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Three-Step Telescoped Synthesis of Monosubstituted Vicinal Diamines from Aldehydes

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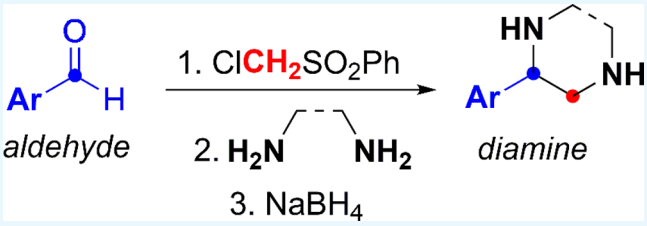
Supporting Information

ABSTRACT: Aldehydes are easily transformed into vicinal diamines and piperazines through a one-pot procedure including a Darzens reaction and treatment with an amine or diamine and then with a reducing agent. Additionally, quinoxalines can be accessed by reaction with 1,2-benzenediamine under oxidative conditions. These transformations are simple methods for the preparation of synthetically interesting monosubstituted diamines, piperazines, and quinoxalines.



INTRODUCTION

Vicinal diamines are important building blocks found in many bioactive molecules (Figure 1),[1] natural products,[2] and metal complexes displaying interesting properties.[3] Also, quinoxalines and piperazines have interesting medical properties. For instance, quinoxaline derivatives display anticancer,[4] antiviral,[5] antibacterial,[6] anti-inflammatory,[7] and antibiotic[8] activities. A piperazine moiety is considered a "privileged scaffold" in medicinal chemistry[9] and is present in many biologically active molecules.

Monosubstituted vicinal diamines are present in potent bioactive compounds such as tetracyclic antidepressants[1] mianserin and mirtazapine or k-opioid antagonist ICI-199441[1e] (Figure 1A). Although interesting approaches have been recently reported for the preparation of monosubstituted[10] and disubstituted[11] diamines, more approaches are welcome.

We report herein the preparation of monosubstituted diamines from aldehydes in a one-pot three-step process. The process comprises first the formation of an epoxysulfone by a Darzens reaction between an aldehyde and chloromethylphenylsulfone and then addition of an amine attacking the β position of the epoxide, affording an α-aminoaldehyde, which upon reductive amination with a second amine gives the corresponding diamine (Figure 1B). This chemical transformation is inspired by our previous work about chemical transformations of nitroepoxides.[11]

RESULTS AND DISCUSSION

We first prepared epoxysulfone **1a** through a Darzens reaction between benzaldehyde and chloromethylphenylsulfone. Then, epoxysulfone **1a** was combined with benzylamine in dichloromethane (DCM) for 8 h at room temperature, and then sodium borohydride was added. The reaction worked satisfactorily, affording diamine **2a** (Scheme 1). However, the conversion of epoxysulfone **1a** into diamine **2a** was very low yielding.

Hence, we turned our attention to a one-pot procedure for the transformation of aldehydes into diamines by combining the four reactions shown in Scheme 1. One-pot procedures represent interesting synthetic approaches,[12] which might improve yields as compared to step-wise sequences. First, benzaldehyde was reacted with chloromethylphenylsulfone previously treated with sodium *tert*-butoxide in dichloromethane. After the mixture was stirred for 1 h at 0 °C and then for 1 h at room temperature, benzylamine (3 equiv.) was added, and the resulting mixture was stirred for 8 h at room temperature and then sodium borohydride (6 equiv.) was added and stirred again for 8 h. Under these experimental conditions, diamines were obtained but chemical yields were not satisfying (Table 1, entries 4, 7, and 9). Under these conditions, the corresponding benzyl *p*-methylbenzyl amine was also isolated when using *p*-tolualdehyde, denoting an undesired attack of the benzylamine on the epoxysulfone (Scheme 2).

To increase the yield, an optimization process was performed by modifying the temperature, solvent, and number of equivalents. Higher yields were obtained when a temperature of 0 °C was kept during the amine treatment, favoring the attack of the amine at the β-position. This slowed the reaction, and the duration for that step had to be increased up to 18 h. Optimized conditions also comprise an increase of the number of equivalents of amine and sodium borohydride (4 and 8, respectively). A screening of solvents gave 1,2-dichloroethane as the best option in all cases (entries 1, 5, 8, and 13). Probably, the improvement of the yield with 1,2-dichloroethane as compared to dichloromethane is due to its lower volatility avoiding losses of solvents after such a long reaction time. Other assayed conditions such as the use of lithium chloride as an additive and tetrahydrofuran (THF) as a

