Table II. ^{13}C NMR Parameters of Protonated Methoxythioanisoles in 11.5 mol % SbF_5-FSO_3H at -60 °C

starting base	^{13}C NMR chemical shifts and multiplicities[a]							
	C1	C2	C3	C4	C5	C6	C7	C8
1	119.4 (s)	186.5 (s)	121.6 (d)	180.8 (d)*	43.4 (br)	179.6 (d)*	66.2 (q)	20.5 (q)
2	121.4 (s)	135.0 (d)*	151.9 (s)	125.3 (d)	122.6 (d)	134.7 (d)*	74.4 (q)	23.0 (q)
3	121.0 (s)	135.9 (d)	121.1 (d)	155.3 (s)	121.1 (d)	135.9 (d)	73.4 (q)	23.2 (q)

[a] ^{13}C NMR chemical shifts are in parts per million from external (capillary) Me_4Si, multiplicities are given in parentheses: s = singlet, d = doublet, q = quartet, br = broad. Resonances which are labeled with asterisks have interchangeable assignments. Numbering of the atoms is the same as in Table I.

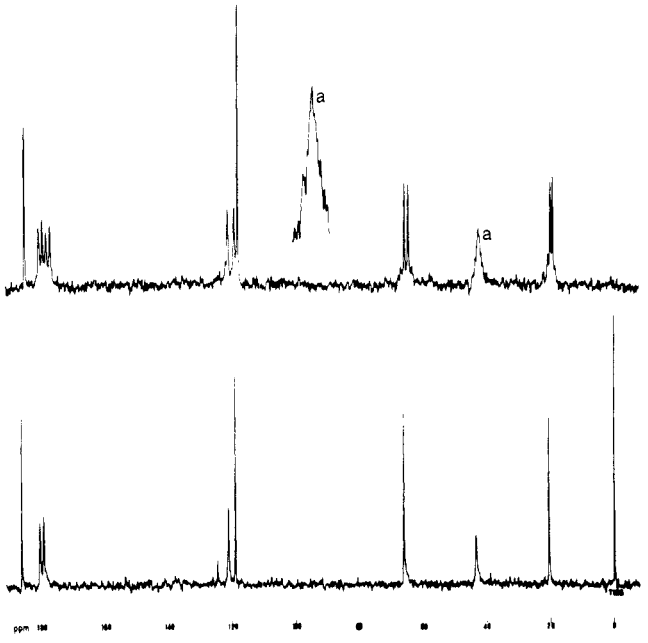

Figure 2. ^{13}C NMR spectra of the *o*-methoxythioanisole **1** in 11.5 mol % SbF_5-FSO_3H solution at -60 °C. The lower portion is the proton-decoupled spectrum, and the upper is the off-resonance proton-decoupled spectrum.

sively at sulfur. The ^1H NMR spectrum of the solution shows a thiomethoxy doublet at δ 3.09 (J = 7 Hz, 3 H), a OCH_3 singlet at δ 4.31 (3 H), a ring-proton multiplet between δ 7.19 and 7.83 (4 H), and an ^+SH quartet centered at δ 8.11 (J = 7 Hz, 1 H).

Contrary to *o*-methoxythioanisole, isomers **2** and **3** did not display ring protonation in 11.5 mol % SbF_5-FSO_3H solution. Both bases give similar ^1H NMR spectra (Table I), indicative of S-protonation. The spectra show a doublet around δ 3.3 assigned to the SCH_3 protons and a rather broad singlet around δ 5.0 ascribed to the methoxy protons. The aromatic protons of protonated base **2** are centered as a multiplet at δ 8.10, while those of protonated isomer **3** show two doublets between δ 7.88 and 8.22 (Table I). The ^{13}C NMR spectra (Table II) of protonated **2** and **3** show also the typical changes of sulfur-protonated ions,[3,8] although on the basis of a significant downfield chemical shift for the methoxy carbon atoms and an observed upfield shift of the ring carbon atom ipso to the OCH_3 group (7.0 ppm for isomer **2** and 3.0 ppm for isomer **3**) attachment of the proton to the oxygen atom cannot be excluded.

