

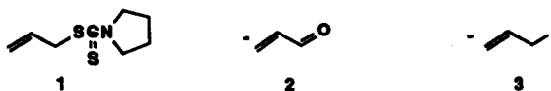
## Allyl Dithiocarbamate as a New $\beta$ -Acyl Vinyl Anion Equivalent

Toshio Hayashi

The Institute of Physical and Chemical Research (RIKEN), Wako, Saitama  
351, Japan

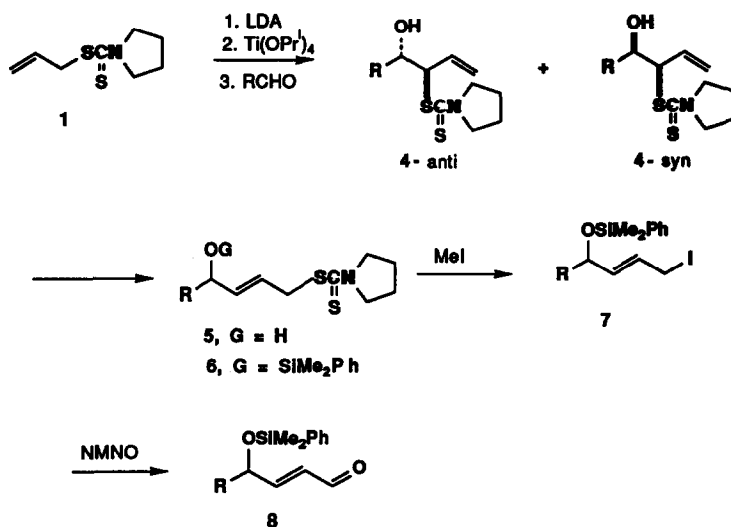
**Abstract:** The title compound can function as synthetic equivalents of  $\beta$ -formyl vinyl and  $\beta$ -halomethyl vinyl anions, as shown by the conversion of aldehydes to 4-hydroxy-2(E)-enals and 4-hydroxy-1-iodo-2(E)-alkenes.

Synthetic equivalent of a  $\beta$ -Formyl vinyl anion (2) can be used as an umpoled synthon <sup>1</sup> for the preparation of 4-oxygenated 2-alkenals (8) which are important features of many natural products including macrocyclic antibiotics, such as pyrenophorin, brefeldin, and cytochalasins,<sup>2</sup> and also serve as a versatile intermediate for other synthetic targets, such as the prostaglandins,<sup>3</sup> coriolic and dismorphelic acids.<sup>4</sup> Although synthon(2) leading to enals has been extensively pursued by a number of investigators<sup>5</sup> since the first report by Corey,<sup>3a</sup> these reagents have not been used for the synthesis of 4-hydroxyenals (8).<sup>5</sup> Herein, we report allyl dithiocarbamate (1)<sup>6</sup> as a new  $\beta$ -formyl vinyl anion equivalent (2) and also  $\beta$ -halomethyl vinyl anion equivalent (3), which transforms aldehydes effectively into 4-oxygenated 2-alkenals (8) and 1-iodoalkenes (7) (Scheme 1). Recently, the iodides (7) has been proved to be useful substrates for the diastereoselective  $S_N2'$  reactions.<sup>7</sup>



The lithium salt of 1, generated with LDA in THF at  $-70^{\circ}\text{C}$  under argon atmosphere, reacts with aldehydes in the presence of  $\text{Ti}(\text{OPr}^i)_4$ , at the  $\alpha$ -site of 1<sup>8,9</sup> to give a diastereomeric mixture of 4-*syn*- and 4-*anti*-isomers in an excellent yield. The mixture, when refluxed in  $\text{CCl}_4$  for 5 h, affords only one isomer of 5 in 95% yield. The hydroxy group is then protected with the dimethylphenylsilyl group according to the conventional method.<sup>10</sup> The transformation of 6 to 7 is straightforward; 6 is dissolved

