= 8.6 Hz, $J_{4,5}$ = 5.2 Hz, 1 H, H4), 3.68 (s, 3 H, COOCH_3), 3.56 (dd, $J_{4,3}$ = 8.6 Hz, $J_{3,2}$ = 9.7 Hz, 1 H, H3), 3.06 (t, $J_{2,3}$ = $J_{2,1}$ = 9.7 Hz, 1 H, H2), 2.70 (dd, $J_{13,13'}$ = 15.0 Hz, $J_{13,1}$ = 3.8 Hz, 1 H, H13), 2.50-2.28 (m, 2 H, H1, H6(eq)), 2.20 (dd, $J_{13,13'}$ = 15.0 Hz, $J_{13',1}$ = 8.8 Hz, 1 H, H13'), 1.51, 1.40, 1.39, 1.35 (s, s, s, s, 12 H), 1.50-1.45 (m, 1 H, H6(ax)); ^{13}C NMR (20 MHz, $CDCl_3$) δ 171.99 ($COOCH_3$), 110.35, 108.92 (C7, C8), 81.69, 78.56, 77.60, 74.20 (C2, C3, C4, C5), 51.40 ($COOCH_3$), 36.94 (C6), 33.16 (C1), 31.59 (C13), 28.38, 26.78, 25.97 (C9, C10, C11, C12); MS m/z 285 (M^+ - 15, 18). Anal. Calcd for $C_{15}H_{24}O_6$: C, 58.31; H, 8.39. Found: C, 58.22; H, 8.31. **49**: mp 35-37 °C; $[\alpha]^{25}_D$ -10° (c 0.6, $CHCl_3$); IR ($CHCl_3$) 2990, 1720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (dd, $J_{2,3}$ = 4.0 Hz, $J_{2,1}$ = 15.8 Hz, 1 H, H2), 6.15 (dd, $J_{1,2}$ = 15.8 Hz, $J_{1,3}$ = 2.0 Hz, 1 H, H1), 4.66 (ddd, $J_{3,2}$ = 4.0 Hz, $J_{3,1}$ = 2.0 Hz, $J_{3,4}$ = 2.4 Hz, 1 H, H3), 3.78 (dd, $J_{5,4}$ = 2.4 Hz, $J_{6,5}$ = 5.4 Hz, 1 H, H5), 3.74 (s, 3 H, COOCH_3), 3.72 (m, 1 H, H6), 3.60 (t, $J_{3,4}$ = $J_{4,5}$ = 2.4 Hz, 1 H, H4), 1.47, 1.45, 1.41, 1.31 (s, s, s, s, 12 H), 1.28 (d, J = 5.9 Hz, 3 H, CH_3-7); MS m/z 285 (M^+ -15, 13). Anal. Calcd for $C_{15}H_{24}O_6$: C, 58.21; H, 8.39. Found: C, 57.99; H, 8.26. Compound **48** (252 mg, 0.8 mmol) was treated with acetic acid/water (7:3, 7 mL) and stirred at room temperature for 24 h. The solvent was evaporated and the residue submitted to chromatography (CH_2Cl_2/methanol, 90:10), giving the polyol **51** (118 mg, 68%): mp 113-115 °C; $[\alpha]^{25}_D$ -52° (c 0.4, CH_3OH); IR (KBr) 3600-3200, 2975, 1730 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.12 (ddd, $J_{5,6(eq)}$ = 3.6 Hz, $J_{5,6(ax)}$ = 2.2 Hz, $J_{5,4}$ = 3.2 Hz, 1 H, H5), 3.83 (s, 3 H, COOCH_3), 3.74 (t, $J_{3,2}$ = $J_{3,4}$ = 9.2 Hz, 1 H, H3), 3.48 (dd, $J_{3,4}$ = 9.2 Hz, $J_{4,5}$ = 3.2 Hz, 1 H, H4), 3.21 (dd, $J_{2,3}$ = 9.2 Hz, $J_{2,1}$ = 10.4 Hz, 1 H, H2), 2.91 (dd, $J_{7,7'}$ = 14.6 Hz, $J_{7,1}$ = 4.0 Hz, 1 H, H7), 2.44 (m, 1 H, H1), 2.32 (dd, $J_{7,7'}$ = 14.6 Hz, $J_{7',1}$ = 8.7 Hz, 1 H, H7'), 2.05 (td, $J_{6(eq),6(ax)}$ = 14.2 Hz, $J_{6(eq),1}$ = $J_{6(eq),5}$ = 3.6 Hz, 1 H, H6(eq)), 1.47 (ddd, $J_{6(ax),5}$ = 2.2 Hz, $J_{6(ax),6(eq)}$ = 14.2 Hz, $J_{6(ax),1}$ = 11.5 Hz, 1 H, H6(ax)). Anal. Calcd for $C_9H_{16}O_6$: C, 49.08; H, 7.32. Found: C, 48.91; H, 7.01.

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Supplementary Material Available: Synthetic procedures and spectral data of the intermediates in the preparation of compounds 4-16 (19 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Metal-Ammonia Reduction and Reductive Alkylation of *N*-Alkylnaphthalenesulfonamides. A New Route to Substituted Naphthalenes[1]

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Conditions have been found for 1,4-reduction of aromatic sulfonamides (conveniently monitored by electrical conductivity), using metals in THF/liquid ammonia on the pre-formed *N*-lithium salts (BuLi), without concomitant C-S reductive cleavage. The resulting 1,4-dihydro compounds could be alkylated, either in situ (in the case of simple unfunctionalized halides only) or, following isolation, after further N-alkylation and then forming the monoanion, or after forming the dianion of the N-monoalkylated dihydrosulfonamide, generally using as base *n*-butyllithium (a simple titration procedure). In the former case functionalized electrophiles (bromo esters, chloroformates) could be utilized. The ratio of α- to γ-alkylation was dependent on the method of alkylation, the reaction medium, the nature of the N-alkyl group(s), and whether a monoanion or a dianion served as substrate. γ-Alkylation products could in some cases be further α-substituted. The α-substituted products aromatized, with loss of SO_2 and amine, by heating, whereas γ-substitution products required hydrolysis by aqueous alkali; this greatly facilitated separation where mixtures were formed. Thus, this dihydrosulfonamide route constitutes a novel and nucleophilic route to 1-substituted, 2-substituted, and, notably, 1,3-disubstituted naphthalenes.

Introduction

The Birch reduction by metals in liquid ammonia continues to be the most effective way of transforming an aromatic system into alicyclic and, ultimately, acyclic compounds.[2] It proceeds with particular ease (with little or no proton donor required) when the aromatic ring is substituted by electron-withdrawing groups, such as carboxyl,[3] carboxylic ester,[4] carboxamide,[5] nitrile,[6] and, noticeably, ketone.[7] In most cases the experimental conditions permit the trapping of a stable carbanion intermediate by an electrophile such as alkyl or alkenyl halide,[2b] epoxide,[8] or α,β-unsaturated ester even when a limited amount of proton donor may have to be present to avoid side reactions.[4-7] This adds greatly to the usefulness of the reaction, particularly when followed by further, often

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ingenious, elaboration of the dihydro product obtained.[10]

Sulfonation is one of a limited number of reactions which introduce an electron-withdrawing group directly into an aromatic ring, and sulfonation in particular of polycyclic systems such as naphthalene,[11] anthracene, and phenanthrene was studied intensively many years ago, albeit mainly for the purpose of providing dyestuff intermediates which to this day continue to be an important outlet for aromatic sulfonation products. As for work reported up to the present on the action of metals in liquid ammonia on aromatic sulfonic acids and their derivatives, this has been either unconvincing or confusing or seems to have convincingly excluded the possibility of 1,4-reduction of the aromatic ring. Thus, benzenesulfonic acid[12] and its salts[13] have been reported to yield only benzene and sulfite anion when using sodium and liquid ammonia, while benzenesulfonamide with additional presence of an alcohol[14] was said to give benzenethiol and/or diphenyl disulfide. On the other hand the sodium–ammonia cleavage of the *N*-tosylamino protective group in peptides, discovered fortuitously in 1937[15] and perfected experimentally since,[16,17] has been used widely.[18] Thorough work by Rudinger and co-workers[19,20] indicated that this reaction proceeds by cleavage of the $ArSO_2$–N bond by two-electron addition to give the free amino group and aryl sulfinate anion (with possible further reduction of the latter to thiophenol). In their work it appears that 1,4-reduction of the aromatic ring was neither detected nor taken into account.

We decided to reexamine this subject, at first in the naphthalene series, for a number of reasons. One was the fact that many substituted naphthalenesulfonic acids and their derivatives had been prepared in the past and their orientation rigorously established.[11] Another was that many of these are still widely used commercially and thus accessible. A third reason was that if Birch reduction of such compounds could be combined with substitution this could possibly open up an unambiguous route to substituted dihydro and perhaps aromatic naphthalenes of predictable orientation, a goal often difficult to achieve by the usual means of electrophilic substitution.[21,22] As for the type of derivative worth investigating, *N*-alkyl- and *N,N*-dialkylsulfonamides appeared to be the most suitable candidates. The sulfonamide group is known to be very stable toward nucleophiles[23] unlike other electron-withdrawing groups; and it offers the additional bonus, prior to possible Birch reduction, of acting as a powerful ortho director in metalation while attached to an aromatic nucleus.[24] At the same time it should be noted that in nonaromatic compounds, unlike the sulfone group, the use of sulfonamide as an activator in α-carbanion formation and subsequent nucleophilic substitution has been rare.[25]

Our work centered mainly on naphthalenesulfonamides with a methoxyl group in the nonsulfonated ring, in view of the latent additional functionality thus provided for at a later stage in synthetic work. The experimental part describes optimized procedures for the O-methylation of naphtholsulfonic acids, conversion into the pertaining sulfonyl chlorides, and thence into N-substituted sulfonamides.

First experiments on *N,N*-dialkylsulfonamides such as **5** and **57**, chosen by analogy to *N,N*-dialkylcarboxamides,[26] were quite unsuccessful, whether or not a proton donor was present during the reduction. Between 3.5 and 5 equiv of metal were consumed, and the main product isolated was that of complete Ar–S bond hydrogenolysis (i.e., naphthalene or 2-methoxynaphthalene), accompanied by intractable, probably polymeric material. *The desired goal was eventually achieved by using N-monoalkyl sulfonamides in the form of their N-lithio or N-sodio derivatives.* Here attention to experimental detail was crucial. The optimum conditions included the following: (a) prior deprotonation of the substrate (usually in THF) using a strong "non-protogenic" base such as *n*-butyllithium or sodium hydride, with the former conveniently exhibiting a colored endpoint (due to incipient ortho metalation); use of alkoxide or amide bases gave inferior results; (b) subsequent addition of liquid ammonia, and then of metal (lithium or sodium) at between −55 and −65 °C (measured in the reaction medium and not in the cooling bath); (c) acidification after attaining the end point (see below) using a large excess of ammonium chloride; and (d) removal of both ammonia and solvent below room temperature in vacuo. In this way generally good yields of crystalline dihydro products could be obtained, with the limitations found as discussed below. When quenching the reaction was preceded by adding an alkyl halide in excess, reductive alkylation could be achieved in many cases; here even greater care had to be exercised in working up the products in view of their sensitivity.

