for $C_{19}H_{21}NO_5$: C, 66.47; H, 6.12; N, 4.08. Found: C, 66.36; H, 6.18; N, 4.33.

(2*R*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-4-phenylbutanoic Acid Methyl Ester (7a). From **3a**: mp 121-122 °C (EtOAc-hexane); $[\alpha]^{25}_{578}$ +6° (*c* 0.98, MeOH); ^{1}H NMR ($CDCl_3$) δ 2.80 (m, 2 H, CH_2Ph), 3.56 (s, 3 H, CH_3), 4.34 (d, 1 H, *J* = 2.9 Hz, C_2-H), 4.40 (m, 1 H, C_3-H), 5.05 (s, 2 H, OCH_2), 5.14 (d, 1 H, *J* = 9 Hz, NH), 7.18-7.63 (m, 10 H, Ph). Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.47; H, 6.12; N, 4.08. Found: C, 66.50; H, 6.09; N, 4.15.

(2*S*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-5-methylhexanoic Acid Methyl Ester (6b). From **3b**: mp 75-76 °C (EtOAc-hexane); $[\alpha]^{25}_{578}$ +57° (*c* 1, MeOH); ^{1}H NMr ($CDCl_3$) δ 0.93 (d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 1.40-1.52 (m, 2 H, C_4-H), 1.63 (m, 1 H, C_5-H), 3.72 (s, 3 H, CH_3), 4.14 (m, 2 H, C_2-H and C_3-H), 5.04 (s, 2 H, OCH_2), 5.10 (d, 1 H, *J* = 10 Hz, NH), 7.30 (m, 5 H, Ph). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.14; H, 7.44; N, 4.53. Found: C, 62.23; H, 7.50; N, 4.62.

(2*R*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-5-methylhexanoic Acid Methyl Ester (7b). From **3b**: mp 64-65 °C (EtOAc-hexane); $[\alpha]^{25}_{578}$ +10° (*c* 1, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.92 (d, 6 H, *J* = 6.5 Hz, $CHCH_3$), 1.29-1.56 (m, 2 H, C_4-H), 1.64 (m, 1 H, C_5-H), 3.81 (s, 3 H, CH_3), 4.16 (m, 1 H, C_3-H), 4.37 (d, 1 H, *J* = 3 Hz, C_2-H), 5.08 (d, 1 H, *J* = 10 Hz, NH), 5.12 (s, 2 H, OCH_2), 7.36 (m, 5 H, Ph). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.14; H, 7.44; N, 4.53. Found: C, 61.98; H, 7.60; N, 4.71.

General Procedure for the Synthesis of 3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy Acids 8a, 8b, 9a, and 9b. To a solution of the methyl esters **6a,b** or **7a,b** (2 mmol), in a 1:1 dioxane-water mixture (50 mL) was added NaOH (2.4 mmol; 1.2 equiv), and the mixture was stirred at room temperature for 1 h. Then the reaction mixture was concentrated (~20 mL), diluted with water (40 mL), and extracted with dichloromethane (3 × 40 mL). The aqueous phase was acidified to pH 3-4 with Dowex 50W-X4 resin. The resin was filtered and washed with dichloromethane (50 mL). The aqueous phase was extracted with dichloromethane (3 × 50 mL), and the organic extracts were dried over Na_2SO_4 and evaporated to give quantitatively the corresponding 3-(*N*-(benzyloxycarbonyl)amino)-2-hydroxy acids **8a,b** or **9a,b**.

(2*S*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-4-phenylbutanoic Acid (8a). From **6a**: mp 152-153 °C (EtOAc-hexane) (lit.[8] mp 154-155 °C); $[\alpha]^{25}_{578}$ +83° (*c* 0.69, AcOH) (lit.[8] $[\alpha]^{25}_{578}$ +83.5°); ^{1}H NMR (DMSO-d_6) δ 2.80 (m, 2 H, CH_2Ph), 3.92 (d, 1 H, *J* = 2.5 Hz, C_2-H), 4.10 (m, 1 H, C_3-H), 4.95 (s, 2 H, OCH_2), 7.26 (m, 10 H, Ph).

