Synthesis J. R. Lizza, G. Moura-Letts Paper

Solvent-Directed Epoxide Opening with Primary Amines for the Synthesis of β-Amino Alcohols

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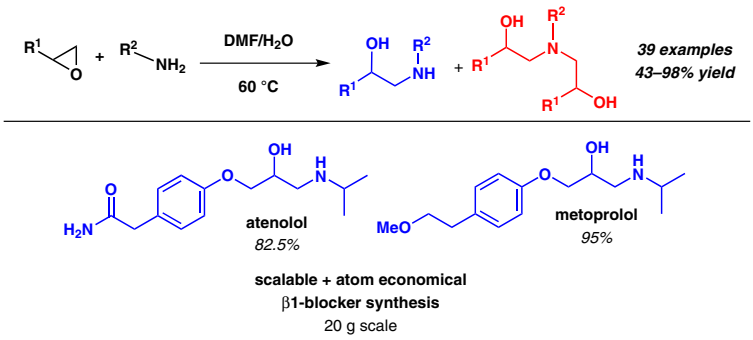

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Abstract An efficient synthesis of β-amino alcohols from a variety of epoxides and primary unbranched amines in the absence of any catalyst in high yields and regioselectivities is reported. A variety of polar mixed solvent systems allow for the selective formation of secondary amino alcohols over tertiary amino alcohols. The reaction scope extends to a wide variety of aromatic and aliphatic substituted epoxides and primary amines bearing complex functionality.

Key words β-amino alcohols, primary amines, epoxide opening reactions, solvent-directed reactions, β-blockers

β-Amino alcohols are an important class of compounds in organic chemistry.[1] Moreover, they can be used as chemical synthons for the synthesis of more complex heterocyclic scaffolds.[2] Their importance also extends to drug discovery due to their high occurrence in commercially available drugs.[3] A long list of methods to construct this scaffold has been reported in the literature.[4] Among these, ring opening of epoxides with amine nucleophiles is one of the most straightforward approaches due to the high availability of either substrates and the comprehensive understanding of nucleophilic substitutions.[5] Most methods rely on high temperatures and high excess of reagents to achieve high conversions and chemoselectivity.[6] Significant efforts have also shown that epoxide aminolysis can be efficiently promoted in the presence of lanthanide triflates, Lewis acids, solid acid supports, or by using solvents such as water.[7] While these methods are effective, the epoxide opening with unhindered primary amines introduces a large number of issues with the chemo- and regioselectivity of this reaction. Double alkylation for this approach is widely reported to lower the productivity and ease of isolation for unbranched primary amines.[8] Moreover, regioselectivity for the least substituted side of the epoxide decreases significantly in the presence of promoters.[9] Thus, there is a clear void for an efficient method for the chemo- and regioselective epoxide opening with unhindered primary amines.

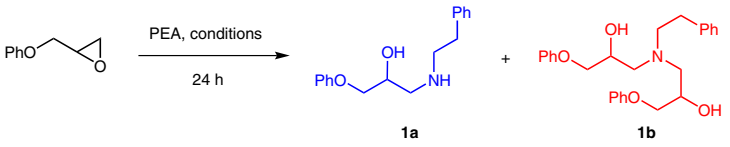
The search for such methods has led us to focus on the development of novel and efficient synthetic methods for the selective introduction of N-nucleophiles for the synthesis of pharmacologically relevant molecular scaffolds.[10] β-Amino alcohols are a highly recurrent scaffold among most β-blockers;[11] however, their production has proven to require longer synthetic sequences due to low selectivities on the key epoxide-opening step.

Herein, we report a chemo- and regioselective approach for the highly selective synthesis of β-amino alcohols with unhindered primary amines.

This study started by assessing the reaction outcomes between phenylglycidyl ether and phenethylamine (PEA) as proof of principle substrates (Table 1). The results showed that in aprotic solvents (heptanes, Et_2O, CH_2Cl_2) at room temperature and after 24 hours, a 2.5:1 mixture of **1a** and **1b** was obtained with very low conversion (Table 1, entries 1, 2, and 3). On the other hand, polar protic solvents (EtOH, TFE, H_2O) provided reaction products with much higher conversions (>84%), but with lower selectivities for monoalkylation product **1a** (entries 4, 5, and 6). The drastic increase in conversion is derived from the protic solvent epoxide activation.[8d] Moreover, under neat conditions the reaction proceeded in >99% conversion and in a 2.5:1 ratio for **1a**:**1b** (entry 7).

Further exploration of solvent effects provided complete selectivity with DMF but low conversion (25%, Table 1, entry 8). Despite the high selectivity with DMF, reaction productivity at 40 °C remained far from ideal (27%, entry 9). The high selectivity could be explained by the reduced nucleophilicity of secondary amine **1a** through intramolecular

Table 1 Reaction Discovery and Optimization



1a **1b**

Entry[a]	Solvent	Concn (M)	Temp (°C)	Conv. (%)[b,c]	Yield (%)[d] **1a**	Yield (%)[d] **1b**
1	heptane	0.1	r.t.	3 (7:3)	–	–
2	Et_2O	0.1	r.t.	5 (7:3)	–	–
3	CH_2Cl_2	0.1	r.t.	5 (7:3)	–	–
4	EtOH	0.1	r.t.	85	70	30
5	TFE	0.1	r.t.	95	48	50
6	H_2O	0.1	r.t.	>99	40	59
7	neat	–	r.t.	>99	71	28
8	DMF	0.1	r.t.	25	95	0
9	DMF	0.1	40	27	91	9
10	DMF	0.1	60	42	90	9
11	DMF	0.1	80	50	75	23
12	DMF	0.1	100	53	79	20
13	DMF	0.1	120	68	72	28
14	DMF/H_2O[e]	0.1	r.t.	25	95	3
15	DMF/H_2O[e]	0.1	40	69	94	5
16	DMF/H_2O[e]	0.1	60	92	94	5
17	DMF/H_2O[e]	0.15	60	99	95	3
18	DMF/H_2O[e]	0.2 M	60	>99	83	16
19	DMF/H_2O[e,f]	0.15 M	60	98	98	<2

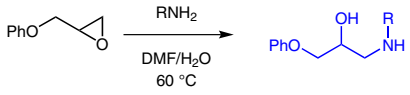
[a] Epoxide/amine ratio = 1:1.5.
[b] Measured by ^1H NMR spectroscopy.
[c] Ratio of **1a**/**1b**.
[d] Isolated yields.
[e] H_2O: 50 equiv.
[f] H_2O added after 12 h.

hydrogen bonding. Nonetheless, the poor conversion arises from poor activation of the epoxide. Higher temperatures did provide a significant increase in conversion (42, 50, 53, 68% conversion, for 60, 80, 100 and 120 °C, entries 10–13, respectively). However, the reaction selectivity decreased proportionally to the increase in conversion. The reaction displayed similar high selectivities when exposed to DMF with 50 equivalents of H_2O at room temperature (25% conversion, 95% of **1a**, entry 14). There was a concern with potential erosion of selectivity at higher temperatures, but it was discovered that at 40 °C the reaction conversion increased to 69% with no erosion on the selectivity (94% **1a**, entry 15). Moreover, at 60 °C the conversion increased to 92% with **1a** as the major isomer (94%, entry 16). Further increasing the reaction temperature failed to improve the reaction selectivity. Based on the S_N2 nature of this reaction, raising the concentration proved to slightly improve the reaction productivity and selectivity (99%, 95% of **1a**, entry 17); however, at 0.2 M the selectivity had begun to erode (83% of **1a**, 16% of **1b**, entry 18). Eventually it was discovered that adding H_2O after 12 hours in DMF provided the ideal results (>99%, 98% of **1a**, entry 19). These results are supported by the decreased nucleophilicity of **1a** relative to the primary amine with H_2O as a reagent rather than as solvent.

The identification of a highly selective set of conditions shifted the focus towards addressing other reaction characteristics. β-Blockers, among other key pharmacophoric scaffolds, share the β-amino alcohol moiety with a variety of substitution pattern on the nitrogen atom. Thus, it is fundamental to fully address the reaction scope to further validate this method as a successful route for this key scaffold. Previous studies on the selective amine opening of epoxides are widely diverse in conversion and scope.[5] Thus, the scope study aimed to provide a comprehensive analysis of steric and electronic factors among different primary

amine substrates (Table 2). Aliphatic primary amines displayed very high conversions and yields for the desired monoalkylated product (entries 1–6). Interestingly, allyl and propargyl amine provided the desired amino alcohol in the highest yields. Sterically hindered α-branched primary amines (cyclohexyl, cyclopentyl, and isopropyl) were also successful at selectively providing the expected products in very high yields (entries 7–9).