In all these reactions intense coloration of the reaction medium (dark-orange or green-brown) usually developed at an early stage, and this made perception of an end point (usually a change to green-black) very difficult. We then found that this difficulty could be overcome very easily

(10) Some recent examples: (a) Pd^{II}-aided cyclization to a bridged-ring system: Kende, A. S.; Battista, R. A.; Sandoval, S. B. *Tetrahedron Lett.* **1984**, *25*, 1341. (b) Halolactonization–free-radical cyclization: Chuang, C.; Galluci, J. C.; Hart, D. J. *J. Org. Chem.* **1988**, *53*, 3210. (c) Selective ozonolysis: Moody, C. J.; Toszek, J. *Tetrahedron Lett.* **1986**, *27*, 5253. (d) Asymmetric alkylation using a chiral amide and further elaboration to chiral product: Schultz, A. G.; Suhaldolnik, J. C.; Kulinig, R. K. *J. Org. Chem.* **1988**, *53*, 2456.

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(21) E.g., the course of electrophilic *tert*-butylation of 2-naphthol: Kessler, H.; Barmel, W.; Griesinger, C.; Hertl, P.; Streich, E.; Rieker, A. *J. Org. Chem.* **1986**, *51*, 596.

(22) For some examples of more involved routes to substituted naphthalenes see the following. By annulation of benzenes: (a) Loozen, H. J. J. *J. Org. Chem.* **1975**, *40*, 520. (b) Wildeman, J.; Borgen, P. C.; Pluim, H.; Rouwette, P. H. F. M.; van Leusen, A. M. *Tetrahedron Lett.* **1978**, *19*, 2213. (c) Teague, S. J.; Roth, G. P. *Synthesis* **1976**, 427. From polyketide precursors: (d) Stossel, D.; Chan, T. H. *J. Org. Chem.* **1988**, *53*, 4901. By Diels–Alder reaction: (e) Coleman, R. S.; Grant, E. B. *J. org. Chem.* **1991**, *56*, 1357. From benzocyclobutene intermediate: (f) Shishido, K.; Yamashita, A.; Hiroya, K.; Fukimoto, K.; Kametani, T. *Tetrahedron Lett.* **1989**, *30*, 111.

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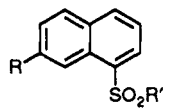
by following the electrical conductivity of the reaction mixture. Addition of even a small (<5% equiv/mol) excess of metal over that usually required for complete reaction (2.2–2.4 equiv/mol) resulted in a sudden increase (usually 100–300%) in the low but measurable and steady conductivity observed before the end point. Moreover, after addition of an alkylating agent this decreased to an ultimately steady value which could serve to monitor completeness of alkylation. We have used this method with success in similar reactions such as reduction using radical anions where such problems are likewise encountered.

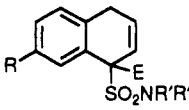
The following will describe and discuss our results and the scope and limitations of their synthetic potential. In view of the difference between results obtained with the 1- and 2-(or 3-)naphthalenesulfonamides on the one hand and the structural interconnection between products obtained in either series on the other, this discussion will be divided between, and refer to, *N*-alkyl-α- and -β-naphthalenesulfonamides.

N-Alkyl-α-naphthalenesulfonamides

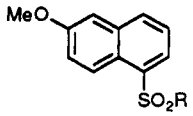
1,4-Reduction. With the unsubstituted (**1**, **2**), 7-methoxy (**4**, **6**, **7**, **8**), and 5-methoxy (**28**, **29**, **30**, **31**)-substituted sulfonamides, metal–ammonia reduction to the corresponding 1,4-dihydrosulfonamides generally proceeds in good to acceptable yield to give products of reasonable stability. The course of, and yields in, these reactions was



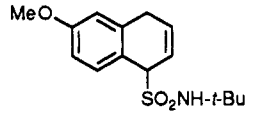
1. R = H, R′ = NH-*t*-Bu
2. R = H, R′ = $NHCMe_2CH_2Me$
3. R = OMe, R′ = Cl
4. R = OMe, R′ = NHMe
5. R = OMe, R′ = NEt_2
6. R = OMe, R′ = NH-*t*-Bu
7. R = OMe, R′ = $NHCMe_2CH_2Me$
8. R = OMe, R′ = $NHCMe_2CH_2CMe_3$
9. R = R′ = Cl
10. R = Cl, R′ = $NHCMe_2CH_2Me$



11. R = E = R′ = H, R″ = *t*-Bu
12. R = OMe, E = R′ = H, R″ = Me
13. R = OMe, E = H, R′ = R″ = Me
14. R = OMe, E = R′ = H, R″ = *t*-Bu
15. R = OMe, E = R′ = H, R″ = CMe_2CH_2Me
16. R = OMe, E = R′ = H, R″ = $CMe_2CH_2CMe_3$
17. R = OMe, E = Me, R′ = H, R″ = *t*-Bu
18. R = OMe, E = *n*-Pr, R′ = H, R″ = *t*-Bu
19. R = OMe, E = allyl, R′ = H, R″ = *t*-Bu
20. R = OMe, E = CH_2Ph, R′ = H, R″ = *t*-Bu
21. R = OMe, E = H, R′ = Me, R″ = *t*-Bu
22. R = OMe, E = CO_2Me, R′ = R″ = Me
23. R = OMe, E = CO_2Me, R′ = Me, R″ = *t*-Bu



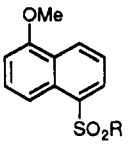
24. R = Cl
25. R = NH-*t*-Bu



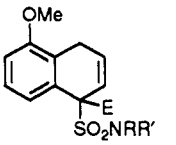
26

not particularly affected by the nature of the N-alkyl group. On balance, *tert*-butyl and 1,1-dimethylpropyl offered advantages in the solubility they bestowed on the substrate (both it and and derived N-metal derivatives) and ease of purification of products. The *N*-methyl group was less advantageous in this regard. In all these reactions the only other products formed were those of Ar–S bond hydrogenolysis, i.e., naphthalene itself and 2- or 1-methoxynaphthalene, and the extent to which these were formed depended entirely on how much or little attention was paid to the critical experimental conditions enumerated above, in particular temperature control inside the reaction medium. A few experiments were conducted using the *N*-sodio derivative (produced with sodium hydride) and sodium metal, but yields were found to be inferior to those experienced with lithium.

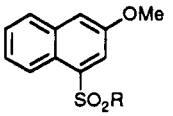
A different situation was encountered when the methoxyl group was at C_6, C_2, and C_3 in the naphthalene nucleus. In the reduction of sulfonamide **25** no clear end



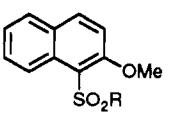
27. R = Cl
28. R = NHMe
29. R = NH-*t*-Bu
30. R = $NHCMe_2CH_2Me$
31. R = $NHCMe_2CH_2CMe_3$



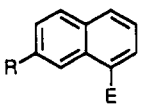
32. E = R = H, R′ = *t*-Bu
33. E = R = H, R′ = CMe_2CH_2Me
34. E = R = H, R′ = $CMe_2CH_2CMe_3$
35. E = CH_2Ph, R = H, R′ = *t*-Bu
36. E = H, R = Me, R′ = *t*-Bu
37. E = CO_2Me, R = Me, R′ = *t*-Bu



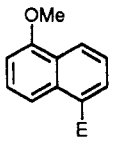
38. R = Cl
39. R = NH-*t*-Bu



40. R = Cl
41. R = NHMe
42. R = NH-*t*-Bu



43. R = H, E = *n*-Bu
44. R = OMe, E = Me
45. R = OMe, E = Et
46. R = OMe, E = Pr
47. R = OMe, E = allyl
48. R = OMe, E = CH_2Ph
49. R = OMe, E = CO_2Me



50. E = CH_2Ph
51. E = CO_2Me

point could be perceived, neither visually nor conductometrically, and the yield of the dihydro product **26** was low, the predominant product being 2-methoxynaphthalene. With the 2-methoxysulfonamides **41** and **42** complete hydrogenolysis to 2-methoxynaphthalene occurred under a variety of conditions. It appeared that inductive nonstabilization of a benzylic carbanion intermediate in this type of reaction by electron-donating groups ortho- or para-situated was responsible; and this supposition was indeed borne out by subsequent results (see below). On the other hand, the behavior of sulfonamide **39**, with methoxyl in the meta position, was unexpected. Reaction of the *N*-lithio derivative with lithium in liquid ammonia was extremely slow under the same conditions as used for its analogues and no dihydro product could be isolated. It was hoped that 1,4-reduction of the sulfonamide-containing group could take precedence over, e.g., dehalogenation; however, the reaction with the 7-chlorosulfonamide **10**, besides being sluggish, led mainly to dehalogenation with formation of sulfonamide **2**.

Reductive Alkylation and Formation of 1-Substituted Naphthalenes. When the metal–ammonia reduction reaction was quenched by addition of simple and reactive alkyl halides 1-alkyldihydrosulfonamides were predominantly produced. These products were considerably less stable than the nonalkylated ones, thermally as well as to conditions of pH higher than 7, and their yields were dependent both on the size of the introduced and of

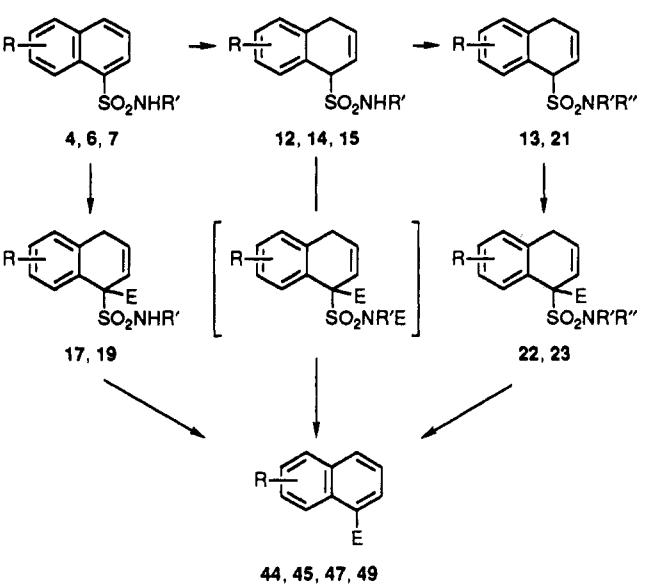
the N-alkyl group. Further acidification of the medium by an excess of ammonium chloride after quenching by alkyl halide was essential. These alkyldihydro products decomposed at or slightly above their melting points, and this decomposition was found to lead to the corresponding alkyl naphthalene in high yield. The latter was in fact found to be the main if not sole byproduct of the reductive alkylation reaction; and for preparation of the alkyl naphthalene by this route it sufficed to perform pyrolysis and distillation of the reduction–alkylation product without isolation of intermediate. This route proved to be an advantageous one to the known substituted naphthalenes **43**, **44**, **45**, and **48**, as well as to the unknown ones **46**, **47**, and **50**.

The thermal fragmentation leading to these latter compounds involves a priori loss of SO_2 and primary amine. During simple distillation of crude alkylated dihydrosulfonamides a crystalline but relatively volatile first sublimate was often observed. Evidently this was a sulfur dioxide–amine complex of the type sporadically reported on in the literature,[27] and there usually described as being a charge-transfer one, but also elsewhere[28] (rather nonevidentially) as an amidosulfurous acid. We are presently attempting to obtain crystals of one of these (highly hygroscopic) complexes suitable for X-ray crystallographic analysis.

Adaptation of this type of route toward functionalized naphthalene derivatives, such as carboxylic acids, faces the difficulty that the type of electrophilic substitution reagent necessary, such as a chloroformate, is always more reactive toward the medium employed (liquid ammonia) than to a stabilized carbanion contained herein. A solution of this problem was found to lay in further N-alkylation (usually methylation) of the simple 1,4-dihydrosulfonamide, followed by C-alkylation or -acylation at C_1, both steps in THF as solvent. In either step *n*-butyllithium could be used to advantage as base, in the first one again by a simple titration. N,N,C-Trisubstituted derivatives were thus usually obtained in good yield and were also found to undergo practically quantitative thermal fragmentation at or slightly above the melting point. This proved to be the best route for introducing a carboxylic ester group. In a number of cases actual isolation and purification of the N,N-dialkyl intermediates proved to be unnecessary (e.g., conversion of **83** into **85**); in others, where the aim was C-alkylation, it was advantageous to perform N,C-"per-alkylation" by use of an excess of sodium hydride and alkyl halide in dimethylformamide (e.g., conversion of **15** into **45**).

