Steric Promotion of Cyclization Reactions: Substituent Effect Studies in the Furan Intramolecular Diels-Alder Reaction

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Seven alkyl and aryl substituted *N*-allyl-*N*-(methylfuran)-sulfonamide compounds have been synthesized and their rates of cyclization and equilibrium product concentrations determined. Increased steric bulk on the sulfonamide substituent has been shown to increase both the rate of cyclization and yields of these reactions. A three-fold increase in rate and 15% increase in yield was observed as the substituent was varied from methyl to triisopropylbenzene.

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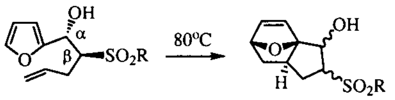
Introduction.

To improve the rates and yields of intramolecular cyclization reactions, substituents on the tethering chain have been studied extensively [1]. There are two main factors controlling cyclization, the Thorpe-Ingold effect [2] and the reactive rotamer effect [3], however, the reactive rotamer effect has been shown to be most influential [4]. The intramolecular Diels-Alder reaction with furan has proven useful in characterizing the reactive rotamer effect due to its sensitivity to substituents on the tethering chain [4,5,6]. A variety of chain lengths have been studied and the three atom tether, which cyclizes to form a five-membered ring, has been examined frequently [5,6].

Initially, disubstitution at the β-carbon (Table 1) was thought to be required for cyclization [7,8] but recent results demonstrated that a single, bulky substituent, such as *t*-butyl, was sufficient [9a]. McNelis and Sternbach further refined this concept by utilizing a sulfone in the β-position which increased the intramolecular Diels-Alder reaction rates and yields as shown in Table 1 [10].

Table 1 [10]



1a-c **2a-c**

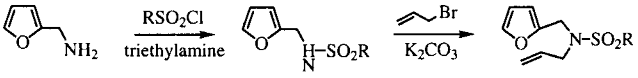
Compound	R	Time (days)	% Yield
1a	Me	9	78
1b	Ph	3	93
1e	*t*-Bu	1.7	97

In the series of compounds **1a-c**, increasing the size of the R-group from methyl to *t*-butyl increased the rate seven-fold and the yield by 19% [10]. In these hydroxysulfone systems, a 1,3-steric interaction between the hydroxyl group and the R-group could be contributing to the observed rate increase. Furthermore, intramolecular hydrogen bonding between the hydroxyl group and the sulfone oxygens could be affecting the rate by maintaining the tethering chain in a reactive conformation as in earlier work by Mukiayama [6k,l]. To determine if the rate and yield increases were due to steric effects of the R-group or the result of hydroxyl-sulfone interactions, sulfonamides **4a-g** [11], with a single substituent on the bridging chain were studied and the results are presented here.

Results and Discussion.

The syntheses of compounds **4a-g** were accomplished in two high yielding steps from furfurylamine using the process shown in Scheme 1. Commercially available sulfonyl chlorides were used for the preparation of **4**, offering a greater variety of alkyl and aryl substituents than in our previous study. By varying the sulfonyl chloride used in the first step of the synthesis, compounds with substituents that increased incrementally in steric bulk were produced.

Scheme 1



3a-g **4a-g**

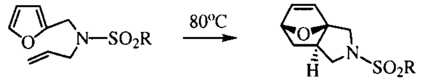
R = **a**, methyl; **b**, ethyl; **c**, propyl; **d**, isopropyl; **e**, phenyl; **f**, mesityl; **g**, 2,4,6-triisopropylphenyl

The intramolecular Diels-Alder reactions under our standard conditions (80° in benzene-d_6, sealed tube) were monitored by ^{1}H nmr and allowed to react until equilibrium had been reached (5-8 half-lives). Reaction kinetics were monitored by observing the disappearance of the furan protons and the appearance of products in the ^{1}H nmr spectrum. Sulfonamide Diels-Alder precursors **4a-g** cyclized with rates and yields given in Table 2, where k_{obs} is the observed first-order rate constant in min^{-1} and the yield is the mole fraction of products **5a-g** at equilibrium as determined by ^{1}H nmr.