(2*R*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-4-phenylbutanoic Acid (9a). From **7a**: mp 172-174 °C (EtOAc-hexane) (lit.[8] mp 175-176 °C); $[\alpha]^{25}_{578}$ +6° (*c* 0.65, AcOH) (lit.[8] $[\alpha]^{25}_{578}$ +5.7°); ^{1}H NMR (DMSO-d_6) δ 2.74 (m, 2 H, CH_2Ph), 4.06 (m, 2 H, C_2-H and C_3-H), 4.90 (s, 2 H, OCH_2), 7.23 (m, 10 H, Ph).

(2*S*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-5-methylhexanoic Acid (8b). From **6b**: mp 91-93 °C (EtOAc-hexane); $[\alpha]^{25}_{578}$ +33° (*c* 0.99, MeOH); ^{1}H NMR (DMSO-d_6) δ 0.85 (d, 6 H, *J* = 6.5 Hz, $CHCH_3$), 1.31 (m, 2 H, C_4-H), 1.55 (m, 1 H, C_5-H), 3.89 (m, 2 H, C_2-H and C_3-H), 4.99 (s, 2 H, OCH_2), 7.34 (m, 5 H, Ph). Anal. Calcd for $C_{15}H_{21}NO_5$: C, 61.02; H, 7.12; N, 4.75. Found C, 61.24; H, 7.29; N, 4.51.

(2*R*,3*R*)-3-(*N*-(Benzyloxycarbonyl)amino)-2-hydroxy-5-methylhexanoic Acid (9b). From **7b**: mp 126-128 °C (EtOAc-hexane); $[\alpha]^{25}_{578}$ +17° (*c* 0.8, MeOH); ^{1}H NMR (DMSO-d_6) δ 0.79 (d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 0.84 (d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 1.01 (m, 1 H, C_4-H), 1.50 (m, 2 H, C_5-H and C_4-H), 3.85 (m, 1 H, C_3-H), 3.96 (d, 1 H, *J* = 4.5 Hz, C_2-H), 5.00 (s, 2 H, OCH_2), 7.33 (m, 5 H, Ph). Anal. Calcd for $C_{15}H_{21}NO_5$: C, 61.02; H, 7.12; N, 4.75. Found: C, 60.92; H, 7.18; N, 4.68.

General Procedure for the Synthesis of the 2-Oxazolidones 10a, 10b, 11a, and 11b. To a solution of the methyl esters **6a,b** or **7a,b** (3 mmol) in methanol (30 mL) was added 6 N NaOH (1 mL), and after stirring at room temperature for 2 h, the reaction mixture was evaporated. The residue was taken up in water (40 mL), washed with dichloromethane (2 × 20 mL), and acidified to pH 3-4 with Dowex 50W-X4 resin. The resin was filtered off and washed with ethyl acetate (30 mL). The aqueous phase was extracted with ethyl acetate (2 × 30 mL), and the combined organic extracts were dried over Na_2SO_4 and evaporated to yield the corresponding 2-oxazolidones (80%) as foams.

(4*R*,5*S*)-4-Benzyl-2-oxo-5-oxazolidinecarboxylic Acid (10a). From **6a**: IR (KBr) 1760 (NH—C=O); ^{1}H NMR (DMSO-d_6) δ 2.71-2.94 (m, 2 H, CH_2Ph), 3.95 (m, 1 H, C_4-H), 4.20 (d, 1 H, *J* = 5 Hz, C_5-H), 7.21-7.31 (m, 5 H, Ph), 7.70 (s, 1 H, NH). Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.58; H, 5.12; N, 6.25.

(4*R*,5*R*)-4-Benzyl-2-oxo-5-oxazolidinecarboxylic Acid (11a). From **7a**: IR (KBr) 1760 (NH—C=O); ^{1}H NMR (DMSO-d_6) δ 2.51-2.90 (m, 2 H, CH_2Ph), 4.34 (m, 1 H, C_4-H), 5.11 (d, 1 H, *J* = 9 Hz, C_5-H), 7.18-7.31 (m, 5 H, Ph), 7.70 (s, 1 H, NH). Anal. Calcd for $C_{11}H_{11}NO_4$: C, 59.73; H, 5.01; N, 6.33. Found: C, 59.61; H, 5.15; N, 6.19.

