simple olefins where steric effects appear to determine the mode of addition.[10]

The reactions involving the sugar derivatives **2** and **3** are significantly more complex. Consideration of the results obtained and examination of molecular models indicate that approach of the organopalladium salt for complexation[10] occurs primarily from the face of the cyclic enol ether ring opposite the allylic acetate substituent.[19] Decomposition of the resulting cis adduct with olefin formation depends on the conformation(s) that this adduct assumes. In Scheme I it is seen that addition of the organopalladium species to **3** produces an adduct which, in its most stable conformation (A), possesses an equatorial palladium function, i.e., a geometry improper for anti elimination of palladium acetate.[10,20,21] The less favorable conformation B, obtained by chair-chair interconversion, possesses the proper geometry for this elimination and presumably gives rise to the minor reaction product **9.** The palladium substituent in conformation A is, however, positioned with respect to the ring oxygen so as to permit anti elimination with alkoxide expulsion,[9,22-25] ring cleavage, and formation of a *Z*-olefinic[14] bond, i.e., the major product (**10**) of the reaction. For the reaction involving **2,** the energy difference between the two conformational isomers corresponding to A and B is less; as a result less selectivity is observed in the adduct decomposition.

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(13) The stereochemistry shown at C-2′ (the anomeric carbon) is that predicted by mechanistic considerations (see Scheme I) and has not been rigorously established.
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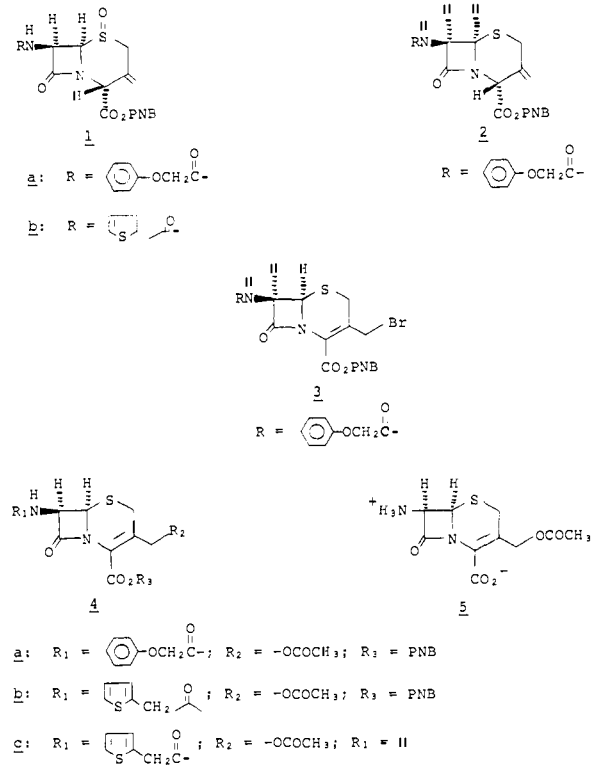
Isamu Arai, G. Doyle Daves, Jr.*
Department of Chemistry and Biochemical Sciences
Oregon Graduate Center, Beaverton, Oregon 97005
Received September 9, 1977

Direct Two-Step Conversion of Penicillins to 3-Acetoxymethylcephems

Sir:

Recently, we reported the transformation of penicillins to 3′-substituted cephems through the intermediate 3-*exo*-methylenecepham **2.**[1,2] Thus, the conversion of **2** to **3** and the subsequent displacement of halogen with the acetate ion afforded **4a.**[2] Such a transformation required initial activation of **2** with base to give the allylic anion which was then trapped with halogen to give **3.**[2] Subsequent transformation converted **4a** to the important intermediate 7-aminocephalosporanic acid (7-ACA, **5**).[2] We have since theorized that, if one could transform the 3-*exo*-methylenecepham **2** to an intermediate which could be intercepted directly by acetate, then the need for the initial conversion to **3** would be obviated.



One possibility which we considered was that 3-*exo*-methylenecepham sulfoxide **1** might be a precursor to the desired activated intermediate **6** which could be trapped at the 3′ carbon by acetate (**1** → **6** → **7**).