Alkyl and aryl sulfonamides differ in rate by roughly a factor of three. In both the alkyl and aryl series, no direct correlation between size and rate was observed, as the propyl and isopropyl sulfonamide were both slower to react than the ethyl sulfonamide and the mesityl was slower than phenyl. Okamura [12] also found only a nominal increase

Table 2

Intramolecular Diels-Alder Kinetics



Compound	R	k_{obs} (min^{-1})	k_{rel}	K_{eq}	Yield [a]
4a	Methyl	5.2 x 10-4	1.0	3.4	77
4b	Ethyl	7.5 x 10-4	1.5	3.6	78
4c	Propyl	5.6 x 10-4	1.1	4.6	82
4d	Isopropyl	5.0 x 10-4	1	4.0	80
4e	Phenyl	1.2 x 10-3	2.4	9.0	90
4f	Mesityl	1.0 x 10-3	2.1	6.1	86
4g	2,4,6-Triisopropylphenyl	1.4 x 10-3	2.9	12	92

[a] Yields were determined by ^{1}H nmr.

in rate with increasing the length of the alkyl substituent in the β-position from ethyl to propyl (increased by a factor of 1.3). Overall, the R-group exerted a modest influence on the rate in these sulfonamide systems, with aryl sulfonamides cyclizing faster than the alkyl sulfonamides.

The magnitude of rate increases observed previously in the hydroxysulfone systems appears to be a function of both the hydroxyl and sulfone substituents and not simply due to the size of the sulfone R-group. Furthermore, DeClercq recently reported that a hydroxyl group significantly increased the rate of the intramolecular Diels-Alder reaction in the *t*-butyl substituted systems as compared to the dehydroxy analog [9b].

The effect of the sulfonamide substituent on the reaction equilibria was consistent with previous findings. Comparing methyl to trisyl, a 15% increase in conversion to products (K_{eq} increased from 3.4 to 12) was observed. An increase in yield has been observed in similar systems, with an increase in length and branching of the β-substituent. In Scheme 2 are two literature examples of yield improvements due to seemingly modest substituent changes two or more atoms removed from the tethering chain (methyl *vs*. benzyl; *o*-hydroxyphenyl *vs*. benzyl) [7,13].

Although substituent effects on rate can vary depending on the overall reactivity of the intramolecular Diels-Alder system being studied, the equilibrium effects are consistent and general to a number of different intramolecular Diels-Alder systems. Previous studies have focused on correlating substituent effects and reaction rates, however, the effect on yield has not been closely examined and is an important consideration for synthetic application of these reactions. This work and the two examples cited above suggest that remote substituents can have a significant effect on the equilibria of the intramolecular Diels-Alder reaction with furan.

EXPERIMENTAL

All reactions were carried out under an atmosphere of dry nitrogen or argon unless otherwise noted. Flash chromatography was performed using 230-400 mesh silica. Tetrahydrofuran was distilled from sodium-benzophenone. Nmr spectra were obtained on a JEOL GSX 400 MHz spectrometer and were taken in deuteriochloroform unless otherwise noted. Elemental analyses were performed by the Microanalytical Lab, University of California, Berkeley, CA 94720. All Diels-Alder reactions were carried out under vacuum in degassed benzene-d_6. These reactions were heated in a constant temperature bath at 80° and were conducted in sealed nmr tubes. In the kinetics studies, yields are reported from the integration in the ^{1}H nmr. First-order rate constants were calculated using a standard linear regression analysis [14], and the correlation coefficients were all greater than 0.99. Small amounts of the Diels-Alder products were isolated by preparative tlc (silica gel 60 Å; 1000 μm) for characterization directly from the nmr tube reactions.