(4*R*,5*S*)-4-Isobutyl-2-oxo-5-oxazolidinecarboxylic Acid (10b). From **6b**: IR (KBr) 1760 (NH—C=O); ^{1}H NMR (DMSO-d_6) δ 0.87 (d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 0.89 (d, 3 H, *J* = 6.5 Hz, $CHCH_3$), 1.42 (m, 2 H, CH_2), 1.70 [m, 1 H, $CH(CH_3)_2$], 3.73 (m, 1 H, C_4-H), 4.61 (d, 1 H, *J* = 4.5 Hz, C_5-H), 8.00 (s, 1 H, NH). Anal. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.21; H, 7.12; N, 7.44.

(4*R*,5*R*)-4-Isobutyl-2-oxo-5-oxazolidinecarboxylic Acid (11b). From **7b**: IR (KBr) 1760 (NH—C=O); ^{1}H NMR (DMSO-d_6) δ 0.83 (d, 3 H, *J* = 6.6 Hz, $CHCH_3$), 0.87 (d, 3 H, *J* = 6.6 Hz, $CHCH_3$), 1.23 (m, 2 H, CH_2), 1.68 [m, 1 H, $CH(CH_3)_2$], 4.09 (m, 1 H, C_4-H), 5.00 (d, 1 H, *J* = 8.7 Hz, C_5-H), 8.00 (s, 1 H, NH). Anal. Calcd for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48. Found: C, 51.47; H, 7.10; N, 7.39.

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Registry No. **1**, 58970-76-6; **2**, 67655-94-1; **3a**, 63219-70-5; **3b**, 70853-26-8; **6a**, 124782-04-3; **6b**, 124782-05-4; **7a**, 124782-06-5; **7b**, 124782-07-6; **8a**, 59969-65-2; **8b**, 70853-12-2; **9a**, 62023-58-9; **9b**, 70853-18-8; **10a**, 100564-98-5; **10b**, 124782-08-7; **11a**, 124820-68-4; **11b**, 124782-09-8; Z-D-Phe-OH, 2448-45-5; Z-D-Leu-OH, 28862-79-5.

Monoalkylation vs Dialkylation of a Sulfone-Stabilized Carbanion[1]

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Alkylation of carbanions is one of the most important processes used in organic synthesis for the formation of carbon-carbon bonds. Typically the carbanion is formed through base-promoted abstraction of an activated hydrogen atom. Although carbonyl plays the major role among the electron-withdrawing groups used to "activate" a carbon-hydrogen bond for proton abstraction from the requisite carbon atom,[3] sulfone is one of a variety of heteroatom substituents that has also been used.[4] Sulfone

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as the activating group has attracted considerable interest because once it serves to direct regiospecific alkylation, it can be removed through reductive desulfurization.[5]

The potential for polyalkylation to occur places some limitation on the use of carbanion alkylation in synthesis. Carbonyl-stabilized carbanions often lead to small or moderate amounts of polyalkylation.[3a,6] However, such a pathway is reported to be much less common with sulfone-stabilized and closely related carbanions.[4e,7] High reaction selectivity is particularly desirable when anion alkylation is a key step in a convergent synthesis involving difficultly prepared precursors. The use of sulfone-stabilized anions for diastereoselective control[8] is another application requiring reaction selectivity.

In the course of another project, we have made use of methyl phenyl sulfone (**1**) as the carbanion precursor on which to build medium-length alkanes and alkenes. Based on reported data, we expected relatively clean monoalkylation that would allow a sequence of different groups to be efficiently added. We were therefore surprised to observe considerable dialkylation, and in one case trialkylation, when methyl phenyl sulfone (**1**) was alkylated under experimental conditions expected to give only monoalkylation. A study was subsequently initiated to investigate the factors that control mono- vs dialkylation of **1**. The results of that work are compiled below.

