S-(+)- and R-(-)-Carvone as Starting Material in the Enantioselective Synthesis of Natural Products

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Conjugate addition of nucleophiles followed by annulation is investigated for R-(-) and S-(+)-carvone to obtain highly functionalised chiral decalins. The isopropenyl group in carvone first serves as a chiral handle. After the addition and annulation, it can be transformed into an alcohol, a double bond, or a carbonyl group, and thus it can be considered as a protecting group for these functionalities. Following these lines, the total syntheses of a number of sesqui- and diterpenes has been realised.

One new approach starts with the conjugate addition of cyanide to the enone in S-(+)-carvone (1), followed by an annulation reaction. In this way a functionalised chiral decalone with a nitrile group at C9 and a potential functional group at C7 is obtained in an easy way and in high yield. This decalone will be applied in the synthesis of Ambrox® (2), drimanes 3 and other flavour compounds. Conjugate addition to S-(+)-carvone followed by annulation also provides an easy access to progesteron receptor ligand eremophilane sesquiterpenes 4.

Mukaiyama or double Mukaiyama reactions can be applied to obtain cadinanes 5, and (homo)steroids from carvone. The application of conjugate addition followed by Mukaiyama-aldol reactions gives excellent intermediates for the enantioselective synthesis of insect antifeedant clerodanes like dihydroclerodin (6).