axial and equatorial methoxy groups in the same molecule. Here again, normal Selectride behavior reemerges in the product, **15**, arising from apparent equatorial delivery of hydride.

These findings can be accommodated within the theoretical construct recently proposed by Cieplak.[16] The following arguments would be advanced. The combination of the conformationally defined equatorial methoxy groups (cf., **3e**, **4e**, and **5e**), in conjunction with the ring oxygen, erodes the capacity of the adjacent C–C bond to stabilize the $\sigma_{\ddagger}^*$ orbital which begins to emerge from equatorial attack on the ketone. Therefore, axial delivery is favored even with L-Selectride. In the case of compound **12**, where the additional methoxy group is absent, normal equatorial delivery pertains.[17,18] In the compounds bearing axial methoxy groups (**3a**, **4a**, and **14**), the steric constraints against axial attack may override the stabilization factor and equatorial delivery preference is observed with L-Selectride.[9]

While the precise reasons for this effect will continue to be appropriate matters for conjecture and experiment, it is already clear that the capacity to control the facial sense of reduction of the 4-pyranone ketone by stereochemical fine tuning of the anomeric center has many implications. The results of investigations which build upon the findings recorded above will be provided in due course.

Acknowledgment. This work was supported by PHS Grant HL 25848. NMR spectra were obtained through the auspices of the Northeast Regional NSF/NMR Facility at Yale University, which was supported by NSF Chemistry Division Grant CHE 7916210. We are grateful for the contribution of Mark Bednarski via the preparation of compound **14** and in the study of its reduction with L-Selectride.

(15) Compound **14** (78%) was prepared from 1,1-dimethoxy-3-[(trimethylsilyl)oxy]-1,3-butadiene and furfural ($Eu(fod)_3$ catalysis) by M. Bednarski of these laboratories. Alcohol **15** was characterized as its acetate. The reduction is apparently stereospecific.

(16) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. A careful reading of the Cieplak paper is necessary to understand the arguments presented herein.

(17) The highly selective reduction of compound **12** stands in contrast to the result obtained by Monti[18] and co-workers and repeated in our laboratory with 2-methyltetrahydropyran-2-one. The weak selectivity for equatorial delivery (3:1) manifested in the monosubstituted case could well reflect its much greater conformational mobility relative to the cis-2,6-disubstituted compound **12**. Thus, in the Monti case, the nature of the reacting conformer is open to considerable question.

(18) Catelani, G.; Monti, L.; Ugazio, M. *J. Org. Chem.* **1980**, *45*, 919.

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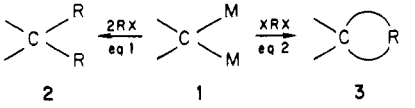
[(Phenylsulfonyl)methylene]dilithium as a Novel Cyclizing and Homologizing Reagent for Bifunctional Organic Substrates[1]

Summary: [(Phenylsulfonyl)methylene]dilithium, generated from methyl phenyl sulfone and 2 equiv of *n*-butyllithium in THF, reacts readily with a series of bifunctional organic substrates, such as dihalides, halo epoxides, halo carbonyls, halo nitriles, dicarbonyls, and α,β-unsaturated carbonyls, to give carbocyclic and homologous derivatives in good to excellent yields.

Sir: The formation of carbon–carbon bonds by the cross-coupling reaction between organometallic reagents and organic halides or sulfonates is a versatile, indispensable mainstay of the synthetic organic chemist.[2,3] Accordingly, an appealing extension of this method has been the generation of reagents bearing geminal carbon–metal bonds (**1**, where, e.g., M = Na,[4] Li,[5] Al,[6] Ti[7-9]), so that

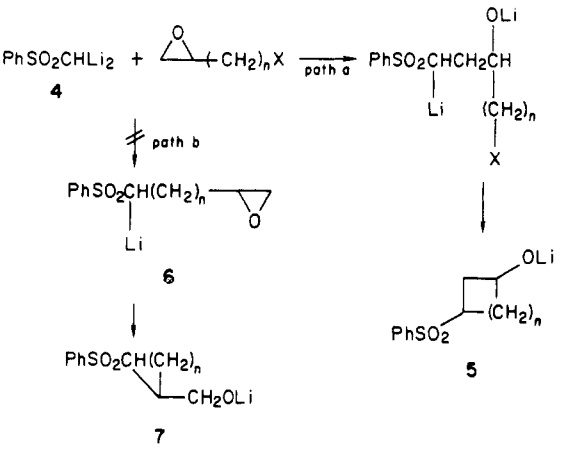


2 1 3

subsequent treatment with carbon electrophiles ($R_2C{=}O$ or 2RX) would lead to the formation of two new carbon–carbon bonds (**2**, eq 1). Alternatively, were a carbon electrophile bearing two reactive centers to be employed, reaction with **1** should lead to carbocyclic products (**3**, eq 2). Indeed, the classic Perkin synthesis of cycloalkanes can be viewed as representing this course of reaction.[10]

