spectrochem, Avra Synthesis or TCI Europe and used as received without purification. Laboratory grade solvents used for reaction, extraction and column chromatography were purchased from Finar chemicals. The progress of reactions was checked by analytical thin-layer chromatography (TLC Silica gel 60 F₂₅₄ plates). The plates were visualized first with short-wavelength UV light, followed by staining with iodine.

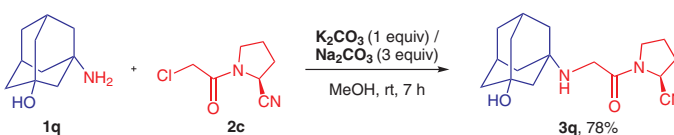
Melting points were determined with an open capillary tube. GC–MS analyses were recorded with a Shimadzu QP–Ultra 2010 GCMS system with MS detector (EI mode, 70 eV) and Rxi–624Sil MS column (30 m, 0.32 mm ID, 1.80 μm). The major signals are quoted in *m/z* with the relative intensity in parentheses. Analyses used an injector temperature of 250 °C; ion source temperature of 200 °C, interface temperature of 260 °C and column flow 5 mL min^{−1} helium, column initial temperature (*T*₀) = 60 °C, hold time (*t*) = 2 min, ramp = 20 °C min^{−1}, final temperature (*T*₁) = 240 °C, hold time (*t*) = 9 to 39 min. LCMS spectra were recorded with a Shimadzu LCMS–8030 system with a triple quadrupole mass spectrometer in electrospray ionization (ESI) mode.

¹H and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-*d*₆ with a Bruker Avance–III 500 MHz spectrometer using TMS as an internal standard. The residual solvent signals were used (CDCl₃: δ_H = 7.16–7.32 ppm, DMSO-*d*₆: δ_H = 2.51 ppm). Infrared spectra were recorded with a Shimadzu IR MIRacle 10 with diamond ATR.

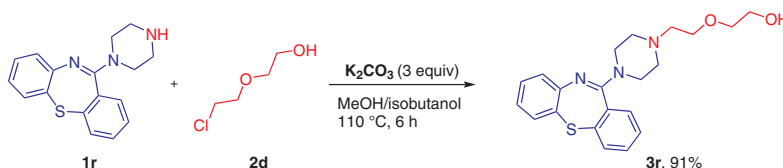
Formal Synthesis of Ticlopidine



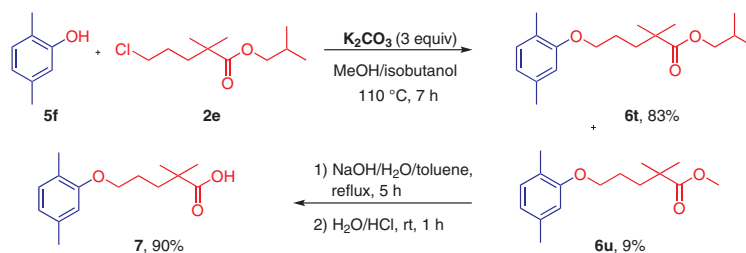
Formal Synthesis of Vildagliptin



Formal Synthesis of Quetiapine



Formal Synthesis of Gemfibrozil



Scheme 2 Formal syntheses of Ticlopidine[®], Vildagliptin[®], Quetiapine[®], and Gemfibrozil[®]

Synthesis of 2-(Arylamino)ethanols; Typical Procedure

To a mixture of amine **1** (0.5 g, 1 equiv) and 2-chloroethanol **2a** (3 equiv) in a round-bottom flask, K_2CO_3 (1 equiv), Na_2CO_3 (3 equiv), and MeOH (2.5 mL) were added and the flask was closed with a septum. The mixture was stirred at r.t. and the progress of reaction was monitored by TLC. After completion, the mixture was diluted with cold water (10 mL) then reaction mass was stirred for 5 minutes and extracted with EtOAc or dichloromethane (10 mL). The organic layer was then washed with cold water (10 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum to obtain the crude mixture of products and unreacted amine. Pure mono-N-alkylated amine **3**, di-N-alkylated amine **4** and unreacted amine **1** were obtained after column chromatography.

Synthesis of 2-Aryloxyethanols; Typical Procedure

To a mixture of phenol **5** (0.5 g, 1 equiv) and 2-chloroethanol **2a** (3 equiv) in a round-bottom flask, K_2CO_3 (3 equiv) and MeOH (2.5 mL) were added and the flask was closed with a septum. The mixture was stirred at r.t. and the progress of the reaction was monitored by TLC. After completion, the mixture was diluted with cold water (10 mL) and 1 M aq. KOH (10 mL), then the reaction mass was stirred for 5 minutes and extracted with dichloromethane (10 mL). The organic layer was then washed with 1 M aq. KOH (10 mL), dried over anhydrous Na_2SO_4 filtered and concentrated under vacuum to obtain the pure product **6** without need for further purification.

Formal Synthesis of Ticlopidine® (3p)

To a mixture of amine **1p** (0.5 g, 1 equiv) and alkyl chloride **2b** (1.2 equiv) in a round-bottom flask, K_2CO_3 (3 equiv) and MeOH (5 mL) were added and the flask was closed with a septum. The mixture was stirred at r.t. and the progress of reaction was monitored by TLC. After completion, the mixture was diluted with cold water (10 mL) then stirred for 5 minutes and extracted with EtOAc (10 mL). The organic layer was washed with cold water (10 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum to obtain the crude product. Column chromatography afforded pure **3p**.

Formal Synthesis of Vildagliptin® (3q)

To a mixture of amine **1q** (0.5 g, 1 equiv) and alkyl chloride **2c** (1.2 equiv) in a round-bottom flask, K_2CO_3 (1 equiv), Na_2CO_3 (1 equiv), and MeOH (2.5 mL) were added and the flask was closed with a septum. The mixture was stirred at r.t. and the progress of the reaction was monitored by TLC. After completion, the mixture was diluted with MeOH (10 mL) and filtered. Evaporation of the solvent gave a residue, which was recrystallized from EtOAc/MeOH (1:1) to obtain pure **3q**.

Formal Synthesis of Quetiapine® (3r)

To a mixture of amine **1r** (0.5 g, 1 equiv) and alkyl chloride **2d** (2.5 equiv) in a round-bottom flask, K_2CO_3 (3 equiv), and MeOH (5 mL)/isobutanol (5 mL) were added and the flask was fitted with a condenser. The mixture was stirred at 110 °C and the progress of the reaction was monitored by TLC. After completion, the mixture was diluted with cold water (10 mL), stirred for 5 minutes and extracted with EtOAc (10 mL). The organic layer was washed with cold water (10 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum to obtain crude **3r**. Column chromatography afforded pure product.

Formal Synthesis of Gemfibrozil® (7)

To a mixture of phenol **5f** (0.5 g, 1 equiv) and alkyl halide **2e** (3 equiv) in a round-bottom flask, K_2CO_3 (3 equiv) and MeOH (1.5 mL)/isobutanol (1.5 mL) were added and the flask was fitted with a condenser. The mixture was stirred at 110 °C and the progress of reaction was monitored by TLC. After completion, the mixture was diluted with cold water (10 mL) and 1 M aq. KOH (10 mL), stirred for 5 minutes and extracted with dichloromethane (10 mL). The organic extract was washed with 1 M aq. KOH (10 mL), dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum to obtain a mixture of products **6t** and **6u**.

In a round-bottom flask the mixture of products **6t** and **6u** was dissolved in 10 M aq. NaOH solution (10 mL) and toluene (10 mL) was added. The mixture was heated to reflux for 5 h and the progress of the reaction was monitored by TLC. After completion, the mixture was cooled, acidified with dilute HCl, stirred for 1 h and extracted with toluene (10 mL). The organic extract was dried over anhydrous Na_2SO_4 , filtered and concentrated under vacuum to obtain pure **7**.

2-(Phenylamino)ethanol (3a)

Yield: 0.5367 g (73%); yellow-brown oil; R_f = 0.60 (hexanes/EtOAc, 65:35).