in an excess of MeI and the mixture is allowed to stand in the dark at room temperature under argon atmosphere for two days.<sup>11</sup> The resulting iodide (7) is extracted with pentane and then purified with silica gel chromatography. The iodides (7) are immediately submitted to the next reaction, where the oxidation of 7 to 8 is achieved by refluxing 7 with N-methyl-morpholine-N-oxide (NMNO)<sup>12</sup> in CH<sub>2</sub>Cl<sub>2</sub>. The aldehydes (8) are purified with silica gel chromatography. The yield of each step is listed in Table 1.





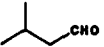

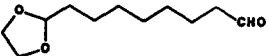
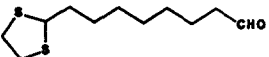
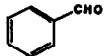
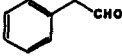
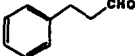
Scheme 1

This  $\beta$ -formyl vinyl anion methodology was applied to the synthesis of coriolic and dismorphelic acids.<sup>4</sup> The coupling reactions of **8d** with the Wittig reagent (9) afforded coriolic ester (10) in 57% yield, and **8f** reacted with the reagent (11) provided the carbon frame (12) of dismorphelic acid in 93% yield (Scheme 2, In each case, the yield of the *trans* isomer is < 3%).<sup>14</sup>

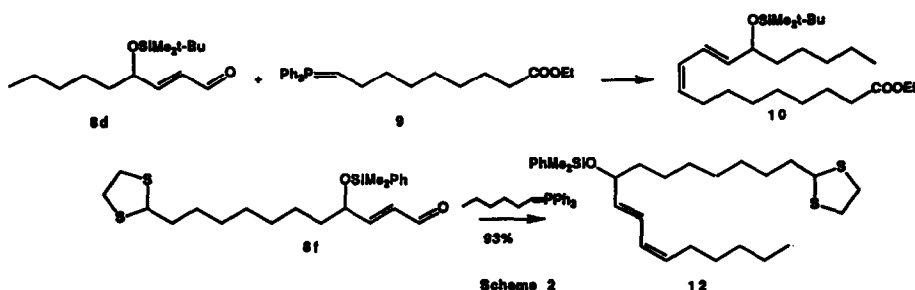
In Summary, aldehydes can be transformed to 4-hydroxy-2-enals and 4-hydroxy-1-iodo-alkenes under mild conditions from commercially available allyl dithiocarbamate.<sup>13</sup> Each step has an excellent yield. This methodology has been successfully applied to the synthesis of coriolic and dismorphelic acids.

**Acknowledgement.** Thanks are due to Dr. Takeshi Oishi of this Institute for his encouragement and useful advice to carry out this work.

Table 1

| entry |   | Yield (%) <sup>a</sup><br>of 4 <sup>b,c</sup> | Yield <sup>a</sup> (%)<br>of 6 <sup>c</sup> | Yield (%) <sup>a</sup><br>of 7 <sup>c</sup> |
|-------|---|---|---|---|
| a     |    | 98  | 88  | 76  |
| b     |    | 97  | 86  | 75  |
| c     |    | 95  | 85  | 76  |
| d     |    | 92  | 85  | 70  |
| e     |    | 99  | 84  | 72  |
| f     |    | 96  | 82  | 75  |
| g     |   | 92  | 80  | 76  |
| h     |  | 89  | 88  | 72  |
| i     |  | 82  | 89  | 70  |

<sup>a</sup> Isolated yield; <sup>b</sup> Mixture of diastereomers.; <sup>c</sup> The structures of the products were determined spectroscopically.



