An Efficient Method for Cleavage of Epoxides with Aromatic Amines

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β-Amino alcohols are an important class of organic compounds which have found much use in medicinal chemistry.[1] Classically, these were synthesized by an opening of epoxides with an excess of amines at elevated temperature. Since the high temperature may not be ideal for certain functional groups, a variety of activators have been introduced in the literature to carry out epoxide opening at room temperature.[2] During the past few years, a variety of metal triflates have also been used to catalyze the opening of epoxides with amines.[3] However, there are still some limitations with the literature methods. For example, deactivated aromatic amines such as *p*-nitroaniline failed to open epoxides or still required higher temperature. While working as a part of our program on asymmetric synthesis using chiral copper complexes of diphenylpybox ligands,[4] we discovered that $Cu(OTf)_2$ catalyzed an epoxide opening reaction with both deactivated and activated aromatic amines. However, it failed to catalyze the reaction with aliphatic amines. This observation was in a sharp contrast to the results from the other known metal triflates[3] which worked on aliphatic and aromatic amines both.[5] The unusual preference in the epoxide cleavage with aromatic amines using $Cu(OTf)_2$ prompted us to look at the reaction in detail, and herein we delineate our results. We also report here that the same reaction can be carried out using tin(II) triflate as a catalyst.

At the outset, the reaction was done using cyclohexene oxide and aniline using 5 mol % of $Cu(OTf)_2$ in ether at room temperature for 30 h, and the product **1a** was obtained in almost quantitative yield. The trans stereochemistry for the amino alcohol **1a** (entry 1) was deduced from the coupling constant (J = 9.9, 9.9, and 4.5 Hz) of the peak at 3.34 ppm (C*H*−OH) in ^{1}H NMR spectrum. Likewise, the peak at 3.14 ppm for C*H*−NHPh showed the similar kind of splitting pattern (ddd, J = 10.8, 9.3, 3.9 Hz). The reaction was then studied in several solvents, and it was found that diethyl ether (95% yield) was superior to CH_2Cl_2 (90% yield), MeCN (75% yield), and THF (71% yield). We also carried out the above reaction using a catalytic amount (5 mol %) of $Sn(OTf)_2$ which took a little shorter time (20 h) in the opening of epoxides with aromatic amines, and the amino alcohol was identical by TLC and NMR with the one obtained from the use of copper triflate. To show the scope of the reaction, we extended it to a variety of aromatic amines and epoxides using both catalysts. In all cases, a very clean reaction was observed and the amino alcohols had trans stereochemistry (Table 1).

The epoxide opening reaction tolerated a varying amount of steric hindrance on aromatic amines such as *o*-methyl and α-naphthyl. However, in case of 2,6-dimethylaniline, the isolated yield of the epoxide opened product was not very high (46−50%). The reaction worked very well on five-, six-, and seven-membered epoxides. In the case of cyclooctene oxide, the reaction required reflux temperature in MeCN and tin triflate was found to be a better catalyst than copper triflate (entry 21). It was gratifying to observe that unsaturated cyclooctene oxide could be opened at room temperature with aromatic amines (entries 22 and 23). In case of acyclic terminal olefins such as 1-dodecene oxide (entry 24), a mixture of two separable regioisomers (**6a** and **6b**) was obtained in a ratio of 8:1 where the major product (**6a**) was formed due to the attack of amine at the terminal carbon. Both regioisomers were isolated and fully characterized in order to avoid ambiguity. The epoxide opening reaction was also smooth in a disubstituted acyclic epxoide such as *cis*-2,3-epoxybutane (entry 25).

