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}.

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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.

(15) Eisch, J. J.; Behrooz, M.; Dua, S. K. *J. Organomet. Chem.* **1985**, *285*, 121.
(16) Cruickshank, P. A.; Fishman, M. *J. Org. Chem.* **1969**, *34*, 4060.

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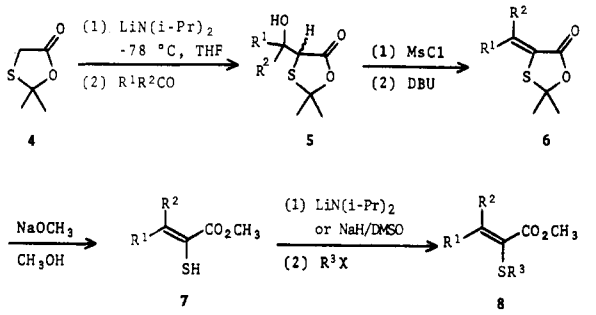
Synthesis of α-Carbalkoxy Enethiols: A Class of Tautomeric Thiopyruvate Derivatives. Application to Griseoviridin[1]

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]

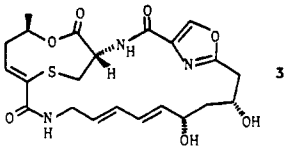
Scheme I



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.
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(8) Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223–228.
(9) Jensen, L.; Thomsen, I.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1977**, *86*, 639–646.

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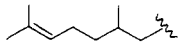
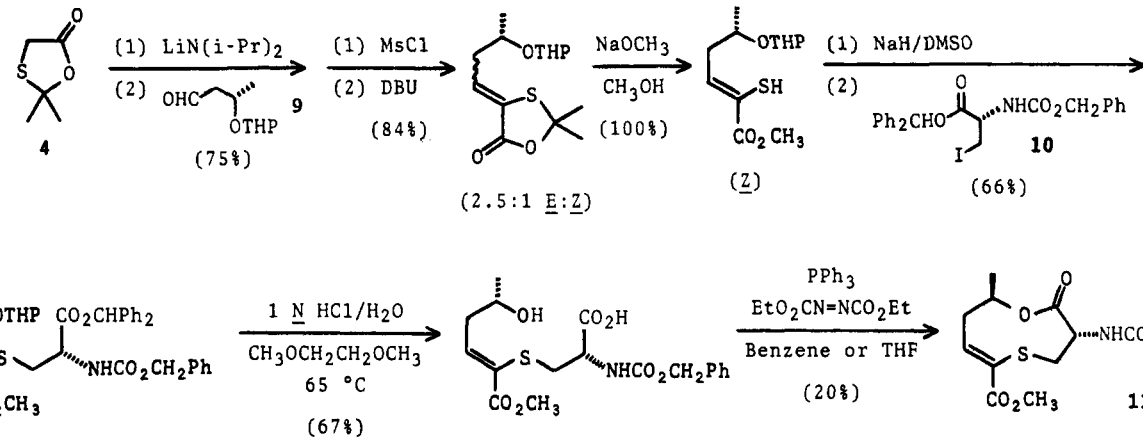
Table I. Preparation of Compounds 5-8

R^1	R^2	products 5-7 and yields, %	R^3X	yield of 8, %
Ph	H	5a, 77; 6a, 94 (*Z* only); 7a, 100	CH_3I	8a, 67
n-C_6H_{13}	H	5b, 70; 6b, 81 (*Z*:*E* = 3:1); 7b, 100	CH_3I	8b$_1$, 85
			$H_2C{=}CHCH_2Br$	8b$_2$, 67
			$PhCH_2Br$	8b$_3$, 57
			n-C_4H_9I	8b$_4$, 62
				8b$_5$, 45
	H	5c, 89; 6c, 88 (*Z*:*E* = 3:2); 7c, 100	CH_3I	8c, 83
$CH_3CH{=}CH$	H	5d, 77; 6d, 91 (*Z*:*E* = 3:2); 7d, 81	CH_3I	8d, 25
CH_3	CH_3	5e, 88; 6e, 73		
$-(CH_2)_5-$		5f, 76		

Scheme II



α-mercaptoacetic acid and acetone.[10] Treatment with lithium diisopropylamide affords the corresponding enolate which then undergoes condensation with aldehydes and ketones as also observed by McIntosh.[11] The resulting diastereomeric mixtures of carbonyl adducts **5** may be subjected to dehydration to give mixtures of the (*E*)- and (*Z*)-alkenes **6**. Cleavage with sodium methoxide then gives the desired α-carbomethoxy enethiols **7** with the *Z* configuration (when R^2 = H) as seen in griseoviridin (**3**). Although the earlier literature indicated the inaccessibility of these compounds,[7] we find that not only may they be prepared but that they may be stored as neat liquids for at least 1 day at −70 °C and may be handled for short times at room temperature.[12] Treatment with base followed by various alkyl halides gives the corresponding alkenyl sulfides 8[13] in high yields (Scheme I, Table I).[14]

In order to demonstrate the applicability of our reaction sequence to complex systems, we have synthesized the unusual sulfur-containing nine-membered lactone system **11** (Scheme II) of griseoviridin (**3**) through use of the optically active aldehyde **9**[15] and iodide **10**.[16] Meyers has reported a synthesis of a derivative of **11** through use of a quite different pathway.[6] In common with the Meyers route, though, we employ a Mitsunobu-type lactonization[17] in the very last step.

