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Note

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Synthesis of *C*-unsubstituted 1,2-Diazetidines and their Ring-opening Reactions via Selective N–N Bond Cleavage

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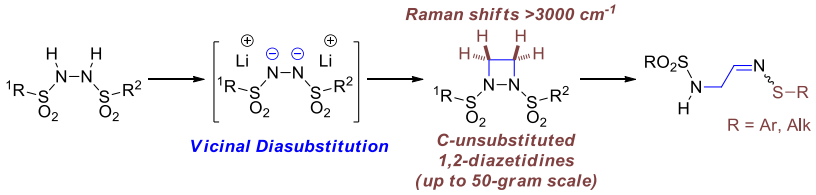
Supporting Information Placeholder

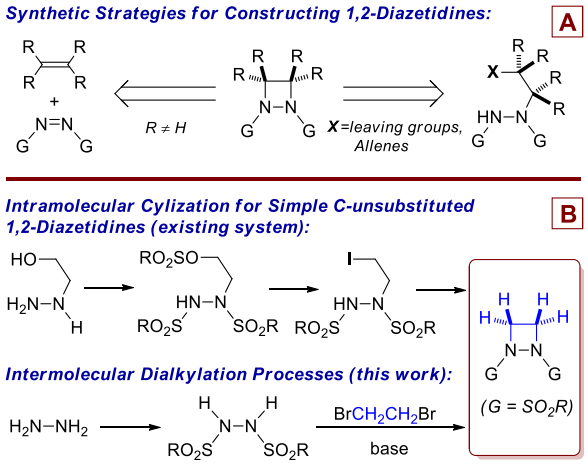


ABSTRACT: *C*-unsubstituted 1,2-diazetidines, a rarely studied type of four-membered heterocyclic compounds, were synthesized through an operationally simple intermolecular vicinal disubstitution reaction. 1,2-Diazetidine derivatives bearing various *N*-arylsulfonyl groups were readily accessed and studied by experimental and computed Raman spectra. Ring-opening reaction of the diazetidine was explored and resulted in the identification of a selective N–N bond cleavage with thiols as nucleophiles, which stereoselectively produced a new class of *N*-sulfenylimine derivatives with *C*-aminomethyl groups.

Among small-ring heterocyclic compounds, 1,2-diazetidine represents one of the most structurally unique classes as the four-membered skeleton contains three types of bonds, C–C, C–N, and N–N.[1] This diversity of the bond types, together with the ring strain, would potentially enable rich synthetic applications. Their structural relationship with β-lactams and 1,2-diazetidinones also makes them biologically and pharmacologically attractive.[1-2] However, none of these promising directions has been extensively explored due to the largely underdeveloped synthetic approaches toward these compounds. Among the limited synthetic strategies, [2+2] cycloaddition of alkenes and azo compounds serves as a classical method, which was often used to construct 1,2-diazetidine derivatives with relatively hindered C-substituents in variable yields (Scheme 1, **A**).[3] Recently, intramolecular ring-closing reactions have been proven successful for accessing several types of 1,2-diazetidine derivatives, either based on intramolecular addition reactions to allenes,[4] or intramolecular substitution reactions (Scheme 1, **A**).[5] While the parent 1,2-diazetidine continues to be unknown, simple 1,2-diazetidines with unsubstituted C3 and C4 were rarely reported. Their synthesis has not been known by using the previous methods for making the *C*-substituted derivatives.[5c]

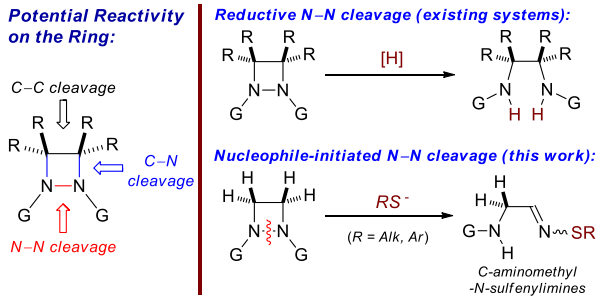
The sole effective synthesis of these simple diazetidines has been demonstrated by Shipman and coworkers' intramolecular ring closure reaction involving an iodide as a "soft" leaving group, affording 1,2-diazetidines with *N*-electron-withdrawing groups (Scheme 1, **B**).[5c] While the ring closure step is productive, the effectiveness of the entire synthesis from commercially

Scheme 1. Synthetic Pathways for Constructing 1,2-Diazetidines



available 2-hydroxyethyl-hydrazine is largely diminished by the tedious trisulfonylation and iodination step for constructing the precursors. In contrast, a more practical access to *C*-unsubstituted 1,2-disulfonyl-1,2-diazetidines would be an intermolecular vicinal disubstitution reaction with dihaloethane and hydrazines (Scheme 1, **B**).[6] Identification of suitable and general conditions for this intermolecular process will offer a more direct and operationally simple pathway.

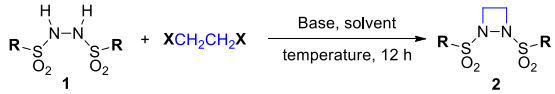
Scheme 2. Ring-opening Reactions of 1,2-Diazetidines.