Experimental Section

The sulfides **1-3** were prepared by methylation of the related thiophenols with methyl sufate in base.[11] Thiophenols were synthetized by routine methods, either from the corresponding anisidines[12] (ortho and meta isomers) or by reduction of the corresponding sulfonyl chloride[13] (para isomer). All compounds were purified by vacuum distillation prior to the protonation study.

The fluorosulfonic acid (Fluka) and antimony pentafluoride (Merck) were purged with dry nitrogen for several hours and distilled in vacuo before use. Ions for NMR measurements were prepared by low-temperature dissolution of base in an excess of superacid under nitrogen.[5] After their NMR analyses, the solutions were quenched as previously described.[5] The starting sulfides were recovered quantitatively in all cases, as indicated by their GC, IR, and NMR analyses.

The ^1H NMR spectra were measured on a JEOL PS-100 spectrometer equipped with a variable-temperature probe. The ^{13}C NMR studies were performed on a JEOL JNM FX-100 spectrometer, also equipped with a variable-temperature probe, by using the Fourier transform method.

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Registry No. 1, 2388-73-0; 1 S-protonated, 73891-69-7; 1 diprotonated, 73953-50-1; 2, 2388-74-1; 2 S-protonated, 73891-70-0; 3, 1879-16-9; 3 S-protonated, 73926-77-9; SbF_5, 7783-70-2; FSO_3H, 7789-21-1.

(10) G. L. Nelson and E. A. Williams, *Prog. Phys. Org. Chem.*, 12, 229-342 (1976), and references therein.
(11) E. I. Vogel "Textbook of Practical Organic Chemistry", 3rd ed., Longmans, Green and Co., London, New York, Toronto, 1956, p 670.
(12) E. Campaigne and S. W. Osborn, *J. Org. Chem.*, 21, 561 (1957).
(13) R. Adams and C. S. Marvel, "Organic Syntheses", Collect. Vol. I, Wiley, New York, 1941, p 504.

A New Route to Simple Monoterpenes by Remote Functionalization

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We have developed a new method which enables remote functionalization of a nonactivated methylene or methine carbon.[1,2] The synthetic utility of this procedure is illustrated by the preparation of some monoterpenes.

We believe that this stereospecific approach, applied here to simple models, could be extended to other synthetic problems such as specific labeling or preparation of new steroid compounds.[3]

(1) (a) J. P. Bégué, M. Charpentier-Morize, and C. Pardo, *Tetrahedron*, 31, 1919 (1975); (b) J. P. Bégué, D. Bonnet, M. Charpentier-Morize, and C. Pardo, *Tetrahedron*, 31, 2505 (1975); (c) D. Baudry, Thèse d'Etat, Université de Paris-Sud, Orsay 91, France, 1975.
(2) (a) D. Baudry, M. Charpentier-Morize, D. Lefort, and J. Sorba, *Tetrahedron Lett.*, 2449 (1974); (b) C. Pardo, Thèse d'Etat, Université de Paris-Sud, Orsay 91, France, 1977.
(3) J. P. Bégué, unpublished results.

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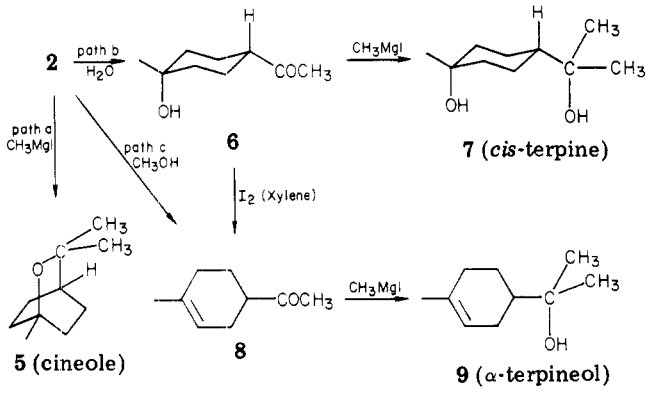
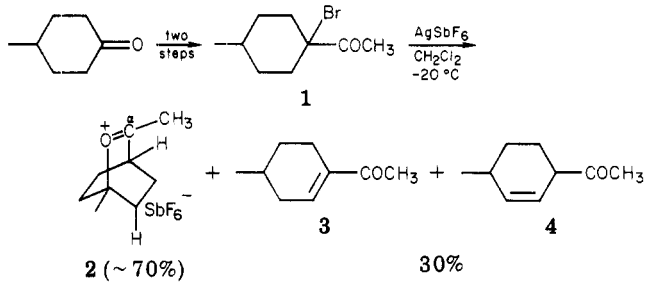
Scheme I



