hexane)pyrrolidine, 81230-62-8; *N*-(2-methylthioheptyl)acetamide, 81230-63-9; 1-(2-methylthioheptyl)pyrrolidine, 81230-64-0; 11-azido-10-(methylthio)undecanoic acid methyl ester, 81230-65-1; 10-azido-11-(methylthio)undecanoic acid methyl ester, 81230-66-2; (*R**,*S**)-1-phenyl-2-(methylthio)propanamine, 81230-67-3; *trans*-*N*-acetyl-1-methyl-2-(methylthio)cyclohexanamine, 81230-68-4; *trans*-*N*-acetyl-2-methyl-2-(methylthio)cyclohexanamine, 81230-69-5; *trans*-1-(1-methyl-2-(methylthio)cyclohexyl)pyrrolidine, 81230-70-8; *trans*-1-(2-methyl-2-(methylthio)cyclohexyl)pyrrolidine, 81230-71-9; *trans*-1-azido-1-methyl-2-(methylthio)cyclohexane, 81230-72-0; *trans*-1-azido-2-methyl-2-(methylthio)cyclohexane, 81230-73-1; (*R**,*S**)-*N*-acetyl-1-phenyl-2-(methylthio)propanamine, 81230-74-2; 4-acetamido-4-((methylthio)methyl)heptane, 81230-75-3.

Nucleophilic Attack on Olefins Initiated by Dimethyl(methylthio)sulfonium Fluoroborate (DMTSF). Cyanosulfenylation and Oxy- and Oxosulfenylation

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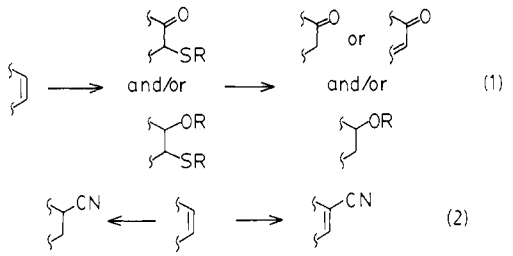
Nucleophilic addition to and substitution in olefins enhances synthetic flexibility by complementing the more usual electrophilic reactions. In exploration of new avenues for such a strategy, attention was focused on nucleophilic introduction of an oxygen substituent and a nitrile group. While the versatile β-hydroxy and β-keto sulfides normally derive from sulfenylation of a carbonyl compound,[1,2] the ready availability of olefins as basic building blocks stimulates a search for simple methods to introduce such functionality directly via the carbon–carbon double bond (eq 1).[3-5] Similarly, very limited methods exist for cyanation of olefins

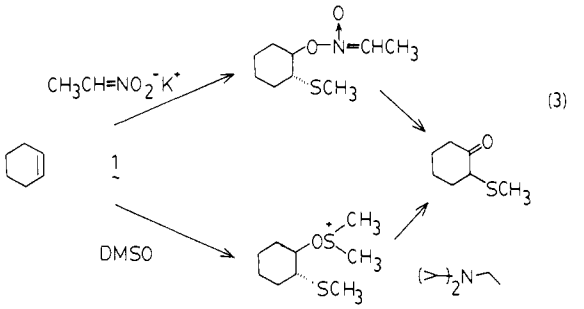


(1) (2)

(eq 2), again a versatile type of substituent.[6-8] The chemoselective activation of olefins for nucleophilic attack by dimethyl(methylthio)sulfonium fluoroborate[9] (DMTSF, **1**), a readily available and convenient reagent that to date has found virtually no synthetic applications,[10,11] offers an attractive solution to both problems.

Three types of oxygen nucleophiles were examined—hydroxide, carboxylate, and Me_2SO as summarized in Table I. Typically, for hydroxide and acetate as the nucleophiles, the olefin and **1** were mixed in the stated organic solvent. Subsequently, either an aqueous carbonate solution (for hydroxide) or anhydrous powdered potassium acetate was added at ambient temperature. While reactions were slow (3–5 days), they were very clean, and pure products were isolated in high yield. In two cases (entries 4 and 6), an advantageous effect on the yield was noted by the addition of a small amount of dimethyl sulfide. Entries 7 and 14 illustrate the chemoselectivity. Complementary regioselectivity is exhibited by these two nucleophiles with hydroxide giving mainly Markovnikov addition (entries 2–4 and 7) and acetate giving mainly anti-Markovnikov addition (entry 5). Entries 4 and 5 nicely illustrate the ability of obtaining both types of products selectively from the same olefin by this simple manipulation of reaction conditions. Spectral analysis allows easy assignment of both the regiochemistry and stereochemistry (i.e., a clean trans addition; see entries 1, 2, 6).