Herein we report a practical synthesis of simple 1,2-disulfonyl-1,2-diazetidines via an intermolecular dialkylation process with 1,2-disulfonylhydrazines and 1,2-dibromoethane. Arylsulfonyl groups with various electronic and steric properties can be tolerated in the cyclization, which is scalable to 50-gram level without column chromatography needed for purification.

Although these four-membered heterocycles would presumably have diverse synthetic applications based on ring-opening reactions,[3g, 5b, 7] their known transformations were mainly reported to occur on the side chain of the ring.[5a, 5b] The *C*-unsubstituted 1,2-diazetidines would serve as ideal model compounds for exploring the transformations on the ring (Scheme 2). Among different modes of ring-opening reactions, N–N bond cleavage is highly attractive as it splits the hydrazine unit into two nitrogen-containing functional groups. To this end, however, only hydrogenation has previously been disclosed (Scheme 2).[7] As an application, we report the first nucleophile-initiated N–N bond cleavage reaction of the 1,2-diazetidines. By treatment with different thiols, facile ring-opening followed by elimination reactions of the 1,2-diazetidines were demonstrated at room temperature in a stereoselective manner, providing a new approach to *N*-sulfenylimine derivatives, a useful class of sulfur analogs of oximes with a N–S bond (Scheme 2).[8]

Table 1. Intermolecular Dialkylation of 1,2-Disulfonylhydrazine[a]

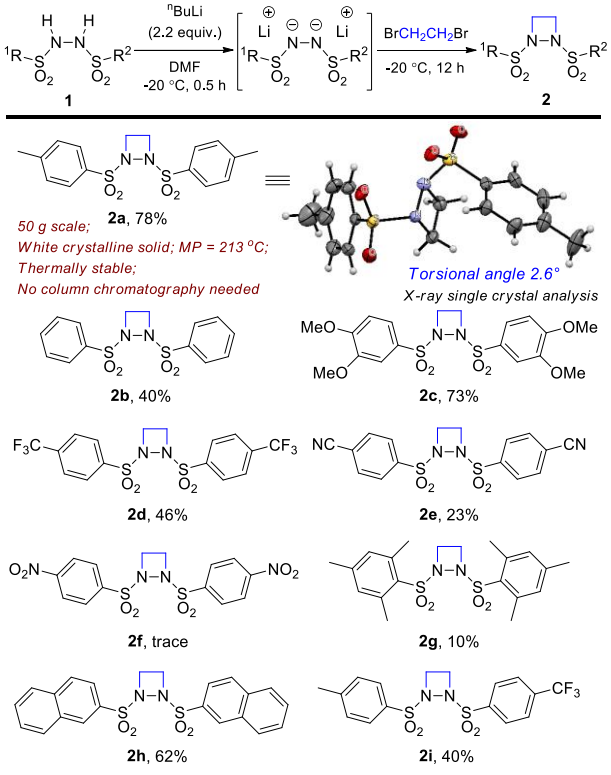


entry	R	X	base	solvent	temp.	yield (%)[b]
1	MeC_6H_4– (**a**)	Br	Cs_2CO_3	MeCN	120 °C	0
2	MeC_6H_4– (**a**)	Br	Cs_2CO_3	DMF	120 °C	0
3	MeC_6H_4– (**a**)	I	Cs_2CO_3	DMF	120 °C	0
4	MeC_6H_4– (**a**)	Br	NaH	DMF	0 °C	trace
5	MeC_6H_4– (**a**)	Br	NaH	DMF	-10 °C	22
6	MeC_6H_4– (**a**)	Br	NaH	DMF	-30 °C	< 10
7	MeC_6H_4– (**a**)	I	NaH	DMF	-20 °C	trace
8	Ph– (**b**)	Br	NaH	DMF	-10 °C	trace
9	MeC_6H_4– (**a**)	Br	^{n}BuLi	THF	-10 °C	<10
10	MeC_6H_4– (**a**)	Br	^{n}BuLi	DMF	-10 °C	26
11	MeC_6H_4– (**a**)	Br	^{n}BuLi	DMF	-20 °C	71
12	MeC_6H_4– (**a**)	I	^{n}BuLi	DMF	-20 °C	trace
13	Ph– (**b**)	Br	^{n}BuLi	DMF	-20 °C	40

[a] Carried out with **1** (1 mmol), 1,2-dihaloethane (1.2 mmol), and base (2.2 mmol) in 4 mL anhydrous solvent. Entries 4 – 13 were carried out under N_2 atmosphere. [b] Isolated yields.