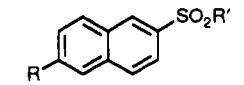
Scheme I summarizes these results.

Scheme I

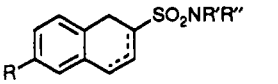


N-Alkyl-β-naphthalenesulfonamides

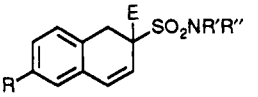
Reduction and Reductive Alkylation. The behavior of *N*-alkyl-β-naphthalenesulfonamides upon metal–ammonia reduction and reductive alkylation was less straightforward than that of the foregoing α-analogues, but proved in the end to be both more interesting and of more varied utility in providing routes to substituted naphthalenes. In all cases where reduction took place without Ar–S cleavage (ring-unsubstituted β-sulfonamides, 6-methoxy 2-sulfonamides, and 8-methoxy 2-sulfonamides), the dihydro products were mixtures of double-bond isomers indistinguishable in polarity (e.g., by TLC); they were also more stable thermally than the α-analogues. Reductive alkylation (methylation) was first tried on β-sulfonamide **58**. This gave in high yield a single isolable product which



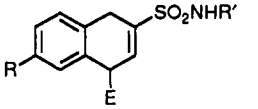
52. R = H, R' = NHMe
53. R = H, R' = NH-*t*-Bu
54. R = H, R' = $NHCMe_2CH_2Me$
55. R = OMe, R' = Cl
56. R = OMe, R' = NHMe
57. R = OMe, R' = NMe_2
58. R = OMe, R' = NH-*t*-Bu



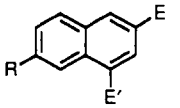
59. R = R' = H, R'' = Me
60. R = H, R' = R'' = Me
61. R = R' = H, R'' = *t*-Bu
62. R = OMe, R' = H, R'' = Me
63. R = OMe, R' = R'' = Me
64. R = OMe, R' = H, R'' = *t*-Bu
65. R = OMe, R' = Me, R'' = *t*-Bu



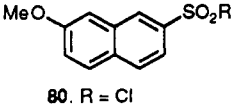
66. R = H, E = allyl, R' = R'' = Me
67. R = H, E = allyl, R' = H, R''= *t*-Bu
68. R = OMe, E = R' = R'' = Me
69. R = OMe, E = allyl, R', R'' = Me



70. R = H, E = allyl, R' = *t*-Bu
71. R = H, E = allyl, R' = CMe_2CH_2Me
72. R = OMe, E = Me, R' = *t*-Bu
73. R = OMe, E = allyl, R' = *t*-Bu



74. R = OMe, E = Me, E' = H
75. R = OMe, E = *n*-Pr, E' = H
76. R = OMe, E = allyl, E' = H
77. R = H, E = $CH_2CMe{:}CH_2$, E' = allyl
78. R = OMe, E = allyl, E' = Me
79. R = OMe, E = CO_2H, E' = allyl



80. R = Cl
81. R = NH-*t*-Bu

unexpectedly showed the introduced *C*-methyl group as a doublet in its ^1H NMR spectrum, indicating that alkylation had taken place at a position other than on the sulfonamide carbon. At the same time the signals due to three alicyclic, nonvinylic, and nonaromatic protons

(27) (a) Hata, T.; Kinumaki, S. *Nature* **1964**, *203*, 1378. (b) van der Helm, D.; Childs, J. D.; Christian, S. D. *J. Chem. Soc., Chem. Commun.* **1969**, 887 and references cited therein.
(28) *Chemical Abstracts*, 11th Collect. Index, 1982–1986, *Chemical Substance Index*, p 2986 CS.

showed up coincidentally as a nonresolvable singlet. The fact that one of these three must be adjacent to the introduced methyl group, as evidenced by the collapse of the doublet upon double irradiation of the three-proton "singlet", did not of course at that stage prove the structure of the alkylation product unequivocally as being **72**, as against two other alternatives (with the methyl group at C_3 or at C_1, with apposite shift of the double bond); that proof was obtained indirectly at a later stage (see below). This γ-directed alkylation was also observed on introduction of an allyl group (product **73**), and likewise in the case of the unsubstituted β-sulfonamides **53** and **54** (products **70** and **71**) though there not exclusively: with the former a small amount of α-alkylation product **67** could be isolated.

These γ-alkylation products were quite stable thermally (no decomposition below 200 °C). They could, however, be aromatized (with formal loss of SO_2 and amine) by vigorous alkaline hydrolysis. In this, as a source for 1-substituted naphthalenes, they did not in most cases appear likely to constitute an alternative to the corresponding α-naphthalenesulfonamide. At the same time their formation raised the dilemma of a feasible route from β-naphthalenesulfonamides to 2-substituted naphthalenes. The phenomenon of γ-alkylation was eventually found to be the outcome of the dianion species involved in the metal–ammonia reaction, the size of the group introduced, and (to a somewhat lesser extent) the size of the N-alkyl group; this subject will be discussed in detail below. A solution was found by further N-methylation of the dihydro-*N*-methylsulfonamide (*n*-butyllithium–iodomethane), followed by further deprotonation to form a monocarbanion and then C-alkylation or methoxycarbonylation. In this route the fact that the intermediates (compounds **59–65**) were double-bond isomers was found to be immaterial in regard to both yield and composition of final product; neither was significantly changed if an intermediate purified by crystallization was used. Except in the case of C-methylation (formation of **68**) the desired α-alkylation was always accompanied even in this variant by formation of the γ-alkylated product, but now separation of the two types of product could be done by taking advantage of the previously observed difference in thermal stability. Heating the product mixture to 140–160 °C (advantageously in diethylene glycol dimethyl ether, diglyme) led to selective aromatization of α-substituted product to give the 2-substituted naphthalene (products **74–79**, E′ = H) which was easily separated in all cases by chromatography from unchanged γ-alkylated dihydrosulfonamide. The latter was then aromatized by alkaline hydrolysis to give the 1-substituted naphthalene isomer.

Perhaps the synthetically most interesting variant was offered by further C-alkylation of the γ-substituted dihydrosulfonamides formed in high yield in the lithium–ammonia alkylative reduction sequence. This could best be done by N,C-"peralkylation" (with sodium hydride–alkyl halide in dimethylformamide) which led exclusively to C-alkylation on the sulfonamide carbon and, hence, to an intermediate aromatizable by pyrolysis alone. Thus were prepared the 1,3-disubstituted naphthalene derivatives **77**, **78**, and **79**, compounds of a type to which alternative synthetic routes would be difficult to visualize. Compound **78**, incidentally, afforded the proof of structure of its starting material **72** which was still lacking. Examination of nuclear Overhauser effect (NOE) interactions in **78** (which will be described in detail elsewhere[29]) provided the picture demonstrated in Figure 1a. In particular, it showed that only one aromatic ring proton interacts with both the allyl and the methyl group. Since the former must be at C_2 the latter has to be at C_4; an alternative location at the periposition C_8 (rather unlikely anyway for mechanistic reasons) can be ruled out by the other interactions found.

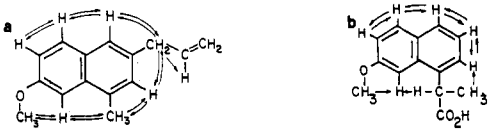
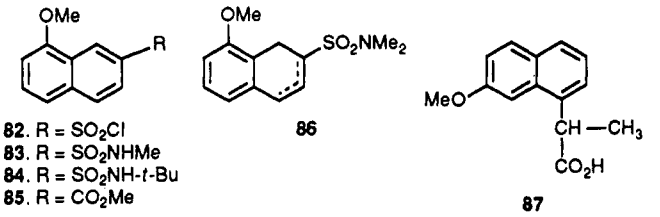


Figure 1. Nuclear Overhauser effect interactions.

After the behavior experienced with the α-naphthalenesulfonamides **25** and **42** it came as no surprise that the lithium–ammonia reduction of the β-sulfonamide **81** was likewise unsuccessful: once again no end point could be perceived and, apart from unchanged starting material, only 2-methoxynaphthalene could be isolated from this reaction. To complete the mechanistic picture it was not necessary to study the methoxynaphthalene sulfonamides **84** or **83** which should undergo the metal–ammonia reduction in high yield. The corresponding 8-hydroxynaphthalene-2-sulfonic acid was not available commercially. We prepared it starting from the trisulfonation of 1-naphthol which has for long been reported to lead to the 2,4,7-trisulfonic acid, though the evidence for the position of the third sulfonic acid group has never been totally convincing. The required sulfonyl chloride **82** was arrived at by way of partial hydrolytic desulfonation, as reported by a number of patents;[30–32] and the orientation of the derived *N*-*tert*-butylsulfonamide has now been rigorously confirmed by 2D-^{1}H NMR studies to be as in **84**, as will be described in detail elsewhere.[29] The corresponding *N*-methylsulfonamide **83** did indeed undergo the metal–ammonia reduction normally, with a sharp end point, and the reduction product after conversion into the dihydro-*N*,*N*-dimethylamide **86** was converted into the unknown 8-methoxynaphthalene-2-carboxylic acid (as its methyl ester **85**).



82. R = SO_2Cl
83. R = SO_2NHMe
84. R = SO_2NH-*t*-Bu
85. R = CO_2Me

86

87

The foregoing routes are illustrated and summarised in Scheme II.

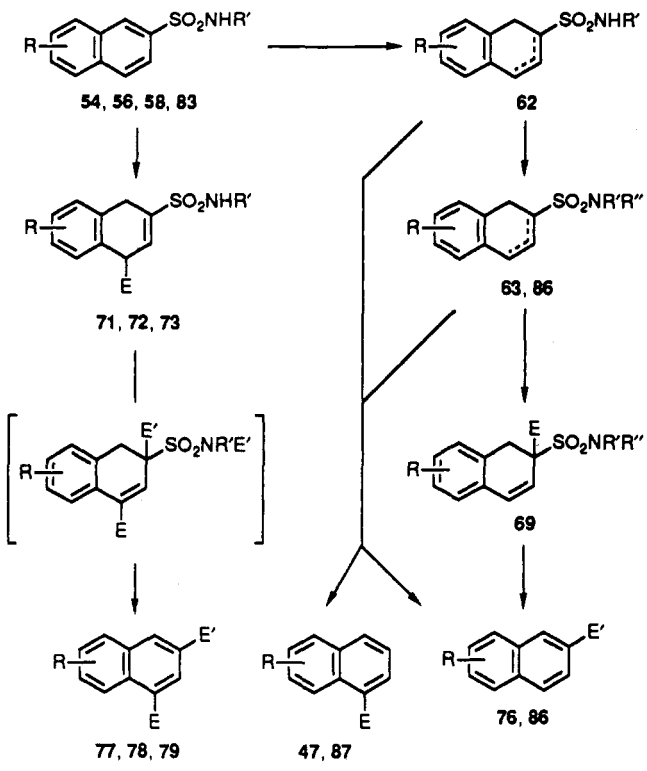
α- versus γ-Substitution

The foregoing account has indicated that the regiochemistry of introduction of a substituent group via dihydrosulfonamide intermediates appeared to depend on a number of factors, in particular in the β-sulfonamide series. Perhaps the most extreme case in the latter was that of the exclusive formation of the carboxylic acid **87**, via alkylation of the monoanion produced from the dihydro-*N*,*N*-dimethylsulfonamide **63** using methyl 2-bromopropanoate, under conditions where alkylation of

(29) Becker, D.; Loewenthal, H. J. E. To be published in *Tetrahedron*.