Table 2 Reaction Scope for Amines[a]



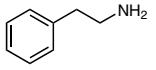
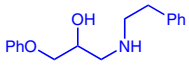
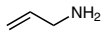
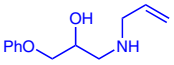
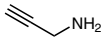
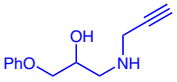
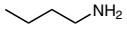
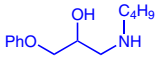
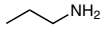
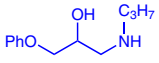
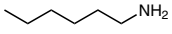
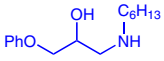
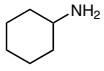
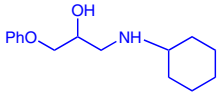
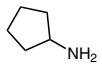
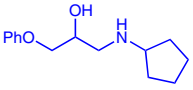
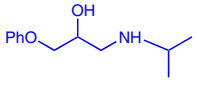
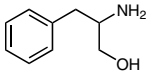
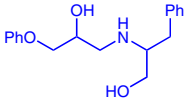
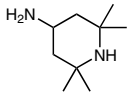
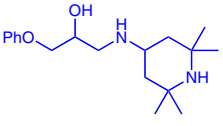
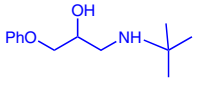
Entry	RNH_2	Product	Yield (%)[b]
1			94
2			95
3			92
4			93
5			91
6			92
7			94
8			92
9			92
10			87
11			86
12			94

Table 2 (continued)

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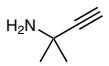
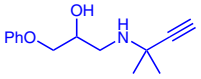
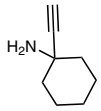
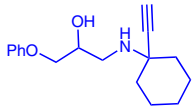
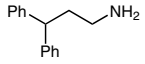
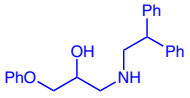
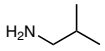
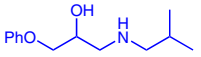
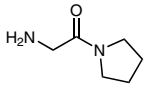
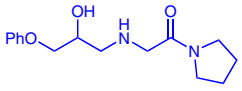
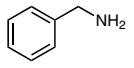
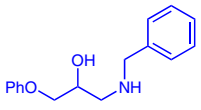
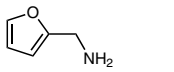
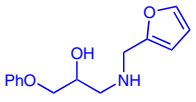
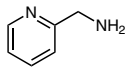
13			76
14			71
15			94
16			90
17			94
18			93
19			90
20			92
21			92
22			86

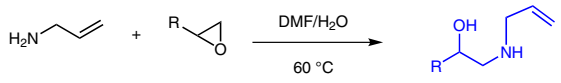
[a] Reaction conditions: Epoxide (1 mmol) and amine (1.5 mmol) were dissolved in DMF and then heated to 60 °C for 12 h, then H_2O (50 mmol) was added and heated for an additional 12 h.
[b] Isolated yields.

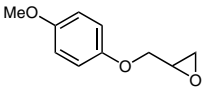
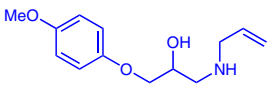
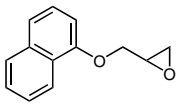
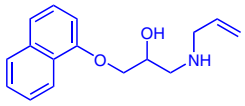
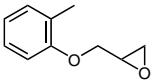
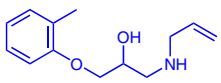
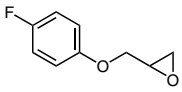
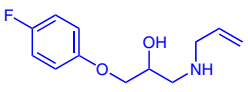
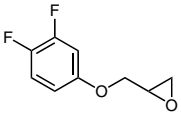
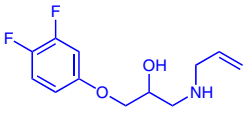
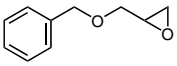
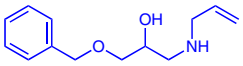
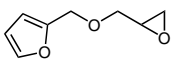
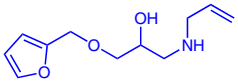
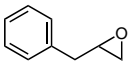
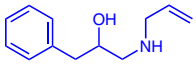
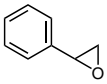
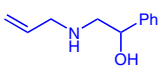
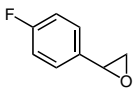
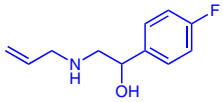
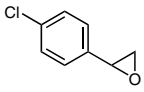
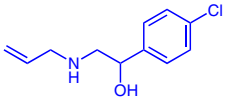
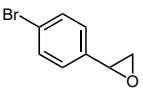
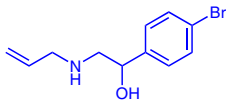
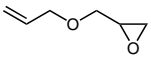
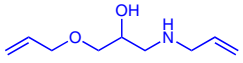
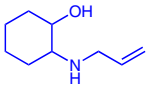
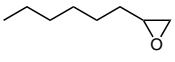
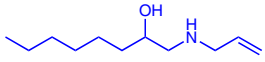
Due to the high recurrence of this scaffold among pharmacophores, functional group tolerance would allow access to a wider variety of more complex scaffolds. Thus, 2-aminophenethyl alcohol and 4-amino-2,2,6,6-tetramethylpiperidine reacted with comparable high yields to provide the expected regioisomer (Table 2, entries 10 and 11). Despite the conflicting reports, α-quaternary amines have been shown to react with lower conversions and selectivities.[12] The reaction of *tert*-butylamine, dimethylpropargylamine, and 1-acetylynecyclohexylamine displayed slightly lower yields for the desired product, but with complete regioselectivity (entries 12–14). Moreover, diphenylpropan-1-amine, isobutylamine, 2-aminopyrrolidinylethanone, and

benzylamine were also successful at providing the respective amino alcohols in very high yields and selectivities (entries 15–18). Added complexity on the amine substrate (furfurylamine, picolylamine, and 2,4-difluorobenzylamine) did not affect the productivity of the reaction and the respective products were obtained in similar high yields (entries 19–21). Further evidence of the highly selective nature of this approach was obtained with 4-(aminomethyl)aniline. This reaction provided the respective amino alcohol with complete selectivity for the primary amine over the aniline epoxide-opening pathway (entry 22).

The success realized among amines of different steric and electronic properties prompted us to turn our focus on the reaction scope for epoxides (Table 3). Aryl glycidyl ethers are widely commercially available and can be easily constructed through the reaction of phenols and epichlorohydrin. Thus, we were interested in assessing the effect of substituents with different electronic properties. Activated phenyl glycidyl ethers proved to undergo epoxide opening with allylamine in excellent yields and regioselectivities (entries 1–3). It has also been established that fluorinated phenyl ethers are good pharmacophores for many biological targets.[3d] The reactions with 4-fluorophenyl and 3,4-difluorophenyl glycidyl ethers also demonstrated to provide the respective amino alcohols in excellent yields and selectivities (entries 4 and 5) providing quick and efficient access to highly relevant pharmacophoric scaffolds.

Table 3 Reaction Scope for Epoxide[a]

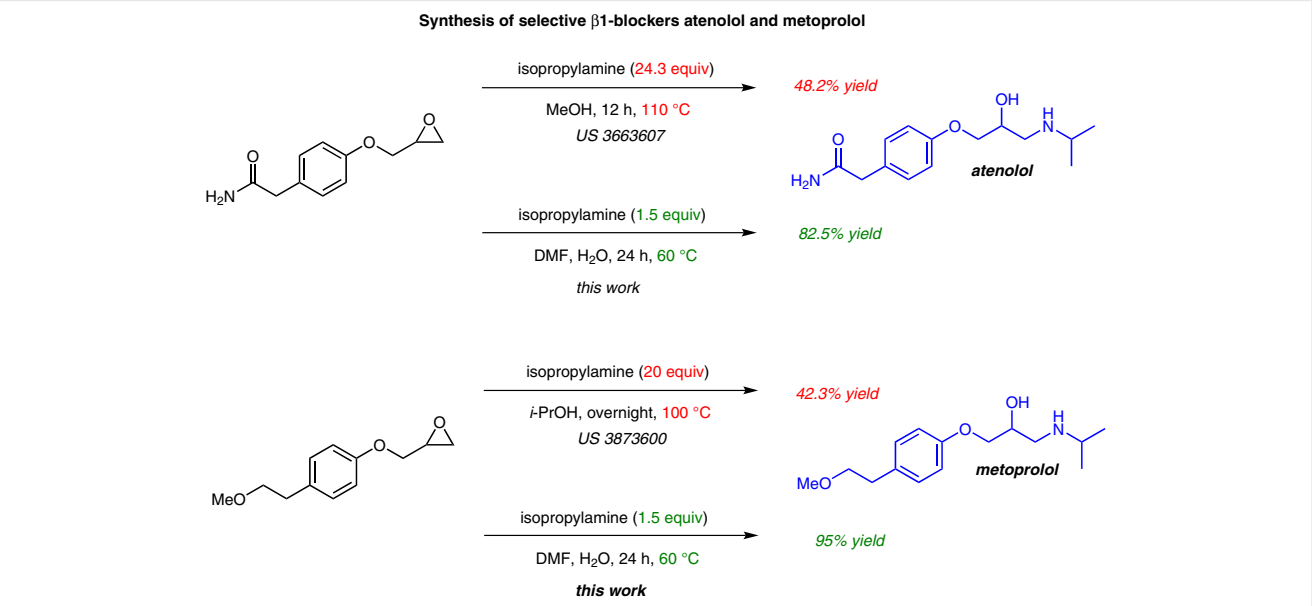


Entry	Epoxide	Product	Yield (%)[b]
1			95
2			94
3			92
4			93
5			91
6			95
7			91
8			94
9			88
10			86
11			85
12			85
13			91
14			43
15			93

[a] Reaction conditions: Epoxide (1 mmol) and amine (1.5 mmol) were dissolved in DMF with H_2O (25 mmol) and then heated to 60 °C for 24 h.
[b] Isolated yields.

