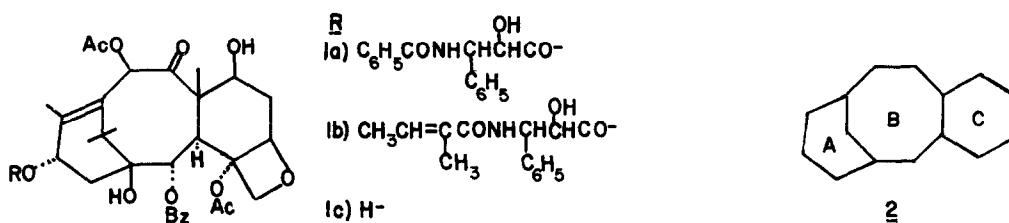


AN APPROACH TO THE D-RING OF BACCATIN III (TAXOL, CEPHALOMANNINE).

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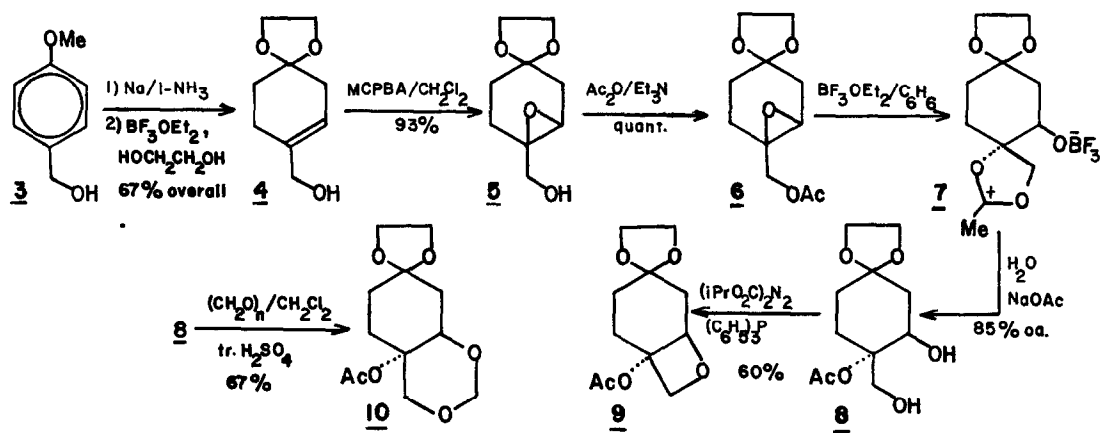
Summary: We report a sequence of reactions applicable to the construction of the oxetane (D-Ring)/tertiary acetate grouping of Baccatin III (Taxol, Cephalomannine).

Taxol<sup>1,2</sup> (**1a**), a Taxane (**2**) derivative with a rare oxetane ring, has attracted considerable attention because of its antileukemic and tumor inhibiting activity. The ability of Taxol to greatly enhance the assembly and stability of microtubules has also been a source of lively interest<sup>3</sup>. Cephalomannine<sup>4</sup> (**1b**), also isolated from a *Taxus* species, incorporates a common polyoxygenated terpenoid fragment, Baccatin III (**1c**).



Whereas the basic A, B, and C rings of Baccatin III, ie. the Taxane skeleton, have been assembled several times in the recent past, little attention has been paid to construction of the oxetane (D) ring<sup>5</sup>. Here we report a sequence of reactions applicable to the conversion of an allylic alcohol into the oxetane/tertiary acetate grouping of Baccatin III.

Allylic alcohol **4** was prepared using the procedure of Isobe<sup>6</sup>: Birch reduction of p-methoxybenzyl alcohol followed by direct ketalization. Epoxidation and acetylation proceeded cleanly, affording **6** in excellent yield. Rearrangement, involving neighboring group participation of the acetoxy group, and catalysed by boron trifluoride etherate<sup>7</sup>, gave a surprisingly good yield of the desired acetoxy-*cis*-diol **8**. The diol was closed to the oxetane **9** by the Mitsunobu procedure<sup>8</sup>, using di-isopropyl diazodicarboxylate. (The diethyl diazoester afforded a hydrazine by-product which was difficult to separate from **9**.) The diol was also converted to dioxolane **10**, an interesting analog, and a latent function for the oxetane (eg. a protected diol).



Initial attempts to open epoxide **5** by acid catalysis led mainly to aromatization. At lower temperatures, however, boron trifluoride etherate in acetic acid afforded the desired tertiary acetate diol **8** in 20% yield.

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Borontrifluoride etherate (11.8 mL, 0.105 mol) was added to a suspension of 21.83 g (0.096 mol) of epoxyacetate **6** suspended in 300 mL of dry benzene, instantly forming a gelatinous white precipitate. This mixture was shaken at room temperature for two minutes, then diluted with 250 mL of 10% aqueous sodium acetate. The mixture was shaken briefly, separated, and the aqueous layer was extracted with four 150 mL portions of ethyl acetate. The combined organic layers were washed with 250 mL of water, dried over magnesium sulfate, and concentrated under reduced pressure, giving 20.0 g (85%) of diol-acetate **8**. The crude diol was purified by flash chromatography (hexane/ethyl acetate:3/2), and further for elemental analysis by preparative TLC (silica, 4% MeOH/CHCl<sub>3</sub>, R<sub>f</sub>=0.3). IR (CHCl<sub>3</sub>): 3490, 1725 cm<sup>-1</sup>. NMR (CDCl<sub>3</sub>): 2.10 (OAc), 3.43 (OH, D<sub>2</sub>O labile), 3.60 and 4.17 (CH<sub>2</sub>OH), 3.75 (CHOH), 3.97 (O-CH<sub>2</sub>-CH<sub>2</sub>-O).

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9] All structures except **7** were confirmed by ir and nmr spectra and elemental analysis.

Acknowledgement: This work was supported in part by a grant from the PSC-BHE Faculty Research Award Program of the City University of New York.

(Received in USA 2 April 1985)