The worthy feature of the reaction is that highly deactivated amines such as *p*-nitroaniline also opened the epoxides in a reasonable yield. Although the isolated yield in the epoxide opening reaction with aromatic amines catalyzed by $Cu(OTf)_2$ and $Sn(OTf)_2$ is comparable, the reaction was faster with the latter catalyst. The unusual feature of this reaction is that only aromatic amines opened the epoxides. Aliphatic amines such as diethylamine, *n*-butylamine, benzylamine, and pyrrolidine failed to react with epoxides at room temperature for 2 days in the presence of a catalytic amount of copper or tin triflate. Although we do not have any proof for the mechanism, we feel that it is ionic in nature. Aliphatic amines by virtue of its higher basicity made stronger complex to the copper and tin triflate which failed to activate the epoxides. This was deduced from an observation that aniline failed to open cyclohexene oxide in the presence of *n*-butylamine and copper or tin triflate under the above condition.

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(2) (a) Fu, X.-L.; Wu, S.-H. *Synth. Commun.* **1997**, *27*, 1677 ($SmCl_3$). (b) V de Weghe, P.; Collin, J. *Tetrahedron Lett.* **1995**, *36*, 1649 (SmI_2). (c) Chini, M.; Crotti, P.; Macchia, F. *J. Org. Chem.* **1991**, *56*, 5939 and references therein (metal salts). (d) Iqbal, J.; Pandey, A. *Tetrahedron Lett.* **1990**, *31*, 575 ($CoCl_2$). (e) Yamada, J.-I.; Yumoto, M.; Yamamoto, Y. *Tetrahedron Lett.* **1989**, *30*, 4255 (R'_3PbNR_2). (f) Overman, L. E.; Flippin, L. A. *Tetrahedron Lett.* **1981**, *22*, 195 (Al amide). (g) Carre, M. C.; Houmounou, J. P.; Caubere, P. *Tetrahedron Lett.* **1985**, *26*, 3107 (Mg amide). (h) Yamada, J.-I.; Yumoto, M.; Yamamoto, Y. *Tetrahedron Lett.* **1989**, *30*, 4255 (Pb amide). (i) Papini, A.; Ricci, A.; Taddei, M.; Seconi, G.; Dembech, P. *J. Chem. Soc. Perkin Trans. 1* **1984**, 2261 (silicon amides). (j) Posner, G. H.; Rogers, D. Z. *J. Am. Chem. Soc.* **1977**, *99*, 8208 (amines adsorbed on alumina).

(3) (a) Auge, J.; Leroy, F. *Tetrahedron Lett.* **1996**, *37*, 7715 (LiOTf). (b) Chini, M.; Crotti, P.; Favero, L.; Macchia, F.; Pineschi, M. *Tetrahedron Lett.* **1994**, *35*, 433 [$La(OTf)_3$]. (c) Meguro, M.; Asao, N.; Yamamoto, Y. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2597 [$(Yb(OTf)_3$]. (d) Fujiwara, M.; Imada, M.; Baba, A.; Matsuda, H. *Tetrahedron Lett.* **1989**, *30*, 739 (Ph_4SbOTf).

(4) (a) Sekar, G.; DattaGupta, A.; Singh, V. K. *J. Org. Chem.* **1998**, *63*, 2961. (b) DattaGupta, A.; Singh, V. K. *Tetrahedron Lett.* **1996**, *37*, 2633. (c) DattaGupta, A.; Bhuniya, D.; Singh, V. K. *Tetrahedron* **1994**, *50*, 13725.

(5) There are two reports (ref 2a,d) in the literature for a similar kind of preference for aromatic amines in the opening of epoxides; however, the yield was modest even for activated aromatic amines and the reaction failed with deactivated aromatic amines such as *p*-nitroaniline.

