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Synthesis of *N*-Aryl β-Amino Alcohols by Trifluoroacetic Acid Promoted Multicomponent Coupling of Aziridines, Arynes, and Water

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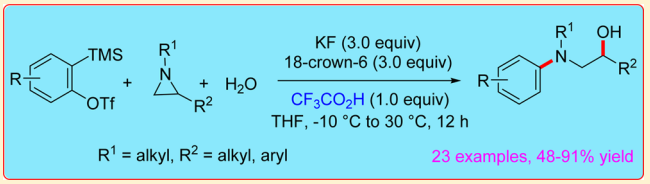
Supporting Information

ABSTRACT: A transition-metal-free, three-component coupling involving *N*-substituted aziridines, arynes, and water promoted by trifluoroacetic acid (TFA) has been reported. The reaction furnished medicinally important *N*-aryl β-amino alcohol derivatives in moderate to good yields. In addition, the use of azetidines in this reaction afforded *N*-aryl γ-amino alcohol derivatives.



β-Amino alcohols are an important class of compounds having widespread applications in the pharmaceutical industry.[1] For example, the β-amino alcohol derivative salbutamol (**A**) is a selective β_2-receptor agonist used in the treatment of asthma (Figure 1).[2] Moreover, terbutaline (**B**) is used in the short term

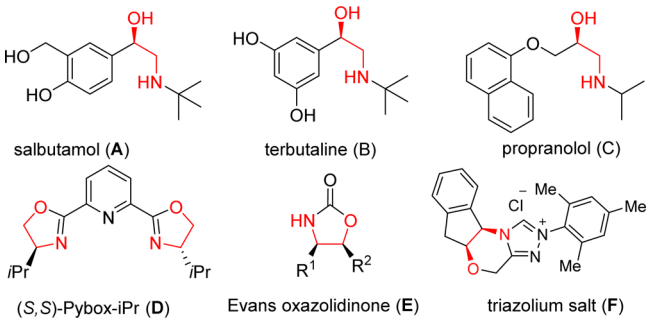
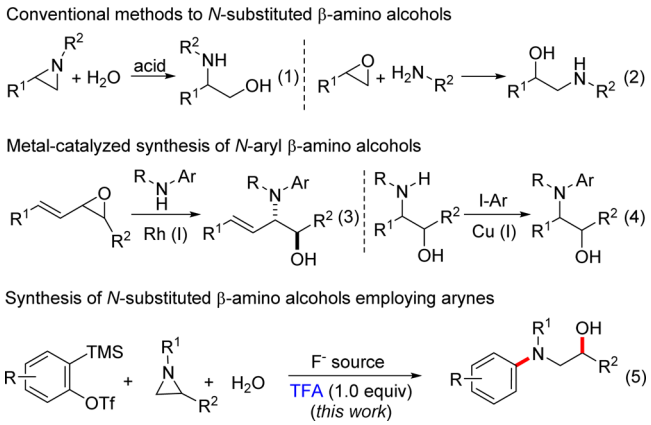


Figure 1. Importance of β-amino alcohol moiety.

asthma treatment,[3] and propranolol (**C**) is used in the treatment of high blood pressure and heart diseases.[4] In addition, β-amino alcohols are used as ligands (pybox ligands **D**) in enantioselective transformations in combination with organometallic reagents.[5] Furthermore, they are used as chiral auxiliaries (Evans's auxiliary **E**) in organic synthesis,[6] and for the synthesis of various N-heterocyclic carbenes (triazolium salt **F**), which are widely used for the umpolung of aldehydes in organocatalysis.[7] Given the importance of β-amino alcohols in drug discovery and in organic synthesis, development of flexible synthetic routes to this moiety is highly desirable.

The ring opening of aziridines with H_2O under the protic or Lewis acid activation is a practical method to access β-amino alcohols (Scheme 1, eq 1).[8] Moreover, the reaction of epoxides with anilines is a useful protocol for accessing the *N*-arylated β-amino alcohols (eq 2).[9] However, this method suffers from limitations such as low reactivity of anilines, use of excess

Scheme 1. Synthesis of *N*-Substituted β-Amino Alcohols



anilines and high temperature, and concerns regarding regioselectivity. In 2000, Fagnou and Lautens developed a Rh-catalyzed aminolysis of vinyl epoxides for the synthesis of *N*-aryl β-amino alcohols (eq 3).[10] Moreover, Job and Buchwald demonstrated the Cu-catalyzed arylation route to the synthesis of *N*-aryl β-amino alcohols (eq 4).[11a] Intriguingly, however, the transition-metal-free synthesis of *N*-aryl β-amino alcohols using arynes[12] as the aryl source, to the best of our knowledge, is unknown. Herein, we report the transition-metal-free, trifluoroacetic acid (TFA)-promoted three-component coupling involving arynes, aziridines, and H_2O for the rapid access to *N*-aryl β-amino alcohols.[13] Notably, the formation of a zwitterion from arynes and aziridines has been known as early as 1972.[12,14] Moreover, the reaction of arynes with aziridines, where the solvent CH_3CN has been incorporated as the third component, has been recently disclosed by Larionov and co-workers.[15]

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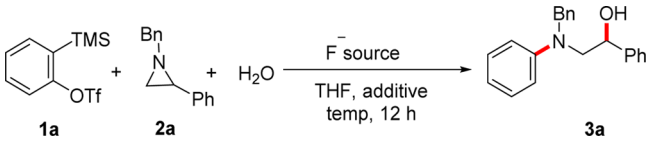
Inspired by the importance of β-amino alcohols in pharmaceutical industry, the present study was initiated by treating the aryne precursor **1a**[16] with *N*-benzyl aziridine **2a** and H_2O. When aryne was generated from **1a** using KF and 18-crown-6, the expected β-amino alcohol **3a** was isolated in 28% yield (Table 1, entry 1). The use of CsF as the fluoride source

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

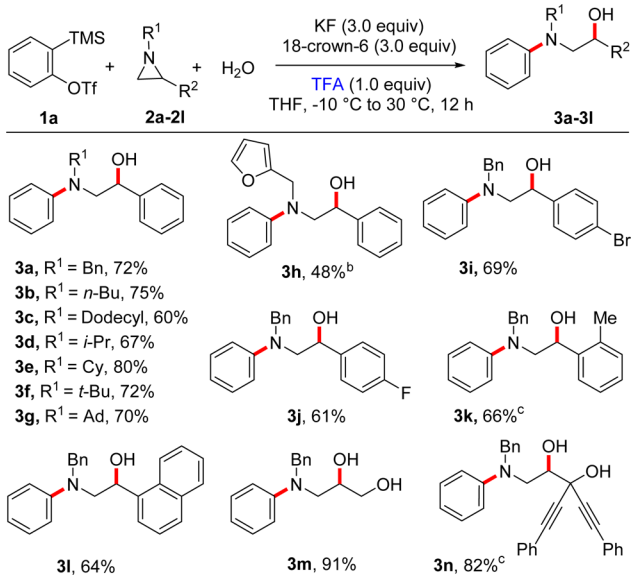
entry	F^- source	additive (mol %)	temp (°C)	yield of **3a** (%)[b]
1	KF/18-crown-6	–	30	28
2[c]	CsF	–	30	13
3	TBAF	–	30	28
4	KF/18-crown-6	–	−10 to 30	10
5	KF/18-crown-6	–	60	19
6	KF/18-crown-6	TFA (20)	30	55
7	KF/18-crown-6	TFA (50)	30	64
8	KF/18-crown-6	TFA (100)	30	69
9	*KF/18-crown-6*	*TFA (100)*	*−10 to 30*	72
10	KF/18-crown-6	TfOH (100)	−10 to 30	<5
11	KF/18-crown-6	*p*TSA·H_2O (100)	−10 to 30	<5
12	KF/18-crown-6	$MeSO_3H$ (100)	−10 to 30	<5
13[c]	CsF	TFA (100)	−10 to 30	20
14	TBAF	TFA (100)	−10 to 30	45