Moreover, potential success with the epoxide opening of benzyl and furfuryl glycidyl ethers would provide further access to complex substituted amino alcohols (Table 3, entries 6 and 7). Alkenyl oxides are another family of relevant electrophiles that can be easily accessed. More importantly, they tend to react with poorer conversion and regioselectivities. The reaction conditions showed that oxides of allylbenzene and allylstyrene provide the desired amino alcohols as the expected regioisomer in very high yields (entries 8 and 9).

Moreover, 4-fluoro-, 4-chloro-, and 4-bromostyrene oxides were also successful at providing the proposed products (Table 3, entries 10–12). Aliphatic oxides also displayed high conversions and selectivities. However, we found that cyclic alkenyl oxides provide complete selectivi-



Scheme 1 Synthesis of commercial β-blockers

ty for the monoalkylated product albeit with poor conversion to the desired amino alcohol (entries 13–15).

The high productivity found for this reaction proposes an important advancement in the search for better methods for the synthesis of highly coveted β-amino alcohols. The commercial synthesis of β-blockers has often relied on harsh conditions to achieve the key epoxide-opening reaction. Thus, the synthesis of known β-blockers (metoprolol and atenolol) would serve as proof of principle to further validate the strength of this method. Moreover, to further assess the scalability of this reaction, we designed the synthesis of these drugs in 20 gram scale (Scheme 1).

This study also intended to compare our results with the industrial standard for obtaining these drugs. We followed patents (US 3663607 and US 3873600)[13] for the synthesis of atenolol and metoprolol as reference approaches.

This comparison showed that our method was more efficient at providing the respective β-blockers (48.2/82.5% for atenolol and 42.3/95% for metoprolol) than the available industrial methods. Moreover, this work is highly atom economical and provides the desired β-amino alcohols. The scale-up for the synthesis of these two molecules provided to be similarly efficient: atenolol was obtained in 82.5% (21.5 g) and metoprolol in 95% (23.3 g).

In summary, we have discovered a more efficient and atom economic approach for the synthesis of β-amino alcohols as potential β-blockers. This reaction allows for the synthesis of such scaffolds with complete regioselectivity and with minimal purification. The scope study demonstrated that a variety of amines with different substitution patterns and orthogonal functional groups could tolerate the reaction conditions and provide the desired product in excellent yields. The reaction has also proven to be highly scalable in comparison to some commercial methods; the respective β-amino alcohols can be obtained in much higher yields. The scaffolds made in this study will be further evaluated for their pharmacological profile as potential β-blockers.

Reagents were obtained from Sigma-Aldrich, Acros Organics, or Alfa Aesar and used without further purification. Solvents were obtained from EMD Miliphore DrySol and degassed with N_2. Solution-phase reactions were performed in glass vials or round bottom flasks without inert atmosphere and magnetic stirring.

TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized under UV light (254 nm) or by staining with $KMnO_4$. Silica gel flash chromatography was performed on E. Merck 230–400 mesh silica gel 60. Automated chromatography was performed on an ISOLERA Prime instrument with 10 g. SNAP silica gel normal phase cartridges. Analytical LC/MS was carried out on an Agilent 1100 UPLC System with Ion Trap MS Detector with a Phenomenex 5 cm, 4.6 mm, 3 µm, 120 Å, C18 reverse phase column. IR spectra were recorded on a Perkin Elmer Spectrum 100 FTIR spectrophotometer. NMR spectra were recorded on Varian Mercury II 400 MHz Spectrometer at 24 °C in $CDCl_3$ unless otherwise indicated. Chemical shifts are expressed in ppm relative to TMS (^{1}H, 0 ppm) or solvent signals: $CDCl_3$ (^{1}H, 7.23 ppm; ^{13}C, 77.0 ppm) coupling constants are expressed in hertz. High-resolution mass spectroscopy was performed on a Agilent 6220 Accurate-Mass Time-of-Flight LC/MS at the Mass Spectrometry facility at Princeton University.

Amino Alcohols from Epoxides and Amines; General Procedure

A 20 mL pressure vessel (for volatile amines) was charged with the appropriate epoxide (1.0 mmol, 1.0 equiv) and the respective amine (1.5 mmol, 1.5 equiv) in reagent grade DMF (6.7 mL). The reaction

vessel fitted with a stir bar, sealed, and heated at 60°C for 12 h, after which the vessel was allowed to cool to r.t. (only for reactions ran in pressure vessels) before adding deionized H_2O (50 equiv) in one portion. The vessel was resealed and stirred at 60 °C for an additional 12 h. Solvent was removed on a rotary evaporator (35 °C/22.5 mbar) and the crude residue loaded directly onto a silica gel column (Tables 2 and 3). Chromatographic purification gave the pure desired product.

1-(Phenethylamino)-3-phenoxypropan-2-ol (T1A)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-phenylethan-1-amine (182 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1A** (255 mg, 94%) as a white solid; R_f = 0.33 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3306, 3062, 2927, 1600 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.12 (m, 7 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.88 (d, *J* = 7.1 Hz, 2 H), 4.04 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.94 (d, *J* = 7.5 Hz, 2 H), 2.93–2.73 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 139.6, 129.4, 128.6, 128.4, 126.1, 120.9, 114.4, 70.3, 68.1, 51.7, 51.0, 36.2.

ESI-MS: *m*/*z* (%) = (pos) 272.2 ($[M + H]^+$, 100); (neg) 270.2 ($[M - H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{17}H_{22}NO_2^+$: 272.16451; found: 272.16438. Absolute difference (ppm): 0.48.

1-(Allylamino)-3-phenoxypropan-2-ol (T1B)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and prop-2-en-1-amine (86 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1B** (197 mg, 95%) as a white solid; R_f = 0.34 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3306, 3074, 2978, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.1 Hz, 2 H), 6.91 (t, *J* = 7.1 Hz, 1 H), 6.88 (d, *J* = 7.1 Hz, 2 H), 5.89 (dddd, *J* = 16.1, 9.9, 7.1, 6.8 Hz, 1 H), 5.18 (d, *J* = 16.1 Hz, 1 H), 5.08 (d, *J* = 9.9 Hz, 1 H), 4.08 (ddt, *J* = 7.5, 7.3, 7.1 Hz, 1 H), 3.94–3.90 (m, 2 H), 3.25 (d, *J* = 7.1 Hz, 2 H), 2.80 (dd, *J* = 7.3, 7.1 Hz, 1 H), 2.68 (dd, *J* = 7.3, 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 136.1, 129.3, 120.7, 116.3, 114.3, 70.5, 68.1, 52.1, 51.3.

ESI-MS: *m*/*z* (%) = (pos) 208.1 ($[M + H]^+$, 100); (neg) 206.1 ($[M - H]^-$, 100).

1-Phenoxy-3-(prop-2-yn-1-ylamino)propan-2-ol (T1C)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and prop-2-yn-1-amine (83 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1C** (189 mg, 92%) as a yellow oil; R_f = 0.31 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3682, 3294, 2924, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 2 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.89 (d, *J* = 7.1 Hz, 2 H), 4.11 (tt, *J* = 7.5, 7.1 Hz, 1 H), 3.98 (d, *J* = 7.5 Hz, 2 H), 3.47 (d, *J* = 7.1 Hz, 2 H), 2.95 (dd, *J* = 7.1, 4.8 Hz, 1 H), 2.84 (dd, *J* = 7.1, 4.8 Hz, 1 H), 2.24 (t, *J* = 4.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 129.4, 120.9, 114.4, 81.6, 71.8, 70.3, 68.3, 50.7, 38.1.

ESI-MS: *m*/*z* (%) = (pos) 206.1 ($[M + H]^+$, 100); (neg) 204.1 ($[M - H]^-$, 100).

1-(Butylamino)-3-phenoxypropan-2-ol (T1D)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and butan-1-amine (110 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1D** (207 mg, 93%) as a white solid; R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3291, 3062, 2957, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 7.1 Hz, 2 H), 6.91 (t, *J* = 7.1 Hz, 1 H), 6.88 (d, *J* = 7.1 Hz, 2 H), 4.11 (dddd, *J* = 7.5, 7.2, 7.1, 6.8 Hz, 1 H), 3.96 (dd, *J* = 7.2, 7.1 Hz, 2 H), 3.47 (br s, 1 H), 2.82 (dd, *J* = 7.1, 6.8 Hz, 1 H), 2.68 (dd, *J* = 7.5, 6.8 Hz, 1 H), 2.66–2.62 (m, 2 H), 1.49 (quint, *J* = 7.1 Hz, 2 H), 1.34 (sext, *J* = 7.1 Hz, 2 H), 0.91 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 70.5, 67.9, 52.0, 49.5, 31.8, 20.3, 13.9.