(30) "Failed" patent application (L 4327), cited by: Friedlander, P.; Taussig, R. *Ber.* **1897**, *30*, 1456.
(31) Hiyama, H.; Dehara, M.; Nakahara, T. *Jap. Patent* 70, 10,935, 1970.
(32) Mejstrik, B.; Valik, J.; Zaloudek, J.; Matoulek, J. *Czech Patent* 155,915, 1974.

Scheme II



the same substrate with less bulky electrophiles had led to substitution predominantly at the sulfonamide carbon. Structure **87**, incidentally, was arrived at also by nuclear Overhauser enhancement measurements[29] (see Figure 1b). It later became clear that this dichotomy was not restricted to the naphthalene-2-sulfonamide series. Reductive *n*-butylation of the 1-sulfonamide **1** led almost entirely directly to a butylnaphthalene owing to instability of the intermediate dihydrosulfonamide, and from the ^{1}H NMR spectrum of the product it was clear that this product was not pure **43** and that some 2-*n*-butylnaphthalene had also been produced. We then decided to undertake a more systematic study on the regiochemistry of substitution, comparing in the first instance the distribution of the same two products (α- and γ-substitution products) as obtained starting from either the 1-sulfonamide or 2-sulfonamide series, and furthermore studying that distribution as affected by the synthetic path chosen (substrate and route) and by the bulk of the N-alkyl group(s), all while using the same electrophile. As for the latter, allyl bromide was chosen, both because allyl appeared to be a group of "medium" size and also because the regioisomers **47** and **76** were easily distinguishable, and their relative proportions estimable, in the ^{1}H NMR spectrum. However, first and foremost it had to be clarified that these two isomers were not interconvertible at some stage by a sigmatropic rearrangement. That this could be ruled out was clear from the fact that pyrolysis of the crystalline dihydro intermediate **19** gave *exclusively* allylnaphthalene **47** and that of **69** gave *exclusively* **76** and also because corresponding reactions where the alkyl group was *n*-propyl gave similar results.

The results obtained are summarized in Table I. In all cases aromatization was done by vigorous alkaline hydrolysis, for reasons explained above. Conditions a and b have been explained adequately in the Experimental Section. As for c, this involved in situ deprotonation and alkylation (NaH, alkyl halide); and since N-deprotonation and -alkylation would surely occur first, one can assume

Table I. Regiochemistry of Allylation. Dependence on Reaction Conditions and on Size of N-Alkyl Group(s)

entry	substrate	condns[a]	ratio 47:76	overall yield (%)
	A. 7-Methoxy-1-sulfonamide Series			
	(i) Reductive Allylation of Sulfonamides			
1	**4**	a	84:16	73.2
2	**6**	a	87:13	77.5
3	**6**	b	78:22	73.0
4	**8**	a	90:10	80.2
	(ii) via Monoanion from Dihydro-*N*,*N*-dialkylsulfonamides			
5	**12**	c	91.5:8.5	65.5
6	**14**	c	92.5:7.5	77.5
7	**16**	c	96:4	65.7
	(iii) via Dianion from Dihydro-*N*-alkylsulfonamide			
8	**14**	d	44:51	56.0
9	**16**	d	53:47	39.7
	B. 6-Methoxy-2-sulfonamide Series			
	(i) Reductive Allylation of Sulfonamides			
10	**56**	a	76:24	35.5
11	**58**	a	79:21	38.5
	(ii) via Monoanion from Dihydro-*N*,*N*-dialkylsulfonamides			
12	**62**	c	25:75	68.0
13	**64**	c	23:77	59.6
14	**63**	c	28:72	74.0
15	**65**	c	27:73	62.9

[a] Conditions (see also Experimental Section): (a) (1) *n*-BuLi/THF, (2) Li/NH_3/THF/−60 °C, CH_2=$CHCH_2Br$, (3) NaOH/EtOH/H_2O/reflux, (4) distil neutral fraction; (b) (1) NaH/THF, (2) Na/NH_3/THF/−60 °C, CH_2=$CHCH_2Br$, (3) and (4) as above; (c) (1) DMF/NaH (excess)/CH_2=$CHCH_2Br$ (excess), −35 °C to rt, then (3) and (4) as above; (d) (1) *n*-BuLi (2.4 equiv)/THF (2.4 equiv)/TMEDA/−70 °C, CH_2=$CHCH_2Br$, to rt, then (3) and (4) as above.

Figure 2. Dihydronaphthalene-1- and -2-sulfonamide dianions.

that the subsequent C-alkylation is on a hybrid monoanion, no matter whether the original substrate is a dihydro-*N*-alkyl- (entries 5, 6, 7, 12, 13) or *N*,*N*-dialkylsulfonamide (entries 14, 15). That this assumption is correct is suggested by comparison of entries 12 and 13 with entries 14 and 15. What we find is that these reaction conditions afforded even higher regiospecificity in the 1-sulfonamide series than that obtained by reductive alkylation, and the greatest extent of α- versus γ-alkylation in the 2-sulfonamide series, irrespective of the nature of the N-alkyl group(s). Conditions d were designed to ensure immediate conversion of the substrate to a dianionic species (Figures 2a,b) (apparently more stable than a monoanionic one), so that subsequent alkylation would occur first on the more highly basic C-anion. These conditions were tried on two dihydro-1-sulfonamides with bulky N-alkyl groups, and the results (entries 8, 9) indicated a clear tendency contrary to that experienced with the corresponding compounds on reductive alkylation (entries 2 and 4), in that the extent of γ-substitution was increased considerably in these 1-sulfonamide derivatives. Here another important factor would appear to be the greater extent of charge separation in the N,γ-dianion. We have recently augmented these two possible factors by using a bulky electrophile in a new approach[33] to the racemate of the important drug naproxen **88**, the regioisomer of carboxylic acid **87**.

However, this cannot be the whole story. The reductive alkylation, with lithium in liquid ammonia and an alkyl-

(33) Loewenthal, H. J. E. *J. Chem. Soc., Chem. Commun.* **1990**, 768.

ating agent, must involve the same dianion (Figure 2b). Yet the fact is that reductive alkylation of sulfonamide 8, with its bulky *N*-1,1,3,3-tetramethylbutyl group was found, if anything, to be even more α-regiospecific (entry 4) than in the case of sulfonamides 4 and 6. Evidently, an additional effect that must be taken into account is that of the reaction medium, i.e., ion–solvent interaction which of course is vastly different in the two conditions a and d.

The problem of α- versus γ-regiospecifity has been encountered in some recent work on the alkylation of α,β-unsaturated carboxamides, notably in the work of Snieckus,[34] of Beak,[35] and of Schultz[36] and their co-workers. There also we find indications that with increasing bulk of alkylating agent (from methyl to allyl to dimethylallyl) the amount of γ-alkylation increases, and also that this is the case when comparing alkylation of a monoanion from an *N,N*-dialkylcarboxamide with that on a dianion from an *N*-alkylcarboxamide. Furthermore, considerable differences in α- against γ-regioselectivity were found on comparing reductive methylation of an aromatic carboxamide with methylation of the corresponding dihydro enolate.[36] The extent of γ-alkylation has also been found to increase considerably on substituting copper for lithium as the countercation.[34] Our attempts to do the same with the unsaturated sulfonamide systems mentioned have so far been unsuccessful. It does seem likely, however, that studying in a systematic way the effect of bulky groups on nitrogen in unsaturated carboxamides (or of the bulk of the ester group in α,β-unsaturated esters) together with that of varying the bulk of the electrophile would also contribute to an increase in γ-substitution in these unsaturated carbonyl system where that happens to be the object.

Conclusions

We have demonstrated the feasibility of using the sulfonamide group in naphthalenes as a key auxiliary in introducing substituents into that aromatic system by nucleophilic substitution methods, via the dihydronaphthalene sulfonamide obtained by metal–ammonia reduction, and have studied the effect of certain other substituents on this synthetic scheme. In all these reactions the unique resistance of the strongly electron-withdrawing sulfonamide group to attack by nucleophiles has been of special advantage. So far this approach has been found suitable only for purely substitution types of reactions. The reaction of the dihydrosulfonamide mono- and dicarbanions described above with a number of carbonyl compounds has been found to lead to net dehydrogenation to the aromatic sulfonamide, apparently via internal proton transfer to oxygen in the initial adduct. The metal–ammonia reduction has given disappointing results with benzenesulfonamides and also with anthracenesulfonamides. In the former, the strong benzylic stabilization of the intermediate carbanion present in dihydronaphthalenes is absent except in very special cases; in the latter the initial step was found to be reduction to a 9,10-dihydroanthracene containing two isolated benzene systems to which the same limitations apply. However, we have had encouraging results with certain biphenyl derivatives which open up some interesting synthetic vistas.

The overall scope of our approach is widened by the fact that sulfonamide groups, in naphthalene or elsewhere, can be introduced by methods other than beginning with sulfonation. The starting point can be a halogen or a nitro group. Thus, aryl(and also alkyl)lithium compounds or Grignard reagents can be made to react with sulfur dioxide to give sulfinate salts which can be oxidatively halogenated (e.g., with sulfuryl chloride) to yield sulfonyl chlorides.[37] Also, aromatic diazonium ions can be made to react in many cases with sulfur dioxide and cupric chloride to give sulfonyl chlorides directly.[38]

In organic sulfur chemistry, sulfides, sulfoxides, and sulfones have been among the most important auxiliary groups for C–C bond formation used in synthetic work in recent years, with almost total disregard of sulfonic acid derivatives. We are hopeful that the work here described will contribute to a change in this situation.

Experimental Section

General. All reactions were carried out under argon, and prior to all reactions carried out under anhydrous conditions the assembled glassware was flamed out while being evacuated. For sources of starting naphthalenesulfonic acids see Acknowledgment. *n*-Butyllithium in cyclohexane was obtained from Metallgesellschaft AG; its concentration was continually monitored by effectual titration against pure substrates (see below). Anhydrous THF was added to the dry reaction vessel against an argon stream by passing through specially activated alumina.[39] Other solvents were dried by distillation from CaH_2 and storage over specially activated (300 °C at 0.05 mmHg) molecular sieves 4A. TLC was done on Merck 60 F-254 silica plates using ethyl acetate–cyclohexane mixtures for development. Nominal and high-resolution mass spectra were measured on a Finnegan MAT 711 instrument (Data System SS 300) and desorption chemical ionization mass spectra (DCI) on a Finnegan TSQ 70B instrument with isobutane as reagent gas (base peaks underlined and only peaks of intensity >10% of base peak given except for molecular peaks). IR spectra were determined in $CHCl_3$; NMR spectra (^{13}C and ^1H) were measured on 400- or 200-MHz Bruker instruments in $CDCl_3$, unless otherwise indicated.