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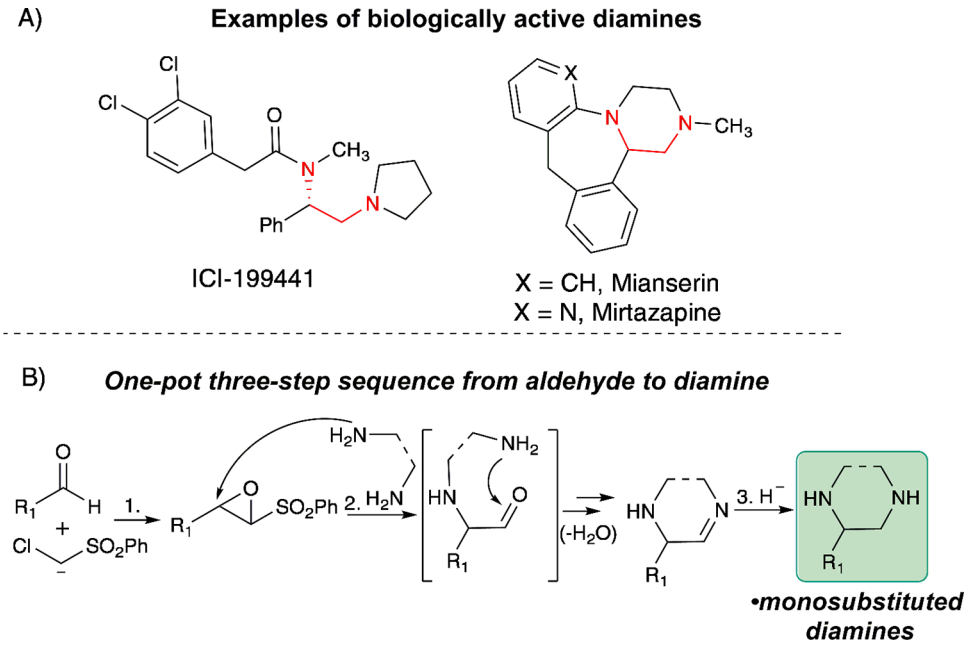


Figure 1. (a) Examples of diamines. (b) Reaction design.

Scheme 1. Synthesis of Diamines through Epoxysulfones

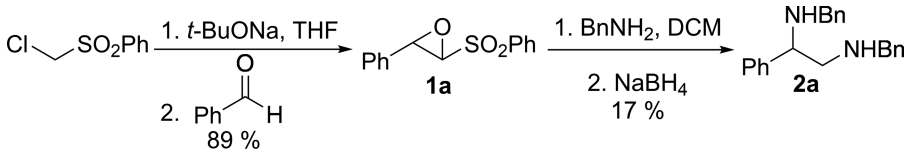
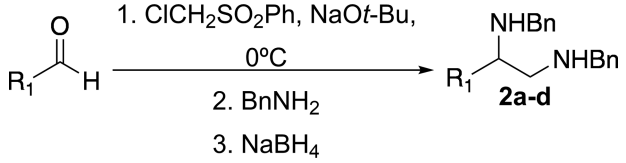


Table 1. Synthesis of Diamines from Aldehydes[a]



entry	R^1	diamine	solvent	yield (%)[b]
1	Ph	**2a**	DCE	44
2	*p*Me-Ph	**2b**	DCM	15
3	*p*Me-Ph	**2b**	THF	34
4	*p*Me-Ph	**2b**	DCE	24[c]
5	*p*Me-Ph	**2b**	DCE	40
6	*p*Cl-Ph	**2c**	DCM	25
7	*p*Cl-Ph	**2c**	DCE	22[c]
8	*p*Cl-Ph	**2c**	DCE	52
9	*p*Cl-Ph	**2c**	THF	4[d]
10	*p*Cl-Ph	**2c**	DCE	23[e]
11	*p*Cl-Ph	**2c**	DCE	5[f]
12	*p*F-Ph	**2d**	DCE	26[c]
13	*p*F-Ph	**2d**	DCE	30

[a]Reactions were performed using benzylamine (4 equiv.) and sodium borohydride (8 equiv.) at 0 °C. [b]Yield of the isolated product. [c]Reactions were carried out at room temperature. [d]The reaction was carried out by adding lithium chloride (10 equiv.). [e]The reaction was carried out under phase-transfer conditions with aq. NaOH (50%) (1 mL/mmol) and tetra-*n*-butyl ammonium bromide (0.2 equiv.). [f]Sodium triacetoxyborohydride (8 equiv.) was used instead of sodium borohydride.

solvent (entry 9), phase-transfer conditions (entry 10), or the use of sodium triacetoxyborohydride instead of sodium borohydride (entry 11) did not improve the yield.

