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SYNTHESIS OF PENEM AND CEPHEM ANTIBIOTICS EMPLOYING CARBENE REACTION

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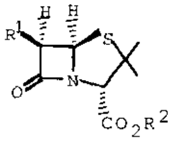
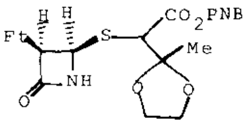
Since the first synthesis of penems reported by Woodward, this important class of non-classical β-lactam antibiotics is becoming an interesting compound with regard to both biology and synthesis. Our synthesis of the above compound starts from readily available 6-aminopenicillanic acid (1). The reaction of 2 with the diazo compound in the presence of rhodium acetate afforded the seco-penicillin derivative in good yield which was easily converted to 3 by two steps. After the introduction of phosphonyl group by the usual way, the phosphorane (4) was converted to the penem (5) by treatment with ozone, followed by an intramolecular Wittig reaction. Whereas the ozonolysis of the seco-penicillin derivative (6) afforded the triester (7), whose conversion into the cephem (8) was effectively achieved by an intramolecular Michael addition. Thus, the conversion of 6-aminopenicillanic acid into the penem (5) and the cephem (8) was successfully carried out by employing carbene reaction as a key step.



1 $R^1 = NH_2$, $R^2 = H$
2 $R^1 = Ft$, $R^2 = Bz$



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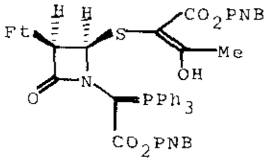

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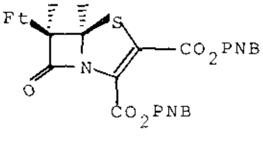

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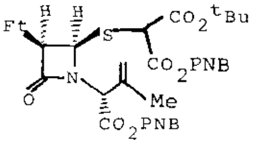

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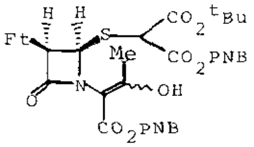

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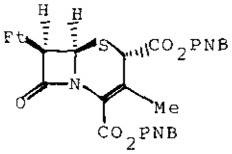

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