References and Notes

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(13) See J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice Hall, Englewood Cliffs, N.J., 1971, p 258–262 and references cited therein, and also G. Berti, *Top. Stereochem.*, **7**, 93 (1973). It has long been recognized that the syn directive effect of allylic alcohols gives rise to varying degrees of stereoselectivity in epoxidation of these compounds by various chemical agents. However, even with the use of chiral epoxidizing agents, only very low optical yields (ca. 5%) of optically active epoxides are obtained from simple prochiral olefins (such as octadiene).
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(15) For example, schemes postulating random generation of *S,R*- and *S,S*-diepoxides from *S*-monoepoxide cannot be ruled out at this time and the same is true of other more complex schemes.

Sheldon W. May,* Michael S. Steltenkamp
School of Chemistry, Georgia Institute of Technology
Atlanta, Georgia 30332

Robert D. Schwartz, Carlton J. McCoy
Corporate Research Laboratories
Exxon Research and Engineering Company
Linden, New Jersey 07036

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Benzoylamination of Uridine Derivatives

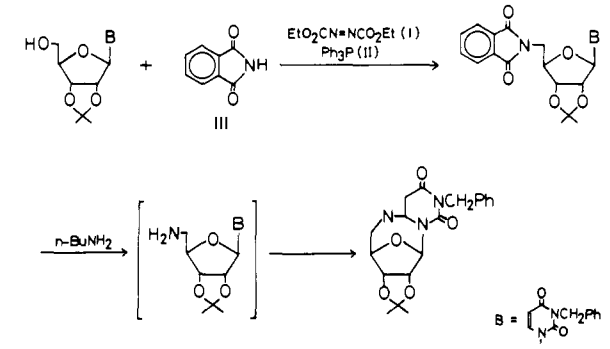
Sir:

Conversion of hydroxyl groups of sugars and nucleosides into acylamino functions is an important reaction for the synthesis of biologically active compounds such as antibiotics.[1] The conversion generally requires many reaction steps, e.g., replacement of the hydroxyl group by an azide group via halides or sulfonates followed by reduction and acylation.[2] In this communication we wish to report an alternative method for the preparation of acylaminonucleosides. N-Protected uridines were utilized in the present study.

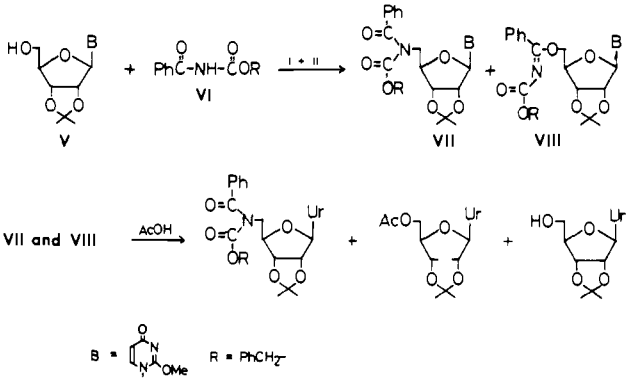
When N^3-benzyl-2′,3′-*O*-isopropylideneuridine (5 mmol) was allowed to react with diethyl azodicarboxylate (I; 6 mmol), triphenylphosphine (II; 6 mmol), and phthalimide (III; 5 mmol) in tetrahydrofuran (THF; 25 ml) at room temperature overnight, 5′-deoxy-5′-phthaloylamino-N^3-benzyl-2′,3′-*O*-isopropylideneuridine (IV) was obtained in a 47% yield (mp 160–161 °C, from ethanol).[3] On treatment with methanol (15 ml)-*n*-butylamine (3 ml) under reflux for 11 h, IV afforded 5′-deoxy-5′,6-epimino-5,6-dihydro-3-benzyl-2′,3′-*O*-isopropylideneuridine in a 28% yield (mp 129–131 °C, from CCl_4) (Scheme I).[4]

Since the N^3-benzyl group of uridine derivatives is difficult to remove,[5] O^2-methyl-2′,3′-*O*-isopropylideneuridine (V)[6] was used as a protected uridine. O^2-Methyl-2′,3′-*O*-isopropylideneuridine reacted smoothly with III in the presence of 1.5 molar equiv each of I and II under the same conditions as above giving 5′-deoxy-5′-phthaloylamino-O^2-methyl-2′,3′-*O*-isopropylideneuridine (77% yield, amorphous solid) which, on treatment with 20% acetic acid under reflux for 16 h, afforded