Aliphatic aldehydes (propionaldehyde and isobutyraldehyde) and ortho-substituted aromatic aldehydes (2-chlorobenzaldehyde) were also assayed under different conditions, but only traces of desired diamines were detected. Then, we assayed the use of two different amines during the process instead of only one. Thus, *N*-benzylmethylamine (4 equiv.) was added first, then benzylamine (4 equiv.) was added when TLC showed total consumption of epoxysulfone and finally sodium borohydride. Following this procedure, diamines **2e−h** were prepared (Scheme 3). However, when benzaldehyde was first treated with benzylamine and *N*-benzylmethylamine was then added, diamine **2a** was obtained. Presumably, the aminoaldehyde intermediate resulting from the opening of epoxysulfone by benzylamine (see Figure 1b) reacts with a second equivalent of benzylamine to give a corresponding imine in contrast with *N*-benzylmethylamine. The same experimental procedure was also used for diamines **2e−h**, using morpholine instead of *N*-benzylmethylamine, and only traces of desired diamines were detected.

Then, we extended the study to the use of other amines different from benzylamines. When optimized experimental conditions (Table 1) were applied but *n*-butylamine was used as a starting material instead of benzylamine, the chemical yield of desired diamines was very low, even when the reaction was performed at room temperature or at reflux. To activate epoxysulfone for the amine attack, Lewis acids were added to the reaction mixture after epoxysulfone formation. Magnesium bromide, magnesium sulfate, and titanium isopropoxide had no

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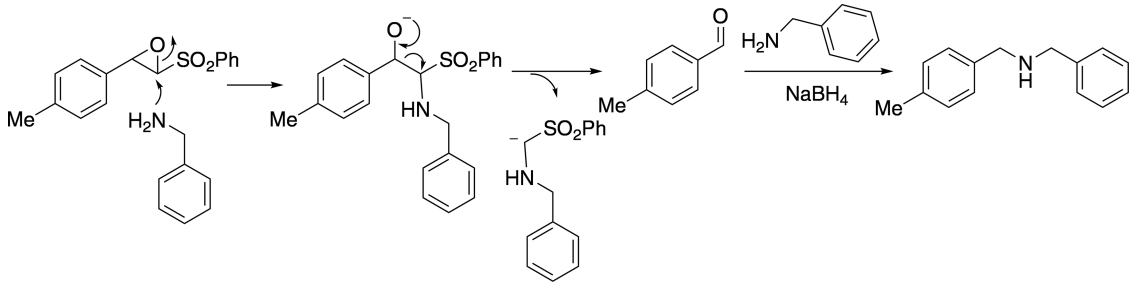
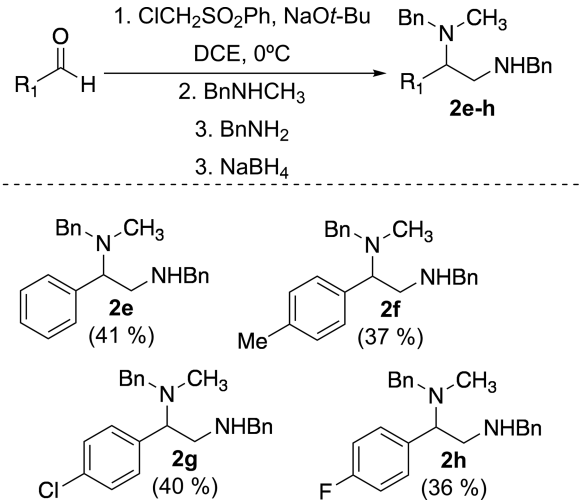
Scheme 2. Formation of Secondary Amines

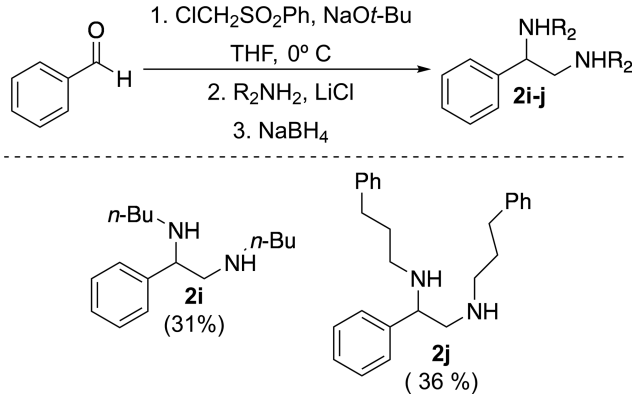


Scheme 3. Synthesis of Differently Substituted Diamines from Aldehydes



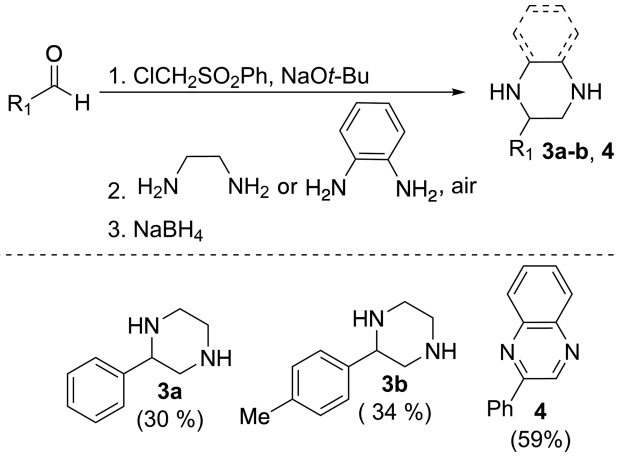
effect on the reactivity of epoxysulfones. However, the addition of lithium chloride (10 equiv.) afforded the desired diamines **2i–j** (Scheme 4). Tetrahydrofuran gave higher yields than dichloroethane probably because of the higher solubility of lithium chloride.