Because of the ease of generating geminal dilithio derivatives from alkyl sulfones,[11] we have been encouraged to investigate the little-studied[12] reaction of such geminal dilithioalkyl sulfones with electrophilic bifunctional organic substrates. We now wish to report our finding of a wide variety of high-yielding carbocyclizations and several most

Scheme I



(1) Part 7 of the series Sulfone Reagents in Organic Synthesis; for Part 6, see: *J. Organomet. Chem.* **1985**, *285*, 121.

(2) House, H. O. "Modern Synthetic Reactions", 2nd ed.; W. A. Benjamin: Menlo Park, CA, 1972; pp 492–595.

(3) Kumada, M. *Pure Appl. Chem.* **1980**, *52*, 669.

(4) Kaiser, E. M.; Solter, L. E.; Schwarz, R. A.; Beard, R. D.; Hauser, C. R. *J. Am. Chem. Soc.* **1971**, *93*, 4237.

(5) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019.

(6) Lehmkuhl, H.; Schäfer, R. *Tetrahedron Lett.* **1966**, 2315.

(7) Tebbe, F. N. Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1980**, *102*, 6149.

(8) Howard, T. R.; Lee, J. B.; Grubbs, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 6876.

(9) Eisch, J. J.; Piotrowski, A. *Tetrahedron Lett.* **1983**, *24*, 2043.

(10) Fuson, R. C. In "Organic Chemistry, An Advanced Treatise"; Gilman, H., Ed.; New York, 1943; Vol. I, pp 82–86.

(11) (a) Truce, W. E.; Christensen, L. W. *J. Chem. Soc., Chem. Commun.* **1971**, 558. (b) Pascali, V.; Tangari, N.; Umani-Ronchi, A. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 1166. (c) Bosworth, N.; Magnus P. *J. Chem. Soc., Perkin Trans. 1*, **1973**, 2319. (d) Kondo, K.; Tunemoto, T. *Tetrahedron Lett.* **1975**, 1397. (e) Bongini, A.; Savoia, D.; Umani-Ronchi, A. *J. Organomet. Chem.* **1976**, *112*, 1. (f) Bartlett,. P. A.; Green, F. R., III; Rose, E. A. *J. Am. Chem. Soc.* **1978**, *100*, 4852.

(12) The reaction between 1,1-dilithioalkyl phenyl sulfones and ω-bromo esters, which leads principally to cyclic vinyl ethers, has been investigated: Mussatto, M. C.; Savoia, D.; Trombini, C.; Umani-Ronchi, A. *J. Chem. Soc., Perkin Trans. 1*, **1980**, 260.

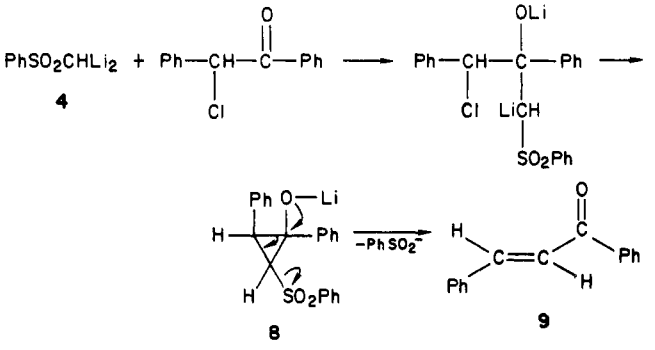
0022-3263/85/1950-3674$01.50/0

Table I. Reactions of [(Phenylsulfonyl)methylene]dilithium (4) with Electrophilic Bifunctional Organic Substrates

