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Zn/CuI-Mediated Coupling of Alkyl Halides with Vinyl Sulfones, Vinyl Sulfonates, and Vinyl Sulfonamides

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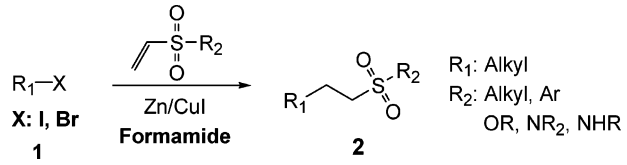
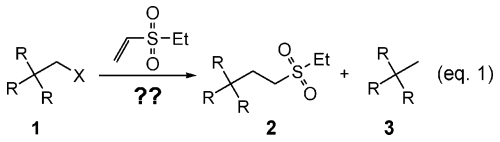


A novel high-yielding Zn/CuI-mediated coupling method of alkyl halides with vinyl sulfones, vinyl sulfonates, and vinyl sulfonamides is described. This protocol is applicable for primary, secondary, and tertiary alkyl iodides and bromides. Alkyl chlorides and aryl and vinyl halides were unreactive under the reaction conditions. Formamide was found to be a superior solvent for obtaining high yields.

Carbon−carbon bond formation is a fundamental reaction in organic synthesis. Metal-mediated couplings of alkyl halides with α,β-unsaturated carbonyl compounds or nitro olefins have been widely utilized in organic synthesis.[1] On the other hand, there are very few reports on analogous reactions with α,β-unsaturated sulfones. Most of the reported procedures require a large excess one coupling partner (4−20 equiv) to obtain a reasonable yield.

Recently, we needed an efficient method for the coupling of a neopentyl alkyl halide with ethyl vinyl sulfone (eq 1). We found that the literature procedures[2−4] gave unsatisfactory results, generally giving significant amounts of the reduced substrates. Therefore, a more efficient method for the coupling of alkyl halides with vinyl sulfones was desired.



We decided to further investigate the Zn/CuI-mediated coupling reaction. First, various solvents were screened. Preliminary results indicated that polar solvents such as DMF, DMAc, NMP, and DMSO were better than less polar solvents and showed higher selectivity for the addition product **2** than protic or aqueous solvent mixtures. Among these solvents, DMF appeared to be the best, affording the coupling product **2** as the main peak based on GC assay. Unfortunately, even under the best conditions, the actual yield was still quite low (∼40%) based on quantitative GC assay. Oligermization was the likely cause for the low yield and the lack of other products detected by GC. Protic solvent mixtures gave variable yields of the coupling product with neopentyl iodide: EtOH/H_2O (2:1), 59%; THF/H_2O (2:1), 32%; THF/MeOH (2:1), 77%. THF alone gave no coupling product.

To further improve the yield, we searched for solvents that are substantially more polar than DMF. On the basis of dielectric constant, only water, formic acid, and formamide qualify, but all of them have acidic protons. Formamide stands out as being the most polar among commonly available solvents. In fact, it is more polar than water based on dielectric constants. The acidity of formamide (pK_a 23) is much lower than that of water, and therefore the premature protonation of the organometallic species should be less pronounced. Gratifyingly, we found that by simply using formamide as a solvent, the yield improved to 94%. Furthermore, only 1.2 equiv of ethyl vinyl sulfone was required.

Screening of various copper sources indicated that CuI was the best. The relative catalytic efficiencies in decreasing order were: CuI > CuBr > CuOAc > Cu(O_2C-thiophene) > copper salicylate > CuOTf > $CuSO_4$. Commercial zinc−copper couple failed to gave any reaction. Substitution of zinc dust with magnesium or aluminum powder did not give satisfactory results.

Next, the scope and utility of this method were investigated. We found that most alkyl iodides including primary, secondary, and tertiary alkyl iodides worked well, affording the coupling products in good to excellent yields as shown in Table 1. Tertiary alkyl iodide gave the best yield (98%) relative to primary or secondary iodides (entries 6−8) consistent with the observations of Luche.[5] We found that substitution on the vinyl moiety of the sulfones strongly influenced the reaction. An α-substituent[6] significantly retarded the reaction, leading to substantially lower yields (entry 10). But for *tert*-butyl iodide, the yield was still acceptable (entry 11). A β-substitution[7] completely blocked the reaction (entry 12).

