Synthesis of Functionalized Cyclic Enamines from Lithium Alkylphenyl Sulfones and *N*-Carbo-*tert*-butoxy Lactams

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Alkylphenyl sulfones **3** are appropriate synthons for the synthesis of 2-phenylsulfonyl alkylidene pyrrolidine or piperidine derivatives **1** in good to moderate yields. The lithium alkyl sulfones **4** are first reacted with the desired protected lactams and then subjected to acidic methanolysis to afford the unusual enamines **1a-e**. NMR studies (COSY ^{1}H-^{1}H, COSY ^{1}H-^{13}C, NOE) showed the *Z* enamines to exist in a dynamic equilibrium with the corresponding imines **2**. The stereochemistry of the described compounds was confirmed by molecular calculations.

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Introduction.

Functionalized enamines can be useful precursors for the synthesis of many biologically active compounds such as the guanidine alkaloids, including ptilomycalin A[2] **6**, and the crambescidins which display antitumor, antifungal, and antiviral activities [1]. In order to further develop a synthetic methodology toward these targets we have envisaged a reaction sequence in which the lithium anions **4a-e** derived from alkylphenyl sulfones **3** are transformed into β-enaminosulfones **1a-e** (Scheme 1). The synthetic utility of alkyl phenylsulfones has been well explored. For example, their magnesium derivatives, formed by reaction with an alkyl Grignard reagent have been added to aldehydes or ketones for the preparation of vinyl sulfones [2]. Some years ago, we used these precursors for the preparation of trisubstituted and tetrasubstituted vinyl ethers [3]. The reports of Giovannini and coworkers that organometallic reagents react with *N*-carbo-*tert*-butoxy lactams, leading to regiospecific ring opening, has made a large variety of cyclic imines readily available [4].

Results and Discussion.

The lithium anions **4a-e**, prepared from sulfones **3**, by direct lithiation with *n*-butyllithium in tetrahydrofuran (THF) at -25 °C, were trapped with *N*-carbo-*tert*-butoxy-2-pyrrolidinone or piperidinone [4] at -78 °C, to give the corresponding *N*-carbo-*tert*-butoxy ω-amino α-phenylsulfonyl ketones **5**. The latter were purified by crystallization from isopropanol and/or recrystallization from hexane/ethyl acetate and identified by their characteristic infrared absorptions near 3460 and 1720 cm^{-1} and also by 1D and 2D NMR techniques. The protected ω-amino keto sulfones **5** were converted into the enamines **1** either by refluxing with methanolic *p*-toluenesulfonic acid or with excess trifluoracetic acid at 0-25 °C. In both cases the resulting products **1** were isolated in 50-75% overall yield after basic workup and crystallization with hexane/ethyl acetate at 0 °C.

These functionalized enamines show characteristic IR absorptions near 3400 and 1610 cm^{-1} and only one spot by silica gel thin layer chromatography. However, ^{1}H-NMR studies indicated that the enamines are in a dynamic equilibrium with the imine tautomers **2**. Enamine **1a** (R = H) was formed in a 5:1 ratio together with imine **2a** which was identified by its absorption at 4.20 ppm corresponding to the exocyclic methylene protons. On the other hand, enamine **1b** (R = *n*-C_3H_7) was formed in a 2:1 ratio with imine **2b**, which showed a doublet of doublets at 4.15 ppm arising from the hydrogen atom adjacent to the phenylsulfonyl group. Enamine **1c** (R = *n*-C_6H_{13}) was formed in a 6:15 ratio together with imine **2c** probably due to the length of the side chain. Enamine **1d** (R = CH_3) was formed in a 5:6 ratio together with imine **2d** and identified by infrared and NMR (^{1}H, and ^{13}C); 2D NMR correlation spectra (^{1}H-^{1}H, ^{1}H-^{13}C) further supported the structure assignments for enamines **1a, b**. The piperidine derivative **1e** (R = H, N = 2) showed a 3:2 ratio with respect to imine **2e**. Contrary to the pyrrolidine derivatives, the ratio for enamine **1e** and imine **2e** was lower presumably because of the ring size difference since an exocyclic double bond in a six-member ring is more stable than that of a five-member ring.

