Tetrahedron Letters,Vol.23,No.18,pp 1955-1956,1982 0040-4039/82/181955-02$03.00/0
Printed in Great Britain

A SIMPLE APPROACH TO CARBOCYCLIC THROMBOXANE A_2 FROM A CYCLOBUTANE

M.F. Ansell[+], M.P.L. Caton* and K.A.J. Stuttle

The Research Laboratories, May & Baker Ltd.,

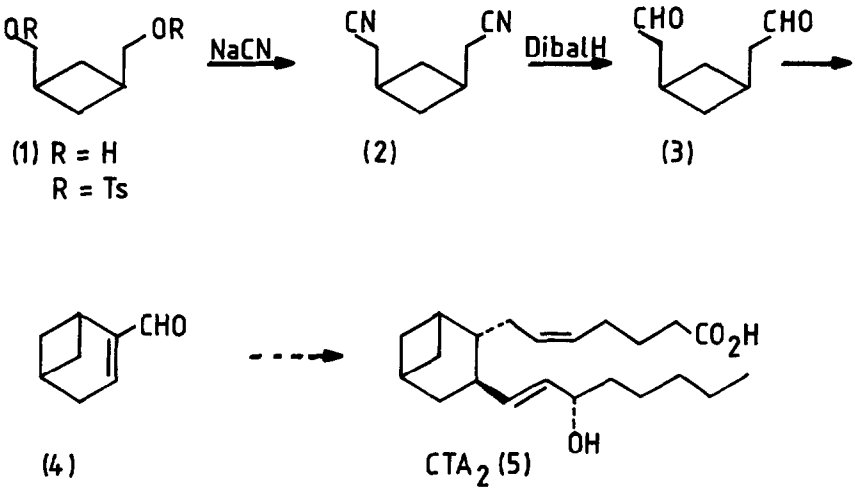
Dagenham, Essex, RM10 7XS

and [+]Department of Chemistry, Queen Mary College

University of London, London, E1 4NS.

Summary - A short route from the cyclobutane derivative (1) to the key intermediate (4) allows easy access to the carbocyclic thromboxane A_2 analogue (5).

Two groups[1,2] have synthesised the stable, biologically active, analogue (5) of thromboxane A_2 in which the ether linkages are replaced by methylene groups. Publication of this work prompted us to report our short and efficient route to this compound from a cyclobutane intermediate (1 R = H) [3,4]. Treatment of the ditosylate of (1) (R=Ts)[3,4] with sodium cyanide in dried DMSO overnight at r.t. gave the nitrile (2) (70%) as a white crystalline solid (m.p. 52-3°), which was readily converted to the dialdehyde (3) (85%) (ν max 2620, 1725 cm^{-1}) by treatment with diisobutylaluminium hydride. The dialdehyde (3) then readily underwent cyclisation to the key intermediate (4) (70%) with piperidinium acetate in refluxing benzene [λmax (EtOH) 241 nm (ε=9,400), ($CDCl_3$) δ 9.4 (s), 6.65 (m), 3.15 (m)]. Intermediate (4) was then elaborated to carbocyclic thromboxane A_2 (5) using a method similar to Nicolaou *et.al.*,[2] namely conjugate addition to introduce the lower chain followed by two consecutive Wittig elaborations.



References

1. S. Ohuchida, N. Hamanaka and M. Hayashi, Tetrahedron Letters, 1979, 3661.

2. K.C. Nicolaou, R.L. Magolda, J.B. Smith, D.A. Aharoni, E.F. Smith and A.M. Lefer, Proc.Nat.Acad.Sci. U.S.A., 1979, 76, 2566.

3. N.L. Allinger and L.A. Tushaus, J.Org.Chem., 1965, 30, 1945.

4. H. Musso, K. Newman and K. Grychtol, Chem.Ber., 1967, 100, 3614.

(Received in UK 1 March 1982)