ESI-MS: *m*/*z* (%) = (pos) 224.1 ($[M + H]^+$, 100); (neg) 222.1 ($[M - H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{22}NO_2^+$: 224.16451; found: 224.16488. Absolute difference (ppm): 1.65.

1-Phenoxy-3-(propylamino)propan-2-ol (T1E)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and propan-1-amine (89 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1E** (190 mg, 91%) as a white solid; R_f = 0.34 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3277, 3079, 2930, 1598 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.23 (d, *J* = 7.1 Hz, 2 H), 6.93–6.86 (m, 3 H), 4.11 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.92 (d, *J* = 7.5 Hz, 2 H), 3.45 (br s, 1 H), 2.82 (dd, *J* = 6.8, 6.4 Hz, 1 H), 2.71 (dd, *J* = 7.1, 6.4 Hz, 1 H), 2.59–2.53 (m, 2 H), 1.52 (sext, *J* = 7.1 Hz, 2 H), 0.91 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 70.5, 67.9, 51.9, 51.6, 22.8, 11.6.

ESI-MS: *m*/*z* (%) = (pos) 210.1 ($[M + H]^+$, 100); (neg) 208.1 ($[M - H]^-$, 100).

1-(Hexylamino)-3-phenoxypropan-2-ol (T1F)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and hexan-1-amine (152 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1F** (231 mg, 92%) as a white solid; R_f = 0.27 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3290, 3062, 2957, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.1 Hz, 2 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.89 (d, *J* = 7.1 Hz, 2 H), 4.11 (ddt, *J* = 7.5, 7.1, 6.6 Hz, 1 H), 3.92 (dd, *J* = 7.2, 7.1 Hz, 2 H), 3.43 (br s, 1 H), 2.84 (dd, *J* = 7.1, 6.6 Hz, 1 H), 2.68 (dd, *J* = 7.5, 7.1 Hz, 1 H), 2.64–2.60 (m, 2 H), 1.49 (quint, *J* = 7.1 Hz, 2 H), 1.29–1.23 (m, 6 H), 0.88 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.8, 114.3, 70.5, 67.8, 52.0, 49.8, 31.6, 29.7, 26.8, 22.5, 13.9.

ESI-MS: *m*/*z* (%) = (pos) 252.1 ($[M + H]^+$, 100); (neg) 250.1 ($[M - H]^-$, 100).

1-(Cyclohexylamino)-3-phenoxypropan-2-ol (T1G)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and cyclohexylamine (149 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1G** (234 mg, 94%) as a white solid; R_f = 0.17 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3305, 3013, 2926, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.1 Hz, 2 H), 6.95–6.86 (m, 3 H), 4.11 (ddt, *J* = 7.5, 7.3, 6.8 Hz, 1 H), 3.96 (t, *J* = 7.3 Hz, 2 H), 3.05 (br s, 1 H), 2.91 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.73 (dd, *J* = 6.8, 6.6 Hz, 1 H), 2.46–2.40 (m, 1 H), 1.92–1.90 (m, 2 H), 1.74–1.69 (m, 2 H), 1.61–1.58 (m, 1 H), 1.29–1.03 (m, 5 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6, 129.3, 120.8, 114.4, 70.5, 68.2, 56.8, 49.0, 33.5, 33.4, 25.9, 24.9.

ESI-MS: *m*/*z* (%) = (pos) 250.2 ([M + H]$^+$, 100); (neg) 248.2 ([M – H]$^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{15}H_{24}NO_2^+$: 250.18016; found: 250.18035. Absolute difference (ppm): 0.76.

1-(Cyclopentylamino)-3-phenoxypropan-2-ol (T1H)

Prepared from 2-(phenoxy methyl)oxirane (150 mg, 1.0 mmol) and cyclopentylamine (128 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1H** (216 mg, 92%) as a white solid; R_f = 0.26 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3299, 3063, 2950, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.1 Hz, 2 H), 6.97–6.88 (m, 3 H), 4.08 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.94–3.89 (m, 2 H), 3.32 (br s, 1 H), 3.05 (quint, *J* = 7.1 Hz, 1 H), 2.82 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.71 (dd, *J* = 6.8, 6.6 Hz, 1 H), 1.87–1.81 (m, 2 H), 1.69–1.63 (m, 2 H), 1.54–1.47 (m, 2 H), 1.37–1.29 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 70.5, 68.1, 59.8, 50.8, 32.9, 32.8, 23.8, 23.7.

ESI-MS: *m*/*z* (%) = (pos) 236.2 ([M + H]$^+$, 100); (neg) 234.2 ([M – H]$^-$, 100).

1-(Isopropylamino)-3-phenoxypropan-2-ol (T1I)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and propan-2-amine (89 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1I** (192 mg, 92%) as a white solid; R_f = 0.26 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3295, 3062, 2967, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (d, *J* = 7.1 Hz, 2 H), 6.93–6.86 (m, 3 H), 4.08 (ddt, *J* = 7.3, 7.1, 6.6 Hz, 1 H), 3.38 (br s, 1 H), 2.88–2.82 (m, 2 H), 2.68 (dd, *J* = 6.8, 6.6 Hz, 1 H), 1.09 (d, *J* = 7.1 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 70.5, 68.1, 49.5, 48.8, 22.7, 22.6.

ESI-MS: *m*/*z* (%) = (pos) 210.1 ([M + H]$^+$, 100); (neg) 208.1 ([M – H]$^-$, 100).

(2*S*)-2-[(2-Hydroxy-3-phenoxypropyl)amino]-3-phenylpropan-1-ol (T1J)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and (*S*)-2-amino-3-phenylpropan-1-ol (227 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1J** (262 mg, 87%) as a white solid; R_f = 0.31 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3357, 3062, 2924, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.13 (m, 7 H), 6.95 (t, *J* = 7.1 Hz, 1 H), 6.84 (d, *J* = 7.1 Hz, 2 H), 4.04 (dddd, *J* = 7.5, 7.3, 7.1, 6.8 Hz, 1 H), 3.89–2.83 (m, 2 H), 3.63–3.58 (m, 1 H), 3.38–3.34 (m, 1 H), 2.91–2.86 (m, 2 H), 2.80–2.75 (m, 2 H), 2.71–2.64 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 138.4, 129.4, 129.1, 128.4, 126.3, 120.9, 114.4, 77.2, 70.1, 68.9, 68.6, 62.7, 62.6, 60.8, 60.5, 49.4, 49.3, 37.7, 37.6.

ESI-MS: *m*/*z* (%) = (pos) 302.2 ([M + H]$^+$, 100); (neg) 300.2 ([M – H]$^-$, 100).

HRMS (ESI): calcd for $C_{18}H_{24}NO_3^+$: 302.17507; found: 302.17564. Absolute difference (ppm): 1.89.

1-Phenoxy-3-[(2,2,6,6-tetramethylpiperidin-4-yl)amino]propan-2-ol (T1K)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2,2,6,6-tetramethylpiperidin-4-amine (234 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1K** (263 mg, 86%) as a clear oil; R_f = 0.31 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3295, 3066, 2956, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 7.1 Hz, 2 H), 6.95–6.88 (m, 3 H), 4.06–4.02 (m, 1 H), 3.98–3.96 (m, 2 H), 2.96–2.92 (m, 2 H), 2.78 (dd, *J* = 7.1, 6.8 Hz, 1 H), 1.89 (dd, *J* = 7.3, 3.5 Hz, 2 H), 1.18 (s, 6 H), 1.12 (s, 6 H), 0.86 (t, *J* = 6.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.4, 120.9, 114.4, 70.4, 68.4, 50.9, 50.0, 48.7, 46.3, 46.1, 35.0, 28.7, 28.5.

ESI-MS: *m*/*z* (%) = (pos) 307.2 ([M + H]$^+$, 100); (neg) 305.2 ([M – H]$^-$, 100).

1-(*tert*-Butylamino)-3-phenoxypropan-2-ol (T1L)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-methylpropan-2-amine (110 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1L** (210 mg, 94%) as a white solid; R_f = 0.18 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3309, 3063, 2965, 1599 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 7.3 Hz, 2 H), 6.93–6.86 (m, 3 H), 4.04–3.91 (m, 3 H), 3.07 (br s, 1 H), 2.82 (dd, *J* = 7.3, 6.4 Hz, 1 H), 2.68 (dd, *J* = 7.1, 6.6 Hz, 1 H), 1.16 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6, 129.3, 120.8, 114.4, 70.5, 68.4, 50.4, 44.8, 28.9.

