104487-40-3; **9**, 104463-71-0; **9**·NaBr, 104463-96-9; **9**·Cs picrate, 104463-98-1; **9**·NH_4 picrate, 104463-82-3; **9**·$MeNH_3$ picrate, 104463-83-4; **9**·$BuNH_3$ picrate, 104463-84-5; **9**·piperidinium picrate, 104463-85-6; **10**, 104463-72-1; **10**·NaBr, 104487-41-4; **10**·$MeNH_3$ picrate, 104487-36-7; **11**, 83604-32-4; **11**·Na picrate, 104464-00-8; **12**, 104463-73-2; **13**, 104463-74-3; **14**, 104463-75-4; **15**, 104463-76-5; **16**, 104463-77-6; **17**, 104463-78-7; **18**, 64726-28-9; **20**, 104463-79-8; **21**, 104463-80-1; **22**, 5345-05-1; **23**, 576-22-7; **24**, 1516-96-7; **25**, 65654-53-7; **26**, 1191-87-3; **27**, 17454-52-3; **28**, 104463-81-2; **29**, 104463-99-2; **37**, 75640-58-3; **38**, 53938-62-8; MeI, 74-88-4; Li picrate, 18390-55-1; Na picrate, 3324-58-1; K picrate, 573-83-1; Rb picrate, 23296-29-9; Cs picrate, 3638-61-7; NH_4 picrate, 131-74-8; $MeNH_3$ picrate, 6032-31-1; *t*-$BuNH_3$ picrate, 38188-68-0; 1,3-bis(bromomethyl)benzene, 626-15-3; 2-bromo-1,3-bis(bromomethyl)benzene, 25006-88-6; methyl 2,6-bis(bromomethyl)benzoate, 56263-51-5; anthrone, 90-44-8.

Electrosynthesis of 1,2-Dithiolane 1-Oxides from Substituted 1,3-Dithianes

Richard S. Glass,* Amorn Petsom, and George S. Wilson

Department of Chemistry, University of Arizona, Tucson, Arizona 85721

Roberto Martínez and Eusebio Juaristi

Departamento de Química, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, 07000-Mexico, D.F., Mexico

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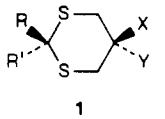
Controlled potential oxidation of a variety of 5-substituted 2-*tert*-butyl-1,3-dithianes in wet acetonitrile, using an undivided electrochemical cell, provide 4-substituted 1,2-dithiolane 1-oxides selectively and in good yields. Adsorption to the electrode surface of the platinum anode, rendering it passive in the electrolysis of these sulfur-containing compounds is a solvable problem. Although acid-sensitive *O*-trimethylsilyl ethers are cleaved under the reaction conditions, *O*-*tert*-butyldimethylsilyl ethers only suffer cleavage to a modest extent, and an ethylene ketal moiety suffers little, if any, cleavage.

Anodic oxidation of dithioacetals and ketals has been studied in detail.[1] Electrochemical oxidation of substituted 1,3-dithianes directly,[2] as well as indirectly[3] via redox catalysis with tri-*p*-tolylamine, affords carbonyl compounds in high yield under mild conditions. Such methodology has been recommended for the unmasking of the carbonyl compound protected in the 1,3-dithiane system.[2,3] The initial papers reported that the sulfur-containing products of oxidation of 1,3-dithianes (1, X = Y = H) were 1,2-dithiolane (**2**, R = H) and a sulfur-containing polymer, probably $[S(CH_2)_3S]_n$, but the yield of 1,2-dithiolane was not given.[1d,2a] The mechanistic implications of these



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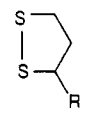

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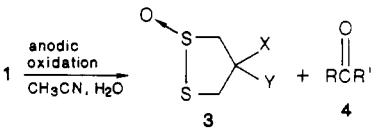
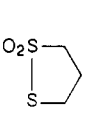
products were commented upon, but use of this method for synthesizing 1,2-dithiolanes was not explored. Very recently, Porter et al.[2b] published a detailed study on the sulfur-containing products obtained by constant current electrolysis of a variety of dithioacetals and dithioketals. Only products from chain contraction, i.e., products in which the carbonyl compound masked in the starting material had been released, were observed. The products included disulfides, thiolsulfinates, and thiolsulfonates. This paper reports our finding that controlled potential electrolysis of substituted 1,3-dithianes in aqueous acetonitrile provides a synthetically useful route to substituted and unsubstituted 1,2-dithiolane 1-oxides as shown in eq 1.



3 4 (1)

Results and Discussion

Despite expectations based on previous reports, no 1,2-dithiolane (**2**, R = H) was isolated from the anodic oxidation of 1,3-dithiane (1, R = R′ = X = Y = H). After controlled potential electrolysis, a mixture of products was obtained, not including 1,2-dithiolane, from which 1,2-dithiolane 1-oxide (**3**, X = Y = H)[4] was isolated in 20% yield, 1,2-dithiolane 1,1-dioxide (**5**) in 6% yield, and 1,3-dithiane 1-oxide (**6**, R = R′ = H)[5] in 22% yield. Porter



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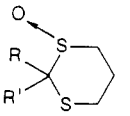

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and co-workers[2b] reported the formation of thiosulfinates and thiolsulfonates analogous to **3**, X = Y = H, and **5**, respectively, on anodic oxidation of dithioacetals and ketals. However, they reported that sulfoxides or sulfones derived from the dithioacetals and -ketals were not formed in contrast to sulfoxide formation on anodic oxidation of phenyl sulfides[6] and our isolation of 1,3-dithiane 1-oxide

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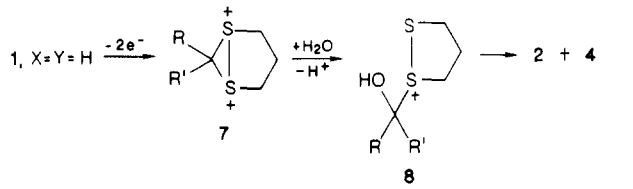
Table I. Anodic Oxidation of 2-Substituted 1,3-Dithianes 1, X = Y = H

cmpd R	cmpd R′	E_p,[a] V	product yield,[b] %
H	H	1.18[c]	20
Me	H	0.75[d]	73[e]
t-Bu	H	0.75	74
p-$MeOC_6H_4$	H	0.74	69
Ph	H	0.73[d]	69
Ph	Me	0.74	52

