higher energies. On the other hand, for bent CO, the energy of the dissociative $^3(d_\pi \rightarrow d_{z^2}^*)$ states becomes comparable to that of $^3(\pi \rightarrow \pi^*)$ states with a value also consistent with the photodissociation experiments. As discussed previously,[18] the bent model may also be representative of model compounds as well as intact proteins. On the basis of these and previous results,[18] the observed low-energy triplet states in CO photodissociation are of $d_\pi \rightarrow d_{z^2}^*$ in nature. The intersystem crossing occurs following the initiation of dissociation by a singlet $d_\pi \rightarrow d_{z^2}^*$ transition consistent with the observed rapid spin conversion associated with the photolysis of HbCO.[36]

In conclusion, contrary to the recent reports,[3,4] our calculations of the triplet state energies of carbonylheme complexes for various ligand geometries show that the energy of the lowest triplet state is too high to accommodate a thermally populated paramagnetic state. The calculated energies of the $^3(d_\pi \rightarrow d_{z^2}^*)$ states in the bent geometry and $^3(\pi \rightarrow \pi^*)$ states in all geometries agree with the experimentally observed data in photodissociations by intermolecular triplet excitation transfer. Because of its dissociative nature, the $^3(d_\pi \rightarrow d_{z^2}^*)$ is identified as the state involved in the intersystem crossing during the photodissociation process.

Acknowledgment. The financial support from NSF Grant No. PCM 7921591 is gratefully acknowledged.

Registry No. H_6CO, 67684-33-7.

(36) Terner, J.; Stong, J. D.; Spiro, T. G.; Nagumo, M.; Nicol, M.; El-Sayed, M. A. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 1313-1317.

Synthesis of Saccharides and Related Polyhydroxylated Natural Products. 3. Efficient Conversion of 2,3-*erythro*-Aldoses to 2,3-*threo*-Aldoses

Albert W. M. Lee, Victor S. Martin, Satoru Masamune,* K. Barry Sharpless,* and Frederick J. Walker

Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Received February 18, 1982

The first communication[1a] of this series outlines a general approach to the synthesis of polyhydroxylated natural products of biological significance, covering a wide range of compounds from simple monosaccharides to the complex molecule palytoxin.[2] The approach basically consists of repetitive addition of a two-carbon unit on a proper starting aldehyde (**1**), creating two chiral hydroxymethylene centers (-*CHOH-) in each cycle of the sequence (Scheme I). The success of this strategy relies heavily upon both the efficiency and stereoselectivity attainable in the titanium-catalyzed asymmetric epoxidation[3] of the intermediate *E*- and *Z*-allylic alcohols (**2** and **3**), which, at the end of the sequence, should yield the acetonides of *erythro*- and *threo*-2,3-dihydroxy aldehydes (**4** and **5**), respectively.[4] Our preliminary examination of this sequence published recently[1] may be summarized as follows: (1) in all cases examined, the sequence leading to the 2,3-erythro products (**4**) through the *E* isomer **2** is satisfactory; (2) in contrast, the asymmetric epoxidation of **3** in the 2,3-threo series (**5**), when R* is chiral, often proceeds intolerably slowly and/or with low stereoselection. For this latter deficiency we now have an effective yet very simple remedy, which is described herein in the context of a unified route to the four possible D-pentoses. With this breakthrough our general approach stands on a solid foundation.

Compare the two structures **4** and **5**. These are epimeric only at C(2), which is α to the aldehyde group and thus epimerizable. From the expected stability of **5** relative to **4**, the latter readily obtainable epimer (**4**) (see above) would very likely be equilibrated to give a mixture enriched in **5**, which thus far has been of limited access. In this sense the selection of acetonide protection in **4** and **5** appears to be most appropriate. Not only is this protecting group definitely necessary to set up the interaction that provides the impetus for the desired epimerization, but at the same time the group would suppress the potential complication of a β elimination. This latter effect is anticipated because the acetonide group would maintain orthogonality between the enolate π system and the β-alkoxy substituent[5] (see **6** and **7** in Scheme I). This analysis of the problem has proven valid.

Thus, treatment of **4a-c** with potassium carbonate in methanol at 25 °C for 2 h effects smooth epimerization, providing the corresponding threo isomers **5a-c**, respectively (**5**:**4** = 20:1, Table I). These examples represent the tetrose, pentose, and hexose series. Incorporation of this critical epimerization technique in our general approach now leads to the satisfactory completion of the pentose synthesis.

