

SYNTHESES OF CARBACEPHAM AND CARBACEPHEM RING SYSTEM BY
EMPLOYING RADICAL CYCLIZATION

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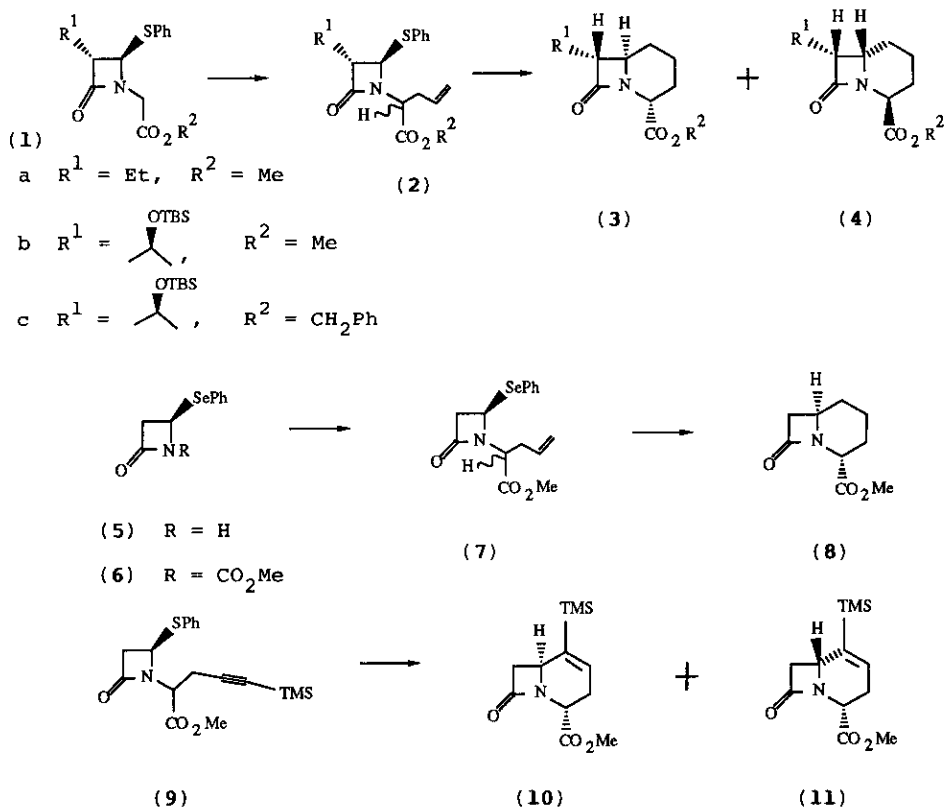
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Abstract — Radical cyclization reaction was successfully
applied to the construction of carbacepham and carbacephem
ring system.

In 1982, we have reported¹ the synthesis of carbacepham ring system by using a radical cyclization reaction. Here, we would like to report a further application of this strategy to the synthesis of 7-substituted carbacephams in addition to the synthesis of carbacephem. 3-Substituted 4-phenylthioazetidinones (1a - c) were converted to the corresponding allyl derivatives (2a - c) in moderate yields. Radical cyclization of (2a - c) using tri-*n*-butyltin hydride in the presence of a catalytic amount of AlBN in refluxing benzene afforded the expected carbacephams (3a - c and 4a - c) in a ratio of ca. 2 : 1 in 50 - 60% yields, where the formation of 1-methylcarbapenam, namely an another possible cyclization product could not be observed. The stereochemistry of the products was determined based on their nmr spectra.² Since a phenylselenenyl group was also recognized as a good progenitor to generate a radical center, we therefore examined the radical cyclization reaction of 4-phenylselenoazetidinone derivative (7), easily derived from (5) via (6) by two steps.³ Treatment of (7) with tri-*n*-butyltin hydride in the presence of AlBN in refluxing benzene furnished the carbacepham (8), identical with an authentic specimen,¹ in 59% yield. Its conversion yield was clearly superior to those of the corresponding 4-phenylthio derivative, the radical cyclization of which afforded (8) in 40 - 45% yield. In order to synthesize a carbacephem skeleton, a propargyl group was introduced into 1-methoxycarbonylmethyl-4-

phenylthio-2-azetidinone to give (9), whose radical cyclization under the similar reaction condition as above afforded the carbacephems (10 and 11) as an inseparable oil in 10.3% yield, in the ratio of ca. 5 : 1.

Thus, we could disclose a construction of carbacepham and carbacephem ring system by employing a radical cyclization reaction as a key step.



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