ESI-MS: *m*/*z* (%) = (pos) 224.2 ([M + H]$^+$, 100); (neg) 222.2 ([M – H]$^-$, 100).

1-[(2-Methylbut-3-yn-2-yl)amino]-3-phenoxypropan-2-ol (T1M)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-methylbut-3-yn-2-amine (125 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1M** (177 mg, 76%) as a white solid; R_f = 0.40 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3291, 3067, 2981, 1600 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 6.9 Hz, 2 H), 6.98–6.91 (m, 3 H), 4.08 (ddt, *J* = 7.5, 7.3, 6.8 Hz, 1 H), 3.98 (d, *J* = 7.3 Hz, 2 H), 2.97 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.86 (dd, *J* = 6.8, 6.6 Hz, 1 H), 2.31 (s, 1 H), 1.38 (s, 3 H), 1.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 129.3, 120.8, 114.4, 88.2, 70.4, 70.1, 68.8, 49.4, 46.5, 29.6, 29.1.

ESI-MS: *m*/*z* (%) = (pos) 234.1 ([M + H]$^+$, 100); (neg) 232.1 ([M – H]$^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{20}NO_2^+$: 234.14886; found: 234.14828. Absolute difference (ppm): 2.48.

1-[(1-Ethynylcyclohexyl)amino]-3-phenoxypropan-2-ol (T1N)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 1-ethynylcyclohexan-1-amine (185 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1N** (194 mg, 71%) as a white solid; R_f = 0.43 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3294, 3063, 2932, 1601 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.3 Hz, 2 H), 6.95–6.88 (m, 3 H), 4.08 (ddt, *J* = 7.3, 7.1, 6.9 Hz, 1 H), 3.96 (d, *J* = 7.1 Hz, 2 H), 2.99 (dd, *J* = 7.3, 6.2 Hz, 1 H), 2.88 (dd, *J* = 6.9, 6.2 Hz, 1 H), 2.37 (s, 1 H), 1.89–1.86 (m, 2 H), 1.67–1.54 (m, 4 H), 1.43–1.32 (m, 2 H), 1.23–1.16 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 87.0, 72.2, 70.4, 68.8, 54.0, 45.4, 37.9, 37.6, 25.5, 22.7, 22.5.

ESI-MS: *m*/*z* (%) = (pos) 274.2 ($[M + H]^+$, 100); (neg) 272.2 ($[M - H]^-$, 100).

1-[(3,3-Diphenylpropyl)amino]-3-phenoxypropan-2-ol (T1O)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 3,3-diphenylpropan-1-amine (317 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1O** (339 mg, 94%) as a white solid; R_f = 0.39 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3305, 3061, 2925, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.12 (m, 13 H), 6.95 (t, *J* = 7.1 Hz, 1 H), 6.84 (d, *J* = 7.1 Hz, 2 H), 4.02–3.96 (m, 2 H), 3.89–3.83 (m, 2 H), 2.73 (dd, *J* = 7.5, 6.8 Hz, 1 H), 2.68 (dd, *J* = 7.1, 6.8 Hz, 1 H), 2.57–2.53 (m, 2 H), 2.24–2.17 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 144.5, 129.4, 128.4, 127.6, 126.1, 120.8, 114.4, 70.3, 68.0, 51.8, 48.9, 48.2, 35.7.

ESI-MS: *m*/*z* (%): (pos) 348.2 ($[M + H]^+$, 100); (neg) 346.2 ($[M - H]^-$, 100).

1-(Isobutylamino)-3-phenoxypropan-2-ol (T1P)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-methylpropan-1-amine (210 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1P** (210 mg, 90%) as a white solid; R_f = 0.24 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3319, 3032, 2954, 1600 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.24 (m, 2 H), 6.95–6.89 (m, 3 H), 4.08 (dddd, *J* = 7.5, 7.3, 7.1, 6.9 Hz, 1 H), 3.94 (dd, *J* = 7.3, 7.1 Hz, 2 H), 3.05 (s, 1 H), 2.82 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.73 (dd, *J* = 6.8, 6.6 Hz, 1 H), 2.48–2.42 (m, 2 H), 1.76 (nonet, *J* = 7.1 Hz, 1 H), 0.91 (d, *J* = 7.1 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 129.3, 120.7, 114.3, 70.4, 67.9, 57.6, 51.9, 28.0, 20.4.

ESI-MS: *m*/*z* (%) = (pos) 224.2 ($[M + H]^+$, 100); (neg) 222.2 ($[M - H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{13}H_{22}NO_2^+$: 224.16451; found: 224.16471. Absolute difference (ppm): 0.89.

2-[(2-Hydroxy-3-phenoxypropyl)amino]-1-(pyrrolidin-1-yl)ethan-1-one (T1Q)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-amino-1-(pyrrolidin-1-yl)ethan-1-one (192 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1Q** (261 mg, 94%) as a white solid; R_f = 0.29 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3370, 3066, 2952, 1628 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.27 (d, *J* = 7.1 Hz, 2 H), 6.93–6.88 (m, 3 H), 4.06–3.96 (m, 3 H), 3.49 (t, *J* = 7.3 Hz, 2 H), 3.41 (s, 2 H), 3.32 (t, *J* = 7.3 Hz, 2 H), 2.93 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.82 (dd, *J* = 6.8, 6.6 Hz, 2 H), 1.96 (quint, *J* = 7.3 Hz, 2 H), 1.89 (quint, *J* = 7.3 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.7, 158.6, 129.3, 120.7, 114.3, 70.0, 68.2, 52.5, 51.2, 45.7, 45.3, 25.9, 23.9.

ESI-MS: *m*/*z* (%) = (pos) 279.2 ($[M + H]^+$, 100); (neg) 277.2 ($[M - H]^-$, 100).

1-(Benzylamino)-3-phenoxypropan-2-ol (T1R)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and benzylamine (161 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1R** (229 mg, 93%) as a white solid; R_f = 0.33 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3305, 3063, 2924, 1599 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.21 (m, 7 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.88 (d, *J* = 7.1 Hz, 2 H), 4.08 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.92 (d, *J* = 7.1 Hz, 2 H), 3.78 (d, *J* = 6.4 Hz, 2 H), 2.84 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.68 (dd, *J* = 6.8, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 139.6, 129.3, 128.4, 128.1, 127.0, 120.8, 114.4, 70.3, 68.2, 53.7, 51.2.

ESI-MS: *m*/*z* (%) = (pos) 258.1 ($[M + H]^+$, 100); (neg) 256.1 ($[M - H]^-$, 100).

1-[(Furan-2-ylmethyl)amino]-3-phenoxypropan-2-ol (T1S)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and furan-2-ylmethanamine (146 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1S** (222 mg, 90%) as a white solid; R_f = 0.31 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3311, 3115, 3066, 2924 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.36 (d, *J* = 2.6 Hz, 1 H), 7.27 (d, *J* = 7.1 Hz, 2 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.89 (d, *J* = 7.1 Hz, 2 H), 6.31 (d, *J* = 2.6 Hz, 1 H), 6.19 (d, *J* = 2.6 Hz, 1 H), 4.06 (ddt, *J* = 7.7, 7.3, 6.9 Hz, 1 H), 3.94 (d, *J* = 7.3 Hz, 2 H), 3.81 (s, 2 H), 2.84 (dd, *J* = 7.7, 6.6 Hz, 1 H), 2.75 (dd, *J* = 6.9, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5, 153.4, 141.9, 129.4, 120.9, 114.4, 110.1, 107.1, 70.2, 68.3, 51.0, 45.9.

ESI-MS: *m*/*z* (%) = (pos) 248.1 ($[M + H]^+$, 100); (neg) 246.1 ($[M - H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{18}NO_3^+$: 248.12812; found: 248.12864. Absolute difference (ppm): 2.09.

1-Phenoxy-3-[(pyridin-2-ylmethyl)amino]propan-2-ol (T1T)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and pyridin-2-ylmethanamine (162 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1T** (237 mg, 92%) as a white semi-solid; R_f = 0.32 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3371, 3308, 2983, 1678 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 6.2 Hz, 1 H), 7.63 (t, *J* = 6.6 Hz, 1 H), 7.29–7.25 (m, 3 H), 7.16 (dd, *J* = 6.6, 6.2 Hz, 1 H), 6.95 (t, *J* = 7.1 Hz, 2 H), 6.88 (d, *J* = 7.1 Hz, 1 H), 4.13 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.98–3.94 (m, 4 H), 2.93 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.84 (dd, *J* = 6.8, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 158.5, 149.1, 136.6, 129.3, 122.2, 122.0, 120.8, 114.4, 70.2, 68.3, 54.7, 51.8.

ESI-MS: *m*/*z* (%) = (pos) 259.1 ($[M + H]^+$, 100); (neg) 257.1 ($[M - H]^-$, 100).

