

## Deoxygenation of 1,4-Endoperoxides to 1,3-Dienes by Low-valent Titanium

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1,4-Endoperoxides are converted into the corresponding 1,3-dienes by reaction with low-valent titanium.

Low-valent titanium, prepared by the action of strong reducing agents on  $\text{TiCl}_3$  or  $\text{TiCl}_4$ , has been shown to be a powerful reducing system with a special ability to accomplish certain deoxygenations.<sup>1</sup>

In connection with our studies on the chemistry of natural steroidal endoperoxides,<sup>2</sup> we now report that low-valent titanium is a suitable reagent to convert endoperoxides into their 1,3-diene precursors.

When the endoperoxides (1)–(4), prepared by photocatalysed oxygenation of the corresponding dienes, were treated, in dry tetrahydrofuran at room temperature under an argon atmosphere, with an excess of low-valent titanium,<sup>†</sup> a smooth deoxygenation took place to give the corresponding diene-type products (6)–(9) respectively, as shown in Table 1. Peroxide (5), which lacks the  $\Delta^6$  double bond present in (4), gave a mixture of diol (10) and a small amount of furan (11).<sup>5</sup>

Mechanistically, the deoxygenation process can be viewed as occurring by an initial reductive cleavage of the O–O bond to give an intermediate (12) with the oxygen atoms bound to the active titanium surface. This then undergoes a similar

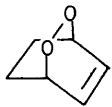

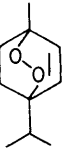
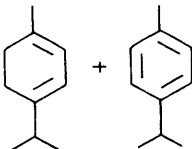
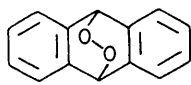
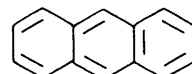
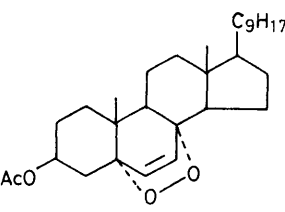
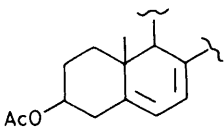
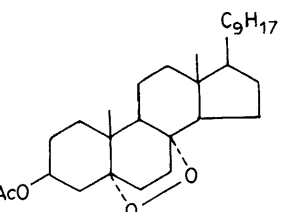
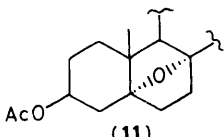
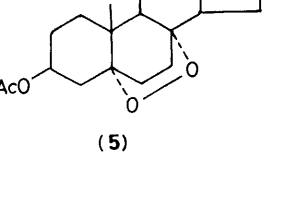
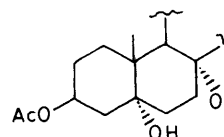
deoxygenation to that postulated in carbonyl coupling reactions with titanium (Scheme 1).<sup>4</sup> The formation of diol (10) and furan compound (11) could occur as shown in Scheme 2. Diol (10) should result from intermediate (13) during the hydrolysis step, while furan compound (11) should result from a C–O radical coupling process. Attempts to carry out these reactions with other deoxygenation agents, such as  $\text{P}_2\text{I}_4$  and a zinc–copper couple, were unsuccessful.

An alternative mechanism can be formulated on the basis of the known thermal and photochemical rearrangement of endoperoxides to bisepoxides<sup>6</sup> [*i.e.* (14)] and the well-established deoxygenation of simple epoxides by low-valent Ti.<sup>1</sup> Therefore a bisepoxide could also be considered as an intermediate in the deoxygenation of endoperoxides. Although we have not detected such an intermediate in our reactions, we found that under deoxygenation conditions ( $\text{TiCl}_3/\text{Zn}-\text{Cu}$ ; 0 °C; 1 h) the bisepoxide (14) gave a very low yield of diene (6) (12%). We have also compared the reactivity of endoperoxides with epoxides, finding that when equal amounts of endoperoxide (4) and 5,6-epoxycholesteryl acetate were subjected to competitive deoxygenation 40% of the initial epoxide was recovered unchanged, when all the endoperoxide had undergone reaction.

Steroidal endoperoxides such as (4) are compounds of increasing interest as they have been isolated from a number of natural sources, including some marine organisms, where they are present as a complex mixture in small amounts, making their isolation difficult. Some authors prefer to treat

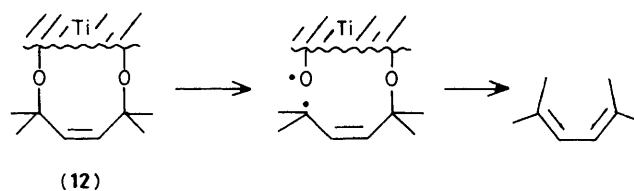
<sup>†</sup> Low-valent titanium was generated from either  $\text{TiCl}_3$  and a Zn–Cu couple<sup>3</sup> or  $\text{TiCl}_3$  and  $\text{LiAlH}_4$ .<sup>4</sup> A  $\text{TiCl}_3$ –endoperoxide molar ratio of 6:1 was used. After 3–5 h of reaction the products were obtained by filtering through a celite pad followed by p.l.c. An alternative method was to pour the reaction mixture into a saturated aqueous potassium carbonate solution followed by extraction of the reaction product.

Table 1

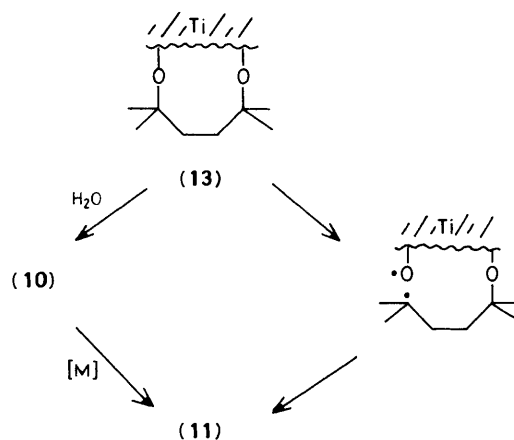
| Substrate   | Product(s)  | % Yield             |
|---|---|---------------------|
|    |    | 35 <sup>a</sup>     |
|    |    | 34, 32 <sup>b</sup> |
|    |    | 48                  |
|   |   | 42                  |
|  |  | 10                  |
|  |  | 72                  |

<sup>a</sup> Isolated as its adduct with tetracyanoethylene. <sup>b</sup> This reaction was carried out at 0 °C and was complete in 30 min. The yields were calculated by g.l.c.

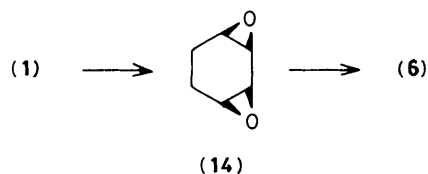
the peroxide mixture with Na-NH<sub>3</sub> and then use g.c.-mass spectrometry to compare the resulting triols, diols, and olefins with those obtained by identical treatment of synthetic endoperoxides.<sup>7</sup> We have found that treatment with low-valent titanium of the endoperoxide mixture isolated from



Scheme 1



Scheme 2



*Aplysia punctata*<sup>2</sup> gives the expected  $\Delta^{5,7}$  sterols which are easily separated and identified by conventional methods such as reverse phase h.p.l.c.

To our knowledge, the present deoxygenation represents the first example of a formal 'retro Diels-Alder' conversion of 1,4-endoperoxides into the corresponding 1,3-dienes.

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