IR (neat): 3341, 3009, 2940, 2870, 1767, 1597, 1504, 1381, 1319, 1242, 1126, 1057, 872, 748, 694, 625, 509 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 7.17 (dd, J = 8.4, 7.4 Hz, 2 H, H_{Ar}), 6.73 (t, J = 7.3 Hz, 1 H, H_{Ar}), 6.62 (d, J = 7.7 Hz, 2 H, H_{Ar}), 3.74 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.26 (br s, 1 H, NH), 3.26 (br s, 1 H, OH), 3.22 (t, J = 5.2 Hz, 2 H, N- CH_2).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 148.05, 129.38 (2C), 118.09, 113.44 (2C), 61.07, 46.22.

GCMS (EI, 70 eV): m/z calcd for $C_8H_{11}NO$: 137.18; found: 137.

2-(o-Tolylamino)ethanol (3b)

Yield: 0.5290 g (75%); dark-brown oil; R_f = 0.55 (hexanes/EtOAc, 65:35).

IR (neat): 3379, 2932, 2855, 1759, 1512, 1450, 1381, 1319, 1250, 1134, 748, 895, 525 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 7.16–7.08 (m, 1 H, H_{Ar}), 7.06 (d, J = 7.3 Hz, 1 H, H_{Ar}), 6.68 (t, J = 7.4 Hz, 1 H, H_{Ar}), 6.63 (d, J = 8.0 Hz, 1 H, H_{Ar}), 3.82 (t, J = 5.3 Hz, 2 H, O- CH_2), 3.30 (t, J = 5.3 Hz, 2 H, O- CH_2), 2.88 (br s, 1 H, NH), 2.88 (br s, 1 H, OH), 2.15 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 146.01, 130.29, 127.17, 122.69, 117.59, 110.18, 61.15, 46.06, 17.53.

GCMS (EI, 70 eV): m/z calcd for $C_9H_{13}NO$: 151.21; found: 151.

2-(p-Tolylamino)ethanol (3c)

Yield: 0.5365 g (76%); brown solid; mp 33–36 °C; R_f = 0.60 (hexanes/EtOAc, 65:35).

IR (neat): 3364, 2955, 2909, 2847, 1759, 1612, 1512, 1450, 1381, 1296, 1242, 1057, 1018, 980, 941, 918, 810, 718, 694, 617, 540, 463 cm^{-1} .

1H NMR (500 MHz, $CDCl_3$): δ = 6.91 (d, J = 8.2 Hz, 2 H, H_{Ar}), 6.49 (d, J = 8.4 Hz, 2 H, H_{Ar}), 3.68 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.15 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.91 (br s, 1 H, NH), 2.91 (br s, 1 H, OH), 2.16 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 145.84, 129.84 (2C), 127.31, 113.59 (2C), 61.22, 46.57, 20.44.

GCMS (EI, 70 eV): m/z calcd for $C_9H_{13}NO$: 151.21; found: 151.

2-(2,4-Dimethylphenylamino)ethanol (3d)Yield: 0.5250 g (77%); brown oil; R_f = 0.65 (hexanes/EtOAc, 60:40).IR (neat): 3310, 2909, 2855, 1759, 1612, 1512, 1443, 1381 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 6.85 (d, J = 8.1 Hz, 1 H, H_{Ar}), 6.82 (s, 1 H, H_{Ar}), 6.48 (d, J = 8.1 Hz, 1 H, H_{Ar}), 3.75 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.22 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.59 (br s, 1 H, NH), 2.59 (br s, 1 H, OH), 2.15 (s, 3 H, CH_3), 2.06 (s, 3 H, CH_3). ^{13}C NMR (126 MHz, CDCl_3): δ = 143.66, 131.17, 127.36, 126.88, 122.93, 110.55, 61.20, 46.42, 20.36, 17.47.GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{15}\text{NO}$: 165.23; found: 165.**2-(2-Methoxyphenylamino)ethanol (3e)**Yield: 0.4480 g (66%); dark-brown oil; R_f = 0.40 (hexanes/EtOAc 50:50).IR (neat): 3418, 2932, 2878, 1759, 1597, 1512, 1450, 1381, 1242, 1134, 1049, 903, 741, 625, 586, 517 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 6.86 (td, J = 7.7, 1.4 Hz, 1 H, H_{Ar}), 6.78 (dd, J = 7.9, 1.2 Hz, 1 H, H_{Ar}), 6.70 (td, J = 7.8, 1.5 Hz, 1 H, H_{Ar}), 6.65 (dd, J = 7.8, 1.3 Hz, 1 H, H_{Ar}), 3.83 (s, 3 H, O- CH_3), 3.822 (t, J = 5.3 Hz, 2 H, O- CH_2), 3.30 (t, J = 5.3 Hz, 2 H, N- CH_2), 3.08 (br s, 1 H, NH), 3.08 (br s, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 147.20, 137.93, 121.28, 117.17, 110.38, 109.61, 61.28, 55.44, 46.00.GCMS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{13}\text{NO}_2$: 167.21; found: 167.**2-(4-Methoxyphenylamino)ethanol (3f)**Yield: 0.5436 g (80%); dark-brown oil; R_f = 0.50 (hexanes/EtOAc, 40:60).IR (neat): 3356, 2943, 2832, 2361, 1759, 1508, 1462, 1234, 1180, 1126, 1030, 899, 822, 629, 567, 521 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 6.81–6.75 (m, 2 H, H_{Ar}), 6.65–6.57 (m, 2 H, H_{Ar}), 3.76 (t, J = 5.2 Hz, 2 H, N- CH_2), 3.74 (s, 3 H, O- CH_3), 3.20 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.03 (br s, 1 H, OH), 3.03 (br s, 1 H, NH). ^{13}C NMR (126 MHz, CDCl_3): δ = 152.53, 142.26, 114.87 (4C), 61.16, 55.82, 47.22.GCMS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{13}\text{NO}_2$: 167.21; found: 167.**2-(3-Nitrophenylamino)ethanol (3g)**Yield: 0.4221 g (64%); dark-red solid; mp 46–50 °C; R_f = 0.60 (hexanes/EtOAc, 50:50).IR (neat): 3395, 2986, 2955, 2932, 2870, 1805, 1767, 1620, 1582, 1520, 1342, 1242, 1165, 1119, 1065, 988, 856, 787, 733, 671, 517 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 7.60–7.46 (m, 1 H, H_{Ar}), 7.38 (d, J = 4.3 Hz, 1 H, H_{Ar}), 7.33–7.21 (m, 1 H, H_{Ar}), 6.90 (dd, J = 8.2, 2.2 Hz, 1 H, H_{Ar}), 4.55 (br s, 1 H, NH), 3.87 (t, J = 4.9 Hz, 2 H, O- CH_2), 3.33 (br s, 2 H, N- CH_2), 2.45 (br d, J = 54.8 Hz, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 149.29, 149.06, 129.78, 119.20, 112.14, 106.43, 60.86, 45.68.GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{N}_2\text{O}_3$: 182.18; found: 182.**2-(2-Chlorophenylamino)ethanol (3h)**Yield: 0.4847 g (72%); yellow oil; R_f = 0.50 (hexanes/EtOAc, 70:30).IR (neat): 3395, 2994, 2940, 2878, 1759, 1597, 1504, 1458, 1373, 1319, 1242, 1142, 1034, 918, 895, 741, 687, 532 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 7.28–7.22 (m, 1 H, H_{Ar}), 7.12 (td, J = 8.2, 1.5 Hz, 1 H, H_{Ar}), 6.71–6.59 (m, 2 H, H_{Ar}), 4.57 (br s, 1 H, NH), 3.81 (t, J = 5.3 Hz, 2 H O- CH_2), 3.31 (t, J = 5.3 Hz, 2 H N- CH_2), 2.45 (br s, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 143.96, 129.29, 127.87, 119.60, 117.72, 111.52, 61.03, 45.75.GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{ClNO}$: 171.62; found: 171.**2-(3-Chlorophenylamino)ethanol (3i)**Yield: 0.4643 g (69%); dark-brown liquid; R_f = 0.50 (hexanes/EtOAc, 70:30).IR (neat): 3348, 3341, 2932, 2870, 1767, 1597, 1481, 1404, 1327, 1242, 1057, 988, 934, 841, 764, 687, 586 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 6.99 (t, J = 8.0 Hz, 1 H, H_{Ar}), 6.61 (dd, J = 7.8, 1.4 Hz, 1 H, H_{Ar}), 6.53 (t, J = 2.1 Hz, 1 H, H_{Ar}), 6.42 (dd, J = 8.2, 2.1 Hz, 1 H, H_{Ar}), 3.72 (t, J = 5.2 Hz, 2 H O- CH_2), 3.17 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.41 (br s, 1 H, NH), 2.41 (br s, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 149.29, 135.06, 130.28, 117.67, 112.74, 111.59, 61.03, 45.84.GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{ClNO}$: 171.62; found: 171.**2-(4-Chlorophenylamino)ethanol (3j)**Yield: 0.4782 g (71%); off-white solid; mp 72–75 °C; R_f = 0.52 (hexanes/EtOAc, 70:30).IR (neat): 3186, 2940, 2901, 2855, 1759, 1597, 1497, 1427, 1396, 1312, 1265, 1242, 1119, 1057, 903 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 7.20–7.06 (m, 2 H, H_{Ar}), 6.58–6.52 (m, 2 H, H_{Ar}), 3.80 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.23 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.81 (br s, 1 H, NH), 2.81 (br s, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 146.72, 129.13 (2C), 122.43, 114.31 (2C), 61.08, 46.15.GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{ClNO}$: 171.62; found: 171.**2-(4-Bromophenylamino)ethanol (3k)**Yield: 0.4648 g (74%); off-white solid; mp 80–84 °C; R_f = 0.60 (hexanes/EtOAc, 60:40).IR (neat): 3302, 3163, 2932, 2847, 1759, 1589, 1489, 1420, 1389, 1312, 1242, 1119, 1057, 995, 903, 810, 679, 594, 509 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 7.29–7.07 (m, 2 H, H_{Ar}), 6.54–6.37 (m, 2 H, H_{Ar}), 3.96 (br s, 1 H, NH), 3.73 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.17 (t, J = 5.2 Hz, 2 H, N- CH_2), 1.96 (br s, 1 H, OH). ^{13}C NMR (126 MHz, CDCl_3): δ = 147.15, 132.00 (2C), 114.78 (2C), 109.45, 61.08, 46.03.GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{BrNO}$: 216.08; found: 216.**2-(3-Fluorophenylamino)ethanol (3l)**Yield: 0.5307 g (76%); brown oil; R_f = 0.55 (hexanes/EtOAc, 70:30).IR (neat): 3379, 2932, 2878, 1759, 1620, 1589, 1497, 1450, 1373, 1335, 1242, 1180, 1150, 1111, 1057, 995, 964, 833, 764, 679, 633, 610, 579, 517 cm^{-1} . ^1H NMR (500 MHz, CDCl_3): δ = 6.99 (dd, J = 15.0, 8.1 Hz, 1 H, H_{Ar}), 6.30 (m, 2 H, H_{Ar}), 6.22 (dt, J = 11.6, 2.2 Hz, 1 H, H_{Ar}), 3.67 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.33 (br s, 1 H, OH), 3.33 (br s, 1 H, NH), 3.12 (t, J = 5.2 Hz, 2 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 163.04 (d, J = 243.3 Hz), 148.87 (d, J = 10.6 Hz), 129.36 (d, J = 10.3 Hz), 108.06 (d, J = 2.3 Hz), 103.15 (d, J = 22.8 Hz), 98.74 (d, J = 25.3 Hz), 59.84, 44.88.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{FNO}$: 155.17; found: 155.