The oxonium salt **2**,[4] the key intermediate, results from dehalogenation ($AgSbF_6$, CH_2Cl_2) of both isomers of α-bromo ketone **1**, prepared by the new method of Durst et al.[5] (In the course of the dehalogenation, a minor competitive process (maximum 30%) takes place, leading to unsaturated ketones **3** and **4**.[6])



Scheme I shows the reactions carried out on **2**, leading to cineole (**5**), *cis*-terpine (**7**), and α-terpineol (**9**). (For practical purposes, the reactions have been carried out on the mixture **2** + **3** + **4**; see Experimental Section.)

In path a, addition of CH_3MgI leads in a stereospecific manner to cineole (**5**; 50% yield from **1**).

In path b, hydrolysis of **2** ($NaHCO_3$, H_2O) leads, also in a stereospecific manner, to the *cis*-hydroxy ketone **6** (65% yield from **1**) which is converted to *cis*-terpine (**7**) by the action of CH_3MgI (90% yield from **6**).

In path c, addition of CH_3OH to **2** leads selectively to the γ-ethylenic ketone **8**. But because the reaction is carried out on the crude dehalogenation mixture, pure **8** is obtained only with difficulty. For this reason, the best way to easily produce α-terpineol (**9**) is by dehydration of **6** to **8** (80% yield), followed by the action of CH_3MgI (55% yield of **9** from **1**).

In both paths a and b, **5** and **6** result from addition of the nucleophilic agent to the carbonyl carbon C_α. (The preliminary formation of the corresponding hemiketal has been demonstrated in other series[1a] and explains the cis configuration of the two functional groups.)

Path c implicates an elimination reaction from **2** in which CH_3OH acts as a base and not as a nucleophile. This specific reactivity of CH_3OH, strikingly different from that of H_2O, has been observed in other cases.[1] Until now, we have had no explanation for this unexpected result.

In conclusion, the formation of these three monoterpenes, **5**, **7**, and **9**, from **2** is an example of the selective reactivity of oxonium salts which permits stereospecific synthesis when the nucleophile reacts at the carbonyl carbon. Furthermore, these reactions, all involving **1** as starting material, are examples of cationic and stereospecific remote functionalizations.

Experimental Section

GLC analyses were obtained on a Girdel "75-FS" with a 1.60-m column containing 5% SE-30 on a Chromosorb support.

The proton NMR chemical shifts were measured at 60 MHz on a Varian T-60 or A-60-D spectrometer, and chemical shifts are reported in parts per million downfield from internal Me_4Si. ^{13}C NMR spectra were recorded at 20 MHz on a Varian CFT-20 spectrometer, using a spectral width of 5200 Hz. The IR spectra were recorded as CCl_4 solutions on a Perkin-Elmer 157 spectrometer and mass spectra with a VG micro-mass 70-70F spectrometer.

1-Bromo-4-methylcyclohexyl Methyl Ketone (1). The α-chloroethyl phenyl sulfone[5] (5 g, 0.024 mol) and 4-methylcyclohexanone (3.3 g, 0.029 mol) were stirred at room temperature for 20 h with 20 mL of 5% NaOH containing 200 mg of tetrabutylammonium hydrogenosulfate. After dilution with water, the reaction mixture was extracted with CH_2Cl_2. The organic solution was washed with water, dried with anhydrous sodium sulfate, and evaporated under reduced pressure. The crude epoxy sulfone (6.5 g) crystallized.[7a]

