product analyzing as $[Ph_4P]_2$ $[S_2MoS_2W(NNMe_2)_2S_2MoS_2]$[13] (**4**), presumably with a structure analogous to **2**.

Acknowledgment. We are grateful to the National Institute of Health for an award (to J.A.Z.) of Grant GM 22566 and to NATO for award (to J.R.D. and J.A.Z.) of Grant 274.80.

Supplementary Material Available: Final positional parameters, final temperature factors, and observed and calculated structure factors (14 pages). Ordering information is given on any current masthead page.

(13) Anal. Calcd for $C_{52}H_{52}N_4Mo_2P_2S_8W$: C, 44.1; H, 3.7; N, 3.9. Found: C, 43.6; H, 3.9; N, 3.7.

Annulated Sugars: The 1,2-*O*-Isopropylidene Ring as a Stereo-, Regio-, and Chemocontrolling Agent[1]

King Mo Sun[2] and Bert Fraser-Reid*

Chemistry Department, University of Maryland College Park, Maryland 20742

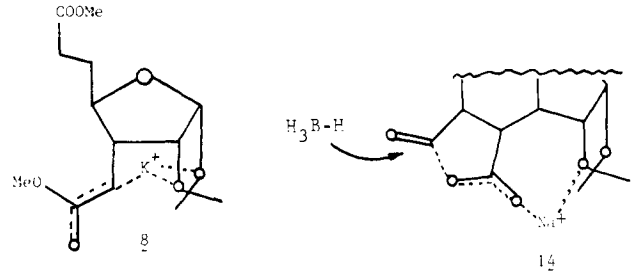
Tim Fat Tam[3]

Guelph-Waterloo Centre for Graduate Work in Chemistry University of Waterloo, Waterloo, Ontario, Canada N22 3G1

Received July 27, 1981

In a recent report from this laboratory we showed that 1,2-*O*-isopropylidenefuranoses such as **1**[4] could serve as precursors for α-methylene-γ-butyrolactones,[5] and consequently annulated furanoses such as **2** may be considered as synthons for sesquiterpene lactones. A survey of this broad family of substances[6] indicates that the absolute configuration at oxygen coincides (usually!) with that at C4 of **1** *whether the lactone is cis or trans fused*,[7] and thus the task is to prepare the 3β and 3α forms of **2** having, respectively, D-xylo and D-ribo configurations on the furanose moiety. In the course of this study we have uncovered remarkable stereocontrolling effects by which each of these forms of **2** may be *prepared and functionalized* with high selectivities.

The work of Rosenthal and Nguyen[8] has shown that the ester **4a** is formed exclusively during hydrogenation of **3**.[8] The derived aldehydic ester **4b**[8,9] was converted into the diester **5a**[10] as indicated in Scheme I. Dieckmann cyclization of **5a** can occur in two possible senses, and indeed treatment with potassium *tert*-butoxide gave a 90% yield of two crystalline compounds in the ratio 10:1. From the 220-MHz ^1H NMR spectra, it was clear that the major isomer was **6a**[10] because of the doublet at 3.44 ppm assignable to H8, the spacing of which (J_{38} = 13.5 Hz) indicated that the methoxycarbonyl group was equatorially oriented. The minor isomer existed entirely in the enolic form **7**[10] as indicated by the IR data (see Scheme I) and the exchangable proton at 12.84 ppm.



Compounds **6a** and **7** result from deprotonation of **5a** at C3[1] and C6, respectively, and one might have expected that the product ratio would be reversed since C3[1] is sterically hindered by the *O*-isopropylidene ring. However, if the influence of the latter were electronic rather than steric, the regiochemical outcome could be readily rationalized, seeing that the C3[1] enolate would be rendered more favorable by chelation of the dioxolane oxygens as in **8**. Thus the 1,2-*O*-isopropylidene ring of **5a** could control the regioselectivity of the cyclization.

In the hope of enhancing the formation of **7**, diester **5a** was treated with a variety of nonchelating bases (Et_3N, DBN, Bu_4NOH), but they all failed to induce cyclization. However, as indicated in Scheme I, *inclusion of two-tenth of an equivalent of 18-crown-6 caused complete suppression of* **6a**. This dramatic example of chelation-mediated regiocontrol was unfortunately soured by the low yield (20%) of **7**; but this reaction has not been optimized, and the direction which must be taken in our future studies is clearly apparent.