[a]Standard conditions: **1a** (0.375 mmol), **2a** (0.25 mmol), H_2O (0.5 mmol), fluoride source (0.75 mmol), THF (1.0 mL), stirred for 12 h. [b]Yields of isolated products are given. [c]The reaction performed using CH_3CN as the solvent.

returned inferior results (entry 2). The utility of tetrabutylammonium fluoride (TBAF) provided comparable results (entry 3), but the reaction also furnished the α-fluoro-β-amino acid derivative recently reported by Wu and Sha in 30% yield.[17] Performing the reaction under cold or hot conditions did not improve the reactivity (entry 4 and 5). At this stage, we considered addition of Brønsted acids as additives. Interestingly, the use of 20 mol % of trifluoroacetic acid (TFA) improved the yield of **3a** to 55% (entry 6).[18] Increasing the amount of TFA enhanced the yield of product **3a** (entries 7 and 8). When the reaction was carried out using 1.0 equiv of TFA at −10 to 30 °C, the desired product **3a** was formed in 72% yield (entry 9).[19] Disappointingly, the use of other Brønsted acids such as triflic acid, *p*-toluenesulfonic acid, and methanesulfonic acid delivered only traces of the expected product (entries 10−12). Moreover, using TFA as additive, the use of CsF and TBAF as fluoride sources were also not found to be beneficial (entry 13 and 14).

Next, the scope and limitations of this reaction were examined. First, we evaluated the variation of aziridines (Scheme 2). A series of aziridines synthesized from linear, branched, and even sterically demanding aliphatic amines underwent a smooth coupling reaction promoted by TFA leading to the formation of the *N*-alkyl *N*-phenyl β-amino alcohols in good yields (**3a**−**3g**). The aziridine derived from furfuryl amine afforded the desired product **3h** in 48% yield by using TBAF as the fluoride source. Disappointingly, aziridines derived from sulfonamides afforded only traces of the *N*-aryl β-amino alcohols. The substituents at the 2-aryl moiety of

Scheme 2. Synthesis of *N*-Aryl β-Amino Alcohols: Scope of Aziridines



[a]General conditions: **1a** (0.75 mmol), **2** (0.50 mmol), H_2O (1.0 mmol), TFA (0.50 mmol), KF (1.5 mmol), 18-crown-6 (1.5 mmol), THF (2.0 mL), −10 to 30 °C, 12 h. Yields of the isolated products are given. [b]Reaction was performed on 0.25 mmol scale with TBAF as fluoride source. [c]Reaction was performed on 0.25 mmol scale.

aziridines did not affect the outcome of the reaction, and in all cases the expected products were isolated in good yields (**3i**−**3l**). Furthermore, alkyl substitution at the 2-position of aziridine was well-tolerated, and the corresponding products were isolated in excellent yields (**3m**, **3n**) thus demonstrating the versatility of the present reaction.

Then, we studied the generality of this reaction with differently substituted arynes (Table 2). Gratifyingly, electronically dissimilar 4,5-disubstituted symmetrical arynes generated from precursors **1b**−**1e** readily afforded the *N*-aryl β-amino alcohols in good yields upon treatment with aziridine **2a** and H_2O promoted by TFA under the optimized conditions (**3o**−**3r**). Moreover, 3,6-dimethyl aryne generated from **1f** and the symmetrical naphthalyne generated from **1g** resulted in the formation of the desired products in moderate yields (**3s**−**3t**). Interestingly, the reaction of **2a** and H_2O with unsymmetrical aryne generated from **1h** furnished 2-naphthyl amino alcohol **3t** in 59% yield and with an excellent regioselectivity of >20:1. Additionally, the unsymmetrical 4-methyl aryne generated from **1i** afforded the mixture of regioisomers in a 1:1 ratio and 70% yield. Furthermore, the 4-fluoroaryne formed from **1j** resulted in the formation of a mixture of regioisomers **3v** and **3v′** in 3:1 ratio and 65% yield, thus further expanding the scope of this aryne three-component coupling.

The proposed mechanism of this TFA-promoted *N*-aryl β-amino alcohol synthesis is shown in Scheme 3. One possibility is the nucleophilic attack of aziridine on aryne[20] derived from **1a** generating the zwitterionic intermediate **G**, which is subsequently protonated by TFA/H_2O to form the quaternary ammonium salt **H**. The nucleophilic attack of trifluoroacetate anion (most likely proceeding via S_N2 pathway) on intermediate **H** generates the ester intermediate **I**, which on hydrolysis affords the desired product **3**. Alternatively, aziridine opening using H_2O promoted by TFA can result in the

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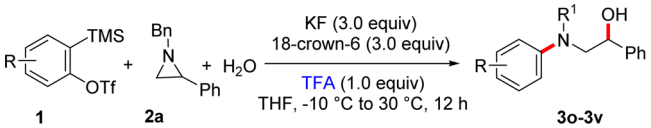
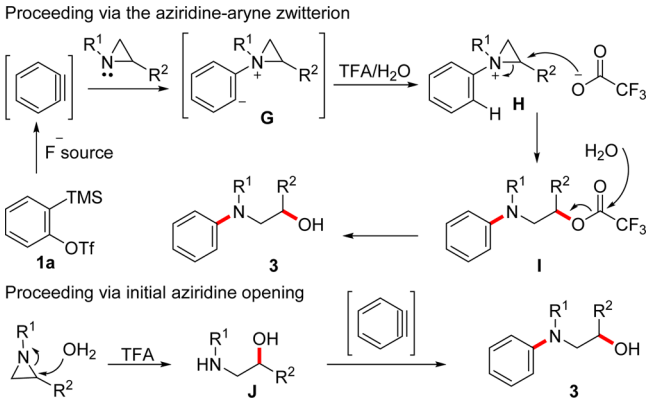
Table 2. Variation of the Aryne Moiety[a]



entry	aryne precursor	product(s), yield (%)
1–4	1b-e	**3o**, R = Me, (60%)[b]; **3p**, R = $(CH_2)_3$, (68%); **3q**, R = $O(CH_2)O$, (66%); **3r**, R = F, (65%)
5	1f	**3s**, (57%)
6	1g	**3t**, (57%)
7	1h	**3t**, (>20:1)[c], (59%); **3t'**
8	1i	**3u**, (1:1)[c], (70%); **3u'**
9	1j	**3v**, (3:1)[c], (65%); **3v'**

[a]General conditions: **1** (0.75 mmol), **2a** (0.50 mmol), H_2O (1.0 mmol), TFA (0.5 mmol), KF (1.5 mmol), 18-crown-6 (1.5 mmol), THF (2.0 mL), −10 to 30 °C, 12 h. Yields of the isolated products are given. [b]Reaction was performed on 0.25 mmol scale. [c]The regioisomer ratio was determined by ^{1}H NMR analysis of crude reaction mixture.

