# Synthesis and Antibacterial Activities of Triphenyltin Cephalosporins

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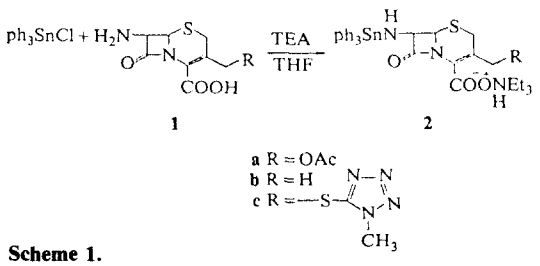
**Sir:**

Although it has been known that organometallic $\beta$-lactam compounds improve the resistance to $\beta$-lactamases as well as their pharmacological activities, only a few results on organometallic $\beta$-lactam antibiotics were reported.[1-4] In the course of our extensive study on the development of new cephalosporins, we were interested in organotin compounds since they show some biological activities.[5] In this communication, we wish to report the first example of organotin cephalosporins and their detailed *in vitro* antibacterial activities.




**Scheme 1.**

Organotin cephalosporins were synthesized as outlined in Scheme 1. A solution of triphenyltin in THF was added slowly to a suspension of 7-aminocephalosporanic acid(**1a**) in the presence of TEA in THF. The contents were stirred for 1hr at room temperature to give the triphenyltinamidocephalosporanic triethylammonium salt(**2a**) in 40% yield. The compound synthesized were characterized by NMR and IR spectral measurement. The IR spectra indicates that the carbonyl group of $\beta$-lactam is not bound to the tin ion.

Table I shows antibacterial spectra of compounds **2a-2c** as compared with those of cefotaxime. Against Gram-positive bacteria, triphenyltin cephalosporins exhibited activities comparable to

**Table I.** ***In vitro*** **antibacterial activity(MIC, $\mu$g/ml)[a] of compounds 2a, 2b, 2c and cefotaxime**

| *Organism* | **2a** | **2b** | **2c** | cefotaxime |
|---|---|---|---|---|
| *Streptococcus faecium* MD 8b | 6.23 | 6.25 | 25 | |
| *Staphylococcus aureus* SG 511 | 1.563 | 1.563 | 1.563 | 1.563 |
| *Staphylococcus aureus* 285 | 3.125 | 1.563 | 1.563 | 3.125 |
| *Staphylococcus aureus* 503 | 1.563 | 1.563 | 0.781 | 1.563 |
| *Escherichia coli* O 55 | 100 | 25 | 100 | 0.013 |
| *Escherichia coli* DC 2 | 6.25 | 6.25 | 6.25 | 0.013 |
| *Escherichia coli* 1507E | 100 | 50 | 100 | 0.049 |
| *Pseudomonas aeruginosa* 9027 | 100 | 100 | 100 | 12.5 |
| *Pseudomonas aeruginosa* 1771 | 100 | 25 | 50 | 6.25 |
| *Pseudomonas aeruginosa* 1771M | 50 | 12.5 | 25 | 0.098 |
| *Klebsiella aerogenes* 1082E | 50 | 25 | 100 | 0.781 |
| *Enterobacter cloacae* P 99 | 100 | 100 | 100 | 100 |

[a]Mueller Hinton Agar; dilution method; 37 °C, 18 hours

those of cafotaxime. The compounds have weak activities against *E. coli* and P. aeruginosa but were inactive against other Gram-negative bacteria. The interesting feature of triphenyltin cephalosporins is the excellent activity against Gram-positive bacteria regardless of the side chain at the C-3 position.

For further improvements and to establish the structure-activity relationship of the metallocene compounds, the synthesis of organometallic $\beta$-lactams is under study now.

## ACKNOWLEDGEMENT

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*IR frequences ($cm^{-1}$) of tin derivatives

| | NH | $\beta$-lactamic CO | $CO_2^-$ |
|---|---|---|---|
| 2a | 3400 | 1767 | 1615 |
| 2b | 3400 | 1767 | 1620 |
| 3c | 3370 | 1768 | 1609 |

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