An ethereal solution of $MgBr_2$ was prepared by reacting Mg (2.75 g, 0.115 mol) with ethylene dibromide (16.3 g, 0.087 mol) in 80 mL of anhydrous ether. To such a solution cooled to 5 °C was added the crude epoxy sulfone (6.5 g) as an anhydrous ether solution (30 mL). After 1 h, the ether layer was washed with ice–water and the solvent dried and evaporated. The crude bromo ketone was purified by chromatography on a Florisil column using pentane. Removal of the solvent gave 1.74 g (38%) of a mixture of the two isomers 1: (**1a**/**1b** 90:10 by GLC analysis) **1a**: ^1H NMR ($CDCl_3$) δ 2.39 (s, 3 H, $COCH_3$), 0.88 (d, 3 H, CH_3). **1b**: ^1H NMR ($CDCl_3$) δ 2.42 (s, 3 H, $COCH_3$), 1.0 (d, 3 H, CH_3); mass spectrum, *m/e* 219 ($M^{+\cdot}$).

Further elution using pentane leads to α,β-unsaturated ketone **3** (61%):[7b,c] ^1H NMR (CCl_4) δ 1.0 (d, 3 H, CH_3), 2.17 (s, 3 H, $COCH_3$), 6.75 (m, 1 H, C=CH); IR (CCl_4) 1645 (C=C), 1675 cm^{-1} (C=O).

Dehalogenation of α-Bromo Ketone 1. $AgSbF_6$ (890 mg, 2.5 mmol) was added to a solution of 500 mg (2.28 mmol) of **1** (**1a**/**1b** 90:10) in 5 mL of CH_2Cl_2. AgBr was filtered through cotton. The residue was evaporated in vacuo and analyzed by NMR to be a mixture of unsaturated ketones **3** and **4** (**4** is described below) and oxonium salt **2**: ^1H NMR ($CDCl_3$) δ 1.86 (s, 3 H, $CH_3CO^+{=}C$), 3.08 (s, 3 H, $-^+O{=}CCH_3$), 3.6 (m, 1 H, $-^+O{=}CCH$); ^{13}C NMR (CD_2Cl_2) δ 246.3 ($C{=}O^+-$), 104.3 ($C-O^+{=}$), 41.8 ($CC{=}O^+$).

For the preparation of cineole (**5**), *cis*-terpine (**7**), and α-terpineol (**9**), the reactions were carried out on the mixture **2** + **3** + **4**, the crude product resulting from dehalogenation of **1**.

Cineole (5). The crude mixture resulting from dehalogenation of **1** (500 mg, 2.28 mmol) was added to a solution of CH_3MgI in Et_2O (10 equiv) and allowed to react for 10 min. The product was hydrolyzed (H_2O, NH_4Cl), extracted with pentane, and worked up in the usual manner. The crude product (315 mg) was chromatographied on a Florisil column (pentane). Pure cineole (**5**; 178 mg, 51%) was isolated and identified by comparison with an authentic sample.

***cis*-Terpine (7).** The crude mixture resulting from dehalogenation of **1** (500 mg, 2.28 mmol) was hydrolyzed ($NaHCO_3$, H_2O) and the product was extracted with CH_2Cl_2. The organic solution was washed with water, dried with anhydrous sodium sulfate, and

(4) The representation of oxonium salt **2** with localized positive charge does not reflect the actual structure: J. P. Bégué and D. Bonnet-Delpon, *Org. Magn. Reson.*, in press.

(5) T. Durst, K. Tin, F. de Reinach-Hirtzbach, J. M. Decesare, and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).

(6) In such dehalogenations, the formation of α,β- and β,γ-unsaturated ketones has already been observed;[1,2] it is always a minor process. In this work, the relative proportions **2**/(**3** + **4**) and **3**/**4** are not known exactly; it depends on unknown parameters (checked experiments have been carried out at different temperatures on the pure isomer **1a** and on different mixtures of **1a** and **1b**).