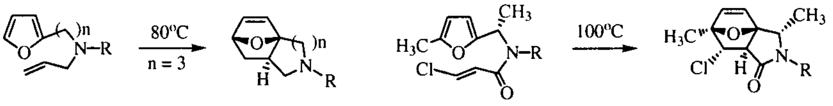
General Procedure to Prepare *N*-(2-furylmethyl)sulfonamides **3a-g**.

To a solution of furfurylamine (1.0 g, 10 mmoles), triethylamine (1.56 g, 15 mmoles), and 4-dimethylaminopyridine (0.12 g, 1 mmole) in 40 ml of dry tetrahydrofuran at 0° was added the sulfonyl chloride (9.5 mmoles) over 15 minutes. The reaction was stirred for 3 hours at 0°, warmed to room temperature and allowed to react for 12 hours. The milky white mixture was diluted to 100 ml with ethyl acetate, washed with 100 ml of water, two 50 ml portions of 5% hydrochloric acid and two 100 ml portions of water. The organic layer was washed with 100 ml of saturated sodium chloride and dried over sodium sulfate. The solvent was removed *in vacuo* to yield the desired sulfonamide.

N-(2-Furylmethyl)methanesulfonamide (**3a**).

Furfurylamine (2.0 g) was treated with methanesulfonyl chloride (1.5 ml) to yield 2.63 g (73%) as a pale yellow oil after purification by flash chromatography; ^{1}H nmr: δ 2.80 (3H, s), 4.35 (2H, d, J = 6.5 Hz), 4.65 (1H, s), 6.32 (1H, d, J = 3 Hz), 6.39 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 39.8, 40.9, 108.5, 110.5, 142.7, 150.1.

Scheme 2 [7,13]



R	% Yield
-H	0
-Me	45
-CH$_2$Ph	75

R	% Yield
-H	0
-*o*-HOPh	74
-CH$_2$Ph	100

Anal. Calcd. for $C_6H_9NO_3S$: C, 41.13; H, 5.18; N, 7.99. Found: C, 41.00; H, 5.08; N, 7.82.

N-(2-Furylmethyl)ethanesulfonamide (**3b**).

Furfurylamine (2.0 g) was treated with ethanesulfonyl chloride (1.85 ml) to yield 2.67 g (74%) as a white solid, mp 34-37°; ^{1}H nmr: δ 1.29 (3H, t, J = 7 Hz), 2.95 (2H, q, J = 7 Hz), 4.31 (2H, d, J = 6 Hz), 4.60 (1H, s), 6.32 (1H, d, J = 3 Hz), 6.39 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 8.5, 40.2, 48.1, 108.7, 110.9, 143.1, 150.6.

Anal. Calcd. for $C_7H_{11}NO_3S$: C, 44.43; H, 5.86; N, 7.40. Found: C, 44.48; H, 6.02; N, 7.38.

N-(2-Furylmethyl)-1-propanesulfonamide (**3c**).

Furfurylamine (2.0 g) was treated with propanesulfonyl chloride (2.20 ml) to yield 3.83 g (96%) as a pale amber solid which was purified by flash chromatography, mp 31-33°; ^{1}H nmr: δ 0.95 (3H, t, J = 7 Hz), 1.75 (2H, m), 2.90 (2H, t, J = 7 Hz), 4.30 (2H, d, 6 Hz), 4.62 (1H, s), 6.30 (1H, d, J = 3 Hz), 6.37 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 12.8, 17.3, 39.9, 55.1, 108.4, 110.9, 142.8, 150.3.

Anal. Calcd. for $C_8H_{13}NO_3S$: C, 47.27; H, 6.45; N, 6.89. Found: C, 46.94; H, 6.52; N, 6.74.

N-(2-Furylmethyl)-2-propanesulfonamide (**3d**).