2-(2,3-Dichlorophenylamino)ethanol (3m)

Yield: 0.5025 g (79%); off-white solid; mp 76–80 °C; R_f = 0.60 (hexanes/EtOAc, 70:30).

IR (neat): 3387, 3341, 3271, 2955, 2878, 2353, 2322, 1759, 1589, 1497, 1450, 1412, 1319, 1250, 1111, 941, 887, 748, 633, 494 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.05 (t, J = 8.1 Hz, 1 H, H_{Ar}), 6.80 (dd, J = 8.0, 1.2 Hz, 1 H, H_{Ar}), 6.57 (dd, J = 8.3, 0.9 Hz, 1 H, H_{Ar}), 4.78 (br s, 1 H, NH), 3.86 (t, J = 5.3 Hz, 2 H, O- CH_2), 3.34 (t, J = 5.3 Hz, 2 H, N- CH_2), 2.01 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 145.48, 133.00, 127.76, 118.32, 117.57, 109.24, 60.97, 45.85.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{Cl}_2\text{NO}$: 206.07; found: 206.

2-(4-Bromo-2-methylphenylamino)ethanol (3n)

Yield: 0.4456 g (72%); off-white solid; mp 74–78 °C; R_f = 0.52 (hexanes/EtOAc, 60:40).

IR (neat): 3310, 2916, 2847, 1759, 1597, 1504, 1458, 1396, 1358, 1319, 1273, 1242, 1142, 1088, 1065, 995, 856, 802 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.18 (dd, J = 8.5, 2.2 Hz, 1 H, H_{Ar}), 7.15 (d, J = 1.8 Hz, 1 H, H_{Ar}), 6.46 (d, J = 8.5 Hz, 1 H, H_{Ar}), 3.82 (t, J = 5.2 Hz, 2 H, O- CH_2), 3.82 (br s, 1 H, NH), 3.26 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.10 (s, 3 H, CH_3), 2.10 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 145.12, 132.61, 129.65, 124.79, 111.57, 109.09, 60.98, 45.97, 17.29.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{BrNO}$: 230.1; found: 230.

2-(3-Fluoro-2-methylphenylamino)ethanol (3o)

Yield: 0.4868 g (72%); yellow-brown solid; mp 58–62 °C; R_f = 0.57 (hexanes/EtOAc, 60:40).

IR (neat): 3395, 3302, 3210, 2932, 2893, 2855, 1759, 1620, 1582, 1520, 1450, 1381, 1319, 1288, 1234, 1134, 1049, 934, 887, 864, 756, 694, 640, 617, 579, 501 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 6.94 (dd, J = 15.0, 8.0 Hz, 1 H, H_{Ar}), 6.38 (t, J = 8.8 Hz, 1 H, H_{Ar}), 6.31 (d, J = 8.2 Hz, 1 H, H_{Ar}), 3.74 (t, J = 5.3 Hz, 2 H, O- CH_2), 3.21 (t, J = 5.2 Hz, 2 H, N- CH_2), 2.71 (br s, 1 H, OH), 2.71 (br s, 1 H, NH), 1.96 (d, J = 1.3 Hz, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 161.50 (d, J = 241.1 Hz), 147.72 (d, J = 7.0 Hz), 127.20 (d, J = 10.7 Hz), 109.16 (d, J = 18.6 Hz), 105.73 (d, J = 2.4 Hz), 104.48 (d, J = 23.85 Hz), 61.04, 46.16, 8.15 (d, J = 6.5 Hz).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{FNO}$: 169.2; found: 169.

2,2'-(Phenylazanediyl)diethanol (4a)

Yield: 0.1451 g (15%); yellow-brown oil; R_f = 0.30 (hexanes/EtOAc, 65:35).

IR (neat): 3287, 2963, 2878, 1767, 1597, 1504, 1358, 1242, 1049, 910, 856, 748, 694, 602, 509 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.25–7.16 (m, 2 H, H_{Ar}), 6.70 (t, J = 7.3 Hz, 1 H, H_{Ar}), 6.64 (d, J = 8.2 Hz, 2 H, H_{Ar}), 4.41 (br s, 2 H, OH), 3.73 (t, J = 4.9 Hz, 4 H, O- CH_2), 3.48 (t, J = 4.9 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 147.80, 129.34 (2C), 116.80, 112.48 (2C), 60.64 (2C), 55.34 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{15}\text{NO}_2$: 181.23; found: 181.

2,2'-(2-Methylphenylazanediyl)diethanol (4b)

Yield: 0.0915 g (10%); yellow oil; R_f = 0.29 (hexanes/EtOAc, 65:35).

IR (neat): 3325, 2940, 2878, 2824, 1759, 1597, 1489, 1443, 1373, 1242, 1157, 1049, 918, 872, 764, 725, 594 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.18 (dd, J = 18.2, 7.7 Hz, 3 H, H_{Ar}), 7.05 (dd, J = 10.2, 4.4 Hz, 1 H, H_{Ar}), 3.58 (t, J = 5.4 Hz, 4 H, O- CH_2), 3.16 (t, J = 5.4 Hz, 4 H, N- CH_2), 3.01 (br s, 2 H, OH), 2.35 (s, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 149.31, 135.71, 131.38, 126.79, 125.02, 124.17, 60.01 (2C), 56.68 (2C), 18.31.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_2$: 195.26; found: 195.