The *Z* geometry for the major enamine isomer **1a** was unambiguously established by 1D NOE studies. Thus, irradiation of the vinylic proton at 4.65 ppm produced a 4% enhancement of the allylic pyrrolidine methylene protons at 2.57 ppm. Correspondingly, irradiation at the 2.57 ppm signal produced a 3% enhancement at the 4.65 ppm resonance. A similar result was obtained for the piperidine analogue **1e** where the signals for the vinylic and allylic protons at 4.45 and 2.30 ppm respectively, showed a 5% enhancement when their partners, *via* dipolar coupling, were irradiated. Interestingly, the NOE studies showed the existence of a dynamic equilibrium between the enamine and imine isomers. Irradiation of the vinylic proton (4.65 ppm) in the pyrrolidine analogue **1a**, simultaneously saturated the 4.25 ppm resonance for the phenyl sulfone methylene in **2a** producing a negative

NOE (-10%) after spectral substraction. Accordingly, irradiation of the 4.25 ppm resonance in **2a** created negatives NOE's on the signals at 7.30 (-22%) and 4.65 (-103%) for the N-H and vinylic protons in **1a**, respectively. Again, very similar results were obtained for the piperidine system **1e/2e**.

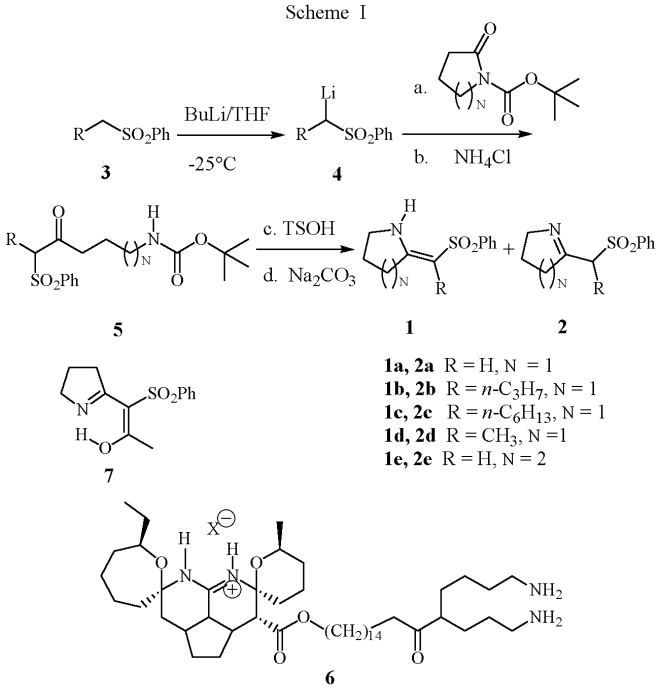
To further study the equilibration process, enamine **1a** was reacted with acetic anhydride under basic conditions to afford the enol imine **7** after column chromatography and crystallization. Its structure determination was based on IR, NMR (^{1}H-^{1}H, ^{1}H-^{13}C) and mass spectroscopy (MS).

Molecular mechanics calculations [5] were performed on the *E* and *Z* isomers of enamines **1a-e**. Also *ab initio* Hartree-Fock 6-31G* calculations were performed on both *E/Z* isomers of enamines **1a** (N = 1, R = H) and **1d** (N = 1, R = CH_3) [6]. Consistently, both calculations showed the *Z* enamines to be more stable than *E* enamine by 3.0-4.0 kcal/mol. This is in agreement with the observed predominance of the *Z* isomer established by NMR studies. This significant difference may be attributable to the intramolecular hydrogen bond stabilization between the N-H hydrogen and the sulfonyl group which is also in agreement with our experimental results.

Conclusions.

Alkyl sulfones are convenient precursors for the preparation of 2-phenylsulfonyl pyrrolidine and piperidine derivatives *via* the corresponding ω-enamino α-phenylsulfonyl ketones. In spite of their dynamic equilibrium with the corresponding imines, the trisubstituted cyclic β-enaminosulfones, with a secondary nitrogen, are the major product. This is due to the higher acidity of the hydrogen alpha to the phenylsulfonyl group. They also show that the α-carbon is more nucleophilic than nitrogen because when **1a** was reacted with *n*-butyllithium followed by addition of acetic anhydride, the enol imine **7** was the predominant product. Meanwhile, for tetrasubstituted cyclic β-enaminosulfones their ratio with imines are side chain dependant.

