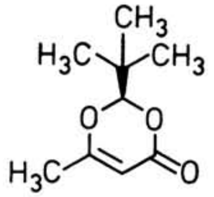
First Fluka-Prize

'Reagent of the Year'

1987

Chiral Aceto Acetic Acid Derivative



20264 (2R)-2(tert.Butyl)-6-methyl-2H, 4H-1, 3-dioxin-4-one, purum 98% (GC)

The Prize Winner 1987: Dieter Seebach

Dieter Seebach, born 1937, studied at the University of Karlsruhe and graduated with a thesis on peroxides under the direction of R. Criegee. After a postdoctoral year with E. J. Corey at Harvard University he became a professor of organic chemistry at the University of Giessen in 1970. In 1977 he was appointed professor of chemistry at the Eidgenössische Technische Hochschule (ETH Zürich) where he has been working since.

The Reagent:

Dieter Seebach's new concept of chirality transfer to an auxiliary stereogenic centre to preserve stereochemical integrity during manipulation on the original centre has led to this new chiral Aceto Acetic Acid Derivative.

Reaction at this Aceto Acetic Acid Derivative forming new stereogenic centers proceed with high diastereoselectivity.

Package sizes 1 and 5 g.

Literature

[1] J. Zimmermann, D. Seebach, Helv. Chim. Acta 70, 1104 (1987).

[2] D. Seebach, J. Zimmermann, U. Gysel, R. Ziegler und Tae-Kyn Ha, J. Am. Chem. Soc. (1988) in the press.

Starting 1987, the Fluka Prize "Reagent of the Year" is awarded anually to a research project, in which a new compounc has been shown to be a reagent of prime importance, useful in organic chemistry, biochemistry or analytical chemistry.

To be eligible for consideration the reagent should have been synthesized for the first time. In exceptional cases, a known compound which has been shown to be a reagent with particular new applications might be considered.

Nominations will be accepted for any scientist or group of scientists working within Universities, Government or privatε Institutes or in industry. The winner will be awarded the sum of sFr. 10'000.–. He will be free of any obligations on behalf of Fluka Chemie AG.

Nominations for the Fluka-Prize "Reagent of the Year" should be submitted to the Fluka-Prize Committee c/o Fluka Chemie AG, CH-9470 Buchs/Switzerland not later than September 30th of the prize year.

Full details regarding the Fluka-Prize are available upon request.

Prize Committee 1987: A. Eschenmoser, ETH Zürich; G. Haas, Ciba-Geigy Basel; H.-J. Hansen, Hoffmann-LaRoche Basel; W. Graf, Fluka Buchs.

Fluka

Fluka Chemie AG
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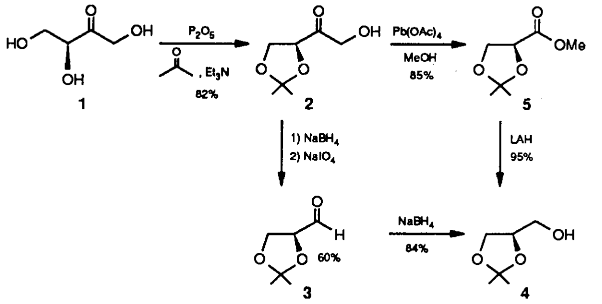
(S)-(+)-Erythrulose Progenitor of C-3 and C-4 Chirons

The elaboration of simple chiral building blocks ("chirons")[1] into complex chiral natural products is an often used and efficacious strategy, provided, of course, that building blocks of high enantiomeric purity are readily available and these suffer no chance racemization in subsequent synthetic transformations.[1,2] **(*S*)-(+)-Erythrulose [1,** L-(+)-erythrulose], a C-4 aldose derivative whose stereogenic center is antipodal to natural sugars is such a building block. This unnatural sugar derivative, heretofore accessible synthetically only with difficulty, is now readily available in significant quantities. Our material is a viscous oil which contains about 9% water by weight to improve its mobility and ease of handling. Anhydrous material can be conveniently prepared without racemization.[3] As indicated below **(*S*)-(+)-erythrulose** and its derived acetonide **2** hold considerable promise as useful chiral building blocks and as progenitors of important C-3 and C-4 chirons.