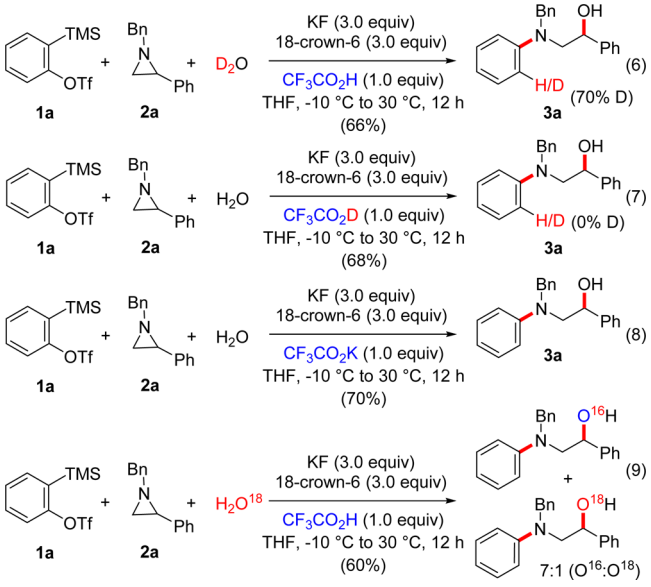
Scheme 3. Plausible Mechanism of the Reaction



formation of the amino alcohol **J**, which on *N*-arylation using aryne can result in the formation of **3**.[21,22]

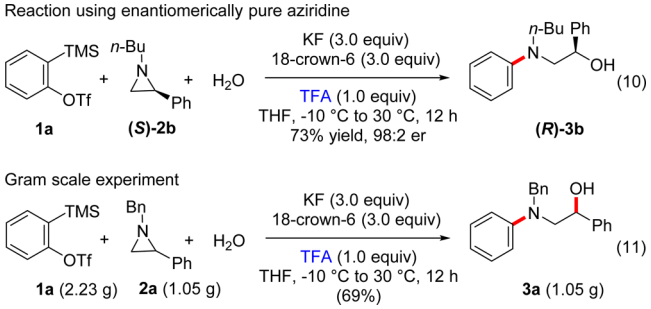
To shed light on the mechanism of this transformation, we have carried out several mechanistic experiments. When the reaction was performed using D_2O instead of H_2O, the desired product **3a** was formed in 66% yield with 70% D incorporation at the 2-position of the ring (Scheme 4, eq 6). This indicates

Scheme 4. Mechanistic Experiments



the role of H_2O in protonating the aryl anion intermediate **G** generated from aziridine and aryne (Scheme 3).[19,23,24] Moreover, to get insight into the role of TFA in the protonation of aryl anion intermediate **G**, a reaction was carried out using TFA-*d* (eq 7). Surprisingly, this reaction afforded **3a** in 68% yield with no incorporation of D at the 2-position of the ring. This shows that TFA is not involved in the protonation of the aryl anion intermediate. To gain information on the role of TFA in this reaction, we have performed additional experiments using CF_3CO_2K (eq 8). Under this condition, **3a** was formed in 70% yield suggesting the formation of CF_3CO_2K under the present reaction conditions. Thus, it is likely that CF_3CO_2K is formed under the reaction conditions from TFA and KF. Furthermore, when the reaction of **1a** and **2a** was performed using O^{18} labeled H_2O, the products incorporating O^{16} and O^{18} were formed in 60% yield and a 7:1 ratio (eq 9). The preferential formation of product incorporating O^{16} indicates that the alcohol oxygen is derived from TFA rather than H_2O.

Furthermore, the reaction of enantiomerically pure aziridine (*S*)-**2b** with **1a** and H_2O under the optimized conditions afforded the chiral *β*-amino alcohol derivative (*R*)-**3b** in 73% yield and a 98:2 enantiomeric ratio (eq 10). The formation of



(*R*)-**3b** in high enantiomeric ratio rules out the possibility of an S_N1 opening of the intermediate **H** (Scheme 3). Moreover, the practical application of the present method has been demonstrated by performing the reaction in gram scale, which afforded the desired product **3a** in 69% yield (eq 11).

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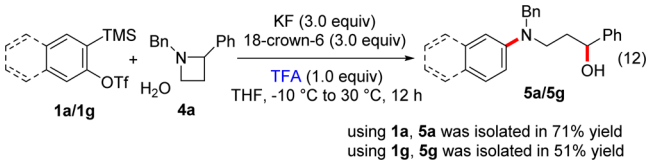
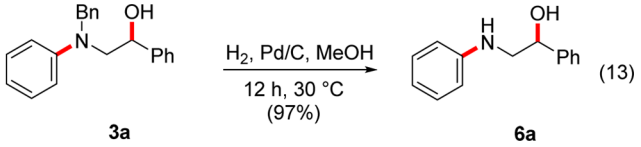
Interestingly, this TFA-promoted reaction is not limited to the synthesis of β-amino alcohols, but instead applicable to the synthesis of γ-amino alcohols as well. Treatment of **1a** with 2-phenyl azetidine **4a** and H_2O in the presence of TFA and KF/18-crown-6 resulted in the formation of the *N*-phenyl γ-amino alcohol **5a** in 71% yield (eq 12). Moreover, the symmetrical naphthalyne generated from **1g** on reaction with **4a** and H_2O afforded the desired γ-amino alcohol **5g** in 51% yield.



Finally, the *N*-aryl β-amino alcohol **3a** has been deprotected under hydrogenation conditions using Pd/C resulting in the formation of unprotected *N*-aryl β-amino alcohol **6a** in 97% yield (eq 13).[25]



In conclusion, we have reported the operationally simple, transition-metal-free, three-component coupling involving aziridines, arynes, and water promoted by TFA. The reaction afforded pharmaceutically relevant *N*-aryl β-amino alcohols in moderate to good yields.[25] In view of the importance of these compounds in medicine, the protocol presented herein may be a practical method to access them.