In Scheme II, compound **8**, which was obtained earlier from **1a** through **2a**, undergoes ring opening[1] to provide **9**, which is converted to the corresponding acetonide **10** under the kinetic acetonation conditions originally developed by Horton et al.[6] Note that the acetonide present in the R group of **9** remains intact during this transformation. Reaction of **10** (0.81 mmol in 10 mL of toluene) with diisobutylaluminum hydride (1.3 mmol, 1 M in toluene) at -78 °C for 1.5 h provides, after aqueous workup and bulb-to-bulb distillation, a product (**11**) (86% yield) shown to be a ribose derivative by comparison with an authentic sample.[7] This reaction proceeds virtually without epimerization.[8] The aldehyde **11** along with the three other aldehydes described below shows a marked proclivity for becoming hydrated[8] and thus exists in two forms. Since a mixture of the aldehyde and its hydrate is difficult to analyze for diastereometric purity, further conformation has been made through the corresponding hydroxy compound, which is readily obtained from **11** by sodium borohydride reduction. Compound **10** is also converted into the C(2) epimer of **11**. Thus, treatment of **10** (0.065 mmol) with potassium carbonate (0.22 mmol) in methanol (0.5 mL) at 25 °C for 2 h causes hydrolysis of the acetoxythioacetal group and epimerization at the C(2) center to give a mixture of aldehydes **12** and **11** in a 98:2 ratio,[8]

(1) (a) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (b) Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. *Ibid.* **1982**, *47*, 1378.

(2) (a) Hirata, Y.; Uemura, D.; Ueda, K.; Takano, S. *Pure Appl. Chem.* **1979**, *51*, 1875. (b) Uemura, D.; Ueda, K.; Hirata, Y.; Naoki, H.; Iwashita, T. *Tetrahedron Lett.* **1981**, *22*, 1909, 2781 and references quoted therein. (c) Scheuer, P. J.; Moore, R. E. *Science (Washington, D.C.)* **1971**, *172*, 495. (d) Moore, R. E.; Bartolini, G. *J. Am. Chem. Soc.* **1981**, *103*, 2491.

(3) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974.

(4) Of the two stereoisomers obtainable from each of **2** and **3**, only one for each series is shown in Scheme I.

(5) (a) Naef, R.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1981**, 1030. (b) Schaffer, R. *J. Am. Chem. Soc.* **1959**, *81*, 5452. (c) Williams, D. T.; Jones, J. K. N. *Can. J. Chem.* **1964**, *42*, 69. (d) Horton, D.; Jewell, J. S.; Just, E. K.; Wander, J. D. *Carbohydr. Res.* **1971**, *18*, 49. (e) Jarrell, H. C.; Szarek, W. A.; Jones, J. K. N.; Dmytraczenko, A.; Rathbone, E. B. *Ibid.* **1975**, *45*, 151. (f) Seebach, D.; Hungerbühler, E. "Modern Synthetic Methods 1980"; Scheffold, R., Ed.; Salle and Sauerland-Verlag: Frankfurt and Aaron, 1980, and references cited therein. (g) See also: Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734, 736, 738.

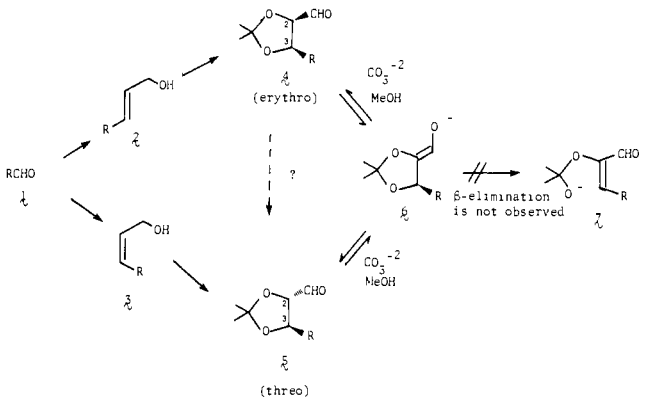
(6) Fanton, E.; Gelas, J.; Horton, D.; Karl, H.; Khan, R.; Lee, C.-K.; Patel, G. *J. Org. Chem.* **1981**, *46*, 4057.