Scheme 4. Synthesis of Diamines from Aliphatic Amines



Cyclic diamines were also prepared. Piperazines **3a** and **3b** were prepared following the same experimental conditions as those for diamines starting from benzaldehyde and tolualdehyde, respectively (Scheme 5). Quinoxaline **4** was prepared using 1,2-benzenediamine and in the presence of air[13] (Scheme 5).

Scheme 5. Synthesis of Cyclic Diamines



CONCLUSIONS

In summary, we reported herein that 1,2-diamines, piperazines, and quinoxalines can be prepared starting from aldehydes. It is a one-pot procedure through three steps: A Darzens reaction with chloromethylsulfone and sodium *tert*-butoxide, treatment with an excess of amines or diamines, and reductive treatment to afford corresponding diamines. Also, quinoxalines can be prepared in a similar manner but using 1,2-benzenediamine upon oxidative conditions. Further research related to the synthetic use of epoxysulfones is going on in our lab and will be reported in the near future.

EXPERIMENTAL SECTION

General Information. All reactions were carried out under a nitrogen atmosphere with magnetic stirring, unless otherwise specified. Used reagents and solvents were obtained from commercial sources and were purified accordingly before use. EM Science Silica Gel 60 was used for column chromatography, whereas TLC was performed with precoated plates (Kieselgel 60, F_{254}, 0.25 mm). ^{1}H NMR spectra and ^{13}C NMR spectra were recorded in $CDCl_3$ (^{1}H, 7.24 ppm; ^{13}C 77.0 ppm) solution at 30 °C on a 300 MHz or a 400 MHz NMR spectrometer. Mass spectra were recorded on a QTOF I (quadrupole–hexapole–TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface.

General Experimental Procedure for the Synthesis of Epoxysulfone 1a. *t*-BuONa (1.1 mmol, 1.1 equiv.) was slowly added to a cold (0 °C) stirred solution of chloromethyl phenyl sulfone (1.1 mmol, 1.1 equiv.) in THF (5 mL). The mixture was stirred for 15 min, followed by dropwise addition of a solution of the corresponding aldehyde (1 mmol, 1 equiv.)

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in THF (5 mL). The reaction mixture was then stirred for 30 min and monitored by TLC. Quenching was done by adding ammonium chloride saturated aqueous solution (10 mL), and then the mixture was allowed to warm to room temperature before being extracted with ethyl ether (3 × 10 mL). The organic layers were washed with 1 M hydrochloric acid (10 mL), then with sodium bicarbonate saturated aqueous solution (10 mL), and finally with brine; then, the layers were dried using Na_2SO_4 and concentrated under vacuum. The crude material was purified using chromatography (silica gel, hexanes/ethyl acetate (9:1 to 7:3)) to give the pure compound.

2-Phenyl-3-(phenylsulfonyl)oxirane (1a). White crystals, mp 105−106 °C (yield 231 mg, 89%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.89 (m, 2H), 7.70−7.63 (m, 1H), 7.61−7.51 (m, 2H), 7.33−7.26 (m, 3H), 7.22−7.19 (m, 2H), 4.52 (d, J = 1.5 Hz, 1H), 4.11 (d, J = 1.6 Hz, 1H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.94, 134.58, 132.72, 129.60, 129.50, 128.88, 128.82, 126.10, 71.05, 57.48 ppm; HRMS (ESI) m/z calcd for $C_{14}H_{12}O_3S$ $[M + H]^+$: 261.0585, found: 261.0582; IR (KBr) ν 3313, 3060, 3025, 2920, 2830, 1757, 1676, 1513, 1495, 1454, 1119, 818, 740, 700 cm^{-1}.

General Experimental Procedure for the Synthesis of Diamines. To an ice-cold, stirred solution of the corresponding epoxysulfone (1 mmol, 1 equiv.) in DCM (10 mL), the corresponding amine (3 mmol, 3 equiv.) was slowly added. The reaction mixture was stirred for 8 h, and then $NaBH_4$ (6 mmol, 6 equiv.) was added portionwise. The reaction mixture was then stirred for 1.5 h and was monitored by TLC. Then, it was quenched by ammonium chloride saturated aqueous solution (10 mL) and was allowed to warm to room temperature before being extracted with DCM (3 × 10 mL). The organic layers resulting from the extraction were washed with 1 M hydrochloric acid (10 mL), then with sodium bicarbonate saturated aqueous solution (10 mL), and finally with brine; then, these layers were dried using Na_2SO_4 and concentrated under vacuum. The resulting crude material was purified by chromatography (silica gel, hexanes/ethyl acetate (7:3 to 1:1)) to give the desired pure compound.