Scheme I



Scheme II



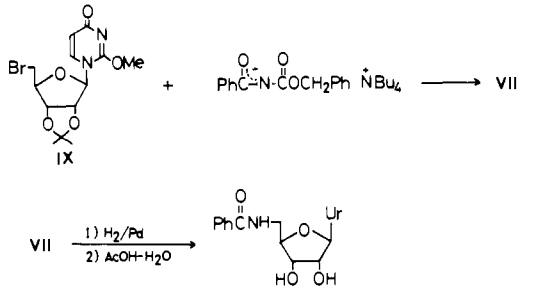
5′-deoxy-5′-phthaloylaminouridine[7] in a yield of 78% (mp 228–229 °C, from 3% aqueous acetic acid).

The conversion of the 5′-hydroxyl group of uridine into the benzoylamino group could be accomplished in a similar way (Scheme II). When V (2 mmol) was allowed to react with 1.5 molar equiv each of I, II, and *N*-benzyloxycarbonylbenzamide (VI) in THF (5 ml) at room temperature overnight, a 50% yield of a condensation product was isolated by preparative layer chromatography (methanol–ethyl acetate = 1:40). The complexity of its ^{1}H NMR spectrum suggested that it was a mixture of 5′-deoxy-5′-(*N*-benzyloxycarbonyl-*N*-benzoyl)amino-O^2-methyl-2′,3′-*O*-isopropylideneuridine (VII) and O^2-methyl-2′,3′-*O*-isopropylideneuridinyl 5′-(*N*-benzyloxycarbonyl)benzenecarboxyimidate (VIII). The mixture was again applied on silica gel plate and developed by the same system. This procedure was repeated three times giving the desired VII in a 20% yield. The VIII was presumably hydrolyzed on the plate during manipulation.[8] Alternatively, on treatment with acetic acid under reflux for 5 h, the mixture of VII and VIII afforded 5′-*O*-acetyl-2′,3′-*O*-isopropylideneuridine, 2′,3′-*O*-isopropylideneuridine, and 5′-deoxy-5′-(*N*-benzyloxycarbonyl-*N*-benzoyl)amino-2′,3′-*O*-isopropylideneuridine (amorphous solid) in 21, 8, and 20% yields, respectively. These products could be easily separated by preparative layer chromatography (the yields are based on V used).

As described in the previous paper,[8] the alkylation of VI by means of I, II, and alcohol gave rise to both *N*- and *O*-alkylated products. On the other hand, the reaction of the sodium salt of VI with primary alkyl halide resulted in the predominant formation of the corresponding *N*-alkylimide. Therefore the reaction of 5′-deoxy-5′-bromo-O^2-methyl-2′,3′-*O*-isopropylideneuridine (IX)[9] was next tried. When IX (1 mmol) was allowed to react with tetrabutylammonium salt of VI (1.5 mmol) in DMF (5 ml) at room temperature for 8 days, VII was, as expected, isolated in a 74% yield without accompanying the formation of VIII (Scheme III).

The deprotection of VII was carried out by usual manners. Thus VII was hydrogenated on Pd in ethanol giving 5′-

Scheme III



deoxy-5′-benzoylamino-2′,3′-*O*-isopropylideneuridine (X) in a 75% yield. The X was treated with 20% acetic acid under reflux for 4 h to give 5′-deoxy-5′-benzoylaminouridine in an 80% yield as amorphous solid.

The reaction sequence disclosed herein may provide a potential method for the synthesis of acylaminosugars and acylaminonucleosides.[10]

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Oyo Mitsunobu,* Susumu Takizawa, Hiroo Morimato

Department of Chemistry, Aoyama Gakuin University Chitosedai, Setagaya-ku, Tokyo 157, Japan

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Specific Effects of Chloride Ion on Epoxide Hydrolysis. The pH-Dependence of the Rates and Mechanisms for the Hydrolysis of Indene Oxide

Sir:

The metabolism of aromatic hydrocarbons is thought to proceed via the intermediacy of arene oxides,[1] and the carcinogenic effects of certain hydrocarbons have been attributed to the covalent binding of the intermediate epoxide to cellular reagents.[2] Recent reports suggest that the principal causative agent in the carcinogenicity of benzo[*a*]pyrene might be a dihydrodiol epoxide in which the epoxide group is located at a benzylic position.[3] A more detailed knowledge of the hydrolysis mechanisms and nucleophilic reactions of non-arene oxides (such as benzylic epoxides) is therefore desirable.