When we treated compound **1a** with mixtures of acetic anhydride and acetic acid at reflux (126 °C), we obtained a mixture of Δ^2,Δ^3-3′-OAc cephems **7a** and **4a,** respectively (R = phenoxyacetyl): IR ($CHCl_3$) 1785 cm^{-1}; NMR (3:1 mixture of Δ^2 and Δ^3) ($CDCl_3$) δ 6.5 (br s, 0.75, Δ^2-C_2 H), 5.8 (dd, 1, C_7 H), 4.6 (s, 2, C_7 side-chain methylene), 3.6 (br s, 0.5, Δ^3 C_2), 2.1-2.2 (ss, 3, Δ^2- and Δ^3-3′-acetoxy).

This reaction presumably proceeds through a Pummerer-type intermediate **6** which is then trapped in a 1,4 manner by

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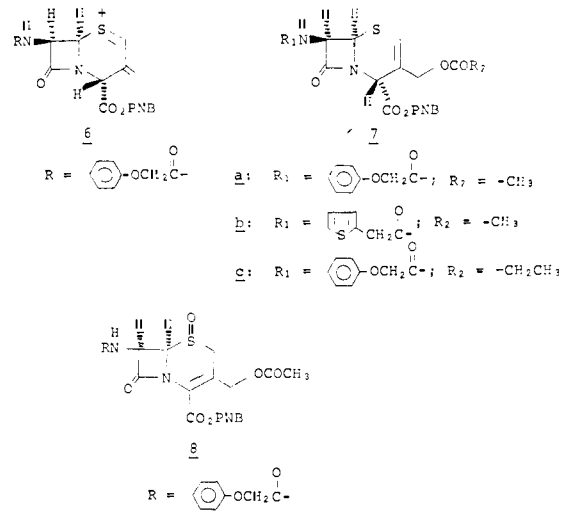

acetate ion.[3-5] The expected product is the Δ^2-3′-OAc cephem **7a.** However, at the reaction temperature of 126 °C, isomerization of the Δ^2 double bond occurs and a 3:1 ratio of Δ^2:Δ^3 isomers is obtained. That high temperature isomerizes the double bond is proven by heating to 70 °C, at which temperature only the Δ^2 product and starting material are obtained.[6]

We found this method to be generally applicable. Apparently, variation of the penicillin side chain is permissible. Thus, thiopheneacetyl-*exo*-methylenecephem sulfoxide **1b** reacts under the above conditions to yield **7b** and **4b** (R = thiopheneacetyl) (IR ($CHCl_3$) 1785 cm^{-1}; NMR ($CDCl_3$) δ 6.4 (br s, 1, Δ^2-C_2 H), 5.6 (dd, 1, C_7 H), 4.6 (br s, 2, $C_{3'}$ methylene), 3.8 (s, 2, C_7 side-chain methylene), 3.8 (s, 2, C_7 methylene), 2.05 (s, 3, 3′-(acetoxy)), which ultimately can be converted to **4c,** an important antibiotic.

Another interesting variation of this method is to change the anhydride and acid. For example, a mixture of propionic anhydride and propionic acid at 120 °C converts **1a** to the 3′-propionate **7c:** NMR ($CDCl_3$) δ 6.45 (br s, 1, Δ^2-C_2 H), 5.7 (dd, 1, C_7 H), 2.3 (q, 2, methylene of propionoxy), 1.1 (t, 3, methyl of propionoxy).

Optimal conditions for the conversion are to heat **1a** in a 2:1 mixture of acetic anhydride–acetic acid, at reflux (126 °C) for 2 h. The mixture of Δ^2,Δ^3-3′-acetoxycephems **7a** and **4a** (R = phenoxyacetyl) is isolated in high yield.

The mixture of isomers is then treated with *m*-chloroperbenzoic acid in methylene chloride and 2-propanol at 0 °C for 45 min. This efficiently yields crystalline Δ^3-3′-acetoxycephem sulfoxide **8.**

The yield for the two steps from **1a** → **8** is 84%. **8** is subsequently treated with PCl_3 and PCl_5 and finally deblocked to yield 7-ACA (**5**).[7]

This adaptation of a 1,4 Pummerer reaction, when combined with the ring expansion of penicillins to **1** as reported by Kukolja, provides a facile and efficient conversion of penicillins to 3′-ester cephalosporins.