Furfurylamine (2.0 g) was treated with 2-propanesulfonyl chloride (2.15 ml) to yield 3.13 g (75%) as a pale amber oil which was purified by flash chromatography; ^{1}H nmr: δ 1.33 (6H, d, J = 7 Hz), 3.08 (1H, m), 4.34 (2H, d, J = 6 Hz), 4.55 (1H, s), 6.30 (1H, d, J = 3 Hz), 6.38 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 16.3, 39.9, 53.8, 108.1, 110.5, 142.5, 150.7.

Anal. Calcd. for $C_8H_{13}NO_3S$: C, 47.27; H, 6.45; N, 6.89. Found: C, 46.95; H, 6.47; N: 6.75.

N-(2-Furylmethyl)benzenesulfonamide (**3e**).

Furfurylamine (2.0 g) was treated with benzenesulfonyl chloride (2.45 ml) to yield 4.37 g (96%) as a white solid, mp 82-83°; ^{1}H nmr: δ 4.21 (2H, d, J = 6 Hz), 4.78 (1H, s), 6.10 (1H, d, J = 3 Hz), 6.23 (1H, dd, J = 2, 3 Hz), 7.23 (1H, d, J = 2 Hz), 7.50 (2H, t, J = 7 Hz), 7.59 (1H, t, J = 7 Hz), 7.85 (2H, d, J = 7 Hz); ^{13}C nmr: δ 40.2, 108.3, 110.4, 127.1, 129.0, 132.7, 139.9, 142.6, 149.4.

Anal. Calcd. for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90. Found: C, 55.72; H, 4.74; N, 5.93.

N-(2-Furylmethyl)-2,4,6-trimethylbenzenesulfonamide (**3f**).

Furfurylamine (1.0 g) was treated with mesityl chloride (2.14 g) to yield 2.45 g (91%) as a white solid, mp 50-51°; ^{1}H nmr: δ 2.29 (3H, s), 2.62 (6H, s), 4.13 (2H, d, J = 6 Hz), 4.89 (1H, s), 6.03 (1H, d, J = 3 Hz), 6.20 (1H, dd, J = 2, 3 Hz), 6.91 (2H, s), 7.21 (1H, d, J = 2 Hz); ^{13}C nmr: δ 20.8, 22.8, 39.6, 107.9, 110.3, 131.8, 133.5, 139.0, 142.2, 142.4, 149.6.

Anal. Calcd. for $C_{14}H_{17}NO_3S$: C, 60.19; H, 6.13; N, 5.01. Found: C, 60.22; H, 6.10; N, 4.91.

N-(2-Furylmethyl)-2,4,6-triisopropylbenzenesulfonamide (**3g**).

Furfurylamine (1.0 g) was treated with 2,4,6-triisopropylbenzenesulfonyl chloride (2.96 ml) to yield 3.46 g (97%) as a white solid after recrystallization from hexane, mp 97-100°; ^{1}H nmr: δ 1.38 (12H, d, J = 7 Hz), 1.40 (6H, d, J = 7 Hz), 3.05 (1H, m), 4.25 (2H, m), 4.30 (2H, d, J = 6 Hz), 4.78 (1H, s), 6.19 (1H, d, J = 3 Hz), 6.35 (1H, dd, J = 2, 3 Hz), 7.37 (1H, d, J = 2 Hz), 7.40 (2H, s); ^{13}C nmr: δ 23.6, 24.8, 29.7, 34.2, 39.8, 108.2, 110.4, 123.7, 132.2, 142.4, 149.7, 150.2, 152.8.

Anal. Calcd. for $C_{20}H_{29}NO_3S$: C, 66.08; H, 8.04; N; 3.85. Found: C, 66.11; H, 8.22; N, 3.84.

General Alkylation Procedure to Prepare *N*-Allyl-*N*-(2-furylmethyl)sulfonamides **4a-g**.