From the standpoint of sesquiterpene syntheses, better yields of **7** would have been appreciated since the carboxymethoxy functionality would make provisions for the ubiquitous C4 methyl group of sesquiterpene lactones.[6] Fortunately, this problem was readily solved by using the propionate $[Ph_3P{=}C(CH_3)COOMe]$ for the Wittig reaction to afford diester **5b**.[10] Cyclization as above led to **6b**.[10]

With the trans annulation of **1** thereby secured, we turned to the cis analogue in which the C3 attachment must be made anti to the 1,2-*O*-isopropylidene ring. A Diels-Alder strategy[11] was conceived which required the diene **9** whose preparation from **1** has been described by us elsewhere.[13] The α- face of compound **9** is rendered completely inaccessible by the *O*-isopropylidene ring, and we could therefore predict that the addition of a dieneophile would be β, forcing H3 into syn relationship with the acetonide. Crotonaldehyde, methyl crotonate, and even α-chloroacrylonitrile all failed to react with **9**. However, after 3 h with maleic anhydride in refluxing toluene, a single product (**10a**) was obtained in 86% yield. The material was crystalline, but it decomposed (retro Diels-Alder) on attempted melting point determination. The critical datum J_{23} = 0.4 Hz from the 360-MHz ^1H NMR spectrum confirmed that addition had indeed occurred from the β face, and the value J_{38} = 5.6 Hz showed that H3 and H8 were also cis related, indicating that the addition had also been exclusively endo. Thus the product of the reaction was established as **10a**.[10]

We now investigated the outcome of hydrogenating the double bond in **10**, and the role that the *O*-isopropylidene ring would play in this process was a source of speculation. In fact under atmospheric pressure and palladium/$BaSO_4$ catalysis, the hydrogenation went smoothly to give **11**[10] as the *exclusive* product isolated in 83% yield. The newly formed stereocenter was readily determined to be as shown in Scheme II in view of the coupling

(1) Presented in part at the "Third International Symposium on Organic Synthesis", Madison WI, June 1980. See "Organic Synthesis Today and Tomorrow"; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: New York, 1981.

(2) Holder of Merck, Sharp and Dohme Graduate Fellowship, University of Maryland. Taken in part from the Ph.D. Thesis of K-M.S., University of Maryland, 1981. Present address of K-M.S.: Shell Development Company, P.O. Box 4238, Modesto, CA 95352.

(3) Holder of an Ontario Graduate Fellowship, University of Waterloo. Taken in part from the Ph.D. Thesis of T.-F. Tam, University of Waterloo, 1980. Present address of T.-F.T.: Syntex Corporation, Missisauga, Ontario, Canada.

(4) 1,2-*O*-Isopropylidene-α-D-*xylo*-furanose, used for the study reported in ref 5, is homomorphous with **1**.

(5) Tam, T. F.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, 556.

(6) Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Prog. Chem. Org. Nat. Prod.* **1979**, *38*, 47.

(7) C4 of **1** coincides with C6 of the trans-fused sesquiterpene lactones but with C8 of the cis-fused series.[6]

(8) Rosenthal, A.; Nguyen, L. *J. Org. Chem.* **1969**, *34*, 1029.

(9) Anderson, R. C.; Fraser-Reid, B. *J. Am. Chem. Soc.*, **1975**, *97*, 3870.

(10) This compound gave satisfactory spectroscopic, microanalytical, and/or high-resolution mass spectrum data.