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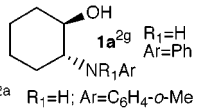
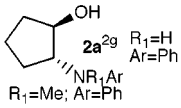
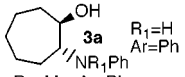
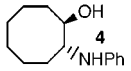
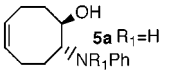
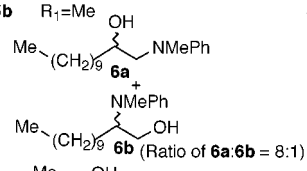
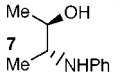
Table 1. Sn(II)- and Cu(II) Triflate Catalyzed Epoxide Opening with Aromatic Amines in Ether at rt for 20−30 h[a]

Entry	Amino alcohols	Isolated Yield (%) $Sn(OTf)_2$	Isolated Yield (%) $Cu(OTf)_2$
1.	 **1a**[2g] R_1=H Ar=Ph	94	95
2.	**1b**[2a] R_1=H; Ar=C_6H_4-*o*-Me	94	92
3.	**1c** R_1=H; Ar=C_6H_4-*m*-Br	94	97
4.	**1d**[2a] R_1=H; Ar=C_6H_4-*p*-OMe	95	97
5.	**1e**[2a] R_1=H; Ar=C_6H_4-*p*-Br	93	88
6.	**1f** R_1=H; Ar=C_6H_3-*o*,*o*'-dimethyl	50	46
7.	**1g**[2a] R_1=H; Ar=α-naphthyl	79	80
8.	**1h** R_1=H; Ar=β-naphthyl	86	81
9.	**1i**[6] R_1=H; Ar=C_6H_4-*o*-OH	93	96
10.	**1j**[7] R_1=H; Ar=C_6H_4-*p*-NO_2	77	66
11.	**1k** R_1=Me; Ar=Ph	86	88
12.	**1l** R_1=Benzyl; Ar=Ph	-	65
13.	 **2a**[2g] R_1=H Ar=Ph	77	75
14.	**2b** R_1=Me; Ar=Ph	74	75
15.	**2c** R_1=Et; Ar=Ph	56	55
16.	**2d** R_1=H; Ar=C_6H_4-*p*-NO_2	57	60
17.	 **3a** R_1=H Ar=Ph	67	64
18.	**3b** R_1=Me; Ar=Ph	55	55
19.	**3c** R_1=Et; Ar=Ph	43	39
20.	**3d** R_1=H; Ar=C_6H_4-*p*-NO_2	39	31
21.	 **4**	30	05
22.	 **5a** R_1=H	61	48
23.	**5b** R_1=Me	48	51
24.	 **6a** + **6b** (Ratio of **6a**:**6b** = 8:1)	84	82
25.	 **7**	85	75

[a] Entry 21 was done in MeCN at 80 °C for 20 h.

Irrespective of a mechanism, the cleavage of epoxides with aromatic amines is unique and will be highly useful in organic synthesis. To the best of our knowledge, the above catalysts are not known to catalyze epoxide opening reaction with aromatic amines. A variety of chiral nonracemic ligands can be complexed with copper or tin triflate for asymmetric version of the reaction which is in progress in our laboratory.

Experimental Section

General Procedure for Epoxide Opening with Aromatic Amines. A solution of an epoxide (1 mmol) and an aromatic amine (1.3 mmol) in anhydrous ether (5 mL) was treated with $Cu(OTf)_2$ (5 mol %) for 30 h or with $Sn(OTf)_2$ (5 mol %) for 20 h at room temperature (except entry 19 which was done in MeCN at reflux temperature). The solvent was removed on a rotary evaporator, and the crude product was purified over silica gel by column chromatography to provide pure trans amino alcohol in high yield (cf. Table 1).

***trans*-2-(Phenylamino)cyclohexanol (1a):**[2g] mp 58−59 °C (lit.[2g] mp 60−62 °C); R_f 0.25 (1:10, EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (m, 1H), 1.34 (m, 3H), 1.75 (m, 2H), 2.12 (m, 2H), 3.04 (bs, 2H, N*H* and O*H*), 3.14 (ddd, *J* = 10.8, 9.3, 3.9 Hz, 1H), 3.34 (ddd, *J* = 9.9, 9.9, 4.5 Hz, 1H), 6.75 (m, 3H), 7.1 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.2, 24.9, 31.5, 33.1, 60.0, 74.3, 114.2, 118.2, 129.2, 147.7.