[a] The peak potentials were determined by cyclic voltammetry using a platinum electrode in acetonitrile, 0.1 M in tetramethylammonium tetrafluoroborate vs. a silver/0.1 M silver nitrate in acetonitrile reference electrode, and a scan rate of 100 mV/s. [b] Isolated yield of pure 1,2-dithiolane 1-oxide (3, X = Y = H). [c] Value reported in ref 1d is +1.10 V at a platinum electrode in acetonitrile, 0.1 M in lithium perchlorate vs. a silver/0.1 M silver ion reference electrode, and a scan rate of 100 mV/s. [d] Value reported in ref 2b is +1.72 V at a platinum bead anode in acetonitrile, 0.1 M in sodium perchlorate vs. a silver/silver iodide reference electrode, and a scan rate of 300 mV/s. [e] Also isolated in 5% yield were *trans*- and *cis*-2-methyl-1,3-dithiane 1-oxide as a 70:30 mixture of isomers. [f] Value reported in ref 2b is +1.60 V vs. a silver/silver iodide reference electrode and a scan rate of 300 mV/s.

from the anodic oxidation of 1,3-dithiane. The formation of 1,2-dithiolane 1-oxide (3, X = Y = H) and 1,2-dithiolane 1,1-dioxide (5) from 1,3-dithiane under our reaction conditions is not surprising. The peak potential for oxidation of 1,3-dithiane is +1.18 V, whereas a representative 1,2-dithiolane; (±)-α-lipoic acid (2, R = $(CH_2)_4CO_2H$)[7] and 1,2-dithiolane 1-oxide (3, X = Y = H) oxidize at +0.75 and +1.15 V, respectively. Furthermore, Gourcy et al.[1d] reported that under their cyclic voltammetric conditions the oxidation potential for 1,3-dithiane is +1.10 V and that repetitive sweeps in wet acetonitrile show an additional peak at less anodic potentials which occurs at the potential for oxidation of authentic 1,2-dithiolane (0.70 V). We have confirmed these results. Thus, in the electrolysis of 1,3-dithiane, 1,2-dithiolane is apparently formed but it is further oxidized under the reaction conditions to 1,2-dithiolane 1-oxide. Some of the 1,2-dithiolane 1-oxide is also further oxidized under the reaction conditions to 1,2-dithiolane 1,1-dioxide.[8]

To favor the selective synthesis of 1,2-dithiolane 1-oxide from 1,3-dithianes, anodic oxidation of various 2-substituted 1,3-dithianes was studied, and the results are summarized in Table I. It was anticipated that 2-alkyl substituents would lower the oxidation potential of 1,3-dithiane because α-branching in dialkyl thioethers lowers their oxidation potentials[9] and ionization potentials.[10,11] As shown in Table I this is indeed the case. This substantial potential lowering allows the selective oxidation to 1,2-dithiolane 1-oxide without further oxidation to the 1,2-dithiolane 1,1-dioxide. It should be noted that the peak potentials for oxidation of the 2-substituted 1,3-dithianes listed in Table I are in the same range as that for 1,2-dithiolane. A second expectation for the effect of a 2-substituent was that ring contraction to 1,2-dithiolane would be favored over sulfoxide formation without ring contraction. As indicated in Table I, anodic oxidation of 2-methyl-1,3-dithiane gives 1,2-dithiolane 1-oxide in 73% isolated yield. *trans*- and *cis*-2-methyl-1,3-dithiane 1-oxides were isolated as a mixture (in a 73:27 isomer ratio, respectively) in only 5% yield, and ^1H NMR spectroscopic analysis of the crude reaction mixture after electrolysis suggested that the combined yield of these isomers is approximately 5%. For the other 2-substituted 1,3-dithianes listed in Table I not even a trace of the corresponding 1,3-dithiane 1-oxide could be detected. Two different mechanisms have been suggested for the formation of ring contracted products on anodic oxidation of dithioacetals.[1,2b] In either case, 2-substituents which stabilize cationic centers would favor ring contraction[6] provided that dication 7 suggested as an intermediate by Simonet and coworkers[1a,c,d] and related to dications isolated and characterized in other systems by Musker et al.[12] undergoes nucleophilic attack at C(2) by water via an S_N1 mechanism to give 8.[13]



As expected, 4 faradays of current are consumed per mole of compound oxidized (n = 4). In the case of 1, R = *p*-$MeOC_6H_4$, R′ = X = Y = H, the other product of the reaction; *p*-methoxybenzaldehyde, was isolated in 93% yield. The overall stoichiometry of these reactions is shown in eq 2. That is, 4 equiv of protons are produced for each

$$1 + 2H_2O - 4e^- \rightarrow 3 + 4 + 4H^+ \qquad (2)$$

equivalent of substituted 1,3-dithiane consumed. Since we were interested in performing these oxidations in the presence of acid-sensitive groups, bases were used to neutralize the acid produced. The electrolyses could be performed in the presence of sodium bicarbonate or, less satisfactorily, with pyridine. However, the simplest and most convenient way to carry out these electrolyses without proton accumulation is to use an *undivided* electrochemical cell. The protons liberated by reaction at the anode are reduced at the cathode or are neutralized by the base produced at the cathode by the reduction of water.

This electrochemical oxidation of 2-substituted 1,3-dithianes to give 1,2-dithiolane 1-oxide appears to be related mechanistically to the hydrolysis of 2,2-disubstituted 1,3-dithianes with ammonium cerium(IV) nitrate in aqueous acetonitrile.[14] Four equivalents of the cerium(IV) salt are required for optimum yield in this reaction, and 1,2-dithiolane 1-oxide (3, X = Y = H) was isolated in 60% yield from the cerium(IV) oxidation of 2,2-dimethyl-1,3-dithiane (1, R = R′ = Me, X = Y = H).[4] The scope of this reaction for the synthesis of substituted 1,2-dithiolane 1-oxides was not explored, and it should be noted that, under these reaction conditions, the solution becomes acidic whereas, under our electrochemical oxidation conditions, the solution remains neutral.

