

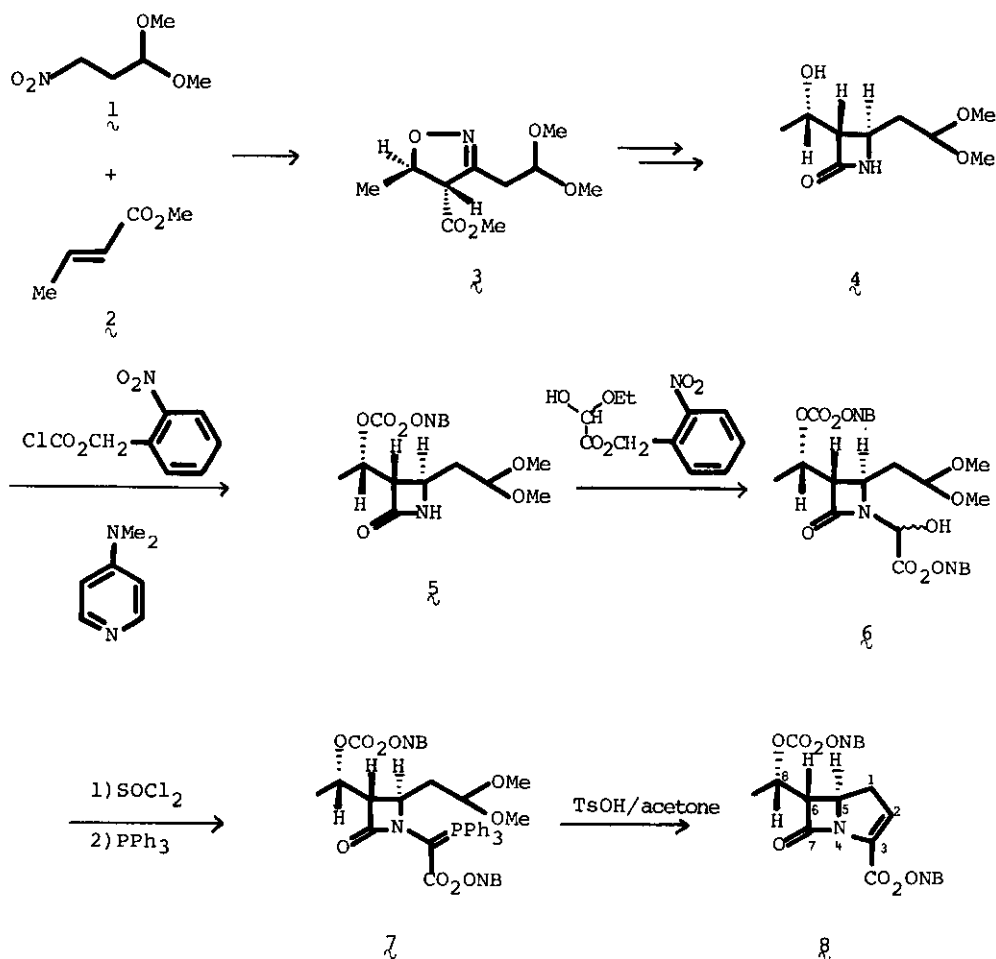
TOTAL SYNTHESIS OF (\pm)-8S^{*}-DESCYSTEAMINYLTHTIENAMYCIN PROTECTED WITH o-NITROBENZYL GROUPS

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Abstract — (\pm)-trans-4-(2',2'-Dimethoxyethyl)-3-(1'S^{*}-hydroxyethyl)-2-azetidinone (**4**), prepared from an isoxazoline derivative (**3**), was converted to (\pm)-8S^{*}-descyteaminylthienamycin protected with o-nitrobenzyl groups (**8**) using an intramolecular Wittig reaction.

Conversion of (\pm)-trans-4-(2',2'-dimethoxyethyl)-3-(1'S^{*}-hydroxyethyl)-2-azetidinone (**4**), prepared as described in a preceding paper,¹ into (\pm)-8S^{*}-descyteaminylthienamycin protected with o-nitrobenzyl groups was accomplished as follows. Reaction of the azetidinone (**4**) with o-nitrobenzyl chloroformate in the presence of N,N-dimethylaminopyridine in methylene chloride at -5 ~ 0°C for 1 h gave trans-4-(2',2'-dimethoxyethyl)-3-(1'S^{*}-o-nitrobenzyloxycarbonyloxyethyl)-2-azetidinone (**5**), $\text{ir } \nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 3450 (NH), 1760, 1750 (C=O); nmr (CDCl₃) δ : 1.46 (3H, d, J = 6.5 Hz, MeCH(OH)), 3.15 (1H, d of d, J = 6 and 2 Hz, C₃-H), 3.34 (6H, s, 2xOMe), 3.65 (1H, t of d, J = 7 and 2 Hz, C₄-H), m/e 383 (M⁺ + 1), in 84 % yield. Condensation of **5** with o-nitrobenzyl glyoxalate ethylhemiacetal, using activated molecular sieves (3A)² in dimethylformamide and toluene at room temperature for 24 h, yielded a epimeric mixture of the alcohol **6**, $\text{ir } \nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 1760 (C=O), nmr (CDCl₃) δ : 3.33 (6H, s, 2xOMe), in 69 % yield. On reaction with thionyl chloride and 2,6-lutidine in tetrahydrofuran at room temperature for 30 min, the alcohol **6** gave the unstable chloro compound, which without purification was converted to the phosphoran (**7**) in 74 % yield after purification by silica gel column chromatography, $\text{ir } \nu_{\text{max}}^{\text{CHCl}_3} \text{ cm}^{-1}$: 1750 (C=O); nmr (CDCl₃) δ : 1.40 (3H, d, J = 6.5 Hz, MeCH(OH)), 3.23 (6H, s, 2xOMe). Deacetalisation was carried out using p-toluenesulfonic acid in acetone at room temperature for 2 h, and on evaporation of the solvent and basification with saturated aqueous sodium hydrogen carbonate spontaneous intramolecular Wittig

Scheme



reaction occurred to give, in 39 % yield, *o*-nitrobenzyl 6-(1'*S*^{*}-*o*-nitrobenzyloxy-carbonyloxyethyl)-1-carba-2-penem-3-carboxylate (8), $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 1778, 1740, 1720 (C=O); nmr (CDCl_3) δ : 1.55 (3H, d, $J = 6.5$ Hz, MeCH(OH)-), 3.46 (1H, d of d, $J = 2$ and 4.5 Hz, $\text{C}_6\text{-H}$), 4.30 (1H, d of t, $J = 2$ and 7 Hz, $\text{C}_5\text{-H}$), 6.60 (1H, t, $J = 2$ Hz, $\text{C}_2\text{-H}$), which would be an important synthetic precursor of (\pm)-8*S*^{*}-descysteaminylthienamycin.³

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