concentrated in vacuo to yield 26.6 mg of a crude oil, which was subsequently purified by HPLC (4:1 hexane/EtOAc). The purified yield was 62% of a mixture of diastereomers **11a** (8.1 mg), **11b** (4.0 mg), **11c** (11.4 mg), and **11d** (3.1 mg) in a 2:1:3:1 ratio.

11a: solid; mp 64–66 °C (crystallized from hexane); *m/e* no peak match for parent, 252.1053 (M + 1, calcd 252.1058, error 1.9 ppm, formula $C_{13}H_{17}O_2N_1S_1$); IR ($CHCl_3$, cm^{-1}) 3330 (N—H), 1735 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 7.40–7.25 (5 H, m), 3.85–3.80 (1 H, m), 3.83 (3 H, s), 3.66 (1 H, br s), 3.51 (1 H, dq, J = 9.7, 6.3 Hz), 1.80 (3 H, s), 1.22 (3 H, d, J = 6.3 Hz).

11b: solid, mp 88–88.5 °C (crystallized from hexane); *m/e* no peak match for parent, 252.1067 (M + 1, calcd 252.1058, error 3.5 ppm, formula, $C_{13}H_{17}O_2N_1S_1$); IR ($CHCl_3$, cm^{-1}) 3330 (N—H), 1730 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 7.35–7.25 (5 H, m), 4.83 (1 H, d, J = 5.1 Hz), 3.76 (3 H, s), 3.69 (1 H, dq, J = 5.1, 6.8 Hz), 2.72 (1 H, br s), 1.91 (3 H, s), 0.89 (3 H, d, J = 6.8 Hz).

11c: solid; mp 94–96 °C (crystallized from hexane); *m/e* no peak match for parent 252.1067 (M + 1, calcd 252.1058, error 3.6 ppm, formula $C_{13}H_{17}O_2N_1S_1$); IR ($CHCl_3$, cm^{-1}): 3300 (N—H), 1730 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 7.42–7.25 (5 H, m), 4.63 (1 H, dd, J = 4.7, 14.5 Hz), 3.87 (1 H, br d, J = 14.5 Hz), 3.85 (3 H, s), 3.80 (1 H, dq, J = 4.7, 7.0 Hz), 1.77 (3 H, s), 0.82 (3 H, d, J = 7.0 Hz).

11d: solid; mp 74–75 °C (crystallized from hexane); *m/e* no peak match for parent; 252.1071 (M + 1, calcd 252.1058, error 5.2 ppm, formula $C_{13}H_{17}O_2N_1S_1$); IR ($CHCl_3$, cm^{-1}) 3300 (N—H), 1730 (C=O); 200-MHz NMR ($CDCl_3$, ppm) 7.45–7.30 (5 H, m), 4.14 (1 H, d, J = 9.25 Hz), 3.79 (3 H, s), 3.55 (1 H, qd, J = 6.4, 9.25 Hz), 2.72 (1 H, br s), 1.82 (3 H, s), 1.20 (3 H, d, J = 6.4 Hz).

Methylation of 11. Preparation of 2-Carbomethoxy-4-phenyl-2,3,5-trimethylthiazolidine (12). To the purified diastereomer **11d** (5.7 mg, 0.029 mmol) dissolved in acetonitrile (3 mL, distilled from CaH_2) was added 1.1 equiv of methyl triflate (MeOTf) (0.003 mL, 0.03 mmol) at room temperature. After 30 min, excess MeOTf (1 equiv) was added to the reaction mixture, and the reaction was followed by TLC until no starting thiazolidine **11d** remained. A crude NMR spectrum indicated the N-protonated ammonium salt of **12**. Filtration through a plug of silica gel (5 g, 10:1 hexane/EtOAc eluent) afforded the single diastereomeric product **12** in quantitative yield (5.8 mg).

12: oil; analytical TLC (silica gel F254), 4:1 hexane/EtOAc, R_f 0.65; *m/e* no peak match for parent, 264.1067 (M − 1, calcd 264.1058, error 3.4 ppm, formula $C_{14}H_{19}O_2N_1S_1$); IR ($CHCl_3$, cm^{-1}) 1723 (C=O); 200-MHz NMR (C_6D_6, ppm) 7.40–7.30 (5 H, m), 4.08 (1 H, d, J = 8.6 Hz), 3.75 (3 H, s), 3.40 (1 H, dd, J = 6.6, 8.6 Hz), 2.11 (3 H, s), 1.76 (3 H, s), 1.20 (3 H, d, J = 6.6 Hz).

Acknowledgment. This work was supported by the National Institutes of Health (CA 17918; also, RRO 2388-01 to support the AM-500 NMR system).

Endocyclic Nucleophilic Substitution at Tetracoordinate Sulfur(VI)[1]

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A search for endocyclic nucleophilic substitution at tetracoordinate sulfur(VI), usually sulfonyl sulfur, was carried out through the use of molecules so constructed that any intramolecular substitution process was forced to proceed through four-, five-, or six-membered cyclic transition states or intermediates with each ring incorporating both the nucleophile, sulfur atom, and leaving group. Three compounds [*N*-methyl-*N*-phenyl-4-toluenesulfonamide (**5**), 2′-(methylamino)phenyl 4-toluenesulfonate (**30**), and 2′-[(*N*-methylamino)methyl]phenyl 4-toluenesulfonate (**38**)] that underwent apparent endocyclic substitution when treated with strong base were synthesized—one for each ring size. Crossover reactions were carried out with mixtures of deuteriated and undeuteriated substrates. These reactions showed that **5** and **30** rearranged intramolecularly to give 2′-(methylamino)phenyl 4-methylphenyl sulfone (**7**) and *N*-(2′-hydroxyphenyl)-4-toluenesulfonamide (**14**), respectively. Although **5** may have rearranged via an endocyclic process, it seems, on the basis of other evidence, that **30** did not. Sulfonate **38** upon treatment with LDA reacted intermolecularly to give *N*-(2′-hydroxybenzyl)-*N*-methyl-4-toluenesulfonamide.

This paper reports the results of a study of nucleophilic substitution at tetracoordinate sulfur(VI) with molecules so constructed that the nucleophile (Nu), leaving group (L), and sulfur atom need not be colinear in the transition state or intermediate.[3] Several earlier studies found that nucleophilic substitution at tetracoordinate sulfur(VI) proceeded with inversion of configuration.[4–7] Usually, a trigonally bipyramidal intermediate or transition state with the sulfur atom at its center and the nucleophile and leaving group at the apical positions was postulated to account for such stereochemistry.[8,9] That is, Nu, the sulfur atom, and L are colinear, or at least closely so, an arrangement analogous to that in an S_N2 transition state. Even though a stable anion that is a model for such an intermediate has been synthesized, it is conceivable that an atom (A), sulfur or otherwise, could undergo substitution via a transition state or intermediate in which Nu, A, and L are far removed from colinearity.[10] A trigonal bipyramidal intermediate (a lone electron pair on sulfur is counted as a ligand) with Nu and L in an apical–equatorial arrangement with respect to one another has been postulated to account for examples of retention of configuration observed in nucleophilic substitution at tricoordinate S(IV).[8] Recently, an analogous intermediate has been postulated involving sulfonyl sulfur.[11]

One approach to test for nonlinearity is to construct a molecule potentially capable of undergoing the desired substitution reaction intramolecularly by having Nu connected to L by a sequence of atoms as depicted below. Nu

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(2) S.C. (Ph.D. Thesis, 1985), D.J.M. (Ph.D. Thesis, 1985), University of New Hampshire.

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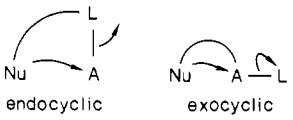
Table I. Analysis of the Mass Spectrum of the Product from the Crossover Reaction of 5 and 9

m/e[a]	267	266	265	264	263	262	261
no. of d atoms	d-6	d-5	d-4	d-3	d-2	d-1	d-0
observed % intensity, 5					5	14	81
observed % intensity, 9	65	20	8	7			
observed % intensity of product	33	9	2	1	4	13	38
calculated % intensity (intramolecular)	32	10	4	3	3	6	41
calculated % intensity (intermolecular)	10	5	4	37	7	6	31

[a] Values normalized to 100%.

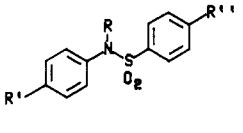
and L may be prevented from attaining colinearity with A by the appropriate length of this sequence. In this way, variation of the Nu–A–L angle from roughly 180 to 90° is possible. The term endocyclic, as opposed to exocyclic, has been used to describe such substitution reactions.[12] If a reaction is suspected to be following an endocyclic pathway, then it must be shown to be intramolecular, not intermolecular (bimolecular), before it can be considered as a possibly true, rather than apparent, example of this mechanism. This approach has been applied to substitution at a variety of atoms.[13-18] Its use in studying nucleophilic substitution at tetracoordinate sulfur(VI) forms the subject of this article.



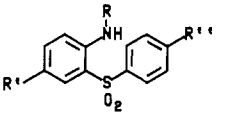
Four variables are attendant in designing a molecule for use in studying endocyclic nucleophilic substitution. These are the nature of the atom undergoing substitution, the nucleophile, the leaving group, and the connection between the latter two. In this study, the atom undergoing substitution was restricted to tetracoordinate sulfur(VI), most commonly exemplified by sulfonyl sulfur. The nucleophile was carbon or nitrogen in an anionic form, and the leaving group was either nitrogen or oxygen. The one, two, or three connecting atoms between Nu and L would lead to four-, five-, or six-membered rings, respectively, in the hoped-for transition states or intermediates. Even with these restrictions, 12 (1 × 2 × 2 × 3) general cases were possible. This paper reports on several of them, beginning with those examples that might involve a four-membered ring in the intermediate or transition state and proceeding to some examples where five- and six-membered rings are hypothetically possible. Stepwise substitution via trigonally bipyramidal intermediates, arising by Nu–S bond formation prior to S–L bond breakage, will be assumed, rather than concerted substitution, for ease of discussion.[19,20] Furthermore, it will be assumed that these intermediates may undergo ligand reorganization by Berry pseudorotation.