***trans*-2-(*o*-Methylphenylamino)cyclohexanol (1b):**[2a] viscous liquid; R_f 0.37 (1:10, EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.08 (m, 1H), 1.38 (m, 3H), 1.78 (m, 2H), 2.16 (m, 2H), 2.18 (s, 3H), 3.00 (bs, 2H, N*H* and O*H*), 3.23 (ddd, *J* = 10.9, 9.3, 3.9 Hz, 1H), 3.44 (ddd, *J* = 10.5, 10.5, 4.8 Hz, 1H), 6.72 (m, 1H), 6.81 (d, *J* = 7.8 Hz, 1H), 7.12 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.62, 24.21, 24.92, 31.75, 33.17, 59.72, 74.44, 111.46, 117.73, 123.00, 127.06, 130.32, 145.62; LCMS (APCI, *m*/*z*) 206 ($M^+ + 1$).

***trans*-2-(*m*-Bromophenylamino)cyclohexanol (1c):** viscous liquid; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.01 (m, 1H), 1.30 (m, 3H), 1.72 (m, 2H), 2.08 (m, 2H), 3.07 (ddd, *J* = 10.6, 9.0, 3.6 Hz, 1H), 3.2 (bs, 2H, N*H* and O*H*), 3.31 (ddd, *J* = 9.9, 9.9, 4.2 Hz, 1H), 6.59 (ddd, *J* = 8.1, 2.1, 0.9 Hz, 1H), 6.83 (m, 2H), 7.00 (dd, *J* = 8.4, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.11, 24.71, 31.39, 33.23, 59.68, 74.22, 112.69, 116.45, 120.67, 123.14, 130.46, 149.14; LCMS (APCI, *m*/*z*) 270 and 271 (1:1, $M^+ + 1$).

***trans*-2-(*p*-Methoxyphenylamino)cyclohexanol (1d):**[2a] mp 58−59 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.00 (m, 1H), 1.30 (m, 3H), 1.71 (m, 2H), 2.05 (m, 2H), 2.97 (ddd, *J* = 10.9, 9.3, 3.9 Hz, 1H), 3.28 (s, 2H, N*H* and O*H*), 3.31 (ddd, *J* = 9.6, 9.6, 3.9 Hz, 1H), 3.73 (s, 3H), 6.68 (d, *J* = 8 Hz, 2H), 6.78 (d, *J* = 8 Hz 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.15, 24.86, 31.25, 33.07, 55.56, 61.48, 74.03, 114.67, 116.28, 141.29, 152.73; LCMS (APCI, *m*/*z*) 222 ($M^+ + 1$).

***trans*-2-(2,6-Dimethylphenylamino)cyclohexanol (1f):** viscous liquid; IR (neat) 3140−3620 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (m, 1H), 1.32 (m, 3H), 1.78 (m, 3H), 2.12 (m, 1H), 2.30 (s, 6H), 2.87 (ddd, *J* = 10.9, 9.3, 3.9 Hz, 1H), 3.42 (ddd, *J* = 10.2, 10.2, 4.5 Hz, 1H), 3.60 (bs, 2H, N*H* and O*H*), 6.85 (dd, *J* = 7.8, 6.9 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (CDCl3, 75 MHz) δ 19.17, 24.26, 25.23, 32.41, 33.02, 63.36, 75.07, 122.25, 129.08, 129.75; LCMS (APCI, *m*/*z*) 220 ($M^+ + 1$).

***trans*-2-(α-Naphthylamino)cyclohexanol (1g):**[2a] mp 84−85 °C; IR (KBr) 3100−3600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.16 (m, 1H), 1.42 (m, 3H), 1.80 (m, 2H), 2.24 (m, 2H), 2.98 (bs, 2H, N*H* and O*H*), 3.39 (ddd, *J* = 10.9, 9.3, 3.9 Hz, 1H), 3.54 (ddd, *J* = 9.6, 9.6, 4.2 Hz, 1H), 6.82 (dd, *J* = 6.3, 0.9 Hz, 1H), 7.30 (m, 2H), 7.45 (m, 2H), 7.84 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.30, 24.92, 31.23, 33.39, 59.84, 74.59, 106.41, 118.32, 119.92, 124.21, 124.87. 125.75, 126.41, 128.76, 134.44, 142.77; LCMS (APCI, *m*/*z*) 242 ($M^+ + 1$).

