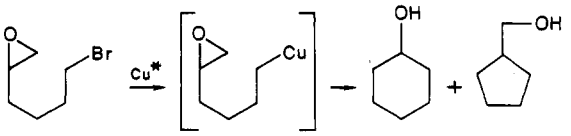
ficiently add to organic halides to form organocopper reagents under very mild conditions. Remarkably, the organic halides can contain a variety of functional groups. These unusual organocopper species can undergo nucleophilic opening of epoxides at the less sterically hindered position. Yields are high and reaction conditions are extremely mild. These results have clearly shown that various functionalities can be tolerated by the activated copper. This, in turn, suggests a number of interesting potentials for use of the highly reactive copper. For example, intramolecular cyclizations via an epoxide cleavage process may be readily carried out using this activated copper under very mild conditions with high regio-, stereo-, and chemoselectivity. Preliminary results show that



(1)

5,6-epoxyhexylcopper generated directly from 5,6-epoxyhexyl bromide and the activated copper will undergo intramolecular epoxide opening at low temperature to give a 55% yield of a mixture of cyclohexanol and cyclopentylmethanol in a 6:1 ratio (eq 1). Further results are forthcoming.

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Tse-Chong Wu, Richard M. Wehmeyer
Reuben D. Rieke*
Department of Chemistry
University of Nebraska—Lincoln
Lincoln, Nebraska 68588-0304
Received July 13, 1987

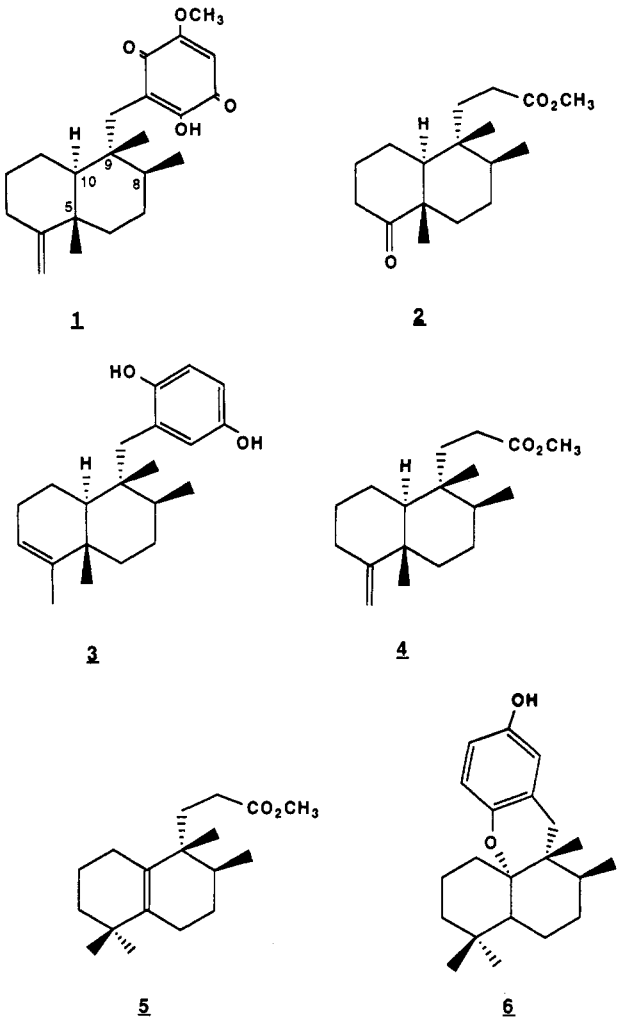
A Revision of the Absolute Stereochemistry of Ilimaquinone

Summary: The absolute stereochemistry of ilimaquinone (1) has been revised following correlation with aureol (6) through a common degradation product.