Initial effort was focused on identifying optimal conditions for the intermolecular dialkylation reactions (Table 1). 1,2-Ditosylhydrazine (**1a**) and 1,2-dibromoethane were used as reactants with conditions similar to Shipman's intramolecular cyclization.[5c] Even at elevated temperature, no desired dialkylation product was observed with cesium carbonate as the base in polar solvents, such as acetonitrile and DMF (entries 1 and 2). The employment of 1,2-diiodoethane, which contains the much "softer" leaving group, was not successful for the intermolecular process (entry 3). Complete bis-deprotonation of the hydrazine with 2.2 equivalents of NaH in DMF followed by immediate introduction of 1,2-dibromoethane at 0 °C resulted in the observation of the desired 1,2-diazetidine **2a** albeit in very low yield (entry 4). Lowering the temperature to -10 °C increased the yield to 22%, presumably because of the prolonged life-time of the dianionic intermediate resulting from the deprotonation (entry 5).[6] However, further decreasing the temperature resulted in poor conversion and caused a large amount of precipitate during the reaction (entry 6). The starting hydrazine could be mostly recovered after quenching the reaction, which suggests the disodium salt of the ditosylhydrazine may be more stabilized under lower temperature. Nevertheless, its solubility is too low even in DMF and thus largely slowed down the reaction. Meanwhile, 1,2-diiodoethane gave dark solution with a complicated system without major product observed (entry 7). Unfortunately, when 1,2-diphenylsulfonylhydrazine (**1b**) was employed, no suitable temperature could be found to allow both the stabilization of the dianion intermediate and a proper solubility (entry 8). The challenge was then addressed by forming the corresponding dilithium diamide intermediate by using n-butyl lithium as the base.

Table 2. Direct Synthesis of Simple 1,2-Disulfonyl-1,2-diazetidines[a]



[a] Carried out under N_2 atmosphere with **1** (1 mmol), 1,2-dibromoethane (1.2 mmol), and ^{n}BuLi (2.2 mmol) in 4 mL anhydrous DMF. Isolated yields are shown. **2a** was synthesized by using 50 grams of 1,2-ditosylhydrazine.

While similar performance was shown at -10 °C (entries 9 and 10), few precipitate was observed in both cases at -20 °C and the desired 1,2-diazetidine **2a** and **2b** were produced in 71% and 40%, respectively (entries 11 and 13). Again, 1,2-diiodoethane, with a softer leaving group, was ineffective for this intermolecular cyclization.[9]

With the optimized conditions, *C*-unsubstituted 1,2-diazetidines bearing different arylsulfonyl groups were synthesized to enrich the number of this less known type of compounds. It was shown that the vicinal dilithiation process worked well for various disulfonylhydrazines with different electronic and steric properties (Table 2). Remarkably, synthesis of 1,2-ditosyl-1,2-diazetidine (**2a**, DTD) was carried out at 50-gram scale with an even higher yield. The white crystalline product, which was purified by only washing with ethanol, is thermally stable at its melting point 213 °C. The structure of **2a** was further confirmed by X-ray analysis on the single crystal. With the simple procedures, 1,2-diazetidine **2b**, as well as **2c** containing electron-donating MeO- groups, were synthesized in 40% and 73% yield, respectively. Electron-withdrawing groups, such as CF_3, could be well tolerated in the cyclization process (**2d**). To our delight, cyano groups, which are sensitive to nucleophiles, could be incorporated into the 1,2-diazetidine product in 23% yield (**2e**), although the nitro group could not be tolerated under the same conditions (**2f**). Moreover, sterically encumbered 1,2-bis(2-mesitylenesulfonyl)hydrazine (**1g**) did not completely disable the disubstitution reactions and afforded 1,2-diazetidine **2g** in 10% yield. Other aryl functionality, as exemplified by a 2-naphthalenesulfonyl group, was shown to produce the corresponding 1,2-diazetidine in good yield (**2h**). Lastly, unsymmetrical hydrazine **1i** was employed and proven to form 1-tosyl-2-(4-(trifluoromethyl)phenylsulfonyl)-1,2-diazetidine (**2i**) in 40% yield, indicating the feasibility of the intermolecular dialkylation for constructing unsymmetrical 1,2-diazetidines. While disulfonylhydrazines were successfully employed, the current method has not been shown effective for hydrazine with two carbonyl groups.

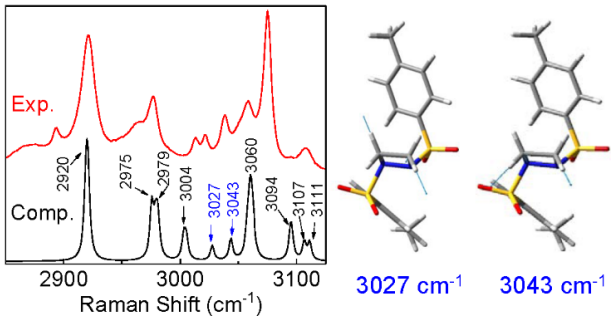
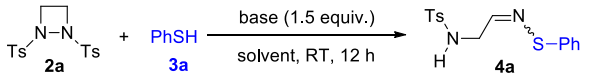


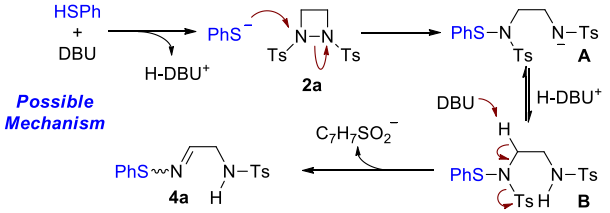
Figure 1. The experimental and computed Raman spectra of **2a** (Left). The vector representation of the Raman peaks associated with methylene C–H stretching (indicated by the arrows) in **2a** (Right). Assignment of other peaks are shown in the supporting information.

