was stirred at 35-40 °C. The reaction proceeded smoothly and

was complete in 45 min to afford 3-allyl-3-cephem 3a (R = allyl) in 85% yield along with a small amount of 2-exo-

methylenepenam 5 (Table 1, entry 1). The formation of 5 can

be reasonably understood by assuming reductive cleavage of the S–S bond of 1 followed by intramolecular attack of thus

formed thiolate ion to the allene moiety.5 The presence of

aluminium and catalytic amounts of $PbBr_2$ and $[NiCl_2(bipy)]$ is indispensable for the formation of 3a, since lack of any of the

components resulted in the formation of no appreciable

amount of 3a. In place of the Al/PbBr2/[NiCl2(bipy)] combina-

tion, use of other metal/metal salt combinations, e.g.,

Zn/NiCl26 and SnCl2/[PdCl2(PhCN)2],7 was attempted for

performing the reaction of 1 and 4a but no detectable amount

redox system may promote a sequential addition/cyclization reaction of the allenecarboxylate 1 via 6 as illustrated in

Scheme 2. The Ni⁰ would be initially formed and regenerated

in the Al/PbBr₂/[NiCl₂(bipy)] system, in which, aluminium would release the required electrons through a Pb⁰–Pb¹¹ redox

The Al/PbBr₂/[NiCl₂(bipy)] system can be successfully

applied to the synthesis of the cephems **3** bearing allylic or benzylic C-3 substituents (entries 2–8). The reaction of **1** with 2-butenyl, 3-phenyl-2-propenyl, and 3-bromo-2-propenyl bromides **4** took place in a regioselective manner to afford the

corresponding α -substituted products 3, exclusively (entries

3-5). When benzylic halides were used in place of the allyl

Although the reaction mechanism is not clear at present, it is likely that an Al⁰-Al¹¹¹, Pb⁰-Pb¹¹, and Ni⁰-Ni¹¹ three-metal

of the desired product 3a was found.

mediatory system.8

A Facile Access to 3-Allyl- and 3-Benzyl-3-cephems *via* Reductive Addition/Cyclization of Allenecarboxylate with Allyl and Benzyl Halides in an Al/Pb/Ni Redox System

Hideo Tanaka, Shin-ichi Sumida, Kouichi Sorajo and Sigeru Torii*

Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushima-naka, Okayama 700, Japan

A sequential reductive addition/cyclization reaction of allenecarboxylate, derived from penicillin G, with allyl and benzyl halides was successfully performed by the aid of aluminium metal and catalytic amounts of PbBr₂ and [NiCl₂(bipy)] to afford 3-allyl- and 3-benzyl-3-cephems, respectively.

Since the pioneering work of Morin et al.,1 conversion of penicillins into cephalosporins has been the keen subject of the synthesis of cephem antibiotics and various synthetic approaches have emerged.² In previous papers, we disclosed a conceptually new strategy for the penicillin \rightarrow cephalosporin conversion involving a sequential addition/cyclization reaction of allenecarboxylate 1, derived from penicillin G, leading to 3-substituted cephems 3 (Scheme 1).³ Independently, Kant and Farina reported an analogous access to the 3-substituted cephems 3.4 In these procedures, heteroatom nucleophiles, organocuprates, and organostannannes were employed as nucleophiles (R⁻) which were introduced at the C-3 position of the cephem framework. Herein we disclose a new device for construction of a cephem framework promoted by reductive addition of allyl or benzyl halides 4 to the allenecarboxylate 1 in an Al/PbBr₂/[NiCl₂(bipy)] three-metal redox system as illustrated in Scheme 2.

The addition/cyclization can be performed by treatment of a mixture of the allenecarboxylate 1 and allyl or benzyl halides 4 with aluminium and catalytic amounts of PbBr₂ and [NiCl₂-(bipy)]. A typical reaction procedure is as follows: A mixture of the allenecarboxylate 1,³ allyl bromide 4a (R = allyl, X = Br; 5 equiv.) aluminium (2.5 equiv.), PbBr₂ (0.05 equiv.), and [NiCl₂(bipy)] (0.1 equiv.) in *N*-methyl-2-pyrrolidone (NMP)

 Table 1 Reaction of allenecarboxylate 1 with allyl and benzyl halides

 4^a

		Yield (%) ^b	
Entry	R-X	3	5
1	Br	85	Trace
2	∕∕ ^{CI}	61	Trace
3	Br	82	-
4	PhBr	60	-
5	Br	31	4
6	Br	73	-
7	CH ₂ Br	83	-
8	Br CH ₂ Br	62	-

^{*a*} Carried out in a similar manner to that described in the text. ^{*b*} Isolated yields after column chromatography.





R = Allyl, benzyl X = Br, Cl

 $\mathbf{R}^2 = \boldsymbol{\rho} \cdot \mathbf{M}_{\theta} \mathbf{O} \mathbf{C}_{\theta} \mathbf{H}_4 \mathbf{C} \mathbf{H}_2$

Scheme 2

halides, the 3-benzyl-3-cephems **3** were obtained in moderate yields (entries 7 and 8). Similar reactions of **1** with vinyl bromide and phenyl iodide were also attempted but no detectable amounts of cyclized products **3** (R = vinyl, phenyl) were observed. Presumably, disproportionation of the vinyl and phenyl nickel(II) complexes (R-Ni-X) would take place preferentially to give buta-1,3-diene and biphenyl, respectively.^{6,7}

In conclusion, we have developed a new methodology for the construction of the cephem framework 3 based on reductive addition/cyclization of the allenecarboxylate 1 with allyl and benzyl halides 4 in the Al/PbBr₂/[NiCl₂(bipy)] system. Further applications of the three-metal redox system are in progress.

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