Results and Discussion

The requisite sulfone-stabilized carbanion **2** was normally prepared in THF at 0 °C using an equivalent amount of butyllithium in hexane or solid potassium hydride. An appropriate haloalkane alkylating agent (**3**) was then added. On workup the product mixtures were analyzed by HPLC.

$$\underset{\mathbf{1}}{C_6H_5SO_2CH_3} \xrightarrow{\text{BuLi/THF}} \underset{\mathbf{2}}{C_6H_5SO_2CH_2^-Li^+} \xrightarrow{\text{RX (3)}}$$

$$\underset{\mathbf{4}}{C_6H_5SO_2CH_2R} + \underset{\mathbf{5}}{C_6H_5SO_2CHR_2} + \underset{\mathbf{6}}{C_6H_5SO_2CR_3}$$

R = **a**, $CH_3CH_2CH_2$; **b**, $CH_3CH_2CH_2CH_2$; **c**, $CH_2{=}CHCH_2CH_2$; **d**, $CH_2{=}CHCH_2$; **e**, $C_6H_5CH_2$

The results of alkylation of **1** by a series of alkylating agents are recorded in Table I. Mono- and dialkylation were observed in all cases even though equivalent quantities of sulfone, base, and alkylating reagent were utilized. Inverse addition (addition of carbanion **2** to the alkylating reagent) had no significant influence on the product mixtures. Trialkylation (product **6**) was normally not observed using equivalent amounts of reagents; however, trialkylated products could be obtained in all cases when using 2 or more equivalents of the base.

Table I. Alkylations of Methyl Phenyl Sulfone (1)

RX (3)	product mixture, % 4	5	6	1
a, $CH_3CH_2CH_2Br$	71	19	0	11
b, $CH_3CH_2CH_2CH_2Br$	66	19	0	16
c, $CH_2{=}CHCH_2CH_2Br$	63	18	0	20
d, $CH_2{=}CHCH_2Br$	40	25	2.5	33
e, $C_6H_5CH_2Br$	36	43	0	21

Table II. Ratios of Monoalkylation (4) to Dialkylation (5) Using Equimolar Quantities of Methyl Phenyl Sulfone (1), Base, and Alkylating Agent (3)

RX (3)	BuLi/THF	BuLi/THF + TMEDA	KH/THF
a, $CH_3CH_2CH_2Br$	3.7	4.7	29
b, $CH_3CH_2CH_2CH_2Br$	3.5	4.2	21
c, $CH_2{=}CHCH_2CH_2Br$	3.5	4.4	–
d, $CH_2{=}CHCH_2Br$	1.6	1.4	2.5
e, $C_6H_5CH_2Br$	0.8	1.5	1.3

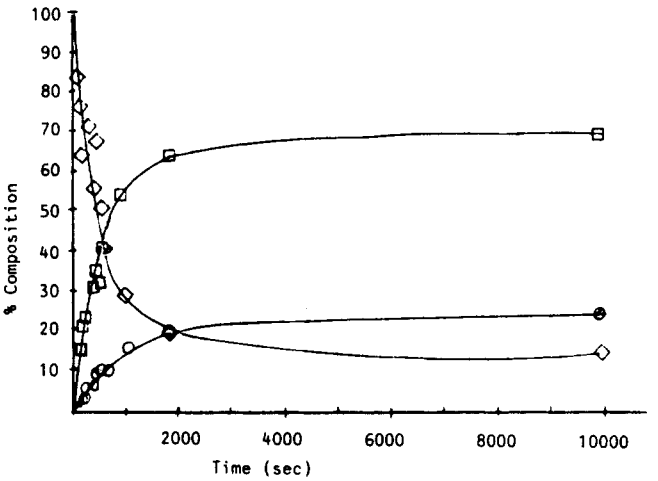

Figure 1. Alkylation of methyl phenyl sulfone (**1**) with 1-bromobutane (**3b**); (◇) methyl phenyl sulfone, (□) monosubstituted sulfone, (○) disubstituted sulfone.

Significant dialkylation was a surprising result of these alkylation reactions, particularly considering the rather sparce mention of similar results in the literature.[4e,7] Furthermore, we had presumed that a difference in acidity of at least 2 pK_a units[9] between **1** and the monoalkylation product **4** would inhibit significant formation of the sulfone stabilized carbanion of **4** and its subsequent alkylation.