The practical synthesis of the *C*-unsubstituted 1,2-diazetidines **2** offers a unique opportunity for comparing and contrasting the structure and property of this four-membered heterocycle and the homocycle in cyclobutane. Investigation by both experimental and computational Raman spectra suggests that the C3 and C4 in 1,2-diazetidines **2a** have substantially more sp^2 characteristics than the carbons in cyclobutane (Fig. 1 and the supporting information). Two bands, calculated at 3027 and 3043 cm^{-1} were attributed to the C–H stretching of the methylene fragment of the 1,2-diazetidine ring. Apparently, they appear above the expected frequencies of methylene C_{sp3}-H bond stretching, which, by the rule of thumb, should appear below 2930 cm^{-1}.[10] Interestingly, the Raman shifts of the methylene C–H stretching in cyclobutane derivatives appear below 3000 cm^{-1}.[11] The contrast may indicate the higher degree of sp^2 character of C3 and C4 carbon atoms in the diazetidine ring of **2a**. Moreover, the C3 and C4 methylene groups in **2a** exhibit much higher torsional strain (H–C3–C4–H torsional angle is 2.6°) than that between two neighboring methylene groups in cyclobutane. Both x-ray analysis and computational model revealed that the four-membered ring in 1,2-dizedidine **2a** is almost planar with a dihedral angle of only 2.6°, while cyclobutanes, including 1,2-disubstituted cyclobutanes, are generally puckered with a 25-30° dihedral angles.[12]

Table 3. Thiolate-initiated Ring-opening N—N Bond Cleavage of 1,2-Ditosyl-1,2-diazetidine (DTD)



entries	base	Solvent	Yield
1	K_2CO_3	THF	0
2	TEA	THF	0
3	DBU	THF	78 %, *E/Z*: 4:1
4	DBU	DMF	76 %, *E/Z*: 10:1

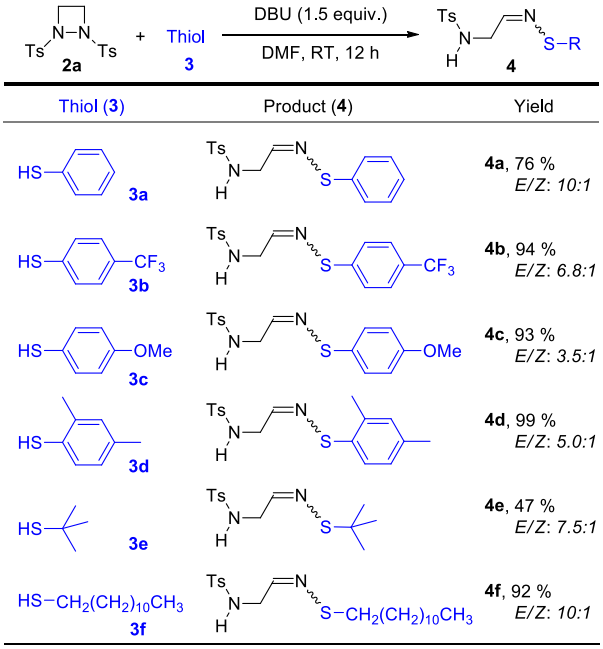


With three types of bonds in the ring, selective bond-breaking events of the *C*-unsubstituted 1,2-diazetidines would be interesting for exploration. Initial results indicated a new and simple approach for *N*-sulfenylimines, which is based on a selective N–N bond cleavage process with thiols as nucleophiles (Table 3). At room temperature, DTD was explored as the ring-opening substrate with thiophenyl (**3a**) as the nucleophile. While K_2CO_3 and triethylamine were not productive (entries 1 and 2), DBU in THF was able to convert DTD into *C*-aminomethyl-*N*-sulfenylimines **4a** in 78% yield and 4:1 *E/Z* ratio (entry 3). The same reaction was carried out in DMF and resulted in comparable yield and increased *E/Z* ratio to 10:1 (entry 4). As illustrated in the proposed mechanism, DBU presumably played two major roles, including the deprotonation of the thiol for the nucleophilic N–N bond cleavage affording intermediate **A**, as well as promoting the subsequent elimination process of intermediate **B**.

The selective N–N cleavage-based ring opening process was effective for various thiols, producing *C*-aminomethyl-*N*-sulfenylimines **4** stereoselectively (Table 4). Thiophenyls with strong electron-withdrawing and -donating groups were successfully transformed into *N*-sulfenylimines **4b** and **4c** in excellent yield and good *E/Z* ratio, respectively. Sterically hindered

thiols, such as 2,4-dimethylphenylthiol (**3d**), were demonstrated to be highly favorable reagents, affording almost quantitative yield with a 5.0:1 *E/Z* ratio. Furthermore, the ring-opening process works equally well for aliphatic thiols, as indicated by bulky *tert*-butylthiol (**3e**) and linear dodecane-1-thiol (**3f**), forming *N*-sulfenylimines **4e** and **4f** in comparably good yields and stereoselectivity.