Alkyl bromides also worked well and thus significantly widened the scope of this chemistry. The reactions were much slower than alkyl iodides, requiring a longer reaction time and higher temperature (20 °C versus 0−5 °C). However, the yields were quite comparable (Table

(1) (a) *Modern Organocopper Chemistry*; Krause, N., Ed.; Wiley-VCH: Weinheim, Germany, 2002. (b) Nakamura, E.; Mori, S. *Angew. Chem., Int. Ed*. **2000**, *39*, 3750−3771. (c) Knochel P.; Perea, J. J. A.; Jones, P. *Tetrahedron* **1998**, *54*, 8275−8319. (d) Knochel, P.; Singer, R. *Chem. Rev.* **1993**, *93*, 2117−2188. (e) Wipf, P. *Synthesis* **1993**, 537−557. (f) Nakamura, E. *Synlett* **1991**, 539−547.

(2) (a) Jang, D. O.; Cho, D. H.; Chung, C.-M. *Synlett* **2001**, 1923−1924. (b) Jang, D. O.; Cho, D. H. *Synlett* **2002**, 1523.

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(4) Perez-Sestelo, J.; Mascarenas, J. L.; Castedo, L.; Mourino, A. *J. Org. Chem.* **1993**, *58*, 118−123.

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(6) Magar, S. S.; Fuchs, P. L. *Tetrahedron Lett*. **1992**, *33*, 745−748.

(7) Inbasekaran, M.; Peet, N. P.; McCarthy, J. R.; Le Tourneau, M. E. *J. Chem. Soc., Chem. Commun*. **1985**, 678−679.

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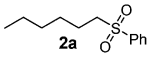
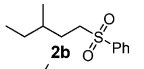
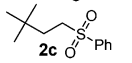
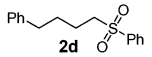
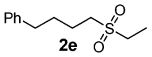
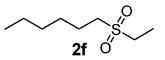
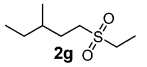
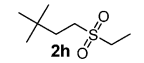
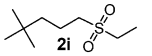
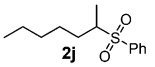
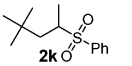
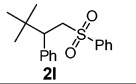
TABLE 1. Coupling of Alkyl Iodides

entry	RX	sulfone	product	yield
1		A	 **2a**	70
2		A	 **2b**	80
3		A	 **2c**	91
4		A	 **2d**	59
5		B	 **2e**	77
6		B	 **2f**	84
7		B	 **2g**	87
8		B	 **2h**	98
9		B	 **2i**	94
10		C	 **2j**	20
11		C	 **2k**	65
12		D	 **2l**	0

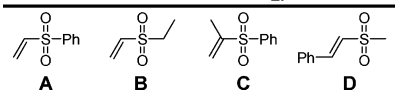
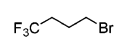
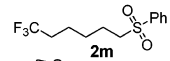
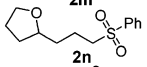
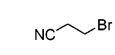
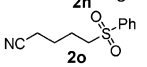
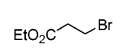
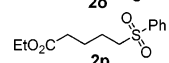
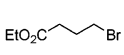
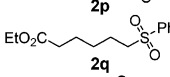
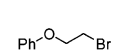
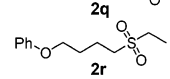
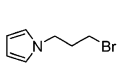
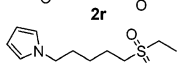
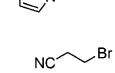

A **B** **C** **D**

TABLE 2. Coupling of Alkyl Bromides

entry	RX	sulfone	product	yield
1		A	 **2m**	80
2		A	 **2n**	62
3		A	 **2o**	72
4		A	 **2p**	75
5		A	 **2q**	67
6		B	 **2r**	88
7		B	 **2s**	80
8		B	**2t**	62
9		B	**2u**	62
10		B	**2v**	61

2). Attempts to accelerate the reaction by adding NaI actually slowed it down. Adding $ZnBr_2$ also retarded the reaction rate significantly. The reaction conditions were compatible with a wide range of functional groups including esters, nitriles, acetals, CF_3, ethers, and so forth.