Results and Discussion

Four-Membered Ring Intermediates. A general reaction that may be an example of endocyclic nucleophilic substitution at sulfonyl sulfur involving a four-membered ring intermediate was independently discovered by Hellwinkel and Closson and their co-workers.[21,22] They showed that N-substituted *N*-arylarenesulfonamides, such as **1**, underwent rearrangement to *o*-amino sulfones, such as **2**, upon treatment with strong bases such as *n*-butyllithium (BuLi).



1, 5, 6, 9

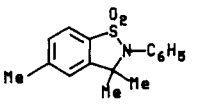


2, 7, 8, 10, 11, 12

	R	R'	R''
1, 2	H	H	Me
5, 7	Me	H	Me
6, 8	Me	MeO	MeO

	R	R'	R''
9, 10	CD_3	H	CD_3
11	CD_3	H	Me
12	Me	H	CD_3

It was postulated that a carbanionic species formed by proton abstraction ortho to the nitrogen atom served as a nucleophile, which attacked the sulfonyl sulfur atom intramolecularly with consequent formation of the *o*-amino sulfone (**2**). Hellwinkel and Supp treated **3** with BuLi and obtained **4** in greater than 90% yield in an apparent endocyclic reaction, suggesting that an endocyclic path is also preferred over an exocyclic one in the rearrangement of sulfonamides such as **1**. An exocyclic reaction would be bimolecular with the carbanionic nucleophile of one molecule attacking the sulfonyl sulfur of the other.



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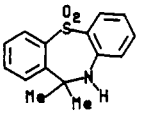

4

Closson and Schaefer treated a mixture of two sulfonamides, **5** and **6**, with methyllithium and found that there was no crossover, i.e., the sulfonamides reacted independently of one another to form their isomeric aminosulfones, **7** and **8**, respectively. Thus, assuming that the two sulfonamides reacted at comparable rates, the rearrangement was deemed to be intra- and not inter-molecular, consistent with an endocyclic pathway. In order to

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(13) Nucleophilic substitution at aliphatic carbon. (a) Reference 12. (b) King, J. F.; McGarrity, M. J. *J. Chem. Soc., Chem. Commun.* **1982**, 175–176.
(14) Nucleophilic substitution at sulfur(II). Hogg, D. R.; Vipond, P. W. *J. Chem. Soc. C* **1970**, 2142–2144.
(15) Nucleophilic substitution at sulfur(IV). (a) Wudl, F.; Lee, T. B. K. *J. Am. Chem. Soc.* **1973**, *95*, 6349–6358. (b) Andersen, K. K.; Malver, O. *J. Org. Chem.* **1983**, *48*, 4803–4807.
(16) Nucleophilic Substitution at sulfur(VI). (a) Reference 3. (b) Hellwinkel, D.; Lenz, R. *Chem. Ber.* **1985**, *118*, 65–85. This reference also contains several references to substitution at other atoms.
(17) Nucleophilic substitution at oxygen and nitrogen. (a) Beak, P.; Loo, D. K. *J. Am. Chem. Soc.* **1986**, *108*, 3834–3835. (b) Beak, P.; Basha, A.; Kokko, B. *J. Am. Chem. Soc.* **1984**, *106*, 1511–1512.
(18) Free radical substitution at sulfur(II). (a) Kampmeier, J. A. *ACS Symp. Ser.* **1978**, No. 69. (b) Beckwith, A. L. J.; Boate, D. R. *J. Chem. Soc., Chem. Commun.* **1986**, 189–190.
(19) Jager, J.; Graafland, T.; Schenk, H.; Kirby, A. J.; Engberts, J. B. F. N. *J. Am. Chem. Soc.* **1984**, *106*, 139–143 and earlier articles cited therein supporting stepwise substitution.
(20) Thea, S.; Guanti, G.; Hopkins, A. R.; Williams, A. *J. Org. Chem.* **1985**, *50*, 3336–3341, and earlier articles cited therein supporting concerted substitution.
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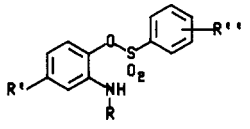
(22) Shafer, S. J.; Closson, W. D. *J. Org. Chem.* **1975**, *40*, 889–892.

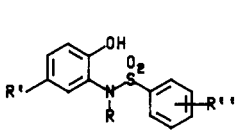
ensure that the sulfonamides were rearranging at comparable rates, we treated an equimolar mixture of **5** and its hexadeuteriated isotopomer, **9**, with BuLi in tetrahydrofuran (THF). Closson had rearranged **5** to **7** in 50% yield; we obtained 37% of a mixture of isotopomers. If the rearrangement was intramolecular (no crossover), four isotopomers—**7**, **10**, **11**, and **12**—should be formed, giving rise to a deuterium ratio of 1:2:1. Analysis of the *o*-amino sulfone product mixture by MS showed that no crossover had occurred (Table I). The rearrangement was intramolecular and therefore may be an example of endocyclic nucleophilic substitution at sulfur(VI). A referee has suggested, as an alternative to this mechanism, elimination of arenesulfinate anion from the carbanoid species to give an iminocarbene followed by recombination of the sulfinate with the carbene to give the *o*-amino sulfone reminiscent of the elimination of arenesulfinate anion from an *N*-arylsulfonylhydrazone in the Bamford–Stevens reaction.

It is interesting to note that aryl arenesulfonates, analogous to the sulfonamides, do not rearrange when treated with strong bases. Instead, the aryl groups are transformed to arynes by 1,2-elimination of the arenesulfonate anion.[23,24]

Five-Membered Ring Intermediates. Earlier, we described the base-induced rearrangement of some arenesulfonate esters (**13**), derived from *o*-aminophenols, to the corresponding sulfonamides (**14**) and considered two mechanisms for this process.[3] One conceivable mechanism was endocyclic substitution at sulfur via a five-membered ring intermediate, **15**. Rearrangement of an equimolar mixture of two sulfonates, **16** and **17**, gave a mixture of their corresponding sulfonamides, **18** and **19**, without any crossover. This observation was consistent with an endocyclic mechanism. The alternative mechanism was 1,4-elimination of an arenesulfinate anion (**20**) followed by addition of this ion to the just-formed *o*-quinonimine **21**. Our finding of a small amount of an azobenzene as a product in two examples of the rearrangement was most easily explained as arising via the elimination–addition mechanism. The products of the crossover experiment were explained as arising from a quinonimine–sulfinate reaction taking place within a solvent cage.



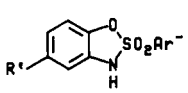
13, 16, 17, 22, 30, 31



14, 18, 19, 24, 32

	R	R'	R''
13, 14	H	H	p-Me
16, 18	H	Me	p-t-Bu
17, 19	H	H	p-MeO

	R	R'	R''
22, 24	H	H	m-CF_3
30, 32	Me	H	p-Me
31	CD_3	H	p-CD_3



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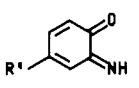
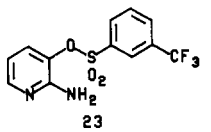


21

Since then, several additional examples of this rearrangement have been found; **22** and **23** yielded **24** and **25**, respectively, upon treatment with LDA in THF. Normally, it was possible to attach the arenesulfonyl group to either the phenolic oxygen or the amino nitrogen of an aminophenol by treating the latter with an arenesulfonyl chloride in the presence of a suitable base. Use of pyridine led to the sulfonamide, but with a stronger base such as triethylamine, the sulfonate was formed.[25] We were unable to use this method to prepare sulfonamide **25**; sulfonate **23** was always obtained. Thus, the rearrangement of **23** was of synthetic utility for the preparation of **25**.



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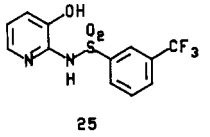
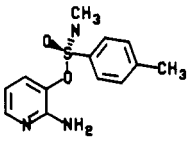


25

It was also found that sulfonimidates rearranged to the corresponding sulfonimidamide, e.g., **26** gave **27** in 45% yield when treated with BuLi. Besides the rearrangement product **27**, however, *N*-methyl-*p*-toluenesulfinamide (**28**) was isolated in 38% yield. An elimination–addition mechanism explains nicely the formation of these products. The anion of sulfinamide **28** and quinonimine **29** are formed from **26** by 1,4-elimination. About half of the anion adds to the quinonimine **29**, perhaps within a solvent cage, to yield sulfonimidamide **27** and about half remains free to give sulfinamide **28**. Quinonimine **29** is undoubtedly kinetically unstable and is the source of intractable byproducts.[26]



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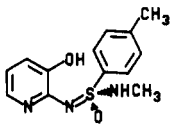

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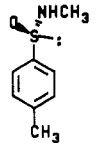

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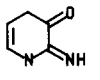
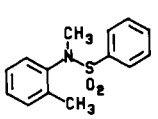


29

To see if the original crossover experiment was correct in indicating an intramolecular process, a rearrangement of an equimolar mixture of **30** and its deuterium isotopomer **31** was carried out. Mass spectral analysis of the product, sulfonamide **32** and its isotopomers, showed no crossover, thus validating the original conclusion that the rearrangement is indeed intramolecular (Table II). If the rearrangement of sulfonimidate **26** is a good model for the rearrangement of the sulfonate esters, then the rearrangement of the latter is also following an elimination–addition and not an endocyclic pathway. Recently, Hellwinkel and Lenz treated **33** with BuLi and obtained products that they believed arose from **34** produced by 1,4-elimination.[16b] Our results and those of Hellwinkel suggest that endocyclic nucleophilic substitution at sulfur(VI) involving a five-membered ring may not be a ready process at least when 1,4-elimination is possible. Alternatively, a five-membered ring intermediate, formed by endocyclic substitution, which fragments in part to a sulfonamide and in part to a quinonimine plus arenesulfinate anion could explain our results.



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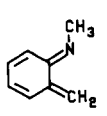

34

(23) Flemming, I.; Mah, T. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1577–1579.
(24) LeHoullier, C. S.; Gribble, G. W. *J. Org. Chem.* **1983**, *48*, 1682–1685.
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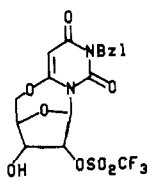
(26) (a) Heine, H. W.; Empfield, J. R.; Golobish, T. D.; Williams, E. A.; Garbauskas, M. F. *J. Org. Chem.* **1986**, *51*, 829–833. (b) Grunanger, P. In *Methoden* der *Organischen Chemie* (*Houben-Weyl*); Grundmann, C., Ed.; Georg Thieme Verlag: Stuttgart, 1979; Vol. VII/3b, pp 233–349.