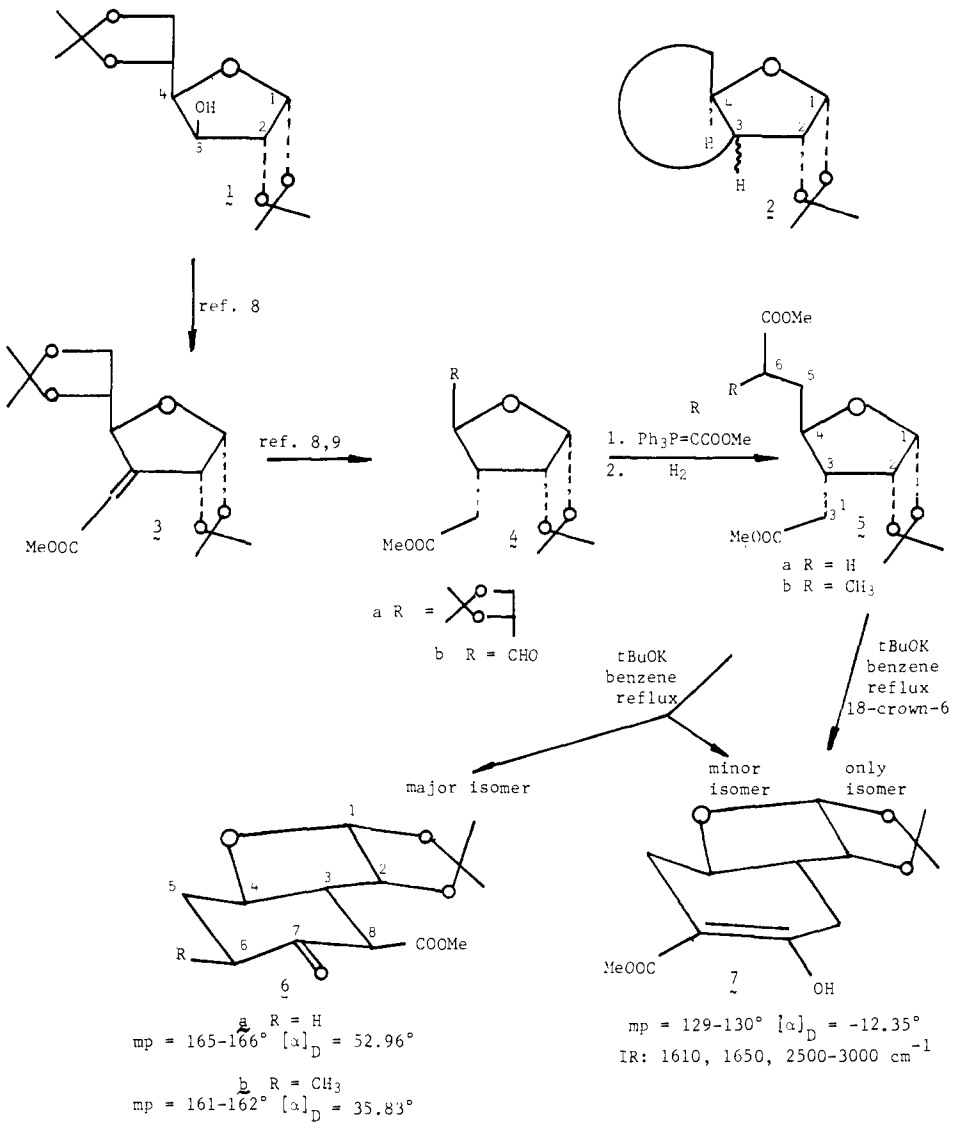
(11) In other approaches to "annulated sugars" we have used the sugar residue as (chiral) dienophile, the diene being achiral.[12] In this present study the roles are reversed.

(12) Primeau, J. L.; Anderson, R. C.; Fraser-Reid, B. *J. Chem. Soc., Chem. Commun.* **1980**, *6*.

(13) Sun, K. M.; Fraser-Reid, B. *Synthesis*, in press.