Sir: During the course of our studies on a number of marine norsesterterpene cyclic peroxides[1] we became aware that CD measurements on 4-keto-5-methyl-*trans*-decalins, obtained as degradation products, were unreliable with respect to assigning absolute stereochemistry, due to their low values.[2] A review of the literature revealed instances[3,4] where the sign of the CD effect, in similar systems of known absolute stereochemistry, was opposite to that predicted. In each case the magnitude of the CD effect was very low. This prompted us to reexamine other assignments of absolute stereochemistry made on related systems.

Ilimaquinone (1) (Chart I) is representative of a class of compounds common to marine sponges. Although the relative stereostructure of 1 was secured by X-ray analysis,[5] an absolute stereochemistry of 5*R*,8*R*,9*S*,10*R* was assigned

Chart I



by interpretation of a weak positive CD measurement ($\Delta\epsilon_{298}$ +0.14) on the 4-keto-5-methyl-*trans*-decalin degradation product **2**.[5] Such an assignment implied that ilimaquinone (1) was "enantiomeric" to avarol (3), a related sponge metabolite whose absolute stereochemistry had been established[6] as 5*S*,8*S*,9*R*,10*S* by interpretation of strong CD effects on two degradation products. Subsequent correlations have resulted in a significant number of marine natural products[7-12] being represented with absolute stereochemistries based on that assigned[5] to ilimaquinone (1). In many of these cases no attempt was made to chemically interrelate the absolute stereochemistry of the natural product under investigation to that of ilimaquinone (1), although the implication was that they had the same absolute stereochemistry. This has resulted in a situation where the majority of sponge metabolites structurally related to ilimaquinone (1) are, without ade-

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quate justification,[7-10,12] depicted as having the same absolute stereochemistry as that of ilimaquinone (1). The hazards of such correlations are highlighted by a recent report[11] in which two compounds, structurally similar to ilimaquinone (1) but "enantiomeric" to it, were found to co-occur with ilimaquinone (1).

We have unambiguously established the absolute stereochemistry of ilimaquinone (1) by the following degradative approach and found it to be opposite to that previously proposed. Basic hydrogen peroxide oxidation of ilimaquinone[13] (1) followed by methylation with diazomethane yielded the ester 4. Acid-catalyzed rearrangement[14,15] of 4 gave the ester 5,[16] which possessed an optical activity ($[\alpha]_D$ -57.6° (*c* 0.25, $CHCl_3$)) comparable to that of the same compound obtained by degradation of aureol (6) (lit.[17,18] $[\alpha]_D$ -48.4° (*c* 0.4, $CHCl_3$)). The absolute stereochemistry of aureol (6) had previously been established[19] by X-ray analysis of a bromoacetate derivative. Thus the absolute stereochemistry of ilimaquinone (1) is the same as that of avarol (3).

Failure of the CD approach to predict the correct absolute stereochemistries in the 4-keto-5-methyl-*trans*-decalins described above highlights the need to exercise caution when attempting to assign absolute stereochemistries by interpreting weak CD effects.

Registry No. 1, 71678-03-0; 2, 109717-96-6; 3, 55303-98-5; 4, 109717-97-7; 5, 76215-39-9; 6, 72853-81-7.

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(15) The possibility that acid-catalyzed isomerization might have induced epimerization or racemization about C8 was addressed by carrying out the reaction with deuteriated reagents (MeOD-DCl-AcOD). The C8 methine proton did not undergo exchange even under prolonged reaction conditions.

(16) The rearranged ester 5 was isolated as a stable colorless oil: ^1H NMR ($CDCl_3$) 0.84 (s, 3 H), 0.84 (d, 3 H, J = 8.0 Hz), 0.95 (s, 3 H), 0.97 (s, 3 H), 3.66 (s, 3 H); ^{13}C NMR ($CDCl_3$) 16.2 (q), 19.9 (t), 20.8 (q), 25.3 (t), 25.7 (t), 27.1 (t), 27.6 (q), 29.3 (q), 29.4 (t), 30.8 (t), 33.8 (d), 34.5 (s), 39.9 (t), 40.4 (s), 51.6 (q), 131.6 (s), 138.0 (s), 175.1 ppm (s); EIMS m/z 278 (M^+, 11%), 191 (100).