EXPERIMENTAL SECTION

General Information. Unless otherwise specified, all reactions were carried out under an atmosphere of argon in flame-dried reaction vessels with Teflon screw caps. 30 °C corresponds to the room temperature of the lab when the experiments were carried out. THF was freshly purified by distillation over Na-benzophenone and was transferred under argon. 18-Crown-6 was recrystallized from dry CH_3CN, and KF was dried by heating at 110 °C for 12 h and left to cool under argon and stored in argon filled glovebox. Trifluoroacetic acid and potassium trifluoroacetate were purchased from commercial sources and used as received without any further purification. All the aziridines and azetidines were prepared following the literature procedure.[26] The 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1a** and the other symmetric and unsymmetric aryne precursors were synthesized following a literature procedure.[16] ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ as solvent. Chemical shifts (δ) are given in ppm. The residual solvent signals were used as references, and the chemical shifts were converted to the TMS scale ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm). HRMS measurements were carried out using an ESI method and ion-trap mass analyzer. Infrared (IR) spectra were recorded on an FT-IR spectrometer as thin films using NaCl plates.

General Procedure for the TFA-Promoted Reaction of Aziridines, Arynes, and H_2O. To a flame-dried screw-capped test tube equipped with a magnetic stir bar was added KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glovebox. THF (2.0 mL) was added outside the glovebox under an argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) with continued stirring for 5 min at 30 °C. After 5 min of stirring, aziridine 2 (0.5 mmol) was added. Then the reaction mixture was cooled to −10 °C and aryne precursor **1** (0.75 mmol) was added. After stirring for 10 min at −10 °C, H_2O (18 μL, 1.0 mmol) was added. Then the reaction mixture was slowly warmed to 30 °C and with maintained stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated, and the crude residue was preadsorbed on silica gel and purified by flash column chromatography (Pet. ether/EtOAc = 95/05) on silica gel to afford the corresponding 2-amino alcohols **3** in moderate to good yields. It may be mentioned that the reaction works well without glovebox techniques, maintaining the isolated yield of **3**.

2-(Benzyl(phenyl)amino)-1-phenylethan-1-ol (3a). Yellow oil, 0.109 g, 72%. R_f (Pet. ether/EtOAc = 80/20): 0.51; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45−7.22 (m, 12H), 6.91 (d, J = 8.3 Hz, 2H), 6.83 (t, J = 7.2 Hz, 1H), 5.09 (t, J = 6.4 Hz, 1H), 4.69 (d, J = 17.1 Hz, 1H), 4.56 (d, J = 17.1 Hz, 1H), 3.68 (d, J = 6.4 Hz, 2H), 2.59 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.8, 142.2, 138. 5, 129.5, 128.7, 128.7, 128.0, 127.0, 126.8, 126.0, 117.5, 113.4, 72.1, 59.8, 55.4. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{21}H_{22}NO$: 304.1696; found: 304.1694. **FTIR (cm^{-1})** 3339, 3055, 2912, 2352, 1687, 1600, 1501.

2-(Butyl(phenyl)amino)-1-phenylethan-1-ol (3b). Yellow oil, 0.101 g, 75%. R_f (Pet. ether/EtOAc = 90/10): 0.51; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47−7.40 (m, 4H), 7.36−7.28 (m, 3H), 6.88 (d, J = 8.0 Hz, 2H), 6.80 (t, J = 7.2 Hz, 1H), 5.00 (dd, J_1 = 9.1, J_2 = 3.9 Hz, 1H), 3.54 (dd, J_1 = 14.7, J_2 = 4.0 Hz, 1H), 3.43 (dd, J_1 = 14.7, J_2 = 9.1 Hz, 1H), 3.37−3.31 (m, 2H), 2.59 (s, 1H), 1.62−1.51 (m, 2H), 1.40−1.31 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.6, 142.1, 129.5, 128.7, 127.9, 126.0, 117.4, 113.8, 71.5, 60.2, 52.3, 28.8, 20.4, 14.1. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{18}H_{24}NO$: 270.1852; found: 270.1863. **FTIR (cm^{-1})** 3357, 3055, 2304, 1710, 1598, 1500.

2-(Dodecyl(phenyl)amino)-1-phenylethan-1-ol (3c). Yellow oil, 0.115 g, 60%. R_f (Pet. ether/EtOAc = 90/10): 0.55; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47−7.10 (m, 7H), 6.75 (d, J = 8.2 Hz, 2H), 6.67 (t, J = 7.2 Hz, 1H), 4.86 (dd, J_1 = 8.9 Hz, J_2 = 3.9 Hz, 1H), 3.41 (dd, J_1 = 14.7 Hz, J_2 = 4.0 Hz, 1H), 3.31 (dd, J_1 = 14.7 Hz, J_2 = 9.0 Hz, 1H), 3.24−3.10 (m, 2H), 2.50 (s, 1H), 1.45 (s, 2H), 1.18 (s, 18H), 0.80 (t, J = 6.7 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.6, 142.1, 129.4, 128.6, 127.9, 126.0, 117.3, 113.8, 71.5, 60.1, 52.6, 32.1, 29.8, 29.6, 29.5, 27.2, 26.7, 22.8, 14.3. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{26}H_{40}NO$: 382.3104; found: 382.3107. **FTIR (cm^{-1})** 3427, 3029, 2924, 2857, 1956, 1600, 1501.

2-(Isopropyl(phenyl)amino)-1-phenylethan-1-ol (3d). Yellow oil, 0.086 g, 67%. R_f (Pet. ether/EtOAc = 90/10): 0.60; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.59−7.34 (m, 7H), 7.13 (d, J = 8.0 Hz, 2H), 6.98 (t, J = 7.2 Hz, 1H), 4.80 (dd, J_1 = 9.9 Hz, J_2 = 3.3 Hz, 1H), 3.96 (dt, J_1 = 13.2 Hz, J_2 = 6.6 Hz, 1H), 3.43 (dd, J_1 = 14.2 Hz, J_2 = 3.4 Hz, 1H), 3.16−3.10 (m, 2H), 1.31 (d, J = 6.7 Hz, 3H), 1.05 (d, J = 6.6 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$** δ 148.9, 142.3, 129.2, 128.5, 127.7, 126.0, 120.5, 119.2, 70.3, 53.2, 53.1, 21.0, 19.1. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{17}H_{22}NO$: 256.1696; found: 256.1698. **FTIR (cm^{-1})** 3442, 3018, 2972, 1596, 1498.

2-(Cyclohexyl(phenyl)amino)-1-phenylethan-1-ol (3e). Yellow oil, 0.118 g, 80%. R_f (Pet. ether/EtOAc = 90/10): 0.60; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.48−7.32 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 6.97 (t, J = 7.2 Hz, 1H), 4.86−4.69 (m, 1H), 3.60−3.40 (m, 2H), 3.17 (dd, J_1 = 13.9 Hz, J_1 = 10.3 Hz, 2H), 2.00 (d, J = 11.7 Hz, 1H), 1.91 (d, J = 12.4 Hz, 1H), 1.80 (d, J = 9.8 Hz, 2H), 1.69 (d, J = 11.5 Hz, 1H), 1.58−1.01 (m, 5H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.9, 142.3, 129.1, 128.5, 127.7, 126.0, 120.3, 119.1, 70.4, 62.0, 54.4, 31.6, 30.1, 26.2. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{20}H_{26}NO$: 296.2009; found: 296.2008. **FTIR (cm^{-1})** 3440, 3018, 2933, 2858, 2404, 1951, 1596, 1497.