Scheme I



EXPERIMENTAL

All melting points were determined on an Electrothermal apparatus and are given uncorrected. Chemicals and solvents were used as received; tetrahydrofuran was distilled from sodium metal in the presence of benzophenone under dry nitrogen. Infrared spectra were determined on a Perking-Elmer 1620 FT-IR spectrophotometer in carbon tetrachloride solutions. The one- and two-dimensional nuclear magnetic resonance spectra were recorded on a Bruker DRX 500 (500.13, 125.77 MHz) spectrometer in deuteriochloroform solutions. The 1D NOE studies were recorded on a G.E. QE-300 (300.15 MHz). Electron impact MS spectra were obtained on a VG Fisons Autospec spectrometer (70 eV) equipped with a direct insertion probe (DIP) attachment. Thin-layer chromatography was carried out utilizing silica gel precoated TLC plates on polyester with 254 nm fluorescent indicator, catalog Z12, 278-5, and E. Merck silica gel 60 F (230-400 mesh) was used for flash chromatography. Combustion analysis were performed by Oneida Research Services, Whitesboro, NY 13492 or Atlantic Microlab, Norcross, GA 30091. Protected lactams and sulfones were prepared following the procedures described by Savoia *et al.* or Jacobs [7]. Computational calculations were done on an Indigo 2 Silicon Graphics workstation.

General Procedure for the Preparation of *N*-Carbo-*tert*-butoxy ω-Amino Keto Sulfones (**5**).

To a magnetically stirred solution of the required sulfone **3** (12 mmoles) in dry tetrahydrofuran (50 mL) was added *n*-butyllithium (13.2 mmoles of a 2.5 *M* solution in hexanes) at -25 °C and stirred for 30 minutes to generate a yellow to orange solution of the corresponding anion. The solution was cooled at -78 °C, at this temperature the protected lactam dissolved in tetrahydrofuran (12 mmoles, 15 mL) was added dropwise and after 3 hours the mixture was quenched by the addition of ammonium chloride (20 mL, saturated aqueous solution). After extraction with diethyl ether, the organic layer was dried with anhydrous magnesium sulfate and concentrated under reduced pressure (25-35 /20-40 torr) to afford the protected ω-*N*-amino keto sulfones **5**.

5-(*N*-Carbo-*tert*-butoxy)amino-1-phenylsulfonyl-2-pentanone [**5a (R = H, N = 1)**].

This compound was recrystallized from isopropanol (60% yield; mp 73-73.5 °C); ir: υ 3463, 3076, 2980, 2932, 1720, 1503, 1460, 1392, 1366, 1330, 1160 cm^{-1}; ^{1}H nmr: δ 7.85 (m, 2H, ArH), 7.7 (m, 1H, ArH), 7.6 (m, 2H, ArH), 4.65 (br s, 1H, NH), 4.20 (s, 2H, CH_2SO$_2$), 3.10 (q, 2H, CH_2N), 2.74 (t, 2H, CH$_2$CH_2CO), 1.74 (qt, 2H, CH$_2$CH_2CH$_2$), 1.40 (s, 9H, (CH_3)$_3$C); ^{13}C nmr: δ 197.7 (C=O), 156.0 (NHC=O), 138.7 (=C-SO$_2$), 134.3, 129.3, 128.2 (ArC), 79.2 (C-O), 66.9

(OC*C*SO_2), 41.3 (C-NH), 39.3 (*C*-C-O), 28.3 [(*C*H_3)$_3$C], 23.7 (CH_2*C*$H_2$$CH_2$).

Anal. Calcd. For $C_{16}H_{23}NO_5S$: C, 56.29; H, 6.79; N, 4.10; S, 9.39. Found: C, 56.17; H, 6.69; N, 4.20; S, 9.42.

1-(*N*-Carbo-*tert*-butoxy)amino-5-phenylsulfonyl-4-octanone [**5b (R = *n*-C_3H_7, N =1)**].