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(18) Preparation of the rearranged ester 5 by degradation of ambliol-B revealed[17] an $[\alpha]_D$ -52.9° (*c* 0.7, $CHCl_3$), which is in good agreement with that obtained from ilimaquinone (1).

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Robert J. Capon,* John K. MacLeod
Research School of Chemistry
Australian National University
Canberra, A.C.T. 2601, Australia
Received April 27, 1987

A Novel Method for Regioselective 2′-O-Methylation and Its Application to the Synthesis of 2′-*O*-Methyl-5-[[(carboxymethyl)amino]methyl]-uridine

Summary: A new modified nucleoside, 5-[[(carboxymethyl)amino]methyl]-2′-*O*-methyluridine, was successfully synthesized by using a two-step O-methylation procedure involving alkylation of the 2′-hydroxyl group with 1,3-benzodithiolium tetrafluoroborate followed by Raney nickel reduction.

Sir: In recent years, much attention has been paid to the molecular mechanism of codon recognition by tRNA[1] since it has been proven that modified uridine derivatives located at the first position of anticodon played an important role in the regulation of rigidity/flexibility of the anticodon of tRNAs.[2] Quite recently, a 2′-O-methylated species (1) of 5-[[(carboxymethyl)amino]methyl]uridine (2) was discovered in the first letter of anticodon of *E. coli* $tRNA^{Leu}$.[3] It is of great interest to know how the 2′-O-methyl group affects the conformation of the sugar moiety. In this paper, we report a synthesis of 1 which involves a new procedure for the regioselective 2′-O-methylation.

Małkiewicz[4] reported the synthesis of 2 by an eight-step reaction from 2′,3′-*O*-isopropylideneuridine via 2′,3′-*O*-isopropylidene-5-(hydroxymethyl)uridine, which was easily obtained by the reaction of 3 with HCOH/KOH.[5,6] Reese[7] also synthesized 2 using displacement of the methiodide of 2′,3′-*O*-isopropylidene-5-(pyrrolidinomethyl)uridine with glycine *tert*-butyl ester. These facts led us to examine the 5-hydroxymethylation[5] and 5-(dialkylamino)methylation[8] of 2′-*O*-methyluridine (4) under similar conditions. However, several attempts to introduce these substituents at the 5-position of 4 have failed. These reactions required essentially the neighboring group participation of the 5′-hydroxyl group, as accounted for by Santi[9] and other workers.[10,11] Therefore, we searched for an alternative route to 2 in which the 2′-O-methylation was planned at a later stage. Reaction of 3 with 37% formalin–piperidine in 50% aqueous ethanol at 80 °C for 8 h gave quantitatively the Mannich base 5. This product was converted in situ to the methiodide 6 by treatment with 5 equiv of methyl iodide in DMF at room temperature for 20 min. The methiodide was allowed to react with 1 equiv of *N*-benzylglycine ethyl ester[12] in the presence of 1 equiv of $(i\text{-Pr})_2NEt$ at 60 °C for 4 h. This one-flask reaction gave finally 2′,3′-*O*-isopropylidene-5-[[*N*-benzyl[(ethoxycarbonyl)methyl]amino]methyl]uridine (7) in an overall yield of 64%. The deacetonization of 7 by the use of 20% acetic acid at 90 °C for 3 h resulted in the triol 8 in 52% yield. Since 8 was unstable under both acidic and basic conditions, the 2′-O-methylation should be done under neutral conditions.

Several methods are known for the 2′-O-methylation of uridine.[13] Moffatt[13b] reported that treatment of 2′,3′-

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(12) Małkiewicz[4] has already reported the use of the N-benzyl group for protection of the secondary amine, since without protection of the amino function decomposition occurred during chromatography. The benzyl group is also used for avoidance of N-alkylation at the branched chain in the conversion of 9 to 10.

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