0002-7863/82/1504-0367$01.25/0

Scheme I

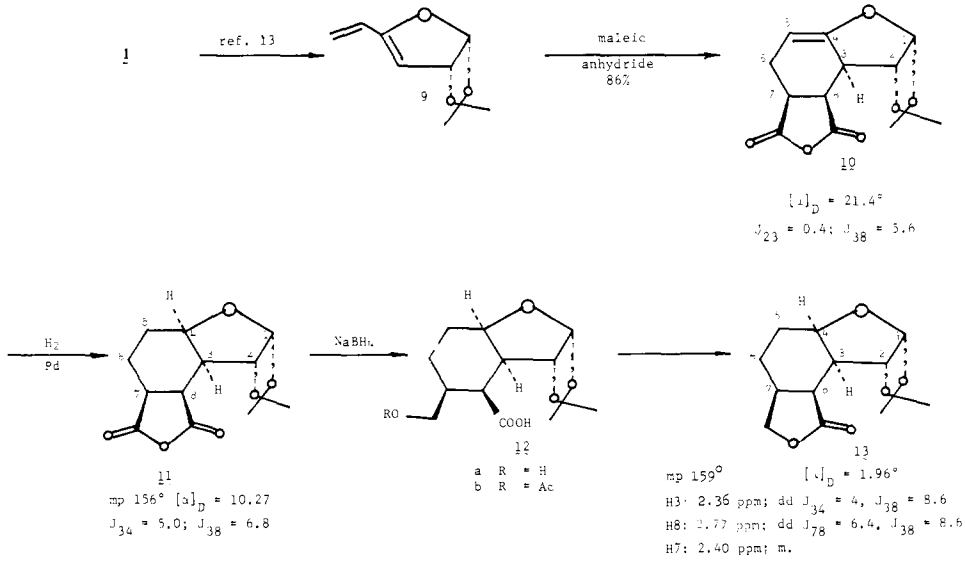


a R = H
mp = 165-166° $[\alpha]_D$ = 52.96°

b R = CH_3
mp = 161-162° $[\alpha]_D$ = 35.83°

mp = 129-130° $[\alpha]_D$ = -12.35°
IR: 1610, 1650, 2500-3000 cm^{-1}

Scheme II



$[\alpha]_D$ = 21.4°
J_{23} = 0.4; J_{38} = 5.6

a R = H
b R = Ac

mp 156° $[\alpha]_D$ = 10.27
J_{34} = 5.0; J_{38} = 6.8

mp 159° $[\alpha]_D$ = 1.96°
H3: 2.36 ppm; dd J_{34} = 4, J_{38} = 8.6
H8: 2.77 ppm; dd J_{78} = 6.4, J_{38} = 8.6
H7: 2.40 ppm; m.

constant J_{34} = 5 Hz. Actually, a study of Drieding models indicates that the double bond of **10** causes (i) the furan ring to be virtually flat and (ii) the carbocyclic ring to be in a boat conformation. As a result, the acetonide is splayed out while the anhydride ring occludes the β face of the double bond. On this basis hydrogenation from the α-face is fully rationalized, in spite of the presence there, of the *O*-isopropylidene ring.

The adducts **10** and **11** are intensively functionalized systems, and their utility for synthesis would therefore require selective access to the functional group of interest. Accordingly we sought

to distinguish between the carbonyl groups of **11** by taking advantage of the well-known phenomenon that sodium borohydride reduction of sterically hindered succinic anhydrides occurs at the *more* hindered center affording a γ-lactone.[14] In the event, reduction of **11** gave a syrupy hydroxy acid, which required 1 week for lactonization, thereby making it possible to prevent the process of acetylation to **12b**. However the 360-MHz ^{1}H NMR spectrum of the lactone showed it to be **13**[10] (see critical data in Scheme II), indicating that it was the *less* hindered carbonyl group that had been reduced.

In the suggested mechanism for the chemoselective reduction of succinic anhydrides to lactones, the surviving carboxyl group is chelated.[15] The opposite course obtained which **11** can therefore be rationalized by the process depicted in **14**.

In summary, a wide variety of functionalized annulated furanoses are readily obtainable from "diacetone glucose" (**1**), the stereo- and regiochemistries of which appear to be determined by the 1,2-*O*-isopropylidene ring exerting control either as a steric (as in **3** → **4** and **9** → **10**) or electronic (as in **5** → **6** and **11** → **12a**) device.

Acknowledgment. We are grateful to Merck, Sharp, and Dohme for financial support for our work in the U.S. and to the Natural Sciences and Engineering Research Council for support in Canada. We are indebted to Dr. Robert Highet of NIH for determining the high-field spectra.

(14) Bailey, D. M.; Johnson, R. E. *J. Org. Chem.* **1979**, *35*, 3574.

(15) Bloomfield, J. J.; Lee, S. L. *J. Org. Chem.* **1967**, *32*, 3919.

Book Reviews

Carcinogenesis: Fundamental Mechanisms and Environmental Effects. Edited by Bernard Pullman, Paul O.P. Ts'o, and Harry Gelboin. D. Reidel Publishing Co., Dordrecht, Holland/Boston, U.S.A./London, England. 1980. viii + 592 pages. 120.00 DFL.

The book is a compendium of papers given at the 13th Jerusalem Symposium on Quantum Chemistry and Biochemistry held April 28–May 2, 1980. There is a distinct biochemical flavor to this book, undoubtedly as a result of the symposium subject matter, but there is enough biology to make the contents interesting even to biologists. Each of the 47 chapters was written by different, often multiple, authors many being undisputed leaders in their fields. In spite of such diversity of authorship, the contents of the book revolve around only a few key questions concerning the metabolism of carcinogens and the chemical interaction between carcinogens and DNA. An additional theme is whether the response of the cell to the presence of adducts or ligands on DNA might be an element in the overall mechanism of carcinogenesis.

In the sense of the sharpness of the focus and the breadth of knowledge contained in it, this book stands as a milestone in this field. It will be of interest to biochemists as well as biologists—those interested in mechanism as well as those interested in methods. While the premise of the book is undoubtedly that damage or repair of DNA is of major importance in carcinogenesis, there are several chapters on promotion in vivo and in vitro in recognition that carcinogenesis may extend beyond DNA damage. There is a short "key word" index at the end of the book and each chapter is well referenced.