To a mixture of the *N*-(2-furylmethyl)sulfonamide (4 mmoles), dried potassium carbonate (5.53 g, 40 mmoles), and tetrabutylammonium iodide (0.148 g, 0.4 mmole) in 30 ml of acetone at room temperature was added allyl bromide (9.68 g, 80 mmoles) in one portion and the reaction was stirred overnight. Acetone was removed by rotary evaporation and the residue taken up in 100 ml of ethyl acetate and washed twice with 100 ml portions of water. The organic layer was washed with saturated sodium chloride and dried over sodium sulfate. The solvent was removed *in vacuo* to yield the desired *N*-allyl-*N*-(2-furylmethyl)sulfonamide.

N-Allyl-*N*-(2-furylmethyl)methanesulfonamide (**4a**).

N-(2-Furylmethyl)methanesulfonamide (0.68 g) was treated with allyl bromide to yield 0.67 g (82%) as a yellow oil; ^{1}H nmr: δ 2.80 (3H, s), 3.80 (2H, d, J = 6.5 Hz), 4.41 (2H, s), 5.30 (2H, m), 5.78 (1H, m), 6.32 (1H, d, J = 3 Hz), 6.39 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 39.9, 42.7, 49.6, 110.3, 111.0, 119.9, 133.1, 143.2, 149.9.

Anal. Calcd. for $C_9H_{13}NO_3S$: C, 50.21; H, 6.09; N, 6.21. Found: C, 50.31; H, 6.11; N, 6.41.

N-Allyl-*N*-(2-furylmethyl)ethanesulfonamide (**4b**).

N-(2-Furylmethyl)ethanesulfonamide (1.06 g) was treated with allyl bromide to yield 1.24 g (87%) as a yellow oil; ^{1}H nmr: δ 1.29 (3H, t, J = 7 Hz), 2.95 (2H, q, J = 7 Hz), 3.85 (2H, d, J = 6 Hz), 4.41 (2H, s), 5.30 (2H, m), 5.79 (1H, m), 6.32 (1H, d, J = 3 Hz), 6.39 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 8.3, 42.6, 47.8, 49.9, 110.0, 110.8, 119.5, 133.3, 143.1, 150.3.

Anal. Calcd. for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59; N, 6.11. Found: C, 52.35; H, 6.74; N, 6.24.

N-Allyl-*N*-(2-furylmethyl)-1-propanesulfonamide (**4c**).

N-(2-Furylmethyl)-1-propanesulfonamide (1.30 g) was treated with allyl bromide to yield 1.49 g (95%) as a yellow oil; ^{1}H nmr: δ 0.95 (3H, t, J = 7 Hz), 1.75 (2H, m), 2.91 (2H, t, J = 7 Hz), 3.83 (2H, d, J = 7 Hz), 4.40 (2H, s), 5.28 (2H, m), 5.78 (1H, m), 6.29 (1H, d, J = 3 Hz), 6.35 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 13.0, 17.0, 42.2, 49.6, 54.9, 109.7, 110.5, 119.2, 133.0, 142.7, 150.0.

Anal. Calcd. for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.04; N, 5.76. Found: C, 54.31; H, 7.24; N, 5.80.

N-Allyl-*N*-(2-furylmethyl)-2-propanesulfonamide (**4d**).

N-(2-Furylmethyl)-2-propanesulfonamide (1.25 g) was treated with allyl bromide to yield 1.58 g (99%) as a yellow oil; ^{1}H nmr: δ 1.33 (6H, d, J = 7 Hz), 3.20 (1H, m), 3.85 (2H, d, J = 6 Hz), 4.40 (2H, s), 5.29 (2H, m), 5.80 (1H, m), 6.30 (1H, d, J = 3 Hz), 6.38 (1H, dd, J = 2, 3 Hz), 7.41 (1H, d, J = 2 Hz); ^{13}C nmr: δ 16.2, 42.0, 49.8, 54.3, 109.3, 110.1, 118.9, 132.9, 142.4, 149.9.

Anal. Calcd. for $C_{11}H_{17}NO_3S$: C, 54.29; H, 7.04; N, 5.76. Found: C, 54.07; H, 7.11; N, 5.92.

N-Allyl-*N*-(2-furylmethyl)benzenesulfonamide (**4e**).

