Absolute Configuration of (−)-Carlosic Acid

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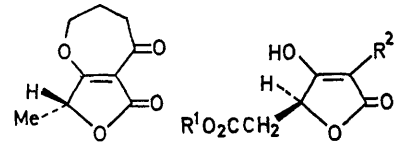
Summary The absolute configuration of (−)-carlosic acid has been shown to be *S*.

THE biosyntheses of carolic acid (**1**) and carlosic acid (**2**) have been studied by several groups.[1] One particularly significant piece of information which has emerged is that (**2**) is apparently the penultimate precursor of (**1**). The relative stereochemistries of (**1**) and (**2**) are therefore of considerable interest. Since (**1**) has been shown to have the *R* configuration,[2] a configuration of *R* for carlosic acid, *i.e.*, the opposite of that shown in (**2**), would be consistent with a simple decarboxylation process in which the asymmetric carbon is not affected, whereas the corresponding *S* form (**2**) as shown would require a considerably more complex biosynthetic conversion into the *R* form (**1**).

Our assignment of configuration for (**2**) rests on the following data. The methyl ester of *S*-malic acid[3] was acetoacetylated with diketen and the resultant ester cyclised to (**3**) using Bu^tOK in Bu^tOH with little modification of a reported procedure[2,4] which is considered not to involve an inversion of the chiral centre. Acidic hydrolysis of (**3**) converted it into (**4**).

Previous work[5] had shown that (**2**) could be converted into (**5**) by bromination, and (**5**) reduced to (**6**) catalytically. When (**4**) was subjected to the same experimental conditions as (**2**), synthetic (**5**) and (**6**) were obtained which were



(**1**)

(**2**) $R^1 = H$, $R^2 = COPr^n$
(**3**) $R^1 = Me$, $R^2 = Ac$
(**4**) $R^1 = H$, $R^2 = Ac$
(**5**) $R^1 = H$, $R^2 = Br$
(**6**) $R^1 = H$, $R^2 = H$

identical both chemically and in the signs of their rotations to the naturally derived substances. The absolute configuration of (**2**) is therefore *S* as shown.

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[1] S. Lybing and L. Reio, *Acta Chem. Scand.*, 1958, **12**, 1575; R. Bentley, D. S. Bhate, and J. G. Keil, *J. Biol. Chem.*, 1962, **237**, 859; J. L. Bloomer, F. E. Kappler, and G. N. Pandey, *J. C. S. Chem. Comm.*, 1972, 243.
[2] P. M. Boll, E. Sorensen, and E. Balieu, *Acta Chem. Scand.*, 1968, **22**, 3251.
[3] H. Arakawa, *Naturwiss.*, 1963, **50**, 441.
[4] R. N. Lacey, *J. Chem. Soc.*, 1954, 832.
[5] P. W. Clutterbuck, H. Raistrick, and F. Reuter, *Biochem. J.*, 1935, **29**, 300, 871.