1-[(2,4-Difluorobenzyl)amino]-3-phenoxypropan-2-ol (T1U)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and (2,4-difluorophenyl)methanamine (110 mg, 1.5 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T1U** (270 mg, 92%) as a white solid; R_f = 0.18 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3269, 3044, 2927, 1600 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 3 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.88 (d, *J* = 7.1 Hz, 2 H), 6.80–6.73 (m, 2 H), 4.08 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.92 (d, *J* = 7.1 Hz, 2 H), 3.81 (s, 2 H), 2.80 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.71 (dd, *J* = 6.8, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.8 (d, *J* = 216 Hz, 1 C), 160.2 (d, *J* = 224 Hz, 1 C), 158.4, 130.9, 129.4, 122.5, 120.9, 114.4, 110.9, 103.7 (t, *J* = 25 Hz, 1 C), 70.3, 68.3, 51.0, 46.5.

ESI-MS: *m*/*z* (%) = (pos) 294.1 ($[M + H]^+$, 100); (neg) 292.1 ($[M – H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{18}F_2NO_2^+$: 294.13001; found: 294.13044. Absolute difference (ppm): 1.46.

1-[(4-Aminobenzyl)amino]-3-phenoxypropan-2-ol (T1V)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 4-aminobenzylamine (183 mg, 1.50 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded amino alcohol **T1V** (237 mg, 86%) as a clear oil; R_f = 0.20 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3345, 3225, 3101, 1615 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.23 (t, *J* = 7.1 Hz, 2 H), 7.01 (d, *J* = 6.9 Hz, 2 H), 6.93 (t, *J* = 7.1 Hz, 1 H), 6.77 (d, *J* = 6.9 Hz, 2 H), 6.53 (d, *J* = 7.1 Hz, 2 H), 4.02 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.81–3.78 (m, 2 H), 3.54 (dd, *J* = 7.3, 7.1 Hz, 2 H), 3.49 (br s, 1 H), 2.75 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.64 (dd, *J* = 6.8, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 145.3, 129.2, 129.1, 120.6, 114.9, 114.3, 70.3, 67.9, 53.0, 51.1.

ESI-MS *m*/*z* (%) = (pos) 273.2 ($[M + H]^+$, 100); (neg) 271.2 ($[M – H]^-$, 100).

1-(Allylamino)-3-(4-methoxyphenoxy)propan-2-ol (T2A)

Prepared from 2-[(4-methoxyphenoxy)methyl)oxirane (150 mg, 0.83 mmol) and prop-2-en-1-amine (71 mg, 1.25 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2A** (188 mg, 95%) as a white semi-solid; R_f = 0.29 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3308, 3077, 2924, 1645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.79 (d, *J* = 6.8 Hz, 4 H), 5.85 (dddd, *J* = 16.0, 10.6, 7.3, 7.1 Hz, 1 H), 5.12 (d, *J* = 16.2 Hz, 1 H), 5.07 (d, *J* = 10.6 Hz, 1 H), 4.02 (ddt, *J* = 7.5, 7.1, 6.8 Hz, 1 H), 3.87 (d, *J* = 7.1 Hz, 2 H), 3.69 (s, 3 H), 3.23 (d, *J* = 7.1 Hz, 2 H), 2.82 (br s, 1 H), 2.77 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.68 (dd, *J* = 6.8, 6.6 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.9, 152.7, 136.2, 116.2, 115.4, 114.5, 71.2, 68.3, 55.6, 52.1, 51.2.

ESI-MS: *m*/*z* (%) = (pos) 238.1 ($[M + H]^+$, 100); (neg) 236.1 ($[M – H]^-$, 100).

1-(Allylamino)-3-(naphthalen-1-yloxy)propan-2-ol (T2B)

Prepared from 2-[(naphthalen-1-yloxy)methyl]oxirane (150 mg, 0.75 mmol) and prop-2-en-1-amine (64 mg, 1.12 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2B** (181 mg, 94%) as an orange oil; R_f = 0.33 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3054, 2924, 1581 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 6.8 Hz, 1 H), 7.78 (d, *J* = 6.8 Hz, 1 H), 7.47–7.39 (m, 3 H), 7.32 (t, *J* = 7.1 Hz, 1 H), 6.79 (d, *J* = 7.1 Hz, 1 H), 5.89 (dddd, *J* = 15.8, 10.2, 7.5, 7.1 Hz, 1 H), 5.16 (d, *J* = 15.8 Hz, 1 H), 5.09 (d, *J* = 10.2 Hz, 1 H), 4.02 (ddd, *J* = 7.5, 7.3, 7.1, 6.8 Hz, 1 H), 4.13–4.06 (m, 2 H), 3.32–3.27 (m, 2 H), 2.94–2.82 (m, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.2, 136.2, 134.4, 127.4, 126.4, 125.8, 125.5, 125.2, 121.8, 120.5, 116.4, 104.9, 70.6, 68.4, 52.2, 51.4.

ESI-MS: *m*/*z* (%) = (pos) 258.1 ($[M + H]^+$, 100); (neg) 256.1 ($[M – H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{16}H_{20}NO_2^+$: 258.14886; found: 258.14926. Absolute difference (ppm): 1.54.

1-(Allylamino)-3-(*o*-tolyloxy)propan-2-ol (T2C)

Prepared from 2-[(*o*-tolyloxy)methyl]oxirane (150 mg, 0.91 mmol) and prop-2-en-1-amine (78 mg, 1.37 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2C** (186 mg, 92%) as a white solid; R_f = 0.23 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3311, 3077, 2923, 1603 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.12–7.08 (m, 2 H), 6.88 (t, *J* = 6.8 Hz, 1 H), 6.79 (d, *J* = 6.8 Hz, 1 H), 5.89 (dddd, *J* = 16.2, 10.4, 7.5, 7.1 Hz, 1 H), 5.14 (d, *J* = 16.2 Hz, 1 H), 5.09 (d, *J* = 10.4 Hz, 1 H), 4.08 (ddt, *J* = 7.3, 7.1, 6.6 Hz, 1 H), 3.98–3.89 (m, 2 H), 3.29–3.27 (m, 2 H), 2.91–2.86 (m, 2 H), 2.79 (dd, *J* = 6.8, 6.6 Hz, 1 H), 2.2 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 136.2, 130.6, 126.8, 126.6, 120.6, 116.3, 111.0, 70.4, 68.3, 52.2, 51.4, 16.2.

ESI-MS: *m*/*z* (%) = (pos) 222.1 ($[M+ H]^+$, 100); (neg) 220.1 ($[M – H]^-$, 100).

1-(Allylamino)-3-(4-fluorophenoxy)propan-2-ol (T2D)

Prepared from 2-[(4-fluorophenoxy)methyl]oxirane (150 mg, 0.89 mmol) and prop-2-en-1-amine (76 mg, 1.34 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2D** (187 mg, 93%) as a white solid; R_f = 0.41 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3315, 3077, 2923, 1602 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.91–6.88 (m, 2 H), 6.79–6.73 (m, 2 H), 5.83 (dddd, *J* = 16.0, 10.8, 7.1, 6.9 Hz, 1 H), 5.12 (d, *J* = 16.0 Hz, 1 H), 5.05 (d, *J* = 10.8 Hz, 1 H), 4.04–3.98 (m, 1 H), 3.87 (d, *J* = 7.1 Hz, 2 H), 3.23 (d, *J* = 6.9 Hz, 2 H), 2.97 (br s, 1 H), 2.78 (dd, *J* = 7.5, 6.8 Hz, 1 H), 2.68 (dd, *J* = 6.9, 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.4, 155.3 (d, *J* = 240 Hz, 1 C), 136.2, 116.3, 115.8, 115.4, 71.2, 68.2, 52.1, 51.2.

ESI-MS: *m*/*z* (%) = (pos) 226.1 ($[M + H]^+$, 100); (neg) 224.1 ($[M – H]^-$, 100).

1-(Allylamino)-3-(3,4-difluorophenoxy)propan-2-ol (T2E)

Prepared from 2-[(3,4-difluorophenoxy)methyl]oxirane (150 mg, 0.81 mmol) and prop-2-en-1-amine (69 mg, 1.21 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2E** (178 mg, 91%) as a white solid; R_f = 0.42 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3309, 3086, 2927, 1608 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 6.98 (dd, *J* = 12.5, 4.8 Hz, 1 H), 6.73 (ddd, *J* = 11.6, 7.1, 4.8 Hz, 1 H), 6.55 (d, *J* = 7.1 Hz, 1 H), 5.78 (dddd, *J* = 15.2, 10.1, 7.5, 7.3 Hz, 1 H), 5.14 (d, *J* = 15.2 Hz, 1 H), 5.10 (d, *J* = 10.1 Hz, 1 H), 4.00 (ddt, *J* = 7.3, 7.1, 6.8 Hz, 1 H), 3.81 (d, *J* = 7.1 Hz, 2 H), 3.23 (d, *J* = 6.9 Hz, 2 H), 3.05 (br s, 1 H), 2.75 (dd, *J* = 7.3, 6.4 Hz, 1 H), 2.64 (dd, *J* = 6.8, 6.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.9 (d, *J* = 8 Hz, 1 C), 150.3 (dd, *J* = 247, 14 Hz, 1 C), 145.1 (dd, *J* = 245, 13 Hz, 1 C), 136.1, 117.1 (d, *J* = 19 Hz, 1 C), 116.4, 109.7, 104.1 (d, *J* = 20 Hz, 1 C), 71.4, 68.0, 52.1, 51.1.