***trans*-2-(β-Naphthylamino)cyclohexanol (1h):** mp 97−99 °C; IR (KBr) 3400−3600 cm^{-1}; R_f 0.20 (1:10, EtOAc in petroleum ether); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05 (m, 1H), 1.40 (m, 3H), 1.78 (m, 2H), 2.20 (m, 2H), 3.02 (bs, 1H, O*H*), 3.30 (ddd, *J* = 9.8, 9.0, 3.9 Hz, 1H), 3.41 (ddd, *J* = 9.3, 9.3, 4.2 Hz, 1H), 6.95 (m, 2H), 7.23 (m, 1H), 7.38 (m, 1H), 7.65 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.26, 24.97, 31.47, 33.22, 60.01, 74.59, 106.46, 118.57, 122.35, 125.96, 126.38, 127.56, 127.86, 129.05, 134.96, 145.41; LCMS (APCI, *m*/*z*) 243 ($M^+ + 2$), 242 ($M^+ + 1$). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.67; H, 7.88; N, 5.81. Found: C, 79.52; H, 7.92; N, 5.88.

***trans*-2-(4-Nitrophenylamino)cyclohexanol (1j):**[7] mp 119−121 °C; IR (KBr) 3500 cm^{-1}; ^{1}H NMR (CD_3OD, 300 MHz) δ 1.30 (bm, 4H), 1.75 (m, 2H), 2.00 (m, 2H), 3.29 (m, 1H), 3.43 (ddd, *J* = 10.2, 10.2, 4.5 Hz, 1H), 4.84 (s, 2H, N*H* & O*H*), 6.65 (d, *J* = 9.3 Hz, 2H), 7.98 (d, *J* = 9.3 Hz, 2H); ^{13}C NMR (CD_3OD, 75 MHz) δ 25.34, 25.53, 32.24, 35.17, 59.22, 74.70, 112.12, 127.28,137.0, 156.16; LCMS (APCI, *m*/*z*) 237 ($M^+ + 1$).

***trans*-2-(*N*-Methyl-*N*-phenylamino)cyclohexanol (1k):** viscous liquid; R_f 0.43 (1:10, EtOAc in petroleum ether); IR (film) 3050−3600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.28 (m, 2H), 1.40 (m, 2H), 1.78 (m, 3H), 2.20 (m, 1H), 2.77 (s, 3H), 3.42 (ddd, *J* = 10.9, 9.6, 3.6 Hz, 1H), 3.67 (ddd, *J* = 10.2, 10.2, 4.8 Hz, 1H), 6.82 (dd, *J* = 6.9, 6.9 Hz, 1H), 6.96 (d, *J* = 8.1 Hz, 2H), 7.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.27, 25.41, 25.98, 31.04, 33.29, 66.92, 69.94, 115.52, 118.45, 129.01, 151.32; LCMS

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(7) Chinnakali, K.; Fun, H.-K.; Sriraghavan, K.; Ramakrishnan, V. T. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1997**, *C53*, 1865.

(APCI, *m*/*z*) 206 ($M^+ + 1$). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.67; H, 7.88; N, 5.81. Found: C, 79.62; H, 7.90; N, 5.90.