Table II. Analysis of the Mass Spectrum of the Product from the Crossover Reaction of 30 and 31

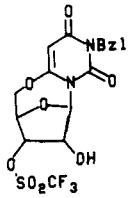
m/e[a] no. of d atoms	283 d-6	282 d-5	281 d-4	280 d-3	279 d-2	278 d-1	277 d-0
observed % intensity, **30**					3	14	83
observed % intensity, **31**	32	42	20	6			
observed % intensity of product	17	22	12	5	4	6	34
calculated % intensity (intramolecular)	16	21	10	3	2	7	41
calculated % intensity (intermolecular)	5	9	6	27	18	8	27

[a] Values normalized to 100%.

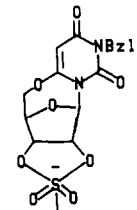
Watanabe et al. found that a pyridine solution of **35** rearranged to **36** and suggested that **37** was an intermediate.[27] If this reaction is truly intramolecular, then it would be an example of endocyclic nucleophilic substitution at sulfur(VI) proceeding via a five-membered ring.



35

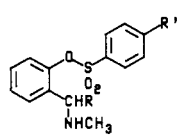


36

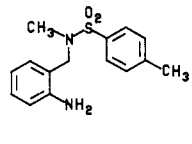


37

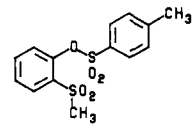
Six-Membered Ring Intermediates. Four compounds having the potential of undergoing an endocyclic reaction were prepared, i.e., **38**–**41**. In **38** and **39**, the intended nucleophiles were formed by deprotonating the amino groups. In **40** and **41**, the nucleophiles were formed by deprotonating the methylsulfonyl groups.



38, 43

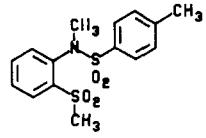


39

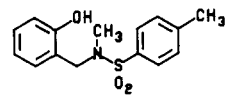


40

	R	R'
38	H	p-Me
43	D	p-CD_3



41



42

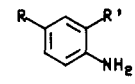
Sulfonate **38**, upon treatment with LDA, yielded sulfonamide **42**, the product expected from an endocyclic reaction. Use of BuLi instead of LDA gave an intractable mixture. When an equimolar mixture of sulfonate **38** and benzylamine was treated with 3 equiv of LDA, sulfonamide **42** was isolated in 24% yield together with 21% of *N*-benzyl-*p*-toluenesulfonamide, apparently formed from reaction of **38** with the anion of benzylamine, the latter functioning as a nucleophile in bimolecular substitution at sulfonyl sulfur. To see if the formation of **42** might also be intermolecular, sulfonate **43**, a deuterium isotopomer of **38**, was synthesized. Treatment of an equimolar mixture of sulfonates **38** and **43** with LDA led to a mixture of sulfonamide **42** and its isotopomers whose deuterium distribution determined by MS was found to be consistent with an inter- and not an intramolecular process (Table III). That is, the rearrangement was not an example of an endocyclic reaction.

Table III. Analysis of the Mass Spectrum of the Product from the Crossover Reaction of 38 and 43

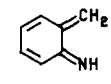
m/e[a] no. of d atoms	295 d-4	294 d-3	293 d-2	292 d-1	291 d-0
observed % intensity, **38**					100
observed % intensity, **43**	51	29	15	5	
observed % intensity of product	19	24	12	22	23
calculated % intensity (intramolecular)	25	15	8	2	50
calculated % intensity (intermolecular)	14	25	8	23	30

[a] Values normalized to 100%.

Sulfonamide **39**, upon treatment with BuLi, did not lead to the hoped-for sulfonamide but instead furnished low yields of *N*-methyl-*p*-toluenesulfonamide (**44**) and *o*-pentylaniline (**45**) as the only identified products. These compounds arose via a 1,4-elimination reaction, which formed **46** and the anion of sulfonamide **44**. Addition of BuLi to **46** led to **45**. That elimination was the mechanism followed, and not substitution on carbon, was substantiated by the treatment of **47**–**49** with BuLi.

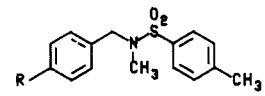


45, 50

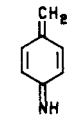


46

	R	R'
45	H	n-Pentyl
50	n-Pentyl	H



47, 48, 49

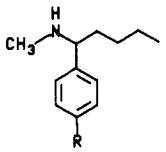


51

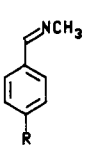
	R
47	NH_2
48	NMe_2
49	H

Treatment of **47** with BuLi gave *p*-pentylaniline (**50**) and sulfonamide **44**. Presumably 1,4-elimination of *N*-methyl-*p*-toluenesulfonamide (**44**) from **47** gave **51**, which then added BuLi to yield aniline **50**. In **48**, such a 1,4-elimination was prevented by dimethylation of the amino group; treatment of **48** with BuLi gave **52** and lithium *p*-toluenesulfinate. Similarly, when the amino group was absent altogether, as in **49**, then the products were **53** and lithium *p*-toluenesulfinate. The reactions of both **48** and **49** with BuLi can be understood as proceeding via 1,2-elimination of *p*-toluenesulfinate anion. The imines thus formed, **54** from **48** and **55** from **49**, added BuLi to give **52** and **53**, respectively.

(27) Pankiewicz, K. W.; Nawrot, B. C.; Watanabe, K. A. *J. Org. Chem.* 1986, *51*, 1525–1529.



52, 53



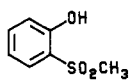
54, 55

R

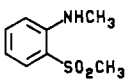
52, 54 NMe_2

53, 55 H

An attempt to detect endocyclic substitution was made with sulfonate **40**. Treatment of **40** with sodium hydride gave no product expected from a rearrangement reaction. Instead, phenol **56** was obtained in almost 80% yield together with some sodium *p*-toluenesulfonate. An attempt to trap the sulfonyl carbanion of **40** by addition of methyl iodide to the reaction mixture led only to the methoxy derivative of **56** formed by methylation on oxygen. Sulfonate **40** was recovered unchanged when treated with LDA in THF. Similar lack of success in detecting an endocyclic reaction was encountered when sulfonamide **41** was treated with sodium hydride in 1,2-dimethoxyethane (DME) at various temperatures, with BuLi in THF, or with LDA in THF. Starting material and various amounts of amino sulfone **57** were isolated. LDA at room temperature led to the highest yield of **57** (53%) and also to lithium *p*-toluenesulfinate (41%). These reactions were not studied further.



56



57

Conclusions

If the Hellwinkel–Closson rearrangement proceeds via nucleophilic substitution at sulfonyl sulfur, it may be concluded that endocyclic substitution through a four-membered ring intermediate or transition state is preferred to exocyclic substitution, at least in this reaction if not in general. The opposite situation appears to prevail if endocyclic substitution is required to proceed via a six-membered ring intermediate or transition state. Our one example is intermolecular, and not intramolecular, as required if the reaction were endocyclic. The situation for molecules constrained to react via five-membered rings, if the reaction is to be endocyclic, is not clear from our results.

Experimental Section

General Methods. Spectra were recorded on a Hitachi-Perkin-Elmer RMU-6E mass spectrometer, a Perkin-Elmer 283B IR spectrometer, and Varian 360A and JEOL FX90Q NMR spectrometers. ^1H and ^{13}C NMR spectra were referenced to internal TMS and ^{19}F NMR spectra to external trifluoroacetic anhydride with all chemical shifts reported in ppm. Elemental analyses were obtained by using a Perkin-Elmer 240B Elemental Analyzer. Solvents were purified and dried by using standard techniques. Reactions were run under nitrogen and usually worked up by addition of water, extraction with an organic solvent, drying of the extracts over magnesium sulfate, and concentration on a rotatory evaporator. The progress of most reactions was monitored by TLC. Silica was used for column chromatography. *n*-Butyllithium was a 1.6 M solution in hexane. Lithium diisopropylamide was freshly prepared as needed by adding BuLi to diisopropylamine in THF.

Analysis of Mass Spectra in the Crossover Reactions. The intensity values calculated for the intramolecular reactions listed in Tables I–III were obtained from the mass spectra of the deuterium-labeled and -unlabeled reactants by dividing their normalized intensities by two. The values calculated for the hypothetical intermolecular reaction of **5** and **9** were obtained by using intensities of appropriate fully and partially labeled fragments observed in the mass spectrum of **9**, i.e., MeNHPh and *p*-$TolSO_2$. A similar calculation was also carried out for the hypothetical intermolecular crossover reaction of **30** and **31** by using intensities of suitable fragments observed in the mass spectrum of **31**, i.e., $C_6H_4ONHCD_3$ and $CD_3C_6H_4$. The calculation of the intensities for the hypothetical intermolecular reaction of **38** and **43** used the intensities found in the molecular ion of the precursor aldehyde used to prepare **43** (for the Me deuterium values) as well as fragments in the spectrum of **43** (for the CHDNMe values).

***N*-Methyl-d_3-*N*-phenyl-4-toluene-d_3-sulfonamide (9).** Reaction of pyridine (0.14 g, 1.8 mmol) and 4-toluene-d_3-sulfonyl chloride (0.321 g, 1.66 mmol), prepared by chlorosulfonation of toluene-d_3 with aniline (0.17 mL, 1.8 mmol) in methylene chloride yielded *N*-phenyl-4-toluene-d_3-sulfonamide: IR (KBr) 3260 (NH), 1920 (CD), 1340 and 1150 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.33 (br s, 0.2 H), 3.55 (br s, 1 H), 6.93–7.70 (m, 9 H), which was dissolved in ethanol (50 mL) and treated with potassium hydroxide (2 eq, 0.19 g, 3.33 mmol) and then iodomethane-d_3 (0.22 mL, 3.3 mmol, Aldrich). Column chromatography (methylene chloride) gave **9**, 45% yield (0.20 g, 0.75 mmol): mp 89–91 °C (lit.[28] mp 94 °C); IR (KBr) 2200 (CD), 2140 (CD), 1345 and 1160 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (br s, 0.4 H), 7.0–7.5 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 143.4, 141.4, 132.7, 129.4, 128.8, 127.9, 127.3, 126.6; MS, *m/e* (intensity) 269 (21, M + 2), 268 (65, M + 1), 267 (330, M), 266 (104), 265 (123), 261 (166), 203 (122), 202 (84), 201 (50), 200 (15), 197 (14).

