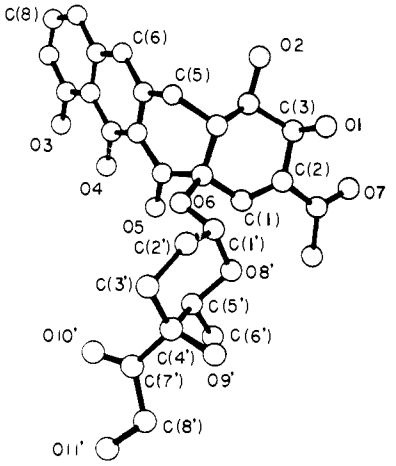
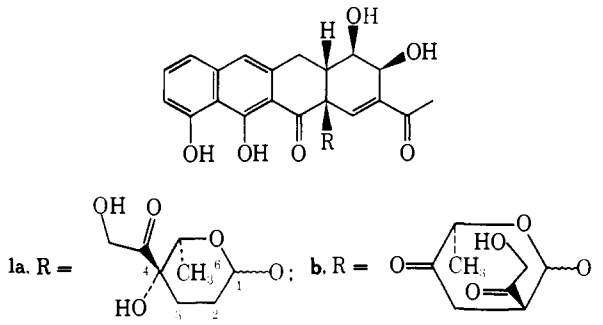


Figure 1. A computer generated perspective drawing of pillaromycin A (**1a**). No hydrogen atoms are shown.

Table I. Field Desorption Mass Spectrum of Pillaromycin A[a,b]

m/e	543	542	540	526	370	336	173
Per cent	29	100	2	2	2	2	1

[a] In ethyl acetate solution. [b] Source 68°; anode 10 kV, 20 mA.



least-squares refinement with anisotropic temperature factors for carbon and oxygen atoms and isotropic temperature factors for the hydrogens converged to a conventional discrepancy index of 0.038 for all of the reflections.[8] Figure 1 is a computer generated drawing of the final X-ray model. All bond distances and angles agree well with generally accepted values for given bond types.

The X-ray experiment, in the absence of anomalous scattering, defines only the relative configuration. The absolute stereochemistry rests upon the earlier crystallographic[9] work on the aglycone. As can be seen clearly in Figure 1 the previously published structure of the aglycone is correct but pillarose must now be reformulated as a 2,3,6-trideoxy-4-*C*-hydroxymethylcarbonyl-L-*threo*-aldohexose.

The molecular formulas for **1a** and **1b** ($C_{28}H_{30}O_{11}$ and $C_{28}H_{28}O_{11}$, respectively) differ by two units −542.2 vs. 540.2. The peaks from the field desorption mass spectrum of pillaromycin A shown in Table I, confirm the molecular weight at 542.[10] The *m/e* 543 peak for $^{13}C^{12}C_{27}H_{30}O_{11}$ is calculated to be 31% and *m/e* 370 represents the aglycone + H, while *m/e* 173 represents the sugar.

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Supplementary Material Available. The fractional coordinates (Table II), important bond distances (Table III), important bond angles (Table IV), and structure factors (Table V), will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.50 for photocopy or $2.50 for microfiche, referring to code number JACS-75-6250.

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(10) It is unlikely that *m/e* 540 is the molecular ion and that *m/e* 542 results from the addition of two hydrogens, since the absence of *m/e* 541 from the addition of one hydrogen would be most unusual.
(11) Camille and Henry Dreyfus Teacher-Scholar Grant Awardee, 1972–1977, and Fellow of the Alfred P. Sloan Foundation, 1973–1975.

John O. Pezzanite, Jon Clardy* [11]
Ames Laboratory US ERDA, Department of Chemistry
Iowa State University
Ames, Iowa 50010

Pui-Yan Lau, Gordon Wood*
Department of Chemistry, University of Windsor
Windsor, Ontario, Canada

David Louis Walker, Bert Fraser-Reid*
Department of Chemistry, University of Waterloo
Waterloo, Ontario, Canada

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Syntheses of "Supposed" and "Real" Pillarose

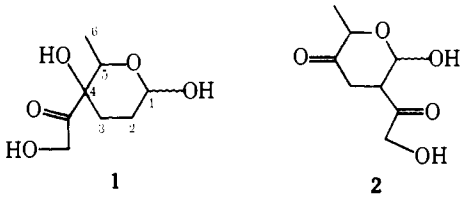
Sir:

In the accompanying paper,[1] crystallographic and mass spectral data are reported which indicate that the structure of pillarose, the sugar component of the antitumor agent pillaromycin A, is **1** and not **2** as originally proposed.[2] In this communication we complement the evidence by describing syntheses of the alkyl D-glycosides **3**–**6** which establish unequivocally that pillarose has the L-threo configuration of formulation **1**.[3] Of additional significance is the fact that the tricarbonyl structure **2** has no naturally occurring congeners, while **1** is obviously related to **7** which has recently been determined as the sugar component of the antibiotic, quinocyclin B.[5]