Table 4. Ring-opening N—N Bond Cleavage for the Syntheses of *N*-Sulfenylimines [a]



[a] Carried out under N_2 atmosphere with **2a** (1 mmol), thiol (1.5 mmol), and DBU (1.5 mmol) in 1.5 mL anhydrous DMF. Isolated yields are shown. *E/Z* ratio was determined by ^{1}H NMR study of the mixture of the stereoisomers.

In summary, a operationally simple and direct synthesis of 1,2-disulfonyl-1,2-diazetidine derivatives has been developed via an intermolecular dialkylation reaction of readily available *N*, *N*'-disulfonylhydrazine and 1,2-dibromoethane. The easy access to *C*-unsubstituted 1,2-diazetidines, even at a 50-gram scale, would encourage the physical study and chemical application of this structurally unique and rarely known class of molecules. Among different types of bonds in the ring, selective N–N bond cleavage of the resulting 1,2-diazetidines was shown and enabled a new pathway for a stereoselective access to *C*-aminomethyl-*N*-sulfenylimines. The facile synthesis, together with the attractive structural features, of these highly strained four-membered heterocycles would encourage the further exploration of their synthetic applications either with other nucleophiles or in catalytic fashions.

EXPERIMENTAL SECTION

General Considerations:

Experimental: All reactions were set up under argon atmosphere, utilizing glassware that was flame-dried and cooled under vacuum. All non-aqueous manipulations were using standard Schlenk techniques. Reactions were monitored using thin-layer chromatography (TLC) on Silica Gel plates. Visualization of the developed plates was performed under UV light (254 nm) or $KMnO_4$ or in iodine chamber. Silica-gel flash column chromatography was performed on SiliCycle Inc. 40-63 μm silica gel.

Materials: Unless otherwise indicated, starting catalysts and materials were obtained from Sigma Aldrich, Oakwood, Strem, or Acros Co. Ltd. Moreover, commercially available reagents were used without additional purification.

Instrumentation: All NMR spectra were run at 500 MHz or 300 MHz in $CDCl_3$ or d-DMSO solution. ^{1}H NMR spectra were internally referenced to TMS. ^{13}C NMR spectra were internally referenced to the residual solvent signal. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m= multiplet, br = broad), coupling constants (*J*) were reported in Hz. High resolution mass spectra (HRMS) were recorded on Bruker MicrOTOF-QII mass instrument (ESI). Melting points of the solid compounds were determined on DgiMelt melting point apparatus. The Raman spectrum was acquired using Horiba LabRam HR Raman microscope system equipped with a 632.8 nm HeNe laser. The Raman shifts were calibration used a neon lamp. The uncertainty in the experimental Raman shift is below 0.5 cm^{-1}. A crystal of compound **2a** were mounted on the end of glass fibers and the X-Ray data was collected with a Bruker Kappa Apex II diffactometer.

Computational modeling: To understand the nature of the Raman vibrational spectroscopy, a density functional theory (DFT)[13] study was carried out using Gaussian 09.[14] The gas-phase geometries were optimized using the B3LYP functional (the B3 exchange functional[15] and LYP correlation functional[16]). For all computations, basis set 1 was utilized (BS1 is defined as LanL2DZ(D,P)+ECP[17] for S and 6-31G(d')[18] basis sets were used for all other atoms; the 6-31G(d') basis sets have the d polarization functions taken from the 6-311G(d)[19] basis sets rather than the default value of 0.8[20] for all other atoms). Default self-consistent field convergence criteria (10^{-8}) were used for all computations. Raman intensities were computed using analytical derivatives,[21] default pruned grids for energies (75, 302), and default pruned coarse grids for gradients and Hessians (35, 110). The computationally-derived Raman spectra were simulated with an in-house Fortran program by convoluting the computed vibrational energies and computed intensities with a Lorentzian line shape and a broadening of 2 cm^{-1}.[22] The computed Raman shifts were scaled by 0.96. Such an adjustment is a commonly accepted practice in aligning DFT-calculated spectra with experimental data.[23]

General Procedure for the preparation of 1,2-ditosyl-1,2-diazetidine (2a, DTD) Tosyl chloride (174 mmol) was added to tosylhydrdazine (139 mmol) in dichloromethane (242 mL) in an ice bath. Pyridine (14.1mL) was added dropwise in a temperature range of 0-10 ^{0}C. TLC analysis was done to monitor the reaction. A mixture of water (250mL) and hexane (250 mL) was added to the solution and stirred vigorously for 30 minutes. The solution was then suction filtered and washed with a 1:1 ratio of acetone and water (100ml). The crystals were then added to acetone (320 mL) and boiled at 80 ^{0}C. Water (150 mL) was added while stirring, and the solution was placed in an ice bath for an hour. The solution was then suction filtered and washed with a small amount of cold diethyl ether. The white solid obtained was used directly in the next step. Other disulfonylhydrazides were synthesized using the same known methods.