2-(*tert*-Butyl(phenyl)amino)-1-phenylethan-1-ol (3f). Yellow oil, 0.097 g, 72%. R_f (Pet. ether/EtOAc = 90/10): 0.45; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43−7.28 (m, 10H), 4.22 (d, J = 10.5 Hz,1H), 4.15 (s, 1H), 3.36 (d, J = 12.6 Hz, 1H), 3.09 (t, J = 11.7 Hz, 1H), 1.20 (s, 9H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 147.3, 142.4, 129.8, 128.7, 128.3, 127.4, 126.3, 126.0, 69.8, 57.6, 55.7, 28.5. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{18}H_{24}NO$: 270.1852; found: 270.1865. **FTIR (cm^{-1})** 3439, 3018, 2974, 2871, 1594, 1486.

2-(Adamantan-1-yl) (phenyl)amino)-1-phenylethan-1-ol (3g). Yellow solid, 0.122 g, 70%. R_f (Pet. ether/EtOAc = 90/10):

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0.54; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37−7.24 (m, 10H), 4.15 (dd, J_1 = 10.6, J_2 = 3.1 Hz, 2H), 3.28 (dd, J_1 = 12.9, J_2 = 3.1 Hz, 1H), 3.09 (dd, J_1 = 12.8, J_2 = 10.7 Hz, 1H), 2.07 (s, 3H), 1.86 (d, J = 10.9 Hz, 3H), 1.62 (d, J = 12.1 Hz, 3H), 1.54 (d, J = 11.8 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.6, 142.5, 130.3, 128.7, 128.3, 127.4, 126.3, 126.0, 69.8, 56.0, 55.7, 41.5, 36.6, 29.9. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{24}H_{30}NO$: 348.2322; found: 348.2328. **FTIR (cm^{-1})** 3432, 3017, 2920, 2855, 1593, 1490.

2-((Furan-2-ylmethyl)(phenyl)amino)-1-phenylethan-1-ol (3h). Yellow oil, 0.035 g, 48%; reaction performed in 0.25 mmol scale using TBAF as the fluoride source). R_f (Pet. ether/EtOAc = 90/10): 0.44; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37−7.21 (m, 6H), 7.21−7.16 (m, 2H), 6.87 (d, J = 8.1 Hz, 2H), 6.73 (t, J = 7.3 Hz, 1H), 6.21 (dd, J_1 = 3.0 Hz, J_2 = 1.9 Hz, 1H), 6.07 (d, J = 2.8 Hz, 1H), 4.90 (dd, J_1 = 9.1 Hz, J_1 = 3.7 Hz, 1H), 4.41 (q, J = 16.7 Hz, 2H), 3.54−3.39 (m, 2H), 2.68 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 152.2, 148.8, 142.1, 141.9, 129.4, 128.7, 128.0, 126.0, 118.4, 114.3, 110.5, 107.8, 71.9, 60.3, 49.4. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{19}H_{20}NO_2$: 294.1489; found: 294.1490. **FTIR (cm^{-1})** 3386, 3020, 2926, 2400, 1599, 1505.

2-(Benzyl(phenyl)amino)-1-(4-bromophenyl)ethan-1-ol (3i). Yellow solid, 0.132 g, 69%. R_f (Pet. ether/EtOAc = 90/10): 0.59; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.51 (d, J = 8.2 Hz, 2H), 7.32−7.18 (m, 9H), 6.89−6.80 (m, 3H), 5.00 (t, J = 6.5 Hz, 1H), 4.65 (d, J = 17.0 Hz, 1H), 4.53 (d, J = 17.0 Hz, 1H), 3.60−3.58 (m, 2H), 2.58 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.7, 141.0, 138.2, 131.7, 129.5, 128.8, 127.7, 127.1, 126.8, 121.7, 117.8, 113.6, 71.4, 59.7, 55.6. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{21}H_{21}NOBr$: 382.0801; found: 382.0804. **FTIR (cm^{-1})** 3440, 3018, 2926, 2404, 1599, 1500.

2-(Benzyl(phenyl)amino)-1-(4-fluorophenyl)ethan-1-ol (3j). Yellow solid, 0.098 g, 61%. R_f (Pet. ether/EtOAc = 90/10): 0.45; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.45−7.15 (m, 9H), 7.07 (t, J = 8.6 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.81 (t, J = 7.3 Hz, 1H), 5.04 (t, J = 6.5 Hz, 1H), 4.65 (d, J = 17.0 Hz, 1H), 4.53 (d, J = 17.1 Hz, 1H), 3.61 (d, J = 6.5 Hz, 2H), 2.55 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 162.5 (d, J = 245.7 Hz), 148.8, 138.3, 137.8 (d, J = 2.7 Hz), 129.5, 128.8, 127.7 (d, J = 8.1 Hz), 127.0, 126.8, 117.7, 115.5 (d, J = 21.3 Hz), 113.5, 71.4, 59.8, 55.5. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{21}H_{21}FNO$: 322.1602; found: 322.1617. **FTIR (cm^{-1})** 3431, 3018, 2920, 2404, 1600, 1504.

2-(Benzyl(phenyl)amino)-1-(*o*-tolyl)ethan-1-ol (3k). Yellow oil, 0.052 g, 66%; reaction performed in 0.25 mmol scale. R_f (Pet. ether/EtOAc = 90/10): 0.48; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.63 (d, J = 7.5 Hz, 1H), 7.37−7.19 (m, 10H), 6.95 (d, J = 8.0 Hz, 2H), 6.83 (t, J = 7.3 Hz, 1H), 5.34 (dd, J_1 = 7.7, J_2 = 5.1 Hz, 1H), 4.70 (d, J = 17.0 Hz, 1H), 4.60 (d, J = 17.0 Hz, 1H), 3.67−3.65 (m, 2H), 2.47 (s, 1H), 2.36 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.0, 140.2, 138.4, 134.7, 130.5, 129.4, 128.7, 127.7, 127.0, 126.9, 126.6, 125.9, 117.7, 113.6, 68.6, 58.5, 55.3, 19.4. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{22}H_{24}NO$: 318.1852; found: 318.1867. **FTIR (cm^{-1})** 3552, 3018, 2935, 2406, 1599, 1500.

2-(Benzyl(phenyl)amino)-1-(naphthalen-1-yl)ethan-1-ol (3l). Yellow oil, 0.112 g, 64%. R_f (Pet. ether/EtOAc = 90/10): 0.50; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.02 (d, J = 7.7 Hz, 1H), 7.93−7.90 (m, 1H), 7.84 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 7.1 Hz, 1H), 7.54−7.48 (m, 3H), 7.35−7.20 (m, 7H), 6.97 (d, J = 8.1 Hz, 2H), 6.84 (t, J = 7.2 Hz, 1H), 5.79 (dd, J = 8.1, 4.4 Hz, 1H), 4.67 (d, J = 16.9 Hz, 1H), 4.59 (d, J = 16.9 Hz, 1H), 3.88−3.78 (m, 2H), 2.65 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 149.1, 138.5, 138.0, 130.6, 129.5, 129.1, 128.8, 128.4, 127.1, 127.0, 126.2, 125.7, 123.8, 123.1, 117.8, 113.9, 69.4, 58.9, 55.5. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{25}H_{24}NO$: 354.1852; found: 354.1870. **FTIR (cm^{-1})** 3554, 3062, 2924, 1598, 1504.