Compound **5b** was obtained in 50% yield (2.30 g) mp 84-85 °C crystallized from isopropanol at -5 °C and recrystallized from hexane/benzene; ir: υ 3458, 3068, 2966, 2940, 2910, 1722, 1586, 1509, 1466, 1448, 1390, 1365, 1323, 1245, 1149 cm^{-1}; ^{1}H nmr: δ 7.66 (d, 2H, ArH), 7.59 (t, 1H, ArH), 7.56 (t, 2H, ArH), 4.68 (br s, 1H, NH), 4.12 (dd, 1H, CHSO_2), 3.11 (m, 2H, C*H*$_2$NH), 2.93 (dt, 1H, COC*Ha*HbCH_2), 2.54 (dt, 1H, COCHa*Hb*CH_2), 1.79 (m, 4H, CH_2CH_2CHSO_2), 1.45 [s, 9H, (C*H*$_3$)$_3$C], 1.22 (sext, 2H, CH_2C*H*$_2$CH_3), 0.91 (t, 3H, C*H*$_3$CH_2); ^{13}C nmr: δ 201.9 (C=O), 156.0 (N*C*O_2), 136.5 (=*C*SO_2), 134.3, 129.4, 129.0 (ArC), 77.4 [O-*C*(CH_3)$_3$], 75.0 (C-SO_2), 42.2 (CH_2N), 39.5 (CH_2*C*H_2CO), 29.1 (CH_2*C*H_2CHSO_2Ph), 28.4 [(*C*H_3)$_3$C], 23.5 (CH_2*C*H_2CH_2NH), 20.3 (CH_3*C*H_2CH_2), 13.7 (*C*H_3CH_2).

Anal. Calcd. for $C_{19}H_{29}NO_5S$: C, 59.50; H, 7.62; N, 3.65; S, 8.36. Found: C, 59.62; H, 7.45; N, 3.70; S, 8.40.

1-(*N*-Carbo-*tert*-butoxy)amino-5-phenylsulfonyl-4-undecanone [**5c (R = *n*-C_6H_{13}, N = 1)**].

Compound **5c** was obtained in 40% yield, mp 70-70.5 °C. Purified by silica gel chromatography with chloroform and recrystallized from isopropanol; ir: υ 3462, 2960, 2930, 1720, 1505, 1448, 1390, 1368, 1324, 1248, 1172, 1084 cm^{-1}; ^{1}H nmr: δ 7.80 (d, 2H, ArH), 7.60 (t, 1H, ArH), 7.50 (m, 2H, ArH), 4.75 (br s, 1H, NH), 4.10 (dd, 1H, CHSO_2), 3.10 (m, 2H, CH_2N), 2.90 (dt, 1H, COC*Ha*HbCH_2), 2.54 (dt, 1H, COCHa*Hb*CH_2), 1.80 (m, 4H, CH_2C*H*$_2$CHSO_2, CH_2C*H*$_2$CH_2NH), 1.48 [s, 9H, (CH_3)$_3$C], 1.20 [br s, 8H, CH_3(C*H*$_2$)$_4$], 0.80 (t, 3H, C*H*$_3$CH_2); ^{13}C nmr: δ 202.0 (C=O), 156.0 (N-CO_2), 136.0 (=CSO_2), 134.0, 129.0, 128.5 (ArC), 79.1 [O-*C*(CH_3)$_3$], 75.0 (*C*-SO_2Ph), 42.1 (*C*H_2N), 39.4 (CH_2*C*H_2CO), 31.5 (CH_2*C*H_2CHSO_2Ph), 29.0 (CH_2*C*H_2CH_2NH), 28.5 [(*C*H_3)$_3$C], 26.8 (CH_2CH_2CH_2CHSO_2Ph), 26.5 (CH_3CH_2*C*H_2), 23.5 (CH_3*C*H_2CH_2), 13.9 (*C*H_3CH_2).

Anal. Calcd. for $C_{22}H_{35}NO_5S$: C, 62.09; H, 8.29; N, 3.29; S, 7.53. Found: C, 61.88; H, 8.14; N, 3.46; S, 7.36.

6-(*N*-Carbo-*tert*-butoxy)amino-2-phenylsulfonyl-2-hexanone [**5d (R = CH_3, N = 1)**].

Compound **5d** was obtained in 40% yield as a colorless oil. Purified by silica gel chromatography with hexane followed by dichloromethane; ir: ν 3458, 3072, 2979, 2925, 1720, 1585, 1504, 1480, 1388, 1366, 1324, 1248, 1152, 1085, 1015 cm^{-1}; ^{1}H nmr: δ 7.66 (d, 2H, ArH), 7.59 (t, 1H, ArH), 7.56 (t, 2H, ArH), 4.68 (br s, 1H, NH), 4.12 (q, 1H, CHSO_2), 3.11 (m, 2H, CH_2NH), 2.93 (dt, 1H, COC*Ha*HbCH_2), 2.54 (dt, 1H, COCHa*Hb*CH_2), 1.79 (qt, 2H, CH_2C*H*$_2$CH_2NH), 1.45 [s, 9H, (CH_3)$_3$C], (d, 3H, C*H*$_3$CHSO_2); ^{13}C nmr: δ 201.9 (C=O), 156.0 (N*C*O_2), 136.5 (=*C*SO_2), 134.3, 129.4, 129.0 (ArC), 77.4 [O-*C*(CH_3)$_3$], 75.0 (C-SO_2), 42.2 (CH_2N), 39.5 (CH_2*C*H_2CO), 28.4 [(*C*H_3)$_3$C], 13.7 (*C*H_3CH).