Under nitrogen atmosphere, n-butyl lithium (2.5M in hexanes, 0.88 mL, 2.2 mmol) solution was added drop wise to a solution of 1,2-ditosylhydrazine (1 mmol) in anhydrous dimethylformamide (4 mL) at -20^{0}C via gas tight syringe, and stirred for 15 minutes. 1,2-Dibromoethane (1.2 mmol) was then added dropwise to the solution at -20 ^{0}C over 10 minutes. The solution was then stirred overnight at -20 ^{0}C. This solution was then allowed to warm to room temperature. The reaction mixture was then added to 20 mL of dilute ammonium chloride solution in a beaker. After thorough precipitation, the solid was then suction filtered, washed with water (10 mL), and then washed with ethanol (5 mL). Then the solid were washed with dichloromethane (10mL) into a clean filter flask, and the filtrate was collected as a yellow solution. Ethanol (10 mL) was then added to the solution and the solution was evaporated at low vacuum to only remove the dichloromethane. The white precipitate formed in the remaining ethanol was then suction filtered and washed with ethanol (2 x 5 mL). 1,2-Ditosyl-1,2-diazetidine (DTD) was produced in 71 % yield. Starting from 1,2-ditosylhydrazine (0.15 mol, 51 g), a large scale reaction with the same procedure led to 78% yield. Detailed X-ray data of the crystal of **2a** is shown in the supporting information. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.3 Hz, 4H), 7.44 (d, *J* = 8.1 Hz, 4H), 3.69 (s, 4H), 2.51 (s, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 145.7, 130.3, 129.7, 129.3, 47.8, 21.8. **HRMS** (ESI) [M+Na] Calcd for $C_{16}H_{18}N_2O_4S_2Na$: 389.0600, found 389.0600. Melting point: 213.0 ^{o}C - 214.0 ^{o}C.

1,2-bis(phennylsulfonyl)-1,2-diazetidine (2b) Synthesis of 1,2-bis(phennylsulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between *N'*-(phenylsulfonyl)benzenesolfonohydrazide and 1,2-dibromoethane was 40 %. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 4H), 7.76 (t, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 4H), 3.68 (s, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 134.1, 131.7, 129.9, 128.7, 47.4. **HRMS** (ESI) Calcd for $C_{14}H_{15}N_2O_4S_2$ [M+H]: 339.0467, found 339.0466. Melting point: 169.3 ^{o}C - 170.8 ^{o}C.

1,2-bis((3,4-dimethoxphenyl)sulfonyl)-1,2-diazetidine (2c) Synthesis of 1,2-bis((3,4-dimethoxphenyl)sulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between *N'*-((3,4-dimethoxyphenyl)sulfonyl)-3,4-dimethoxybenzenesulfonohydrazide and 1,2-dibromoethane was 73 %. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.63 (dd, *J* = 8.5, 1.8 Hz, 2H), 7.48 (d, *J* = 1.7 Hz, 2H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.99 (s, 6H), 3.97 (s, 6H), 3.71 (s, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 154.0, 148.9, 124.3, 123.4, 112.5, 110.3, 56.3, 56.2, 47.7. **HRMS** (ESI) Calcd for $C_{18}H_{22}N_2O_8S_2Na$ [M+Na]: 481.0709, found 481.0709. Melting point: 198.2 ^{o}C - 198.9 ^{o}C

1,2-bis((4-(trifluoromethyl)phenyl)sulfonyl)-1,2-diazetidine (2d) Synthesis of 1,2-bis((4-(trifluoromethyl)phenyl)sulfonyl)-1,2-diazetidine was followed general procedure with some modification. 4-(trifluromethyl)-*N'*-((4-trifluromethyl)phenyl)sulfonyl)benzenesulfonohydrazide was added to the round bottom flask and purge with nitrogen gas. DMF was added to the mixture and followed by 1,2-dibromoethane was added and mixed until dissolved. Round bottom flask was place in cooling bath at -20 ^{o}C and treated with n-BuLi and reaction mixture was stirred for 12h. Round bottom flask was remove from the cooling bath and warm up room temperature. Ammonium chloride solution was added to the mixture and extracted with ethyl acetate for three times. Ethyl acetate was evaporated under reduced pressure and got yellow color residue. Residue was washed with ethanol and got white color residue as product and percentage yield was 46 %. **^{1}H NMR** (500 MHz, DMSO) δ 8.21 (d, *J* = 8.4 Hz, 4H), 8.17 (d, *J* = 8.4 Hz, 4H), 3.73 (s, 4H). **^{13}C NMR** (125 MHz, DMSO) δ 135.6, 134.4 (q, *J* = 32.4 Hz), 131.0, 126.8 (d, *J* = 3.7 Hz), 123.4 (q, *J* = 260.0 Hz), 48.6. **HRMS** (ESI) Calcd for $C_{16}H_{12}F_6N_2O_4S_2K$ [M+K]: 512.9774, found 512.9771. Melting point was not measured due to degradation of the compound at 195.0 ^{o}C.