(7) (a) The crude product is a mixture of the two stereoisomers (probably 90:10). (b) D. F. Taber and B. P. Gunn, *J. Org. Chem.*, **44**, 450 (1979). (c) The proportion (**1**/**3**) resulting from the addition of $MgBr_2$ to the epoxy sulfone is dependent on the configuration of the latter. This problem is under consideration in our laboratory and the results will be discussed in a forthcoming publication.

evaporated under reduced pressure. Chromatography on a Florisil column using pentane gave 62 mg of a mixture of unsaturated ketones 3 + 4[6] (GLC, ^{1}H NMR). 4: ^{1}H NMR δ 5.71 (d, 2 H, HC=CH), 2.10 (s, 3 H, $COCH_3$). Further elution with Et_2O leads to 6: 233 mg (yield 66%); ^{1}H NMR ($CDCl_3$) δ 1.16 (s, 3 H, CH_3), 2.08 (s, 3 H, $COCH_3$); IR (CCl_4) 3400 (OH), 1705 cm^{-1} (C=O).

A solution of 6 (233 mg, 1.5 mmol) in 10 mL of Et_2O was added to a solution of CH_3MgI (5mmol) in 20 mL of Et_2O at room temperature. The mixture was stirred for 15 min and then hydrolyzed ($H_2O/NH_4Cl/Et_2O$). After extraction with ethyl acetate (3 times) the usual workup yielded 235 mg (92%) of *cis*-terpine (7), mp 108 °C, which was identified by comparison with an authentic sample.

α-Terpineol (9). A few drops of anhydrous MeOH was added to the mixture resulting from the dehalogenation of 600 mg of α-bromoketone 1. The solution was allowed to stir for 1 h at 40 °C and then was hydrolyzed (H_2O, $NaHCO_3$) and worked up. The crude product was a mixture (GLC and NMR) of the unsaturated ketones 3 and 4 (30%) and the γ,δ-unsaturated ketone 8 (70%) already described.[8]

8: ^{1}H NMR ($CDCl_3$) δ 1.65 (m, 3 H, CH_3C=C), 2.07 (s, 3 H, $COCH_3$), 5.32 (m, 1 H, HC=O); IR 1675 (C=C) 1720 cm^{-1} (C=O).

The separation of pure 8 from 3 and 4 was difficult. The following procedure was a better mode of preparation of 8.

A solution of hydroxy ketone 6 (359 mg, 2.3 mmol) in 15 mL of toluene was refluxed for 15 min in the presence of some crystals of I_2. After removal of the solvent in a rotatory evaporator, the residue was diluted in pentane, washed with an aqueous solution of $NaHSO_3$ and then twice with saturated $NaHCO_3$ aqueous solution, and dried (Na_2SO_4). Filtration on a Florisil column led to pure 8 (257 mg, 81%).

A solution of 8 (155 mg, 1.12 mmol) in 5 mL of Et_2O was added to an ethereal solution of CH_3MgI (4 mmol) and allowed to stir for 15 min at room temperature. The mixture was then hydrolyzed (H_2O, NH_4Cl), and the aqueous layer was extracted twice with CH_2Cl_2. The organic layers were gathered, washed with water, dried (Na_2SO_4), and concentrated. Filtration on a Florisil column (pentane–ether 3:1) gave 146 mg (85%) of α-terpineol (9). The spectra data of 9 are identical with literature data:[9] ^{1}H NMR ($CDCl_3$) δ 1.12 (s, 6 H, Me_2C), 1.64 (m, 3 H, CH_3C=C), 5.35 (m, 1 H, HC=C); IR 3375 (OH), 1680 cm^{-1} (C=C).

Registry No. *cis*-1, 73839-18-6; *trans*-1, 73839-19-7; 2, 43103-57-7; 3, 22273-97-8; 4, 19876-42-7; 5, 470-82-6; 6, 61187-22-2; 7, 565-48-0; 8, 6090-09-1; 9, 98-55-5; 4-methylcyclohexanone, 589-92-4.

(8) J. H. Babler, D. O. Olsen, and W. H. Arnold, *J. Org. Chem.*, 39, 1656 (1974).
(9) J. G. Grasselli, "Atlas of Spectral Data and Physical Constants for Organic Compounds", CRC Press, Cleveland, OH, 1973.