Preparation of Methoxynaphthalenesulfonyl Chlorides. The following procedure for the preparation of **55** was typical for all hydroxynaphthalenesulfonyl chlorides and was based on procedures reported by Knuesli[40] and by Bosshard.[41] Sodium 6-hydroxynaphthalene-2-sulfonate (technical, 60 g) was suspended in water (600 mL), and NaOH (21 g) was added with stirring. To the solution was added dropwise dimethyl sulfate (51 mL) during 1 h, maintaining the temperature at 50–55 °C. NaCl (100 g) was added, and after stirring to dissolve the latter the methoxynaphthalene sulfonate was filtered off, washed with concd NaCl solution and then with toluene (to remove 2-methoxynaphthalene formed in the reaction), pressed dry, and dried overnight at 80 °C. A small additional amount of this product could usually be obtained by further saturating the filtrate with NaCl and stirring overnight. Of the total product (51.4 g, negative $FeCl_3$ test in

(34) Majewski, M.; Mpango, G. B.; Thomas, M. T.; Wu, A.; Snieckus, V. *J. Org. Chem.* **1981**, *46*, 2029.
(35) Beak, P.; Kempf, D. J.; Wilson, R. D. *J. Am. Chem. Soc.* **1985**, *107*, 4745.
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dilute acetic acid) ca. half was suspended in dry dimethylformamide (DMF) (50 mL), and with stirring thionyl chloride (25 mL) was added dropwise, together with the rest of the methoxy salt in portions, keeping the internal temperature below 15 °C by external cooling. After the mixture was stirred for another 3 h at room temperature, ice and water were added, and the product was removed by filtration, washed with ice–water, and dissolved in dichloromethane (ca. 100 mL). The water layer was removed, and the dried (Na_2SO_4) organic extract passed through a short column of Florisil. Recrystallization of the crude product, obtained by solvent removal, from *tert*-butyl methyl ether (TBME), finally at 0 °C, gave **6-methoxynaphthalene-2-sulfonyl chloride (55)** (25.0 g, 40% overall yield assuming 100% purity for starting material), mp 97–97.5 °C (lit.[40] mp 93 °C): ^{1}H NMR (200 MHz) δ 3.96 (s, 3 H), 7.27 (m, 2 H), 7.69 (m, 3 H), 8.47 (s, 1 H). Overall yields in other cases appeared to be of the same order; however, the purity of starting material salts was not ascertained and appeared to vary from batch to batch.

Preparation of *N*-Alkylnaphthalenesulfonamides. General Procedure. The solid sulfonyl chloride was added in portions to a vigorously stirred two-phase mixture of a solution of the corresponding primary amine (1.3 equiv) in dichloromethane (or $CHCl_3$ in the case of products of mp above 150 °C) (10–20 mL/g of chloride) and of 2 N NaOH (1.5 equiv) (in the case of *N*-methyl and *N,N*-dimethylamides 5 equiv of the aqueous solutions of the amines was used instead of the 2 N NaOH), starting at 0–10 °C and raising to rt during 3–5 h. The organic phase was separated, washed with water and dilute HCl, dried (Na_2SO_4), and passed through a short column of Florisil (1 g/g of product), the solvent removed, and the residue recrystallized, usually from $CHCl_3$–cyclohexane. The yields throughout were in the range 85–95%.

7-Methoxy-*N*-methylnaphthalene-1-sulfonamide (4): mp 183.5–139 °C, IR 3380, 2940, 1630, 1600, 1465, 1330, 1160 cm^{-1}; ^{1}H NMR δ (400 MHz) 2.58 (s, 3 H), 3.95 (s, 3 H), 4.56 (s, 1 H), 7.25–7.40 (m, 2 H), 7.85 (d, 1 H), 8.00 (d, 2 H), 8.25 (d, 1 H); ^{13}C NMR δ 159.35, 133.85, 131.75, 130.6, 130.5, 128.6, 121.35, 119.5, 103.2, 55.5, 28.45; nominal mass spectrum *m/z* 252 (M + 1$^+$), 251 (M$^+$), 173, 158, 157, 142, 128, 127, 115, 114, 113; exact mass *m/z* calcd for $C_{12}H_{13}NO_3S^+$ 251.0616, found 251.0625.

7-Methoxy-*N*-(1′,1′-dimethylethyl)naphthalene-1-sulfonamide (6): mp 178–178.5 °C; ^{1}H NMR (200 MHz) δ 1.17 (s, 9 H), 3.94 (s, 3 H), 4.93 (s, 1 H), 7.24–7.36 (m, 2 H), 7.80 (d, 1 H), 7.80 (d, 2 H), 9.25 (d, 1 H); ^{13}C NMR (50 MHz) δ 159.25, 136.4, 133.65, 130.5, 129.85, 129.75, 121.9, 119.45, 103.7, 55.85, 55.0, 30.1, 29.7; nominal mass spectrum *m/z* 294 (M + 1$^+$), 293 (M$^+$), 279, 278, 237, 222, 221, 173, 158, 157, 142, 139, 128, 127, 114, 113; exact mass *m/z* calcd for $C_{15}H_{19}NO_3S^+$ 293.1086, found 293.1096.

7-Methoxy-*N*-(1′,1′-dimethylpropyl)naphthalene-1-sulfonamide (7): mp 136.5–137 °C; IR 3380, 2940, 1630, 1465, 1325, 1130 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.73 (t, 3 H), 1.095 (s, 6 H), 1.50 (q, 2 H), 3.92 (s, 3 H), 4.92 (s, 1 H), 7.21–8.27 (m, 6 H); ^{13}C NMR δ 159.15, 136.2, 133.5, 130.4, 129.8, 129.6, 121.4, 103.75, 57.75, 55.6, 35.75, 28.95, 8.1; nominal mass spectrum *m/z* 307 (M$^+$), 279, 278, 221, 173, 158, 157, 142, 139, 114; exact mass *m/z* calcd for $C_{16}H_{21}NO_3S^+$ 307.1242, found 307.1281.

***N*-(1′,1′-Dimethylpropyl)naphthalene-2-sulfonamide (54)**: mp 109–109.5 °C; IR 3380, 2930, 1325, 1150, 1130 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.81 (t, 3 H), 1.14 (s, 6 H), 1.53 (q, 2 H), 4.92 (s, 1 H), 7.59 (m, 2 H), 7.65–7.95 (m, 4 H), 8.45 (s, 1 H); ^{13}C NMR (50 MHz) δ 134.6, 132.2, 129.2, 129.1, 128.5, 127.85, 127.3, 122.65, 57.55, 35.65, 27.1, 8.2: nominal mass spectrum *m/z* 277 (M$^+$), 249, 248, 191, 128, 127, 117; exact mass *m/z* calcd for $C_{15}H_{19}NO_2S^+$ 277.1136, found 277.1181.

6-Methoxy-*N*-methylnaphthalene-2-sulfonamide (56): mp 139.5–140 °C; IR 3400, 1635, 1395, 1335, 1160 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.65 (d, 3 H), 3.93 (s, 3 H), 4.60 (d, 1 H), 7.14–7.25 (m, 2 H), 7.77–7.85 (m, 3 H), 8.33 (s, 1 H); ^{13}C NMR δ 159.5, 133.95, 130.6, 130.5, 129.95, 129.9, 121.8, 119.5, 103.45, 55.55, 29.4; nominal mass spectrum *m/z* 252 (M + 1$^+$), 251 (M+), 221, 173, 158, 157, 142, 114; exact mass *m/z* calcd for $C_{12}H_{113}NO_3S^+$ 251.0616, found 251.0601.

6-Methoxy-*N*-(1′,1′-dimethylethyl)naphthalene-2-sulfonamide (58): mp 114–114.5 °C; IR 3380, 2960, 2940, 1628, 1388, 1325, 1265, 1150, 1000 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.295 (s, 9 H), 4.015 (s, 3 H), 5.05 (s, 1 H), 7.25–7.38 (m, 2 H), 7.85–7.95 (m, 3 H), 8.45 (s, 1 H); ^{13}C NMR (50 MHz) δ 159.8, 138.05, 136.3, 130.65, 137.8, 127.75, 127.55, 123.35, 120.25, 106.0, 55.45, 54.65, 30.2; nominal mass spectrum *m/z* 293 (M$^+$), 279, 278, 221, 173, 157, 127, 114; exact mass *m/z* calcd for $C_{15}H_{19}NO_3S^+$ 293.1085, found 293.1092.

8-Methoxy-*N*-methylnaphthalene-2-sulfonamide (83): mp 115–116 °C; IR 3390, 2935, 2840, 1625, 1578, 1460, 1330, 1160, 1110 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.65 (d, 3 H), 4.00 (s, 3 H), 4.50 (m, 1 H), 6.89 (d, 1 H), 7.42–7.57 (m, 2 H), 7.635–7.915 (m, 2 H), 8.83 (s, 1 H); ^{13}C NMR (100 MHz) δ 156.15, 135.8, 134.65, 129.15, 128.85, 124,35, 123.3, 122.95, 105.2, 55.55, 29.3; mass spectrum (CI) *m/z* 252.2 (M + 1$^+$), 251.1, 250.1, 221.1.

Metal–Ammonia Reduction and Reductive Alkylation of Naphthalenesulfonamides. General Procedure. In a 100-mL three-necked flask with low-temperature thermometer and solid CO_2 condenser leading via a drying tube to an argon trap the sulfonamide (5–10 mmol) was dissolved in anhydrous THF (12–15 mL), and the cooled solution was titrated with *n*-butyllithium in cyclohexane (2.0–2.3 M), keeping the temperature below 15 °C, until a permanent orange to red color was just produced. The solution was cooled to −40 °C, and liquid ammonia (25–30 mL), passed through drying towers containing solid KOH, CaO, and CaH_2 in series, was condensed into the flask. With *N*-methylsulfonamides the *N*-lithio derivative precipitated at this stage but it redissolved in the course of further reaction. Against argon pressure the reaction mixture was cooled to −55 to −65 °C, and with steady magnetic stirring lithium (total of 2.2–2.5 equiv.) was introduced in portions of 5–15 mg, keeping the internal temperature throughout in the above range. An intense color, usually deep orange to dark brown, soon developed. When about half the lithium had been added a conductivity electrode (two 5- × 5-mm Pt electrodes ca. 3 mm apart) was immersed in the reaction mixture; the conductivity at this stage was ca. 3–5 mmho. Further metal additions were made through the thermometer neck; addition of metal just beyond the end point (change to green-black if perceptible) led to a sudden 2- to 5-fold increase in conductivity. At this stage either ammonium chloride (12–15 equiv) was added (reduction) or (reductive alkylation) the respective halide (iodomethane, 2.0 equiv; 3-bromo-1-propene or bromomethylbenzene, 1.5 equiv) was added rapidly dropwise below −50 °C, followed by ammonium chloride addition as above after conductivity had reattained a steady value. The apparatus was then attached to water-pump vacuum and both ammonia and THF were removed, cautiously at first, until the internal temperature had risen to ambient, after which water and dichloromethane were added. The organic layer was separated, dried (Na_2SO_4), and passed through a short column of Florisil (1 g/g of substrate), the solvent removed, and the product recrystallised, usually first from pentane at 0 °C and then from dichloromethane–hexane. When the metal was sodium, then the *N*-sodio derivative was formed with sodium hydride (pentane-washed, 1.2 equiv); the initial and final conductivities were higher in this case. The following products were obtained:

1,4-Dihydro-7-methoxy-*N*-methylnaphthalene-1-sulfonamide (12) from 4: 85% yield, mp 81.5–82 °C; IR 3400, 2940–2900, 1615, 1500, 1325, 1130 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.56 (d, 3 H), 3.45 (m, 2 H), 3.75–3.95 (m, 1 H), 3.83 (s, 3 H), 4.92 (s, 1 H), 6.12 (m, 1 H), 6.37 (m, 1 H), 6.90–7.23 (m, 3 H); ^{13}C NMR (100 MHz) δ 157.85, 133.1, 129.2, 128.3, 128.05, 119.45, 115.1, 114.9, 64.2, 55.4, 30.45, 29.75; nominal mass spectrum *m/z* 253 (M$^+$), 160, 159, 158, 144, 128, 127, 116, 115; exact mass *m/z* calcd for $C_{12}H_{15}NO_3S^+$ 253.0773, found: 253.0780.