(7) Sodium borohydride reduction of **11** gave (2,3:4,5-diisopropylidene ribitol ($[\alpha]^{27}_D$ +7.0° (*c* 0.96, EtOH) which was identical (^{1}H NMR, IR, TLC, GLC, $[\alpha]_D$) with a sample prepared by kinetic acetonation[6] of 2,3-isopropylidene ribitol (see: Hughes, N. A.; Speakman, P. R. K. *Carbohydrate Res. I* **1965**, 171). Compound **12** and its $NaBH_4$ reduction product ($[\alpha]^{27}_D$ +12.2° (*c* 0.7, EtOH)) were identical in all respects with 2,3:4,5-diisopropylidene arabinose and its corresponding pentitol prepared from D-arabinose, respectively (see: Zinner, H.; Wittenburg, E.; Rembarz, G. *Chem. Ber.* **1959**, 1614). The lyxose series (**14**) was correlated by preparation of lyxitol pentaacetate ($[\alpha]^{22}_D$ = +40.5° (*c* 1.8, EtOH)) as previously described (see ref 1a), and finally the stereochemistry of the xylose series (**13**) follows from a process of elimination.

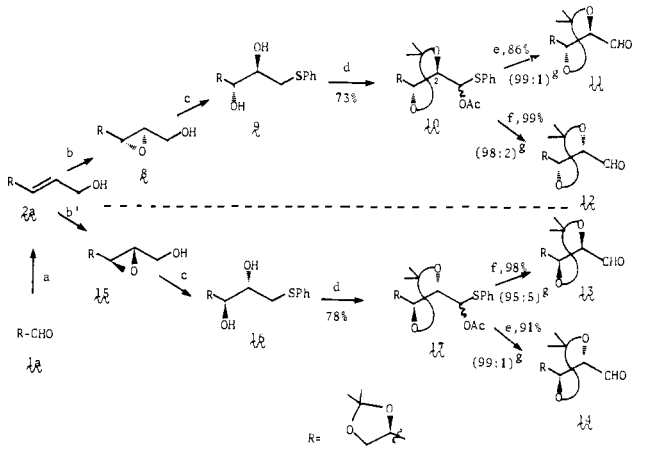
(8) The ratio of epimers was determined by integration of NMR spectra and GLC analysis of the sodium borohydride reduction products [i.e., the (2,3)-(4,5)-diisopropylidene-1-pentitols] of **14**, **13**, **12**, and **11** [retention times 16.1, 15.4, 13.4, and 12.6 min, respectively, 30 M fused silica capillary column, Carbowax 20 M (J & W Scientific, Inc.) 120 °C for 4 min, then program rate of 8 °C/min]. This observed high ratio (98:2) is likely due to the relative stability of the two methyl hemiacetals that form from **12** and **11** in methanol. We thank Professor W. R. Roush for this suggestion.

0002-7863/82/1504-3515$01.25/0

Scheme I

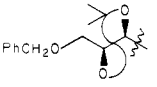


Scheme II.[a] Pentose Synthesis[b]



[a] This scheme shows a complete cycle of the iterative sequence for adding two new chiral centers in any one of the four possible ways. [b] Letters a-g refer to the following: (a) See ref 1, (i) $Ph_3P{=}CHCHO$ (toluene) 0 °C, 39 h, (ii) $NaBH_4$ (MeOH) −40 °C, 10 min; (b) $Ti(O\text{-}i\text{-}Pr)_4$, (−)-DET, TBHP ($CH_2Cl_2$) −20 °C, 15 h; (b') $Ti(O\text{-}i\text{-}Pr)_4$, (+)-DET, TBHP ($CH_2Cl_2$) −20 °C, 15 h; (c) PhSH, 0.5 N NaOH, $(CH_3)_3COH$ (1:1) 100 °C, 3 h; (d) (i) $CH_3(CCH_2)OMe$, camphorsulfonic acid (CH_2Cl_2) 25 °C, 3 h, (ii) *m*-CPBA (CH_2Cl_2) −78 °C, 1 h, (iii) Ac_2O, NaOAc, reflux, 8 h; (e) see text; (f) see text; (g) see footnote 8.