TABLE 3. Coupling to Vinyl Sulfonates

entry	RX	sulfonate	product	yield
1		E	**4a**	84
2		E	**4b**	85
3		E	**4c**	72
4		F	**4d**	83
5		F	**4e**	59
6		F	**4f**	70
7		F	**4g**	81
8		F	**4h**	42
9		G	**4i**	60
10		G	**4j**	87

R: Ph Et *i*-Pr
E **F** **G**

In contrast to alkyl iodides and bromides, alkyl chlorides were unreactive under the reaction conditions. Surprisingly, aryl halides, α-iodo, and bromo carbonyl compounds also failed to react. Benzenesulfonates, toluenesulfonates, or 4-nitro-benzenesulfonates of alcohols were also unreactive. Triflates of alcohols, on the other hand, gave some product albeit in low yield. Benzyl bromide gave mostly the homocoupling product.

The scope of the vinyl sulfur compounds was also investigated. We found that vinyl sulfonates[8] sulfonamides[9] including those with free NH group were also good coupling partners for the reaction. The results are summarized in Tables 3 and 4, respectively.

As for the mechanism of the reaction, there was an obvious reaction when zinc dust and CuI were mixed in formamide. Evidence for the formation of a new species includes the substantial heat evolution as well as the changes in appearance. The temperature climbed as much as 15 °C within 5−10 min of adding 0.5 equiv of CuI to zinc dust. Meanwhile, the mixture also changed from a thin gray slurry to a thick black one. Another observation also lends support. We found that the Zn/CuI mixture was much more active than zinc dust alone. While alkyl bromides were essentially inert toward zinc dust in formamide at room temperature, the Zn/CuI mixture cleanly converted the bromides to the desired coupling product. In the absence of a Michael acceptor, they were cleanly reduced.

(8) Adamczyk, M.; Chen, Y.-Y.; Mattingly, P. G. *Tetrahedron Lett.* **2001**, *42*, 4285−4287.

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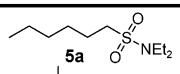
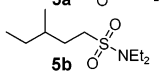
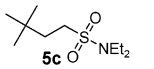
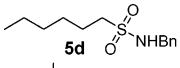
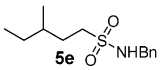
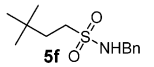
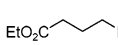
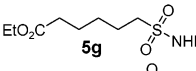
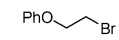
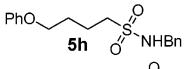
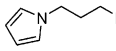
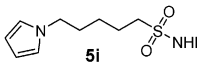
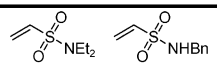
TABLE 4. Coupling to Vinyl Sulfonamide

entry	RX	sulfonamide	product	yield
1		H	 **5a**	88
2		H	 **5b**	83
3		H	 **5c**	94
4		I	 **5d**	70
5		I	 **5e**	91
6		I	 **5f**	76
7		I	 **5g**	85
8		I	 **5h**	66
9		I	 **5i**	88



H I

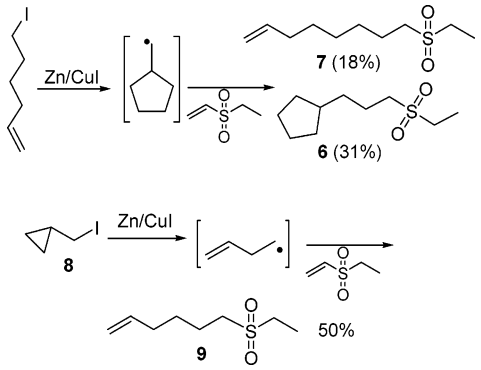
We also noticed that the quality of the Zn/CuI complex degraded with time and should be used almost immediately following its preparation. The deterioration was more rapid at higher temperature. Thus, the mixing should be performed with efficient cooling. This aging effect was less apparent for alkyl bromides, however, and satisfactory results were obtained at room temperature. For larger scale reactions (>20 mmol), CuI was added in portions to maintain the temperature of the mixture at 0−10 °C. Curiously, reversing the order of addition (i.e., adding zinc dust in portions to a CuI slurry) gave significantly inferior results.

When an alkyl iodide was added, more heat was generated. The temperature rise was apparent during addition of the first 50% of the substrate only, indicating a rapid reaction for the first 50% of the substrate followed by a much slower reaction for the remainder. This implies that the turnover of copper catalyst is relatively slow.

Competing reactions include protonation of the R−Zn−Cu−I species and oligomerization by reaction of the initial adduct with a second vinyl sulfone. The pK_a of the solvent may be very important. If it is too low such as alcohols or water (pK_a 14−16), premature protonation of R−Zn−Cu−I would dominate. If it is too high, oligomerization would become a problem. The key to the success of formamide may be its high polarity and an appropriate pK_a.