1,4-Dihydro-7-methoxy-*N*-(1′,1′-dimethylethyl)naphthalene-1-sulfonamide (14) from 6: 89% yield; mp 151.5–152 °C; IR 3375, 2960–2910, 1610, 1315, 1125 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.21 (s, 9 H), 3.22 (d, 1 H), 3.51 (d, 1 H), 3.75–4.00 (m, 1 H), 3.82 (s, 3 H), 4.83 (s, 1 H), 6.10 (m, 1 H), 6.35 (m, 1 H), 6.82–7.23 (m, 3 H); ^{13}C NMR δ 157.75, 133.3, 129.05, 128.8, 128.55, 119.8, 115.2, 114.95, 66.4, 55.45, 55.35, 30.4, 29.55; nominal mass spectrum *m/z* 295 (M$^+$), 160, 159, 158, 144, 115; exact mass *m/z* calcd for $C_{15}H_{21}NO_3S^+$ 295.1242, found 295.1252. When this reduction was done using NaH and Na metal the yield fell to 55%.

1,4-Dihydro-7-methoxy-*N*-(1′,1′-dimethylpropyl)naphthalene-1-sulfonamide (15) from 7: 86.6% yield, mp

98.5–99 °C; IR 3380, 2950, 1612, 1500, 1315, 1125 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.84 (t, 3 H), 1.15 (split s, 6 H), 1.54 (m, 2 H), 3.47 (ABq, 2 H), 3.79 (s, 3 H), 3.84 (s, 1 H)), 4.81 (br s, 1 H), 6.12 (m, 1 H), 6.40 (m, 1 H), 6.85–7.28 (m, 3 H); ^{13}C NMR δ 158.0, 133.65, 129.05, 119.9, 115.25, 115.05, 66.6, 55.4, 36.05, 29.35, 27.3, 27.05, 8.35; nominal mass spectrum m/z 309 (M^+), 159, 158, 144, 128, 127, 115; exact mass m/z calcd for $C_{16}H_{23}NO_3S^+$ 309.1399, found 309.1398.

1,4-Dihydro-7-methoxy-1-methyl-*N*-(1′,1′-dimethylethyl)-naphthalene-1-sulfonamide (17) from 6: 58% yield, mp 136–136.5 °C dec; ^{1}H NMR (400 MHz) δ 1.05 (s, 9 H), 1.90 (s, 3 H), 3.45 (m, 3 H), 3.80 (s, 3 H), 5.85 (m, 1 H), 6.28 (m, 1 H), 6.85–7.22 (m, 3 H); ^{13}C NMR δ 158.1, 133.8, 131.0, 128.9, 127.2, 114.8, 114.0, 56.0, 55.5, 30.3, 30.2, 28.0, 23.6; nominal mass spectrum m/z 309 (M^+), 189, 174, 173, 172, 171, 159, 158, 157, 129, 128; exact mass m/z calcd for $C_{16}H_{23}NO_3S^+$ 309.1397, found 309.1384. The mother liquor of this product contained almost exclusively **44** (see below).

1,4-Dihydro-*N*-(1′,1′-dimethylethyl)-7-methoxy-1-(2′-propenyl)naphthalene-1-sulfonamide (19) from 6: 61.5% yield, mp 129–130 °C, dec 132 °C; IR 3365, 2960–2900, 1612, 1500, 1312, 1135 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.03 (s, 9 H), 2.94 (m, 1 H), 3.30–3.55 (m, 4 H), 3.79 (s, 3 H), 5.00 (m, 2 H), 5.37 (m, 1 H), 5.80 (d, 1 H), 6.32 (m, 1 H), 6.82 (dd, 1 H), 7.08 (d, 1 H), 7.20 (d, 1 H); ^{13}C NMR (100 MHz) δ 157.9, 132.8, 131.0, 129.0, 128.7, 125.5, 118.8, 114.8, 113.9, 76.65, 56.0, 55.4, 39.1, 30.3, 30.0, 27.6; nominal mass spectrum m/z 200, 199, 198, 183, 171, 167, 165, 158, 155, 153, 152, 128, 115, no molecular peak.

Dihydro-6-methoxy-*N*-methylnaphthalene-2-sulfonamide, mixture of double bond isomers **62** from **56**: 92% yield, mp 82–95 °C; one spot on TLC unresolved by four developments; IR 3400, 1610, 1500, 1320, 1128 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.50 and 2.51 (2d, ratio ca. 69:31), 3.77 (s).

1,4-Dihydro-*N*-(1′,1′-dimethylpropyl)-1-(2′-propenyl)-naphthalene-3-sulfonamide (71) from 54: 49% yield, mp 74.5–75.5 °C; IR 3380, 2930, 1640, 1325, 1145 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.15 (t, 3 H), 1.515 (s, 6 H), 1.86 (q, 2 H), 2.60–2.90 (m, 2 H), 3.97 (br s, 3 H), 4.59 (s, 1 H), 5.21–5.32 (m, 2 H), 5.83–6.08 (m, 1 H), 7.24 (s, 1 H), 7.48–7.59 (m, 4 H); ^{13}C NMR (50 MHz) 136.5, 135.6, 134.45, 132.45, 128.45, 127.75, 126.75, 126.6, 117.9, 57.35, 41.25, 40.5, 35.75, 28.15, 27.05, 26.7, 8.3; nominal mass spectrum m/z 290, 278, 248, 215, 214, 191, 169, 144, 141, 129, 128, 127, 115, no molecular peak.

1,4-Dihydro-7-methoxy-1-methyl-*N*-(1′,1′-dimethylethyl)-naphthalene-3-sulfonamide (72) from 58: 71% yield, mp 139.5–140 °C, IR 3380, 2960–2940, 1612, 1500, 1320, 1145 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.29 (s, 9 H), 1.37 (d, 3 H, collapses to s on irradiation at 3.65) 3.65 (s, 3 H), 3.79 (s, 3 H), 4.39 (s, 1 H), 6.90–7.25 (m, 4 H); nominal mass spectrum m/z 309 (M^+), 238, 173, 172, 158, 157, 129, 115; exact mass m/z calcd for $C_{16}H_{23}NO_3S^+$ 309.1398, found 309.1463.

1,4-Dihydro-7-methoxy-*N*-(1′,1′-dimethylethyl)-1-(2′-propenyl)naphthalene-3-sulfonamide (73) from 58: 64% yield, mp 89.5–90 °C; IR 3380, 2960–2910, 1612, 1500, 1320, 1145 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.30 (s, 9 H), 2.46 (m, 1 H), 2.57 (m, 1 H), 3.58–3.75 (m, 2 H), 3.80 (s, 3 H), 4.45 (s, 1 H), 5.04 (m, 2 H), 5.70 (m, 1 H), 6.75–7.12 (m, 4 H); ^{13}C NMR (100 MHz) δ 158.35, 139.45, 136.7, 136.25, 134.4, 129.3, 124.45, 117.9, 112.75, 112.65, 55.3, 54.4, 41.25, 40.7, 30.1, 27.45; nominal mass spectrum m/z 335 (M^+), 294, 293, 230, 174, 159, 158, 115; exact mass m/z calcd for $C_{18}H_{25}NO_3S^+$ 335.1555, found 335.1568.

Further N-Methylation of Dihydro-*N*-alkylnaphthalenesulfonamides. General Procedure. A solution of the dihydrosulfonamide in anhydrous THF (5–7 mL/mmol), cooled to −50 °C (some *N*-methylsulfonamides crystallized out but redissolved on further reaction), was titrated with *n*-butyllithium/cyclohexane (2.1–2.25 M) until a permanent color (usually orange) just persisted, keeping the internal temperature at −45 to −40 °C. After the solution was cooled to −60 °C iodomethane (1.8 equiv) was added rapidly with stirring, after which the solution was allowed immediately to reach rt and was then warmed to 35–40 °C for 20 min. The THF was removed in vacuo, water was added, and the product was isolated with CH_2Cl_2 and recrystallized, usually from CH_2Cl_2–hexane. The following products were obtained.

1,4-Dihydro-7-methoxy-*N*,*N*-dimethylnaphthalene-1-sulfonamide (13) from 12: 55.5%, mp 135.5–136 °C; IR 2940, 1615, 1500, 1330, 1128 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.65 (s, 6 H), 3.43 (m, 2 H), 3.81 (s, 3 H), 4.93 (br s, 1 H), 6.10 (m, 1 H), 6.32 (m, 1 H), 6.87–7.10 (m, 3 H); ^{13}C NMR δ 157.9, 132.5, 129.2, 128.4, 128.0, 119.9, 115.3, 115.0, 64.6, 55.4, 38.3, 29.8; nominal mass spectrum m/z 267 (M^+), 169, 160, 159, 158, 145, 144, 143, 129, 128, 127, 116, 115; exact mass m/z calcd for $C_{13}H_{17}NO_3S^+$ 267.0929, found 267.0895.

1,4-Dihydro-7-methoxy-*N*-(1′,1′-dimethylethyl)-*N*-methylnaphthalene-1-sulfonamide (21) from 14: 80.9% yield, mp 115.5–116 °C; IR 2940, 2840, 1615, 1500, 1465, 1370, 1325 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.40 (s, 9 H), 2.67 (s, 3 H), 3.35 (dd, 1 H), 3.56 (d, 1 H), 3.82 (s, 3 H), 4.79 (br s, 1 H), 6.05 (m, 1 H), 6.38 (m, 1 H), 6.85–7.25 (m, 3 H); ^{13}C NMR δ 157.7, 133.7, 129.2, 128.95, 119.95, 115.35, 114.9, 67.2, 59.05, 55.45, 33.95, 30.05, 29.65, 29.25; nominal mass spectrum m/z 309 (M^+), 159, 158, 144, 128, 115; exact mass m/z calcd for $C_{16}H_{23}NO_3S^+$ 309.1398, found 309.1378.

1,2-Dihydro-6-methoxy-*N*,*N*-dimethylnaphthalene-2-sulfonamide (63) from 62: 84% yield, mp (recryst) 120–120.5 °C; IR 2940, 2840, 1605, 1575, 1500, 1325, 1260, 1130 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.57 (s, 6 H), 3.18 (m, 1 H), 3.37 (m, 1 H), 3.80 (s, 3 H), 4.03 (m, 1 H), 6.06 (m, 1 H), 6.64–7.10 (m, 4 H); ^{13}C NMR δ 158.8, 132.9, 132.8, 128.7, 124.0, 121.0, 113.5, 112.7, 59.2, 55.3, 38.0, 27.8; nominal mass spectrum m/z 267 (M^+), 160, 159, 158, 144, 128, 127, 115; exact mass m/z calculated for $C_{13}H_{17}NO_3S^+$ 267.0929, found 267.0932. Material formed in other runs with lower mp (112–118 °C) was just as satisfactory for further reaction.

1,2-Dihydro-8-methoxy-*N*,*N*-dimethylnaphthalene-2-sulfonamide (86) (directly from **83** by methylation of the crude Li/NH_3 reduction product according to the general procedure): 61% overall yield of double-bond isomer mixture homogeneous by TLC and suitable for further reaction; mp of **86** after recrystallization 90–91 °C; ^{1}H NMR (400 MHz) δ 2.57 (spl s, 6 H), 2.99 (q, 1 H), 3.63–3.69 (2d, 1 H), 3.82 (s, 3 H), 4.05 (m, 1 H), 6.04 (m, 1 H), 6.65 (d, 1 H), 6.74–7.24 (m, 3 H); ^{13}C NMR (100 MHz) δ 156.3, 132.75, 132.6, 127.55, 120.45, 119.75, 119.5, 110.85, 58.55, 55.5, 37.9, 21.3; mass spectrum (CI) 268.1 ($M + 1^+$), 266.1, 160.1.