While the hydroxy sulfides can be envisioned as precursors to β-keto sulfides, direct conversion to β-keto sulfides would be desirable. Two approaches were examined (eq 3). In the first,



O-alkylation of a nitronate salt by the olefin-**1** complex followed by elimination of nitrosoethane would generate the desired product. While this expectation was fulfilled, substantial amounts of the corresponding β-hydroxy sulfide, which presumably arose by simple hydrolysis of the nitronate intermediate, accompanied it. Surprisingly, Me_2SO proved to be a sufficient nucleophile.[12,13] Addition of diisopropylethylamine to the initial adduct completed the conversion to the desired β-keto sulfide. Three procedures were employed. In the first, the olefin was reacted sequentially with **1**, Me_2SO, and then base at room temperature (entries 8, 13, 14). In the second, the olefin was mixed with **1**, Me_2SO, and base in CCl_4 and then heated to 60 °C (entry 9). In the third and preferred method, the olefin and **1** were mixed in methylene chloride and, after 15 min, Me_2SO, HgO, and diisopropylethylamine added in rapid succession (entries 10–13), all at room temperature.

A typical procedure for cyanosulfenylation involves mixing DMTSF (1 equiv) with the olefin (1–2 equiv) in acetonitrile followed by addition of finely powdered sodium cyanide at room temperature. Use of acetonitrile containing 1–3% (v/v) of dimethyl sulfide sometimes improved the yield. While this reaction is slow (1–3 days), it proceeds cleanly, which allows isolation of the products in good yield by simple distillation as summarized

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(9) Meerwein, H.; Zenner, K. F.; Gipp, R. *Justus Liebigs Ann. Chem.* **1965**, *688*, 67. Helmkamp, G. K.; Cassey, H. N.; Olsen, B. A.; Pettitt, D. J. *J. Org. Chem.* **1965**, *30*, 933. Smallcombe, S. H.; Caserio, M. C. *J. Am. Chem. Soc.* **1971**, *93*, 5826.
(10) For reactions of **1** and related salts with olefins see: Helmkamp, G. K.; Olsen, B. A.; Koskinen, J. R. *Ibid.* **1965**, *30*, 1623. Capozzi, G.; DeLucchi, O.; Lucchni, V.; Modena, G. *Tetrahedron Lett.* **1975**, 2603.
(11) For a synthetic application of this most intriguing reagent see: Trost, B. M.; Murayama, E. *J. Am. Chem. Soc.* **1981**, *103*, 6529.
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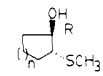
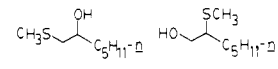
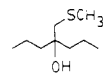
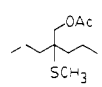
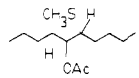
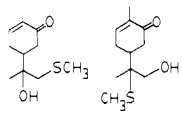
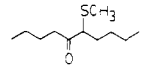
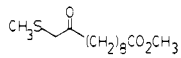
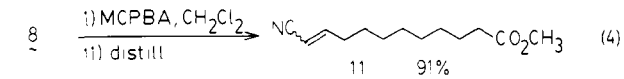
Table I. Oxy- and Oxo-Sulfenylation of Olefins

entry	olefin	nucleophile (solvent)	product[e]	yield,[f] %
	 2		 3	
1	2, R = H; n = 2	$NaHCO_3$, $H_2O(CH_3CN)$	3, R = H; n = 2	92
2	2, R = CH_3; n = 2	$CaCO_3$, $H_2O(CH_2Cl_2)$	3, R = CH_3; n = 2	93
3	1-heptene	$NaHCO_3$, $H_2O(CH_3NO_2)$	 55 45	76
4	2-propyl-1-pentene 4	$CaCO_3$, H_2O (CH_2Cl_2-DMS[a])		97
5	4	KOAc(CH_3CN)	 [b]	97
6	(E)-5-decene	KOAc(CH_3CN-DMS[a])		98
7	carvone	$NaHCO_3$, $H_2O(CH_3CN)$	 79 21	83
			 5	
8	2, R = H; n = 2	Me_2SO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_3NO_2)$	5, n = 2	72
9	2, R = H; n = 4	Me_2SO, $(i\text{-}C_3H_7)_2NC_2H_5(CCl_4)$	5, n = 4	87
10	2, R = H; n = 8	Me_2SO, HgO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_2Cl_2)$	5, n = 8	88
11	(E)-5-decene	Me_2SO, HgO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_2Cl_2)$		79
12	cycloocta-1,5-diene	Me_2SO, HgO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_2Cl_2)$		71
13	(E)-1-phenylpropene			
a		Me_2SO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_2Cl_2)$		83[c]
b		Me_2SO, HgO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_2Cl_2)$		81
14	methyl 10-undecenoate (6)	Me_2SO, $(i\text{-}C_3H_7)_2NC_2H_5(CH_3NO_2)$		84[d]