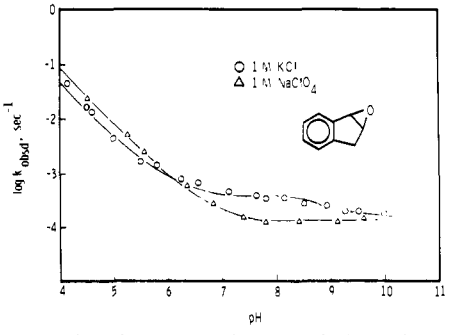
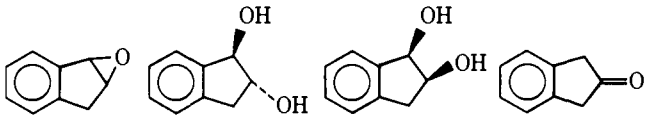


Figure 1. Plots of log k_{obsd} vs. pH for the hydrolysis of indene oxide in 1 M $NaClO_4$ and 1 M KCl solutions at 25 °C.

The rates and mechanisms for hydrolysis of various arene and non-arene oxides have been studied as a function of pH. It is common practice to carry out the hydrolysis studies of a given epoxide in solutions held at a constant ionic strength by addition of an electrolyte, and potassium chloride is often the electrolyte chosen.[4] In this paper we wish to report the specific effects of added chloride ion on the hydrolysis of indene oxide, and to caution against the use of nucleophilic reagents such as potassium chloride to maintain constant ionic strength in solutions used for hydrolysis of epoxides highly susceptible to nucleophilic reagents.

Various reports of the stereochemistry of the products from the hydrolysis of indene oxide (**1**) have appeared. Several publications have stated that trans and cis diols **2** and **3** from the hydrolysis of **1** are formed in ratios that depend on pH, reaction times, and reaction conditions.[5] A more recent publication appeared in which the authors obtained the same ratio (69:31) of **3** and **2** from the hydrolysis of **1** in both 0.1 and 1.0 N sulfuric acid at room temperature, and demonstrated that some of the differences in the product distributions reported previously were not due to differences in acid concentration, but rather to secondary transformations of the diol products under reaction conditions.[6]



1 **2** **3** **4**

Because of discrepancies in the published data on the hydrolysis of **1** at pH >1, and due to the importance of understanding the mechanisms of epoxide hydrolyses, we undertook a study of the kinetics and stereochemical outcome of the hydrolysis of **1** as a function of pH. Our results reveal that the product distributions and mechanisms for the hydrolysis of **1** at pH 4–10 are indeed pH dependent, and are reported here.

The rate expression for the hydrolysis of **1** in buffered aqueous 1 M $NaClO_4$ solutions, in which the rates were extrapolated to zero buffer concentration, is given by eq 1.[7] The

$$k_{obsd} = k_{H^+}a_{H^+} + k_0 \quad (1)$$

values for the rate constants k_{H^+} and k_0 are 8.9×10^2 M^{-1} s^{-1} and 1.3×10^{-4} s^{-1}, respectively. The pH-rate profile for the hydrolysis of **1** in 1 M $NaClO_4$ solutions is given in Figure 1. Two distinct regions in the pH-rate profile between pH 4 and 10 are apparent, one region at pH ca. 6 in which $k_{H^+}a_{H^+} > k_0$, and a plateau at pH ca. 7.5, where $k_0 > k_{H^+}a_{H^+}$. From analysis of eq 1 (or the pH-rate profile), it is clear that there are two distinct mechanisms for the hydrolysis of indene oxide in 1 M $NaClO_4$. At pH 2 the acid-catalyzed mechanism predominates, and yields 30% of **2** and 70% of **3**. At pH 8.3, however, $k_0 \gg k_{H^+}a_{H^+}$, and the product mixture from hy-