6-(*N*-Carbo-*tert*-butoxy)amino-1-phenylsulfonyl-2-hexanone [**5e (R = H, N = 2)**].

Compound **5e** was obtained in 70% yield, mp 92-93 °C, recrystallized from isopropanol; ir: υ 3460, 3069, 2978, 1720, 1503, 1448, 1326, 1157 cm^{-1}; ^{1}H nmr: δ 7.84 (d, 2H, ArH), 7.65-7.50 (m, 3H, ArH), 4.71 (br s, 1H, NH), 4.14 (s, 2H, PhSO_2C*H*$_2$), 3.02 (q, 2H, CH_2C*H*$_2$NH), 2.67 (t, 2H, CH_2C*H*$_2$CO), 1.46-1.28 (m, 4H, COCH_2C*H*$_2$C*H*$_2$CH_2NH), 1.38 [s, 9H, (C*H*$_3$)$_3$C]; ^{13}C nmr: δ 197.9 (C=O), 163.1 (N*C*O_2), 138.6 (=*C*SO_2), 134.2, 129.3, 128.5, 128.1 (ArC), 79.0 [O*C*(CH_3)$_3$], 66.6 (*C*H_2SO_2), 43.8 (*C*H_2N), 39.9 (*C*H_2C=O), 29.0 (*C*H_2CH_2NH), 28.3[(*C*H_3)$_3$C], 20.0 (COCH_2*C*H_2CH_2CH_2N).

Anal. Calcd. for $C_{17}H_{25}NO_5S$: C, 57.44; H, 7.09; N, 3.94; S, 9.02. Found: C, 57.05; H, 6.96; N, 3.94; S, 9.02.

General Procedure for the Preparation of Enamines (**1**).

A mixture of the appropriate *N*-carbo-*tert*-butoxy amino keto sulfone **5** (10 mmol), *p*-toluenesulfonic acid (10 mmol) and methanol (40-50 mL) was refluxed while the reaction progress was monitored by thin layer chromatography (hexane/ethyl acetate 1:1). Methanol was removed under vacuum, the residue dissolved with water (20 mL), washed with diethyl ether and basified with solid sodium carbonate. After extraction with methylene chloride, the organic layer was dried with anhydrous magnesium sulfate and concentrated under reduced pressure (25-35 °C/20-40 torr) to give the enamines **1**.

Z-2-(Phenylsulfonylmethylene)pyrrolidine [**1a (R = H, N = 1)**].

Compound **1a** was obtained in 71% yield, mp 80-82 °C, recrystallized from hexane/ethyl acetate; ir: υ 3400, 3068, 2982, 2872, 1613, 1487, 1446, 1328, 1286, 1134 cm^{-1}; ^{1}H nmr: δ 7.80 (m, 2H, ArH), 7.50 (m, 3H, ArH), 7.19 (br s, 1H, NH), 4.65 (s, 1H, =CHSO_2), 3.47 (t, 2H, CH_2C*H*$_2$N), 2.57 (t, 2H, CH_2C*H*$_2$C=), 1.92 (qt, 2H, CH_2C*H*$_2$CH_2); ^{13}C nmr: δ 161.7 (=C-N), 145.4 (=CSO_2), 131.6, 128.7, 125.4 (ArC), 82.6 (=CHSO_2), 47.4 (CH_2N), 33.0 (*C*H_2C=), 21.5 (CH_2*C*H_2CH_2); Ms; m/z 158 (100%), 223 (M^+).

Anal. Calcd. for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27; S, 14.36. Found: C, 58.85; H, 5.84; N, 6.21; S, 14.58.

2-(Phenylsulfonylmethyl)-1,2-dehydropyrrolidine [**2a (R = H, N = 1)**].