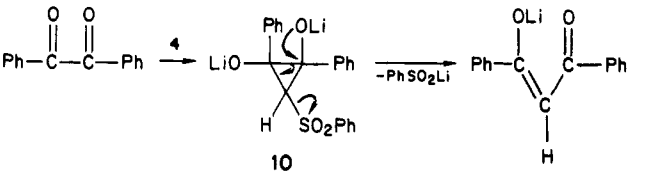
entry	organic substrate	product (% yield)
1	1,2-dichloroethane	(phenylsulfonyl)cyclopropane (60)[a]
2	1,4-diiodobutane	(phenylsulfonyl)cyclopentane (72)[b]
3	3-chloro-1,2-epoxypropane	3-(phenylsulfonyl)cyclobutanol (80)[c]
4	4-bromo-1,2-epoxybutane	3-(phenylsulfonyl)cyclopentanol (84)[c]
5	5-bromo-1,2-epoxypentane	3-(phenylsulfonyl)cyclohexanol (64)[d]
6	4-bromobutanenitrile	cyclopropyl (phenylsulfonyl)methyl ketone (75)[d]
7	(*E*)-1,3-diphenyl-2-propen-1-one	4-(phenylsulfonyl-1,3-diphenyl-1-butanone (60)[d]
8	quinoline	2-[(phenylsulfonyl)methyl]quinoline (53)[e]
9	quinoxaline	2,3-bis[(phenylsulfonyl)methyl]-1,2,3,4-tetrahydroquinoxaline (75)[d]
10	benzil	1,3-diphenyl-1,3-propanedione (40)[f,i] benzoin (27)
11	2-chloro-1,2-diphenyl-1-ethanone	(*E*)-1,3-diphenyl-2-propen-1-one (83)[a,i]
12	2-chlorocyclohexanone	2-cycloheptenone (45)[g,i]
13	2-chloro-1-phenyl-1-ethanone	homopolymer of 1-phenyl-2-propen-1-one (85)[h,i]

[a] Identified by spectral and mixture mp comparison with an authentic sample. [b] Truce, W. E.; Hollister, K. R.; Lindy, L. B.; Parr, J. E. *J. Org. Chem.* **1968**, *33*, 43. [c] Mixture of cis,trans isomers: Decesare, J. M.; Corbel, B.; Durst, T.; Blount, J. M., *Can. J. Chem.* **1981**, *59*, 1415. [d] Identified by elemental analysis and MS, NMR, and IR data. [e] Kauffmann, T.; Jouben, R. *Chem. Ber.* **1977**, *110*, 3930. [f] Allen, C. F. H.; Abell, R. D.; Normington, J. B. "Organic Syntheses"; Wiley: New York, 1951; Collect. Vol. 1, p 205. [g] Garbisch, E. W., Jr. *J. Org. Chem.* **1965**, *30*, 2109. [h] Various attempts to generate phenyl vinyl ketone often lead to its homopolymer: Scaiano, J.; Lissi, E. A.; Stewart, L. C. *J. Am. Chem. Soc.* **1984**, *106*, 1539. [i] Between 85% and 95% of benzenesulfinic acid was recovered from acidification of the aqueous extract of the hydrolyzed reaction mixture.

Scheme II



Scheme III



unusual homologizations. These homologizations can lead either to chain-lengthening or ring-expansion (Table I).

As our test reagent we chose the dilithio derivative of methyl phenyl sulfone, [(phenylsulfonyl)methylene]dilithium (**4**), which can easily be prepared from the sulfone and 2 equiv of *n*-butyllithium in tetrahydrofuran (THF). As can be seen from entries 1–5 in Table I, reagent **4** reacts readily with α,ω-dihalides or halo epoxides to produce homologized cycloalkane derivatives in high yields. That the halo epoxides react to yield the cycloalkanol of the maximum ring size (**5**) argues for an initial attack of **4** on the epoxide function, followed by carbocyclization by lithium halide loss (path a, Scheme I). Were initial attack to occur instead on the carbon–halogen center, then the resulting intermediate **6** would have cyclized to give the smaller cycloalkane **7**, as has been shown by previous workers.[13]

α-Chloro carbonyl derivatives (entries 11–13) also react initially with the oxygen-containing functional group and appear then to form a labile cyclopropanolate (**8**), whose rupture and elimination of the benzenesulfinate anion then consummate the homologization (**9**, Scheme II).

Certain other carbonyl derivatives, such as 2,3-butanedione and 4-bromobutanenitrile (entry 6), react with **4** to undergo abstraction of a proton α to the unsaturated function. Such a reaction with the nitrile leads to cyclization to cyclopropanenitrile, which then adds $PhSO_2CH_2Li$.

In the case of competing unsaturated carbon electrophilic centers (C=O, C=N, or C=C), as in entries 7–10, attack has been found to occur at exclusively one (entries 7 and 8) or both centers (entries 9 and 10). Thus, quinoline undergoes only 1,2-addition, while chalcone ((*E*)-1,3-diphenyl-2-propen-1-one) reacts only in a 1,4-fashion. The unusual homolization of benzil suggests the formation of labile cyclopropanediolate **10** and its subsequent decomposition (Scheme III). In this reaction, electron transfer (ET) is a significant competing process, for benzoin can be isolated in up to 30% yield. Such ET processes appear to play a major role in other reactions of **4** with dicarbonyl and related substrates. Thus both 9,10-phenanthraquinone and quinoxaline undergo some ET reduction with **4**, although the diadduct of **4** with quinoxaline (entry 9) could be isolated. A thorough study of experimental conditions has not yet been made, but preliminary results indicate that the competition between addition and ET processes occurring with **4** depends upon the choice of solvent and temperature for the reaction.