In the original investigation,[2] pillarose had been characterized as its benzoylated methyl glycoside whose salient physical constants and ^1H NMR parameters are shown in Table I. Our objective was therefore the synthesis of the epimeric benzoates related to formulation **2**, viz., **3** and **4**, one of which would possess the skeleton proposed for pillarose.[5]

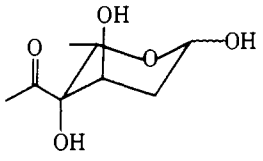
Table I. Physical Data for Pillarosides and Their Analogs

Compound	^{1}H NMR data (ppm), $CDCl_3$ (TMS)					
	H-1	H-2(H'-2)	H-3,H'-3	H-5	CH_3	OCH_3
"Benzoylated methyl Pillaroside"[2] Mp 103–105° $[\alpha]^{23}D$ −98.8°	4.6 doublet	1.9	1.7–2.3	4.29	1.14	3.32
3c[11] Mp 85.5–86° $[\alpha]^{23}D$ +219.0°	5.15 doublet	3.24	2.50	4.23	1.32	—
4c[11] Mp 85.5–87° $[\alpha]^{23}D$ +77.2	5.38 doublet	3.58	2.94, 2.54	4.26	1.29	—
5b Oil $[\alpha]^{23}D$ +74.8	4.82 triplet	2.0		3.98	1.22	3.39
6b Mp 107–108° $[\alpha]^{23}D$ +94.6°	4.7 broad singlet	1.6–2.3		4.22	1.15	3.34



1

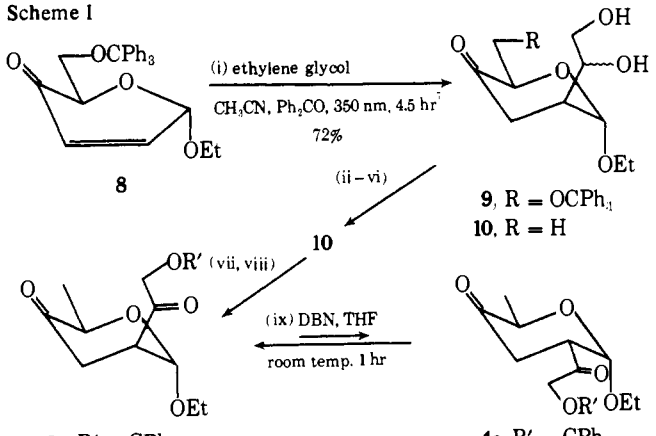
2



7

The pivotal reaction was the photoalkylation of enone **8** to the diol **9** (72%) with ethylene glycol as previously described[7] (Scheme I). Conversion of **9** to the 6-deoxy derivative **10** (65% yield) was achieved by the well-established protocol ((ii–vi) Scheme I) involving respectively, acetylation, detritylation, *p*-toluenesulfonylation, iodinolysis, hydrogenolysis, and finally deacetylation. Tritylation of the primary alcohol followed by oxidation with Collins' reagent[10] (vii and viii, Scheme I) afforded the diketone **3a**, which upon treatment with diazabicyclononene in THF, gave an equilibrium mixture of **3a** and **4a** in the ratio 3:2. Detritylation (x) and chromatographic separation gave the alcohols **3b** and **4b**, which were benzoylated (ix) to the esters **3c**[11a] and **4c**,[11b] critical data for which are shown in Table I.