It has been suggested that the addition of alkyl halides to enones promoted by Zn/CuI involves a radical intermediate.[5] This was supported by three key observations: (1) the reaction works in protic/aqueous solvents, (2) the order of reactivity of the alkyl halides parallels the stability of their corresponding radicals, and (3) the reaction was inhibited by the addition of cumene. Our observations are consistent with (1) and (2) above; however, we found that addition of the radical inhibitors galvinoxyl (0.5 equiv) or cumene (2 equiv) had no impact on the reaction in formamide. The reactions with 1-iodo-5-hexene and with cyclopropylmethyl iodide both showed the expected rearrangements consistent with formation of radical intermediates.[10] Such radicals may be formed by an initial single-electron transfer from the Zn/CuI adduct as suggested by Luche (Scheme 1).

SCHEME 1. Radical Mechanism?



In summary, we have developed a general and high-yielding Zn/CuI-mediated coupling of alkyl iodides and bromides to vinyl sulfones, sulfonates, and sulfonamides. Primary, secondary, and tertiary alkyl halides all work equally well. This protocol is also compatible with a wide range of functional groups. Formamide is found to be crucial for obtaining high yields by virtue of being exceedingly polar and possessing a suitable pK_a.

Experimental Section

^{1}H NMR and ^{13}C NMR spectra were taken in $CDCl_3$ at 400 and 100 MHz, respectively. All reagents and solvents were purchased and used without further purification unless otherwise noted. Zinc dust (<10 μm) purchased from Aldrich performed well. Zinc dust from other vendors may perform differently.

General Procedure. A mixture of zinc dust (20 mmol, <10 μm, Aldrich) and CuI (5.0 mmol) in formamide (10 mL) was stirred for 15 min at 0−10 °C. The vinyl sulfone, sulfonamide, or sulfonate (12 mmol) was added followed by the alkyl iodide (10 mmol). The mixture was aged at 0 °C for a few hours, then warmed to room temperature, and stirred until the reaction was complete. EtOAc (30 mL) was added, and the precipitate was filtered off and rinsed with EtOAc (Caution! the Zn/CuI residue should not be sucked completely dry as it may self-ignite in air, particularly on larger scale. It should be covered by water after the filtration and EtOAc rinse). To the filtrate were added HCl (0.6 N, 30 mL) and heptane (15 mL). The product was in the organic layer and was isolated either by crystallization or silica gel column purification. On larger scales, to control the temperature to <10 °C, CuI was added in portions. For alkyl bromides, the reaction mixture was warmed to room temperature after charging the substrate since the reaction was slow at 0−5 °C.

Sulfones.

Phenyl Hexyl Sulfone (2a): From R−I, yield, 70%; oil. ^{1}H NMR δ 7.91−7.93 (m, 2H), 7.64−7.68 (m, 1H), 7.55−7.60 (m, 2H), 3.06−3.11 (m, 2H), 1.68−1.74 (m, 2H), 1.32−1.40 (m, 2H), 1.21−1.30 (m, 4H), 0.86 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 139.1, 133.5, 129.1, 127.8, 56.1, 31.0, 27.7, 22.4, 22.1, 13.7; Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.44; H, 8.02.

(10) It should be noted that cyclopropylmethylmagnesium halides also undergo virtually complete rearrangement to the butenylmagnesium halides at room temperature: (a) Patel, D. J.; Hamilton, C. L.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 5144−5148. 5-Hexenylmagnesium halides do not rearrange at room temperature: (b) Eisch, J. J.; Behrooz, M.; Galle, J. E. *Tetrahedron Lett.* **1984**, *25*, 4851−4854.

Phenyl 3-Methylpentyl Sulfone (2b): from R−I; yield, 80%; oil. ^{1}H NMR δ 7.88 (d, J = 7.2 Hz, 2H), 7.61−7.64 (m, 1H), 7.52−7.56 (m, 2H), 2.98−3.12 (m, 2H), 1.65−1.74 (m, 1H), 1.45−1.54 (m, 1H), 1.34−1.42 (m, 1H), 1.20−1.29 (m, 1H), 1.06−1.15 (m, 1H), 0.77−0.82 (m, 6H); ^{13}C NMR δ 139.3, 133.7, 129.3, 128.1, 54.5, 33.5, 29.0, 28.8, 18.8, 11.2; Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.55; H, 8.16.