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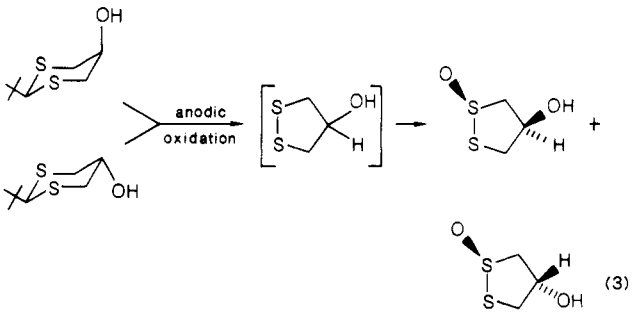
Table II. Anodic Oxidation of 2,5-Disubstituted 1,3-Dithianes 1

compound					product yield,
R	R′	X	Y	E_p,[a] V	%
p-$MeOC_6H_4$	H	OH	H	0.75, 1.70	62 (55:45)[b]
t-Bu	H	OH	H	0.75	33 (3:2)[b]
t-Bu	H	H	OH	0.73	41 (3:2)[b]
t-Bu	H	OMe	H	0.77	73 (1:2)[c]
t-Bu	H	H	$OSiMe_3$	0.83	25 (1:1)[b,d]
t-Bu	H	$OSiMe_2$-(*t*-Bu)	H	0.96	48 (2:3),[e] 13 (3:2)[b]
t-Bu	H	H	$OSiMe_2$-(*t*-Bu)	1.05	39 (2:3),[e] 17 (3:2)[b]
t-Bu	H	OCH_2CH_2O		0.85	72

[a] The peak potentials were determined by cyclic voltammetry using a platinum electrode in acetonitrile, 0.1 M in tetramethylammonium tetrafluoroborate vs. a silver/0.1 M silver nitrate in acetonitrile reference electrode, and a scan rate of 100 mV/s. [b] Yield after isolation of 4-hydroxy-1,2-dithiolane 1-oxide as a mixture of geometric isomers. The approximate ratio of brugierol to isobrugierol is given in parentheses. [c] Yield after isolation of 4-methoxy-1,2-dithiolane 1-oxide as a mixture of geometric isomers. The approximate cis/trans ratio of isomers is given in parentheses. [d] No 4-(trimethylsiloxy)-1,2-dithiolane 1-oxide was isolated. [e] Yield after isolation of 4-[(*tert*-butyldimethylsilyl)oxy]-1,2-dithiolane 1-oxide as a mixture of geometric isomers. The approximate ratio of cis/trans isomers is given in parentheses. [f] Yield of isolated, pure 3, X,Y = OCH_2CH_2O. No hydrolysis product was isolated in this reaction.

To explore the utility of this synthetic method, the preparation of 4-substituted 1,2-dithiolane-1-oxides **3** from 2,5-disubstituted 1,3-dithianes **1** was studied. The results are shown in Table II. Cyclic voltammetric studies on *cis*-2-(*p*-methoxyphenyl)-5-hydroxy-1,3-dithiane (**1**, R = *p*-$MeOC_6H_4$, X = OH, R′ = Y = H)[15] showed two irreversible anodic peak potentials at +0.75 and +1.7 V. Controlled potential oxidation of this substrate at +1.0V in an individual cell resulted in an "*n*" value of 4. A mixture of brugierol and isobrugierol[16] in an 55:45 ratio was isolated in 62% yield. Similarly the separated, chemically pure cis and trans isomers of 2-*tert*-butyl-5-hydroxy-1,3-dithiane were separately electrolyzed. However, in both cases the current diminished to zero after the passage of only 1.2 and 1.3 F/mol, respectively. Analysis of the product revealed substantial amounts of unreacted starting material and only modest amounts of brugierol and isobrugierol. This incomplete electrolysis is due to adsorption on the electrode surface. The yields of brugierol and isobrugierol can be improved by intermittent cleaning, by flaming, of the electrode surface. In this way, both cis and trans isomers of 2-*tert*-butyl-5-hydroxy-1,3-dithiane produced the same isomeric mixture of brugierol and isobrugierol, within experimental error, in 33% and 41% yields, respectively, as shown in eq 3.

This result is consistent with the mechanism already suggested for these reactions. Both cis and trans isomers of 2-*tert*-butyl-5-hydroxy-1,3-dithiane would give the same intermediate 4-hydroxy-1,2-dithiolane, as shown in eq 3. Thus, the ratio of stereoisomers of the product is independent of the stereochemistry of the 1,3-dithiane precursors. Nevertheless, the relatively low yield of products in these electrolyses is unsatisfactory. Adsorption to the



(3)

electrode surface is not a problem in the controlled potential electrolysis of *cis*-2-*tert*-butyl-5-methoxy-1,3-dithiane (**1**, R = *t*-Bu, X = OMe, R′ = Y = H). As shown in Table II, this compound affords 4-methoxy-1,2-dithiolane 1-oxide as cis/trans mixture in 73% isolated yield. Therefore, the electrochemistry of the silyl ether derivatives of 2-*tert*-butyl-5-hydroxy-1,3-dithiane were studied with hope that, in analogy with the corresponding methyl ether, adsorption would not be a problem and, subsequent to electrolysis, the silyl group could be selectively cleaved.