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(4) For another example of a 1,4 Pummerer reaction, see Uda, *J. Chem. Soc., Chem. Commun.*, 193 (1975).
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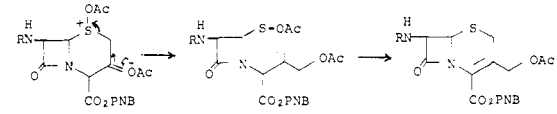
(6) An alternate mechanism for the conversion (**1a** → **7a** and **4a**) would be an S_N2' displacement followed by readdition of sulfenate. However, the major product should be Δ^3, **4a.** At low temperature, the product is exclusively Δ^2, **7a.**



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G. A. Koppel,* L. J. McShane*
The Lilly Research Laboratories, Eli Lilly and Company
Indianapolis, Indiana 46206

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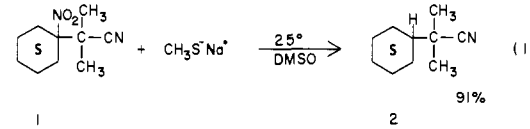
Replacement of the Nitro Group by Hydrogen[1]

Sir:

It was not until 1954 that the first useful synthesis of tertiary nitroparaffins was described. Since then a number of other reactions which also give excellent yields of pure aliphatic and alicyclic tertiary nitro compounds have been found.[1-10] All of these reactions employ mild conditions and most of them are carbon–carbon bond-forming processes. It is of especial interest that they give rise to highly branched compounds—many of them all but unobtainable by other means. Still another important feature of these reactions is that they are capable of providing tertiary nitro compounds in which other functional groups are present, e.g., cyano, keto, and ester.

With such a wide variety of unusual structures readily available it is apparent that any process which results in the replacement of a nitro group by other atoms or groups of atoms has considerable value. In this communication we describe a new reaction—the replacement of a nitro group by hydrogen. This occurs at room temperature when the nitro compound is treated with the sodium salt of methyl mercaptan. Equation 1 is illustrative and Table I summarizes our results; it should be emphasized that yields refer to pure, isolated products.



(1)

91%

1 2

The mechanism of this transformation appears to be

$$R_3C\text{-}NO_2 + CH_3S^- \rightarrow R_3C\text{-}NO_2^{-}\cdot + CH_3S\cdot \quad (2)$$

$$R_3C\text{-}NO_2^{-}\cdot \rightarrow R_3C\cdot + NO_2^- \quad (3)$$

$$R_3C\cdot + H_3C\text{-}S^- \rightarrow R_3C\text{-}H + H_2\dot{C}\text{-}S^- \quad (4)$$

$$H_2\dot{C}\text{-}S^- + R_3C\text{-}NO_2 \rightarrow H_2C{=}S + R_3C\text{-}NO_2^{-}\cdot \quad (5)$$

The first two steps (eq 2 and 3) are fully consistent with what is known about electron-transfer reactions of aliphatic nitro compounds.[10] The last two (eq 4 and 5), which provided the initiative for this work, were suggested by the studies of Bunnett, Boyle, and Wamser[11] on the free-radical chemistry of methoxide ion. Although mechanistic studies are not yet complete, it has already been established that several of the reactions of Table I are completely inhibited by 20 mol % of di-*tert*-butyl nitroxide. This, and the fact that these reactions are greatly accelerated by exposure to two 20-W ordinary fluorescent lights, provides support for the proposed electron-transfer chain mechanism of eq 2-5.[10]

A typical example follows. Under N_2 the sodium salt of methyl mercaptan[12] (10.50 g, 150 mmol) was dissolved in 150 mL of Me_2SO[13] and, then, 9.80 g (50 mmol) of **1**[7] was added without opening the system. The resulting solution was stirred for 10 h, under N_2, with exposure to two 20-W fluorescent lights and, then, was poured into water. The aqueous Me_2SO solution was extracted with pentane, the pentane was washed

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