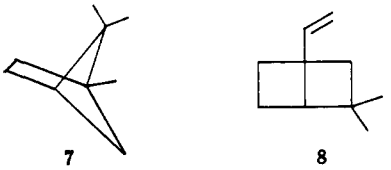
probably the most definitive feature of the spectrum. Structures **6** and **8** are the only products of internal cycloaddition which would have intact vinyl groups. There is no precedent for the expectation that any of the single protons of **8** would absorb at very high field. On the other hand the spectra of bicyclo[2.1.1]cyclohexane[6] and its derivatives[6,7] have high-field signals (τ 9.13 in the parent compound and 9.11 in **8**) attributed to the *endo* protons on methylene bridges. A slightly distorted A_2B_2 group (relative area 4.0) centered at about τ 8.35 is assigned to the protons attached to the two-carbon bridge of **6** and an unresolved broad signal (relative area 2.0) centered at τ 7.96 must include the *exo*-methylene and bridgehead protons. The only surprising feature of the spectrum is the relatively high-field position of the latter signal. However, the spectrum of **7** shows a signal at τ 8.01, probably due to the proton attached to the bridgehead, and the bridgehead protons in tricyclo[3.3.0.$0^{2,6}$] octane occur at τ 8.18.[8]



7 **8**

Since myrcene is converted smoothly to 5,5-dimethyl-1-vinylbicyclo[2.1.1]hexane (**6**) in the sensitized reaction, we conclude that in the direct irradiation[5] the excited diene system does not cross, or at best, inefficiently crosses, to the triplet manifold prior to cyclization. In view of the simplicity of the procedure and the current interest in highly strained, polycyclic systems, we suggest that this and similar sensitized cyclization reactions may have significant synthetic utility.

(7) J. Meinwald and A. Lewis, *J. Am. Chem. Soc.*, **83**, 2769 (1961).
(8) R. Srinivasan, *ibid.*, **85**, 819 (1963).

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RECEIVED MARCH 3, 1964

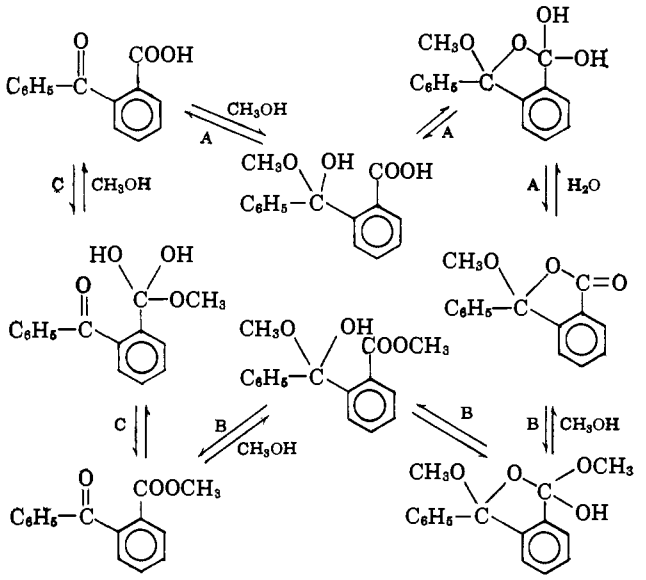
Mechanisms of Esterification of 2-Benzoylbenzoic Acids[1]

Sir:

From the fact that methyl 2-benzoyl-6-methylbenzoate (I) underwent alkaline hydrolysis more rapidly than methyl 2-benzoylbenzoate (II), the conclusion was drawn that the mechanism of hydrolysis of I involved mainly attack of the hydroxyl ion on the ketonic function and that the 6-methyl group provided steric assistance in the subsequent intramolecular hydrolysis.[2] However, it was not possible to estimate the amount of hydrolysis which took place by attack at the ketonic and ester functions in methyl 2-benzoylbenzoate (II) if, indeed, both mechanisms were competitive in this case.

On acid-catalyzed esterification with methanol, 2-benzoylbenzoic acids are converted into normal and/or pseudo-methyl esters.[3] Accordingly we turned to this reaction to find out if it proceeded by attack at the carboxy or the keto functions. We now report that 2-benzoylbenzoic acid *first forms pseudo-methyl 2-benzoylbenzoate*. The pseudo-ester is then rapidly converted to the normal ester under esterification conditions.

The reason 2-benzoylbenzoic acid has always been reported[3] to form normal ester on esterification is that previous workers allowed the reaction to proceed long enough to ensure that equilibrium was attained. The following scheme illustrates the processes involved (no attempt is made to locate the protons involved in catalysis).