Controlled potential electrolysis of the trimethylsilyl ether derived from *trans*-2-*tert*-butyl-5-hydroxy-1,3-dithiane (**1**, R = *t*-Bu, Y = $OSiMe_3$, R′ = X = H) resulted in electrode passivation. Since brugierol and isobrugierol were isolated from this electrolysis in 25% yield and none of the corresponding *O*-trimethylsilyl derivatives, the *O*-trimethylsilyl group is cleaved under the reaction conditions. Therefore, the more stable *tert*-butyldimethylsilyl ethers were studied. Controlled potential electrolysis of the *O*-*tert*-butyldimethylsilyl derivatives of *cis*- and *trans*-*tert*-butyl-5-hydroxy-1,3-dithiane separately, showed only a modest amount of cleavage of the *tert*-butyldimethylsilyl group, and adsorption on the electrode surface was not a problem. The combined yields of the isomeric 4-(*tert*-butyldimethylsiloxy)-1,2-dithiolane 1-oxides (**3**, X = (*t*-$BuMe_2Si$)O, Y = H) and 4-hydroxy-1,2-dithiolane 1-oxides (**3**, X = OH, Y = H) are good as shown in Table II. Again the cis/trans isomer ratios of the products are comparable with either isomeric starting material, as expected. Hydrolysis of the *tert*-butyldimethylsilyl ether group occurred selectively and in quantitative yield with 1% hydrochloric acid in 95% ethanol. The brugierol and isobrugierol produced in these reactions and those mentioned previously were separated and found to be identical with authentic samples.[16,18,19] Their identities were further confirmed by their conversion to the corresponding *N*-ethylcarbamates. These carbamates showd undepressed mixture melting points when admixed with authentic samples.

As already pointed out, under our electrolysis conditions, the solution overall remains neutral. However, at or near the anode the solution may be acidic. During electrolysis an *O*-trimethylsilyl group is apparently completely hydrolyzed; an *O*-*tert*-butyldimethylsilyl group is hydrolyzed to a modest extent, and an ethylene ketal is hydrolyzed slightly if at all. As shown in Table II controlled potential electrolysis of the ketal-containing **1**, R = *t*-Bu, R^1 = H, X,Y = OCH_2CH_2O, gives **3**, X,Y = OCH_2CH_2O with the ketal moiety intact in 72% isolated yield.

In sum, the controlled potential electrolysis of substituted 1,3-dithianes reported in this paper provides a selective synthesis of 1,2-dithiolane 1-oxides in good yields

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(19) Spectra of authentic brugierol and isobrugierol and authentic samples of the corresponding *N*-ethylcarbamates were kindly supplied by Professor A. Kato.

under mild conditions. Adsorption to the electrode surface is a solvable problem and the experimental apparatus is relatively simple. This method for synthesizing 1,2-dithiolane 1-oxides offers advantages over existing methods. The conventional method for such syntheses is the chemical oxidation of a 1,3-propanedithiol to the corresponding 1,2-dithiolane followed by chemical oxidation to the desired 1,2-dithiolane 1-oxide **3**.[18,20] The 1,3-dithiane **1** used in the electrochemical synthesis is obtained from a 1,3-propanedithiol but can serve as a stable protecting group[21,22] for the dithiol and 1,2-dithiolane, so that a variety of chemical reactions can be effected elsewhere in the molecule. Furthermore, although the 1,3-dithiane moiety is stable under a variety of conditions, it can be selectively electrolyzed in the presence of a variety of other functional groups to 1,2-dithiolane 1-oxides in one step. As already shown, the acid-sensitive ethylene ketal moiety is not cleaved to any substantial extent, if at all, under the reaction conditions and *tert*-butyldimethylsilyl ethers suffer cleavage only to a modest extent.

Experimental Section

All melting points are uncorrected and were taken using a Thermolyne melting point apparatus. IR spectra were obtained with a Perkin-Elmer Model 983 spectrophotometer. NMR spectra were measured with a Bruker WM-250 spectrometer at 250 MHz for ^1H and 62.89 MHz for ^{13}C on samples containing tetramethylsilane as an internal standard. Mass spectra were measured with a Varian MAT 311A mass spectrometer equipped with a Varian SS-200 data system. Elemental microanalysis was performed at Atlantic Microlab, Inc., Atlanta, GA. High-resolution mass spectra were done at the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE (National Science Foundation Regional Instrumentation Facility). Preparative thin-layer plates were prepared by using Merck HF-254 (Type 60) silica gel supplied by Brinkmann Instruments, Inc. HPLC was performed on an Ultrasphere ODS column (4.6 × 150 mm) supplied by Beckman Instruments. An Altex/Beckman 110A pump and a Spectra Physics Model 8400 UV/VIS detector set at 230 or 254 nm were used. Filtered, AR grade acetonitrile was used as the eluting solvent. Technical grade acetonitrile supplied by Fisher Scientific Company was purified by drying over activated 3A molecular sieve and distillation sequentially from a mixture of sodium carbonate–potassium permanganate and finally phosphorus pentoxide under a nitrogen atmosphere. This purified acetonitrile was used in cyclic voltammetric experiments and had a working range between +1.8 and −1.8 on a platinum electrode using a Ag/0.1 M $AgNO_3$ in acetonitrile reference electrode when tetramethylammonium tetrafluoroborate, used as received from Fluka AG, was used as supporting electrolyte. Pivalaldehyde was also used as received from Aldrich Chemical Company.

Cyclic Voltammetry Measurements. Cyclic voltammetry was performed in a separated electrochemical cell with acetonitrile solutions 0.1 M in tetramethylammonium tetrafluoroborate and approximately 10^{-4} M in substrate. The working electrode was a platinum flag with an area of 0.35 cm^2. The counter electrode was also a platinum flag. The reference electrode was a silver wire in acetonitrile solution 0.1 M in silver nitrate. The working electrode was cleaned by burning before each experiment. The scan rate was 100 mV/s. The measurements were made with a Princeton Applied Research Model 362 scanning potentiostat equipped with a Houston Model 200 XY-recorder. The data acquisition and data processing systems have been described previously.[23]

Controlled Potential Electrolyses. An undivided cell equipped with a platinum gauze working electrode and a (2.6 × 2.6 cm^2) platinum sheet counter electrode was used. The electrolysis was controlled with an ECO Model 551 potentiostat and the current monitored with a Princeton Applied Research Model 379 digital coulometer. The applied potential was approximately 100 mV more anodic than the peak potential determined by cyclic voltammetry. A typical experiment follows.

