

## Conservation of the Chair-like Transition State by Base-catalysed Epimerization of *meso*-Tetramethyl Hexa-1,5-diene-2,3,4,5-tetracarboxylate prior to its Cope Rearrangement

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*meso*-Tetramethyl hexa-1,5-diene-2,3,4,5-tetracarboxylate (5) rearranges at 20–50 °C in the presence of sodium carbonate to (*E,E*)-tetramethyl hexa-1,5-diene-1,2,5,6-tetracarboxylate (7), by base-catalysed epimerization followed by Cope rearrangement of the resulting ( $\pm$ )-tetraester (6) *via* the expected four-centred, chair-like transition state. In the absence of base the *meso*-tetraester (5) undergoes [3,3] sigmatropic rearrangement to produce (*E,Z*)-tetramethyl hexa-1,5-diene-1,2,5,6-tetracarboxylate (8) exclusively.

IN recent contributions<sup>1-3</sup> from this laboratory the stereospecific formation of the vinyl sulphide (1) *via* Michael addition of the sulphonium ylide (2) to the sulphonium bromide (3), followed by demethylation of the resulting salt (4) by bromide ion, was described. Chemical proof of the structure of the vinyl sulphide (1) was provided by mild desulphurization with Raney nickel, which produced the crystalline tetraester (5) as the major cleavage product together with a smaller quantity of the isomeric (*E,E*)-tetraester (7).<sup>2</sup> In order to determine the relative configuration at the chiral centres of the vinyl sulphide (1), the stereochemical outcome of the Cope rearrangement of the tetraester (5) was invoked.<sup>3</sup> It was found that when heated (115 °C; 24 h) the ester (5) smoothly rearranged to produce the (*E,Z*)-tetraester (8) as the sole product.<sup>3</sup> This result is in accord with the expected stereochemical outcome of the Cope rearrangement of the *meso*-tetraester (5) *via* a four-centred, chair-like transition state<sup>4</sup> to produce the (*E,Z*)-tetraester (8) (Scheme 1). Furthermore, it dictates the indicated relative configuration at the chiral centres of the vinyl sulphide (1).

Various pathways may account for the formation of the (*E,E*)-tetraester (7) during desulphurization of the vinyl sulphide (1) with Raney nickel. It is evident that Cope rearrangement of the *meso*-tetraester (5) can only yield the (*E,E*)-tetraester (7) *via* the 'second-best' six-centred, boat-like transition state (Scheme 2).<sup>5</sup> Although it is a well documented fact that the six-centred

transition state is energetically accessible to systems having special geometrical restraints,<sup>5-7</sup> the four-centred, chair-like transition state generally remains the preferred geometry for Cope rearrangements of normal acyclic diallyls.<sup>7</sup> Stabilization of the boat-like conformation by co-ordination of the 1,5-diene system (5) to nickel centres during desulphurization cannot be totally excluded, but recent contributions<sup>8</sup> demonstrated strikingly that co-ordination effectively inhibits the Cope rearrangement of otherwise thermally labile 1,5-dienes.

Formation of the (*E,E*)-tetraester (7) may more reasonably be rationalized as being the result of partial epimerization of the vinyl sulphide (1) or the *meso*-tetraester (5) in the presence of residual alkali on the Raney nickel catalyst, followed by Cope rearrangement of the resulting ( $\pm$ )-tetraester (6) *via* the normal four-centred, chair-like transition state (Scheme 2).

In our hands the vinyl sulphide (1) appeared to resist epimerization in the presence of sodium carbonate in dimethyl sulphoxide (60 °C; 30 h) or methanolic 20% potassium hydroxide (65 °C; 6 h). Both the *meso*-tetraester (5) and the vinyl sulphide (1) were likewise unaffected by prolonged treatment with Raney nickel in methanol at room temperature. However, treatment of the *meso*-tetraester (5) with sodium carbonate in methanol (30 °C; 2 h) produced a mixture which comprised the ( $\pm$ )-tetraester (6) (46%) [ $\delta$  6.32 (H<sub>a</sub>) and

<sup>1</sup> J. E. Baldwin, J. A. Walker, A. J. H. Labuschagne, and D. F. Schneider, *Chem. Comm.*, 1971, 1382.

<sup>2</sup> C. F. Garbers, A. J. H. Labuschagne, C. J. Meyer, and D. F. Schneider, *J.C.S. Perkin I*, 1973, 2016.