Aliphatic hydrogen and carbon chemical shift assignments. ^{1}H nmr: δ 4.20 (s, 2H, CH_2SO_2), 3.73 (t, 2H, CH_2C*H*$_2$N), 2.68 (t, 2H, CH_2C*H*$_2$C=), 1.90 (qt, 2H, CH_2C*H*$_2$CH_2); ^{13}C nmr: δ 166.7 (=CN), 133.9 (=CSO_2), 129.1, 127.9 (ArC), 61.3 (C-CH_2SO_2), 60.4 (CH_2N), 37.7 (CH_2C=), 22.7 (CH_2*C*H_2CH_2).

2-(1-Phenylsulfonylbutylidene)pyrrolidine [**1b (R = *n*-C_3H_7, N = 1)**].

Compound **1b** was obtained in 58% yield, mp 83-85 °C, recrystallized from hexane/ether/ethyl acetate; ir: υ 3396, 3068, 2962, 2870, 1614, 1446, 1321, 1288, 1151, 1132, 1050 cm^{-1}; ^{1}H nmr: δ 7.80 (m, 2H, ArH), 7.65 (m, 1H, ArH), 7.50 (m, 2H, ArH), 7.30 (br s, 1H, NH), 3.50 (t, 2H, CH_2C*H*$_2$NH), 2.60 (t, 2H, CH_3CH_2C*H*$_2$C=), 1.95 (t, 2H, CH_2C*H*$_2$C=), 1.85 (sext, 2H, CH_2C*H*$_2$CH_3), 1.40 (qt, 2H, CH_2C*H*$_2$CH_2), 0.80 (t, 3H, C*H*$_3$CH_2); ^{13}C nmr: δ 171.0 (=C-N), 144.2, 133.6, 128.9, 128.6, 126.0 (ArC), 94.0 (=*C*(SO_2)CH_2CH_2), 48.0 (CH_2N), 37.0 (=C*C*H_2CH_2C), 29.0 [=C(N)CH_2CH_2], 27.5 (CH_2CH_2CH_3), 23.0 (CH_2CH_2CH_2), 14.5 (*C*H_3CH_2).

Anal. Calcd. for $C_{14}H_{19}NO_2S$: C, 63.36; H, 7.22; N, 5.28; S, 12.08. Found: C, 63.54; H, 7.10; N, 5.45; S, 11.87.

2-(1-Phenylsulfonylbutyl)-1,2-dehydropyrrolidine [**2b (R = *n*-C_3H_7, N = 1)**].

Aliphatic hydrogen and carbon (aliphatic & olefinic) NMR chemical shift assignments. ^{1}H nmr: δ 4.15 (dd, 1H, $PhSO_2CHCH_2$), 3.65 (m, 2H, CH_2CH_2NH), 2.70 (t, 2H, CH_2CH_2C=), 2.00 (m, CH_2CH_2CH), 1.85 ($CH_2CH_2CH_2$), 1.30 ($CH_2CH_2CH_3$), 0.90 (t, 3H, CH_3CH_2); ^{13}C nmr: δ 160.0 (C=N), 70.0 ($CHSO_2$), 61.0 (CH_2N), 33.0 (CH_2CH_2C=), 32.0 ($CHCH_2CH_2$), 24.0 ($CH_2CH_2CH_3$), 21.0 ($CH_2CH_2CH_3$), 14.0 (CH_3CH_2).

2-(1-Phenylsulfonylheptylidene)-pyrrolidine [**1c (R = *n*-C_6H_{13}, N = 1)**].

Compound **1c** was obtained in 70% yield, as a yellow oil. Purified by silica gel chromatography with 1:1 cyclohexane/ethyl acetate; ir: ν 3398, 3063, 2953, 2929, 2859, 1614, 1479, 1466, 1447, 1374, 1321, 1282, 1151, 1135, 1085, 1024 cm^{-1}; ^{1}H nmr: δ 7.82 (m, 2H, ArH), 7.62 (m, 1H, ArH), 7.40 (m, 2H, ArH), 7.25 (br s, 1H, NH), 3.45 (t, 2H, CH_2NH), 2.55 [t, 2H, $CH_2(CH_2)_4$], 1.92 (t, 2H, $NC{=}CCH_2CH_2$), 1.85 [m, 4H, $CH_2CH_2CH_2NH$, $CH_2CH_2(CH_2)_3CH_3$], 1.18 [m, 6H, $CH_2(CH_2)_3CH_3$], 0.80 [t, 3H, $CH_2(CH_2)_3CH_3$]; ^{13}C nmr: δ 159.5 (=*C*-NHCH$_2$), 144.2, 1131.7, 128.6, 126.2 (Ar*C*), 93.4 (=*C*-SO_2-Ph), 47.3 (CH_2CH_2NH), 31.4 (CH_2CH_2C=C), 31.3 [=$CCH_2(CH_2)_4$], 30.3 ($CH_2CH_2CH_2NH$), 29.0 [$CH_2CH_2(CH_2)_3CH_3$], 28.7 [$CH_2CH_2(CH_2)_3CH_3$], 26.8 [$CH_2(CH_2)_3CH_2CH_3$], 22.5 [$(CH_2)_4CH_2CH_3$], 13.9 [$CH_2(CH_2)_4CH_3$].