A solution of 2-*tert*-butyl-1,3-dithiane (91 mg, 0.52 mmol) dissolved in acetonitrile containing 1% water and 0.05 M in tetramethylammonium tetrafluoroborate (80 mL) was placed in a 100-mL beaker. The stirred solution was electrolyzed at +0.85 V. The progress of the reaction was monitored by both HPLC and by coulometry. After the anodic current dropped to a negligible value, the electrolysis was stopped and solvent evaporated under reduced pressure. The residue was triturated several times with ethyl acetate. The combined ethyl acetate extracts (approximately 50 mL total volume) were concentrated by using a rotary evaporator. The residue was chromatographed on a silica gel preparative TLC plate by eluting with ethyl acetate/dichloromethane (1:1). The proper band was separated and extracted with ethyl acetate. The extracts were filtered and concentrated on a rotary evaporator to afford 1,2-dithiolane 1-oxide as a colorless, viscous liquid (47 mg, 75% yield): IR (CCl_4) 1097, 1070 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.85–3.00 (m, 3 H), 3.25–3.38 (m, 1 H), 3.60–3.66 (m, 1 H), 3.72–3.80 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 29.9, 38.2, 63.5; mass spectrum, *m/z* 122 (M^+), 74 ($M^+ - SO$).

Controlled Potential Oxidation of 1, R = *p*-MeOC$_6$H$_4$, R′ = X = Y = H. A sample of **1**, R = *p*-$MeOC_6H_4$, R′ = X = Y = H (203 mg, 0.90 mmol), was oxidized according to the general procedure at a potential maintained at +1.0 V. On workup **3**, X = Y = H, was isolated in 69% yield (75.6 mg) together with *p*-methoxybenzaldehyde in 93% yield (114 mg).

Controlled Potential Oxidation of 1,3-Dithiane. A sample of 1,3-dithiane (114 mg, 0.95 mmol) was oxidized according to the general procedure at a potential maintained at +1.3 V. On workup **3**, X = Y = H, was isolated in 20% yield (23 mg), together with **6**, R = R′ = H, in 22% yield (29 mg) and **5** in 6% yield (7 mg). The spectroscopic data of **6** were previously reported.[24] The spectroscopic data of **5** were as follows: IR (CCl_4) 1355 (s), 1323 (s), 1153 (s), 1133 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 2.58 (quintet, 2 H, *J* = 6.6 Hz), 3.40 (t, 2 H, *J* = 6.6 Hz), 3.70 (t, 2 H, *J* = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 24.9, 36.7, 58.2; mass spectrum, *m/z* 138 (M^+), 74 ($M^+ - SO_2$).

Controlled Potential Oxidation of 1, R = Me, R′ = X = Y = H. A sample of **1**, R = Me, R′ = X = Y = H (84 mg, 0.63 mmol), was oxidized at +0.75 V according to the general procedure. On workup **3**, X = Y = H, was isolated in 73% yield (56 mg), together with **5** in 6% yield (5 mg) and **6**, R = Me, R′ = H, as a 27:73 mixture of cis and trans isomers in 5% yield (5 mg). The NMR spectra of *cis*-**6**, R = Me, R′ = H, and *trans*-**6**, R = H, R′ = Me, were consistent with those reported by Carey and co-workers.[25]

Controlled Potential Oxidation of *cis*-1, R = *p*-MeOC$_6$H$_4$, X = OH, R′ = Y = H. A sample of *cis*-**1**, R = *p*-$MeOC_6H_4$, X = OH, R′ = Y = H (186 mg, 0.77 mmol), was oxidized according to the general procedure at a potential maintained at +0.9 V in acetonitrile containing 5% water. On workup brugierol and isobrugierol were isolated in 62% total yield (66 mg) together with *p*-methoxybenzaldehyde in 86% yield (90 mg). The mixture of brugierol and isobrugierol was further purified by prepartive TLC on silica gel using ethyl acetate/dichloromethane (1:1) as eluant.

Brugierol: ^1H NMR ($CDCl_3$, 250 MHz) δ 2.93 (dd, 1 H, *J* = 4.3, 13.1 Hz), 3.59 (dd, 1 H, *J* = 4.3, 12.3 Hz), 4.07 (ddd, 1 H, *J* = 2.2, 2.2, 13.1 Hz), 4.10 (ddd, 1 H, *J* = 2.2, 2.2, 12.3 Hz), 5.42 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 43.7, 70.5, 76.0.

Isobrugierol: ^1H NMR ($CDCl_3$, 250 MHz) δ 3.44 (dd, 1 H, *J* = 5.3, 12.3 Hz), 3.45 (dd, 1 H, *J* = 5.3, 13.1 Hz), 3.60 (dd, 1 H, *J* = 6.6, 13.1 Hz), 3.86 (dd, 1 H, *J* = 5.3, 12.3 Hz), 5.36 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 48.2, 67.1, 80.4.

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Brugierol *N*-ethylcarbamate: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.12 (t, 3 H, J = 7.3 Hz), 3.20 (dq, 2 H, J = 6.0, 7.3 Hz), 3.27 (dd, 1 H, J = 4.8, 13.8 Hz), 3.66 (dd, 1 H, J = 5.1, 12.0 Hz), 3.84 (dd, 1 H, J = 1.7, 13.8 Hz), 4.00 (dd, 1 H, J = 2.6, 12.0 Hz), 5.00 (br s, 1 H), 6.07 (septet, 1 H, J = 2.7 Hz).

Isobrugierol *N*-ethylcarbamate: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 1.11 (t, 3 H, J = 7.3 Hz), 3.18 (dq, 2 H, J = 6.6, 7.2 Hz), 3.58 (dd, 1 H, J = 5.1, 13.8 Hz), 3.60 (dd, 1 H, J = 4.0, 12.2 Hz), 3.75 (dd, 1 H, J = 4.5, 13.8 Hz), 4.03 (dd, 1 H, J = 4.4, 12.2 Hz), 4.80 (br s, 1 H), 6.04 (quintet, 1 H, J = 4.4 Hz).