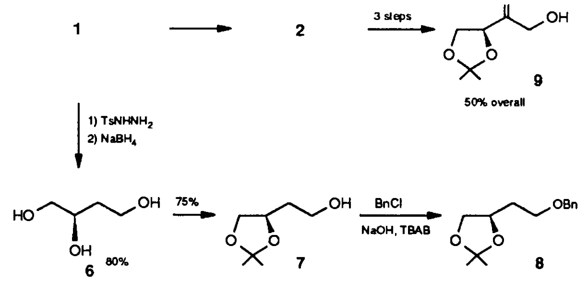
C-3 Chirons

Vandewalle and co-workers[3] have recently demonstrated that **1** *via* its readily prepared acetonide **2** is a convenient source of important enantiomerically pure[4] C-3 chiral building blocks such as the acetonides of L-glyceraldehyde **(3)**, L-glycerol **(4)**, and L-methyl glycerate **(5)**. Aldehyde **3**, which has also been prepared recently in three steps from L-ascorbic acid,[5] provides access *via* Wittig reaction to valuable intermediates for carbapenem synthesis.[6] The use of **3** and its enantiomer in stereoselective organic synthesis has been reviewed recently.[7] L-Glycerol acetonide **(4)** was recently employed in the synthesis of a chiral diene which holds potential for enantioselective cyclic terpene synthesis.[8] L-Methyl glycerate acetonide **(5)** has been employed in a synthesis of (+)-dropropizine.[9] Treatment of **5** with methyllithium at low temperature affords a good yield of the corresponding methyl ketone.[10]

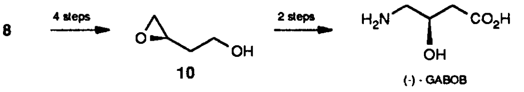


C-4 Chirons

Vandewalle and coworkers[11] have demonstrated that **1** and **2** are also useful precursors to optically pure,[12] synthetically useful C-4 chiral building blocks.



Triol **6** has been transformed in high yield to (*R*)-3-hydroxytetrahydrofuran on treatment with tosic acid[13] and provided a key intermediate for the synthesis of okadaic acid.[14] Acetonide **8** proved useful for the synthesis of the epoxy alcohol **10**, which can be converted to (-)-γ-amino-β-hydroxybutyric acid [(-)-GABOB].[15]



References and Notes:

(1) Hanessian, S. *Total Synthesis of Natural Products: The 'Chiron' Approach;* Pergamon Press, Inc.: New York, 1984. (2) Morrison, J.D. *Asymmetric Synthesis;* Scott, J.W., Ed.; Academic Press, Inc.: New York, 1984; Vol. 4. (3) DeWilde, H.; DeClerq, P.; Vandewalle, M. *Tetrahedron Lett.* **1987,** *28,* 4757. (4) Conversion of **3** and **5** into L-glycerol acetonide followed by ^{1}H NMR examination in the presence of a chiral shift reagent revealed one enantiomer only. (5) Hubschwerlen, C. *Synthesis* **1986,** 962. (6) Matsunaga, H. *et al. Tetrahedron Lett.* **1983,** *24,* 3009. (7) Jurczak, J. *et al. Tetrahedron* **1986,** *42,* 447. (8) Maier, M.S.; Breitmaier, E. *Ann.* **1987,** 385. (9) Borsa, M. *et al.* Eur. Patent Appl. 147847, 1985; *Chem. Abstr.* **1985,** *103,* 215734y. (10) Tanner, D.; Somfai, P. *Synth. Commun.* **1986,** *16,* 1517. (11) Van der Eycken, E.; DeWilde, H.; Deprez, L.; Vandewalle, M. *Tetrahedron Lett.* **1987,** *28,* 4759. (12) Optical rotations of **6** and **7** as reported in ref. 11 compare very favorably with literature values. (13) Tandon, V.K. *et al. J. Org. Chem.* **1983,** *48,* 2767. (14) Isobe, M. *Tetrahedron Lett.* **1985,** *26,* 5203. (15) Rossiter, B.E.; Sharpless, K.B. *J. Org. Chem.* **1984,** *49,* 2767.

32,985-1 (*S*)-(+)-Erythrulose hydrate, 97% (1)
5g $19.00; 25g $63.00

30,971-0	**(*R*)-(+)-1,2,4-Butanetriol, 98% (6)**	**1g $14.50**
29,667-8	**(*S*)-(-)-1,2,4-Butanetriol, 98%**	**5g $17.00; 25g $51.00**
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23,774-4	**(*S*)-(+)-2,2-Dimethyl-1,3-dioxolane-4-methanol, 98% (4)**	**1g $23.55**
25,460-6	**(*S*)-(-)-Methyl dimethyl-1,3-dioxolane-4-carboxylate, 98% (5)**	**1g $9.90; 5g $30.90**
30,864-1	**Methyl (4*S*)-*trans*-2,2,5-trimethyl-1,3-dioxolane-4-carboxylate, 97%**	**1g $7.50; 5g $25.00**

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