2-(1-Phenylsulfonylheptyl)-1,2-dehydropyrrolidine [**2c (R = *n*-C_6H_{13}, N = 1)**].

Aliphatic hydrogen and carbon (aliphatic & olefinic) NMR chemical shift assignments. ^{1}H nmr: δ 4.15 (dd, 1H, $PhSO_2CHCH_2$), 3.65 (m, 2H, CH_2CH_2NH), 2.70 (t, 2H, CH_2CH_2C=), 2.00 (m, CH_2CH_2CH), 1.85 ($CH_2CH_2CH_2$), 1.30 ($CH_2CH_2CH_3$), 0.90 (t, 3H, CH_3CH_2); ^{13}C nmr: δ 160.0 (C=N), 70.0 ($CHSO_2$), 61.0 (CH_2N), 33.0 (CH_2CH_2C=), 32.0 ($CHCH_2CH_2$), 24.0 ($CH_2CH_2CH_3$), 21.0 ($CH_2CH_2CH_3$), 14.0 (CH_3CH_2).

2-(1-Phenylsulfonylethylidene)-pyrrolidine [**1d (R = CH_3, N = 1)**].

Compound **1d** was obtained in 60% yield, mp 74-75 °C, crystallized from hexane/ethyl acetate; ir: υ 3403, 3072, 2980, 2943, 1624, 1587, 1479, 1442, 1322, 1292, 1152, 1133, 1089, 1066 cm^{-1}; ^{1}H nmr: δ 7.80 (m, 2H, ArH), 7.64 (t, 1H, ArH), 7.55 (m, 2H, ArH), 7.27 (br s, 1H, NH), 3.45 (t, 2H, CH_2CH_2NH), 2.52 (t, 2H, CH_2CH_2C=N), 1.93 (qt, 2H, $CH_2CH_2CH_2$), 1.70 (s, 3H, CH_3C=); ^{13}C nmr: δ 158.9 (C=*C*-N), 136.9, 131.9, 129.0, 126.3 (ArC), 89.6 (CH_3CSO_2), 47.6 (CH_2NH), 35.3 (C=C-CH_2), 22.5 ($CH_2CH_2CH_2$), 13.4 (CH_3C=).

Anal. Calcd. for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90; S, 13.51. Found: C, 60.88; H, 6.28; N, 6.02; S, 13.27.

2-(Phenylsulfonylethyl)-1,2-dehydropyrrolidine [**2d (R = CH_3, N = 1)**].

Hydrogen and carbon NMR chemical shift assignments. ^{1}H nmr: δ 7.80 (m, 2H, ArH), 7.50-7.42 (m, 3H, ArH), 4.20 (q, 1H, $CHCH_3$), 3.52 (t, 2H, CH_2CH_2N=), 2.72 (t, 2H, CH_2CH_2C=N), 1.88 (qt, 2H, $CH_2CH_2CH_2$), 1.55 (d, 3H, $CHCH_3$); ^{13}C nmr: δ 171.9 (-C=N), 143.1, 134.0, 128.9, 128.7 (ArC), 64.1 ($CHSO_2Ph$), 60.9 (CH_2N=*C*), 36.1 (CH_2C=C), 21.7 ($CH_2CH_2CH_2$), 12.3 ($CHCH_3$).

Z-2-(Phenylsulfonylmethylene)-piperidine [**1e, R = H, N = 2)**].