Scheme I



8

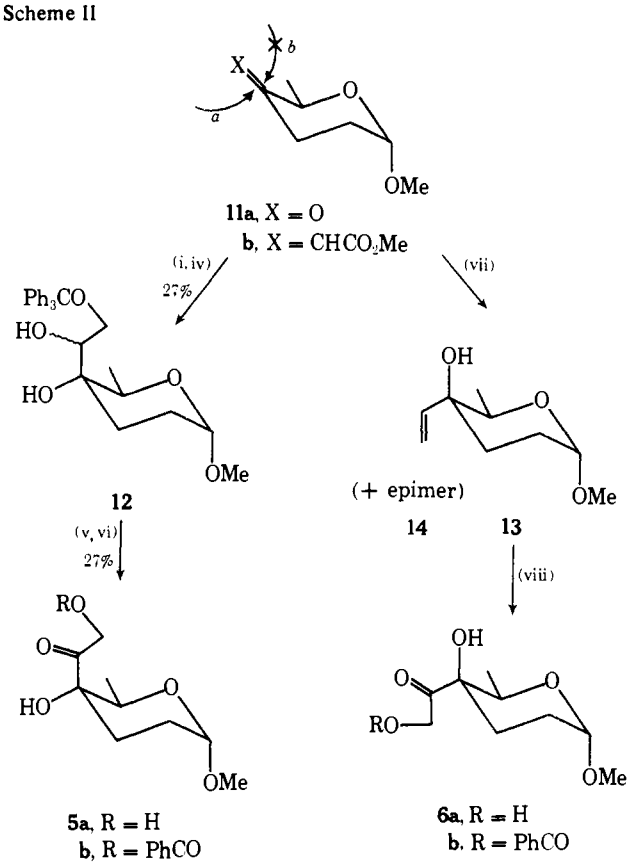
9, R = $OCPh_3$
10, R = H

3a, R′ = CPh_3
b, R′ = H
c, R′ = COPh

4a, R′ = CPh_3
b, R′ = H
c, R′ = COPh

(ii) Ac_2O, py, room temp, 7 hr, 94%
(iii)[8] $CHCl_3$, HCL, −30°, 0.5 hr, 84%
(iv)[9a] TsCl, py, O°, 24 hr, 94%
(v)[9b] NaI, butanone, reflux, 1.5 hr, 93%
(vi) MeOH–H_2O–Et_3N (5:4:1), room temp, 4 hr, 98%
(vii) Ph_3CCl, py, room temp, 48 hr, 75%
(viii)[10] CrO_3·2py, CH_2Cl_2, room temp, 1 hr, 93%
(x) as in (iii) 37%
(xi) PhCOCl, py, O°, 12 hr, 91%

Scheme II



11a, X = O
b, X = $CHCO_2Me$

12

14 13

5a, R = H
b, R = PhCO

6a, R = H
b, R = PhCO

(i)[15b] trimethylphosphono acetate
(ii) $LiAlH_4$, ether, O°, 0.5 hr
(iii) Ph_3CCl, py, room temp, 18 hr
(iv) OsO_4·py, room temp, 24 hr
(v)[17] DMSO, DCC, CF_3COOH, py
(vi) CH_3Cl, HCl, room temp
(vii) C_2H_3MgBr, THF, O°, 0.75 hr
(viii) OsO_4, *t*-BuOH, H_2O_2, 18 hr

The ^{1}H NMR parameters for entries 1 to 3 (Table I)

particularly the chemical shifts for H-2, led to the belief that the proposed skeleton of benzoylated methyl pillaroside was neither **3** nor **4.** This doubt was intensified by the observation that **3b** and **4b** were destroyed when treated with 50% H_2O–HOAC followed by MeOH–HCl under conditions used to obtain methyl pillaroside from pillaromycin A.[2]

In the light of the crystallographic study,[1] the epimers **5** and **6** were synthesized from the ketone **11**[12] (Scheme II). The strategy adopted was based on the premise that reagents would approach the trigonal center in **11** from the direction *a* rather than *b*. Thus the desired stereochemistries in **5** and **6** would be generated by oxidation or alkylation of suitable receptors.

With this approach in mind, the acrylate ester **11b** obtained from Wadsworth-Emmons-Wittig[15a] reaction of **11a**[15b] was reduced with $LiAlH_4$, tritylated, and hydroxylated to give the diol **12**[16] in 27% yield from **11.** Oxidation of **12** with the Moffatt reagent[17,18] followed directly by detritylation,[8] gave **5a** in 27% yield after chromatography. Upon benzoylation, **5b** was obtained as an oil (91%).

For preparation of the epimer **6** (Scheme II) ketone **11** was treated with vinyl magnesium bromide,[19] and the resulting alcohols, **13**[16] and **14**,[16] were separated chromatographically. Reaction of **13** with OsO_4–H_2O_2[20] afforded, among other products,[21] the dihydroxy ketone **6a** (21%) which was benzoylated to **6b.** (Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.40; H, 6.42.)

Perusal of the data in Table I provides conclusive evidence that the benzoylated methyl pillaroside in entry 1 is the L-enantiomer of **6b.**[3] Furthermore, this skeleton for pillarose (**1**)[3] better accommodates the periodate oxidation analysis[2] than does **2.** This analysis will be discussed in detail in the full paper.

Acknowledgment. We are grateful to the National Research Council of Canada and Bristol Laboratories (Syracuse) for financial assistance.