Controlled Potential Oxidation of *cis*-1, R = *t*-Bu, X = OH, R′ = Y = H. (A) A solution of 0.05 M tetramethylammonium tetrafluoroborate in anhydrous acetonitrile (80 mL) was placed in an undivided electrochemical cell and distilled water (0.05 mL, 2.8 mmol) was added. The solution was preelectrolyzed at a controlled potential of +0.9 V until the current dropped to an insignificant value. While the potential was maintained at +0.85V, a solution of *cis*-1, R = *t*-Bu, X = OH, R′ = Y = H (115 mg, 0.60 mmol), in anhydrous acetonitrile (2 mL) was added dropwise at such a rate that the current did not exceed 70 mA. When the current decreased to an insignificant value, the polarity of the working electrode and the counter electrode was reversed and then switched back and the electrolysis continued. This switching was discontinued when there was no increase in current. At this point, the electrolysis was ended (η = 1.2 F/mol). The acetonitrile was removed by rotary evaporation under reduced pressure. The resulting solid was triturated with ethyl acetate, and the extracts were filtered and concentrated. Analysis of this crude product (101 mg) quantitatively by ^{1}H NMR spectroscopy, using piperonal as an internal standard, revealed unreacted starting material (31%) and brugierol and isobrugierol (4% in a 70:30 ratio respectively). An uncharacterized chloroform and water insoluble material was observed.

(B) To optimize the yield of brugierol and isobrugierol a modification of the preceding experiment was carried out, as follows, and the products were isolated. A wet acetonitrile solution was prepared and preelectrolyzed as above. A sample of *cis*-1, R = *t*-Bu, X = OH, R′ = Y = H (40 mg, 0.21 mmol), was added and electrolyzed at a constant potential of +0.8 V. When the current decreased to zero, the polarity of the working and counter electrodes was switched and then back again repeatedly. In addition, the electrodes were removed occasionally and cleaned in an open flame. The electrolysis was stopped after η = 4 F/mol. The acetonitrile was removed by rotary evaporation under reduced pressure. The resulting residue was triturated with ethyl acetate (3 × 20 mL). The combined, filtered extracts were concentrated and then chromatographed on a layer of silica gel by eluting with a 3:2 solution of ethyl acetate/dichloromethane. A mixture of brugierol and isobrugierol (10 mg, 33% yield) was obtained which by ^{1}H NMR analysis contained no other materials, and the ratio of isomers was 57:43, respectively.

Controlled Potential Oxidation of *trans*-1, R = *t*-Bu, R′ = X = H, Y = OH. (A) The oxidation of *trans*-1, R = *t*-Bu, R′ = X = H, Y = OH (74 mg, 0.38 mmol), was carried out in the same way as the oxidation of *cis*-1, R = *t*-Bu, X = OH, R′ = Y = H, using procedure A. At the end of the electrolysis η = 1.3 F/mol. Quantitative ^{1}H NMR spectroscopic analysis of the crude product (48 mg) as before revealed starting material (42%) and brugierol and isobrugierol (16% in a 70:30 ratio). An uncharacterized chloroform and water-insoluble material was also observed.

Controlled potential oxidation of a sample of *trans*-1, R = *t*-Bu, R′ = X = H, X = OH (50 mg, 0.26 mmol), was also done in the same way as the oxidation of *cis*-1, R = *t*-Bu, X = OH, R′ = Y = H, using procedure B. On workup a mixture of brugierol and isobrugierol was isolated in a ratio of 53:47 (15 mg, 41% yield).

Controlled Potential Oxidation of *cis*-1, R = *t*-Bu, X = OMe, R′ = Y = H. A sample of *cis*-1, R = *t*-Bu, X = OMe, R′ = Y = H (100 mg, 0.49 mmol), prepared by the procedure of Eliel and Juaristi,[17] was oxidized according to the general procedure at a potential maintained at +0.8 V. On workup **3**, X = OMe, Y = H, was isolated as a mixture of cis and trans isomers in a ratio of 1:2 (54 mg, 73%): IR (neat) 1050–1120 cm^{-1}; mass spectrum, m/z calcd for $C_4H_8O_2S_2$ 151.9966, found 151.9971. These isomers can be separated by preparative thin-layer chromatography on silica gel, eluting with ethyl acetate/dichloromethane (1:1).

Cis isomer: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.22 (dd, 1 H, J = 4.4, 13.1 Hz) 3.45 (s, 3 H), 3.48 (dd, 1 H, J = 4.4, 10.9 Hz), 3.78 (dd, 1 H, J = 3.9, 13.1 Hz), 3.97 (ddd, 1 H, J = 1.8, 4.4, 10.9 Hz), 4.74 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 42.6, 57.8, 65.9, 86.4.

Trans isomer: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 3.41 (s, 3 H), 3.41 (dd, 1 H, J = 6.6, 13.1 Hz), 3.44 (dd, 1 H, J = 5.7, 10.9 Hz), 3.56 (dd, 1 H, J = 4.3, 13.1 Hz), 3.85 (dd, 1 H, J = 4.3, 10.9 Hz), 4.94 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 39.7, 58.1, 66.7, 84.8.

Preparation of 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_3$. A sample of 1, R = *t*-Bu, R′ = X = H, Y = OH (234 mg, 1.20 mmol), was dissolved in dry tetrahydrofuran (20 mL) and placed in a 100-mL three-necked flask equipped with a magnetic stirrer and three septa. The solution was purged with nitrogen and freshly distilled triethylamine (1.0 mL, 7.2 mmol) was added. By means of a syringe, trimethylchlorosilane (0.5 mL, 3.9 mmol) was added to the well-stirred solution. The progress of the reaction was monitored by TLC analysis on silica gel eluting with dichloromethane. After the mixture was stirred overnight, the white precipitate of triethylammmonium hydrochloride was filtered off and the tetrahydrofuran evaporated under reduced pressure by using a rotary evaporator. Diethyl ether was added to the residue and filtered removing more of the triethylammonium hydrochloride. The ether solution was concentrated, and the residue was chromatographed on a layer of silica gel by eluting with hexane to afford 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_3$, as a white solid (293 mg, 91%), and an analytical sample was prepared by sublimation: mp 50–52 °C; ^{1}H NMR ($CDCl_3$, 250 MHz) 0.12 (s, 9 H), 1.11 (s, 9 H), 2.67–2.85 (m, 4 H), 3.86 (s, 1 H), 3.84–3.98 (m, 1 H). Anal. Calcd for $C_{11}H_{24}OS_2Si$: C, 50.00; H, 9.09; S, 24.24. Found: C, 50.03; H, 9.17; S, 24.29.