Phenyl 3,3-Dimethylbutyl Sulfone (2c): from R−I; yield, 91% white solid, mp 65.6−66.3 °C. ^{1}H NMR δ 7.93 (d, J = 7.6 Hz, 2H), 7.65−7.69 (m, 1H), 7.57−7.61 (m, 2H), 3.05−3.09 (m, 2H), 1.59−1.64 (m, 2H), 0.98 (s, 9 H); ^{13}C NMR δ 139.3, 133.7, 129.4, 128.1, 53.0, 35.7, 30.1, 29.0; Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02. Found: C, 63.84; H, 8.10.

Phenyl 4-Phenylbutyl Sulfone (2d): from R−I; yield, 59%; white solid, mp 74.9−75.4 °C. ^{1}H NMR δ 7.88−7.92 (m, 2 H), 7.64−7.69 (m, 1H), 7.55−7.59 (m, 2H), 7.24−7.28 (m, 2H), 7.16−7.20 (m, 1H), 7.11 (d, J = 7.2 Hz, 2H), 3.11 (t, J = 7.2 Hz, 2H), 2.60 (t, J = 7.2 Hz, 2H), 1.67−1.82 (m, 4H); ^{13}C NMR δ 141.4, 139.4, 133.8, 129.5, 128.6, 128.5, 128.3, 126.2, 56.3, 35.5, 30.2, 22.5; Anal. Calcd for $C_{16}H_{18}O_2S$: C, 70.04; H, 6.62; S, 11.69. Found: C, 70.04; H, 6.61; S, 11.99.

Ethyl 4-Phenylbutyl Sulfone (2e): from R−I; yield, 77%; oil. ^{1}H NMR δ 7.27−7.32 (m, 2H), 7.17−7.23 (m, 3H), 2.94−2.99 (m, 4H), 2.68 (t, J = 7.6 Hz, 2H), 1.85−1.93 (m, 2H), 1.76−1.84 (m, 2H), 1.39 (t, J = 7.6 Hz, 3H); ^{13}C NMR δ 141.4, 128.7, 128.6, 126.3, 52.0, 47.3, 35.5, 30.4, 21.7, 6.8; Anal. Calcd for $C_{12}H_{18}O_2S$: C, 63.68; H, 8.02; S, 14.17. Found: C, 63.32; H, 8.24; S, 14.31.

Phenyl 6,6,6-Trifluorohexyl Sulfone (2m): from R−Br; yield, 80%; oil. ^{1}H NMR δ 7.90 (d, J = 8.0 Hz, 2H), 7.65−7.69 (m, 1H), 7.57−7.61 (m, 2H), 3.10 (t, J = 8.4 Hz, 2H), 1.99−2.11 (m, 2H), 1.73−1.80 (m, 2H), 1.43−1.57 (m, 4H); ^{13}C NMR δ 139.4, 134.0, 129.6, 128.2, 127.3 (q, $^1J_{C-F}$ = 276.0 Hz), 56.1, 33.6 (q, $^2J_{C-F}$ = 29.0 Hz), 27.6, 22.6, 21.7; Anal. Calcd for $C_{12}H_{15}F_3O_2S$: C, 51.42; H, 5.39. Found: C, 51.12; H, 5.33.

Phenyl 3-(2-Tetrahydrafuranyl)propyl Sulfone (2n): from R−Br; yield, 62%; oil. ^{1}H NMR δ 7.90 (d, J = 8.0 Hz, 2H), 7.64−7.68 (m, 1H), 7.56−7.60 (m, 2H), 3.73−3.84 (m, 2H), 3.65−3.72 (m, 1H), 3.09−3.23 (m, 2H), 1.92−2.00 (m, 1H), 1.77−1.89 (m, 4H), 1.55−1.62 (m, 2H), 1.38−1.46 (m, 1H); ^{13}C NMR δ 139.2, 133.7, 129.3, 128.1, 78.5, 67.8, 56.3, 34.1, 31.4, 25.7, 20.0.

