New Stereoselective Synthesis of 9-Methyl-*cis*-decalin Derivatives by Double Michael Reaction of 3,5-Dimethyl-4-methylenecyclohex-2-enone and Dimethyl 3-Oxoglutarate; *X*-Ray Crystal and Molecular Structure of Two of the Products

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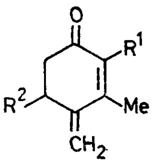
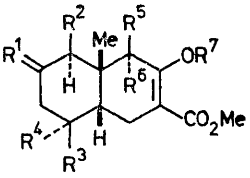
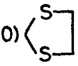
Summary Double Michael reaction of 3-methyl-, 2,3-dimethyl-, and 3,5-dimethyl-4-methylenecyclohex-2-enone with dimethyl 3-oxoglutarate in dimethyl sulphoxide in the presence of potassium fluoride as a catalyst gave stereoselectively 9-methyl-, 1,9-dimethyl-, and 4,9-dimethyl-6,8-dimethoxycarbonyl-2,7-dioxo-*cis*-decalin, respectively.

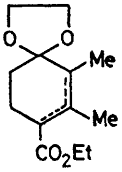
A number of methods for constructing the decalin system, a common constituent of the skeleton of sesquiterpenes, have been used so far, Robinson annelation being the most widely applied method. The first stage of this annelation involves cyclohexanone derivatives as Michael donors and methyl vinyl ketone and its equivalents as Michael acceptors. We report a new type of annelation in which cyclic ketones are the Michael acceptors and open-chain compounds are the Michael donors.



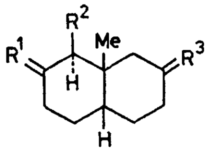
	R^1	R^2
(1)	H	H
(2)	H	Me
(3)	Me	H

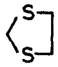
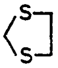


	R^1	R^2	R^3	R^4	R^5	R^6	R^7
(4)	O	H	H	H	CO_2Me	H	H
(5)	O	H	H	H	H	CO_2Me	H
(6)	O	H	Me	H	CO_2Me	H	H
(7)	O	H	H	Me	CO_2Me	H	H
(8)	O	H	H	Me	CO_2Me	H	Me
(9)	O	Me	H	H	CO_2Me	H	H
(10)		Me	H	H	CO_2Me	H	H
(11)	H_2	Me	H	H	CO_2Me	H	H



(12)



	R^1	R^2	R^3
(13)	O	H	O
(14)		H	
(15)	H_2	H	H_2
(16)	H_2	Me	O

Treatment of 3-methyl-4-methylene-cyclohex-2-enone (**1**)[1] with dimethyl 3-oxoglutarate in dimethyl sulphoxide in the presence of potassium fluoride at 55—60 °C for 2 days gave a mixture of the stereoisomeric diketo-diesters (**4**) and (**5**), separable by column chromatography on silica gel with chloroform, in 40% and 1% yield (isolated yield of crystalline compounds, respectively. Both gave the same diketone (**13**) on hydrolysis with sodium chloride in dimethyl sulphoxide–water,[2] indicating that they were stereoisomers at the C-8 position.† Treatment of the diketone (**13**) with ethanedithiol and boron trifluoride gave the dithioacetal (**14**) which yielded 9-methyl-*cis*-decalin (**15**) on reduction with Raney nickel. The ^{13}C n.m.r. and i.r. spectra of (**15**) were identical with those reported,[3] confirming that the Michael products have a *cis*-ring junction.

The double Michael reaction of the cyclohexenone (**2**)[4] with dimethyl 3-oxoglutarate similarly gave two crystalline products (**6**) and (**7**) in 22 and 11% yield (isolated yield of crystalline compounds), respectively. The structures of these diketo-diesters were confirmed by *X*-ray crystallography.

Crystal data: (**6**), $C_{16}H_{22}O_6$, monoclinic prisms, m.p. 146—147 °C, from ether–hexane, space group $P2_1/a$, $a = 17{\cdot}70$, $b = 6{\cdot}87$, $c = 13{\cdot}50$ Å, $\beta = 94°$, $Z = 4$, $D_c = D_m = 1{\cdot}257$ g cm^{-3}. Intensity data around the *b* and *c* axes were measured with a SYNTEX AD-1 densitometer from equi-inclination Weissenberg photographs taken with Cu-K_α radiation. The structure was solved by the direct method and was refined by block-diagonal least-sqaures to an *R*-factor of 8·7% for 1410 reflections.‡ Since the minor product (**7**) did not form crystals suitable for *X*-ray analysis, it was converted into the methyl ether (**8**) with diazomethane in the usual manner. The methyl ether (**8**), $C_{17}H_{24}O_6$, forms orthorhombic prisms, m.p. 113–115 °C, from methanol, space group *Pbca*, $a = 28{\cdot}55$, $b = 11{\cdot}98$, $c = 10{\cdot}11$ Å, $Z = 8$, $D_c = 1{\cdot}247$ g cm^{-3}, $D_m = 1{\cdot}217$ g cm^{-3}. Intensity data obtained as for (**6**) were similarly to an *R*-factor of 8·2% for 1318 reflections. The structure established for the methyl ether (**8**) suggests that a non-bonded interaction between the C(4)-methyl group and the C(8)-hydrogen, which would be significant if (**8**) adopted a steroid conformation, compels it to adopt a distorted non-steroid conformation.

In order to extend the applicability of the procedure, the cyclohexenone (**3**) was prepared. Acetalisation of 2,3-dimethyl-4-ethoxycarbonylcyclohex-2-enone[5] (Hagemann's ester) gave a mixture of the acetals (**12**) (isomeric with respect to the position of the double bond, as shown by g.l.c.–mass spectroscopy). Reduction of the mixture with lithium aluminium hydride in ether followed by acid hydrolysis with dilute hydrochloric acid in acetic acid furnished the dienone (**3**), b.p. 71—75 °C at 10 mmHg, in 18% yield from Hagemann's ester. Double Michael reaction of (**3**) with dimethyl 3-oxoglutarate gave the *cis*-decalin (**9**) (enol form is shown). Thioacetalisation of the diketo-diester (**9**) gave the monothioacetal (**10**) which, on reduction with Raney nickel, gave the keto-diester (**11**). Hydrolysis of (**11**) with sodium chloride in dimethyl sulphoxide–water gave the ketone (**16**), the n.m.r. and i.r. spectra of which were identical with those of an authentic sample,[6] confirming the *cis*-ring junction in the Michael product. Since the ketone (**16**) has been transformed into (±)-eremophilenolide, (±)-furanoeremophilane,[6] and (±)-fukinone,[7] its synthesis represents an alternative formal synthesis of these sesquiterpenes.

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† The stereochemistry at the C(8) was proposed from Dreiding models based on a plausible steroid conformation of these compounds.

‡ All the computations were performed using the KPAX system including the UNICS programs on a FACOM M-190 computer in the Data Processing Center of Kyoto University. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

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