<sup>3</sup> A. J. H. Labuschagne, C. J. Meyer, H. S. C. Spies, and D. F. Schneider, *J.C.S. Perkin I*, 1975, 2129.

<sup>4</sup> W. von E. Doering and W. R. Roth, *Tetrahedron*, 1962, **18**, 67.

<sup>5</sup> J. A. Berson and P. B. Dervan, *J. Amer. Chem. Soc.*, 1972, **94**, 7597.

<sup>6</sup> (a) R. Hoffmann and R. B. Woodward, 'The Conservation of Orbital Symmetry,' Academic Press, New York, 1970, pp. 148–150; (b) R. Hoffmann and R. B. Woodward, *J. Amer. Chem. Soc.*, 1965, **87**, 4389.

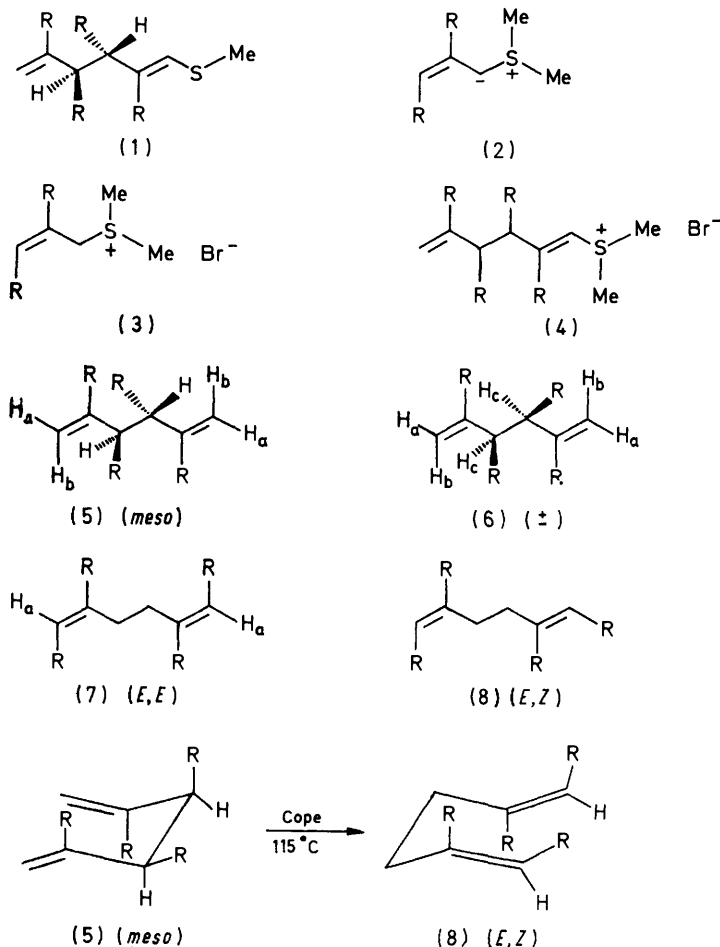
<sup>7</sup> (a) R. P. Lutz, S. Bernal, R. J. Boggio, R. O. Harris, and M. W. McNicholas, *J. Amer. Chem. Soc.*, 1971, **93**, 3985; (b) R. P. Lutz, H. A. J. Berg, and P. J. Wang, *J. Org. Chem.*, 1976, **41**, 2048.

<sup>8</sup> (a) V. Aris, J. M. Brown, and B. T. Golding, *J.C.S. Chem. Comm.*, 1972, 1206; (b) V. Aris, J. M. Brown, and B. T. Golding, *J.C.S. Perkin II*, 1974, 700.