In summary, we have developed a general approach to a class of enethiols which were previously inaccessible.

(10) Pihlaja, K.; Nikkila, A.; Neuvonen, K.; Keskinen, R. *Acta Chem. Scand., Ser. A* **1976**, *A30*, 457-460.

(11) McIntosh and co-workers have recently reported alkylations and condensations of the oxathiolanone **4** but have indicated few further transformations of the resulting products. See: McIntosh, J. M.; Mishra, P.; Siddiqui, M. A. *J. Org. Chem.* **1984**, *49*, 1036-1040.

(12) Spectral data is given for **7b** as a representative compound of this series: ^{1}H NMR ($CDCl_3$) δ 6.88 (t, *J* = 7.2 Hz, 1 H, C=CH), 3.88 (s, 1 H, SH), 3.79 (s, 3 H, CH_3 ester), 2.20 (m, 2 H, C=CCH_2), 1.30 (m, 8 H, $(CH_2)_4$), 0.85 (br t, 3 H, CH_2CH_3); IR (neat film) 2920 (CH), 2575 (SH), 1708 cm^{-1} (C=O); mass spectrum (70 eV), *m*/*z* (relative intensity) 204 (5, M^+ + 2), 203 (12, M^+ + 1), 202 (75, M^+) 142 (33), 132 (42), 110 (43), 113 (53), 109 (100), 100 (97), 87 (32), 86 (45), 85 (39), 71(82), 67 (40).

(13) To date, the best conditions for accomplishing these alkylations are to form the enethiolate anion at −78 °C with lithium diisopropylamide as the base in THF, to add 1 equiv of hexamethylphosphoric triamide, and then to warm the mixture to −15 °C before adding the alkylating agent. An alternative is to employ sodium hydride/dimethyl sulfoxide.

(14) We have found that a related sequence of reactions may be performed starting with ethyl *S*-trimethylsilyl α-mercaptoacetate and aliphatic aldehydes, although previous uses of this sequence have been limited to aromatic aldehydes; see: Hayashi, T.; Midorikawa, H. *Tetrahedron Lett.* **1973**, 2461-2462. The yields, however, are much higher when reagent **4** is used.

(15) (a) Seuring, B.; Seebach, D. *Helv. Chim. Acta* **1977**, *60*, 1175-1181. (b) Wipf, B.; Kupfer, E.; Bertazzi, R.; Leuenberger, H. G. W. *Ibid.* **1983**, *66*, 485-488. (c) Seebach, D.; Sutter, M. A.; Weber, R. H.; Züger, M. F. *Org. Synth.* **1984**, *63*, 1-9. (*S*)-Ethyl 3-hydroxybutyrate was protected (dihydropyran, pyridinium tosylate, CH_2Cl_2), reduced to the alcohol ($LiAlH_4$, ether), and oxidized ($(COCl)_2$, Me_2SO, Et_3N) to afford the optically active aldehyde **9**: $[\alpha]^{20}_D$ +12.48°; ^{1}H NMR ($CDCl_3$) δ 8.25 (m, 1 H, C(O)H), 4.55 (br s, 1 H, OCHO), 4.25 (m, 1 H, CH_3CH), 3.25-4.00 (m, 2 H, OCH_2), 2.50 (m, 2 H, CH_2CHO), 1.50 (m, 6 H, $(CH_2)_3$), 1.29 (d, *J* = 8 Hz, CH_3 of one diastereomer), 1.21 (d, *J* = 8 Hz, CH_3 of the other diastereomer); IR (neat film) 2970 (CH), 2750 (CHO), 1725 cm^{-1} (C=O).

(16) D-Serine was protected ($PhCH_2OCOCl$, $NaHCO_3$, H_2O), esterified (Ph_2CN_2), and converted to **10** (CH_3SO_2Cl, Et_3N; NaI, acetone) in analogy to transformations of serine and cysteine employed in our synthesis of sparsomycin. See: Hwang, D.-R.; Helquist, P.; Shekhani, M. S. *J. Org. Chem.* **1985**, *50*, 1264. We have also developed a route to **11** starting with L-serine (ref 1b).

(17) Mitsunobu, O. *Synthesis* **1981**, 1-28.

Applications of this methodology and further uses of the oxathiolanone **4** and its derivatives are being investigated.

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