To demonstrate that acidities were in the expected order under our typical reaction conditions, equimolar quantities of **1**, **4**, and butyllithium were mixed in THF and then quenched with D_2O. Only deuterated **1** was observed based upon NMR analysis of the separated components. A control reaction in which **4** alone was treated in this way resulted in complete deuterium exchange. These data confirm that the anions of **1** and **4** can readily form and that **1** is the more acidic.

The results, as compiled in Table II, show that alkylating agents **3a–c** all produce mono- to dialkylation in a ratio of about 3.6 whereas the allylic halide **3d** and particularly the benzylic halide **3e** yield relatively more dialkylated product. The order of increasing dialkylation is also the

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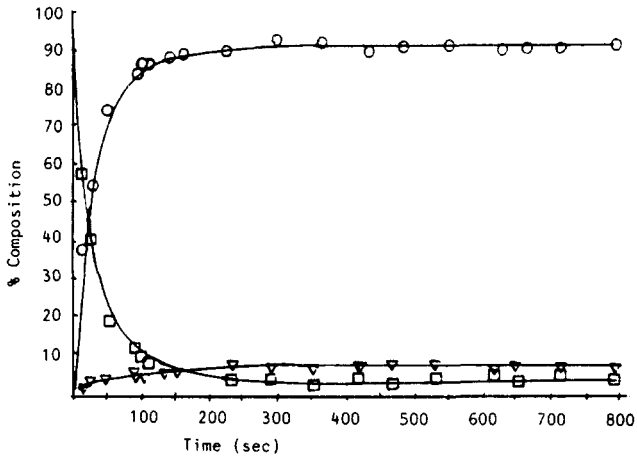

Figure 2. Alkylation of pentyl phenyl sulfone (**4b**) with 1-bromobutane (**3b**); (□) monosubstituted sulfone, (○) disubstituted sulfone, (▽) trisubstituted sulfone.

order of increasing reactivity of the alkylating agents in nucleophilic substitution.[10]

We assumed, based on acidity and steric considerations, that competitive formation and alkylation of the monosubstituted carbanion derived from **4** would be considerably less favorable than the similar reactions of **1**. Yet the results suggest that these processes may be competitive for the two sulfones. To establish reactivities in the two cases we carried out an investigation of the rates of alkylation of **1** and **4b**. The results (Figures 1 and 2) show that alkylation of the monosubstituted sulfone (**4b**) is approximately 20 times faster than alkylation of the unsubstituted sulfone (**1**). The thermodynamically less stable carbanion is the more reactive.

A quenching experiment on **2** using deuteriosulfuric acid to avoid subsequent exchange showed that this carbanion is formed rapidly on reaction of sulfone **1** with butyllithium, i.e., the base is consumed prior to addition of the alkylating agent. Thus **7**, the carbanion that is derived from the initial alkylation product **4** and that leads to dialkylation product **5**, must be formed during the reaction through equilibration of **4** with unreacted **2**.

$$\underset{\mathbf{2}}{C_6H_5SO_2CH_2^-Li^+} + \underset{\mathbf{4}}{C_6H_5SO_2CH_2R} \rightleftharpoons \underset{\mathbf{1}}{C_6H_5SO_2CH_3} + \underset{\mathbf{7}}{C_6H_5SO_2CH^-RLi^+}$$

$$\underset{\mathbf{7}}{C_6H_5SO_2CH^-RLi^+} + \underset{\mathbf{3}}{RX} \rightarrow \underset{\mathbf{5}}{C_6H_5SO_2CHR_2}$$

Although our acidity data suggest that only a low concentration of **7** is present, its greater reactivity (compared to **2**) leads to significant alkylation to give **5**. It has been suggested that the ratio of polyalkylation to monoalkylation of ketone enolates is a function of the rate of equilibration between the requisite enolates.[11] Our results suggest that equilibration between **2** and **7** and their conjugate acids **1** and **4** is more rapid than the substitution reaction. Although the dianion of **1** has been reported[4g] and could lead directly to **5**, this species seems unlikely to be formed under the reaction conditions of our investigation.[12]

The different reactivity of **2** and **7** in the alkylation sequence may well reflect the "freeness" of the respective nucleophilic carbon atoms. Ion aggregation and ion pairing are important factors in such reactivity considerations.[13] We have addressed both possibilities in our investigation.

