

The Norbornadiene Route to Prostaglandin I₂ and Other Prostaglandins: Preparation and Rearrangement of 7-Substituted Norbornadienes

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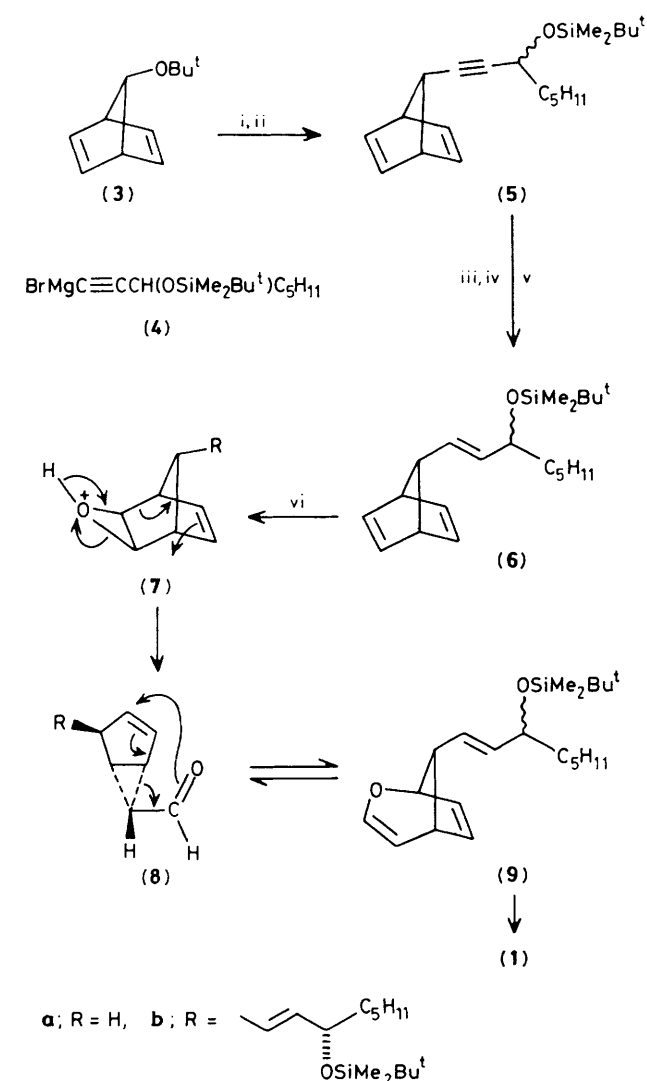
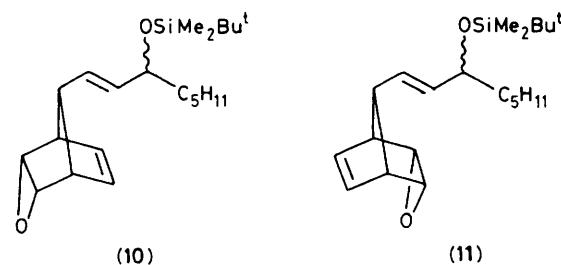
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The cyclopentenylacetaldehyde (**1**) required for the synthesis of prostacyclin (prostaglandin I₂) and other prostanoids is now readily available from the preparation and rearrangement of 7-substituted norbornadienes.

The first *de novo* synthesis of prostacyclin (PGI₂) (**2**),¹ a potent inhibitor of blood platelet aggregation, involves eighteen steps from cyclopentadiene and requires the cyclopentenylacetalde-

hyde (**1**)² as the key intermediate (Scheme 1).¹ We have improved and simplified this synthesis by a study of the preparations and peracid oxidations of 7-substituted nor-



- 1 R. F. Newton, S. M. Roberts, B. J. Wakefield, and G. T. Woolley, *J. Chem. Soc., Chem. Commun.*, 1981, 922; A. D. Baxter, S. M. Roberts, B. J. Wakefield, G. T. Woolley, and R. F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1809.
- 2 S. M. Ali, M. A. W. Finch, S. M. Roberts, and R. F. Newton, *J. Chem. Soc., Chem. Commun.*, 1979, 679; 1980, 74; S. M. Ali, C. B. Chapleo, M. A. W. Finch, S. M. Roberts, G. T. Woolley, R. C. Cave, and R. F. Newton, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2093. For another lengthy route to this cyclopentenyl-acetaldehyde system see C. Gandolfi and G. Doria, *Farmaco, Ed. Sci.*, 1974, **29**, 405.
- 3 P. R. Story and S. R. Farenholtz, *J. Org. Chem.*, 1963, **28**, 1716.
- 4 S. C. Clark and B. C. Johnson, *Tetrahedron*, 1968, **24**, 5067.
- 5 J. Stapersma and G. W. Klumpp, *Tetrahedron*, 1981, **37**, 187.
- 6 F. Binns, unpublished work; A. D. Baxter, F. Binns, M. D. Lynch, R. F. Newton, S. M. Roberts, P. Sadler, F. Scheinmann, B. J. Wakefield, and G. T. Woolley, *Adv. Prostaglandin, Thromboxane Leukotriene Res.*, 1983, **11**, 307.
- 7 J. Meinwald, S. S. Labana, and K. S. Chada, *J. Am. Chem. Soc.*, 1963, **85**, 582.
- 8 M. Rey and A. S. Dreiding, *Helv. Chim. Acta*, 1965, **48**, 1985.