2,2'-(4-Methylphenylazanediyl)diethanol (4c)

Yield: 0.1365 g (15%); dark-brown oil; R_f = 0.30 (hexanes/EtOAc, 60:40).

IR (neat): 3296, 2916, 2862, 1759, 1612, 1512, 1443, 1350, 1242, 1180, 1042, 910, 856, 802, 710, 610, 571, 509 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 6.94 (d, J = 8.4 Hz, 2 H, H_{Ar}), 6.51 (d, J = 8.6 Hz, 2 H, H_{Ar}), 3.88 (br s, 2 H, OH), 3.66 (t, J = 4.9 Hz, 4 H, O- CH_2), 3.38 (t, J = 4.9 Hz, 4 H, N- CH_2), 2.16 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 145.75, 129.85 (2C), 126.29, 113.01 (2C), 60.70 (2C), 55.53 (2C), 20.20.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_2$: 195.26; found: 195.

2,2'-(2,4-Dimethylphenylazanediyl)diethanol (4d)

Yield: 0.1030 g (12%); yellow oil; R_f = 0.32 (hexanes/EtOAc, 60:40).

IR (neat): 3356, 2940, 2878, 1497, 1443, 1366, 1265, 1196, 1150, 1042, 1150, 1042, 872, 818, 571, 525 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.02 (d, J = 8.0 Hz, 1 H, H_{Ar}), 6.94 (s, 1 H, H_{Ar}), 6.91 (d, J = 8.1 Hz, 1 H, H_{Ar}), 3.50 (t, J = 5.4 Hz, 4 H, O- CH_2), 3.06 (t, J = 5.4 Hz, 4 H, N- CH_2), 2.81 (br s, 2 H, OH), 2.24 (s, 3 H), 2.20 (s, 3 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 146.61, 135.51, 134.67, 132.02, 127.48, 124.15, 60.07 (2C), 56.99 (2C), 20.82, 18.17.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{12}\text{H}_{19}\text{NO}_2$: 209.28; found: 209.

2,2'-(2-Methoxyphenylazanediyl)diethanol (4e)

Yield: 0.1275 g (15%); dark-brown oil; R_f = 0.20 (hexanes/EtOAc, 50:50).

IR (neat): 3372, 2940, 2878, 2839, 1805, 1744, 1589, 1497, 1458, 1373, 1242, 1157, 1049, 910, 856, 748, 594, 532, 494 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.20 (dd, J = 7.8, 1.5 Hz, 1 H, H_{Ar}), 7.14 (td, J = 8.1, 1.6 Hz, 1 H, H_{Ar}), 6.96 (td, J = 7.6, 1.2 Hz, 1 H, H_{Ar}), 6.92 (dd, J = 8.2, 0.9 Hz, 1 H, H_{Ar}), 3.86 (s, 3 H, O- CH_3), 3.50 (t, J = 5.2 Hz, 4 H, O- CH_2), 3.25 (br s, 2 H, OH), 3.20 (t, J = 5.2 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 155.45, 138.15, 125.93, 125.08, 121.58, 111.64, 59.80, 57.31 (2C), 55.55 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_3$: 211.26; found: 211.

2,2'-(4-Methoxyphenylazanediyl)diethanol (4f)

Yield: 0.0430 g (5%); brown oil; mp 44–48 °C; R_f = 0.22 (hexanes/EtOAc, 40:60).

IR (neat): 3271, 2940, 2909, 2862, 2839, 1759, 1705, 1512, 1443, 1366, 1281, 1242 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 6.84–6.78 (m, 2 H, H_{Ar}), 6.73–6.66 (m, 2 H, H_{Ar}), 3.82 (br s, 2 H, OH), 3.74 (s, 3 H, O- CH_3), 3.71 (t, J = 5.0 Hz, 4 H, O- CH_2), 3.39 (t, J = 5.0 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 152.22, 142.60, 115.57 (2C), 114.88 (2C), 60.51, 55.98, 55.81.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{17}\text{NO}_3$: 211.26; found: 211.

2,2'-(4-Nitrophenylazanediyl)diethanol (4g)

Yield: 0.0414 g (5%); dark-yellow oil; mp 92–94 °C; R_f = 0.30 (hexanes/EtOAc, 50:50).

IR (neat): 3210, 2955, 2893, 2862, 1759, 1620, 1520, 1481, 1373, 1335, 1281, 1234, 1173, 1126, 1080, 1034, 995, 887, 849, 779, 733, 664, 594, 540 cm^{-1} .

^1H NMR (500 MHz, $\text{DMSO}-d_6$): δ = 7.47 (s, 1 H, H_{Ar}), 7.42–7.34 (m, 2 H, H_{Ar}), 7.19–7.09 (m, 1 H, H_{Ar}), 4.85 (t, J = 5.2 Hz, 2 H, OH), 3.60 (dd, J = 11.3, 5.7 Hz, 4 H, O- CH_2), 3.51 (t, J = 6.1 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, $\text{DMSO}-d_6$): δ = 149.49, 149.48, 130.40, 118.06, 109.61, 105.35, 58.34 (2C), 53.51 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_4$: 226.23; found: 226.

2,2'-(2-Chlorophenylazanediyl)diethanol (4h)

Yield: 0.0681 g (8%); yellow oil; R_f = 0.25 (hexanes/EtOAc, 70:30).

IR (neat): 3294, 3063, 2932, 2870, 1759, 1636, 1589, 1474, 1373, 1242, 1119, 1049, 910, 864, 756, 671, 579, 525 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.40 (dd, J = 8.0, 1.4 Hz, 1 H, H_{Ar}), 7.31 (dd, J = 8.0, 1.6 Hz, 1 H, H_{Ar}), 7.25 (td, J = 7.6, 1.5 Hz, 1 H, H_{Ar}), 7.10 (td, J = 8.0, 1.7 Hz, 1 H, H_{Ar}), 3.59 (t, J = 5.3 Hz, 4 H, O- CH_2), 3.27 (t, J = 5.3 Hz, 4 H, N- CH_2), 2.92 (br s, 2 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 146.95, 132.55, 130.58, 127.89, 126.64, 126.30, 59.93 (2C), 56.72 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{ClNO}_2$: 215.68; found: 215.

2,2'-(3-Chlorophenylazanediyl)diethanol (4i)

Yield: 0.1094 g (13%); white solid; mp 88–93 °C; R_f = 0.25 (hexanes/EtOAc, 70:30).

IR (neat): 3233, 3140, 2631, 2600, 2399, 2222, 2106, 1967, 1913, 1721, 1589, 1489, 1211, 988, 833, 764, 687 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.03 (t, J = 8.2 Hz, 1 H, H_{Ar}), 6.60 (dd, J = 7.8, 1.3 Hz, 1 H, H_{Ar}), 6.54 (t, J = 2.2 Hz, 1 H, H_{Ar}), 6.44 (dd, J = 8.5, 2.3 Hz, 1 H, H_{Ar}), 4.19 (br s, 2 H, OH), 3.70 (t, J = 4.8 Hz, 4 H, O- CH_2), 3.43 (t, J = 4.9 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 148.92, 135.20, 130.22, 116.67, 112.32, 110.62, 60.55 (2C), 55.30 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{ClNO}_2$: 215.68; found: 215.

2,2'-(4-Chlorophenylazanediyl)diethanol (4j)

Yield: 0.1017 g (12%); off-white solid; mp 95–99 °C; R_f = 0.26 (hexanes/EtOAc, 70:30).

IR (neat): 3264, 2916, 2862, 1775, 1589, 1489, 1358, 1173, 1065, 910, 856, 802, 633, 563, 494 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.19–7.11 (m, 2 H, H_{Ar}), 6.62–6.55 (m, 2 H, H_{Ar}), 4.05 (br s, 2 H, OH), 3.77 (t, J = 4.9 Hz, 2 H, O- CH_2), 3.51 (t, J = 4.9 Hz, 2 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 146.42, 129.06 (2C), 121.74, 113.70 (2C), 60.54 (2C), 55.39 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{ClNO}_2$: 215.68; found: 215.

2,2'-(4-Bromophenylazanediyl)diethanol (4k)

Yield: 0.0456 g (6%); off-white solid; mp 88–93 °C; R_f = 0.29 (hexanes/EtOAc, 60:40).

