Total Synthesis of (*S*)-(+)-Solanone

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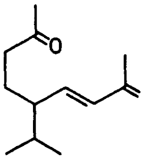
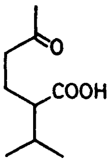
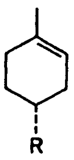
Summary Optically active solanone was synthesized from (*R*)-(+)-*p*-menthene, and the (*S*)-configuration was confirmed for the natural product.

Solanone (**1**) is a member of the tobacco terpenoids and represents a unique structure in that it apparently violates the isoprene rule. Its structure was elucidated and confirmed by the synthesis of the racemate by Johnson and Nicholson in 1965.[1] However, the stereochemistry of solanone remains controversial: Johnson and Nicholson[1] assigned the (*R*)-configuration by comparing the optical rotation of the tetrahydro-derivative of the product of natural origin with that of the compound synthesized from (*R*)-(+)-*p*-menthene, while Fukuzumi and his co-workers assigned the (*S*)-configuration in view of the optical rotations of the carboxylic acids (**2**) of natural and synthetic origin.[2] An attempt to synthesize optically active solanone gave a product which was mixed with by-products and the optical activity was not measured.[1] A number of solanone-related constituents have been isolated from tobacco since then, and the (*S*)-configuration has been tentatively assigned to all of them,[3] in compliance with the assignment made by Fukuzumi and his co-workers. The present report describes the unambiguous synthesis of (*S*)-(+)-solanone from (*R*)-(+)-*p*-menthene and demonstrates that the natural product has the (*S*)-configuration.

Previously we found that the iron(III) chloride-catalysed photo-oxidation of 1-methylcyclohexene (**3a**) produced the *gem*-dichloro-ketone (**4a**) in 47% yield.[4] The same reaction with (*R*)-(+)-*p*-menthene (**3b**) gave (**4b**) in 26% yield, and, in contrast with the reaction of (**3a**), also gave (**5**) (43%) and (**6**) (12%) as by-products. Their formation may be interpreted in terms of the steric effect of the isopropyl group.[5] The chloro-ketone (**5**) was removed by distillation and a mixture of (**4**) and (**6**), after acetalization, was treated with lithium di-isopropylamide in tetrahydrofuran at −10 to 0 °C. Distillation gave the acetylenic acetal (**7a**) almost pure. The acetal group was removed with dilute HCl, and the acetylenic ketone (**7b**) was treated successively with catechol–borane and isopropenyl bromide–$Pd(Ph_3P)_4$–


(1)


(2)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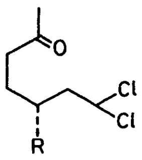
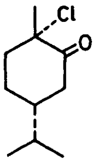

(4)

a; R = H; b; R = Pr^i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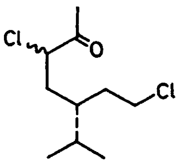
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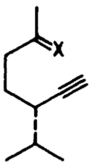
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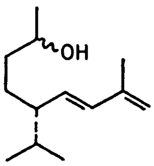
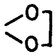

(8)

a: X = 

b: X = O

NaOEt[6] to give the alcohol (**8**). Jones oxidation of (**8**) gave the (*S*)-ketone (**7**) which was found to be identical with the natural product by its mass, i.r., and n.m.r. spectra, and optical rotation ($[\alpha]_D^{18\cdot3}$ + 10·4°; lit.:[1] $[\alpha]_D$ + 13·6°).

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