Crossover Reaction of 5 and 9 with BuLi. BuLi (2 equiv) was added to equimolar mounts of sulfonamide **5** (0.136 g, 0.522 mmol) and **9** (0.140 g, 0.522 mmol) in THF (15 mL). After 15 min, the reaction was quenched with water (2 mL) and worked up. Column chromatography (methylene chloride) gave an isotopomeric mixture of **7**, 37% yield (0.101 g): mp 130 °C (lit.[35] mp 134–135 °C); IR (KBr) 3400 (NH), 2040 (CD), 1960 (CD), 1325 and 1140 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.4 (s, 2.4 H), 2.8 (d, 1.6 H), 3.17 (br s, 1 H), 6.1–7.9 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 147.9, 143.8, 139.2, 135.2, 130.3, 129.6, 126.8, 121.6, 115.9, 111.7, 30.1, 21.5; MS, *m/e* (intensity) 269 (12, M + 2), 268 (39, M + 1), 267 (124, M), 266 (114), 265 (15), 264 (12), 263 (169), 262 (117), 261 (351).

2′-Aminophenyl 3-(Trifluoromethyl)benzenesulfonate (22). Powdered 3-(trifluoromethyl)benzenesulfonyl chloride (14.3 g, 0.0587 mol) was added to 2-aminophenol (6.11 g, 0.0561 mol) and triethylamine (5.92 g, 0.0585 mol) suspended in methylene chloride (50 mL) at 0 °C. After 1 h at room temperature, the mixture was worked up to give **22**, 55% yield from chloroform–petroleum ether (9.71 g, 0.0306 mol): mp 106–107 °C; IR (KBr) 3495 and 3405 (NH_2), 1370 and 1195 (SO_2O), 1330 (CF) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.7 (br s, 2 H), 6.4–8.13 (m, 8 H); ^{13} C NMR ($CDCl_3$) δ 139.6, 135.9, 132.7, 131.8, 131.0 ($^3J_{CF}$ = 4.4 Hz),[29] 130.0, 128.3, 125.7 ($^3J_{CF}$ = 4.4 Hz), 123.0 ($^1J_{CF}$ = 2.72 Hz), 122.7, 118.4, 117.4; ^{19}F NMR ($CDCl_3$) δ 14.62; MS, *m/e* (intensity) 317 (27, M), 209 (129), 145 (112), 108 (1000). Anal. Calcd for $C_{13}H_{10}F_3NO_3S$: C, 49.21; H, 3.18; N, 4.41. Found: C, 49.14; H, 3.00; N, 4.45.

***N*-(2′-Hydroxyphenyl)-3-(trifluoromethyl)benzenesulfonamide (24).** Pyridine (0.452 mL, 5.01 mmol) and then a solution of 3-(trifluoromethyl)benzenesulfonyl chloride (1.11 g, 4.55 mmol) in methylene chloride (5 mL) were added to 2-aminophenol (0.994 g, 9.11 mmol) suspended in methylene chloride

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(35) Muller, E., Ed. *Houben-Weyl Methoden der Organischen Chemie*; Georg Thieme Verlag: Stuttgart, 1955; Vol 9, p 424.

(20 mL) at −78 °C. After 5 h at room temperature the mixture was worked up. Column chromatography (ethyl acetate) gave **24**, 83% yield from carbon tetrachloride (1.19 g, 3.75 mmol): mp 125–126 °C; IR (KBr) 3460 (OH), 3260 (NH), 1330 and 1170 (SO_2N), 1130 (CF) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (s, 1 H), 5.90 (s, 1 H), 6.6–7.9 (m, 8 H); ^{13}C NMR (acetone-d_6) δ 150.8, 142.4, 132.1, 131.7, 131.4 ($^2J_{CF}$ = 33.0 Hz), 131.0, 130.1 ($^3J_{CF}$ = 3.7 Hz), 127.8, 125.7, 124.9 ($^3J_{CF}$ = 4.2 Hz), 124.5 ($^1J_{CF}$ = 272 Hz), 120.7, 116.4; ^{19}F NMR (acetone-d_6) δ 17.96. Anal. Calcd for $C_{13}H_{10}F_3NO_3S$: C, 49.21; H, 3.18; N, 4.41. Found: C, 49.59; H, 3.11; N, 4.47.

Reaction of 2′-Aminophenyl 3-(Trifluoromethyl)-benzenesulfonate (22) with LDA. A solution of LDA (3 equiv) at −78 °C in THF (5 mL) was added by cannula to a solution of **22** (0.50 g, 1.6 mmol) in THF (60 mL) at −78 °C. After 30 min, the solution was kept at 0 °C for 4 h. Workup and recrystallization from carbon tetrachloride and petroleum ether gave sulfonamide **24**, 25% yield (0.124 g, 0.391 mmol): mp 124–125.5 °C; IR (KBr) 3460 (OH), 3260 (NH), 1330 and 1170 (SO_2N), 1130 (CF) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.63 (s, 1 H), 5.90 (s, 1 H), 6.6–7.9 (m, 8 H); MS, m/e 317 (M).

3′-(2′-Amino)pyridyl 3-(trifluoromethyl)benzenesulfonate (23) was prepared from 2-amino-3-hydroxypyridine (1.01 g, 9.16 mmol) and 3-(trifluoromethyl)benzenesulfonyl chloride (2.39 g, 9.82 mmol) via the procedure used to prepare **24**. Recrystallization from carbon tetrachloride gave **23**, 67% yield (1.95 g, 6.11 mmol): mp 111–113.5 °C; IR (KBr) 3500 and 3330 (NH_2), 1390 and 1160 (SO_2O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.70 (br s, 2 H), 6.43–8.13 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 152.2, 146.9, 136.5, 133.0, 131.7, 131.6 ($^3J_{CF}$ = 5.9 Hz), 130.3, 129.1, 125.6 ($^3J_{CF}$ = 3.9 Hz), 122.9 ($^1J_{CF}$ = 272 Hz), 113.9; ^{19}F NMR ($CDCl_3$) δ 11.71. Anal. Calcd for $C_{12}H_9F_3N_2O_3S$: C, 45.28; H, 2.85; N, 8.80. Found: C, 45.08; H, 2.91; N, 8.66.

Reaction of 3′-(2′-Amino)pyridyl 3-(Trifluoromethyl)-benzenesulfonate (23) with LDA. Sulfonate **23** (0.25 g, 0.78 mmol) in THF (40 mL) was treated at −78 °C with a solution of LDA (3 equiv) in THF (5 mL) as described above for **24**. After 1 h at −78 °C and 2 h at 0 °C, the reaction was quenched with 10 mL of 5% aqueous hydrochloric acid and worked up to give **23**, 13% yield from carbon tetrachloride (0.0311 g, 0.098 mmol) identified by mp (109–112 °C) and IR and ^1H NMR spectra. The aqueous layer from the extraction was acidified with 10% aqueous hydrochloric acid and reextracted three times with methylene chloride (90 mL). Workup gave *N*-[2′-(3′-hydroxy)pyridyl]-3-(trifluoromethyl)benzenesulfonamide (**25**), 52% yield from carbon tetrachloride (0.13 g, 0.41 mmol): mp 136–138 °C; IR (KBr) 3485 (OH), 3300 (NH), 1330 and 1150 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.50–8.13 (m, 9 H); ^{19}F NMR ($CDCl_3$) δ 13.27. Anal. Calcd for $C_{12}H_9F_3N_2O_3S$: C, 45.16; H, 2.70; N, 8.56. Found: C, 45.19; H, 2.71; N, 8.58.

3′-(2′-Amino)pyridyl *N*-Methyl-4-toluenesulfonimidate (26). *tert*-Butyl hypochlorite (6.48 g, 0.06 mmol) in carbon tetrachloride (825 mL) precooled to 0 °C was added to *N*-methyl 4-toluenesulfinamide (5.07 g, 0.0300 mol) in carbon tetrachloride (40 mL) at 0 °C in dim light.[30] After 1 h at 0 °C, the mixture was concentrated under reduced pressure at 0 °C. The crude sulfonimidoyl chloride was immediately dissolved in methylene chloride (15 mL) and added to a solution of 3-hydroxy-2-aminopyridine (3.0 g, 0.027 mol) and triethylamine (2.80 g, 25.5 mmol) in methylene chloride (50 mL) at 0 °C. After 1 h at room temperature, the reaction mixture was filtered and the filtrate was washed twice with water. The organic layer was worked up. Column chromatography (ether) gave **26**, 34% yield (2.37 g, 8.56 mmol): mp 121–122 °C dec; IR (KBr) 3430, 3330 (NH), 1635, 1475, 1450, 1295 and 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.96–7.66, 7.40–6.90, and 6.67–6.32 (m, 7 H), 4.51 (br, 2 H), 3.01 (s, 3 H), 2.39 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 152.5, 144.9, 144.5, 134.3, 133.5, 129.5, 127.6, 113.7, 29.0, 21.5; MS, m/e 277. Anal. Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.32; H, 5.42; N, 15.16. Found: C, 56.41, H, 5.36, N, 15.08.

Reaction of 3′-(2′-Amino)pyridyl *N*-Methyl-4-toluenesulfonimidate (26) with BuLi. BuLi (4.5 mL of a 1.6 M solution, 7.2 mmol) was added to **26** (0.50 g, 1.8 mmol) in THF (40 mL) at 0 °C. After 1 h at room temperature, the cloudy reaction mixture was quenched with saturated aqueous ammonium chloride (10 drops) and concentrated. The residue was taken up in methylene chloride and washed once with water. The water layer was acidified with 10% sulfuric acid and then extracted several times with methylene chloride. The combined organic layers were worked up to give 0.50 g of product. TLC (ether) showed two spots. Column chromatography (ether) yielded *N*-[2′-(3′-hydroxy)pyridyl]-*N*-methyl-4-toluenesulfonimidamide (**27**) [47% yield (0.23 g, 0.83 mmol): mp 126–127 °C; IR ($CDCl_3$) 3450 (br), 3290, 1450, 1400, 1220, 1100, 1075, 1050 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.88–6.67 (m, 8 H), 2.70 (s, 3 H), 2.41 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 147.0, 144.6, 143.6, 137.2, 136.2, 129.7, 127.1, 119.6, 117.4, 28.4, 21.5. Anal. Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.32; H, 5.42; N, 15.16. Found: C, 56.06; H, 5.37; N, 14.99] and *N*-methyl-*p*-toluenesulfinamide (**28**) identified by melting point and by comparison of spectra with those from an authentic sample, 37% yield (0.11 g, 0.65 mmol): mp 56–57 °C.