A New 7-Ring Cycloaddition Reaction[1]

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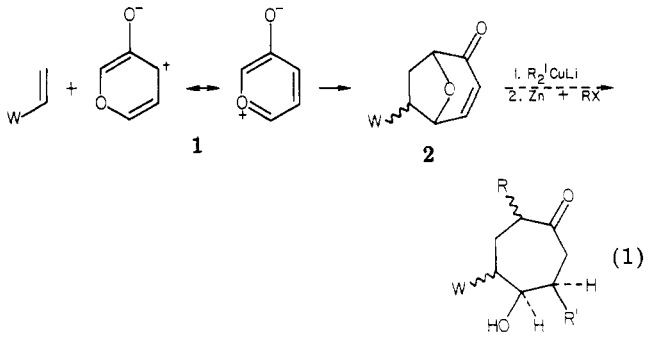
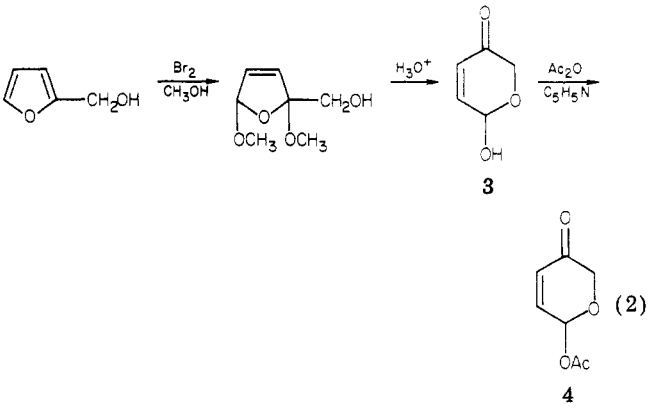
Received January 30, 1980

Whereas syntheses of three-, four- and six-membered carbocyclic rings are often efficiently constructed by cycloaddition reactions, there are no analogous general routes to five- and seven-membered rings. We focused on a ($_4\pi$ + $_2\pi$) cycloaddition for the latter and sought a $_4\pi$ component which would be rigid and cisoid in the reactant and rigid for later synthetic stereocontrol in the adduct. Such a model diene for six-membered rings is furan and this expands to 1 for seven-membered rings, with the oxygen anion substituent for regiospecificity and electron enrichment. The product 2 is a multiply functionalized rigid bicyclic system, presumably capable of subsequent synthetic elaboration by conjugate or direct addition from the upper (exo) face and zinc reduction to free the ether bridge as well as to create a specific enolate for α-alkylation by RX as projected in eq 1.



The preparation of a precursor (4) for the pyrylium zwitterion (1) was available from Achmatowicz[2] as summarized in eq 2.



A number of cycloadditions were then examined (summarized in Table I) with a view to examining the scope and the regio- and stereoselectivity of the cycloaddition. In general, the cycloaddition occurred on heating to 130-135 °C for 5–18 h and was monitored by NMR ($CDCl_3$) in sealed NMR tubes. When no adduct was formed (or 4 was heated alone), the precursor 4 was completely consumed and no product from 4 alone could be isolated; unreacted dienophile was generally recovered and acetic acid was always formed. The regiospecificity was secure as predicted for all adducts but the stereoselectivity varied, generally favoring the exo adduct, in contrast to Alder rule expectations based on furan adducts.[3,4] In general, the dienophiles which did not react were less active or more substituted, the latter especially evident in the methyl substitutions on acrolein. The stereochemistry of the adducts was determined by NMR; the exo adducts (e.g., entry 3) have a dihedral angle of ~90° between H-4 and H-5 so that the H-4 absorption at δ 5.46 is only a doublet and becomes a singlet on irradiation of H-3 at δ 7.41. The same reasoning assigns the major adduct stereochemistry

(1) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

(2) O. Achmatowicz, Jr., P. Bukowski, B. Szechner, Z. Zwierzchowska, and A. Zamojski, *Tetrahedron*, 27, 1973 (1971).
(3) J. Sauer, *Angew. Chem., Intl. Ed. Engl.*, 5, 211 (1966); 6, 16 (1967).
(4) We subsequently found that analogous cycloadditions were studied by Katritzky,[5] using oxypyridinium zwitterions with similar results and regiospecificity. The nitrogen bridges formed there, however, are not as easily cleaved or synthetically transformable to other functions.
(5) N. Dennis, A. Katritzky, and Y. Takeuchi, *Angew. Chem., Int. Ed. Engl.*, 15, 1 (1976).

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