[a] 0.7–1% (v/v) of dimethyl sulfide added. [b] This product was an 84:16 ratio of the two regioisomers with only the major regioisomer depicted. [c] In addition, 5% of the regioisomeric product was isolated by prep TLC. [d] The major regioisomer of the product is depicted. The ratio of the two regioisomers varied from 2.5–4:1. [e] All products have been fully characterized by spectral analysis. New compounds have also been characterized by combustion analysis and/or high-resolution mass spectroscopy. [f] All yields are for isolated pure products. Isolation was typically by distillation, and regioisomers, when present, were separated chromatographically.

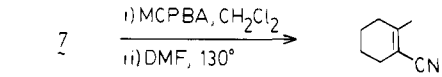
in Table II. In several instances (cyclopentene and methyl 10-undecenoate) substantial amounts of vicinal disulfenylation arising from demethylation of the olefin adduct of **1** complicated the reaction.[14] This problem was eliminated by mixing the olefin with **1** in nitromethane, evaporating in vacuo, and then adding an aqueous or methanolic solution which is 4 M in sodium cyanide and 2 M in fluoroboric acid (**Caution**: in situ HCN generation!).

The most critical question is that of regioselectivity. With a monosubstituted olefin, only the anti-Markovnikov addition product was observed (entry 9). Verification of this assignment, which also demonstrates the equivalent of nucleophilic substitution, utilized elimination to the conjugated nitrile **11** (eq 4), which was



(4)

produced as a 1:1 E/Z mixture.[15,16] In the cases of the 1,1-di- or trisubstituted olefins, the regiochemistry depended upon the nucleophilicity of the cyanide source. Decreasing the nucleophilicity of the cyanide enhanced the Markovnikov adduct (entries 5–12), which became the dominant to exclusive adduct upon using trimethylsilyl cyanide. The orientation was deduced from the NMR spectra and confirmed in the cases of **3** and **6** by elimination to the conjugated nitriles (eq 5 and 6). Each adduct capable of



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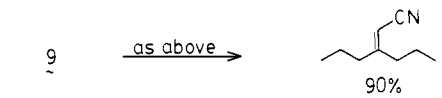

(6)

forming mixtures of stereoisomers is assumed to be trans except

(14) Cf. ref 10. For some recent studies see: Kim, J. K.; Caserio, M. C. *J. Org. Chem.* **1979**, *44*, 1897. Kline, M. L.; Beutow, N.; Kim, J. K.; Caserio, M. C. *Ibid.* **1979**, *44*, 1904.

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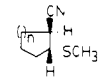
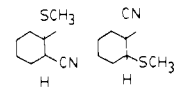
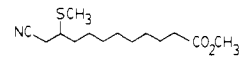
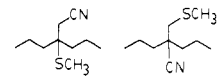
(16) Cf. Heathcock, C. H.; Brattesam, D. N. *Tetrahedron Lett.* **1974**, 2279.

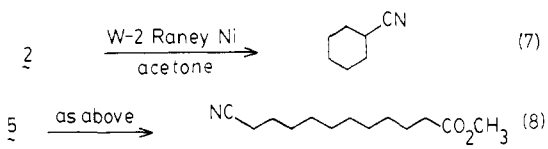
Table II. Cyanosulfenylation of Olefins

entry	olefin	nucleophile[a]	solvent	product[h]		yield,[i] %
				 6		
1	cyclopentene	NaCN, HBF_4	CH_3NO_2, H_2O[b]	6, $n = 1$		79
2	cyclopentene	NaCN, HBF_4	CH_3NO_2, CH_3OH	6, $n = 1$		68
3	cyclohexene	NaCN	CH_3CN	6, $n = 2$		94
4	cyclohexene	NaCN, HBF_4	CH_3NO_2, H_2O[b]	6, $n = 2$		80
	1-methylcyclohexene			 7		
5		KCN	CH_3CN[c]	92	8	99
6		NaCN	CH_3CN[d,f]	87	13	
7		LiCN, $LiClO_4$	CH_3CN[d,f]	79	21	
8		Me_3SiCN	CH_2Cl_2[d]	31	69	72[j]
	methyl 10-undecenoate			 8		
9		NaCN, HBF_4	CH_3NO_2, CH_3OH[b]			81[k]
	2-propyl-1-pentene (4)			 9	10	
10		NaCN	CH_3CN, $(CH_3)_2S$	98	2	99
11		LiCN, $LiClO_4$	CH_3CN, CF_3CH_2OH[d-f]	95	5	
12		Me_3SiCN	CH_2Cl_2[f,g]	35	52	