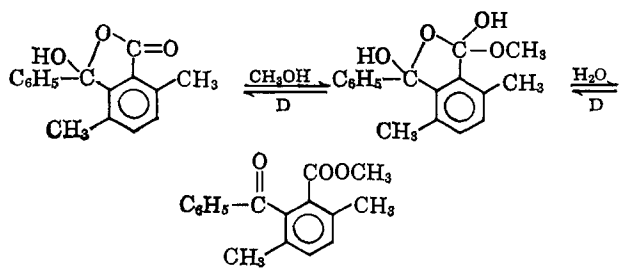
Pseudo-ester is first formed by route A. The pseudo-ester is then rapidly transformed into normal ester by route B. Some normal ester is probably formed directly *via* route C, but the following experiments show that little is so formed. When 2-benzoylbenzoic acid in methanol (0.2 *N* in hydrochloric acid) was held at 55.5° for 15 min., 13.5% was converted into ester of composition 70.5% normal–29.5% pseudo.[4] When an exactly comparable solution of pseudo-methyl ester was held at 55.5° for 15 min., *the ester obtained was 94% normal*. Thus the rate of conversion of pseudo to normal ester is much greater than the rate of esterification. At equilibrium the esters are 98% normal–2% pseudo. From these results one can readily see that little normal ester is formed from 2-benzoylbenzoic acid by route C. Kinetic studies are under way to determine just how much.

Turning to 3,6-dimethyl-2-benzoylbenzoic acid, an acid which forms 85% pseudo–15% normal ester at equilibrium,[3] we find another surprising result: *after 15 min. the ester formed in 6.7% yield is over 80% normal*. This result is explained by noting that this acid exists mainly (86%) as the hydroxylactone form[3] which is esterified as shown in Scheme I.

Thus we see that 2-benzoylbenzoic acid, which is present mainly in the keto acid form[3] and whose normal methyl ester is more stable, forms pseudo-ester preferentially under kinetic control, whereas 3,6-dimethyl-2-benzoylbenzoic acid, which is present mainly in the

(1) This research was supported by grant GP-718 of the National Science Foundation.
(2) M. S. Newman and S. Hishida, *J. Am. Chem. Soc.*, **84**, 3582 (1962). See also M. L. Bender and M. S. Silver, *ibid.*, **84**, 4589 (1962), and F. Ramirez, B. Hansen, and N. B. Desai, *ibid.*, **84**, 4588 (1962).
(3) For references and results see M. S. Newman and C. W. Muth, *ibid.*, **73**, 4627 (1951).
(4) The analysis was carried out by n.m.r. The normal methyl ester had τ 6.56 and the pseudo had τ 6.84, following the lead of P. T. Lansbury and J. F. Bieron [*J. Org. Chem.*, **28**, 3564 (1963)].

SCHEME I



hydroxylactone form[3] and whose pseudo-ester is more stable, forms mainly normal ester under kinetic control.

In a comparable 15-min. experiment, 6-methyl-2-benzoylbenzoic acid forms *in 44% yield* a mixture of 40% normal–60% pseudo-ester whereas at equilibrium the ester is 63% normal–37% pseudo. These results may be rationalized by using a combination of esterifications *via* routes comparable to A, B, and D, route C being less involved because of conventional steric hindrance. We believe that the accelerative effect of the 6-methyl group on route A is largely responsible for the increase in rate of esterification, as in the case of alkaline hydrolysis.[2]

How general the above effects are in the cases of other keto acids is under investigation.

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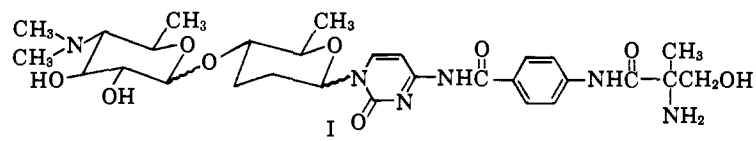
Synthesis of 2,3-Didehydro-2,3-dideoxy and 2,3-Dideoxy Sugar Nucleosides of Known Configuration

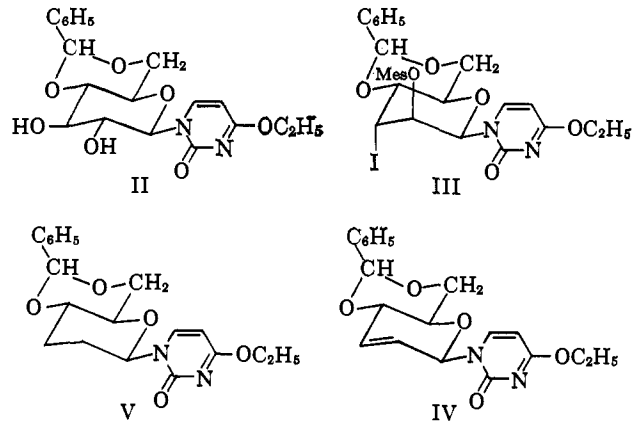
Sir:

The antibiotic amicetin has been shown to have the structure I.[1] Initially reported in 1953,[2] the antibiotic



represents the first reported nucleoside containing a 2,3-dideoxy sugar. Two of the most important problems associated with the chemistry of this new class of compounds are the determination of the stereochemistry of the nucleoside bond and the synthesis of a 2,3-dideoxy sugar nucleoside of known configuration. This paper presents the first synthesis of a such a nucleoside *via* a 2,3-didehydro-2,3-dideoxy sugar nucleoside. Further, a 2,3-dideoxy sugar was converted directly into a nucleoside and the stereochemistry of nucleoside linkage established.