One explanation for the lower lower reactivity of **2** relative to **7** may be inhibition of alkylation by aggregation about the lithium cation.[6c,14] The less crowded anion would be expected to be the more aggregated. To investigate the possible role of aggregation we added to the reaction mixture an equivalent quantity of tetramethylethylenediamine (TMEDA), a compound often used to complex lithium and reduce aggregation.[15] An increase in monoalkylation of **1** did take place (Table II), though the change was slight and probably not synthetically significant. However, TMEDA might not effectively compete with sulfone to reduce any aggregation.[16] Furthermore, it has been suggested that TMEDA does not compete well with THF in solvating lithium cations.[17] This information coupled with the data of Table II suggest that ion aggregation is not occurring. In fact, Streitwieser and co-workers have not found ion aggregation to be important with lithium salts in THF at low concentrations.[17]

We also considered how the degree of cation–anion association might affect reactivity. Tight (or contact) ion pairing would be expected to decrease anion reactivity in nucleophilic substitution. It is known that ion association decreases as the counterion is changed from lithium to potassium.[6c,13a] Thus if tight ion pairing does indeed inhibit alkylation by **2**, change to a potassium counterion should enhance reactivity of **2** relative to **7**. To test this we carried out the alkylation reactions by forming the anion using potassium hydride in THF. The results (Table II) are quite clear. The mono- to dialkylation increases significantly for haloalkanes **3a–c** and somewhat less for the more reactive (and less selective) **3d,e**. The more free and sterically less encumbered primary carbanion **2**, which is present in higher concentration, increases its alkylation relative to the secondary carbanion **7**. Thus a rather simple change in base reagent markedly enhances the selectivity of this synthetic method.

Conclusion

We have found that alkylation of methyl phenyl sulfone using a lithium base can lead to significant polyalkylation even under experimental conditions expected to give principally monoalkylation. Resultant product mixtures can limit the synthetic utility of the alkylation process. The polyalkylation is believed to occur by equilibration between the initially formed sulfone-stabilized carbanion and the alkylated product (or products), followed by alkylation of the new sulfone-stabilized carbanion. Use of a potassium base markedly enhances formation of monosubstituted product, presumably by decreasing ion pairing.

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Experimental Section

General. Reactions were carried out in an inert atmosphere using predried (sodium benzophenone ketyl) and distilled THF. Haloalkanes were obtained commercially. Product mixtures were separated to obtain analytical data by medium-pressure chromatography using an EM Lobar Si 60 column with 10% diethyl ether–90% ligroin (60–80 °C) as eluent. Quantitative analysis of the reaction mixtures was accomplished on a Waters 6000 HPLC using an IBM silica column with 15% diethyl ether–85% ligroin (60–80 °C). The UV detector was calibrated on known product mixtures. NMR spectra were obtained using a Varian EM-390 spectrometer.

General Alkylation Procedure. One millimole each of the sulfone and base were added to 7–15 mL of THF and allowed to stir for 1 h at 0 °C. One millimole of the alkylating agent was added at that same temperature, and the mixture was allowed to stir at room temperature for 5 h. Addition of 5 mL of water, ether extraction, drying with $MgSO_4$, and removal of the solvent via a rotary evaporator provided the product mixture.

Kinetic Reactions. Six millimoles of the appropriate sulfone in THF and of butyllithium were mixed at 0 °C. After 1 h the slurry was brought to room temperature, and then 6 mmol of bromoalkane was added. Alliquots (1 mL) were removed and quenched with water at specific times. The samples were recovered as above and analyzed by HPLC.

Equilibration–Deuterium Quench. An equimolar mixture of butyllithium, sulfone 1, and sulfone **4a** were stirred for 1 h at 0 °C in 7 mL of THF. Deuterium oxide was added to the mixture, and the products were recovered as above, separated by medium-pressure chromatography, and analyzed for deuterium content by NMR spectroscopy.

Deuterium Quench. An equimolar mixture of 1 and butyllithium were stirred in 7 mL of THF at 0 °C for 1 h. Deuteriosulfuric acid (1 M) was added, and the product was recovered as above and analyzed for deuterium content by NMR spectroscopy.