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(3) In keeping with literature precedents,[4] pillarose is named 2,3,6-trideoxy-4-*C*-(oxo(hydroxymethyl)methyl-L)-*threo*-hexopyranose.
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(6) We have been informed by Professor Dr. H. Paulsen of the University of Hamburg that the methyl α-L-*erythro*-glycoside related to formulation **2** has been synthesized in his laboratory using an altogether different route than the one described here.
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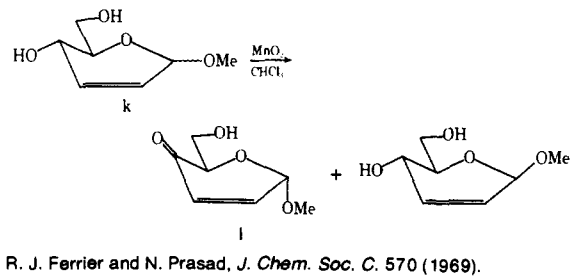
(10) J. C. Collins, W. W. Hess, and F. J. Frank, *Tetrahedron Lett.*, 3363 (1968).
(11) Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found (a) for **3c**: C, 63.78; H, 6.31. (b) for **4c**: C, 63.85; H, 6.53.
(12) Ketone **11** was readily prepared from the anomeric mixture k[13] by MnO_2 oxidation in $CHCl_3$, whereupon only the α-glycoside was oxidized[14] to enone l. The unreacted β-diol was then removed by extraction into water.



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(16) The stereochemistry at C-4 of the compounds in Scheme II was not known with certainty until compound **6b** had been finally obtained. Our choice of olefin **13** for further study was based on the observation that the H-1 ^1H NMR signal had the appearance of a doublet, such as that reported for methyl pillaroside[2] (see Table I). By contrast, H-1 in **14** was a triplet. The successful conversion of **13** to **6** confirmed these stereochemical assignments. The triplet pattern for H-1 of **5b** indicated stereochemical relationship to **14** rather than to **13.**
(17) J. G. Moffatt, *J. Am. Chem. Soc.*, **89**, 2697 (1967); **90**, 740 (1968).
(18) With Collins' reagent,[10] **12** underwent over oxidation to regenerate ketone **11.**
(19) D. Seyferth and F. G. A. Stone, *J. Am. Chem. Soc.*, **79**, 515 (1957).
(20) B. Magerlein and J. Hogg, *J. Am. Chem. Soc.*, **80**, 2226 (1958).
(21) These products will be described in the full paper.

David Louis Walker, Bert Fraser-Reid*
Chemistry Department, University of Waterloo
Waterloo, Ontario, Canada
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CIDNP in Reactions Initiated by Tetramethyl-1,2-dioxetane

Sir:

Excited states of the carbonyl compounds produced in thermal decomposition of 1,2-dioxetanes have been identified by chemiluminescence measurement[1] and by their chemical intra-[2] or intermolecular[3,4] reactions which generally are in quite low yield.[5] Tetramethyl-1,2-dioxetane (TMD), which is most extensively investigated, is known to produce excited triplet acetone efficiently in its thermal decomposition in systems free or carefully purged of metal salts.[3] Chemically induced dynamic nuclear polarization (CIDNP) has been so well explored as to offer an independent way of characterizing the multiplicity of the radical pair responsible for the polarization. Thus the thermal decomposition or direct irradiation of benzoyl peroxide in carbon tetrachloride (via a singlet radical pair) produces an emission signal in the ^1H NMR spectrum of the product chlorobenzene, while photosensitized decomposition in carbon tetrachloride, with acetophenone as sensitizer (via a triplet radical pair), leads to chlorobenzene showing an *enhanced absorption* CIDNP signal, the reversal being associated with decomposition from the triplet rather than the singlet state.[6,7]

We have found that at 87° in carbon tetrachloride, benzoyl peroxide (0.18 *M*) is caused to decompose by a sixfold excess of TMD. Enhanced ^1H NMR absorption at δ 7.2 due to chlorobenzene was seen 15 sec after insertion of the sample into the preheated probe. The signal reached a maximal intensity after 45 sec, and disappeared after 200 sec. (In the absence of TMD no CIDNP was seen under these conditions and no perceptible decomposition of the benzoyl peroxide in 200 sec. The ^1H NMR signal of the originally 1 *M* TMD also disappeared as the enhanced absorption declined. The results were similar in chloroform-*d* at 80°, but in this case the strong enhanced absorption of benzene-*d* at δ 7.30 was accompanied by less intense emission at δ 7.23 due to phenyl benzoate. Both signals were seen 30 sec after insertion of the sample into the heated probe; both reached a maximal intensity after 105 sec. Those CIDNP spectra were also observable in the presence of 0.2 *M* TMD.

These experiments confirm that the peroxide decomposition is initiated by energy uptake from triplet acetone, as in the photosensitized BPO decomposition, in harmony with the observations cited above.[6,7] Addition of acetophenone (0.3 *M*) to our solution made no significant difference in the NMR signals seen; however, addition of 9-fluorenone or