Method A. *t*-BuONa (1.2 mmol, 1.2 equiv.) was added to a 0 °C cold solution of chloromethyl phenyl sulfone (1.2 mmol, 1.2 equiv.) in DCE (5 mL). The resulting mixture was stirred for 15 min, and then the corresponding aldehyde (1 mmol, 1 equiv.) dissolved in DCE (5 mL) was added dropwise. The mixture was stirred for 1 h in a cold ice-bath and then for 1 h at room temperature until complete formation of epoxysulfone as monitored by TLC. Then, the reaction mixture was cooled at 0 °C and the amine (4 mmol, 4 equiv.) was slowly added. The reaction mixture was kept for 18 h at −8 °C, and then $NaBH_4$ (8 mmol, 8 equiv.) was slowly added. The resulting mixture was stirred for 8 h. Then, it was quenched with saturated ammonium chloride aqueous solution (10 mL) and was allowed to warm up to room temperature and extracted with DCM (3 × 10 mL). The organic layers were washed with 1 M hydrochloric acid (10 mL), saturated sodium bicarbonate aqueous solution (10 mL), and brine; dried using Na_2SO_4; and concentrated under vacuum. The crude mixture was purified by chromatography (silica gel, hexanes/ethyl acetate (7:3 to 1:1)) to afford the pure compound.

*N^1,N^2-Dibenzyl-1-phenylethane-1,2-diamine (**2a**)*. Yellowish oil (yield 139 mg, 44%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.07 (m, 15H), 3.71−3.56 (m, 4H), 3.40 (d, J = 13.2 Hz, 1H), 2.72−2.65 (m, 2H), 2.21 (br s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.50, 140.70, 140.27, 128.66, 128.50, 128.46, 128.34, 128.22, 127.48, 127.43, 127.07, 126.96, 61.72, 56.07, 53.73, 51.42 ppm; HRMS (ESI) m/z calcd for $C_{22}H_{24}N_2$ $[M + H]^+$: 317.2018, found: 317.2015; IR (KBr) ν 3421, 3281, 3062, 3029, 2957, 2921, 2864, 1630, 1497, 1462, 1445, 1370, 1316, 1291, 1239, 1170, 1131, 1111, 1080, 1048, 1031, 1005, 952, 919, 901, 862, 817, 762, 745, 695 cm^{-1}.

*N^1,N^2-Dibenzyl-1-(p-tolyl)ethane-1,2-diamine (**2b**)*. Yellowish oil (yield 132 mg, 40%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23−7.12 (m, 12H), 7.10−7.05 (m, 2H), 3.69−3.61 (m, 3H), 3.62 (d, J = 13.4 Hz, 1H), 3.42 (d, J = 13.2 Hz, 1H), 2.73−2.64 (m, 2H), 2.26 (s, 3H), 2.16 (br s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.67, 140.23, 139.32, 136.96, 129.31, 128.43, 128.39, 128.29, 128.17, 128.14, 127.32, 127.00, 126.88, 61.33, 56.06, 53.70, 51.31, 21.18 ppm; HRMS (ESI) m/z calcd for $C_{23}H_{26}N_2$ $[M + H]^+$: 331.2174, found: 331.2169; IR (KBr) ν 3329, 3062, 3027, 2922, 2834, 1604, 1509, 1455, 1350, 1223, 1158, 1122, 1054, 837, 742, 700 cm^{-1}.

*N^1,N^2-Dibenzyl-1-(4-chlorophenyl)ethane-1,2-diamine (**2c**)*. Yellowish oil (yield 182 mg, 52%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.14 (m, 14H), 3.70−3.63 (m, 3H), 3.61 (d, J = 13.6 Hz, 1H), 3.41 (d, J = 13.3 Hz, 1H), 2.75−2.60 (m, 2H), 1.70 (br s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.05, 140.42, 140.19, 128.86, 128.49, 128.41, 128.39, 128.16, 128.04, 127.16, 127.00, 126.91, 66.74, 63.11, 61.11, 55.99, 53.70, 51.32, 51.16 ppm; HRMS (ESI) m/z calcd for $C_{22}H_{23}ClN_2$ $[M + H]^+$: 351.1628, found: 351.1634; IR (KBr) ν 3310, 3061, 3026, 2920, 2831, 1755, 1603, 1494, 1454, 1361, 1204, 1126, 1073, 1029, 746, 701 cm^{-1}.