[a] The KCN and NaCN were ground into fine powders and dried. [b] In this case, after the initial reaction of the olefin with 1, the solvent listed first was evaporated and the solvent listed second was added. [c] Reaction performed at −10 °C for 2 days, 0 °C for 30 h. [d] Reaction performed at 0 °C. [e] A 3:4 mixture of solvents was employed. [f] Only the relative ratio of products was determined. [g] The remaining 13% was the thiohydrin. [h] All the products except 10 were isolated pure and completely characterized spectrally and the elemental composition determined either by combustion analysis or high-resolution mass spectroscopy. [i] In all cases except where otherwise noted the pure products were isolated by simple distillation. [j] Each pure regioisomer was obtained by flash chromatography. [k] In this case, the product isolated by simple distillation in quantitative yield contained four small impurities as determined by GLC. HPLC (6:1 hexane/ethyl acetate) separation provided the pure product in the stated yield.

for **6**, $n = 2$, where the NMR spectrum permits unambiguous assignment of the trans stereochemistry.

For explicit demonstration of the equivalent of nucleophilic addition to an olefin, adducts **2** and **5** were desulfurized with W-2 Raney Ni (eq 7 and 8).[17] Thus, this method holds promise as a versatile approach for nucleophilic addition and substitution of simple olefins.



The convenience and mildness of this method for oxo- and oxysulfenylation are particularly noteworthy. This method has greater versatility in the choice of the oxygen and sulfur substitution than other recently reported oxysulfenylations.[3] Multistep procedures proceeding through sulfenyl halides suffer because of the inherent instability of such compounds, their low regio- and chemoselectivity, and the relative inertness of the initial olefin adducts.[4] Reductive desulfurization of these adducts constitutes a net conversion of an olefin to a ketone[18] or to a hydration of an olefin.[11,12] The ability to control the regiochemistry of the nucleophilic attack then translates into a Markovnikov or an anti-Markovnikov hydration—a type of flexibility generally lacking in other approaches. The flexibility of the nitrile in terms of conversion to esters,[20] ketones,[21] aldehydes,[22] and amines[22,23] converts cyanosulfenylation into a versatile functionalization of an olefin. The generality of this type of approach for nucleophilic functionalization of an olefin is being actively pursued. The question of the involvement of episulfonium ions, while appealing, is not necessarily required or in complete accord with the reactivity patterns observed for such species.[5] On the other hand, direct displacement of the known initial olefin adducts of **1** is precluded by the overall trans stereochemistry. The question of mechanism will be probed in future work.

Acknowledgment. We thank the National Science Foundation for their generous support of our programs.

Registry No. **1**, 8799-67-7; **2** (R = H, $n = 2$), 110-83-8; **2** (R = CH_3, $n = 2$), 591-49-1; **2** (R = H, $n = 4$), 931-88-4; **2** (R = H, $n = 8$), 1501-82-2; **3** (R = H, $n = 2$), 41578-04-5; **3** (R = CH_3, $n = 2$), 81230-76-4; **4**, 15918-08-8; **5** ($n = 2$), 52190-35-9; **5** ($n = 4$), 52190-37-1; **5** ($n = 8$), 52190-38-2; **6** ($n = 1$), 81230-77-5; **6** ($n = 2$), 81230-78-6; **7**, isomer I, 81230-79-7; **7**, isomer II, 81230-80-0; **8**, 81230-81-1; **9**, 81230-82-2; **10**, 81230-83-3; 5-(2-hydroxy-3-(methylthio)prop-2-yl)-2-methyl-3-oxo-1-cyclohexene, 81230-88-8; 5-(3-hydroxy-2-(methylthio)-prop-2-yl)-2-methyl-3-oxo-1-cyclohexene, 81230-89-9; 6-(methylthio)-5-oxodecane, 81230-90-2; 6-(methylthio)-5-oxocyclooctene, 81230-91-3; 2-(methylthio)-1-phenyl-1-propanone, 14236-72-7; 11-(methylthio)-10-oxoundecanoic acid methyl ester, 81230-92-4; 1-cyano-2-methylcyclohexene, 4883-65-2; 4-(cyanomethylene)heptane, 54353-88-7.

(17) Hauptmann, H.; Walter, W. F. *Chem. Rev.* **1962**, *62*, 347.
(18) Cf. methods via epoxide (House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin: Menlo Park, CA, 1972) or via a Wacker type of reaction (Tsuji, J.; Shimizu, I.; Yamamoto, K. *Tetrahedron Lett.* **1976**, 2975. Fahey, D. R.; Zuech, E. A. *J. Org. Chem.* **1974**, *39*, 3276).
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