Preparation of 1, R = *t*-Bu, R′ = Y = H, X = OSiMe$_2$(*t*-Bu). A sample of *tert*-butyldimethylchlorosilane (1 g, 6.6 mmol) and diisopropylethylamine (1.5 mL, 8.6 mmol) was added to a solution of 1, R = *t*-Bu, R′ = Y = H, X = OH (1.02 g, 5.29 mmol), in *N*,*N*-dimethylformamide (5 mL), and the reaction mixture was stirred overnight. Water (5 mL) was added to the reaction mixture, and stirring was continued for 10 min. Diethyl ether (15 mL) and a saturated aqueous solution of sodium bicarbonate (10 mL) were added, and the stirring was continued for another 15 min. The ether layer was separated and the aqueous layer was extracted with diethyl ether (2 × 15 mL). The combined ether extracts were dried (anhydrous Na_2SO_4) and then concentrated on a rotary evaporator. The crude product was purified by preparative TLC on silica gel and eluting with hexane to afford unreacted starting material (0.12 g) and 1, R = *t*-Bu, R′ = Y = H, X = OSiMe$_2$(*t*-Bu), as a colorless, viscous liquid (1.18 g, 73%), and an analytical sample was prepared by preparative GLC: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.05 (s, 6 H), 0.88 (s, 9 H), 1.08 (s, 9 H), 2.78 (m, 4 H), 3.74 (s, 1 H), 3.99 (quintet, 1 H). Anal. Calcd for $C_{14}H_{30}OS_2Si$: C, 54.90; H, 9.80; S, 20.92. Found: C, 54.93; H, 9.89; S, 20.83.

Preparation of 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_2$(*t*-Bu). A sample of *tert*-butyldimethylchlorosilane (200 mg, 1.33 mmol) and diisopropylethylamine (0.3 mL, 1.7 mmol) was added to a solution of 1, R = *t*-Bu, R′ = X = H, Y = OH (161 mg, 0.84 mmol), in *N*,*N*-dimethylformamide (2.5 mL). The progress of the reaction was monitored by TLC analysis on silica gel eluting with dichloromethane. After workup as above, 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_2$(*t*-Bu), was isolated as a colorless liquid, which solidified upon standing (226 mg, 88%), and an analytical sample was prepared by preparative GLC: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 0.06 (s, 6 H), 0.86 (s, 9 H), 1.11 (s, 9 H), 2.73 (d, 2 H, J = 5.0 Hz), 2.75 (d, 2 H, J = 8.9 Hz), 3.86 (s, 1 H), 3.84–3.98 (m, 1 H). Anal. Calcd for $C_{14}H_{30}OS_2Si$: C, 54.90; H, 9.80; S, 20.92. Found: C, 54.78; H, 9.90; S, 20.83.

Controlled Potential Oxidation of 1, R = *t*-Bu, Y = OSiMe$_3$, R′ = X = H. A sample of 1, R = *t*-Bu, X = OSiMe$_3$, R′ = Y = H (54 mg, 0.20 mmol), was oxidized in dry acetonitrile, according to the general procedure, at a potential maintained at +1.0 V. When the current dropped to an insignificant value, the electrolysis was terminated (η = 2.7 F/mol). On workup, a mixture of brugierol and isobrugierol was isolated in a ratio of 49:51 (7 mg, 25%) as determined by ^{1}H NMR analysis.

Controlled Potential Oxidation of 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_2$(*t*-Bu). A sample of 1, R = *t*-Bu, R′ = X = H, Y = OSiMe$_2$(*t*-Bu) (76 mg, 0.25 mmol), was oxidized in dry

acetonitrile, according to the general procedure, at a potential maintained at +1.0 V. On workup, a mixture of brugierol and isobrugierol was isolated in a ratio of 58:42 (5 mg, 17%) together with **3**, X = H, Y = $OSiMe_2(t\text{-Bu})$, as a mixture of cis and trans isomers in a ratio of 38:62 (26 mg, 39%) as determined by ^1H NMR analysis.

Controlled Potential Oxidation of 1, R = t-Bu, X = $OSiMe_2(t\text{-Bu})$, R′ = Y = H. A sample of **1**, R = *t*-Bu, X = $OSiMe_2(t\text{-Bu})$, R′ = Y = H (88 mg, 0.29 mmol), was oxidized in dry acetonitrile, according to the general proedure, at a potential maintained at +1.0 V. On workup, a mixture of brugierol and isobrugierol was isolated in a ratio of 58:42 (5 mg, 13%) together with **3**, X = $OSiMe_2(t\text{-Bu})$, Y = H, which was isolated as a colorless viscous liquid composed of a mixture of cis and trans isomers in a ratio of 41:59 (35 mg, 48%): IR (CCl_4) 1051, 1077, 1097 cm^{-1}; mass spectrum, *m/z* cacld for $C_9H_{21}O_2S_2Si$ (M^+ + H) 253.0753, found 253.0741; calcd for $C_5H_{11}O_2SSi$ ($M^+ - C_4H_9$) 194.9970, found 194.9967. These isomers can be separated by preparative HPLC on a silica column (Altex Ultrasil-Si, 10 × 250 mm), eluting with ethyl acetate/hexane (1:3) at a flow rate of 3 mL/min, and a UV detector set at 280 nm was used as a monitor.

Cis isomer: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.09 (s, 3 H), 0.10 (s, 3 H), 0.88 (s, 9 H), 3.23 (dd, 1 H, *J* = 6.2, 13.2 Hz), 3.38 (dd, 1 H, *J* = 5.0, 11.4 Hz), 3.72 (dd, 1 H, *J* = 6.3, 13.2 Hz), 3.82 (dd, 1 H, *J* = 7.4, 11.4 Hz), 4.78 (m, 1 H); ^{13}C NMR (CD_3COCD_3), δ −4.8, 18.5, 26.0, 45.7, 70.4, 78.9.

Trans isomer: ^1H NMR ($CDCl_3$, 250 MHz) δ 0.11 (s, 6 H), 0.87 (s, 9 H), 3.26 (dd, 1 H, *J* = 8.8, 12.6 Hz), 3.28 (dd, 1 H, *J* = 7.3, 10.4 Hz), 3.46 (dd, 1 H, *J* = 4.4, 12.6 Hz), 3.70 (dd, 1 H, *J* = 5.5, 10.4 Hz), 5.38 (m, 1 H); ^{13}C NMR (CD_3COCD_3) δ −4.8, 18.5, 26.0 43.4, 77.8.