IR (neat): 3271, 2947, 2862, 1759, 1582, 1489, 1358, 1242, 1173, 1103, 1057, 1011, 910, 849, 802, 640, 548, 548, 494 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.30–7.26 (m, 2 H, H_{Ar}), 6.53 (d, J = 9.1 Hz, 2 H, H_{Ar}), 4.00 (br s, 2 H, OH), 3.77 (t, J = 4.8 Hz, 2 H, O- CH_2), 3.50 (t, J = 4.8 Hz, 2 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 146.80, 131.95 (2C), 114.16 (2C), 108.78, 60.49 (2C), 55.32 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{BrNO}_2$: 260.13; found: 260.

2,2'-(3-Fluorophenylazanediyl)diethanol (4l)

Yield: 0.1340 g (15%); dark-brown oil; R_f = 0.25 (hexanes/EtOAc, 70:30).

IR (neat): 3256, 2955, 2878, 1759, 1612, 1497, 1358, 1242, 1157, 1057, 849, 756, 610, 517 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.12 (dd, J = 15.5, 8.2 Hz, 1 H, H_{Ar}), 6.39 (m, 2 H, H_{Ar}), 6.32 (dt, J = 12.9, 2.3 Hz, 1 H, H_{Ar}), 4.62 (br s, 2 H, OH), 3.75 (t, J = 4.9 Hz, 4 H, O- CH_2), 3.48 (t, J = 4.9 Hz, 4 H, N- CH_2).

^{13}C NMR (126 MHz, CDCl_3): δ = 150.62 (d, J = 242.6 Hz), 149.55 (d, J = 10.5 Hz), 130.32 (d, J = 10.4 Hz), 107.94 (d, J = 2.0 Hz), 103.12 (d, J = 21.6 Hz), 99.34 (d, J = 26.2 Hz), 60.41 (2C), 55.35 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{FNO}_2$: 199.22; found: 199.

2,2'-(2,3-Dichlorophenylazanediyl)diethanol (4m)

Yield: 0.0235 g (3%); yellow oil; R_f = 0.30 (hexanes/EtOAc, 70:30).

IR (neat): 3302, 2932, 2870, 2708, 2029, 1921, 1759, 1574, 1450, 1242, 1042, 918, 718, 617, 532 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.29–7.26 (dd, J = 8.1, 1.7 Hz, 1 H, H_{Ar}), 7.23 (dd, J = 8.1, 1.7 Hz, 1 H, H_{Ar}), 7.18 (t, J = 7.9 Hz, 1 H, H_{Ar}), 3.60 (t, J = 5.3 Hz, 4 H, O- CH_2), 3.29 (t, J = 5.3 Hz, 4 H, N- CH_2), 2.79 (br s, 2 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 149.01, 134.03, 131.11, 127.57, 126.93, 124.77, 59.98 (2C), 56.25 (2C).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{13}\text{Cl}_2\text{NO}_2$: 250.12; found: 250.

2,2'-(2-Methyl-4-bromophenylazanediyl)diethanol (4n)

Yield: 0.0889 g (12%); dark-brown oil; R_f = 0.27 (hexanes/EtOAc, 60:40).

IR (neat): 3279, 2940, 2878, 1913, 1759, 1643, 1481, 1242, 1057, 818, 571 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.33 (d, J = 2.1 Hz, 1 H, H_{Ar}), 7.27 (dd, J = 8.4, 2.1 Hz, 1 H, H_{Ar}), 7.06 (d, J = 8.5 Hz, 1 H, H_{Ar}), 3.56 (t, J = 5.3 Hz, 4 H O- CH_2), 3.35 (br s, 2 H, OH), 3.11 (t, J = 5.3 Hz, 4 H, N- CH_2), 2.30 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 148.60, 138.19, 133.99, 129.69, 125.91, 117.85, 59.83 (2C), 56.52 (2C), 18.12.

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{16}\text{BrNO}_2$: 274.15; found: 274.

2,2'-(2-Methyl-4-fluorophenylazanediyl)diethanol (4o)

Yield: 0.0588 g (7%); yellow solid; mp 54–60 °C; R_f = 0.28 (hexanes/EtOAc, 60:40).

IR (neat): 3372, 3310, 2878, 1775, 1582, 1466, 1242, 1049, 787, 718, 633 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.11 (dd, J = 14.9, 7.9 Hz, 1 H, H_{Ar}), 6.99 (d, J = 8.0 Hz, 1 H, H_{Ar}), 6.82 (t, J = 8.7 Hz, 1 H, H_{Ar}), 3.59 (t, J = 5.4 Hz, 4 H, O- CH_2), 3.17 (br s, 2 H, OH), 3.17 (t, J = 5.4 Hz, 4 H, N- CH_2), 2.25 (d, J = 2.4 Hz, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 162.10 (d, J = 242.5 Hz), 151.15 (d, J = 6.6 Hz), 126.68 (d, J = 10.2 Hz), 122.92 (d, J = 15.9 Hz), 119.38 (d, J = 2.9 Hz), 111.50 (d, J = 23.0 Hz), 60.01 (2C), 56.46 (2C), 9.90 (d, J = 5.2 Hz).

GCMS (EI, 70 eV): m/z calcd for $\text{C}_{11}\text{H}_{16}\text{FNO}_2$: 213.25; found: 213.

2-Phenoxyethanol (6a)

Yield: 0.7265 g (99%); colorless oil; R_f = 0.55 (hexanes/EtOAc, 90:10).

IR (neat): 3341, 2924, 1759, 1597, 1489, 1242, 1049, 910, 756, 602, 517 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.26–7.14 (m, 2 H, H_{Ar}), 6.88 (t, J = 7.4 Hz, 1 H, H_{Ar}), 6.82 (d, J = 7.9 Hz, 2 H, H_{Ar}), 3.97 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.85 (t, J = 4.6 Hz, 2 H, O- CH_2), 2.52 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 158.62, 129.52 (2C), 121.21, 114.59 (2C), 69.14, 61.41.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_{10}\text{O}_2$: 138.16; found: 138.

2-(*o*-Tolyloxy)ethanol (6b)

Yield: 0.6758 g (96%); pale-yellow liquid; R_f = 0.50 (hexanes/EtOAc, 90:10).

IR (neat): 3302, 2916, 2866, 2361, 1890, 1755, 1655, 1589, 1493, 1454, 1373, 1308, 1242, 1123, 1049, 918, 822, 748, 714, 606 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.14 (t, J = 7.2 Hz, 2 H, H_{Ar}), 6.87 (td, J = 7.5, 0.7 Hz, 1 H, H_{Ar}), 6.81 (d, J = 8.3 Hz, 1 H, H_{Ar}), 4.05 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.95 (br t, J = 4.6 Hz, 2 H, O- CH_2), 2.44 (br t, J = 5.2 Hz, 1 H, OH), 2.23 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 156.73, 130.85, 126.90, 126.85, 120.89, 111.3, 69.24, 61.62, 16.27.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_2$: 152.19; found: 152.

2-(*m*-Tolyloxy)ethanol (6c)

Yield: 0.6967 g (99%); colorless liquid; R_f = 0.52 (hexanes/EtOAc, 90:10).

IR (neat): 3351, 2916, 2870, 2361, 2338, 1674, 1585, 1489, 1450, 1377, 1261, 1157, 1049, 949, 899, 856, 772, 741, 691 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.08 (t, J = 7.8 Hz, 1 H, H_{Ar}), 6.73–6.68 (m, 1 H, H_{Ar}), 6.68–6.60 (m, 2 H, H_{Ar}), 3.96 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.85 (br d, J = 3.9 Hz, 2 H, O- CH_2), 2.46 (br s, 1 H, OH), 2.24 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 157.57, 138.54, 128.22, 120.90, 114.36, 110.39, 68.04, 60.38, 20.46.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_2$: 152.19; found: 152.

2-(*p*-Tolyloxy)ethanol (6d)

Yield: 0.6967 g (99%); colorless liquid; R_f = 0.50 (hexanes/EtOAc, 90:10).

IR (neat): 3337, 2936, 2870, 2361, 2342, 1759, 1690, 1589, 1481, 1447, 1373, 1277, 1246, 1161, 1134, 1061, 1038, 918, 791, 745, 691, 602, 540, 509, 474 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.07 (t, J = 5.4 Hz, 2 H, H_{Ar}), 6.84–6.77 (m, 2 H, H_{Ar}), 4.03 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.92 (t, J = 4.5 Hz, 2 H, O- CH_2), 2.53 (br s, 1 H, OH), 2.28 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 156.5, 130.39, 130.00 (2C), 114.47 (2C), 69.34, 61.48, 20.49.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_2$: 152.19; found: 152.