N-(2-Furylmethyl)benzenesulfonamide (0.95 g) was treated with allyl bromide to yield 1.09 g (98%) as a yellow oil; ^{1}H nmr: δ 3.81 (2H, d, J = 6 Hz), 4.41 (2H, s), 5.19 (2H, m), 5.64 (1H, m), 6.15 (1H, d, J = 3 Hz), 6.26 (1H, dd, J = 2, 3 Hz), 7.23 (1H, d, J = 2 Hz), 7.48 (2H, t, J = 7 Hz), 7.57 (1H, t, J = 7 Hz), 7.79 (2H, d, J = 7 Hz); ^{13}C nmr: δ 42.6, 49.7, 109.5, 110.3, 119.3, 127.2, 128.9, 132.4, 132.4, 140.3, 142.4, 149.6.

Anal. Calcd. for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.56; H, 5.27; N, 4.99.

N-Allyl-*N*-(2-furylmethyl)-2,4,6-trimethylbenzenesulfonamide (**4f**).

N-(2-Furylmethyl)-2,4,6-trimethylbenzenesulfonamide (1.0 g) was treated with allyl bromide to yield 1.09 g (94%) as a yellow oil; ^{1}H nmr: δ 2.30 (3H, s), 2.61 (6H, s), 3.71 (2H, d, J = 6 Hz), 4.33 (2H, s), 5.18 (2H, m), 5.67 (1H, m), 6.12 (1H, d, J = 3 Hz), 6.27 (1H, dd, J = 2, 3 Hz), 6.94 (2H, s), 7.31 (1H, d, J = 2 Hz); ^{13}C nmr: δ 21.0, 22.7, 41.3, 48.5, 109.5, 110.3, 119.6, 131.9, 132.4, 132.9, 140.4, 142.5, 142.5, 149.7.

Anal. Calcd. for $C_{17}H_{23}NO_3S$: C, 63.92; H, 6.63; N, 4.38. Found: C, 63.70; H, 6.65; N, 4.35.

N-Allyl-*N*-(2-Furylmethyl)-2,4,6-triisopropylbenzenesulfonamide (**4g**).

N-(2-Furylmethyl)-2,4,6-triisopropylbenzenesulfonamide (1.07 g) was treated with allyl bromide to yield 1.17 g (98%) as a yellow oil; ^{1}H nmr: δ 1.22 (12H, d, J = 7 Hz), 1.28 (6H, d, J = 7 Hz), 2.93 (1H, m), 3.73 (2H, d, J = 7 Hz), 4.15 (2H, m), 4.39 (2H, s), 5.20 (2H, m), 5.75 (1H, m), 6.14 (1H, d, J = 3 Hz), 6.29 (1H, dd, J = 2, 3 Hz), 7.18 (2H, s), 7.32 (1H, d, J = 2 Hz); ^{13}C nmr: δ 23.6, 24.8, 29.3, 34.2, 40.9, 48.6, 109.6, 110.4, 119.8, 123.9, 131.3, 132.6, 142.4, 149.7, 151.5, 153.1.

Anal. Calcd. for $C_{23}H_{33}NO_3S$: C, 68.45; H, 8.24; N, 3.47. Found: C, 68.06; H, 8.52; N, 3.45.

General Diels-Alder Reaction Procedure for **5a-g**.

A solution of the *N*-Allyl-*N*-(2-furylmethyl)sulfonamide (25-30 mg) in 0.75 mL of benzene-d_6 was heated to 80° in a vacuum-sealed nmr tube and the progress of the reaction monitored by ^{1}H nmr. After the reaction had reached equilibrium, the solvent was removed *in vacuo* and the Diels-Alder product was isolated by preparative tlc (2:1 hexane: ethyl acetate).

(+/-)-*N*-Methylsulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5a**).