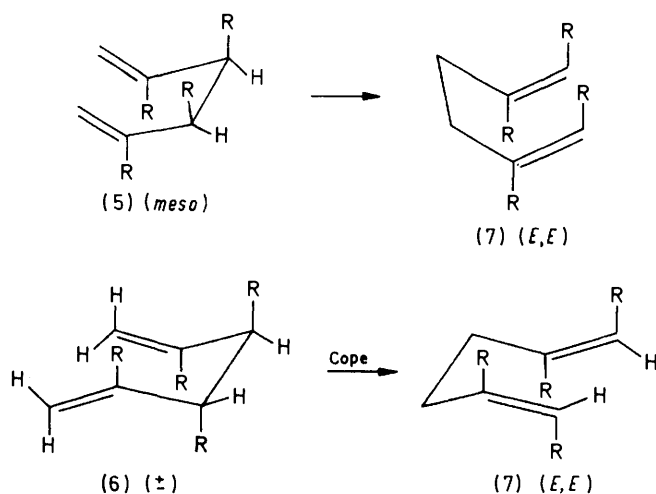
5.73 ( $H_b$ ), unchanged *meso*-tetraester (5) (36%) [ $\delta$  6.41 ( $H_a$ ) and 5.89 ( $H_b$ )],<sup>2</sup> and (*E,E*)-tetraester (7) (18%) [ $\delta$  6.77 ( $H_a$ )].<sup>2</sup>

Separation by preparative t.l.c. on silica gel produced

the pure (*E,E*)-tetraester (7) and a mixture which contained the ( $\pm$ )-tetraester (6) (44%), the *meso*-tetraester (5) (44%), and the (*E,E*)-tetraester (7) (12%). All efforts to separate this mixture by repeated t.l.c. failed



SCHEME 1



SCHEME 2

owing to the ready Cope rearrangement of the labile ( $\pm$ )-tetraester (6) during attempted chromatographic separation. When the mixture was heated (50 °C; 1½ h), rearrangement took place to produce the relatively stable *meso*-tetraester (5) (42%), the (*E,E*)-tetraester (7) (45%), and unchanged ( $\pm$ )-tetraester (6) (13%).

These results demonstrated that the (*E,E*)-tetraester (7) was produced *via* base-catalysed epimerization of the *meso*-tetraester (5) and Cope rearrangement of the resulting ( $\pm$ )-tetraester (6). The thermal lability of the ( $\pm$ )-tetraester (6) is an indication that the four-centred transition state leading to *E,E*-geometry is more effectively stabilized by the ethoxycarbonyl substituents than the corresponding transition state leading to *E,Z*-geometry.

#### EXPERIMENTAL

<sup>1</sup>H N.m.r. spectra were recorded for solutions in [<sup>2</sup>H]-chloroform with a Varian HA-60IL spectrometer and tetramethylsilane as internal standard.

*Base-catalysed Epimerization of meso-Tetramethyl Hexa-1,5-diene-2,3,4,5-tetracarboxylate* (5).—A suspension of sodium carbonate (0.06 g, 0.6 mmol) in a solution of the tetraester (5) (0.2 g, 0.6 mmol) in methanol (10 ml) was stirred for 4 h at 30 °C. The mixture was then added to water (20 ml) and the aqueous solution repeatedly extracted with ether. Separation of the residue (0.16 g) from the dried (MgSO<sub>4</sub>) organic phase by preparative t.l.c. on silica gel GF<sub>254</sub> (Merck) with ether-petroleum (b.p. 40–60 °C) (1 : 1) as mobile phase yielded (*E,E*)-tetramethyl hexa-1,5-diene-1,2,5,6-tetracarboxylate (7)<sup>2</sup> (30 mg, 15%) and a mixture (70 mg) which comprised ( $\pm$ )-tetramethyl hexa-1,5-diene-2,3,4,5-tetracarboxylate (6) (44%),  $\delta$  6.32 (2 H, s), 5.73 (2 H, s), 4.22 (2 H, s), 3.71 (3 H, s), and 3.69 (3 H, s), the *meso*-tetraester (5)<sup>2,3</sup> (44%), and the (*E,E*)-

tetraester (7)<sup>2</sup> (12%) (composition determined by n.m.r. analysis).

*Cope Rearrangement of ( $\pm$ )-Tetramethyl Hexa-1,5-diene-2,3,4,5-tetracarboxylate* (6).—A sample of the foregoing mixture of tetraesters (5) (44%), (6) (44%), and (7) (12%), was heated at 50 °C for 1½ h in [<sup>2</sup>H]chloroform in a n.m.r. tube. N.m.r. analysis of the product revealed that the ( $\pm$ )-tetraester (6) had largely rearranged to the (*E,E*)-tetraester (7), thus yielding a mixture of the *meso*-tetraester (5) (42%), the (*E,E*)-tetraester (7) (45%), and the ( $\pm$ )-tetraester (6) (13%).

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