2-(2,4-Dimethylphenoxy)ethanol (6e)

Yield: 0.6596 g (97%); white solid; mp 52–56 °C; R_f = 0.55 (hexanes/EtOAc, 90:10).

IR (neat): 3256, 2940, 2916, 2862, 2361, 2330, 1759, 1609, 1504, 1450, 1377, 1354, 1300, 1250, 1223, 1161, 1134, 1084, 1053, 934, 907, 883, 799, 768, 710, 579, 544 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 6.98–6.90 (m, 2 H, H_{Ar}), 6.71 (d, J = 8.1 Hz, 1 H, H_{Ar}), 4.04 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.94 (br d, J = 4.0 Hz, 2 H, O- CH_2), 2.25 (s, 3 H, CH_3), 2.23 (br s, 1 H, OH), 2.20 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 154.61, 131.67, 130.15, 127.06, 126.64, 111.55, 69.59, 61.71, 20.47, 16.18.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$: 166.22; found: 166.

2-(2,5-Dimethylphenoxy)ethanol (6f)

Yield: 0.6598 g (97%); yellow liquid; R_f = 0.55 (hexanes/EtOAc, 90:10).

IR (neat): 3352, 2920, 2870, 2361, 1755, 1582, 1508, 1454, 1412, 1254, 1130, 1042, 949, 899, 802, 718, 667, 586 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.00 (d, J = 7.5 Hz, 1 H, H_{Ar}), 6.68 (d, J = 7.5 Hz, 1 H, H_{Ar}), 6.63 (s, 1 H, H_{Ar}), 4.03 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.93 (br d, J = 4.2 Hz, 2 H, O- CH_2), 2.56 (br s, 1 H, OH), 2.30 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 156.62, 136.69, 130.57, 123.67, 121.44, 112.49, 69.37, 61.64, 21.41, 15.84.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$: 166.22; found: 166.

2-(4-Methoxyphenoxy)ethanol (6g)

Yield: 0.6707 g (99%); off-white solid; mp 64–70 °C; R_f = 0.45 (hexanes/EtOAc, 85:15).

IR (neat): 3291, 3013, 2928, 2870, 2361, 1751, 1504, 1439, 1377, 1292, 1227, 1088, 1030, 930, 891, 826, 725, 671, 571, 532, 501 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 6.87–6.80 (m, 4 H, H_{Ar}), 4.02 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.92 (br dd, J = 8.8, 4.6 Hz, 2 H, O- CH_2), 3.76 (s, 3 H, O- CH_3), 2.48 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 154.09, 152.78, 115.60 (2C), 114.71 (2C), 69.96, 61.51, 55.73.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_{12}\text{O}_3$: 168.19; found: 168.

2-(3-Nitrophenoxy)ethanol (6h)

Yield: 0.5465 g (83%); white solid; mp 87–91 °C; R_f = 0.30 (hexanes/EtOAc, 90:10).

IR (neat): 3279, 3078, 2936, 2866, 2361, 1763, 1616, 1524, 1450, 1342, 1292, 1242, 1053, 953, 895, 864, 791, 733, 671, 613, 540, 486 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.83 (ddd, J = 8.2, 2.0, 0.7 Hz, 1 H, H_{Ar}), 7.74 (t, J = 2.3 Hz, 1 H, H_{Ar}), 7.44 (t, J = 8.2 Hz, 1 H, H_{Ar}), 7.26 (ddd, J = 8.3, 2.5, 0.6 Hz, 1 H, H_{Ar}), 4.17 (t, J = 4.5 Hz, 2 H, O- CH_2), 4.03 (br d, J = 3.7 Hz, 2 H, O- CH_2), 2.38 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 159.20, 149.13, 130.08, 121.62, 116.10, 108.91, 69.95, 61.10.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{NO}_4$: 183.16; found: 183.

2-(4-Nitrophenoxy)ethanol (6i)

Yield: 0.4409 g (67%); pale-yellow solid; mp 79–83 °C; R_f = 0.27 (hexanes/EtOAc, 90:10).

IR (neat): 3252, 2947, 2361, 1759, 1593, 1501, 1331, 1261, 1173, 1072, 1038, 914, 837, 752, 687, 656, 521 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 8.23–8.17 (m, 2 H, H_{Ar}), 7.01–6.97 (m, 2 H, H_{Ar}), 4.21–4.17 (m, 2 H, O- CH_2), 4.06–4.01 (m, 2 H, O- CH_2), 2.31 (br s, 1 H).

^{13}C NMR (126 MHz, CDCl_3): δ = 163.73, 141.71, 125.97 (2C), 114.54 (2C), 70.01, 61.06.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{NO}_4$: 183.16; found: 183.

2-(2-Chlorophenoxy)ethanol (6j)

Yield: 0.6178 g (92%); brown liquid; R_f = 0.50 (hexanes/EtOAc, 85:15).

IR (neat): 3383, 2920, 2870, 2361, 2330, 1612, 1508, 1454, 1377, 1288, 1238, 1177, 1042, 914, 806, 737, 702, 667, 637, 559, 509 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.35 (dd, J = 7.8, 1.6 Hz, 1 H, H_{Ar}), 7.23–7.15 (m, 1 H, H_{Ar}), 6.96–6.85 (m, 2 H, H_{Ar}), 4.11 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.97 (t, J = 4.5 Hz, 2 H, O- CH_2), 2.92 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 154.17, 130.32, 127.86, 123.02, 121.92, 113.97, 70.67, 61.18.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{ClO}_2$: 172.61; found: 172.

2-(3-Chlorophenoxy)ethanol (6k)

Yield: 0.6579 g (98%); colorless liquid; R_f = 0.60 (hexanes/EtOAc, 85:15).

IR (neat): 3345, 3314, 2924, 2870, 2361, 2334, 1759, 1597, 1489, 1369, 1285, 1242, 1169, 1088, 1049, 914, 826, 741, 667, 563, 509 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.85 (dd, J = 8.1, 1.7 Hz, 1 H, H_{Ar}), 7.59–7.51 (m, 1 H, H_{Ar}), 7.11 (dd, J = 8.4, 0.8 Hz, 1 H, H_{Ar}), 7.08–7.03 (m, 1 H, H_{Ar}), 4.24 (t, J = 4.5 Hz, 2 H, O- CH_2), 3.98 (dt, J = 9.3, 4.8 Hz, 2 H, O- CH_2), 3.01 (t, J = 6.4 Hz, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 152.28, 139.82, 134.50, 125.79, 120.86, 115.14, 71.33, 60.86.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{ClO}_2$: 172.61; found: 172.

2-(4-Chlorophenoxy)ethanol (6l)

Yield: 0.6044 g (90%); dark-brown liquid; R_f = 0.47 (hexanes/EtOAc, 85:15).

IR (neat): 3526, 3360, 2943, 2874, 2361, 2330, 1921, 1759, 1690, 1643, 1605, 1582, 1520, 1485, 1450, 1350, 1277, 1254, 1165, 1072, 1038, 914, 853, 775, 745, 698, 667, 602, 567, 517 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.26–7.19 (m, 2 H, H_{Ar}), 6.87–6.80 (m, 2 H, H_{Ar}), 4.04 (t, J = 4.5 Hz, 2 H, O- CH_2), 3.95 (dd, J = 9.4, 5.3 Hz, 2 H, O- CH_2), 2.30 (t, J = 6.0 Hz, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 157.24, 129.42 (2C), 126.01, 115.84 (2C), 69.53, 61.34.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{ClO}_2$: 172.61; found: 172.

2-(2,4-Dichlorophenoxy)ethanol (6m)

Yield: 0.4129 g (65%); yellow liquid; R_f = 0.47 (hexanes/EtOAc, 85:15).

IR (neat): 3364, 2928, 2874, 2361, 1967, 1751, 1585, 1389, 1246, 1061, 868, 802, 733, 652, 571, 559 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.35 (d, J = 2.5 Hz, 1 H, H_{Ar}), 7.16 (dd, J = 8.8, 2.6 Hz, 1 H, H_{Ar}), 6.85 (d, J = 8.8 Hz, 1 H, H_{Ar}), 4.09 (t, J = 4.5 Hz, 2 H, O- CH_2), 3.98 (dd, J = 9.4, 5.1 Hz, 2 H, O- CH_2), 2.81 (t, J = 6.1 Hz, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 153.02, 130.00, 127.71, 126.25, 123.70, 114.57, 71.00, 61.10.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_8\text{Cl}_2\text{O}_2$: 207.05; found: 207.

