Tetrahedron Letters, Vol.27, No.8, pp 993-994, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF SESBANIMIDE : AN APPROACH FOR THE SYNTHESIS OF RING C

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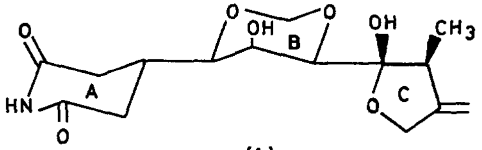
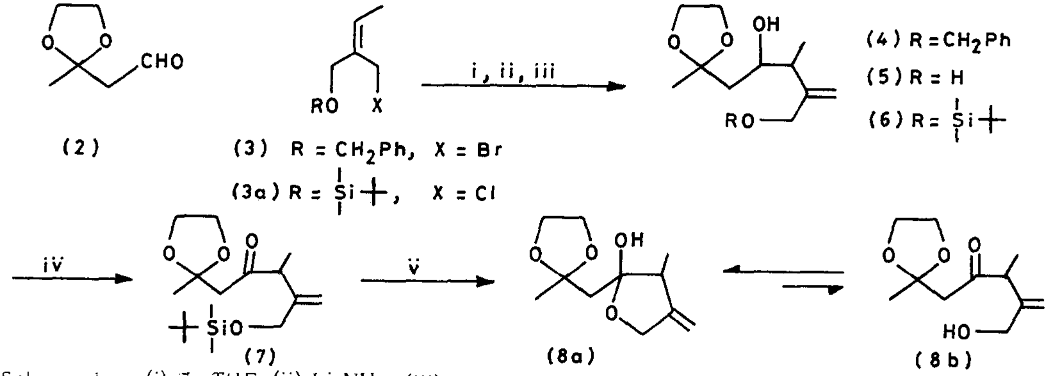
ABSTRACT *A simple method for the construction of C-ring of sesbanimide utilizing the condensation of 2-benzyloxymethylcrotyl bromide with an aldehyde in the presence of zinc as the key step is described.*

Sesbanimide (1) isolated from the seeds of Sesbania drummondii, possesses potent antitumour activity against p-388 lymphocytic leukaemia. It has unique structural features in that its three rings are connected by single bonds[1].



(1)

Although reports describing the synthesis of ring A and rings AB have appeared[2], the total synthesis of sesbanimide has not yet been achieved for want of an appropriate method for the synthesis of ring C. This communication describes a simple and elegant method for synthesis of ring C of sesbanimide as shown in Scheme 1.



Scheme 1 : (i) Zn,THF; (ii) Li-NH_3; (iii) t-butyldimethylchlorosilane,imidazole; (iv) PCC-NaOAc, CH_2Cl_2; (v) n-Bu_4NF, THF

Condensation of the bromide (3) (see Scheme 2[3]) with aldehyde (2) was initially attempted in the presence of magnesium or lithium metal, but the yields were poor. This problem was solved by employing Zaitzev reaction[4] in which the bromide (3) was reacted

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*Present address : Regional Research Laboratory, Hyderabad 500 007, India with the aldehyde (2) in the presence of activated zinc dust and iodine as catalyst to give 4 in 85% yield. Although the reaction was not stereoselective as judged by NMR spectrum, high degree of regioselectivity was observed. Since the chirality of the carbon bearing the hydroxyl group was destroyed at later stages, the nonstereoselectivity of the Zaitzev reaction will not affect the synthetic plan.

Hydrogenolysis of 4 with lithium in liquid ammonia was smooth and gave the diol (5) in high yield. The primary hydroxyl group in 5 was selectively protected with t-butyl-dimethylsilyl (TBDMS) group to afford 6 in almost quantitative yield. In an alternative approach, compound 6 was directly prepared in one step from the aldehyde (2) and TBDMS protected chloride (3a) by employing similar conditions, but the yield was low.

Oxidation of the secondary hydroxyl group 6 with PCC-NaOAc in CH_2Cl_2 gave the ketone (7) in 75% yield. Subsequent treatment of 7 with one molar solution of tetrabutylammonium fluoride in tetrahydrofuran resulted in the desired hemiketal (8) as a recemic mixture with 80% yield. The NMR spectrum of 8 in $CDCl_3$ showed that the product existed in both forms, closed (8a) and open (8b) in a ratio of 4:1. Further work, incorporating the C-ring on the AB ring synthon of sesbanimide, is in progress.

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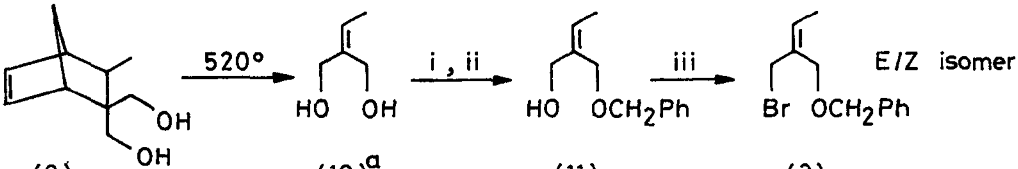
3. The bromide (3) was prepared as depicted in Scheme 2.



Scheme 2: (i) $PhCH(OMe)_2,H^+$; (ii) LAH-$AlCl_3$; (iii) PBr_3

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NCL Communication No. 3902

(Received in UK 12 December 1985)