***trans*-2-(*N*-Benzyl-*N*-phenylamino)cyclohexanol (1l):** viscous liquid; IR (neat) 3000−3600 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.38 (m, 4H), 1.80 (m, 2H), 1.94 (m, 1H), 2.19 (m, 1H), 2.84 (bs, 1H, O*H*), 3.65 (m, 2H), 4.48 (d, J = 10.5 Hz, 2H), 6.82 (m, 1H), 7.00 (m, 2H), 7.25 (m, 3H), 7.36 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 24.19, 25.38, 26.99, 33.60, 48.91, 66.38, 70.62, 116.21, 118.62, 126.62, 126.76, 128.60, 128.96, 139.58, 149.7. Anal. Calcd for $C_{19}H_{23}NO$: C, 81.14; H, 8.19; N, 4.98. Found: C, 81.42; H, 8.32; N, 5.08.

***trans*-2-(Phenylamino)cyclopentanol (2a):**[2g] mp 54−55 °C (lit.[2g] mp 57−58 °C);); R_f 0.13 (1:10, EtOAc in petroleum ether); IR (KBr) 3100−3580 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (m, 1H), 1.62 (m, 1H), 1.78 (m, 2H), 1.98 (m, 1H), 2.10 (m, 1H), 3.12 (bs, 2H, N*H* and O*H*), 3.60 (m, 1H), 4.03 (m, 1H), 6.70 (m, 3H), 7.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.83, 30.95, 32.59, 61.92, 77.94, 113.31, 117.42, 129.15, 147.63.

***trans*-2-(*N*-Methyl-*N*-phenylamino)cyclopentanol (2b):** viscous liquid; R_f 0.35 (1:10, EtOAc in petroleum ether); IR (neat) 3100−3580 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.58−2.08 (bm, 6H + O*H*), 2.80 (s, 3H), 3.97 (m, 1H), 4.21 (m, 1H), 6.74 (dt, J = 7.2, 0.6 Hz, 1H), 6.89 (d, J = 8.7 Hz, 2H), 7.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.83, 24.39, 31.50, 32.24, 68.09, 74.49, 114.23, 117.44, 129.10, 151.08; LCMS (APCI, *m*/*z*) 192 ($M^+ + 1$).

***trans*-2-(*N*-Ethyl-*N*-phenylamino)cyclopentanol (2c):** viscous liquid; R_f 0.37 (1:10, EtOAc in petroleum ether); IR (neat) 3100−3580 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (t, J = 6.9 Hz, 3H), 1.6 (m, 2H), 1.8 (m, 2H), 2.0 (m, 2H), 3.28 (m, 2H), 3.91 (m, 1H), 4.20 (m, 1H), 6.74 (m, 1H), 6.88 (tt, J = 7.2, 0.9 Hz, 1H), 7.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.63, 19.72, 25.69, 31.53, 40.55, 67.60, 74.93, 114.76, 117.33, 129.13, 149.37; LCMS (APCI, *m*/*z*) 206 ($M^+ + 1$). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.10; H, 9.27; N, 6.83. Found: C, 76.32; H, 9.22; N, 6.90.

***trans*-2-(4-Nitrophenylamino)cyclopentanol (2d):** semisolid; R_f 0.27 (1:4, EtOAc in petroleum ether); IR (KBr) 3100−3580 cm^{-1}; ^1H NMR (CD_3OD, 300 MHz) δ 1.40−2.02 (m, 5H), 2.22 (m, 1H), 3.65 (m, 1H), 3.75 (bs, O*H*), 3.85 (bs, N*H*), 4.02 (m, 1H), 6.65 (d, J = 9.3 Hz, 2H), 8.00 (d, J = 9.3 Hz, 2H); ^{13}C NMR (CD_3OD, 75 MHz) δ 22.29, 31.17, 33.69, 62.48, 78.37, 112.24, 127.20, 137.92, 155.65; LCMS (APCI, *m*/*z*) 223 ($M^+ + 1$).