2-(4-Fluorophenoxy)ethanol (6n)

Yield: 0.6683 g (96%); colorless liquid; R_f = 0.50 (hexanes/EtOAc, 90:10).

IR (neat): 3375, 2932, 2874, 2361, 1759, 1504, 1454, 1373, 1296, 1204, 1042, 914, 826, 745, 648, 633, 563, 513 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.04–6.91 (m, 2 H, H_{Ar}), 6.89–6.80 (m, 2 H, H_{Ar}), 4.03 (t, J = 4.5 Hz, 2 H, O- CH_2), 3.94 (br s, 2 H, O- CH_2), 2.54 (br s, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 157.45 (d, J = 239.0 Hz), 154.75 (d, J = 2.1 Hz), 115.89 (d, J = 23.1 Hz) (2C), 115.59 (d, J = 8.0 Hz) (2C), 69.89, 61.37.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_8\text{H}_9\text{FO}_2$: 156.15; found: 156.

2-(3-(Trifluoromethyl)phenoxy)ethanol (6o)

Yield: 0.4577 g (72%); colorless liquid; R_f = 0.50 (hexanes/EtOAc, 85:15).

IR (neat): 3345, 3306, 2932, 2878, 2361, 1755, 1674, 1593, 1493, 1450, 1323, 1238, 1169, 1119, 1061, 937, 883, 787, 745, 698, 656, 610, 517 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.38 (t, J = 8.0 Hz, 1 H, H_{Ar}), 7.22 (d, J = 7.7 Hz, 1 H, H_{Ar}), 7.14 (s, 1 H, H_{Ar}), 7.08 (dd, J = 8.3, 2.3 Hz, 1 H, H_{Ar}), 4.10 (t, J = 4.5 Hz, 2 H, O- CH_2), 3.98 (br dd, J = 9.2, 4.9 Hz, 2 H, O- CH_2), 2.55 (br t, J = 5.8 Hz, 1 H, OH).

^{13}C NMR (126 MHz, CDCl_3): δ = 158.76, 131.89 (q, J = 32.4 Hz), 130.08, 123.92 (q, J = 408.2 Hz), 118.01 (d, J = 1.0 Hz), 117.80 (q, J = 3.9 Hz), 111.36 (q, J = 3.8 Hz), 69.52, 61.20.

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_9\text{H}_9\text{F}_3\text{O}_2$: 206.16; found: 206.

2-(4-(2,4,4-Trimethylpentan-2-yl)phenoxy)ethanol (6p)

Yield: 0.5948 g (98%); pale-yellow liquid; R_f = 0.55 (hexanes/EtOAc, 90:10).

IR (neat): 3325, 2951, 2870, 2361, 2268, 2118, 2064, 2041, 1944, 1883, 1759, 1639, 1609, 1512, 1458, 1366, 1242, 1042, 918, 829, 683, 586, 517 cm^{-1} .

^1H NMR (500 MHz, CDCl_3): δ = 7.28–7.25 (m, 2 H, H_{Ar}), 6.87–6.81 (m, 2 H, H_{Ar}), 4.06 (t, J = 4.6 Hz, 2 H, O- CH_2), 3.94 (br s, 2 H, O- CH_2), 2.33 (br s, 1 H, OH), 1.70 (s, 2 H, CH_2), 1.34 (s, 6 H, CH_3), 0.71 (s, 9 H, CH_3).

^{13}C NMR (126 MHz, CDCl_3): δ = 156.23, 142.74, 127.16 (2C), 113.75 (2C), 69.12, 61.55, 56.99, 37.98, 32.35, 31.80 (3C), 31.71 (2C).

GC-MS (EI, 70 eV): m/z calcd for $\text{C}_{16}\text{H}_{26}\text{O}_2$: 250.38; found: 250.

Methyl 3-(2-Hydroxyethoxy)benzoate (6q)

Yield: 0.6123 g (95%); colorless liquid; R_f = 0.30 (hexanes/EtOAc, 90:10).

IR (neat): 3483, 3406, 3352, 3337, 2943, 2866, 2361, 1717, 1585, 1443, 1277, 1045, 926, 895, 756, 683, 610, 555, 517 cm^{-1} .

¹H NMR (500 MHz, CDCl₃): δ = 7.66–7.64 (m, 1 H, H_{Ar}), 7.57 (dd, *J* = 2.4, 1.6 Hz, 1 H, H_{Ar}), 7.34 (t, *J* = 8.0 Hz, 1 H, H_{Ar}), 7.12 (dd, *J* = 7.9, 3.0 Hz, 1 H, H_{Ar}), 4.13 (t, *J* = 4.6 Hz, 2 H, O-CH₂), 3.98 (br dd, *J* = 9.0, 4.8 Hz, 2 H, O-CH₂), 3.91 (s, 3 H, O-CH₃), 2.48 (br t, *J* = 5.7 Hz, 1 H, OH).

¹³C NMR (126 MHz, CDCl₃): δ = 166.94, 158.62, 131.46, 129.51, 122.39, 119.98, 114.72, 69.44, 61.30, 52.24.

GC-MS (EI, 70 eV): *m/z* calcd for C₁₀H₁₂O₄: 196.2; found: 196.

2-(2-Hydroxyethoxy)benzaldehyde (6r)

Yield: 0.4080 g (60%); yellow oil; *R*_f = 0.30 (hexanes/EtOAc, 90:10).

IR (neat): 3379, 3364, 2932, 2870, 2361, 1759, 1678, 1597, 1454, 1396, 1242, 1161, 1045, 918, 833, 760, 656, 517 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 10.43 (s, 1 H, CHO), 7.80 (dd, *J* = 7.7, 1.8 Hz, 1 H, H_{Ar}), 7.60–7.50 (m, 1 H, H_{Ar}), 7.05 (t, *J* = 7.5 Hz, 1 H, H_{Ar}), 7.00 (d, *J* = 8.4 Hz, 1 H, H_{Ar}), 4.20 (t, *J* = 4.6 Hz, 2 H, O-CH₂), 4.03 (t, *J* = 4.5 Hz, 2 H, O-CH₂), 3.13 (br s, 1 H, OH).

¹³C NMR (126 MHz, CDCl₃): δ = 190.24, 160.87, 136.08, 129.71, 125.00, 121.13, 112.94, 70.21, 61.07.

GC-MS (EI, 70 eV): *m/z* calcd for C₉H₁₀O₃: 166.17; found: 166.

2-(Quinolin-8-yloxy)ethanol (6s)

Yield: 0.6256 g (96%); pale-brown solid; mp 112–116 °C; *R*_f = 0.40 (hexanes/EtOAc, 40:60).

IR (neat): 3387, 2994, 2855, 1759, 1666, 1574, 1504, 1450, 1373, 1319, 1250, 1119, 1072, 903, 764, 733, 633, 571, 532 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 8.82 (dd, *J* = 4.2, 1.6 Hz, 1 H, H_{Ar}), 8.13 (dd, *J* = 8.3, 1.5 Hz, 1 H, H_{Ar}), 7.45 (t, *J* = 7.9 Hz, 1 H, H_{Ar}), 7.41–7.37 (m, 2 H, H_{Ar}), 7.07 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 5.87 (br s, 1 H, OH), 4.26 (t, *J* = 4.4 Hz, 2 H, O-CH₂), 4.11 (t, *J* = 4.4 Hz, 2 H, O-CH₂).

¹³C NMR (126 MHz, CDCl₃): δ = 154.37, 148.67, 139.85, 136.54, 129.49, 127.02, 121.70, 119.89, 109.61, 70.96, 60.83.

GC-MS (EI, 70 eV): *m/z* calcd for C₁₁H₁₁NO₂: 189.21; found: 189.

5-(2-Chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (3p)⁵⁵

Yield: 0.9013 g (95%); colorless oil; *R*_f = 0.70 (hexanes/EtOAc, 85:15).