ESI-MS: *m*/*z* (%) = (pos) 244.1 ($[M + H]^+$, 100); (neg) 242.1 ($[M – H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{16}F_2NO_2^+$: 244.11436; found: 244.11453. Absolute difference (ppm): 0.71.

1-(Allylamino)-3-(benzyloxy)propan-2-ol (T2F)

Prepared from 2-[(benzyloxy)methyl]oxirane (150 mg, 0.91 mmol) and prop-2-en-1-amine (78 mg, 1.37 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2F** (192 mg, 95%) as a clear oil; R_f = 0.31 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3066, 2907, 1644 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.27 (m, 5 H), 5.83 (dddd, *J* = 16.0, 10.6, 7.3, 6.9 Hz, 1 H), 5.12 (d, *J* = 16.0 Hz, 1 H), 5.07 (d, *J* = 10.6 Hz, 1 H), 4.53 (s, 2 H), 3.89 (ddt, *J* = 7.5, 7.3, 6.8 Hz, 1 H), 3.47–3.43 (m, 2 H), 3.21 (d, *J* = 7.1 Hz, 2 H), 3.09 (br s, 1 H), 2.68 (dd, *J* = 7.5, 6.9 Hz, 1 H), 2.62 (dd, *J* = 6.9, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8, 136.2, 128.1, 127.4, 116.0, 73.1, 72.9, 68.5, 51.9, 51.3.

ESI-MS: *m*/*z* (%) = (pos) 222.2 ($[M + H]^+$, 100); (neg) 220.2 ($[M – H]^-$, 100).

1-(Allylamino)-3-(furan-2-ylmethoxy)propan-2-ol (T2G)

Prepared from 2-[(oxiran-2-ylmethoxy)methyl)]furan (150 mg, 0.97 mmol) and prop-2-en-1-amine (83 mg, 1.46 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2G** (187 mg, 91%) as a clear oil; R_f = 0.26 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3316, 3116, 2910, 1644 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32 (s, 1 H), 6.24 (d, *J* = 6.8 Hz, 2 H), 5.81 (dddd, *J* = 18.0, 11.6, 7.5, 6.8 Hz, 1 H), 5.09 (d, *J* = 18.0 Hz, 1 H), 5.03 (d, *J* = 11.6 Hz, 1 H), 4.42 (s, 2 H), 3.81 (ddt, *J* = 7.3, 7.1, 6.8 Hz, 1 H), 3.41–3.32 (m, 2 H), 3.18 (d, *J* = 7.1 Hz, 2 H), 2.77 (br s, 1 H), 2.60 (dd, *J* = 7.3, 6.9 Hz, 1 H), 2.53 (dd, *J* = 6.9, 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.4, 142.6, 136.3, 116.1, 110.1, 109.3, 72.7, 68.6, 65.0, 52.0, 51.2.

ESI-MS *m*/*z* (%) = (pos) 212.1 ($[M + H]^+$, 100); (neg) 210.1 ($[M – H]^-$, 100).

1-(Allylamino)-4-phenylbutan-2-ol (T2H)

Prepared from 2-benzyloxirane (150 mg, 1.12 mmol) and prop-2-en-1-amine (96 mg, 1.68 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2H** (201 mg, 94%) as a clear oil; R_f = 0.37 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3065, 2919, 1644 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.18 (m, 5 H), 5.81 (dddd, *J* = 18.1, 12.1, 7.5, 7.1 Hz, 1 H), 5.12 (d, *J* = 18.1 Hz, 1 H), 5.09 (d, *J* = 12.1 Hz, 1 H), 3.85 (ddt, *J* = 7.5, 7.3, 6.8 Hz, 1 H), 3.21–3.16 (m, 2 H), 2.73–2.64 (m, 5 H), 3.21 (dd, *J* = 6.9, 6.8 Hz, 1 H), 2.22 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.3, 136.4, 129.3, 128.3, 126.2, 116.1, 70.6, 54.0, 52.0, 45.4, 41.7.

ESI-MS: *m*/*z* (%) = (pos) 192.1 ($[M + H]^+$, 100); (neg) 190.1 ($[M – H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{12}H_{18}NO^+$: 192.13829; found: 192.13864. Absolute difference (ppm): 1.82.

2-(Allylamino)-1-phenylethan-1-ol (T2I)

Prepared from 2-phenyloxirane (150 mg, 1.25 mmol) and prop-2-en-1-amine (107 mg, 1.87 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2I** (195 mg, 88%) as a white semi-solid; R_f = 0.33 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3065, 2982, 1645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.23 (m, 5 H), 5.81 (dddd, *J* = 18.4, 12.6, 7.5, 7.3 Hz, 1 H), 5.09 (d, *J* = 18.4 Hz, 1 H), 5.05 (d, *J* = 12.6 Hz, 1 H), 4.75 (dd, *J* = 7.5, 7.1 Hz, 1 H), 3.41 (br s, 1 H), 3.17 (d, *J* = 7.4 Hz, 2 H), 2.73–2.64 (m, 2 H), 2.28 (s, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.0, 136.0, 128.2, 127.3, 125.7, 116.3, 71.7, 56.3, 51.7.

ESI-MS: *m*/*z* (%) = (pos) 178.1 ($[M+H]^+$, 100); (neg) 176.1 ($[M–H]^-$, 100).

2-(Allylamino)-1-(4-fluorophenyl)ethan-1-ol (T2J)

Prepared from 2-(4-fluorophenyl)oxirane (150 mg, 1.09 mmol) and prop-2-en-1-amine (93 mg, 1.63 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2J** (182 mg, 86%) as a white solid; R_f = 0.37 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3309, 3077, 2982, 1645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.29 (dd, *J* = 8.4, 7.3 Hz, 2 H), 6.99 (t, *J* = 7.1 Hz, 2 H), 5.81 (dddd, *J* = 18.2, 12.8, 7.5, 7.3 Hz, 1 H), 5.12 (d, *J* = 18.2 Hz, 1 H), 5.10 (d, *J* = 12.8 Hz, 1 H), 4.71 (dd, *J* = 7.7, 7.1 Hz, 1 H), 3.27 (br s, 1 H), 3.23–3.18 (m, 2 H), 2.75 (dd, *J* = 7.7, 6.9 Hz, 1 H), 2.66 (dd, *J* = 7.1, 6.9 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.1 (d, *J* = 244 Hz, 1 C), 138.6, 136.0, 127.3, 116.4, 115.1 (d, *J* = 22 Hz, 1 C), 71.1, 56.4, 51.8.

ESI-MS: *m*/*z* (%) = (pos) 196.1 ($[M + H]^+$, 100); (neg) 194.1 ($[M – H]^-$, 100).

2-(Allylamino)-1-(4-chlorophenyl)ethan-1-ol (T2K)

Prepared from 2-(4-chlorophenyl)oxirane (150 mg, 0.97 mmol) and prop-2-en-1-amine (83 mg, 1.46 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded amino alcohol **T2K** (175 mg, 85%) as a white semi-solid; R_f = 0.27 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3082, 2923, 1645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.25 (m, 4 H), 5.85 (dddd, *J* = 17.8, 11.8, 7.3, 7.1 Hz, 1 H), 5.16 (d, *J* = 17.8 Hz, 1 H), 5.12 (d, *J* = 11.8 Hz, 1 H), 4.71 (dd, *J* = 7.9, 6.9 Hz, 1 H), 3.27–3.21 (m, 2 H), 3.18 (br s, 1 H), 2.82 (dd, *J* = 7.9, 6.8 Hz, 1 H), 2.66 (dd, *J* = 7.9, 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.2, 135.9, 133.1, 128.4, 127.1, 116.6, 71.0, 56.2, 51.7.

ESI-MS: *m*/*z* (%) = (pos) 212.1 ($[M + H]^+$, 100); (neg) 210.1 ($[M – H]^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{15}ClNO^+$: 212.08367; found: 212.08397. Absolute difference (ppm): 1.41.

2-(Allylamino)-1-(4-bromophenyl)ethan-1-ol (T2L)

Prepared from 2-(4-bromophenyl)oxirane (150 mg, 0.75 mmol) and prop-2-en-1-amine (65 mg, 1.13 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2L** (164 mg, 85%) as a clear oil; R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3311, 3077, 2998, 1645 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, *J* = 7.3 Hz, 2 H), 6.97 (d, *J* = 7.3 Hz, 2 H), 5.85 (dddd, *J* = 18.8, 10.8, 7.1, 6.9 Hz, 1 H), 5.16 (d, *J* = 18.8 Hz, 1 H), 5.12 (d, *J* = 10.8 Hz, 1 H), 4.68 (dd, *J* = 7.5, 6.9 Hz, 1 H), 3.29–3.23 (m, 2 H), 3.05 (br s, 1 H), 2.82 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.66 (dd, *J* = 6.9, 6.6 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.7, 136.1, 131.4, 127.5, 121.2, 116.4, 71.1, 56.2, 51.8.