Fredric J. Burns, *New York University Medical Center, Institute of Environmental Medicine*

Advances in Physical Organic Chemistry. Volume 17. Edited by V. Gold and D. Bethell. Academic Press, London. 1980. viii + 518 pp. $84.50.

This volume of an established and valuable series presents five reviews of rather widely different topics: M. J. Perkins on spin trapping (64 pages); John L. Kice on mechanisms and reactivity of organic oxyacids of sulfur and their anhydrides (117 pages); Anthony J. Kirby on effective molarities for intramolecular reactions (96 pages); F. De Jong and D. N. Reinhoudt on stability and reactivity of crown ether complexes (155 pages); Toyoki Kunitake and Seiji Shinkai on catalysis by micelles, membranes, and other aqueous aggragates as models of enzyme action (75 pages).

The chapter by Perkins on spin trapping extends somewhat other reviews of this technique whereby a transient, reactive free radical undergoes addition to a diamagnetic compound to produce a more persistent radical which lends itself to more ready detection and identification. This review emphasizes the chemical and spectroscopic features which must be considered when utilizing the technique and includes a number of applications with emphasis on mechanistic and kinetic information which may be extracted by this method.

Kice's chapter on the organic oxyacids of sulfur reviews an expansive field including sulfenic (RSOH), sulfinic (RSO_2H), and sulfonic (RSO_3H) acid derivatives. Separate sections dealing with the corresponding anhydrides or mixed anhydrides are included because of the distinctive chemistry exhibited by these derivatives.

The review of effective molarities by Kirby addresses in a quantitative manner the efficiency of intramolecular catalysis. The effective molarity is defined as the concentration of the catalytic agent required to make the intermolecular reaction go at the observed rate of the intramolecular process; effective molarities can range from zero to 10^{16} M. Extensive, critical tabulations classified according to reaction mechanism make this review particularly informative.

The longest review is that by De Jong and Reinhoudt dealing with the physical organic chemistry of crown ether complexes with metal cations, protonated amines, arenediazonium salts, and neutral molecules. Topics include the thermodynamic and kinetic stabilities of complexes, spatial arrangement and electron density at the binding sites, solvent effects, anion effects, chiral recognition, and chemical reactivity of complexes.

Kunitake and Shinkai's chapter on micellar catalysis begins with a discussion of the various aqueous micellar aggregates. The catalytic action of these aggregates is then presented in relation to enzyme catalysis; the underlying theme is the hydrophobic effect.

Although this volume is considerably longer than preceding volumes, the diversity of topics and price will be unappealing to most potential individual subscribers. It is imperative, of course, for libraries and other institutions to sustain their holdings of this series.

Wayne C. Danen, *Kansas State University*

Analytical Applications of FT-IR to Molecular and Biological Systems. Proceedings of the NATO Advanced Study Institute, Florence, Italy, August 31–September 12, 1979. Edited by James R. Durig. D. Reidel Publishing Co., Hingham, MA. 607 pages. $68.50 (hardcover).

Fourier transform infrared (FT-IR) spectrometers have two significant advantages compared to their dispersive relatives—the increased sensitivity associated with the various improvements of signal-to-noise of the interferometric measurement, and the improved photometric accuracy and general convenience of use of the small instrumentation computer usually built in to the spectrometer. Since the costs of FT-IR spectrometers are dropping to the levels of conventional machines, it seems probable that FT-IR will become the normal mode of oepration within the next few years. This book is then particularly timely. It contains 26 didactic articles grouped under the headings Instrumentation and Theory (four articles), Techniques (eight), and Applications (fourteen). It provides a very convenient entry to the FT-IR area, and its literature.

As the editor indicates in his preface, the articles are pedagogical and are, with exceptions, neither sufficiently complete or critical to qualify as review articles. Within this constraint, the articles are well written and generally have the right mixture of theory, experimental background, results, and cookbook details. The range of subjects covered is very wide, including Hadamard spectroscopy, matrix isolation techniques, industrial applications, polymers, inorganic species, surface and crystal phenomena, and conformational analysis. The stress in the title on analytical applications is misleading. Only a fraction of the articles are related to component identification or measurement; for example, seven pages suffice for Chromatography and FT-IR Spectroscopy. The "Biological" of the title has a similar relation to content; 15 pages suffice to review spectra of proteins, and elsewhere biology receives another reference or two in passing.

This book should be most useful to those teaching graduate courses