IR (neat): 3055, 2901, 2770, 2275, 2361, 2060, 1921, 1763, 1674, 1566, 1443, 1358, 1254, 1165, 1107, 1038, 903, 837, 752, 702, 590 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.45 (dd, *J* = 7.6, 1.6 Hz, 1 H, H_{Ar}), 7.27 (dd, *J* = 7.8, 1.3 Hz, 1 H, H_{Ar}), 7.16–7.08 (m, 2 H, H_{Ar}), 6.97 (d, *J* = 5.1 Hz, 1 H, H_{Ar}), 6.61 (d, *J* = 5.1 Hz, 1 H, H_{Ar}), 3.73 (s, 2 H, N-CH₂), 3.54 (s, 2 H, N-CH₂), 2.80 (d, *J* = 5.0 Hz, 2 H, N-CH₂), 2.78–2.74 (m, 2 H, CH₂).

¹³C NMR (126 MHz, CDCl₃): δ = 135.06, 133.16, 132.85, 132.35, 129.55, 128.38, 127.13, 125.66, 124.20, 121.56, 57.40, 52.06, 49.68, 24.48.

GCMS (EI, 70 eV): *m/z* calcd for C₁₄H₁₄ClNS: 263.79; found: 263.

(2S)-1-[2-[(3-Hydroxy-1-adamantyl)amino]acetyl]pyrrolidine-2-carbonitrile (3q)⁵⁶

Yield: 0.7075 g (78%); off-white solid; mp 112–116 °C; *R*_f = 0.50 (EtOAc/MeOH, 90:10).

IR (neat): 3291, 2913, 2847, 2361, 2330, 1755, 1655, 1547, 1512, 1450, 1404, 1354, 1308, 1250, 1188, 1153, 1119, 1034, 964, 910, 826, 791, 671, 637, 602, 552, 513, 463 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 4.89–4.75 (m, 1 H, N-CH), 3.70–3.58 (m, 1 H, CH), 3.52–3.38 (m, 3 H, CH, CH₂), 2.40–2.12 (m, 8 H, CH₂), 1.68–1.49 (m, 12 H, CH₂).

¹³C NMR (126 MHz, CDCl₃): δ = 170.60, 170, 47, 118.33, 118.28, 69.45, 53.76, 53.46, 49.92, 49.84, 46.58, 46.53, 46.30, 45.48, 44.34, 44.30, 43.37, 41.26, 41.20, 41.11, 41.04, 35.11, 35.07, 32.28, 30.65, 30.64, 29.88, 25.05, 22.77

LCMS (ESI): *m/z* [M + H]⁺ calcd for [C₁₇H₂₅N₃O₂]⁺: 304.4; found: 304.

2-[2-(4-Benzo[b][1,4]benzothiazepin-6-yl)piperazin-1-yl]ethoxyethanol (3r)⁵⁷

Yield: 0.5907 g (91%); pale-yellow viscous liquid; *R*_f = 0.45 (hexanes/EtOAc, 30:70).

IR (neat): 2913, 2855, 2361, 2338, 1593, 1574, 1555, 1454, 1404, 1369, 1304, 1242, 1146, 1111, 1061, 1011, 949, 883, 833, 741, 691, 667, 617, 590, 505, 463 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 7.49 (d, *J* = 7.6 Hz, 1 H, H_{Ar}), 7.38 (dd, *J* = 7.7, 1.3 Hz, 1 H, H_{Ar}), 7.32–7.27 (m, 3 H, H_{Ar}), 7.17–7.14 (m, 1 H, H_{Ar}), 7.07 (dd, *J* = 8.0, 1.2 Hz, 1 H, H_{Ar}), 6.87 (td, *J* = 7.6, 1.3 Hz, 1 H, H_{Ar}), 3.70–3.57 (m, 10 H, N-CH₂), 3.57 (br s, 1 H, OH), 2.58 (dt, *J* = 14.8, 6.5 Hz, 6 H, O-CH₂).

¹³C NMR (126 MHz, CDCl₃): δ = 160.68, 148.87, 139.89, 134.06, 132.21, 132.18, 130.85, 129.13, 128.99, 128.33, 128.00, 125.32, 122.86, 72.46, 67.54, 61.84, 57.97, 53.10.

LC-MS (ESI): *m/z* [M + H]⁺ calcd for [C₂₁H₂₅N₃O₂S]⁺: 384.51; found: 384.

Isobutyl 5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanoate (6t)⁵⁴

Yield: 0.4854 g (83%); colorless liquid; *R*_f = 0.77 (hexanes/EtOAc, 95:5).

IR (neat): 2955, 2870, 2361, 2330, 1759, 1724, 1612, 1582, 1508, 1470, 1416, 1389, 1312, 1261, 1192, 1130, 1045, 995, 941, 841, 802, 768, 714, 667, 586, 517 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 6.99 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.65 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.60 (s, 1 H, H_{Ar}), 3.92–3.88 (m, 2 H, O-CH₂), 3.85 (d, *J* = 6.5 Hz, 2 H, O-CH₂), 2.30 (s, 3 H, CH₃), 2.17 (s, 3 H, CH₃), 1.93 (dp, *J* = 13.3, 6.7 Hz, 1 H, CH), 1.73 (s, 4 H, CH₂), 1.22 (s, 6 H, CH₃), 0.94 (d, *J* = 6.7 Hz, 6 H, CH₃).

¹³C NMR (126 MHz, CDCl₃): δ = 177.83, 156.98, 136.46, 130.31, 123.61, 120.69, 111.93, 70.53, 67.97, 42.21, 37.20, 27.82, 25.24 (3C), 21.43, 19.15 (2C), 15.79.

GC-MS (EI, 70 eV): *m/z* calcd for C₁₉H₃₀O₃: 306.44; found: 306.

Methyl 5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanoate (6u)⁵⁸

Yield: 0.0531 g (9%); colorless liquid; *R*_f = 0.68 (hexanes/EtOAc, 95:5).

IR (neat): 2947, 2866, 2361, 2334, 1732, 1612, 1585, 1508, 1474, 1389, 1312, 1261, 1196, 1153, 1130, 1045, 991, 941, 849, 802, 772, 714, 671, 586, 544, 505 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ = 6.99 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.65 (d, *J* = 7.5 Hz, 1 H, H_{Ar}), 6.60 (s, 1 H, H_{Ar}), 3.90 (t, *J* = 5.5 Hz, 2 H, O-CH₂), 3.66 (s, 3 H, O-CH₃), 2.30 (s, 3 H, CH₃), 2.17 (s, 3 H, CH₃), 1.76–1.69 (m, 4 H, CH₂), 1.22 (s, 6 H, CH₃).

¹³C NMR (126 MHz, CDCl₃): δ = 178.30, 156.93, 136.42, 130.28, 123.55, 120.66, 111.89, 67.83, 51.71, 42.09, 37.11, 25.19, 25.18 (2C), 21.40, 15.75.

GC-MS (EI, 70 eV): *m/z* calcd for C₁₆H₂₄O₃: 264.36; found: 264.

5-(2,5-Dimethylphenoxy)-2,2-dimethylpentanoic Acid (7)⁵⁴

Yield: 0.5463 g (90%); off-white solid; mp 62–65 °C; R_f = 0.50 (EtOAc/MeOH, 90:10).

IR (neat): 2959, 2916, 2870, 2361, 2342, 1759, 1705, 1612, 1582, 1512, 1474, 1400, 1327, 1269, 1211, 1157, 1126, 1045, 995, 937, 864, 802, 748, 586, 555 cm^{-1} .

¹H NMR (500 MHz, CDCl_3): δ = 6.99 (d, J = 7.5 Hz, 1 H, H_{Ar}), 6.65 (d, J = 7.5 Hz, 1 H, H_{Ar}), 6.60 (s, 1 H, H_{Ar}), 3.92 (t, J = 6.0 Hz, 2 H, O- CH_2), 2.30 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3), 1.84–1.71 (m, 4 H, CH_2), 1.25 (s, 6 H, CH_3).

¹³C NMR (126 MHz, CDCl_3): δ = 184.97, 156.98, 136.48, 130.35, 123.64, 120.75, 111.98, 67.93, 42.03, 36.91, 25.18 (2C), 25.01, 21.45, 15.81.

LC-MS (ESI): m/z [M + H]⁺ calcd for $[\text{C}_{15}\text{H}_{22}\text{O}_3]^+$: 251.33; found: 251.

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Supporting Information

Supporting information for this article is available online at <https://doi.org/10.1055/s-0039-1690334>.

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