N-Allyl-*N*-(2-furylmethyl)methanesulfonamide was heated at 80° to yield a white solid, mp 98-101°; ^{1}H nmr: δ 1.49 (1H, dd, J = 8, 12 Hz), 1.80 (1H, m), 2.21 (1H, m), 2.83 (3H, s), 2.89 (1H, m), 3.67 (1H, d, J = 12 Hz), 3.89 (1H, dd, J = 8, 9 Hz), 3.94 (1H, d, J = 12 Hz), 5.08 (1H, dd, J = 2, 5 Hz), 6.38 (1H, d, J = 7 Hz), 6.44 (1H, dd, J = 2, 5 Hz); ^{13}C nmr: δ 31.2, 34.1, 42.7, 49.4, 53.6, 80.2, 95.2, 133.6, 137.7.

Anal. Calcd. for $C_9H_{13}NO_3S$: C, 50.21; H, 6.09; N, 6.51. Found: C, 50.27; H, 6.05; N, 6.45.

(+/-)-*N*-Ethylsulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5b**).

N-Allyl-*N*-(2-furylmethyl)ethylsulfonamide was heated at 80° to yield an oil; ^{1}H nmr: δ 1.39 (3H, t, J = 8 Hz), 1.47 (1H, dd, J = 12, 7 Hz), 1.79 (1H, ddd, J = 12, 4.5, 3 Hz), 2.2 (1H, m), 2.97 (1H, t, 10 Hz), 3.04 (2H, q, J = 7 Hz), 3.74 (1H, d, J = 12 Hz), 3.93 (1H, dd, J = 8, 8 Hz), 3.98 (1H, d, J = 12 Hz), 5.09 (1H, dd, J = 5, 2 Hz), 6.38 (1H, d, J = 6 Hz), 6.43 (1H, dd, J = 5, 2 Hz); ^{13}C nmr: δ 7.9, 31.1, 42.7, 43.8, 49.3, 53.4, 80.3, 95.4, 133.8, 137.6.

Anal. Calcd. for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59; N, 6.11. Found: C, 52.10; H, 6.36; N, 5.72.

(+/-)-*N*-Propylsulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5c**).

N-Allyl-*N*-(2-furylmethyl)-1-propanesulfonamide was heated at 80° to yield an oil; ^{1}H nmr: δ 0.98 (3H, t, J = 8 Hz), 1.40 (1H, dd, J = 12, 7 Hz), 1.71 (1H, ddd, J = 12, 4.5, 3 Hz), 2.12 (1H, m), 1.80 (2H, m), 2.89 (3H, m), 3.65 (1H, d, J = 12 Hz), 3.84 (1H, dd, J = 8, 8 Hz), 3.90 (1H, d, J = 12 Hz), 5.02 (1H, dd, J = 5, 2 Hz), 6.31 (1H, d, J = 6 Hz), 6.36 (1H, dd, J = 5, 2 Hz); ^{13}C nmr: δ 13.2, 16.9, 31.0, 42.7, 49.2, 50.8, 53.3, 80.3, 95.3, 133.8, 137.5.

Anal. Calcd. for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.05; N, 5.76. Found: C, 53.84; H, 7.17; N, 5.54.

(+/-)-*N*-Isopropylsulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5d**).

N-Allyl-*N*-(2-furylmethyl)-2-propanesulfonamide was heated at 80° to yield an oil; ^{1}H nmr: δ 1.31 (6H, dd, J = 7, 1.5 Hz), 1.38 (1H, dd, J = 12, 7 Hz), 1.70 (1H, ddd, J = 12, 4.5, 3 Hz), 2.10 (1H, m), 2.95 (1H, t, 10 Hz), 3.20 (1H, m), 3.69 (1H, d, J = 12 Hz), 3.93 (1H, dd, J = 8, 8 Hz), 3.98 (1H, d, J = 12 Hz), 5.02 (1H, dd, J = 5, 2 Hz), 6.31 (1H, d, J = 6 Hz), 6.35 (1H, dd, J = 5, 2 Hz); ^{13}C nmr: δ 16.7, 30.9, 42.8, 49.7, 53.4, 53.8, 80.4, 95.7, 134.0, 137.5.