*N^1,N^2-Dibenzyl-1-(4-fluorophenyl)ethane-1,2-diamine (**2d**)*. Yellowish oil (yield 100 mg, 30%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.12 (m, 12H), 7.02−6.92 (m, 2H), 3.69−3.63 (m, 3H), 3.61 (d, J = 12.7 Hz, 1H), 3.41 (d, J = 13.3 Hz, 1H), 2.75−2.61 (m, 2H), 1.77 (br s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.06 (d, J = 244.9 Hz), 140.52, 140.30, 138.17 (d, J = 3.0 Hz), 128.84 (d, J = 7.8 Hz), 128.48, 128.40, 128.37, 128.16, 128.04, 126.97, 126.89, 115.30 (d, J = 21.1 Hz), 61.06, 56.16, 53.72, 51.31 ppm; HRMS (ESI) m/z calcd for $C_{22}H_{23}FN_2$ $[M + H]^+$, found 335.1913: 335.1912; IR (KBr) ν 3428, 3062, 3027, 2923, 2848, 1649, 1612, 1493, 1455, 1421, 1351, 1092, 1037, 1015, 828, 743, 701 cm^{-1}.

*N^1,N^2-Dibenzyl-N^1-methyl-1-phenylethane-1,2-diamine (**2e**)*. Yellowish oil (yield 135 mg, 41%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.20 (m, 15H), 3.98−3.84 (m, 3H), 3.58 (d, J = 13.3 Hz, 1H), 3.38−3.23 (m, 2H), 3.20 (br s, 1H), 2.92 (dd, J = 11.9, 5.7 Hz, 1H), 2.11 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.58, 137.29, 128.91, 128.81, 128.50, 128.47, 128.32, 128.27, 128.21, 127.60, 127.14, 126.96, 66.63, 58.59, 53.59, 49.77, 37.48 ppm; HRMS (ESI) m/z calcd for $C_{23}H_{26}N_2$ $[M + H]^+$: 331.2174, found: 331.2167; IR (KBr) ν 3416, 3060, 3026, 2931, 2858, 1656, 1603, 1496, 1455, 1385, 751, 702 cm^{-1}.

*N^1,N^2-Dibenzyl-N^1-methyl-1-(p-tolyl)ethane-1,2-diamine (**2f**)*. Yellowish oil (yield 127 mg, 37%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27−7.13 (m, 12H), 7.10−6.99 (m, 2H), 3.83−3.76 (m, 2H), 3.73 (d, J = 13.3 Hz, 1H), 3.51 (br s, 1H), 3.44 (d, J = 13.3 Hz, 1H), 3.24−3.08 (m, 2H), 2.78 (dd, J = 11.9, 5.7 Hz, 1H), 2.27 (s, 3H), 1.97 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.61, 139.40, 137.25, 133.94, 128.92, 128.84, 128.52, 128.44, 128.33, 127.19, 126.96, 66.13, 58.56, 53.51, 49.71, 37.42, 21.17 ppm; HRMS (ESI) m/z calcd for $C_{24}H_{28}N_2$ $[M + H]^+$: 345.2331, found: 345.2328; IR (KBr) ν 13C NMR (400 MHz) δ 3433, 3062, 3028, 2923, 2849, 2796,

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1672, 1645, 1604, 1510, 1454, 1368, 1226, 1160, 1016, 837, 740, 701 cm^{-1}.

*N^1,N^2-Dibenzyl-1-(4-chlorophenyl)-N^1-methylethane-1,2-diamine (**2g**).* Yellowish oil (yield 145 mg, 40%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.35−7.14 (m, 12H), 7.12−7.04 (m, 2H), 3.86−3.75 (m, 3H), 3.42 (d, J = 13.3 Hz, 1H), 3.22 (d, J = 13.3 Hz, 1H), 3.18 (s, 1H), 3.14 (dd, J = 12.0, 8.9 Hz, 1H), 2.80 (dd, J = 12.0, 5.7 Hz, 1H), 1.97 (s, 3H) ppm; HRMS (ESI) m/z calcd for $C_{23}H_{25}ClN_2$ $[M + H]^+$: 365.1788, found: 365.1788.; ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.10, 135.51, 133.47, 130.11, 128.77, 128.63, 128.60, 128.56, 128.42, 128.39, 128.38, 127.43, 127.11, 65.63, 58.59, 53.29, 49.27, 37.34 ppm; IR (KBr) ν 3345, 3061, 3027, 2926, 2846, 2795, 1674, 1638, 1603, 1495, 1454, 1368, 1124, 1077, 1025, 745, 702 cm^{-1}.