Phenyl 4-Cyanobutyl Sulfone (2o): from R−Br, yield, 72%; white solid; mp 58.5−59.3 °C. ^{1}H NMR δ 7.93 (d, J = 7.6 Hz, 2H), 7.68−7.71 (m, 1H), 7.58−7.62 (m, 2H), 3.14 (t, J = 7.2 Hz, 2H), 2.39 (t, J = 6.8 Hz, 2H), 1.88−1.96 (m, 2 H), 1.79−1.86 (m, 2H); ^{13}C NMR δ 138.7, 133.9, 129.3, 127.9, 118.9, 55.0, 23.9, 21.8, 16.7; Anal. Calcd for $C_{11}H_{13}NO_2S$: C, 59.17; H, 5.87; N, 6.27. Found: C, 58.96; H, 5.68; N, 5.98.

Sulfonates.

Phenyl 3-Methylpentanesulfonate (4a): from R−I; yield, 84%; oil. ^{1}H NMR δ 7.40−7.44 (m, 2H), 7.27−7.34 (m, 3H), 3.15−3.31 (m, 2H), 1.95−2.06 (m, 1H), 1.75−1.85 (m, 1H), 1.49−1.60 (m, 1H), 1.34−1.44 (m, 1H), 1.18−1.29 (m, 1H), 0.94 (d, J = 6.4 Hz, 3H), 0.92 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 149.4, 130.1, 127.3, 122.3, 48.9, 33.6, 29.9, 29.1, 18.9, 11.3.

Phenyl 3,3-Dimethylbutanesulfonate (4b): from R−I; yield, 85%; oil. ^{1}H NMR δ 7.41−7.44 (m, 2H), 7.23−7.34 (m, 3H), 3.21−3.26 (m, 2H), 1.87−1.92 (m, 2H), 0.97 (s, 9H); ^{13}C NMR δ 149.4, 130.2, 127.4, 122.2, 47.4, 36.8, 30.4, 29.1; Anal. Calcd for $C_{12}H_{18}O_3S$: C, 59.47; H, 7.49. Found: C, 59.36; H, 7.62.

Phenyl 5-Cyanopentanesulfonate (4c): from R−Br; 72% yield; oil. ^{1}H NMR δ 7.42−7.45 (m, 2H), 7.32−7.36 (m, 1H), 7.28 (d, J = 8.4 Hz, 2H), 3.28 (t, J = 7.6 Hz, 2H), 2.41 (t, J = 6.8 Hz, 2H), 2.00−2.08 (m, 2H), 1.64−1.79 (m, 4H); ^{13}C NMR δ 149.2, 130.2, 127.4, 122.1, 119.3, 50.1, 27.2, 25.0, 23.0, 17.0.

Ethyl Hexanesulfonate (4d): from R−I; yield, 83%; oil. ^{1}H NMR δ 4.28 (q, J = 7.2 Hz, 2H), 3.07 (t, J = 8.0 Hz, 2H), 1.81−1.89 (m, 2H), 1.38−1.46 (m, 2H), 1.40 (t, J = 7.2 Hz, 3H), 1.28−1.35 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 66.0, 50.7, 31.3, 28.0, 23.6, 22.4, 15.3, 14.1.

Sulfonamides.

***N,N*-Diethyl Hexanesulfonamide (5a):** from R−I; yield, 88%; oil. ^{1}H NMR δ 3.30 (q, J = 7.2 Hz, 4H), 2.91 (t, J = 8.0 Hz, 2H), 1.75−1.83 (m, 2H), 1.37−1.44 (m, 2H), 1.28−1.34 (m, 4H), 1.21 (t, J = 7.2 Hz, 6H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 52.6, 41.7, 31.5, 28.3, 23.7, 22.6, 14.7, 14.2; Anal. Calcd for $C_{10}H_{23}NO_2S$: C, 54.26; H, 10.47; N, 6.33. Found: C, 54.35; H, 10.52; N, 6.18.

***N,N*-Diethyl 3-Methylpentanesulfonamide (5b):** from R−I; yield, 83%; oil. ^{1}H NMR δ 3.30 (q, J = 7.2 Hz, 4H), 2.85−2.99 (m, 2H), 1.77−1.87 (m, 1H), 1.56−1.66 (m, 1H), 1.41−1.50 (m, 1H), 1.30−1.41 (m, 1H), 1.17−1.24 (m, 1H), 1.21 (t, J = 7.2 Hz, 6H), 0.91 (d, J = 7.1 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 50.6, 41.7, 33.7, 29.8, 29.1, 18.9, 14.6, 11.3; Anal. Calcd for $C_{10}H_{23}NO_2S$: C, 54.26; H, 10.47; N, 6.33. Found: C, 54.23; H, 10.52; N, 6.27.