Anal. Calcd. for $C_{11}H_{17}NO_3S$: C, 54.30; H, 7.05; N, 5.76. Found: C, 54.53; H, 7.10; N, 5.64.

(+/-)-*N*-Benzenesulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5e**).

N-Allyl*N*-(2-furylmethyl)benzenesulfonamide was heated at 80° to yield a white solid, mp 121-123°; ^{1}H nmr: δ 1.36 (1H, dd, J = 8, 12 Hz), 1.64 (2H, m), 2.07 (1H, m), 2.71 (1H, dd, J = 9, 10 Hz), 3.54 (1H, d, J = 12 Hz), 3.91 (1H, dd, J = 8, 9 Hz), 3.96 (1H, d, J = 12 Hz), 4.94 (1H, dd, J = 2, 5 Hz), 6.36 (2H, m), 7.56 (3H, m), 7.84 (2H, d, J = 6 Hz); ^{13}C nmr: δ 30.2, 42.6, 49.3, 53.3, 80.2, 95.1, 127.4, 129.1, 132.7, 134.0, 136.9, 137.3.

Anal. Calcd. for $C_{14}H_{15}NO_3S$: C, 60.63; H, 5.45; N, 5.05. Found: C, 60.41; H, 5.40; N, 4.99.

(+/-)-*N*-2,4,6-Trimethylbenzenesulfonyl-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5f**).

N-Allyl-*N*-(2-furylmethyl)-2,4,6-trimethylbenzenesulfonamide was heated at 80° to yield an oil; ^{1}H nmr: δ 1.41 (1H, dd, J = 12, 8 Hz), 1.73 (2H, ddd, J = 12, 4, 3 Hz), 2.15 (1H, m), 2.29 (3H, s), 2.63 (6H, s), 2.87 (1H, t. J = 10 Hz), 3.63 (1H, d, J = 12 Hz), 3.80 (1H, dd, J = 10, 8 Hz), 3.87 (1H, d, J = 12 Hz), 5.05 (1H, dd, J = 4, 2 Hz), 6.37 (2H, m), 6.95 (2H, s); ^{13}C nmr: δ 20.9, 22.9, 30.7, 42.9, 47.9, 52.1, 80.3, 95.5, 131.9, 132.8, 134.1, 137.3, 140.1, 142.4.

Anal. Calcd. for $C_{17}H_{21}NO_3S$: C, 63.92; H, 6.63; N, 4.38. Found: C, 63.61; H, 6.67; N, 4.12.

(+/-)-*N*-2,4,6-Triisopropylbenzenesulfonyl)-3a,4,5,7a-tetrahydro-5,7a-epoxyisoindoline (**5g**).

N-Allyl-*N*-(2-furylmethyl)-2,4,6-triisopropylbenzenesulfonamide was heated at 80° to yield a white solid, mp 144-145°; ^{1}H nmr: δ 1.25 (18H, d, J = 6 Hz), 1.41 (2H, dd, J = 8, 12 Hz), 1.74 (1H, m), 2.13 (1H, m), 2.91 (2H, m), 3.64 (1H, d, J = 12 Hz), 3.80 (1H, dd, J = 8, 9 Hz), 3.87 (1H, d, J = 12 Hz), 4.23 (2H, m), 5.06 (1H, dd, J = 2, 5 Hz), 6.38 (2H, m), 7.16 (2H, s); ^{13}C nmr: δ 23.6, 24.8, 29.3, 30.5, 34.2, 43.1, 47.7, 52.1, 80.3, 95.5, 123.8, 131.5, 134.3, 137.3, 151.2, 152.9.

Anal. Calcd. for $C_{23}H_{33}NO_3S$: C, 68.45; H, 8.24; N, 3.47. Found: C, 68.47; H, 8.27; N, 3.53.

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