3-(Benzyl(phenyl)amino)propane-1,2-diol (3m). Yellow oil, 0.117 g, 91%. R_f (Pet. ether/EtOAc = 60/40): 0.54; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 (t, J = 7.2 Hz, 2H), 7.26−7.18 (m, 5H), 6.79 (d, J = 8.1 Hz, 2H), 6.75 (t, J = 7.3 Hz, 1H), 4.66−4.57 (m, 2H), 4.06−4.03 (m, 1H), 3.71 (dd, J_1 = 11.4 Hz, J_2 = 3.2 Hz, 1H), 3.53 (dd, J_1 = 11.4 Hz, J_2 = 5.8 Hz, 1H), 3.48 (d, J = 6.5 Hz, 2H), 2.92 (s, 1H), 2.68 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.8, 138.4, 129.4, 128.8, 127.0, 126.8, 117.5, 113.4, 69.9, 64.4, 55.5, 53.8. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{16}H_{20}NO_2$: 258.1489; found: 258.1482. **FTIR (cm^{-1})** 3424, 3021, 2928, 2254, 1599, 1503.

1-(Benzyl(phenyl)amino)-5-phenyl-3-(phenylethynyl)pent-4-yne-2,3-diol (3n). White solid, 0.094 g, 82%; reaction performed in 0.25 mmol scale). R_f (Pet. ether/EtOAc = 70/30): 0.46; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.36 (d, J = 7.5 Hz, 2H), 7.32−7.24 (m, 12H), 7.18 (t, J = 8.0 Hz, 3H), 7.08 (d, J = 8.2 Hz, 2H), 6.78 (t, J = 7.2 Hz, 1H), 5.04 (d, J = 17.2 Hz, 1H), 4.95 (d, J = 17.2 Hz, 1H), 4.73 (dd, J_1 = 7.9 Hz, J_2 = 5.2 Hz, 1H), 4.41 (dd, J_1 = 11.7 Hz, J_2 = 5.0 Hz, 1H), 4.21 (dd, J_1 = 11.6 Hz, J_2 = 8.1 Hz, 1H), 3.57 (s, 1H), 2.04 (s, 1H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 150.0, 139.6, 131.0, 131.9, 129.1, 129.0, 128.7, 128.4, 128.4, 126.9, 126.8, 121.8, 121.7, 118.9, 116.4, 88.0, 87.7, 86.1, 85.8, 69.9, 66.7, 61.5, 49.2. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{32}H_{28}NO_2$: 458.2115; found: 458.2098. **FTIR (cm^{-1})** 3413, 3020, 2403, 2239, 1598.

2-(Benzyl(3,4-dimethylphenyl)amino)-1-phenylethan-1-ol (3o). Yellow oil, 0.050 g, 60%; reaction performed in 0.25 mmol scale. R_f (Pet. ether/EtOAc = 90/10): 0.45; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.44−7.38 (m, 10H), 7.04 (d, J = 8.3 Hz, 1H), 6.76 (s, 1H), 6.68 (dd, J_1 = 8.2 Hz, J_2 = 2.3 Hz, 1H), 5.04 (dd, J_1 = 8.5 Hz, J_2 = 4.3 Hz, 1H), 4.57 (dd, J_1 = 45.7 Hz, J_2 = 16.8 Hz, 2H), 3.59 (qd, J_1 = 14.8 Hz, J_2 = 6.5 Hz, 2H), 2.61 (s, 1H), 2.27 (s, 3H), 2.23 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$** δ 147.2, 142.2, 138.7, 137.4, 130.5, 128.6, 128.6, 127.8, 127.0, 126.9, 125.98, 115.7, 111.7, 71.8, 60.0, 55.8, 20.5, 18.7. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{23}H_{26}NO$: 332.2009; found: 332.2006. **FTIR (cm^{-1})** 3445, 3018, 2927, 2405, 1955, 1878, 1611, 1569, 1507.

2-(Benzyl(2,3-dihydro-1*H*-inden-5-yl)amino)-1-phenylethan-1-ol (3p). Yellow oil, 0.091 g, 68%. R_f (Pet. ether/EtOAc = 90/10): 0.50; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.43−7.38 (m, 4H), 7.33 (t, J = 7.51 Hz, 3H), 7.28−7.22 (m, 3H), 7.13 (d, J = 8.2 Hz, 1H), 6.85 (s, 1H), 6.73 (dd, J_1 = 8.2 Hz, J_2 = 1.8 Hz, 1H), 5.04 (dd, J_1 = 8.5 Hz, J_2 = 4.3 Hz, 1H), 4.64 (d, J = 16.8 Hz, 1H), 4.52 (d, J = 16.8 Hz, 1H), 3.59 (qd, J_1 = 14.7 Hz, J_2 = 6.5 Hz, 2H), 2.89 (dd, J_1 = 16.7 Hz, J_2 = 7.7 Hz, 4H), 2.63 (s, 1H), 2.10 (p, J = 7.4 Hz, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.0, 145.7, 142.2, 138.7, 133.8, 128.7, 128.6, 127.9, 127.1, 126.9, 126.0, 124.9, 112.5, 110.5, 71.8, 60.3, 56.2, 33.5, 32.0, 25.8. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{24}H_{26}NO$: 344.2009; found: 344.2010. **FTIR (cm^{-1})** 3425, 3063, 3012, 2950, 2868, 2845, 1615, 1573, 1498.

2-(Benzo[*d*][1,3]dioxol-5-yl(benzyl)amino)-1-phenylethan-1-ol (3q). Yellow oil, 0.114 g, 66%. R_f (Pet. ether/EtOAc = 90/10): 0.46; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.39 (d, J = 4.3 Hz, 4H), 7.36−7.24 (m, 4H), 7.21 (d, J = 7.1 Hz, 2H), 6.73 (d, J = 8.5 Hz, 1H), 6.57 (d, J = 2.4 Hz, 1H), 6.35 (dd, J = 8.5, 2.5 Hz, 1H), 5.89 (d, J = 0.9 Hz, 2H), 4.96 (dd, J = 8.8, 4.2 Hz, 1H), 4.53 (d, J = 16.4 Hz, 1H), 4.43 (d, J = 16.4 Hz, 1H), 3.54−3.42 (m, 2H), 2.81 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 148.5, 144.9, 142.0, 140.5, 138.3, 128.6, 128.6, 127.9, 127.3, 127.1, 126.0, 108.5, 107.7, 100.9, 98.4, 71.6, 60.9, 57.1. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{22}H_{22}NO_3$: 348.1594; found: 348.1604. **FTIR (cm^{-1})** 3442, 3019, 2886, 2404, 1621, 1496.