***trans*-2-(Phenylamino)cycloheptanol (3a):** mp 59−60 °C; R_f 0.27 (1:10, EtOAc in petroleum ether); IR (KBr) 3140−3600 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.2−1.8 (bm, 9H), 1.98 (m, 1H), 3.05 (bs, 1H, O*H*), 3.24 (ddd, J = 9.3, 9.3, 3.3 Hz, 1H), 3.46 (ddd, J = 8.4, 8.4, 3.6 Hz, 1H), 6.72 (m, 3H), 7.24 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.13, 24.03, 27.18, 30.24, 32.79, 62.76, 114.92, 118.73, 129.36, 147.47; LCMS (APCI, *m*/*z*) 206 ($M^+ + 1$). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.10; H, 9.27; N, 6.83. Found: C, 76.42; H, 9.12; N, 6.90.

***trans*-2-(*N*-Methyl-*N*-phenylamino)cycloheptanol (3b):** viscous liquid; R_f 0.50 (1:10, EtOAc in petroleum ether); IR (neat) 3140−3600 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.38−1.80 (bm, 9H), 2.08 (m, 1H), 2.74 (s, 3H), 3.06 (bs, 1H, O*H*), 3.48 (ddd, J = 9.3, 9.3, 2.4 Hz, 1H), 3.74 (ddd, J = 9.3, 9.3, 3.6 Hz, 1H), 6.84 (tt, J = 7.5, 0.9 Hz, 1H), 6.97 (m, 2H), 7.26 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.74, 24.35, 25.43, 26.68, 31.35, 32.66, 69.51, 72.38, 116.21, 119.03, 129.08, 151.33; LCMS (APCI, *m*/*z*) 220 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.71; H, 9.59; N, 6.39. Found: C, 76.42; H, 9.42; N, 6.20.

***trans*-2-(*N*-Ethyl-*N*-phenylamino)cycloheptanol (3c):** viscous liquid; R_f 0.63 (1:10, EtOAc in petroleum ether); IR (neat) 3140−3600 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (dt, J = 6.9, 1.8 Hz, 3H), 1.30−1.80 (bm, 9H), 2.02 (m, 1H), 3.20 (m, 2H), 3.33 (m, 1H), 3.70 (m, 1H), 6.82 (tt, J = 7.5, 0.9 Hz, 1H), 6.97 (m, 2H), 7.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.40, 21.68, 24.55, 26.10, 26.73, 32.57, 39.19, 70.85, 72.69, 117.77, 119.40, 129.04, 149.30; LCMS (APCI, *m*/*z*) 234 ($M^+ + 1$).

***trans*-2-(4-Nitrophenylamino)cycloheptanol (3d):** semisolid; R_f 0.39 (1:3, EtOAc in petroleum ether); IR (KBr) 3140−3600 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.42−1.90 (bm, 10H), 3.43 (m, 1H), 3.55 (bs, O*H*), 3.69 (ddd, J = 8.1, 3.9 Hz, 1H), 6.61 (d, J = 9.3 Hz, 2H), 8.02 (d, J = 9.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.52, 25.30, 29.56, 31.26, 35.26, 61.93, 77.11, 112.32, 127.32, 140.37, 157.17; LCMS (APCI, *m*/*z*) 251 ($M^+ + 1$).

***trans*-2-(Phenylamino)cyclooctanol (4):** viscous liquid; IR (neat) 3120−3620 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.6 (m, 8H), 1.86 (m, 4H), 3.22 (bs, 2H, N*H* and O*H*), 3.45 (m, 1H), 3.56 (ddd, J = 9.5, 6.6, 2.7 Hz, 1H), 6.78 (m, 3H), 7.24 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.27, 25.17, 25.67, 26.74, 29.63, 31.10, 60.02, 74.93, 115.11, 118.84, 129.35, 147.50; LCMS (APCI, *m*/*z*) 220 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{21}NO$: C, 76.71; H, 9.59; N, 6.39. Found: C, 76.82; H, 9.62; N, 6.28.

