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SYNTHESIS OF β-LACTAM ANTIBIOTICS VIA THE SULFENO-CYCLOAMINATION

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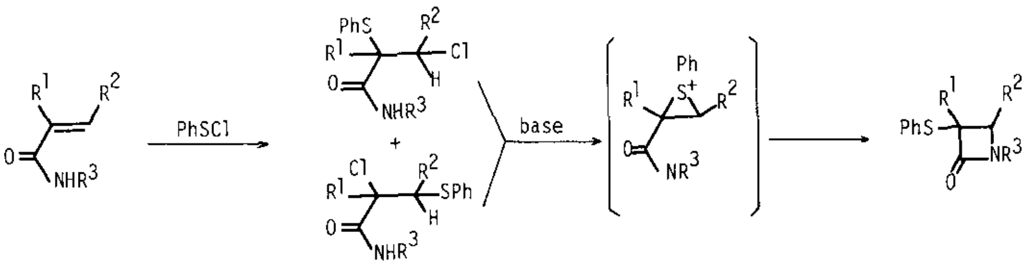
β-Lactam linkage and carbapenam ring system were constructed by the sulfeno-cycloamination as follows.

Construction of β-Lactam Linkage

Novel β-lactam synthesis was achieved efficiently by succesive two processes; addition of phenylsulfenyl chloride to α,β-unsaturated amides (1) followed by base treatment. The cyclization has following distinguished characteristics. The reaction proceeds via a most probable episulfonium ion intermediate (3) under mild conditions without separation of regio-isomers of adducts (2) and the resulting sulfenyl group is readily removable as well as useful for introduction of other functional group. Key synthetic intermediates of monobactams and nocardicin derivatives were obtained via this method.



Construction of Carbapenam Ring System

Reaction of olefinic azetidinones (5) with the sulfenyl chloride gave the N-sulfenylated adducts (6), which were cyclized to carbapenam derivatives (8) after removal of the N-sulfenyl group with sodium borohydride.