Methyl phenyl sulfone (1): via oxidation of methyl phenyl sulfide with 30% hydrogen peroxide in acetic acid;[18] 91%; mp 87.4–89.6 °C (lit.[18b] mp 86–88 °C); ^{1}H NMR ($CDCl_3$) δ 3.0 (s, 3), 7.5–7.8 (m, 5).

Butyl phenyl sulfone (4a): ^{1}H NMR (CCl_4) δ 0.9 (t, 3, J = 6 Hz), 1.1–1.9 (m, 4), 3.0 (t, 2, J = 6 Hz), 7.3–7.9 (m, 5). Anal. Calcd for $C_{10}H_{14}O_2S$: C, 60.58; H, 7.12. Found: C, 60.71; H, 7.20.

4-Heptyl phenyl sulfone (5a): ^{1}H NMR (CCl_4) δ 0.9 (t, 6, J = 6 Hz), 1.1–1.9 (m, 8), 2.6–2.9 (m, 1), 7.2–7.9 (m, 5). Anal. Calcd for $C_{13}H_{20}O_2S$: C, 64.96; H, 8.39. Found: C, 64.79; H, 8.07.

4-(4-Propylheptyl) phenyl sulfone (6a): ^{1}H NMR ($CDCl_3$) δ 0.8 (t, 9, J = 6 Hz), 1.2–1.8 (m, 12), 7.3–7.8 (m, 5). Anal. Calcd for $C_{16}H_{26}O_2S$: C, 68.04; H, 9.27. Found: C, 67.93; h, 9.29.

Pentyl phenyl sulfone (4b): ^{1}H NMR (CCl_4) δ 0.8 (t, 3, J = 6 Hz), 1.0–1.9 (m, 6), 2.8–3.1 (m, 2), 7.3–8.0 (m, 5). Anal. Calcd for $C_{11}H_{16}O_2S$: C, 62.23; H, 7.60. Found: C, 62.18; H, 7.64.

5-Nonyl phenyl sulfone (5b): ^{1}H NMR (CCl_4) δ 0.8 (6 t, J = 6 Hz), 1.0–2.0 (m, 12), 2.6–2.8 (m, 1), 7.4 (m, 3), 7.8 (m, 2). Anal. Calcd for $C_{15}H_{24}O_2S$: C, 67.12; H, 9.01. Found: C, 67.31; H, 8.83.

5-(5-Butylnonyl) phenyl sulfone (6b): ^{1}H NMR ($CDCl_3$) δ 0.7–1.8 (m, 27), 7.3–7.8 (m, 5). Anal. Calcd for $C_{19}H_{32}O_2S$: C, 70.32; H, 9.93. Found: C, 70.23; H, 9.94.

4-Pentenyl phenyl sulfone (4c): ^{1}H NMR (CCl_4) δ 1.5–2.4 (m, 4), 2.8–3.1 (m, 2), 4.8–5.1 (m, 2), 5.4–5.9 (m, 1), 7.4–7.9 (m, 5). Anal. Calcd for $C_{11}H_{14}O_2S$: C, 62.83; H, 6.71. Found: C, 62.82; H, 6.63.

5-(1,8-Nonadienyl) phenyl sulfone (5c): ^{1}H NMR (CCl_4) δ 1.4–2.4 (m, 8), 2.7–2.9 (m, 1), 4.7–5.1 (m, 4), 5.3–5.8 (m, 2), 7.4–7.8 (m, 5). Anal. Calcd for $C_{15}H_{20}O_2S$: C, 68.14; H, 7.62. Found: C, 68.26; H, 7.70.

5-[5-(3-Butenyl)-1,8-nonadienyl] phenyl sulfone (6c): ^{1}H NMR (CCl_4) δ 1.5–1.8 (m, 6), 1.9–2.3 (m, 6), 4.7–5.1 (m, 6), 5.4–5.8 (m, 3), 7.3–7.8 (m, 5). Anal. Calcd for $C_{19}H_{26}O_2S$: C, 71.66; H, 8.23. Found: C, 71.36; H, 8.29.

3-Butenyl phenyl sulfone (4d): ^{1}H NMR (CCl_4) δ 2.1–2.5 (m, 2), 2.8–3.1 (m, 2), 4.8–5.1 (m, 2), 5.3–5.8 (m, 1), 7.2–7.9 (m, 5). Anal. Calcd for $C_9H_{10}O_2S$: C, 61.20; H, 6.16. Found: C, 61.13; H, 6.23.