*N^1,N^2-Dibenzyl-1-(4-fluorophenyl)-N^1-methylethane-1,2-diamine (**2h**).* Yellowish oil (yield 125 mg, 36%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.27−7.08 (m, 12H), 7.01−6.90 (m, 2H), 3.83−3.69 (m, 3H), 3.42 (d, J = 13.3 Hz, 1H), 3.34 (br s, 1H), 3.24−3.07 (m, 2H), 2.77 (dd, J = 11.9, 5.8 Hz, 1H), 1.96 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.23 (d, J = 245.8 Hz), 139.32, 139.29, 133.05 (d, J = 3.3 Hz), 130.31 (d, J = 7.9 Hz), 128.77, 128.54, 128.38, 128.29, 127.25, 127.06, 115.07 (d, J = 21.0 Hz), 65.80, 58.57, 53.51, 49.75, 37.38 ppm; HRMS (ESI) m/z calcd for $C_{23}H_{25}FN_2$ $[M + H]^+$: 349.2080, found: 349.2078; IR (KBr) ν 3367, 3062, 3027, 2924, 2850, 2796, 1659, 1596, 1494, 1455, 1396, 1093, 1016, 828, 741, 701 cm^{-1}.

Method B. *t*-BuONa (1.2 mmol, 1.2 equiv.) was added to an ice-cold solution of chloromethyl phenyl sulfone (1.2 mmol, 1.2 equiv.) in THF (5 mL). The mixture was stirred for 15 min; then, the corresponding aldehyde (1 mmol, 1 equiv.) was slowly added as a solution in THF (5 mL). The reaction mixture was then stirred for 1 h at 0 °C and for 1 h at room temperature. When TLC showed complete formation of epoxysulfone, the reaction was cooled at −8 °C and the corresponding amine (4 mmol, 4 equiv.) was added followed by addition of LiCl (10 mmol, 10 equiv.). The reaction mixture was kept for 18 h at −8 °C. Then, $NaBH_4$ (8 mmol, 8 equiv.) was added portionwise, and the resulting mixture was stirred for additional 8 h. Finally, the reaction mixture was quenched with saturated ammonium chloride aqueous solution (10 mL) and was then allowed to warm up to room temperature. Then, it was extracted with DCM (3 × 10 mL). The resulting organic layers were washed with 1 M hydrochloric acid (10 mL), then with sodium bicarbonate saturated aqueous solution (10 mL), and finally with brine. Washed organic portion was dried using Na_2SO_4 and concentrated under vacuum. The resulting crude material was purified by chromatography (silica gel, hexanes/ethyl acetate (7:3 to 1:1)) to give the desired compound.

*N^1,N^2-Dibutyl-1-phenylethane-1,2-diamine (**2i**).* Yellow oil (yield 76 g, 31%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.35−7.23 (m, 5H), 3.80 (dd, J = 7.6, 6.3 Hz, 1H), 3.45 (br s, 2H), 2.91−2.83 (m, 2H), 2.68 (qt, J = 11.6, 7.3 Hz, 2H), 2.51−2.39 (m, 2H), 1.55−1.40 (m, 4H), 1.37−1.24 (m, 4H), 0.89 (t, J = 7.4 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.66, 128.63, 128.49, 127.22, 127.06, 62.00, 55.42, 48.93, 47.10, 32.03, 31.28, 20.38, 20.27, 13.87, 13.81 ppm; HRMS (ESI) m/z calcd for $C_{16}H_{28}N_2$ $[M + H]^+$: 249.2331, found: 249.2329; IR (KBr) ν 3411, 3061, 3029, 2961, 2929, 2869, 1653, 1602, 1552, 1458, 1385, 762, 704 cm^{-1}.

*1-Phenyl-N^1,N^2-bis(3-phenylpropyl)ethane-1,2-diamine (**2j**).* Yellow oil (yield 144 g, 39%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.42−7.14 (m, 15H), 3.78 (dd, J = 8.6, 5.1 Hz, 1H), 2.90−2.79 (m, 2H), 2.77−2.61 (m, 8H), 2.61−2.51 (m, 2H), 1.93−1.77 (m, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.34, 142.21, 141.91, 128.58, 128.41, 128.32, 127.39, 127.22, 125.86, 125.74, 62.50, 56.11, 48.97, 47.03, 33.60, 33.50, 31.77, 31.28 ppm; HRMS (ESI) m/z calcd for $C_{26}H_{32}N_2$ $[M + H]^+$: 373.2644, found: 373.2641; IR (KBr) ν 3164, 3068, 3034, 2994, 1583, 1494, 1478, 1460, 1449, 1401, 1326, 1314, 1288, 1232, 1192, 1181, 1166, 1152, 1087, 1077, 1059, 1025, 999, 982, 936, 909, 857, 809, 786, 762, 742, 716, 700, 687 cm^{-1}.