2-(Benzyl(3,4-difluorophenyl)amino)-1-phenylethan-1-ol (3r). Yellow oil, 0.110 g, 65%. R_f (Pet. ether/EtOAc = 90/10): 0.48; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.41−7.31 (m, 7H), 7.26 (t, J = 7.3 Hz, 1H), 7.16 (d, J = 7.3 Hz, 2H), 6.99 (dd, J_1 = 19.1 Hz, J_2 = 9.3 Hz, 1H), 6.62 (ddd, J_1 = 13.8 Hz, J_2 = 6.6 Hz, J_3 = 3.1 Hz, 1H), 6.49−6.47 (m, 1H), 5.01 (dd, J_1 = 8.3 Hz, J_1 = 4.5 Hz, 1H), 4.58 (d, J = 17.1 Hz, 1H), 4.47 (d, J = 17.1 Hz, 1H), 3.60 (qd, J_1 = 15.1, J_2 = Hz, 2H), 2.40 (s, 1H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 150.8 (dd, J_1 = 244.6, J_2 = 13.4 Hz), 146.0 (d, J = 8.2 Hz), 143.0 (dd, J_1 = 236.9, J_2 = 12.7 Hz), 141.9, 137.7, 128.9, 128.8, 128.2, 127.2, 126.7, 125.99, 117.5 (d, J = 17.3 Hz), 108.5, 102.4 (d, J = 21.7 Hz), 72.2, 60.1, 55.7. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{21}H_{20}F_2NO$: 340.1507; found: 340.1508. **FTIR (cm^{-1})** 3429, 3069, 3019, 2968, 2866, 2404, 1599, 1517.

2-(Benzyl(2,5-dimethylphenyl)amino)-1-phenylethan-1-ol (3s). Yellow oil, 0.094 g, 57%. R_f (Pet. ether/EtOAc = 90/10): 0.53; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.33−7.29 (m, 8H), 7.21−7.19 (m, 2H), 7.13 (d, J = 7.9 Hz, 1H), 6.91 (d, J = 6.9 Hz, 2H), 4.63 (dd, J_1 = 10.3, J_2 = 3.2 Hz, 1H), 4.14 (d, J = 13.8 Hz, 1H), 4.07 (d, J = 13.8 Hz, 1H), 3.41 (s, 1H), 3.29 (dd, J_1 = 13.0, J_2 = 3.2 Hz, 1H), 2.94 (dd, J_1 = 13.0, J_2 = 10.3 Hz, 1H), 2.36 (s, 3H), 2.30 (s, 3H). **^{13}C NMR (100**

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MHz, $CDCl_3$) δ 149.0, 142.1, 137.6, 136.3, 131.3, 129.4, 128.4, 128.4, 127.6, 127.5, 126.1, 125.7, 124.1, 70.4, 60.8, 60.2, 21.2, 18.2. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{23}H_{26}NO$: 332.2009; found: 332.2022. **FTIR (cm^{-1})** 3441, 3019, 2927, 2405, 1604, 1501.

2-(Benzyl(naphthalen-2-yl)amino)-1-phenylethan-1-ol (3t). Yellow oil, 0.101 g, 57%. R_f (Pet. ether/EtOAc = 90/10): 0.57; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.78 (d, J = 8.9 Hz, 2H), 7.70 (d, J = 8.2 Hz, 1H), 7.49−7.26 (m, 13H), 7.15 (s, 1H), 5.17 (dd, J_1 = 7.6, J_2 = 5.2 Hz, 1H), 4.79 (d, J = 17.0 Hz, 1H), 4.66 (d, J = 17.0 Hz, 1H), 3.96−3.60 (m, 2H), 2.66 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 146.6, 142.2, 138.3, 135.0, 129.2, 128.7, 128.0, 127.5, 127.4, 126.7, 126.4, 126.1, 122.5, 116.7, 107.5, 72.1, 59.7, 55.5. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{25}H_{24}NO$: 354.1852; found: 354.1855. **FTIR (cm^{-1})** 3417, 3020, 2926, 2403, 1629, 1597, 1507.

2-Amino Alcohols 3u and 3u′ (1:1). Yellow oil, 0.111 g, 70%. R_f (Pet. ether/EtOAc = 90/10): 0.54; **^{1}H NMR of 3u (400 MHz, $CDCl_3$)** δ 7.46−7.21 (m, 10H), 7.12 (d, J = 8.25 Hz, 2H), 6.85 (d, J = 8.67 Hz, 2H), 5.11−5.07 (m, 1H), 4.71−4.73 (m, 2H), 3.67−3.57 (m, 2H), 2.66 (s, 1H), 2.38 (s, 3H). **^{13}C NMR of 3u (100 MHz, $CDCl_3$)** δ 146.7, 142.1, 138.6, 129.3, 128.6, 127.9, 126.9, 126.9, 114.2, 110.7, 71.9, 59.7, 55.4, 20.4. **^{1}H NMR of 3u′ (400 MHz, $CDCl_3$)** δ 7.46−7.21 (m, 10H), 7.18 (d, J = 7.8 Hz, 1H), 6.75−6.72 (m, 2H), 6.67 (d, J = 7.6 Hz, 1H), 5.07−5.04 (m, 1H), 4.57−4.51 (m, 2H), 3.67−3.57 (m, 2H), 2.58 (s, 1H), 2.34 (s, 3H). **^{13}C NMR of 3u′ (100 MHz, $CDCl_3$)** δ 148.9, 142.2, 139.1, 130.0, 128.7, 128.7, 127.9, 127.0, 126.0, 118.5, 114.1, 72.0, 60.1, 55.8, 22.1. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{22}H_{24}NO$: 318.18524; found: 318.18527. **FTIR (cm^{-1})** 3442, 3018, 2405, 1955, 1877, 1812, 1605, 1508.

2-Amino Alcohols 3v and 3v′ (3:1). Yellow oil, 0.104 g, 65%. R_f (Pet. ether/EtOAc = 90/10): 0.47; **^{1}H NMR of Major isomer 3v (400 MHz, $CDCl_3$)** δ 7.42−7.14 (m, 10H), 6.96 (t, J = 8.7 Hz, 2H), 6.83−6.80 (m, 2H), 4.99 (dd, J = 7.8, 5.0 Hz, 1H), 4.68−4.47 (m, 2H), 3.61−3.52 (m, 2H), 2.57 (s, 1H). **^{13}C NMR of Major isomer 3v (100 MHz, $CDCl_3$)** δ 157.4, 150.5 (d, J = 10.4 Hz), 142.0, 138.2, 130.5 (d, J = 10.4 Hz), 128.8, 127.2, 127.1, 126.0, 115.9, 115.7, 103.6 (d, J = 22.1 Hz), 100.1 (d, J = 25.3 Hz), 72.0, 60.6, 56.4. **^{1}H NMR of Minor isomer 3v′ (400 MHz, $CDCl_3$)** δ 7.42−7.14 (m, 11H), 6.60 (dd, J_1 = 8.3 Hz, J_2 = 1.9 Hz, 1H), 6.54 (d, J = 12.8 Hz, 1H), 6.46 (t, J = 8.1 Hz, 1H), 5.08 (dd, J = 7.9, 4.7 Hz, 1H),), 4.68−4.47 (m, 2H), 3.71−3.64 (m, 2H), 2.34 (s, 1H). **Representative ^{13}C NMR peaks of Minor isomer 3v′ (100 MHz, $CDCl_3$)** δ 155.0, 137.9, 128.2, 128.1, 126.6, 115.5 (d, J = 7.2 Hz), 108.6, 72.3, 59.6, 55.2. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{21}H_{21}FNO$: 322.1602; found: 322.1604. **FTIR (cm^{-1})** 3245, 3018, 2926, 2404, 1892, 1600, 1504.

