Synthesis of an Aromatic Sesquiterpene, (±)-Cuparene, *via* Construction of a Quaternary Carbon Centre by an Intramolecular Carbenoid Displacement Reaction

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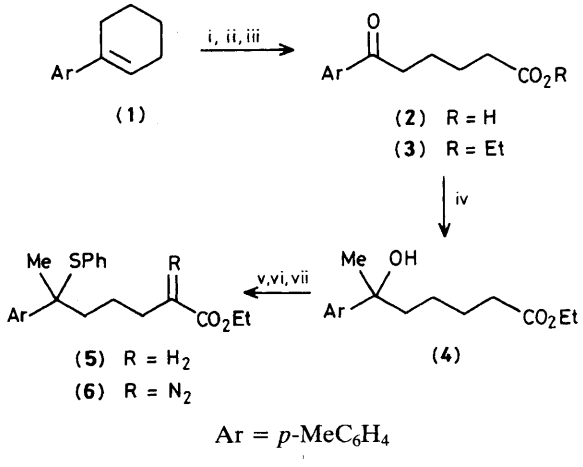
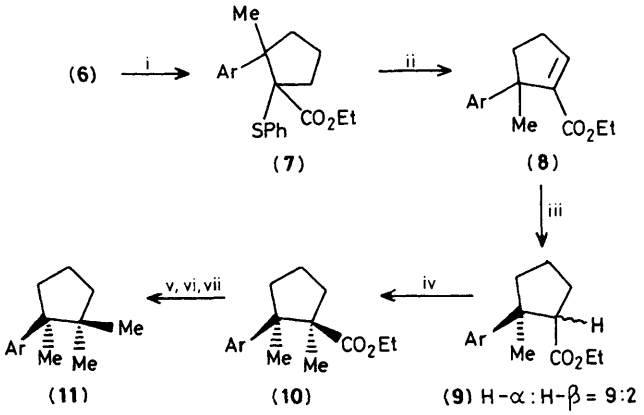
The synthesis of (±)-cuparene (**11**), which includes as the key step an intramolecular carbenoid displacement reaction at the benzylic position of a benzyl sulphide derivative, is described.

Interest in the development of new methods for construction of quaternary carbon centres continues unabated,[1] not only for synthetic reasons, but also because of the observation of such centres in a variety of natural products. A number of aromatic sesquiterpenes contain the 1-aryl-1,2,2-trimethylcyclopentane ring system, which involves a quaternary carbon centre. We report here a novel synthesis of this ring system. The key feature of our approach to the synthesis of an aromatic sesquiterpene, (±)-cuparene (**11**), is based on our earlier work[2] and involves the formation of a new carbon–carbon bond at the benzylic position to construct the quaternary carbon centre by employing an intramolecular carbenoid displacement reaction of the benzyl sulphide derivative.

The requisite starting material was prepared as follows. Ozonolysis of the cyclohexene derivative (**1**), followed by Jones oxidation, afforded the acid (**2**) in 49% yield. After esterification of the acid (**2**), the ester (**3**) was treated with methyl-lithium to give the tertiary alcohol (**4**). Displacement reaction of the hydroxy group in (**4**) with benzenethiol[3] in 1,2-dichloroethane in the presence of zinc iodide as catalyst furnished the sulphide (**5**) in 85% yield, which was converted into the desired diazo-compound (**6**) on treatment with



Scheme 1. *Reagents:* i, O_3, CH_2Cl_2; Me_2S, −78 °C; ii, Jones oxidation, acetone; iii, EtOH, H_2SO_4, reflux; iv, MeLi, benzene, 0 °C; v, PhSH, ZnI_2, $ClCH_2CH_2Cl$, room temp.; vi, $LiNPr^i_2$, tetrahydrofuran (THF), HCO_2Et, −78 °C; vii, *p*-MeC_6H_4-SO_2N_3, Et_3N, CH_2Cl_2, room temp.



Scheme 2. *Reagents:* i, $Rh_2(OAc)_4$, benzene, reflux; ii, *m*-$ClC_6H_4CO_3H$, CH_2Cl_2, aq. $NaHCO_3$, room temp.; iii, $NiCl_2 \cdot 6H_2O$, $NaBH_4$, MeOH, room temp.; iv, $LiNPr^i_2$, THF–hexamethylphosphoramide, MeI, room temp.; v, $LiAlH_4$, Et_2O, room temp.; vi, pyridinium chlorochromate, CH_2Cl_2, room temp.; vii, $H_2NNH_2 \cdot H_2O$, Na, $(HOCH_2CH_2)_2O$, $HOCH_2CH_2OH$, 185 °C.

lithium di-isopropylamide and ethyl formate and subsequently tosyl azide in methylene chloride[4] in 78% yield from (**5**).

The intramolecular carbenoid displacement reaction of (**6**) was carried out in refluxing benzene in the presence of rhodium acetate as catalyst to bring about the formation of the quaternary carbon centre yielding the cyclopentane derivative (**7**), whose oxidative elimination afforded the α,β-unsaturated ester (**8**) in 52% yield from (**6**). Since the carbon framework for (±)-cuparene had thus been constructed, attention was then focused on the conversion of (**8**) into the natural compound. Reduction of the α,β-unsaturated ester (**8**) with sodium borohydride and nickel chloride[5] in methanol afforded the saturated ester (**9**) as an epimeric mixture, in quantitative yield, whose methylation with methyl iodide gave the ester (**10**), which was transformed by a known procedure[6] into (±)-cuparene (**11**), whose spectral data were identical with those reported.[7]

Thus the intramolecular carbenoid displacement reaction, a novel method for construction of a quaternary carbon centre at a benzylic position, was successfully applied to the synthesis of (±)-cuparene.

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