Preparation of Substituted Naphthalenes. 7-Methoxy-1-methylnaphthalene (44). Method a, from 17. The latter sulfonamide (0.65 g) was heated at 150–170 °C (25 mmHg), and then the residue was distilled at 0.1 mmHg (Kugelrohr ot 100 °C) to give **44** (0.28 g), mp 45.5–46.5 °C (lit.[50] mp 47–49 °C); ^{1}H NMR (400 MHz) δ 2.65 (s, 3 H), 3.95 (s, 3 H), 7.15–7.72 (total 6 H); in good agreement with the reported spectrum.[50] **Method b, Directly from 4.** The crude reductive methylation product obtained from **4**, as described by the preparation of **17**, was heated and then distilled as described in **a**, to give crude **44** (^{1}H NMR spectrum identical to product from **method a**) in 83% overall yield (no trace of peak at δ 2.49 in the ^{1}H NMR spectrum due to **74**).

1-Ethyl-7-methoxynaphthalene (45). Dihydrosulfonamide **15** (0.706 g) and iodoethane (0.55 mL, 3 equiv) were added to a suspension of sodium hydride (from 0.30 g of pentane-washed 49% oil suspension, 2.7 equiv) in dry DMF (2.5 mL) at −35 °C with stirring which was continued while the reaction mixture slowly warmed to rt overnight. Water was added, and the product which was isolated with CH_2Cl_2 was heated at 180 °C (20 mmHg) for 10 min. The residue in diethyl ether was passed through a short column of Al_2O_3 and the eluate distilled at 110–120 °C (Kugelrohr ot) (0.08 mmHg) to give **45** (0.39 g, 92% overall yield): ^{1}H NMR (200 MHz) δ 1.33 (t, 3 H), 3.00 (q, 2 H), 3.88 (s, 3 H), 7.06–7.72 (total 6 H), in excellent agreement with the published spectrum[50] and with no trace of peak at δ 3.10–3.45 due to 2-ethyl-6-methoxynaphthalene.

7-Methoxy-1-(2′-propenyl)naphthalene (47). Dihydrosulfonamide **19** (0.74 g) was heated and distilled as described for the preparation of **46** under **method a** to give **47**, 0.35 g (80% yield), bp 110 °C (Kugelrohr ot) (0.05 mmHg): IR 2955, 2900, 2835, 1632, 1605, 14580, 1385, 1260, 1120 cm^{-1}; ^{1}H NMR (400

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MHz) δ 3.89 (d, 2 H), 4.02 (s, 3 H), 5.22 (d, 2 H), 6.22 (m, 1 H), 7.25–7.85 (total 6 H); ^{13}C NMR (100 MHz) δ 157.55, 136.8, 134.65, 133.05, 130.1, 129.25, 126.75, 126.65, 123.3, 117.9, 116.05, 102.85, 55.2, 37.65; nominal mass spectrum m/z 199 ($M + 1^+$), 198 (M^+), 183, 171, 167, 165, 155, 153, 152, 128; exact mass m/z calcd for $C_{14}H_{14}O^+$ 198.1044, found 198.1050.

2-Methoxy-6-(2′-propenyl)naphthalene (76). Dihydrosulfonamide **63** (1.473 g) was deprotonated and alkylated as above for **75** but using 3-bromo-1-propene (1.0 mL) after which the stirred reaction mixture was immediately allowed to reach rt. Removal of THF, isolation with CH_2Cl_2, and 2 recrystallizations (diisopropyl ether) gave **1,2-dihydro-6-methoxy-*N*,*N*-dimethyl-2-(2′-propenyl)naphthalene-2-sulfonamide (69)**: 0.86 g, mp 99.5–100 °C dec from 150 °C; IR 2930, 1238, 1600, 1572, 1315, 1135 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.43 (s, 6 H), 2.5–3.3 (m, total 4 H), 3.765 (s, 3 H), 5.065–5.145 (m, total 2 H), 5.625–5.825 (m, total 2 H), 6.60–7.05 (total 4 H); ^{13}C NMR (100 MHz) δ 158.55, 132.65, 132.25, 128.55, 126.15, 124.7, 119.4, 113.25, 112.7, 67.2, 55.35, 40.7, 38.45, 31.9. This product (0.50 g) was heated at 170 °C (20 mmHg) for 10 min and then passed in TBME through Florisil and distilled at 120–125 °C (Kugelrohr ot) (0.08 mmHg) to give **76** (0.28 g, 86.6%) which immediately crystallized: mp 48–48.5 °C; IR 2935, 2900, 2840, 1632, 1608, 1480, 1388, 1260, 1120 cm^{-1}; ^{1}H NMR (400 MHz) δ 3.505 (d, 2 H), 3.90 (s, 3 H), 5.09–5.16 (m, total 2 H), 5.95–6.11 (m, total 1 H), 7.095–7.67 (total 6 H); ^{13}C NMR (50 MHz) δ 157.3, 137.55, 135.2, 133.15, 129.15, 128.9, 127.85, 126.6, 126.5, 118.65, 115.8, 105.75, 75.55, 55.25, 40.15; nominal mass spectrum m/z 198 (M^+), 197, 183, 171, 167, 165, 155, 152, 128; exact mass m/z calcd for $C_{14}H_{14}O^+$ 198.1045, found 198.1015. The mother liquors of sulfonamide **69** were hydrolyzed under reflux with NaOH in EtOH–H_2O as described for the more polar fractions of the chromatogram of **75** (see above) and the neutral product distilled; it was found to contain isomer **47** by ^{1}H NMR. The amount and composition (relative integration of the ^{1}H NMR doublets at δ 3.505 and 3.89, respectively) established that the total yield in the allylation of **63** was 87.6% and the ratio of **76** to **47** was 82:18, respectively.

Methyl 7-Methoxynaphthalene-1-carboxylate (49). To dihydrosulfonamide **13** (1.33 g) in anhydrous THF (12 mL) at −40 °C was added *n*-butyllithium in cyclohexane (2.17 M, 2.41 mL) with stirring, followed after cooling to −65 °C by addition of methyl chloroformate (redistilled, 0.64 mL). The stirred solution was allowed to reach rt during 3 h and then warmed to 35 °C for 20 min. Removal of THF, isolation with CH_2Cl_2, and recrystallization (CH_2Cl_2–hexane) gave **methyl 1,4-dihydro-1-(*N*,*N*-dimethylsulfamoyl)-7-methoxynaphthalene-1-carboxylate (22)** (1.32 g (81.5% yield): mp 126–127 °C dec 133 °C; IR 2970, 1743, 1615, 1335, 1140 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.59 (s, 6 H), 3.50 (s, 2 H), 3.79 (s, 3 H), 3.81 (s, 3 H), 6.18 (d, 1 H), 6.38 (m, 1 H), 6.91–7.37 (total 3 H); ^{13}C NMR (100 MHz) δ 168.2, 157.7, 131.5, 129.4, 127.7, 127.1, 121.2, 116.0, 114.8, 75.35, 55.45, 53.35, 39.2, 29.45; mass spectrum (CI): 326.2 ($M + 1^+$), 308.1, 217.1, 216.1, 185.0. Heating this product (0.30 g) at 155 °C (20 mmHg) and then distilling (150 °C (Kugelrohr ot) (0.08 mmHg) gave the methyl ester **49** (0.197 g), identical (^{1}H NMR spectrum) with the product obtained as reported by a different route.[54] Similar results and yields were obtained via methoxycarbonylation of **21**, with the intermediacy of **methyl 1,4-dihydro-1-[*N*-(1′,1′-dimethylethyl)-*N*-methylsulfamoyl]-7-methoxynaphthalene-1-carboxylate (23)**: mp 90.0–90.5 °C; IR 2950, 1740, 1610, 1330, 1135 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.15 (s, 9 H), 2.60 (s, 3 H), 3.40 (br s, 2 H), 3.72 (s, 6 H), 6.12–6.35 (m, 2 H), 6.67–7.40 (m, 3 H); ^{13}C NMR δ 168.15, 157.8, 131.25, 129.15, 128.0, 127.6, 122.0, 116.1, 115.2, 76.55, 60.75, 55.45, 53.3, 35.4, 29.45, 29.2.

Methyl 8-Methoxynaphthalene-2-carboxylate (85). The dihydrosulfonamide **86** (double-bond isomer mixture, 1.47 g) was deprotonated with *n*-butyllithium and methoxycarbonylated, as described in the previous examples. The crude product (1.94 g) was heated in diglyme (3 mL) to 150–165 °C for 20 min, water was added, and the crude pyrolysis product obtained after the usual workup chromatographed (SiO_2, 15 g). The first fractions, eluted with CH_2Cl_2–hexane (1:10 to 1:5), homogenous by TLC were distilled to give **85** (0.30 g, 26% overall yield), mp 57–58 °C: IR 2940, 2840, 1710, 1628, 1575, 1460, 1370, 1280, 1118 cm^{-1}; ^{1}H NMR (400 MHz) δ 3.95 (s, 3 H), 3.995 (s, 3 H), 6.82 (d, 1 H), 7.395–7.48 (m, 2 H), 7.79 (d, 1 H), 8.04 (d, 1 H), 8.995 (s, 1 H); ^{13}C NMR (100 MHz) δ 167.35, 156.4, 136.55, 128.55, 127.6, 126.6, 125.85, 125.4, 124.75, 119.85, 104.45, 55.55, 52.1; nominal mass spectrum m/z 217, 216 (M^+), 185, 173, 127, 114; exact mass m/z calcd for $C_{13}H_{12}O_3^+$ 216.0787, found 216.0798. The more polar fractions from the above chromatogram, eluted with $CHCl_3$, were combined and hydrolyzed with NaOH in EtOH–H_2O as described in foregoing examples, the acidic portion obtained from this was sublimed and esterified with diazomethane, and the ester was redistilled. The crystalline product (0.10 g) was identified (^{1}H NMR) as the ester **51**, containing only 2.4% of **85** as shown by detailed analysis of the aromatic portion of the ^{1}H NMR spectrum (intensity of doublets at δ 8.42 and 8.04, respectively).

2-(7′-Methoxy-1′-naphthyl)propanoic Acid (87). Dihydrosulfonamide **63** (1.00 g) was deprotonated in THF under conditions described in foregoing examples, and the anion was alkylated with methyl α-bromopropionate (0.67 mL, 1.5 equiv). The product obtained by the usual workup was heated in diglyme to 160–165 °C and then chromatographed. The initially eluted fractions (0.27 g) showed no ester carbonyl band in the IR spectrum and gave no acidic fraction on alkaline hydrolysis. The more polar, $CHCl_3$-eluted fractions (0.60 g) were hydrolyzed with NaOH in EtOH/H_2O under reflux for 3 h, and after removal of EtOH and extraction of neutral material, acidification gave material which was distilled (160–180 °C (Kugelrohr ot) (0.05 mmHg)) and then crystallized from CH_2Cl_2–hexane to give acid **87**: 0.20 g, mp 96.0–96.5 °C; IR 3500–2930, 2830, 1710, 1628, 1603, 1450, 1250–1180 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.76 (d, 3 H), 3.86 (s, 3 H), 4.40 (t, 1 H), 7.10–7.80 (m, total 6 H); ^{13}C NMR δ 180.75, 158.2, 134.55, 132.6, 130.5, 129.5, 127.8, 125.25, 123.3, 118.25, 102.05, 55.3, 41.65, 17.4; nominal mass spectrum m/z 231, 230 (M^+), 186, 185, 170, 154, 153, 141, 115; exact mass m/z calculated for $C_{14}H_{14}O_3^+$ 230.0943, found 230.0969.