Procedure for the TFA-Promoted Reaction of Azetidine, Arynes, and H_2O. To a flame-dried screw-capped test tube equipped with a magnetic stir bar were added KF (87 mg, 1.5 mmol) and 18-crown-6 (0.396 g, 1.5 mmol) inside a glovebox. THF (2.0 mL) was added outside the glovebox under an argon atmosphere. To this solution was added trifluoroacetic acid (0.057 g, 39 μL, 0.50 mmol) with continued stirring for 5 min at 30 °C. After 5 min of stirring, 1-benzyl-2-phenylazetidine **4a** (0.112 g, 0.5 mmol) was added. Then the reaction mixture was cooled to −10 °C and **1** (0.75 mmol) was added. After stirring for 10 min at −10 °C, H_2O (18 μL, 1.0 mmol) was added. Then the reaction mixture was slowly warmed to 30 °C with continued stirring for 12 h. After 12 h, the reaction was stopped, the solvent was evaporated, and the crude residue was preadsorbed on silica gel and purified by flash column chromatography (Pet. ether/EtOAc = 93/7) on silica gel to afford the product as a yellow oil **5**. It may be mentioned that the reaction works well without glovebox techniques maintaining the isolated yield of **5**.

3-(Benzyl(phenyl)amino)-1-phenylpropan-1-ol (5a). Yellow oil, 0.113 g, 71%. R_f (Pet. ether/EtOAc = 80/20): 0.40; **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.38−7.20 (m, 12H), 6.77−6.72 (m, 7.7 Hz, 3H), 4.77 (t, J = 6.4 Hz, 1H), 4.57 (s, 2H), 3.65−3.51 (m, 2H), 2.28 (s, 1H), 2.10 (dd, J = 13.8, 7.2 Hz, 2H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 148.7, 144.5, 139.0, 129.3, 128.7, 127.8, 126.9, 126.9, 125.8, 116.8, 113.1, 72.9, 55.1, 48.2, 36.3. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{22}H_{24}NO$: 318.1852; found: 318.1847. **FTIR (cm^{-1})** 3425, 3060, 2926, 2253, 1640, 1601, 1501.

3-(Benzyl(naphthalen-2-yl)amino)-1-phenylpropan-1-ol (5g). Yellow oil, 0.094 g, 51%. R_f (Pet. ether/EtOAc = 80/20): 0.45; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77−7.66 (m, 4H), 7.56 (d, J = 8.2 Hz, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.39−7.18 (m, 9H), 7.14−7.11 (m, 1H), 6.91 (s, 1H), 4.79 (t, J = 6.3 Hz, 1H), 4.66 (s, 2H), 3.71−3.57 (m, 2H), 2.33−2.11 (m, 3H). **^{13}C NMR (100 MHz, $CDCl_3$)** 146.5, 144.5, 138.8, 135.1, 129.1, 128.7, 127.9, 127.7, 127.5, 127.1, 127.0, 126.4, 126.3, 125.9, 124.1, 122.9, 122.2, 116.6, 105.0, 72.9, 55.2, 48.2, 36.3. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{26}H_{26}NO$: 368.2009; found: 368.2005. **FTIR (cm^{-1})** 3422, 3055, 2929, 2254, 1641, 1610.

(*R*)-2-(Butyl(phenyl)amino)-1-phenylethan-1-ol ((*R*)-3b). Yellow oil, 0.098 g, 73%. R_f (Pet. ether/EtOAc = 90/10): 0.51; er = 98:2, $[\alpha]_D^{26}$ = −11.2 (*c* 1.0, $CHCl_3$), HPLC (Chiralpak AD, 95:05 (Hexane/IPA, 1.0 mL/min), Major: 8.7 min, Minor: 8.1 min. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.47−7.40 (m, 4H), 7.37−7.29 (m, 3H), 6.89 (d, J = 8.0 Hz, 2H), 6.81 (t, J = 7.2 Hz, 1H), 4.99 (dd, J_1 = 8.9 Hz, J_2 = 4.1 Hz, 1H), 3.54 (dd, J_1 = 14.7 Hz, J_2 = 4.1 Hz, 1H), 3.45 (dd, J_1 = 14.7 Hz, J_2 = 9.0 Hz, 1H), 3.37−3.30 (m, 2H), 2.67 (s, 1H), 1.62−1.55 (m, 7.7, 2.7 Hz, 2H), 1.39−1.33 (m, 7.5 Hz, 2H), 0.97 (t, J = 7.4 Hz, 3H). **^{13}C NMR (125 MHz, $CDCl_3$)** δ 148.5, 142.1, 129.4, 128.6, 127.9, 126.0, 117.3, 113.8, 71.5, 60.1, 52.3, 28.8, 20.4, 14.1. **HRMS (ESI)** calculated $[M + H]^+$ for $C_{18}H_{24}NO$: 270.1852; found: 270.1855. **FTIR (cm^{-1})** 3451, 3018, 2958, 2872, 2404, 1598, 1501.

Gram Scale Synthesis of 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol. An oven-dried round bottomed flask with a magnetic stir bar was charged with KF (0.870 g, 15.0 mmol) and 18-crown-6 (3.96 g, 15.0 mmol) inside a glovebox. THF (20 mL) was added outside of the glovebox under an argon atmosphere. To this solution was added trifluoroacetic acid (0.570 g, 0.390 μL, 5.0 mmol) with continued stirring for 5 min at 30 °C. After 5 min of stirring, 1-benzyl-2-phenylaziridine **2a** (1.05 g, 5.0 mmol) was added. Then the reaction mixture was cooled to −10 °C and 2-(trimethylsilyl)phenyl trifluoromethanesulfonate **1a** (2.23 g, 1.82 mL, 7.5 mmol) was added. After stirring for 10 min at −10 °C, H_2O (180 μL, 10.0 mmol) was added. Then the reaction mixture was slowly warmed to 30 °C with stirring maintained for 12 h. After 12 h the reaction was stopped, the solvent was evaporated, and the crude residue was preadsorbed on silica gel and purified by flash column chromatography (Pet. ether/EtOAc = 95/05) on silica gel to afford the 2-(benzyl(phenyl)amino)-1-phenylethan-1-ol as yellow oil **3a** (1.05 g, 69% yield). It may be mentioned that the reaction works well without glovebox techniques, maintaining the isolated yield of **3**.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01798.

Details on mechanistic experiments, copies of ^{1}H and ^{13}C NMR spectra of all products, HPLC data for (*R*)-**3b** (PDF)

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Notes

The authors declare no competing financial interest.

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