## References

1. a) Corey, E.J. *Pure Appl. Chem.*, **1967**, 14, 19 ; b) Hase, H.A. "Umpeoled Syn-  
thons" **1987**, John Wiley, New York.
2. a) Bakuzis, P., Bakuzis, M.L.F., Weingartner, T.F. *Tetrahedron Lett.*, **1978**,  
2371; b) "The Total Synthesis of Natural Products" vol.8, ed. by J. Sp-  
Simon, p. 102, **1988**, John Wiley, New York.
3. a) Corey, E.J., Erickson, B.W., Noyori, R. *J. Am. Chem. Soc.*, **1971**, 93, 1724.  
b) Bindra, J.S., Bindra, R. "Prostaglandin Synthesis" Academic Press, New  
York
4. de Montarby, L., Tourbah, H., Gree, R. *Bull. Soc. Chim. France*, **1988**, 419.  
and the literatures cited herein.
5. a) Leroux, Y., Montione, R. *Tetrahedron Lett.*, **1971**, 591, 593.; b) Hirai, K.,  
Kishida, Y. *ibid.* **1972**, 2743.; c) Nakai, T., Shiono, H., Okawara, M. *ibid.*  
**1974**, 3625.; d) Hori, I., Hayashi, T., Midorikawa, H. *Synthesis*, **1975**, 727.;  
e) Oshima, K., Yamamoto, H., Nozaki, H. *Bull. Chem. Soc. Japan*, **1975**, 48,  
1567 ; f) Cohen, T., Bennett, D.A., Mura, A.J. *J. Org. Chem.*, **1976**, 41, 2506  
; g) Lansbury, P.T., Britt, R.W. *J. Am. Chem. Soc.*, **1976**, 98, 4577.; h)  
Wada, M., Nakamura, H., Taguchi, T., Takei, T. *Chem. Lett.*, **1977**, 345.; i)  
Piers, E., Morton, H.E. *J. Org. Chem.*, **1979**, 44, 3437.; j) Reich, J.H., Clark  
M.C., Willis Jr., W.W. *ibid.* **1982**, 47, 1618.; k) Rud, K.O., BiEkogha, C.B.,  
Julia, S.A. *Tetrahedron Lett.*, **1983**, 24, 4827.; l) Crombie, C.C., Fisher, D.,  
*ibid.* **1985**, 26, 2477.; m) Najera, C., Yus, M. *Tetrahedron Lett.*, **1987**, 28,  
8709.; For the preparaation of 4-hydroxy-enals, see n) Funk, R.L. Bolton,  
G.L., *J. Am. Chem. Soc.*, **1988**, 110, 1920.; o) Chabert, P., Ousset, J.B.,  
Mioskowski, C., *Tetrahedron Lett.*, **1989**, 30, 179.
6. a) Hayashi, T., *Tetrahedron Lett.*, **1974**, 339.; b) Hayashi, T., *J. Syn.*  
*Org. Chem. Japan*, **1986**, 44, 245.
7. Nakamura, E., Sekiya, K., Arai, M., Aoki, S. *J. Am. Chem. Soc.*, **1989**, 111, 3091
8. Ikeda, Y., Furuta, K., Meguriya, N., Ikeda, N., Yamamoto, H. *J. Am. Chem. Soc.*, **1982**  
104, 7663.
9. Hayashi, T., Ikeda, K., Oishi, T., *J. Chem. Soc. Japan.*, **1987**, 1403.
10. Colvin, E.W. "Silicon Reagents in Organic Synthesis" p. 93, **1988**,  
Academic Press, New York.
11. Sakurai, A., Hayashi, T., Hori, I., Jindo, Y., Oishi, T., *Synthesis*, **1978**, 370.
12. These oxides were used by Otera et al., see, Suzuki, S., Onishi, T., Fujita,  
Y., Misawa, H., Otera, J., *Bull. Chem. Soc. Japan*. **1986**, 59, 3287.
13. The reagent (1) can be purchased from Tokyo Kasei Kogyo Co., LTD.
14. 10 and 11 can be easily converted to coriolic and dimorphecolic acids.

(Received in Japan 13 April 1990)