***trans*-2-(Phenylamino)cyclooct-5-en-1-ol (5a):** mp 48−50 °C; IR (KBr) 3140−3580 cm^{-1}; R_f 0.34 (1:10, EtOAc in petroleum ether); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.5 (m, 1H), 1.72 (m, 1H), 2.04 (m, 2H), 2.38 (m, 4H), 3.45 (m, 1H + N*H* and O*H*), 3.65 (ddd, J = 8.1, 8.1, 3.3 Hz, 1H), 5.58 (m, 1H), 5.75 (m, 1H), 6.7 (m, 2H), 6.78 (m, 1H), 7.20 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.82, 23.35, 32.15, 33.32, 59.04, 72.94, 115.04, 119.04, 127.67, 129.21, 130.74, 147.93. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.42; H, 8.76; N, 6.45. Found: C, 77.62; H, 8.72; N, 6.58.

***trans*-2-(*N*-Methyl-*N*-phenylamino)cyclooct-5-en-1-ol (5b):** viscous liquid; IR (neat) 3000−3600 cm^{-1}; R_f 0.62 (1:10, EtOAc in petroleum ether); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.56−1.90 (bm, 3H), 2.02 (m, 1H), 2.4 (bm, 4H), 2.77 (s, 3H), 3.42 (bs, 1H, O*H*), 3.85 (m, 2H), 5.52 (m, 1H), 5.72 (m, 1H), 6.85 (m, 1H), 6.92 (m, 2H), 7.27 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.93, 24.16, 25.98, 32.50, 64.06, 70.28, 116.08, 119.17, 126.52, 129.09, 131.54; LCMS (APCI, *m*/*z*) 256 ($M^+ + 1$). Anal. Calcd for $C_{17}H_{21}NO$: C, 80.00; H, 8.24; N, 5.49. Found: C, 79.82; H, 8.12; N, 5.52.

1-(*N*-Methyl-*N*-phenylamino)dodecan-2-ol (6a):[8] viscous liquid; R_f 0.52 (1:5, EtOAc in petroleum ether); IR (neat) 3100−3620 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, J = 6.9 Hz, 3H), 1.28 (bs, 16H), 1.5 (m, 2H), 1.57 (m, 1H), 2.2 (bs, 1H, O*H*), 2.96 (s, 3H), 3.24 (m, 2H), 3.92 (m, 1H), 6.78 (dd, J = 7.5, 7.5 Hz, 1H), 6.82 (d, J = 8.4 Hz, 2H), 7.26 (dd, J = 8.7, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.11, 22.68, 25.69, 29.32, 29.60, 29.76, 31.90, 34.53, 39.27, 60.66, 69.27, 113.40, 117.50, 129.14, 150.48; LCMS (APCI, *m*/*z*) 292 ($M^+ + 1$).

2-(*N*-Methyl-*N*-phenylamino)dodecanol (6b):[8] viscous liquid; R_f 0.47 (1:5, EtOAc in petroleum ether); IR (neat) 3100−3620 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.88 (t, J = 6.9 Hz, 3H), 1.20 (bs, 17H), 1.5 (m, 1H), 1.95 (bs, 1H, O*H*), 2.74 (s, 3H), 3.62 (m, 2H), 3.95 (m, 1H), 6.78 (dd, J = 7.5, 7.5 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.24 (dd, J = 8.7, 7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.10, 22.65, 26.45, 28.56, 29.26, 29.37, 29.51, 29.57, 29.83, 31.86, 61.56, 62.57, 114.40, 117.80, 129.12, 150.48; LCMS (APCI, *m*/*z*) 292 ($M^+ + 1$).

***trans*-3-(Phenylamino)butan-2-ol (7):** viscous liquid; IR (neat) 3140−3640 cm^{-1}; R_f 0.28 (1:10, EtOAc in petroleum ether); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (d, J = 6.3 Hz, 3H), 1.25 (d, J = 6.0 Hz, 3H), 2.82 (bs, N*H* and O*H*), 3.33 (m, 1H), 3.67 (m, 1H), 6.68 (m, 2H), 6.74 (m, 1H), 7.18 (m, 2H); MS (EI, *m*/*z*) 165 (M^+). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.14; N, 8.48. Found: C, 72.42; H, 9.02; N, 8.42.

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