2′-Formamidylphenyl 4-Toluenesulfonate. 2′-Aminophenyl 4-toluenesulfonate (10.0 g, 0.079 mol) was formylated[31] with acetic formic anhydride prepared in situ from acetic anhydride (15.5 g, 0.1512 mol) and formic acid (6.12 g, 0.133 mol) to give the title compound, 80% yield from ethanol (8.84 g, 0.0303 mol): mp 130–132 °C; IR (KBr) 3325 (NH), 1680 (C=O), 1380 and 1170 (SO_2O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.46 (s, 3 H), 6.86–7.86 (m, 8 H), 8.23 and 8.33 (2 s, 2 H). Anal. Calcd for $C_{14}H_{13}NO_4S$: C, 57.72; H, 4.50; N, 4.81. Found: C, 57.62; H, 4.52; N, 4.81.

2′-(Methylamino)phenyl 4-Toluenesulfonate (30). Borane–tetrahydrofuran complex (2.5 equiv, 5.46 mL, 2.18 mmol) was added to 2′-formamidylphenyl 4-toluenesulfonate (0.636 g, 2.18 mmol) in THF.[31] After gas evolution had ceased, the mixture was heated for 1 h and allowed to cool to room temperature, and methanol (10 mL) was added. Workup gave **30**, 74% yield from ethanol (0.450 g, 1.62 mmol): mp 64–65 °C (lit.[3] mp 66–67 °C); IR (KBr) 3460 (NH), 1370 and 1200 (SO_2O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 (s, 3 H), 2.56 (d, 3 H), 3.96 (br s, 1 H), 6.26–7.7 (m, 8 H); ^{13}C NMR ($CDCl_3$) 145.4, 142.2, 136.8, 132.7, 129.7, 128.4, 128.0, 122.1, 116.0, 111.7, 30.0, 21.7; MS, m/e (intensity) 278 (4, M + 1), 277 (25, M), 155 (33), 122 (1000), 108 (121), 91 (340).

Reaction of 30 with LDA. Sulfonate **30** (0.296 g, 1.069 mmol), dissolved in THF (30 mL), was treated with LDA (3 equiv) at room temperature. After 1 h the reaction was quenched with 10% aqueous hydrochloric acid (2 mL). Workup and column chromatography (methylene chloride) gave *N*-methyl-*N*-(2′-hydroxyphenyl)-4-toluenesulfonamide (**32**), 44% yield (0.130 g, 0.468 mmol): mp 122–123 °C (lit.[3] mp 125–126 °C); IR (KBr) 3480 (OH), 1335 and 1150 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H), 3.16 (s, 3 H), 6.35–7.63 (m, 9 H).

2′-(Methyl-d_3-amino)phenyl 4-Toluene-d_3-sulfonate (31). 2′-Formamidyl-d_1-phenyl 4-toluene-d_3-sulfonate was prepared according to the procedure for the nondeuteriated analogue except that the 2′-aminophenyl 4-toluenesulfonate (0.079 g, 0.297 mmol), obtained from the tosylation of 2-aminophenol using 4-toluene-d_3-sulfonyl chloride, was formylated with acetic formic-d_1 anhydride (prepared from acetic anhydride, freshly distilled from dimethylaniline, and formic-d_2 acid). The crude product was recrystallized from ethanol: ^1H NMR ($CDCl_3$) δ 2.46 (br s, 0.29 H), 6.86–7.86 (m, 8 H), 8.23 and 8.33 (2 s, 1.1 H). The crystals and residue from the mother liquor were dissolved in THF and then reduced with BD_3–THF (2.5 equiv, 0.742 mmol) according to the procedure for the nondeuteriated analogue. Column chromatography (methylene chloride) gave **31**, 43% yield (0.0359 g, 0.1268 mmol): mp 63–64 °C (lit.[3] mp 66–76 °C); IR (KBr) 3460 (NH), 1950 (CD), 1365 and 1185 (SO_2O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 and 2.56 (2 s, 1.38 H), 3.96 (br s, 1 H), 6.26–7.7 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 145.3, 142.2, 136.8, 132.8, 129.7, 128.9, 128.0, 122.1, 116.0, 111.7, 30.0; MS, m/e (intensity) 284 (14, M + 1), 283 (51, M), 282 (67), 281 (32), 280 (11), 158 (16), 125 (791), 124 (1000), 123 (354), 122 (20), 94 (146), 93 (53), 92 (35), 91 (19).

Crossover Reaction of 30 and 31 with LDA. Sulfonate esters **30** (0.0212 g, 0.0765 mmol) and **32** (0.0226 g, 0.0798 mmol) in THF (50 mL) were treated with a solution of LDA (3 equiv, 0.48 mmol) in THF (20 mL) under nitrogen. After 1 h, the reaction was quenched with 10% aqueous sulfuric acid. Workup and column chromatography (methylene chloride) gave the isotopomeric sulfonamides **32**, 54% yield (0.0236 g): mp 121–122 °C (mp of **32**, 125–126 °C); IR (KBr) 3480 (OH), 1335 and 1145 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 1.5 H), 3.16 (s, 1.5 H), 6.35–7.63 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 153.8, 144.4, 132.3, 129.6,

129.5, 128.4, 128.1, 126.0, 120.4, 117.6, 39.3, 21.6; MS, *m/e* (intensity) 284 (15), 283 (72), 282 (93), 281 (53), 280 (20), 279 (16), 278 (27), 277 (142).

Toluene-d_3 was prepared from benzotrichloride:[32] bp 110 °C (lit.[16] bp 110 °C); ^{1}H NMR ($CDCl_3$) δ 2.3 (br s, 0.37 H), 7.2 (s, 5 H); MS, *m/e* (intensity), 96 (76, M + 1), 95 (1000, M), 94 (846), 93 (656), 92 (214), 91 (76).

4-Toluene-d_3-sulfonyl chloride was prepared from methyl-d_3-benzene,[33] 26% yield from hexane: mp 65.5–67 °C (lit.[34] mp 67–68 °C); IR (KBr), 1370 and 1170 (SO_2Cl) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.43 (br s, 0.4 H), 7.33–8.01 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 146.6, 141.8, 130.2, 127.1; MS, *m/e* (intensity) 195 (55, M + 2), 194 (32, M + 1), 193 (157, M), 192 (47), 191 (20), 160 (21), 159 (49), 158 (394), 157 (121), 156 (56), 155 (13), 94 (1000), 93 (323), 92 (176), 91 (67).

2′-(*N*-Methylforiminyl)phenyl 4-Toluenesulfonate. A mixture of aqueous methylamine solution (6 equiv, 12 mL of a 40% solution) and 2′-formylphenyl 4-toluenesulfonate (40.7 g, 0.147 mol) in methanol (800 mL) was stirred for 12 h to give the ester, 89% yield from cyclohexane (37.9 g, 0.131 mol): mp 80–81 °C; IR (KBr) 1650 (C=N), 1380 and 1190 (SO_2O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3 H), 3.30 (s, 3 H), 7.06–7.95 (m, 8 H), 8.15 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 156.4, 148.8, 145.8, 132.1, 131.4, 129.9, 129.5, 128.5, 127.6, 127.3, 123.3, 48.3, 21.7. Anal. Calcd for $C_{15}H_{15}NO_3S$: C, 62.27; H, 5.23; N, 4.84. Found: C, 62.53; H, 5.22; N, 4.83.

2′-[(*N*-Methylamino)methyl]phenyl 4-Toluenesulfonate (38). Sodium borohydride (2.4 equiv, 0.782 g, 0.0207 mol) was added gradually to the imine (2.50 g, 8.65 mmol) in dry methanol (150 mL). After 12 h, the mixture was worked up to give a brown oil, which was distilled in a Kugelrohr apparatus (160 °C, 0.2 mm) to give **38**, 80% yield (2.02 g, 6.93 mmol): IR (neat) 3345 (NH), 1380 and 1200 (SO_2O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 1 H), 2.34 (s, 3 H), 2.44 (s, 3 H), 3.57 (s, 2 H), 7.10–7.93 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 147.9, 145.5, 133.6, 132.9, 130.4, 129.9, 128.3, 128.0, 127.1, 122.2, 49.8, 36.0, 21.7; MS, *m/e* (intensity), 291 (80, M), 276 (47), 155 (53), 136 (1000), 120 (158), 91 (410). Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81. Found: C, 61.47; H, 6.00; N, 4.72.

Reaction of 38 with LDA. LDA (3 equiv) in THF (20 mL) was added to sulfonate **38** (0.533 g, 1.83 mmol) in THF (30 mL). Both solutions were at −78 °C. After 20 min, the reaction was quenched at −78 °C with aqueous ammonium chloride solution. Workup and preparative plate chromatography (ethyl acetate) yielded three bands. One band was a very small amount of a highly colored oil, which was not identified. Another band was shown by mass spectrometry to consist of many compounds. No further work was done on this band. The third band was repurified by column chromatography (chloroform) to yield *N*-(2′-hydroxybenzyl)-*N*-methyl-4-toluenesulfonamide (**42**), 33% yield (0.175 g, 0.601 mmol): mp 91–93 °C; IR (KBr) 3410 (OH), 1325 and 1150 (SO_2N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3 H), 2.66 (s, 3 H), 4.06 (s, 2 H), 6.81–7.85 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 155.9, 144.2, 133.3, 130.5, 130.3, 130.1, 127.7, 120.1, 120.0, 117.2, 51.3, 34.4, 21.6; MS, *m/e* (intensity) 291 (99, M), 185 (195), 155 (204), 136 (192), 91 (1000). Anal. Calcd for $C_{15}H_{17}NO_3S$: C, 61.83; H, 5.88; N, 4.81. Found: C, 61.61; H, 5.91; N, 4.70. Repetition of the reaction at room temperature gave a 40% yield of **42**.