Hydrolysis of a Mixture of 3, X = $OSiMe_2(t\text{-Bu})$, Y = H, and 3, X = H, Y = $OSiMe_2(t\text{-Bu})$. A mixture of **3**, X = $OSiMe_2(t\text{-Bu})$, Y = H, and **3**, X = H, Y = $OSiMe_2(t\text{-Bu})$ (31 mg, 0.12 mmol, 59:41 mixture), was dissolved in 1% hydrochloric acid in 95% ethanol (4 mL), and the solution was stirred overnight and analyzed periodically by TLC on silica gel eluting with a 1:1 solution of ethyl acetate/dichloromethane. After completion of the reaction (about 36 h), a small amount of solid sodium bicarbonate was added to neutralize the acid. The mixture was filtered, and the filtrate was concentrated under reduced pressure by using a rotary evaporator. The crude product was subjected to preparative TLC on silica gel eluting with a 1:1 solution of ethyl acetate/dichloromethane to obtain brugierol and isobrugierol (16 mg, 94% yield) in a ratio of 36:64 as determined by ^1H NMR analysis.

Controlled Potential Oxidation of 1, R = t-Bu, R′ = H, X,Y = OCH_2CH_2O. A sample of **1**, R = *t*-Bu, X,Y = OCH_2CH_2O (73 mg, 3.1 mmol), prepared by the procedure of Eliel and Juaristi,[17] was oxidized, according to the general procedure, at a potential maintained at +0.8 V. On workup **3**, X,Y = OCH_2CH_2O, was isolated (41 mg, 72%): IR (neat) 1035–1120 cm^{-1}; ^1H NMR ($CDCl_3$, 250 MHz) δ 3.49 (d, 1 H, *J* = 11.6 Hz), 3.50 (d, 1 H, *J* = 13.6 Hz), 3.60 (d, 1 H, *J* = 13.6 Hz), 3.90 (d, 1 H, *J* = 11.6 Hz), 4.05 (m, 2 H), 4.14 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 42.4, 65.3, 67.5 (×2); mass spectrum, *m/z* calcd for $C_5H_8O_3S_2$ 179.9915, found 179.9913.

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Registry No. **1** (R = R′ = X = Y = H), 505-23-7; **1** (R = Me, R′ = X = Y = H), 6007-26-7; **1** (R = *t*-Bu, R′ = X = Y = H), 6007-21-2; **1** (R = *t*-Bu, X = OH, R′ = Y = H), 14044-03-2; **1** (R = *t*-Bu, R′ = X = H, Y = OH), 14044-04-3; **1** (R = *t*-Bu, X = OMe, R′ = Y = H), 68449-87-6; **1** (R = *t*-Bu, R′ = X = H, Y = OTMS), 104574-99-4; **1** (R = *t*-Bu, R′ = Y = H, X = $OSiMe_2(t\text{-Bu})$), 104575-00-0; **1** (R = *t*-Bu, R′ = X = H, Y = $OSiMe_2(t\text{-Bu})$), 104575-01-1; **1** (R = *t*-Bu, R′ = H, X, Y = OCH_2CH_2O), 104575-02-2; **1** (R = Ph, R′ = X = Y = H), 5425-44-5; **1** (R = Ph, R′ = Me, X = Y = H), 6331-22-2; **1** (R = *p*-$MeOC_6H_4$, R′ = X = Y = H), 24588-72-5; **1** (R = *p*-$MeOC_6H_4$, X = OH, R′ = Y = H), 104574-96-1; **3** (X = Y = H), 79032-16-9; *cis*-**3** (X = OMe, Y = H), 104574-97-2; *trans*-**3** (X = H, Y = OMe), 104574-98-3; **3** (X, Y = OCH_2CH_2O), 104575-03-3; *cis*-**3** (X = $OSiMe_2(t\text{-Bu})$, Y = H), 104598-33-6; *trans*-**3** (X = H, Y = $OSiMe_2(t\text{-Bu})$), 104598-34-7; **5**, 18321-16-9; **6** (R = R′ = H), 16487-10-8; *cis*-**6** (R = Me, R′ = H), 60349-78-2; *trans*-**6** (R = H, R′ = Me), 60349-75-9; brugierol, 36437-85-1; isobrugierol, 36437-86-2; *p*-methoxybenzaldehyde, 123-11-5; brugierol *N*-ethylcarbamate, 75663-85-3; isobrugierol *N*-ethylcarbamate, 75655-76-4.

A New Synthesis of β-Keto Phosphonates and β-Keto Silanes

Paul Sampson, Gerald B. Hammond, and David F. Wiemer*†

Department of Chemistry, University of Iowa, Iowa City, Iowa 52242

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A new preparation of β-keto phosphonates from α-bromo ketones, by reaction of dialkyl chlorophosphate electrophiles with the dilithiated derivative of the bromo ketone, is described. This umpolung approach is complementary to the classical Arbuzov synthesis in two important ways. It extends the range of possible ketone substrates, allowing use of secondary α-halo ketones or α-bromo ketones where the Arbuzov reaction often fails. It also extends the variety of phosphonates available, by allowing, for example, the direct preparation of bis(trifluoroethyl) phosphonates. These fluoroalkyl phosphonates are not readily available via the Arbuzov reaction, because tris(trifluoroethyl) phosphite is only weakly nucleophilic. From our efforts to employ (trialkylsiloxy)vinyl bromides and *n*-butyllithium to generate an intermediate vinyllithium reagent, in place of forming the lithium enolate and using *tert*-butyllithium, a facile migration of trialkylsilyl groups from oxygen to the α-carbon has been discovered. This has been exploited in the development of a new route from α-bromo ketones to α-trialkylsilyl ketones.

β-Keto phosphonates are often used for the preparation of α,β-unsaturated ketones via the Horner–Wadsworth–Emmons reaction,[1] and new variations on this reaction appear destined to further increase its usefulness.[2] Unfortunately, synthetic routes to β-keto phosphonates are rather limited. One common route, the acylation of alkyl phosphonate anions,[3] is restricted by the limited availa-

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