

The Spirodienone Route for the Methylene Functionalization of Calixarenes

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The calixarenes are macrocyclic compounds which are presently extensively studied as building blocks for the construction of molecular hosts. The name "calixarenes" (coined by C. D. Gutsche) was bestowed to this family, since a space-filling model of a derivative containing four phenolic rings resembled a Greek calix crater. Mild oxidation of calixarenes affords their spirodienone derivatives. These derivatives are useful synthetic intermediates for the selective functionalization of calixarenes. The presence of several functionalities (carbonyl, ether, diene) within the macrocyclic scaffold enables a large number of synthetic transformations.

A synthetic route allowing the functionalization of two distal (i.e., non-vicinal) methylene groups of a calix[4]arene in a *trans* fashion has been developed. The method is based in a sequence of reactions involving addition of two equivalents of bromine to the bis(spirodienone) derivative, bis-dehydrobromination of the tetrabromo derivative, and finally nucleophilic attack on the exocyclic double bonds (a process accompanied by double bond shifts and expulsion of the bromine atoms). In the *cone* conformation of calixarenes possessing two opposite bridges substituted in a *trans* fashion by a pair of groups, one group must necessarily be located in an axial position. The steric interactions ensuing from the presence of an axial group destabilize the *cone* conformation, rendering the *1,2-alternate* form the lowest energy conformation in some derivatives.