Reaction of 38, Benzylamine and LDA. Sulfonate **38** (0.496 g, 1.70 mmol) and benzylamine (0.19 mL, 1.7 mmol) in THF (27 mL) were treated with LDA (3 equiv, 3.4 mmol) at −78 °C as above. After 1.5 h, the reaction was quenched with water (2 mL) at −78 °C and worked up. Preparative plate chromatography gave **42** [24% yield (0.120 g, 0.412 mmol): mp 91–93 °C; IR (KBr) 3410 (OH), 1325 and 1150 (SO_2N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3 H), 2.66 (s, 3 H), 4.06 (s, 2 H), 6.81–7.85 (m, 9 H)] and *N*-benzyl-4-toluenesulfonamide, 21% yield (0.0914 g, 0.350 mmol): mp 113–114 °C (lit.[28] mp 115–116 °C); IR (KBr) 3290 (NH), 1330 and 1170 (SO_2N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3 H), 4.05 (d, 2 H), 5.13 (t, 1 H), 7.20–7.80 (m, 9 H).

2′-[(*N*-Methylamino)methyl-d_1]phenyl 4-Toluene-d_3-sulfonate (43). 2′-Formylphenyl 4-toluene-d_3-sulfonate was prepared from salicylaldehyde (2 eq, 0.82 mL, 7.7 mmol) and 4-toluene-d_3-sulfonyl chloride (0.739 g, 3.83 mmol). Excess salicylaldehyde was removed by Kugelrohr distillation, and the residue was purified by recrystallization from cyclohexane, 83% yield (0.887 g, 3.18 mmol): mp 59–61 °C (lit.[61] mp 63–64 °C); IR (KBr) 2760 (CHO), 1975 and 1950 (CD), 1695 (C=O), 1380 and 1195 (SO_2O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.13–7.96 (m, 8 H), 10.06 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 187.3, 151.3, 146.2, 135.3, 131.6, 130.1, 129.4, 128.7, 128.5, 127.5, 123.8; MS, *m/e* (intensity) 280 (27, M + 1), 279 (118, M), 278 (115), 277 (16). This sulfonate ester (0.887 g, 3.18 mmol) was converted to the imine according to the procedure for the nondeuteriated analogue. The ^{1}H NMR spectrum showed the imine CH peak at 8.15 ppm and the *N*-methyl at 3.33 ppm. Without further purification, the imine was reduced with sodium borodeuteride (1.5 eq, 0.199 g, 4.76 mmol, Aldrich) in methanol (50 mL) according to the procedure for the synthesis of the nondeuteriated analogue **38**. Column chromatography (ethyl acetate) gave **43**, 74% yield (0.698 g, 2.37 mmol): IR (neat, NaCl plates) 3340 (NH), 2120 (CD), 1930 (CD), 1370 and 1185 (SO_2O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.66 (br s, 1 H), 2.33 (s, 3.1 H), 3.56 (br s, 1 H), 7.06–7.85 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 147.9, 145.5, 133.1, 132.8, 130.5, 129.9, 128.4, 128.1, 127.1, 122.3, 49.6 ($^1J_{CD}$ = 21 Hz), 36.0; MS, *m/e* (intensity) 295 (21.75, M), 294 (12.50), 293 (6.45), 292 (2.15), 291 (0.08), 158 (21), 137 (1000), 136 (238).

Crossover Reaction of 38 and 43 (0.05 M Solution) with LDA. LDA (3 equiv, 3.0 mmol) in THF (20 mL) was added to equimolar amounts of the sulfonate esters **38** (0.144 g, 0.495 mmol) and **43** (0.146 g, 0.495 mmol) in THF (20 mL). Both solutions were at −78 °C. The reaction was monitored by TLC (0.6 hexane–0.4 ethyl acetate). The reaction was quenched after 15 min with methanol (10 mL) to which two drops of sulfuric acid had been added. The mixture was worked up. Preparative plate chromatography (6 hexane–4 ethyl acetate) gave the rearranged product, 21% (0.0605 g): mp 90–93 °C (mp of **42** is 91–93 °C); IR (KBr) 3330 (OH), 1925 (CD), 1810 (CD), 1330 and 1160 (SO_2N) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 1.6 H), 2.66 (s, 3 H), 4.06 (s, 1.4 H), 6.81–7.85 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 155.9, 144.2, 133.3, 130.5, 130.3, 130.0, 127.7, 120.1, 117.2, 51.3, 34.4, 21.5; MS, *m/e* (intensity) 295 (185), 294 (243), 293 (122), 292 (222), 291 (228). Repetition of the reaction at 0.0051 M concentration gave a 14% yield of **42** and its isotopomers.

***N*-Methyl-*N*-(2′-nitrobenzyl)-4-toluenesulfonamide** was prepared from 2-nitrobenzyl bromide (7.26 g, 0.0390 mol) in 95% ethanol (50 mL) added to a paste made from *N*-methyl-4-toluenesulfonamide (8.5 g, 0.039 mol), powdered potassium hydroxide (3.0 g, 0.058 mol), and a small amount of 95% ethanol.[35] Workup gave **41**, 83% yield (10.35 g, 0.0323 mol); mp 118–119 °C (ethanol); IR (KBr) 1530 and 1350 (NO_2), 1350 and 1170 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.20–7.30 (m, 8 H), 4.60 (s, 2 H), 2.75 (s, 3 H), 2.49 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.9, 143.9, 134.4, 133.8, 132.2, 129.9, 129.6, 128.4, 127.3, 124.9, 51.1, 35.8 and 21.5. Anal. Calcd for $C_{15}H_{16}N_2O_4S$: C, 56.24; H, 5.04; N, 8.74. Found: C, 56.60; H, 5.08; N, 8.82.

***N*-Methyl-*N*-(4′-nitrobenzyl)-4-toluenesulfonamide** was prepared in the same manner as above in 76% yield: mp 125–128 °C; IR (KBr) 1515 and 1360 (NO_2), 1340 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.45–7.10 (s, 8 H), 4.28 (s, 2 H), 2.65 (s, 3 H), 2.48 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 147.6, 143.9, 143.5, 134.0, 129.8, 128.8, 127.3, 123.8, 53.5, 34.8, and 21.5. Anal. Calcd for $C_{15}H_{16}N_2O_4S$: C, 56.24; H, 5.04; N, 8.74. Found: C, 56.24; H, 5.02; N, 8.75.

***N*-Benzyl-*N*-methyl-4-toluenesulfonamide** was prepared in the same manner as above in 83% yield: mp 93–94 °C; IR (KBr) 1345 and 1170 cm^{-1} (SO_2); ^{1}H NMR ($CDCl_3$) δ 7.95–7.68, 7.55–7.18 (m, 8 H), 4.15 (s, 2 H), 2.58 (s, 3 H), 2.46 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 143.4, 135.7, 134.4, 129.7, 128.5, 128.3, 127.8, 127.4, 54.1, 34.3, and 21.5. Anal. Calcd for $C_{15}H_{17}NO_2S$: C, 65.67; H, 6.25; N, 5.11. Found: C, 65.68; H, 6.30; N, 4.99.

***N*-Methyl-*N*-(2′-aminobenzyl)-4-toluenesulfonamide (39).** A solution of stannous chloride (5.30 g, 0.0235 mol) in concentrated hydrochloric acid (10 mL) was added with stirring to *N*-methyl-*N*-(2′-nitrobenzyl)-4-toluenesulfonamide (2.08 g, 6.50 mmol) in 95% ethanol (175 mL). The mixture was heated for three h, made basic with 5.5 N NaOH, and worked up to give **39**, 80% yield: mp 121–122 °C; IR (KBr) 3490 and 3400 (NH_2), 1235 and 1160 (SO_2) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 9.90–6.43 (m, 8 H), 4.40 (br, 2 H), 3.93 (s, 2 H), 2.55 (s, 3 H), 2.41 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.5, 133.2, 131.1, 129.8, 129.7, 127.7, 117.9, 117.3, 115.9, 52.6, 34.0, and 21.5. Anal. Calcd for $C_{15}H_{18}N_2O_2S$: C, 62.04; N, 9.65; H, 6.25. Found: C, 62.37; N, 9.55; H, 6.36.

The following compounds were prepared by reduction of the corresponding nitro compounds with tin and HCl in boiling aqueous ethanol.

N-Methyl-N-(4′-aminobenzyl)-4-toluenesulfonamide (47) was separated from the crude solid product by Soxhlet extraction (ether–solvent) in 76% yield: mp 153–154 °C; IR (KBr) 3500 and 3410 (NH_2) 1355 and 1155 cm^{-1} (SO_2); ^1H NMR ($CDCl_3$) δ 7.95–7.69, 7.65–7.00, and 6.85–6.60 (AA′BB′, 8 H), 4.02 (s, 2 H), 3.65 (s, 2 H), 2.56 (s, 3 H), 2.46 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.2, 143.2, 134.4, 129.6, 127.4, 125.0, 115.0, 53.7, 33.9, and 22.1. Anal. Calcd for $C_{15}H_{18}N_2O_2S$: C, 62.04; H, 6.25; N, 9.65. Found: C, 61.70; H, 6.31; N, 9.56.

N-Methyl-N-[4′-(dimethylamino)benzyl]-4-toluenesulfonamide (48). 4-(Dimethylamino)-N-methylbenzylimine (3.8 g, 0.023 mol), prepared from 4-(dimethylamino)benzaldehyde, and $NaBH_4$ (0.87 g, 0.023 mol) in dry methanol (380 mL) were stirred at room temperature for 11 h.[36] Workup gave a yellow liquid, which was used without further purification: IR (neat) 3340 (br, NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.02 and 6.88–6.25 (AA′BB′, 4 H), 3.60 (s, 2 H), 2.90 (s, 7 H), 2.35 (s, 3 H). Pyridine (1 mL) and then 4-toluenesulfonyl chloride (1.9 g, 0.012 mol) were added to crude N-methyl-4-(dimethylamino)benzylamine (2.0 g, 0.012 mol) in dichloromethane (20 mL) with cooling in an ice–salt bath. After 2 h, the reaction mixture was worked up to give 2.48 g of **48**, 64% yield from 95% ethanol: mp 130–131 °C; IR (KBr) 1335 and 1165 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.89–7.62, 7.62–7.00, and 6.81–6.65 (AA′BB′, 8 H), 4.02 (s, 2 H), 2.99 (s, 6 H), 2.55 (s, 3 H), 2.45 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 150.2, 143.1, 134.5, 129.5, 127.5, 123.0, 112.5, 53.6, 40.5, 33.8, and 21.4. Anal. Calcd for $C_{17}H_{22}N_2O_2S$: C, 64.12; H, 6.96; N, 8.80. Found: C, 63.67; H, 7.09; N, 8.58.