4-(1,6-Heptadienyl) phenyl sulfone (5d): ^{1}H NMR (CCl_4) δ 2.1–2.7 (m, 4), 2.8–3.2 (m, 1), 4.8–5.2 (m, 4), 5.4–6.0 (m, 2), 7.3–8.0 (m, 5). Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 66.18; H, 6.75.

4-[4-(2-Propenyl)-1,6-heptadienyl] phenyl sulfone (6d): ^{1}H NMR (CCl_4) δ 2.4 (d, 6, J = 9 Hz), 4.8–5.2 (m, 6), 5.5–6.1 (m, 3), 7.3–7.9 (m, 5). Anal. Calcd for $C_{16}H_{20}O_2S$: C, 69.53; H, 7.29. Found: C, 69.41; H, 7.24.

2-Phenylethyl phenyl sulfone (4e): ^{1}H NMR (CCl_4) δ 2.7–3.3 (m, 4), 7.0 (s, 5), 7.2–7.9 (m, 5). Anal. Calcd for $C_{14}H_{14}O_2S$: C, 68.27; H, 5.73. Found: C, 68.33; H, 5.35.

2-(1,3-Diphenylpropyl) phenyl sulfone (5e): ^{1}H NMR ($CDCl_3$) δ 2.5–3.4 (m, 5), 6.6–7.8 (m, 15). Anal. Calcd for $C_{21}H_{20}O_2S$: C, 74.97; H, 5.99. Found: C, 74.92; H, 6.03.

2-Benzyl-1,3-diphenylpropyl phenyl sulfone (6e): ^{1}H NMR ($CDCl_3$) δ 3.2 (s, 6), 7.2 (s, 20). Anal. Calcd for $C_{28}H_{26}O_2S$: C, 78.84; H, 6.14. Found: C, 78.74; H, 6.24.

Registry No. 1, 3112-85-4; **3a**, 106-94-5; **3b**, 109-65-9; **3c**, 5162-44-7; **3d**, 106-95-6; **3e**, 100-39-0; **4a**, 16823-62-4; **4b**, 34009-04-6; **4c**, 41795-36-2; **4d**, 67100-44-1; **4e**, 27846-25-9; **5a**, 124992-95-6; **5b**, 105494-88-0; **5c**, 125023-16-7; **5d**, 124992-96-7; **5e**, 124992-97-8; **6a**, 124992-98-9; **6b**, 124992-99-0; **6c**, 124993-00-6; **6d**, 124993-01-7; **6e**, 124993-02-8; MeSPh, 100-68-5.

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Synthesis of 2-Octalones from Quinaldine

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The addition of a methyl vinyl ketone unit to a cyclic ketone to form a new carbocyclic ring (the Robinson annulation[1]) has found many applications in the synthesis of organic compounds.[2] Since the reaction in its original form suffers from low yields and only moderate regiochemical control, synthetic chemists have developed various alternatives, many of which have been applied to the total synthesis of natural products.[3] In this connection, heterocycles in which lie "hidden" or "masked" ketones or enols have proven especially fruitful.[4]

We have developed a synthetic method by which one can efficiently convert 2-alkylquinolines into 2-octalones, which are important intermediates in many steroid and terpenoid total syntheses.[2] Such a transformation is of significant potential importance in view of the commercial availability of a variety of quinolines and tetrahydroquinolines,[5] as well as the many heterocycle syntheses by which virtually any substituted quinoline may be prepared.[6]

In this paper we report the conversion of the tar distillate product quinaldine (1) into 2-octalone **3**. We then demonstrate that quinaldine may be functionalized by alkylation and subsequently converted into 1-substituted-2-octalones.

As shown in Scheme I, quinaldine was hydrogenated in neat trifluoroacetic acid (TFA) as described by Vierhapper and Eliel.[7] The methiodide **2** was formed by allowing the above compound to stir in iodomethane followed by recrystallization from 2-propanol/ether. This material was not very hygroscopic and was easy to handle when prepared in this way. Birch reduction and hydrolysis provided

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