Table I. Base-Catalyzed Epimerization of *erythro*-4 to *threo*-5 Acetonides

erythro isomer	threo isomer	R in 4 and 5	5:4 (equilibrium)
4a	5a	$PhCH_2OCH_2$-	97:3
4b	5b		98:2[a]
4c	5c		>95:5

[a] The ratio observed for 12; see Scheme II.

an even better ratio than we had anticipated at the outset! The major product was shown to have the arabinose configuration in a manner similar to that employed for correlation of **11**. The acetonides (**13** and **14**) of the two remaining pentoses, xylose and lyxose, are prepared in exactly the same manner. The transformation of **2a** through **15** and **16** to **17** proceeds smoothly, and conversions of **17** into **13** and **14** are effected flawlessly. In this way a highly efficient route from the same intermediate to either the *erythro*- or the *threo*-2,3-dihydroxy aldehydes has been established.

A pleasing quality of the sequence shown in Scheme II is its symmetry. With an achiral R group, all structures and reaction steps (including reagents) above and below the dotted line have a perfect mirror image relationship. With a chiral R group, it will be recognized that the titanium-catalyzed epoxidation with a (+)- or (−)-tartrate overrides the influence of the preexisting chirality in the allylic alcohol by exhibiting high enantiofacial selection.[9] Now that efficient, practical routes from a chiral or achiral aldehyde to all of the four possible homologated aldehydes have been established, these four final products are ready for a second two-carbon extension, a central feature incorporated in our approach. Thus, the tetroses should lead to saccharides with an even carbon number and the pentoses to those with an odd number. Our efforts toward these larger saccharides including fragments of palytoxin have been successful even in the case of labile 2,3-erythro aldehydes such as **11** and **14**. These results will be documented in due course.

Acknowledgment. We are grateful to the National Science Foundation, Eli Lilly (unrestricted grant to K.B.S.) and Hoffmann-La Roche (unrestricted grant to S.M.) for generous financial support. V.S.M. thanks the Fundacion Juan March of Spain for a fellowship. High-resolution mass spectra were provided by the facility supported by the National Institutes of Health (Grant RR 00317, the Biotechnology Resources Branch, Division of Resarch Resources).

Registry No. 2a, 80532-35-0; **4a**, 81801-08-3; **4b**, 50866-82-5; **4c**, 81789-99-3; **5a**, 81801-09-4; **5b**, 13039-93-5; **5c**, 81769-40-6; **8**, 80532-36-1; **9**, 81769-41-7; **10**, isomer 1, 81769-42-8; **10**, isomer 2, 81769-43-9; **11**, 50866-82-5; **12**, 13039-93-5; **13**, 13039-94-6; **14**, 81801-10-7; **15**, 80581-19-7; **16**, 81801-11-8; **17**, isomer 1, 81769-44-0; **17**, isomer 2, 81769-45-1.

Supplementary Material Available: Listing of spectra data and specific optical rotations for all new compounds prepared in this work (2 pages). Ordering information is given on any current masthead page.

(9) Excellent stereochemical *control* in the construction of acyclic systems can often be achieved through the use of a enantioface-selective reagent, which outweighs the many other factors influencing the stereochemical course of a reaction. For a recent clear demonstration of this strategy, see: Masamune, S.; Ali, Sk. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557. For an applications, see: Masamune, S.; Hirama, M.; Mori, S.; Ali, Sk. A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568.

(10) **Note Added in Proof**: After the submission of this manuscript a report similar, in content, to our first communication[1a] appeared: Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109.

Planar *cis*-[10]Annulene and Azulene Revisited

Robert C. Haddon* and Krishnan Raghavachari*

Bell Laboratories, Murray Hill, New Jersey 07974

Received November 6, 1981

Aromatic character has proven to be a particularly enduring concept.[1] The central issue in the area of annulene chemistry revolves around the question of the ring size at which [4*n* + 2]annulenes become nonaromatic. This is generally taken to be the point at which the C–C bonds of the perimeter are no longer of equal length but alernate so as to produce a cyclopolyene with a succession of conjugated single and double bonds.[2-3] For some time now attention has been focused on [18]annulene in the belief that this molecule might well be close to the demarcation point between bond equalization and bond alternation in the annulenes.[2-4] Recently, however, theoretical work has suggested that

(1) Garratt, P. J. "Aromaticity"; McGraw-Hill; London, 1971.

(2) Longuet-Higgins, H. C.; Salem, L. *Proc. Roy. Soc. Ser. A* **1959**, *251*, 172.

(3) Salem, L. "Molecular Orbital Theory of Conjugated Systems"; Benjamin: New York, 1966, Chapter 8.

0002-7863/82/1504-3516$01.25/0