Reaction of N-Methyl-N-(2′-aminobenzyl)-4-toluenesulfonamide (39) with BuLi. THF (15 mL) and then BuLi (2.12 mL, 1.3 M, 2.76 mmol) were added to sulfonamide **39** (0.20 g, 0.69 mmol) with cooling in an ice bath. After 7 h five drops of water were added. A white precipitate was filtered, and the mixture was worked up to give a yellow oil. TLC (ether–hexane) showed six spots. Preparative TLC allowed separation of two compounds (A and B). Compound A, R_f 0.3 (ether–hexane), was a white solid (0.048 g, 25%) whose ^1H NMR, IR, melting point, and mixed melting point were identical with those obtained for N-methyl-4-toluenesulfonamide (**44**). Compound B, a thick oil (0.0253 g, 15%), was identified as 2-pentylaniline (**45**): R_f 1.3 (ether–hexane); IR (neat) 3460 and 3370 (NH_2), 2980–2870 (aliphatic CH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.3–6.59 (m, 4 H), 3.58 (br, 2 H), 2.52 (t, 2 H), 1.85–0.65 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 144.0, 129.4, 127.0, 126.8, 118.7, 115.5, 31.9, 31.2, 28.4, 22.6, and 14.0; MS, m/e (intensity) 163 (287, M), 164 (39, M + 1), 162 (16, M − 1), 107 (168), 106 (1000), 77 (119). When the reaction was quenched after 1 h by adding methyl iodide, **44** was found along with two other compounds. One was identified as 2-pentyl-N,N-dimethylaniline (11%): IR (neat) 2980, 2800, and 2780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.45–7.00 (m, 4 H), 2.61 (s, 8 H), 1.85–0.65 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 152.7, 137.7, 129.5, 126.2, 123.2, 119.3, 45.1, 32.0, 30.6, 30.3, 22.6, and 14.0. The other compound was identified as N-methyl-N-[2′-(dimethylamino)benzyl]-4-toluenesulfonamide: mp 104–105 °C; IR (KBr) 1345 and 1165 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.92–7.01 (m, 8 H), 4.31 (s, 2 H), 2.60 (s, 6 H), 2.53 (s, 3 H), 2.46 (s); ^{13}C NMR ($CDCl_3$) δ 143.2, 134.9, 129.9, 129.7, 129.2, 128.1, 127.5, 123.6, 119.1, 48.9, 45.1, 34.4, and 21.5.

Reaction of N-methyl-N-benzyl-4-toluenesulfonamide (49) with BuLi. The procedure used for the reaction of **39** with BuLi was followed. A white precipitate formed as soon as the BuLi was added. The reaction was complete in 1 h (TLC). Four drops of water were added. The precipitate was filtered, and the filtrate was worked up. Three compounds were indicated by a TLC of the filtrate. They were separated by preparative TLC, and the major band, an oily liquid, (0.0803 g, 25%), was identified as 1-(methylamino)-1-phenylpentane (**53**): IR (neat) 2980–2780 (aliphatic CH), 3320 (br, NH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.34 (m, 5 H), 3.45 (t, 1 H), 2.26 (s, 3 H), 2.05 (br, 1 H), 1.80–0.80 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 144.2, 128.3, 127.2, 126.8, 65.6, 37.7, 34.5, 28.6, 22.7, and 13.9; MS, m/e (intensity) 177 (40, M), 176 (61, M − 1), 121 (551), 120 (1000). The white precipitate was identified as lithium 4-toluenesulfinate by matching its IR and NMR spectra with those obtained from an authentic sample.

Reaction of N-Methyl-N-(4′-aminobenzyl)-4-toluenesulfonamide (47) with BuLi. The above procedure was followed. TLC ($CHCl_3$) showed more than six spots. Only two compounds were separated by preparative TLC. One (0.0693 g, 22%) was identified as N-methyl-4-toluenesulfonamide (**44**) by agreement of its melting point and IR and NMR spectra with published data.[37a] The other compound, an oily liquid (0.0330 g, 12%), was identified as 4-pentylaniline (**50**): IR (neat) 3480 and 3380 (NH_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.16–6.9 and 6.8–6.55 (AA′BB′, 4 H), 3.32 (br, 2 H), 2.68–2.31 (t, 2 H), 1.80–0.65 (m, 9 H), MS, m/e (intensity) 163 (178, M), 164 (34, M + 1), 107 (206), 108 (1000).

Reaction of N-Methyl-N-[4′-(dimethylamino)benzyl]-4-toluenesulfonamide (48) with BuLi. The procedure was the same as above. Two products were isolated. One was identified as lithium 4-toluenesulfinate (0.189 g, 77%) by agreement of its IR and NMR spectra with published spectra.[37b] The other, a semisolid, was identified as 1-(methylamino)-1-[4′-(dimethylamino)phenyl]pentane (**52**) (0.0478 g, 25%): IR (neat) 2970, 2940, 2860, 2800 (aliphatic CH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38–7.02 and 6.89–6.60 (AA′BB′, 4 H), 3.40 (t, 1 H), 2.95 (s, 6 H), 1.91–0.65 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 149.0, 127.9, 127.3, 111.5, 63.5, 39.5, 35.3, 27.5, 21.5, and 12.9; MS, m/e 220 (47, M), 189 (218), 163 (1000), 160 (537).

2′-(Methylthio)phenyl 4-Toluenesulfonate. 2-Hydroxyphenyl methyl sulfide[38] was treated with equimolar amounts of triethylamine and 4-toluenesulfonyl chloride in dichloromethane to give the sulfonate in 66% yield: mp 66–68 °C (95% ethanol); IR (KBr) 1360 and 1170 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00–7.80 and 7.5–7.2 (m, 8 H), 2.42 (s, 3 H), 2.30 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.7, 145.3, 133.0, 129.6, 128.6, 127.3, 125.7, 122.3, 75.5, and 21.7. Anal. Calcd for $C_{14}H_{14}O_3S_2$: C, 57.12; H, 4.79. Found: C, 57.06; H, 4.76.

2′-(Methylsulfonyl)phenyl 4-Toluenesulfonate (40). 2′-(Methylthio)phenyl 4-toluenesulfonate (6.49 g, 0.022 mol) in acetic acid (150 mL) was treated with a solution of 30% hydrogen peroxide (9.46 mL, 0.110 mol) in acetic acid (25 mL) for 4 days at room temperature[39] to give **40** after workup, 77% yield (5.5 g, 0.017 mol): mp 114–115 °C; ^1H NMR ($CDCl_3$) δ 8.20–7.25 (m, 8 H), 3.15 (s, 3 H), 2.24 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 146.2, 135.2, 130.3, 129.9, 129.0, 128.8, 126.6, 121.8, 43.8, and 21.7. Anal. Calcd for $C_{14}H_{14}O_5S_2$: C, 51.53; H, 4.29. Found: C, 51.75; H, 4.34.

Reaction of 40 with Sodium Hydride. A solution of sulfonate **40** (0.50 g, 15 mmol) in THF (20 mL) was added to a mixture of sodium hydride (0.30 g, 75 mmol) and THF (5 mL). After 2 h, no reaction had occurred (TLC). After 12 h at room temperature, water was added to the milky mixture to destroy unreacted sodium hydride. The precipitate was filtered, and the filtrate was concentrated. The residue was taken up in dichloromethane. Some insoluble material was removed by filtration. The dichloromethane solution yielded starting material, identified by TLC (0.0123 g, 2.5%). The air-dried precipitate was identified as sodium 4-toluenesulfonate by NMR spectroscopy. The material insoluble in dichloromethane was dissolved in water, acidified with hydrochloric acid, and then extracted with chloroform to give 2-(methylsulfonyl)phenol (**56**), 75% yield (0.20 g), purified by column chromatography (ethyl acetate), and identified by comparison of its melting point and spectra with those in the literature: mp 80–81 °C (lit.[38] mp 80–83 °C).

N-[2′-(Methylthio)phenyl]-4-toluenesulfonamide. Pyridine (6.4 mL, 0.079 mol) and then 4-toluenesulfonyl chloride (22.6 g, 0.118 mol) were added to 2-(aminothio)anisole[40] (11 g, 0.079 mol) in ether (250 mL) at 0 °C. After 18 h at room temperature, the mixture was worked up to give the sulfonamide, 83% yield from 95% ethanol (19.2 g, 0.0654 mol): mp 146–147 °C; IR (KBr) 3260

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(NH), 1320 and 1140 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.16 (s, 3 H), 2.36 (s, 3 H), 7.2–7.83 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 143.9, 141.1, 137.4, 136.2, 133.4, 129.5, 129.0, 127.3, 125.1, 120.3, 21.5, 19.1. Anal. Calcd for $C_{14}H_{15}NO_2S_2$: C, 57.33; H, 5.16; N, 4.78. Found: C, 57.67; H, 5.12; N, 4.87.

***N*-Methyl-*N*-[2′-(methylthio)phenyl]-4-toluenesulfonamide.** Dimethyl sulfate (0.20 mL, 2.0 mmol), *N*-[2′-(Methylthio)phenyl]-4-toluenesulfonamide (0.199 g, 0.678 mmol), and 5.5 N potassium hydroxide (20 mL) were heated in ethanol (10 mL) to give the sulfonamide, 71% yield from ethanol (0.147 g, 0.478 mmol): mp 126–127 °C; IR (KBr) 1350 and 1160 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40 and 2.43 (2 s, 6 H), 3.1 (s, 3 H), 6.78–7.85 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 143.6, 141.2, 138.5, 135.7, 129.5, 129.0, 128.2, 127.9, 125.4, 124.7, 38.3, 21.6, 14.8. Anal. Calcd for $C_{15}H_{17}NO_2S_2$: C, 58.62; H, 5.58; N, 4.56. Found: C, 58.63; H, 5.57; N, 4.55.