3-(2′-Methyl-2′-propenyl)-1-(2′-propenyl)naphthalene (77). The dihydrosulfonamide **71** (0.97 g) and 3-bromo-2-methyl-1-propene (1.44 g, 3.5 equiv) were added to a stirred suspension of sodium hydride (from 0.52 g of pentane-washed 49% suspension) in anhydrous DMF (3.5 mL) at −35 °C (acetonitrile/solid CO_2). With stirring the mixture attained rt overnight, and then water was added and the product, isolated with CH_2Cl_2, heated to 180 °C/20 min. Passage in TBME through a SiO_2 column and distillation gave **77**: bp 120–130 °C (Kugelrohr ot) (0.05 mmHg); IR 2810, 1640, 1605, 1440, 1380 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.71 (s, 3 H), 3.455 (s, 2 H), 3.615 (d, 2 H), 4.82 (d, 2 H), 5.035–5.125 (m, 2 H), 6.04 (m, 1 H), 7.20–8.01 (m, total 6 H); ^{13}C NMR (50 MHz) δ 144.95, 137.05, 136.95, 136.05, 134.1, 130.75, 128.3, 128.1, 126.15, 125.55, 125.15, 123.7, 116.0, 112.15, 44.75, 37.2, 22.1; nominal mass spectrum m/z 223, 222 (M^+), 207, 182, 180, 179, 178, 168, 167, 166, 165, 153, 152, 141, 115; exact mass m/z calcd for $C_{17}H_{18}^+$ 222.1409, found 222.1402.

7-Methoxy-1-methyl-3-(2′-propenyl)naphthalene (78). Dihydrosulfonamide **72** (0.80 g) and 3-bromo-1-propene (0.66 mL) were added to a stirred suspension of NaH (from 0.38 g of pentane-washed 49% suspension) in anhydrous DMF at −50 °C and the suspension left to reach rt overnight. The product obtained by adding water and extractive workup was heated at 150 °C/20 min and then distilled at 160 °C(ot) (0.05 mmHg) to give **78**: 0.36 g (65.5%); IR 2930, 2835, 1608, 1500, 1462, 1432, 1255–1195 cm^{-1}, ^{1}H NMR (400 MHz) δ 2.62 (s, 3 H), 3.47 (d, 2 H), 3.93 (s, 3 H), 5.10 (t, 2 H), 6.02 (m, 1 H), 7.12–7.67 (total 5 H); ^{13}C NMR (100 MHz) δ 157.3, 137.7, 134.8, 133.0, 132.3, 129.6, 129.25, 128.6, 124.9, 117.9, 115.7, 102.9, 55.3, 40.1, 19.4; nominal mass spectrum m/z 213, 212 (M^+), 211, 197, 172, 165; exact mass m/z calculated for $C_{15}H_{16}O^+$ 212.1201, found 212.1211.

6-Methoxy-4-(2′-propenyl)naphthalene-2-carboxylic Acid (79). Dihydrosulfonamide **73** (1.195 g) in anhydrous THF (7 mL) was titrated with *n*-butyllithium/cyclohexane to a dark-red endpoint at −60 °C, followed by addition of iodomethane (0.44 mL), after which the stirred mixture was warmed to rt and then to 35 °C for 30 min. The usual workup (see preparation of **60**) gave a product, homogeneous by TLC, which could not be crystallized. It was redissolved in anhydrous THF (8 mL), and

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butyllithium/cyclohexane (1.05 equiv) was added at -40 °C, and then to the dark-red solution at -65 °C methyl chloroformate (0.6 mL) was added. Warming to room temperature and the usual workup (see above) left an oil which was hydrolyzed with NaOH in EtOH/H_2O (see for preparation of **51**) under reflux for 3.5 h. The product after acidification, taken up in TBME, was fractionated by fractional extraction[55] starting with small quantities of 2% sodium bicarbonate, proceeding in base strength up to 5% sodium carbonate. The fractions obtained crystalline after acidification were combined and extracted with $CHCl_3$/THF (3:1) to give acid **79** (0.35 g, 42.4% overall yield); recrystallization from toluene gave mp 197-197.5 °C: IR 3400-2950, 1690, 1625, 1475, 1280-1180 cm^{-1}, ^1H NMR (200 MHz) δ 3.865 (d, 2 H), 3.98 (s, 3 H), 5.15 (d, 1 H), 5.22 (s, 1 H), 6.15 (m, 1 H), 7.22-7.99 (total 5 H), 8.55 (s, 1 H); ^{13}C NMR (50 MHz) δ 171.6, 159.9, 136.65, 136.15, 135.25, 131.95, 130.9, 128.25, 126.3, 123.8, 116.95, 116.7, 103.05, 55.35, 37.2; nominal mass spectrum m/z 243, 242 (M^+), 197, 167, 165, 153, 152; exact mass m/z calcd for $C_{15}H_{14}O_3^+$ 242.0943, found 242.0998.

Experiments on Regiochemistry of Allylation (Table I). Conditions. (a) The sulfonamide (4 mmol) was deprotonated in THF with *n*-butyllithium/cyclohexane and then reduced in THF-liquid NH_3 with lithium metal, followed by quenching with 3-bromo-1-propene (0.8 mL) and then workup as described in the General Procedure (see above). The total crude product, isolated with CH_2Cl_2, was hydrolyzed by heating under reflux in ethanol (4 mL) and 3 N NaOH (3 mL) for 3 h, followed by removal of the ethanol, extraction with hexane, passage through a short column (1-1.5 g) of alumina, and distillation (flask to vial[56]) at 110 °C (Kugelrohr ot) (0.08 mmHg). The proportion of regioisomers **47** to **76** in the distilled product was determined in the ^1H NMR spectrum by integration of the doublets centered at δ 3.89 and 3.505, respectively.

(b) The same procedure was followed except for the use of NaH instead of *n*-BuLi and of Na metal instead of Li.

(c) Sodium hydride suspension (0.38 g) was washed free of oil with pentane and covered with anhydrous DMF (2.5 mL), the suspension cooled to -35 °C (acetonitrile-solid CO_2 bath), and the dihydrosulfonamide (4 mmol) and 3-bromo-1-propene (0.8 mL) added with stirring which was continued as the reaction mixture reached rt overnight, after which water was added and the product isolated with CH_2Cl_2. Thereafter hydrolysis was effected as in a.

(d) To anhydrous THF (8 mL) and anhydrous TMEDA (distilled from sodium, 1.38 mL, 2.5 equiv) was added *N*-benzylbenzamide indicator (4 mg) and to the solution at -20 °C was added dropwise with stirring *n*-butyllithium in cyclohexane to a blue color and then at -70 °C a total of 2.4 equiv of *n*-butyllithium in cyclohexane. The dihydro-*N*-alkylsulfonamide (4 mmol) was then added as a solid and stirring continued at -70 °C until it had all dissolved to give a red solution (1.5-2.5 h). Thereafter, 3-bromo-1-propene (0.95 mL) was added, the solution allowed to reach rt during 2-4 h, the THF removed in vacuo, the product taken up in CH_2Cl_2, and the TMEDA extracted with 2 M aqueous citric acid. Thereafter, the product was hydrolyzed and worked up as in a.

Registry No. **1**, 29083-07-6; **2**, 139633-35-5; **3**, 56875-61-7; **4**, 121429-55-8; **5**, 139633-36-6; **6**, 121429-56-9; **7**, 139633-37-7; **8**, 139633-38-8; **9**, 102153-62-8; **10**, 139633-39-9; **11**, 121429-58-1; **12**, 121429-59-2; **13**, 121429-72-9; **14**, 121429-60-5; **15**, 139633-40-2; **16**, 139633-41-3; **17**, 121429-63-8; **18**, 139633-42-4; **19**, 121429-62-7; **20**, 139633-43-5; **21**, 121429-73-0; **22**, 121429-74-1; **23**, 121429-75-2; **24**, 66413-57-8; **25**, 139633-44-6; **26**, 139633-45-7; **27**, 56875-56-0; **28**, 139633-46-8; **29**, 121429-57-0; **30**, 139633-47-9; **31**, 139633-48-0; **32**, 121429-61-6; **33**, 139633-49-1; **34**, 139633-50-4; **35**, 121429-64-9; **36**, 139633-51-5; **37**, 139655-47-3; **38**, 139633-52-6; **39**, 139633-53-7; **40**, 96362-60-6; **41**, 139633-54-8; **42**, 139633-55-9; **43**, 1634-09-9; **44**, 2825-01-6; **45**, 23076-74-6; **46**, 139633-56-0; **47**, 121429-80-9; **48**, 109250-93-3; **49**, 91903-17-2; **50**, 121429-81-0; **51**, 91903-16-1; **52**, 7147-68-4; **53**, 24293-49-0; **54**, 139633-57-1; **55**, 56875-59-3; **56**, 121429-65-0; **57**, 139633-58-2; **58**, 121429-66-1; **59**, 139633-80-0; **60**, 139633-82-2; **61**, 139633-84-4; 1,2-dihydro-**61**, 139633-59-3; **62**, 139633-78-6; **63**, 121429-76-3; **64**, 139633-76-4; **65**, 121429-78-5; **66**, 139633-60-6; **67**, 139633-61-7; **68**, 121429-77-4; **69**, 139633-62-8; **70**, 139633-63-9; **71**, 139633-64-0; **72**, 121429-69-4; **73**, 121429-70-7; **74**, 26386-94-7; **75**, 94134-18-6; **76**, 139633-65-1; **77**, 139633-66-2; **78**, 121429-82-1; **79**, 139633-67-3; **80**, 56875-60-6; **81**, 139633-68-4; **82**, 139633-69-5; **83**, 139633-70-8; **84**, 139633-71-9; **85**, 33295-54-4; **86**, 139633-74-2; **87**, 139633-72-0; CH_2=$CHCH_2Br$, 106-95-6; sodium 6-hydroxynaphthalene-2-sulfonate, 135-76-2.

Supplementary Material Available: Experimental procedures and data for **3**, **24**, **27**, **38**, **40**, **9**, **80**, **82**, **1**, **2**, **5**, **8**, **10**, **25**, **28**, **29**, **30**, **39**, **41**, **42**, **53**, **57**, **81**, **84**, **11**, **16**, **26**, **32**, **33**, **34**, **18**, **20**, **35**, **59**, **61**, **64**, **70**, **67**, **60**, **65**, **46**, **48**, **50**, **74**, **68**, **75** and **51** and the ^1H or ^{13}C NMR spectra for 1-87 (97 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(55) Reference 39, p 145.
(56) Reference 39, p 202.

Addition of Amino Amides to Vinyl Vicinal Tricarbonyls. Formation of Tricyclic 3-Azadethiacephams

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Amino amides react as trinucleophiles with vinyl vicinal tricarbonyl esters. Reaction of the primary amino group takes place at the β-position of the α,β-unsaturated ketone along with addition to the central carbonyl group. In a third-stage reaction, the amide residue adds to the iminium ion formed from the intermediate carbinolamine. The resulting product is a bicyclic or tricyclic (acylamino)pyrrolidone carboxylate. A novel tricyclic 3-azadethiacepham of biological interest has been prepared using this reaction.

Introduction

In earlier work, we have reported the reactions of the polyelectrophilic vinyl vicinal tricarbonyl system with donor reagents having multiple nucleophilic capability. Thus, a primary amine attached to an auxiliary nucleophilic center undergoes addition in conjugate fashion to the reagent **1** along with attack at the central carbonyl group to generate an intermediate carbinolamine which then gives rise to the iminium ion **2**. The auxiliary nucleophile then adds to **2** to form the bicyclic product as

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