The starting nucleoside II, of known β-configuration, was prepared from 1(tetra-*O*-acetyl-β-D-glucopyranosyl)-4-ethoxy-2(1*H*)pyrimidone which in turn was made by the classic procedure of Hilbert and Jansen.[3] The four acetate groups were removed with catalytic amounts of ethoxide ion and the resulting product was treated with benzaldehyde and zinc chloride to give 63% of II, 1(4,6-*O*-benzylidene-β-D-glucosyl)4-ethoxy-2(1*H*)pyrimidone, m.p. 228–230°, $[\alpha]^{23}D$ +33.5° (*c* 1.3, $CHCl_3$).



Compound II was converted to a 2,3-epoxide by a procedure recently described by Goodman and Christensen.[4] Treatment with 1.2 equiv. of *p*-toluenesulfonyl chloride followed by excess acetic anhydride gave a monotosyl monoacetate in 47% yield, m.p. 143–144°, $[\alpha]^{24.5}D$ +7.2° (*c* 2.09, $CHCl_3$). The monotosyl monoacetate gave a crystalline oxide in 73% yield when allowed to react with 5 equiv. of ethoxide ion. The oxide, m.p. 184–185°, $[\alpha]^{21}D$ +70.6° (*c* 1.47, $CHCl_3$). is assigned the *manno* configuration on the basis of previous data[5] which indicate the initial tosylation takes place on the 2-carbon.

The oxide was opened with sodium iodide, acetic acid, and small amounts of sodium acetate in acetone to give 92% of an iodohydrin, m.p. 220–221°, $[\alpha]^{25}D$ +92.2° (*c* 1.14, $CHCl_3$). On the basis of diaxial opening, the iodohydrin is assigned the *altro* configuration. Mesylation at room temperature gave 67% of III, 1(4,6-*O*-benzylidene-3-deoxy-3-iodo-2-*O*-methylsulfonyl-β-D-altrosyl)-4-ethoxy-2(1*H*)pyrimidone, m.p. 182–183°, $[\alpha]^{25}D$ +78.8° (*c* 1.84, $CHCl_3$).

The 2,3-unsaturated nucleoside IV, which to our knowledge represents the first such nucleoside reported in the chemical literature, was prepared in 99% yield from III with excess sodium iodide in acetone. The product, 1(4,6-*O*-benzylidene-2,3-didehydro-2,3-dideoxy-β-D-*erythro*-aldohexosyl)4-ethoxy-21(*H*)pyrimidone, IV, had m.p. 174–176°, $[\alpha]^{25.5}D$ +72.0° (*c* 0.7, $CHCl_3$).

Reduction of IV with platinum oxide in methanol was stopped after 1-mole uptake. Thin layer chromatography indicated a small amount of benzylidene reduction, but 60% of pure, recrystallized 2,3-dideoxy sugar nucleoside (V) was isolated.

This product V, 1(4,6-*O*-benzylidene-2,3-dideoxy-β-D-*erythro*-aldohexosyl)-4-ethoxy-2(1*H*)pyrimidone, had m.p. 181–182°; $[\alpha]^{25}D$ +69.5° (*c* 1.2, $CHCl_3$).

(1) C. L. Stevens, P. Blumbergs, and F. A. Daniher, *J. Am. Chem. Soc.*, **85**, 1552 (1963), C. L. Stevens, K. Nagarajan, and T. H. Haskell, *J. Org. Chem.*, **27**, 2991 (1962).

(2) J. W. Hinman, E. L. Caron, and C. DeBoer, *J. Am. Chem. Soc.*, **75**, 5864 (1953); E. H. Flynn, J. W. Hinman, E. L. Caron, and D. O. Woolf, Jr., *ibid.*, **75**, 5867 (1953).

(3) G. E. Hilbert and E. F. Jansen, *ibid.*, **58**, 60 (1936).

(4) L. Goodman and J. E. Christensen, *J. Org. Chem.*, **28**, 158 (1963).

(5) G. J. Robertson and C. F. Griffith, *J. Chem. Soc.*, 1193 (1935); H. R. Bollinger and D. A. Prins, *Helv. Chim. Acta*, **28**, 465 (1945); also *cf.* ref. 4.