***N,N*-Diethyl 3,3-Dimethylbutanesulfonamide (5c):** from R−I; yield, 94%; oil. ^{1}H NMR δ 3.31 (q, J = 7.2 Hz, 4H), 2.89−2.93 (m, 2H), 1.66−1.70 (m, 2H), 1.21 (t, J = 7.2 Hz, 6H), 0.93 (s, 9H); ^{13}C NMR δ 49.2, 41.7, 36.9, 30.3, 29.3, 14.7; Anal. Calcd for $C_{10}H_{23}NO_2S$: C, 54.26; H, 10.47; N, 6.33; S, 14.49. Found: C, 54.04; H, 10.55; N, 6.06; S, 14.81.

***N*-Benzyl 5-Ethoxycarbonylpentanesulfonamide (5g):** from R−Br; yield, 85%; white solid, mp 45.5−45.9 °C. ^{1}H NMR δ 7.29−7.41 (m, 5H), 4.48 (br, t, J = 6.8 Hz, 1H), 4.31 (d, J = 6.8 Hz, 2H), 4.13 (q, J = 7.2 Hz, 2H), 2.93 (t, J = 7.2 Hz, 2H), 2.29 (t, J = 7.2 Hz, 2H), 1.75−1.82 (m, 2H), 1.58−1.65 (m, 2H), 1.36−1.44 (m, 2H), 1.27 (d, J = 7.2 Hz, 3H); ^{13}C NMR δ 173.6, 137.4, 129.1, 128.3, 128.1, 60.6, 53.3, 47.4, 34.0, 27.8, 24.5, 23.5, 14.4; Anal. Calcd for $C_{15}H_{23}NO_4S$: C, 57.48; H, 7.40; N, 4.47. Found: C, 57.46; H, 7.42; N, 4.44.

***N*-Benzyl 4-Phenoxybutanesulfonamide (5h):** from R−Br; 66%; white solid; mp 85.0−86.0 °C. ^{1}H NMR δ 7.38−7.27 (m, 5H), 7.27−7.32 (m, 2H), 6.96 (t, J = 7.2 Hz, 1H), 6.87 (d, J = 9.2 Hz, 2H), 4.47 (br, t, J = 6.8 Hz, 1H), 4.32 (d, J = 6.8 Hz, 2H), 3.95 (t, J = 6.0 Hz, 2H), 3.03 (t, J = 7.6 Hz, 2H), 1.95−2.03 (m, 2H), 1.83−1.90 (m, 2H); ^{13}C NMR δ 158.9, 137.1, 129.7, 129.1, 128.3, 128.2, 121.1, 114.7, 67.0, 53.2, 47.4, 28.0, 21.0; Anal. Calcd for $C_{17}H_{21}NO_3S$: C, 63.92; H, 6.63; N, 4.39. Found: C, 63.76; H, 6.42; N, 4.24.

***N*-Benzyl 5-(1*H*-Pyrrol-1-yl)-pentanesulfonamide (5i):** from R−Br; yield, 88%; oil. ^{1}H NMR δ 7.29−7.39 (m, 5H), 6.62−6.65 (m, 2H), 6.13−6.16 (m, 2H), 4.49 (br t, J = 6.0 Hz, 1H), 4.29 (d, J = 6.0 Hz, 2H), 3.87 (t, J = 7.2 Hz, 2H), 2.89 (t, J = 8.0 Hz, 2H), 1.71−1.79 (m, 4H), 1.30−1.38 (m, 2H); ^{13}C NMR δ 137.0, 129.1, 128.4, 128.2, 120.7, 108.3, 53.4, 49.3, 47.5, 31.2, 25.6, 23.5; Anal. Calcd for $C_{16}H_{22}N_2O_2S$: C, 62.71; H, 7.24; N, 9.14. Found: C, 62.67; H, 7.30; N, 9.06.

Acknowledgment. We dedicate this paper to Professor Iwao Ojima on the occasion of his 60th birthday. We thank Pete Dormer and Robert Reamer for NMR assistance.

Supporting Information Available: Characterization data including ^{1}H, ^{13}C, and elemental analysis for **2f**−**2k**, **2p**−**2v**, and **4e**−**4j**, and **5d**−**5f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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