As the following illustrative procedure shows, the ease of generating **4** in situ and permitting it to react with readily accessible substrates makes **4** a convenient, valuable reagent for producing cycloalkane and homologized open-chain derivatives. Furthermore, an array of well-developed methods is at hand for the aryldesulfonylation of such carbon skeletons,[14] so that the corresponding sulfur-free organic derivatives thereby also become accessible.

A typical procedure for preparing **4** and thereafter preparing 3-(phenylsulfonyl)cyclopentanol is as follows.

(13) (a) Decesare, J. M.; Corbel, B.; Durst, T.; Blount, J. F. *Can. J. Chem.* **1981**, *59*, 1415. (b) Corbel, B.; Decesare, J. M. Durst, T. *Can. J. Chem.* **1978**, *56*, 505.

(14) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R., *Tetrahedron Lett.* **1976**, 3477.

A solution of 1.50 g (9.6 mmol) of methyl phenyl sulfone[15] in 30 mL of anhydrous THF was cooled at 0 °C under nitrogen and thereafter treated dropwise with a solution of 14 mL (21.1 mmol) of *n*-butyllithium in hexane. Upon the addition, a yellow suspension began to form. After a further hour of stirring at 0 °C, the suspended reagent **4** was treated dropwise with a solution of 1.45 g (9.6 mmol) of 4-bromo-1,2-epoxybutane[16] in 10 mL of anhydrous THF. The reaction mixture was stirred for 30 min at 0 °C and then allowed to attain room temperature. Quenching with water and workup with an ether–water mixture gave an organic layer that was separated, dried over anhydrous $MgSO_4$, evaporated in vacuo, and subjected to column chromatography on silica gel. Elution with a EtOAc–hexane pair (4:1, v/v) gave 1.81 g (84%) of 3-(phenylsulfonyl)cyclopentanol as a cis,trans isomeric mixture: mp 103–108 °C[13]; ^1H NMR ($CDCl_3$) 1.7–2.4 (6 H, m), 2.9–3.1 (1 H, hydroxyl), 3.5–3.9 (1 H, m), 4.2–4.6 (1 H, m), 7.4–7.8 (5 H, m); IR (mineral oil) 3500 (OH),1300, 1150 cm^{-1}.

Acknowledgment. This research was supported by Grant CA 28335 from the National Cancer Institute of the Public Health Service.

Registry No. **4**, 59807-81-7; **9**, 614-47-1; *cis*-3-(phenylsulfonyl)cyclopentanol, 97861-58-0; *trans*-3-(phenylsulfonyl)-cyclopentanol, 97861-59-1; 5-bromo-1,2-epoxypentane, 21746-87-2; 2-chloro-1,2-diphenyl-1-ethanone, 447-31-4; 2-chloro-1-phenyl-1-ethanone, 532-27-4; (phenylsulfonyl)cyclopropane, 17637-57-9; (phenylsulfonyl)cyclopentane, 14633-46-6; *cis*-3-(phenylsulfonyl)cyclobutanol, 97861-60-4; *trans*-3-(phenylsulfonyl)-cyclobutanol, 97861-61-5; 3-(phenylsulfonyl)cyclohexanol, 65288-09-7; cyclopropyl (phenylsulfonyl)methyl ketone, 74480-95-8; 4-(phenylsulfonyl)-1,3-diphenyl-1-butanone, 97861-62-6; 2-[(phenylsulfonyl)methyl]quinoline, 65492-27-5; 2,3-bis(phenylsulfonyl)-1,2,3,4-tetrahydroquinoxaline, 97861-63-7; 1,2-diphenyl-1,3-propanedione, 5669-11-4; poly(1-phenyl-2-propen-1-one), 26742-84-7; methyl phenyl sulfone, 3112-85-4; 4-bromo-1,2-epoxybutane, 13287-42-8; 1,2-dichloroethane, 107-06-2; 1,4-diiodobutane, 628-21-7; 3-chloro-1,2-epoxypropane, 106-89-8; 4-bromobutyronitrile, 5332-06-9; (*E*)-1,3-diphenyl-2-propen-1-one, 614-47-1; quinoline, 91-22-5; quinoxaline, 91-19-0; benzil, 134-81-6; 2-chlorocyclohexanone, 822-87-7; 2-cycloheptenone, 1121-66-0.