***N*-Methyl-*N*-[2′-(methylsulfonyl)phenyl]-4-toluenesulfonamide (41).** *N*-Methyl-*N*-[2′-(methylthio)phenyl]-4-toluenesulfonamide (11.4 g, 0.0371 mol) and 30% hydrogen peroxide (5 equiv, 1.5 mL) in glacial acetic acid (150 mL) were refluxed for 24 h.[41] Sulfonamide **41** was obtained upon workup, 77% yield from ethanol (9.71 g, 0.0286 mol): mp 194–195 °C; IR (KBr) 1350 and 1160 (SO_2N) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H), 3.26 (s, 3 H), 3.47 (s, 3 H), 6.7–8.26 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 144.6, 140.9, 134.7, 134.4, 130.6, 129.9, 129.5, 128.4, 45.1, 40.8, 21.6; MS, *m/e* (intensity) 340 (9, M), 324 (137), 307 (68), 274 (68), 260 (100). Anal. Calcd for $C_{15}H_{17}O_4NS_2$: C, 53.09; H, 5.05; N, 4.13. Found: C, 53.36; H, 5.40; N, 4.18.

Reaction of 41 with Sodium Hydride. Sulfonamide **41** (0.20 g, 0.59 mmol), sodium hydride (6 equiv) and THF (10 mL) were stirred at room temperature for 18 h. D_2O (1 mL) was added to quench the reaction. Workup yielded 68% of starting material. In a similar way, sulfonamide **41** (0.24 g, 0.71 mmol), sodium hydride (3 equiv), and DME (40 mL) gave after 4 h at room temperature, starting material (80% yield from ethanol) and 2-(methylamino)phenyl methyl sulfone (**57**) (13% yield). Both compounds were identified by comparison of their melting points and IR and NMR spectra with those obtained from authentic samples. Repetition of the reaction at 85 °C for 9.5 h gave a 62% recovery of **41** and a negligible amount of sulfone **57**. Starting material was recovered quantitatively when the reaction was run for 5 h at 10 °C.

Reaction of 41 with BuLi. BuLi (2 equiv, 1.8 mL of a 1.6 M solution in hexane, 2.9 mmol) was added to sulfonamide **41** (0.496 g, 1.45 mmol) in THF (55 mL). After 2 h, the reaction was quenched with water (1 mL). Column chromatography (methylene chloride) gave starting material, 35% yield (0.172 g, 0.504 mmol) and sulfone **57**, 9.8% yield (0.0266 g, 0.144 mmol).

Reaction of 41 with LDA. LDA (3 equiv) in THF (20 mL) was added to a solution of sulfonamide **41** (0.513 g, 1.50 mmol) in THF (30 mL) at room temperature. After 3 h, the reaction was quenched with water (1 mL). The solution was filtered and worked up. Column chromatography (methylene chloride, ethyl acetate) gave starting material, 11% yield (0.0585 g, 0.172 mmol) and sulfone **57**, 42% yield (0.116, 0.627 mmol). The vacuum-dried solid (filtered from the THF solution) was identified as 4-toluenesulfinic acid by matching its proton NMR spectrum with that of an authentic sample; 33% yield (0.0809 g, 0.499 mmol).

2-Acetamidophenyl Methyl Sulfide. Triethylamine (11.2 mL, 0.0810 mol) and acetic anhydride (10.2 mL, 0.108 mol) were added simultaneously to 2-(aminothio)anisole (7.50 g, 0.0540 mol) in chloroform (100 mL). After 1 h at room temperature and heating for 1 h, work up gave the sulfide, 90% yield from cyclohexane (8.88 g, 0.0488 mmol): mp 101–103 °C; IR (KBr) 3220 (NH), 1650 (C=O), 1570, 1540 (amide II band) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.23 (s, 3 H), 2.38 (s, 3 H), 6.98–8.36 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 168.4, 138.2, 132.5, 128.6, 125.5, 124.5, 121.0, 24.7, 18.7. Anal. Calcd for $C_9H_{11}NOS$: C, 59.65; H, 6.12; N, 7.73. Found: C, 59.64; H, 6.22; N, 7.84.

2-Acetamidophenyl Methyl Sulfone. A solution of 30% hydrogen peroxide (2.5 mL, 0.43 mol) and 2-acetamidophenyl methyl sulfide (7.80 g, 0.0430 mol) in acetic acid (200 mL) was refluxed for 10 days. Workup gave the sulfone, which was purified by column chromatography (ethyl acetate) and then by recrystallization from carbon tetrachloride 53% yield (4.86 g, 0.0229 mol): mp 144–145 °C; IR (KBr) 3320 (NH), 1685 (C=O), 1300 and 1145 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (s, 3 H), 2.98 (s, 3 H), 7.02–8.00 (m, 4 H), 9.47 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 168.6, 137.1, 135.4, 129.3, 127.1, 124.2, 123.0, 44.3, 25.1; MS, *m/e* (intensity), 215 (39, M + 2), 214 (80, M + 1), 213 (597, M), 171 (1000), 156 (453), 108 (886), 92 (1000). Anal. Calcd for $C_9H_{11}NO_3S$: C, 50.69; H, 5.20; N, 6.57. Found: C, 50.54; H, 5.17; N, 6.58.

2-Aminophenyl Methyl Sulfone. 2-Acetamidophenyl methyl sulfone (0.324 g, 1.52 mmol) and aqueous sodium hydroxide (2 mL of 5 N solution) in ethanol 820 mL) were refluxed for 8 h. Workup gave the sulfone, 86% yield from carbon tetrachloride (0.223 g, 1.31 mmol): mp 83 °C; IR (KBr) 3460 and 3370 (NH_2), 1300 and 1140 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.03 (s, 3 H), 5.20 (br s, 2 H), 6.68–7.82 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 146.4, 135.1, 129.3, 121.9, 117.8, 117.7, 42.3. Anal. Calcd for $C_7H_9NO_2S$: C, 49.09; H, 5.30; N, 8.19. Found: C, 49.09; H, 5.25; N, 8.16.

2-(Methylamino)phenyl Methyl Sulfone (57). N-Monomethylation of 2-aminophenyl methyl sulfone was accomplished by following Krishnamurthy's procedure[31] for formylation of the amine group with acetic formic anhydride followed by in situ reduction of the formamide with borane–methyl sulfide complex. 2-Aminophenyl methyl sulfone (0.979 g, 5.72 mmol) was thus converted to **57**, 89% yield (0.943 g, 5.10 mmol): mp 91–92 °C; IR (KBr) 3430 (NH), 1300 and 1140 (SO_2) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.87 (s, 3 H), 3.02 (s, 3 H), 6.13 (br s, 1 H), 6.67–7.90 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 147.8, 135.5, 129.7, 121.5, 116.1, 111.8, 42.3, 30.0. Anal. Calcd for $C_8H_{11}NO_2S$: C, 51.88; H, 5.99; N, 7.57. Found: C, 52.08; H, 6.02; N, 7.70.

Registry No. **5**, 599-62-2; **7**, 53973-85-6; **9**, 115562-36-2; **9** (R = H), 115590-78-8; **13**, 1216-96-2; **13** (R = CHO), 115562-43-1; **22**, 115562-37-3; **23**, 115562-39-5; **24**, 115562-38-4; **25**, 115562-40-8; **26**, 115562-41-9; **27**, 115562-42-0; **30**, 81256-16-8; **31**, 115562-45-3; **31** (R = CDO), 115562-44-2; **32**, 81256-17-9; **38**, 107555-81-7; **38** (imine), 92851-33-7; **39**, 115562-52-2; **39** (2-nitro deriv), 115562-50-0; **39** (*N,N*-dimethyl deriv), 115562-56-6; **40**, 115562-59-9; **41**, 115562-60-2; **41** (sulfide), 3982-28-3; **41** (*N*-demethylsulfide), 4908-08-1; **42**, 115562-46-4; **43**, 115562-49-7; **43** (imine), 115562-48-6; **44**, 640-61-9; **45**, 53334-33-1; **45** (*N,N*-dimethyl deriv), 115562-55-5; **47**, 115562-53-3; **47** (R = NO_2), 115562-51-1; **48**, 115562-54-4; **49**, 3695-02-1; **50**, 33228-44-3; **52**, 115562-57-7; **53**, 13509-75-6; **56**, 27489-33-4; **57**, 10224-69-8; $C_6H_5NH_2$, 62-53-3; *p*-$CD_3C_6H_4SO_2Cl$, 65596-99-8; *m*-$CF_3C_6H_4SO_2Cl$, 777-44-6; *o*-$NH_2C_6H_4OH$, 95-55-6; *p*-$MeC_6H_4S(O)NHMe$, 6873-56-9; *o*-$OHCC_6H_4OSO_2C_6H_4$-*p*-Me, 19820-56-5; $C_6H_5CH_2NH_2$, 100-46-9; *p*-$MeC_6H_4SO_2NHCH_2C_6H_5$, 1576-37-0; *o*-$OHCC_6H_4OH$, 90-02-8; *o*-$OHCC_6H_4OSO_2C_6H_4$-*p*-CD_3, 115562-47-5; *o*-$NO_2C_6H_4CH_2Br$, 3958-60-9; *p*-$MeC_6H_4SO_2NHMe$, 640-61-9; *p*-$NO_2C_6H_4CH_2Br$, 100-11-8; $C_6H_5CH_2Br$, 100-39-0; *p*-$Me_2NC_6H_4CH{=}NMe$, 24431-17-2; *p*-$Me_2NC_6H_4CH_2NHMe$, 55096-85-0; *p*-$MeC_6H_4SO_2Cl$, 98-59-9; *p*-$MeC_6H_4SO_2Li$, 16844-27-2; *o*-$MeSC_6H_4OH$, 1073-29-6; *o*-$MeSC_6H_4OSO_2C_6H_4$-*p*-Me, 115562-58-8; *o*-$NH_2C_6H_4SMe$, 2987-53-3; *p*-$MeC_6H_4SO_2H$, 536-57-2; *o*-$CH_3CONHC_6H_4SMe$, 6310-41-4; *o*-$CH_3CONHC_6H_4SO_2Me$, 20628-27-7; *o*-$NH_2C_6H_4SO_2Me$, 2987-49-7; 2-amino-3-hydroxypyridine, 16867-03-1.

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