1,2-bis(4-cyanophenylsulfonyl)-1,2-diazetidine (2e) Synthesis of 1,2-bis((4-cyanophenyl)sulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between 4-cyano-*N*-((4cyanophenyl)sulfonyl)benzenesulfonohydrazide and 1,2-dibromoethane was 23 %. **^{1}H NMR** (500 MHz, DMSO-d_6) δ 8.26 (d, *J* = 8.0 Hz, 4H), 8.15 (d, *J* = 8.0 Hz, 4H), 3.74 (s, 4H). **^{13}C NMR** (125 MHz, DMSO-d_6) δ 135.6, 133.6 130.6, 117.5, 117.4, 48.6. **HRMS** (ESI) Calcd for $C_{16}H_{12}N_4O_4S_2K$ [M+K]: 426.9931, found 426.9931. Melting point was not measured due to degradation of the compound at 195.0 ^{o}C.

1,2-bis(mesitylsulfonyl)-1,2-diazetidine (2g) Synthesis of 1,2-bis(mesitylsulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between *N'*-((3,4-dimethoxyphenyl)sulfonyl)-3,4-dimethoxybenzenesulfonohydrazide and 1,2-dibromoethane was 10 %. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 6.65 (s, 4H), 4.52 (s, 4H), 2.45 (s, 12H), 2.24 (s, 6H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 143.7, 141.8, 131.8, 128.3, 48.3, 23.2, 21.2. **HRMS** (ESI) Calcd for $C_{20}H_{26}N_2O_4S_2K$ [M+K]: 461.0965, found 461.0962. Melting point: 212.9 ^{o}C - 213.4 ^{o}C

1,2-bis(naphthalene-2-ylsulfonyl)-1,2-diazetidine (2h) Synthesis of 1,2-bis(naphthalene-2-ylsulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between *N'*-(naphthalen-2-ylsulfonyl)naphthalen-2-ylsolfonohydrazide and 1,2-dibromoethane was 62 %. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.58 (s, 2H), 8.02 (br, 4H), 8.03 (d, *J* = 8.0 Hz, 2H), 7.95 (d, *J* = 8.0 Hz, 2H), 7.74 – 7.69 (m, 2H), 7.68 – 7.64 (m, 2H), 3.76 (s, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 135.7, 132.3, 131.9, 129.7, 129.6, 129.4, 129.2, 128.0, 127.8, 124.7, 47.9. **HRMS** (ESI) Calcd for $C_{22}H_{18}N_2O_4S_2Na$ [M+Na]: 461.0600, found 461.0600. Melting point: 196.8 ^{o}C - 197.4 ^{o}C.

1-tosyl-2-(((4-trifluoromethyl)phenyl)sulfonyl)-1,2- diazetidine (2i) Synthesis of 1,2-bis((3,4-dimethoxphenyl)sulfonyl)-1,2-diazetidine was followed general procedure and percentage yield of reaction between 4-methyl-*N*-((4-trifluoromethyl)phenyl)sulfonyl)benzenesulfonohydrazide and 1,2-dibromoethane was 40 %. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.2 Hz, 2H), 7.91 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 3.72 (s, 4H), 2.50 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.0, 136.0 (q, *J* = 33.2 Hz), 130.8, 130.3, 129.9, 128.9, 126.2 (q, *J* = 3.6 Hz), 122.2 (q, *J* = 271.2 Hz), 47.8, 21.8. **HRMS** (ESI) Calcd for $C_{16}H_{15}F_3N_2O_4S_2Na$ [M+Na]: 443.0317, found 443.0318. Melting point: 211.3 ^{o}C - 212.8 ^{o}C.

General procedure for synthesis of *N*-(2-((phenylthio)imino)ethyl)-4-methylbenzenesulfonamide (4a) 1,2-dithosyl-1,2-diazetidine (DTD, **2a**) (0.1 mmol) was added to the Schlenk tube and vacuum was applied to remove air from the tube. Schenk tube was filled with nitrogen gas and thiophenol (0.15 mmol) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.15 mmol) and dimethylformamide (0.5 mL) were added to the Schlenk tube and closed properly with Teflon cap. Reaction mixture was stirred at room temperature for 12 hours. Water (3 mL) and dichloromethane (DCM) (1 mL) were added to the reaction mixture and shake well. DCM layer was separated and solvent was removed under reduced pressure. 4-Methyl-*N*-(2-

((phenylthio)imino)ethyl)benzenesulfonamide **4a** was isolated by column chromatography with 1:1 hexane and ethyl acetate mixture in 76% yield. *E/Z* ratio was determined by the ^{1}H NMR to be 10:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 2H), 7.29 – 7.24 (m, 2H), 7.23 – 7.21 (m, 3H), 7.17-7.16 (m, 2H), 7.10 (t, *J* = 5.9 Hz, 1H), 3.61 (d, *J* = 5.9 Hz, 2H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 146.7, 144.2, 135.1, 134.1, 129.7, 129.6, 128.9, 127.8, 126.5, 35.0, 21.6. **HRMS** (ESI) Calcd for $C_{15}H_{16}N_2O_2S_2Na$ [M+Na]: 343.0545, found 343.0541. Melting point: 141.3 ºC - 142.9 ºC.