Compound **1e** was obtained in 70% yield, mp 73.5-74 °C, recrystallized from hexane/ethyl acetate); ir: υ 3353, 3056, 2953, 2867, 1604, 1331, 1282, 1156, 1080 cm^{-1}; ^{1}H nmr: δ 7.85 (m, 2H, ArH), 7.63 (m, 1H, ArH), 7.55 (m, 2H, ArH), 7.49 (m, 3H, NH & ArH), 4.45 (s, 1H, =$CHSO_2$), 3.25 (br s, 2H, CH_2CH_2N), 2.30 (br s, 2H, CH_2CH_2C=), 1.80 (br s, 2H, $CH_2CH_2CH_2C$=), 1.65 (br s, 2H, $CH_2CH_2CH_2$); ^{13}C nmr: δ 158.1 (=C-N), 145.4 (=*C*H-SO_2Ph), 131.7, 128.7, 128.5, 125.4 (ArC), 85.6 (=CH-SO_2), 41.4 (NCH_2), 29.6 (CH_2-C=), 22.4 ($NCH_2CH_2CH_2$), 19.6 ($CH_2CH_2CH_2C$=). Ms: m/z 172 (100%), 237(M^+).

Anal. Calcd. for $C_{12}H_{15}NO_2S$: C, 60.73; H, 6.37; N, 5.90; S, 13.51. Found: C, 60.37; H, 6.29; N, 5.87; S, 13.91.

2-(Phenylsulfonylmethyl)-1,2-dehydropiperidine [**2e (R = H, N = 2)**].

Hydrogen and carbon NMR for compound **2e**. ^{1}H nmr: δ 7.85 (m, 2H, ArH), 7.55 (m, 3H, ArH), 3.90 (s, 2H, CH_2SO_2), 3.50 (br s, 2H, CH_2N), 2.40 (br s, 2H, CH_2C=), 1.75 (br s, 2H, $CH_2CH_2CH_2N$), 1.50 (br s, 2H, ($CH_2CH_2CH_2C$=); ^{13}C nmr: δ 160.7 (-C=N), 138.5 (=C-SO_2), 133.8, 129.0, 128.2, 125.2 (ArC), 66.6 (CH_2SO_2), 50.0 (CH_2N), 30.3 (CH_2-C=), 21.1 ($CH_2CH_2CH_2N$), 19.9 ($CH_2CH_2CH_2C$=).

Acylation of 2-(Phenylsulfonylmethylene)-pyrrolidine (**1a**).

To a magnetically stirred solution of enamine **1a** (0.65 g, 2.91 mmol) in 15 mL dry tetrahydrofuran was added *n*-butyllithium (1.3 mL of a 2.5 *M* solution in hexanes) at -50 °C, stirred for 35 minutes. The orange solution was cooled at -78 °C, and reacted with acetic anhydride (0.30 g, 2.91 mmol) in 3 mL dry tetrahydrofuran while stirring and then allowing the temperature bath to raise to -28 °C. The reaction mixture was quenched with ammonium chloride (5 mL, saturated aqueous solution) and extracted with methylene chloride. The organic layer was dried with anhydrous magnesium sulfate, concentrated under reduced pressure (25-35/20-40 torr) and the residue crystallized (hexane/ethyl acetate, -10 °C) to afford the iminodienol **7** (0.25 g, 36%), mp 139.5-141.5 °C ir: υ 3068, 3000, 2982, 1600, 1552, 1479, 1460, 1310, 1236, 1150, 1095 cm^{-1}; ^{1}H nmr: δ 11.95 (br s, 1H, OH), 7.80 (m, 2H, ArH), 7.50 (m, 2H, ArH), 3.61 (t, 2H, CH_2CH_2N), 3.25 (t, 2H, CH_2CH_2C=), 2.28 (s, 3H, CH_3), 1.98 (qt, 2H, $CH_2CH_2CH_2$); ^{13}C nmr: δ 194.0 (=C-O), 173.0 (=N-C-SO_2), 145.0 (=C-SO_2), 132.0, 128.0, 126.0 (ArC), 106.0 (-C=N), 48.0 (CH_2N), 35.0 (CH_2CH_2C=), 30.0 (CH_3), 21.0 ($CH_2CH_2CH_2$); Ms: m/z 200 (100%), 266 (M^+ + 1).

Anal. Calcd. for $C_{13}H_{15}NO_3S$: C, 58.85; H, 5.70; N, 5.28; S, 12.08. Found: C, 58.42; H, 5.59; N, 5.19; S, 12.31.

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