2-Phenylpiperazine (3a). White crystals, mp 115−119 °C[14] (yield 49 mg, 30%): ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.32 (m, 5H), 3.79 (dd, J = 11.3, 2.8 Hz, 1H), 3.54 (br s, 1H), 3.33−3.21 (m, 2H), 3.00 (td, J = 12.5, 2.7 Hz, 1H), 2.89−2.76 (m, 1H), 2.67 (dt, J = 13.3, 11.5 Hz, 1H), 1.69 (br s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.0, 128.9, 128.2, 126.5, 60.7, 59.0, 52.3, 46.4 ppm; HRMS (ESI) m/z calcd for $C_{10}H_{14}N_2$ $[M + H]^+$: 163.1233, found: 163.1235; IR (KBr) ν 3166, 3092, 3071, 3059, 3035, 3002, 2232, 1918, 1904, 1800, 1602, 1584, 1493, 1480, 1451, 1422, 1386, 1324, 1311, 1287, 1267, 1227, 1189, 1161, 1147, 1115, 1102, 1088, 1070, 1056, 1041, 1025, 1013, 999, 928, 909, 855, 834, 808, 790, 749, 721, 704, 682 cm^{-1}.

*2-Methyl-3-(p-tolyl)piperazine (**3b**).* White crystals, mp 161−163 °C[15] (yield 60 mg, 34%): ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.1 Hz, 1H), 7.09 (d, J = 7.9 Hz, 1H), 3.66 (dd, J = 11.2, 2.7 Hz, 1H), 3.29 (br s, 1H), 3.22−3.12 (m, 2H), 2.91 (td, J = 12.4, 2.6 Hz, 1H), 2.74 (ddd, J = 25.2, 12.4, 3.3 Hz, 1H), 2.59 (dt, J = 13.2, 11.6 Hz, 1H), 2.27 (s, 3H), 1.47 (br s, 2H) ppm; ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.3, 138.2, 129.5, 126.8, 60.5, 59.0, 52.3, 46.2, 21.1 ppm; HRMS (ESI) m/z calcd for $C_{11}H_{17}N_2$ $[M + H]^+$: 177.1390, found: 177.1392; IR (KBr) ν 3283, 3150, 3055, 3026, 2871, 2435, 2390, 2311, 2265, 2161, 2033, 1977, 1769, 1600, 1519, 1493, 1327, 1313, 1211, 1165, 1130, 1074, 1042, 1022, 1006, 953, 895, 859, 832, 801 cm^{-1}.

2-Phenylquinoxaline (4). Orange crystals, mp 69−70 °C[16] (yield 121 mg, 59%): ^1H NMR (300 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.13−7.97 (m, 4H), 7.71−7.57 (m, 2H), 7.49−7.38 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.86, 143.39, 142.32, 141.60, 136.80, 130.31, 130.22, 129.66, 129.57, 129.18, 129.15, 127.58 ppm; HRMS (ESI) m/z calcd for $C_{14}H_{14}N_2$ $[M + H]^+$: 207.0922, found: 207.0922; IR (KBr) ν δ 3088, 3075, 3066, 2998, 1908, 1606, 1582, 1513, 1478, 1449, 1434, 1405, 1392, 1326, 1314, 1292, 1273, 1236, 1191, 1181, 1168, 1154, 1101, 1086, 1074, 1059, 1026, 1014, 999, 952, 937, 916, 865, 846, 802, 769, 757, 719, 688 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acsomega.8b03030.

Graphical NMR spectra of all compounds: ^1H NMR spectrum of **1a** (Figure S1); ^{13}C NMR spectrum of **1a** (Figure S2); ^1H NMR spectrum of **2a** (Figure S3); ^{13}C NMR spectrum of **2a** (Figure S4); ^1H NMR spectrum of **2b** (Figure S5); ^{13}C NMR spectrum of **2b** (Figure S6); ^1H NMR spectrum of **2c** (Figure S7); ^{13}C NMR spectrum of **2c** (Figure S8); ^1H NMR spectrum of **2d** (Figure S9); ^{13}C NMR spectrum of **2d** (Figure S10); ^1H NMR spectrum of **2e** (Figure S11); ^{13}C NMR spectrum

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of **2e** (Figure S12); ^{1}H NMR spectrum of **2f** (Figure S13); ^{13}C NMR spectrum of **2f** (Figure S14); ^{1}H NMR spectrum of **2g** (Figure S15); ^{13}C NMR spectrum of **2g** (Figure S16); ^{1}H NMR spectrum of **2h** (Figure S17); ^{13}C NMR spectrum of **2h** (Figure S18); ^{1}H NMR spectrum of **2i** (Figure S19); ^{13}C NMR spectrum of **2i** (Figure S20); ^{1}H NMR spectrum of **2j** (Figure S21); ^{13}C NMR spectrum of **2j** (Figure S22); ^{1}H NMR spectrum of **3a** (Figure S23); ^{13}C NMR spectrum of **3a** (Figure S24); ^{1}H NMR spectrum of **3b** (Figure S25); ^{13}C NMR spectrum of **3b** (Figure S26); ^{1}H NMR spectrum of **4** (Figure S27); ^{13}C NMR spectrum of **4** (Figure S28) (PDF)

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Notes

The authors declare no competing financial interest.

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