***N*-(2-(((4-(trifluoromethyl)phenyl)thio)imino)ethyl)-4-methylbenzenesulfonamide (4b)** Synthesis of 4-methyl-*N*-(2-(((4-(trifluoromethyl)phenyl)thio)imino)ethyl)benzenesulfonamide was followed general procedure and percentage yield of reaction between 4-trifluoromethylbenzenethiol and 1,2-ditosyl-1,2-diazetidine was 94 %. E/Z: 6.8:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.85 (br, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.30 (m, 4H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.09 (t, *J* = 5.8 Hz, 1H), 3.71 (d, *J* = 5.8 Hz, 2H), 2.44 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 145.4, 132.1, 129.9, 129.6, 128.1, 127.5, 125.7(q, *J* = 3.7 Hz), 124.0 (q, *J* = 271.0 Hz), 33.7, 21.6. **HRMS** (ESI) Calcd for $C_{16}H_{16}F_3N_2O_2S_2$ [M+H]: 389.0599, found 389.0594. Melting point: 141.3 ºC - 142.5 ºC.

***N*-(2-(((4-methoxyphenyl)thio)imino)ethyl)-4-methylbenzenesulfonamide (4c)** Synthesis of *N*-(2-(((4-methoxyphenyl)thio)imino)ethyl)-4-methylbenzenesulfonamide was followed general procedure and percentage yield of reaction between 4-methoxybenzenethiol and 1,2-ditosyl-1,2-diazetidine was 93 %. E/Z: 3.5:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.01 (br, 1H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.11 (t, *J* = 5.9 Hz, 1H), 6.71 (d, *J* = 8.7 Hz, 2H), 3.77 (s, 3H), 3.49 (d, *J* = 5.9 Hz, 2H), 2.43 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 159.4, 147.3, 144.2, 135.2, 135.1, 129.7, 127.8, 124.0, 114.6, 55.3, 37.0, 21.6. **HRMS** (ESI) Calcd for $C_{16}H_{18}N_2O_3S_2K$ [M+K]: 389.0390, found 389.0390. Melting point: 133.7 ºC – 134.8 ºC.

***N*-(2-(((2,4-dimethylphenyl)thio)imino)ethyl)-4-methylbenzenesulfonamide (4d)** Synthesis of *N*-(2-(((2,4-dimethylphenyl)thio)imino)ethyl)-4-methylbenzenesulfonamide was followed general procedure and percentage yield of reaction between 2,4-dimethylbenzenethiol and 1,2-ditosyl-1,2-diazetidine was 99 %. E/Z: 5.0:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.12 – 7.04 (m, 2H), 6.92 (s, 1H), 6.80 – 6.70 (m, 1H), 3.53 (d, *J* = 5.9 Hz, 2H), 2.44 (s, 3H), 2.26 (s, 3H), 2.25 (s, 3H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 147.1, 144.1, 138.5, 136.7, 135.3, 131.2, 130.2, 129.6, 127.9, 127.2, 34.9, 21.6, 20.9, 20.3. **HRMS** (ESI) Calcd for $C_{17}H_{21}N_2O_2S_2$ [M+H]: 349.1039, found 349.1036. Melting point: 91.7 ºC - 93.1 ºC.

***N*-(2-((tert-butylthio)imino)ethyl)-4-methylbenzenesulfonamide (4e)** Synthesis of *N*-(2-((tert-butylthio)imino)ethyl)-4-methylbenzenesulfonamide was followed general procedure and percentage yield of reaction between tert-butylthiol and 1,2-ditosyl-1,2-diazetidine was 47 %. E/Z: 7.5:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.09 (t, *J* = 6.0 Hz, 1H), 3.28 (d, *J* = 6.0 Hz, 2H), 2.43 (s, 3H), 1.18 (s, 9H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 149.0, 144.3, 135.3, 129.7, 128.0, 43.3, 3.0, 30.7, 21.6. **HRMS** (ESI) Calcd for $C_{13}H_{20}N_2O_2S_2Na$ [M+Na]: 323.0858, found 323.0855. Melting point: 115.8 ºC - 117.8 ºC.

***N*-(2-((dodecylthio)imino)ethyl)-4-methylbenzenesulfonamide (4f)** Synthesis of *N*-(2-((dodecylthio)imino)ethyl)-4-methylbenzenesulfonamide was followed general procedure and percentage yield of reaction between 1-dodecanethiol and 1,2-ditosyl-1,2-diazetidine was 92 %. E/Z: 10:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.83 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.09 (t, *J* = 6.1 Hz, 1H), 3.16 (d, *J* = 6.1 Hz, 2H), 2.44 (s, 3H), 2.16 (t, *J* = 7.2 Hz, 2H), 1.46-1.20 (m, 20H), 0.90 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 144.2, 135.1, 129.7, 128.0, 32.6, 31.9, 30.7, 29.7, 29.6, 29.6, 29.6, 29.4, 29.3, 29.1, 28.7, 22.7, 21.6, 14.1. HRMS (ESI) Calcd for $C_{21}H_{36}N_2O_2S_2Na$ [M+Na]: 435.2110, found 435.2111. Melting point: 77.8 ºC - 79.5 ºC.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

Experimental procedures, additional experimental data, and compounds characterization data (PDF)

Crystallographic data (excluding structure factors) for the structure in this paper has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1832697. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail:deposit@ccdc.cam.ac.uk).

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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