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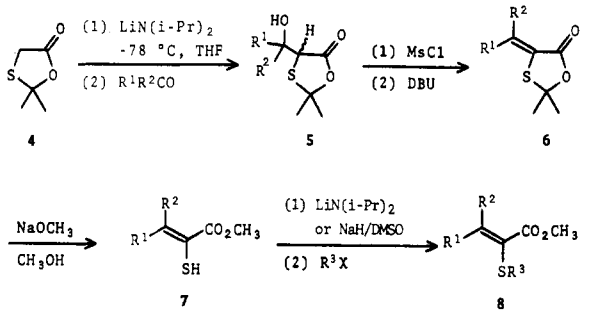
Synthesis of α-Carbalkoxy Enethiols: A Class of Tautomeric Thiopyruvate Derivatives. Application to Griseoviridin[1]

Summary: A general approach to previously inaccessible α-carbalkoxy enethiols **1** is described (e.g., **4** → **5** → **6** → **7**), and the use of such substances in synthesis is illustrated (**11**).

Sir: The α-carbalkoxy enethiols **1** are an unusual class of compounds which may be regarded as tautomers of α-thioketo esters or thiopyruvate derivatives **2** (eq 1). An important naturally occurring compound that contains this functionality as an *S*-alkyl derivative is griseoviridin (**3**), a member of the streptogramin family of antibiotics.[3-5] Also, α-carboxy enethiols have been used as synthetic intermediates leading to other systems.[6]

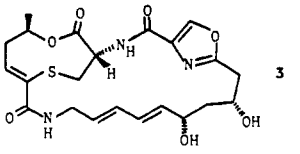
Scheme I



4 5 6 7 8

(1)

1 2



3

Although various procedures have been reported for the preparation of enethiols and thioketones, these methods are not very general.[7] They are commonly limited to aryl-substituted systems rather than being useful for the aliphatic derivatives in which we are interested as a broader representation of these compounds. Indeed, we have attempted to employ Lawesson's reagent[8] and rhodanine derivatives,[7a] but we have been uniformly unsuccessful in our aliphatic systems. Therefore, we have elected to explore new methodology which we describe herein as a general solution to this problem and which we have applied to griseoviridin.

With precedents in work of Lawesson,[9] we have developed the 1,3-oxathiolanone **4** as a quite useful reagent for our purposes. This compound is easily prepared from

(1) (a) This work was presented in part at the 186th National Meeting of the American Chemical Society, Aug 1983, Washington, D.C.: Abstr. No. ORGN 120. (b) Taken in part from Butera, J. Ph.D. Dissertation, State University of New York at Stony Brook, 1985.

(2) Address correspondence to this author at the Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556.
(3) For the isolation and structural studies of griseoviridin, see: (a) Ehrlich, J.; Coffey, G. L.; Fisher, M. W.; Galbraith, M. M.; Knudsen, M. P.; Sarber, R. W.; Schlingman, A. S.; Smith, R. M.; Weston, J. K. *Antibiot. Ann.* **1954–1955**, 790–805. (b) Birnbaum, G. I.; Hall, S. R. *J. Am. Chem. Soc.* **1976**, *98*, 1926–1931. (c) Bycroft, B. W.; King, T. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1996–2004.
(4) For studies on the mechanism of action of griseoviridin, see: Barbacid, M.; Contreras, A.; Vazquez, D. *Biochim. Biophys. Acta* **1975**, *395*, 347–354, and references cited therein.
(5) For studies directed toward the synthesis of griseoviridin, see: Meyers, A. I.; Lawson, J.; Amos, R. A.; Walker, D. G.; Spohn, R. F. *Pure Appl. Chem.* **1982**, *54*, 2537–2544.
(6) Ogawa, K.; Yamada, S.; Terada, T.; Yamazaki, T.; Honna, T. *Synthesis* **1984**, 595 and references cited therein.
(7) (a) Campaigne, E. *Chem. Rev.* **1946**, *39*, 1–77. (b) Mayer, R.; Morgenstern, J.; Fabian, J. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 277–286. (c) Ohno, A. In "Organic Chemistry of Sulfur"; Oae, S., Ed.; Plenum Press: New York, 1977; Chapter 5. For some reactions in which α-carboxy enethiols are generated in low yields as side products, see: (d) Sado, M.; Abe, H.; Inuzuka, N.; Shirai, K.; Kumamoto, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1665. (e) Matsui, S. *Ibid.* **1984**, *57*, 426–434.
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(9) Jensen, L.; Thomsen, I.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1977**, *86*, 639–646.

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