ESI-MS: *m*/*z* (%) = (pos) 256.0 ([M + H]$^+$, 100); (neg) 254.0 ([M – H]$^-$, 100).

1-(Allylamino)-3-(allyloxy)propan-2-ol (T2M)

Prepared from 2-[(allyloxy)methyl]oxirane (150 mg, 1.31 mmol) and prop-2-en-1-amine (113 mg, 1.97 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2M** (205 mg, 91%) as a clear oil, R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3311, 3080, 2981, 1645 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85–5.72 (m, 2 H), 5.18–4.95 (m, 4 H), 3.89 (d, *J* = 7.5 Hz, 2 H), 3.78 (ddt, *J* = 7.5, 7.3, 6.9 Hz, 1 H), 3.34–3.29 (m, 2 H), 3.14 (d, *J* = 7.3 Hz, 2H), 2.88 (br s, 1 H), 2.60 (dd, *J* = 7.5, 6.6 Hz, 1 H), 2.51 (dd, *J* = 6.9, 6.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.2, 134.4, 116.9, 116.0, 72.9, 72.1, 68.6, 52.0, 51.4.

ESI-MS: *m*/*z* (%) = (pos) 172.1 ([M + H]$^+$, 100); (neg) 170.1 ([M – H]$^-$, 100).

2-(Allylamino)cyclohexan-1-ol (T2N)

Prepared from cyclohexene oxide (150 mg, 1.53 mmol) and prop-2-en-1-amine (131 mg, 2.29 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2N** (102 mg, 43%) as a clear oil; R_f = 0.14 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3300, 3081, 2930, 1645 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87 (dddd, *J* = 16.8, 12.5, 7.3, 7.1 Hz, 1 H), 5.12 (d, *J* = 16.8 Hz, 1 H), 5.07 (d, *J* = 12.5 Hz, 1 H), 3.38 (dd, *J* = 7.3, 6.6 Hz, 1 H), 3.21–3.01 (m, 2 H), 2.40 (br s, 1 H), 2.19 (ddd, *J* = 7.3, 7.1, 6.4 Hz, 1 H), 2.08–1.94 (m, 2 H), 1.69–1.65 (m, 2 H), 1.27–1.16 (m, 3 H), 1.01–0.91 (m, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.7, 116.1, 73.6, 62.9, 49.2, 33.4, 30.3, 25.1, 24.3.

ESI-MS: *m*/*z* (%) = (pos) 156.1 ([M + H]$^+$, 100); (neg) 154.1 ([M – H]$^-$, 100).

HRMS (ESI): *m*/*z* calcd for $C_9H_{18}NO^+$: 156.13829; found: 156.13871. Absolute difference (ppm): 2.68.

1-(Allylamino)octan-2-ol (T2O)

Prepared from 2-hexyloxirane (150 mg, 1.17 mmol) and prop-2-en-1-amine (100 mg, 1.75 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **T2O** (202 mg, 93%) as a pale yellow oil; R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3310, 3078, 2957, 1645 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.81 (dddd, *J* = 18.3, 12.7, 7.5, 7.3 Hz, 1 H), 5.09 (d, *J* = 18.3 Hz, 1 H), 5.03 (d, *J* = 12.7 Hz, 1 H), 3.58–3.52 (m, 1 H), 3.23–3.14 (m, 2 H), 2.73 (br s, 1 H), 2.62 (dd, *J* = 7.5, 6.9 Hz, 1 H), 2.39 (dd, *J* = 7.3, 6.9 Hz, 1 H), 1.41–1.29 (m, 3 H), 1.25–1.16 (m, 7 H), 0.82 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.3, 116.2, 69.5, 54.6, 52.0, 35.2, 31.7, 29.3, 25.6, 22.5, 14.0.

ESI-MS: *m*/*z* (%) = (pos) 186.2 ([M + H]$^+$, 100); (neg) 184.2 ([M – H]$^-$, 100).

3,3′-(Phenethylazanediyl)bis(1-phenoxypropan-2-ol) (1b)

Prepared from 2-(phenoxymethyl)oxirane (150 mg, 1.0 mmol) and 2-phenylethan-1-amine (182 mg, 1.50 mmol). Purification by silica gel chromatography (isocratic, 4% MeOH/$CHCl_3$) afforded **1b** (211 mg, 50%) as a white solid; R_f = 0.45 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3399, 3028, 2928, 1599 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.29 (m, 6 H), 7.25–7.18 (m, 4 H), 7.01 (t, *J* = 7.1 Hz, 2 H), 6.93 (d, *J* = 7.3 Hz, 3 H), 4.13–4.06 (m, 2 H), 3.97–3.92 (m, 4 H), 2.93–2.88 (m, 2 H), 2.84–2.79 (m, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6, 140.0, 129.6, 128.8, 128.6, 126.3, 121.1, 114.6, 70.0, 68.1, 67.5, 58.0, 57.5, 57.4, 33.6, 33.5.

ESI-MS: *m*/*z* (%) = (pos) 422.2 ([M + H]$^+$, 100); (neg) 420.2 ([M – H]$^-$, 100).

2-{4-[2-Hydroxy-3-(isopropylamino)propoxy]phenyl}acetamide (Atenolol)

4-Hydroxyphenylacetamide (20 g, 95.55 mmol) and propan-2-amine (8.56 g, 143.30 mmol) were combined in DMF and heated to 60 °C in a pressure vessel for 12 h, after which the vessel was allowed to cool to r.t. before adding deionized H_2O (32.28 mL, 50 equiv) in one portion. The flask was resealed and allowed to react for an additional 12 h at 60 °C. Solvent and excess amine were removed on a rotary evaporator (35 °C/22.5 mbar) and purification was accomplished in accordance with the procedure described in the US patent 3 663 607[13a] to furnish the atenolol freebase (21.2 g, 82.5%) as a white solid.; R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3350, 3162, 2965, 1635 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.43 (br s, 1 H), 7.18 (d, *J* = 7.1 Hz, 2 H), 7.18 (d, *J* = 7.1 Hz, 2 H), 3.89 (ddt, *J* = 7.5, 7.3, 6.9 Hz, 1 H), 3.83 (d, *J* = 7.3 Hz, 2 H), 3.29 (s, 2 H), 2.71–2.66 (m, 2 H), 2.53 (sept, *J* = 7.1 Hz, 1 H), 0.99 (d, *J* = 6.8 Hz, 6 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 172.7, 157.3, 130.0, 128.4, 114.2, 70.9, 68.4, 50.1, 48.3, 41.4, 23.0, 22.9.

ESI-MS: *m*/*z* (%) = (pos) 267.2 ([M + H]$^+$, 100); (neg) 265.2 ([M – H]$^-$, 100).

1-(Isopropylamino)-3-[4-(2-methoxyethyl)phenoxy]propan-2-ol (Metoprolol)

2-{[4-(2-Methoxyethyl)phenoxy]methyl}oxirane (20 g, 93.1 mmol) and propan-2-amine (8.34 g, 139.7 mmol) were combined in DMF and heated to 60 °C in a pressure vessel for 12 h, after which the vessel was allowed to cool to r.t. before adding deionized H_2O (32.28 mL, 50 equiv) in one portion. The flask was resealed and allowed to react for an additional 12 h at 60 °C. Solvent and excess amine were removed on a rotary evaporator (35 °C/22.5) to afford 24.5 g (95%) of metoprolol freebase as a white semi-solid in >95% purity (^{1}H NMR); R_f = 0.28 (1:9 MeOH/$CHCl_3$).

IR (thin film): 3299, 3034, 2966, 1613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (d, *J* = 7.1 Hz, 2 H), 6.77 (d, *J* = 7.1 Hz, 2 H), 4.00 (ddt, *J* = 7.5, 7.3, 6.8 Hz, 1 H), 3.83–5.09 (m, 2 H), 3.49 (t, *J* = 7.5 Hz, 2 H), 3.27 (s, 3 H), 3.23 (br s, 1 H), 3.78–3.72 (m, 4 H), 2.71 (dd, *J* = 6.8, 6.6 Hz, 1 H), 1.03 (d, *J* = 6.9 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 131.0, 129.5, 114.2, 73.6, 70.6, 68.1, 58.4, 59.5, 48.7, 35.1, 22.7, 22.6.

ESI-MS: *m*/*z* (%) = (pos) 268.2 ([M + H]$^+$, 100); (neg) 266.2 ([M – H]$^-$, 100).

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588356. Copies of all ^{1}H and ^{13}C NMR spectra are included.

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