New Syntheses of Racemic Nuciferal, ar-Turmerone, and Ipsdienol by a Ready Regio- and Stereo-specific Allylic Oxidation

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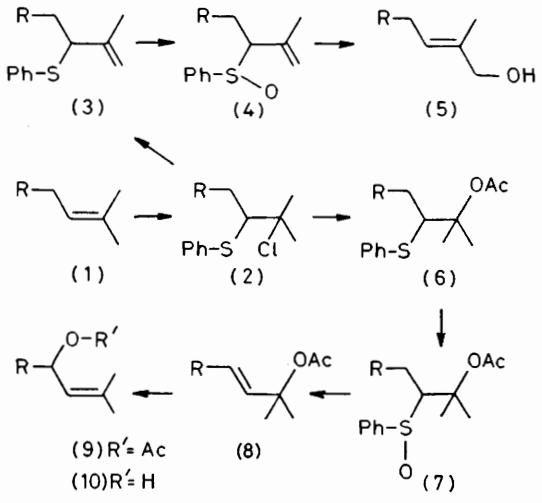
Summary A simple regio- and stereo-specific terminal and internal allylic oxidation *via* benzenesulphenyl chloride addition is reported; using this method racemic nuciferal (**11**) and ar-turmerone (**12**) were synthesized from racemic α-curcumene (**1a**), and racemic ipsdienol (**10c**) from myrcene (**1c**).

TERMINAL and internal allylic oxidation of the isopropylidene terminus of isoprenoids with regio- and stereochemical control offers potential for the synthesis of a range of biologically important oxygenated terpenes. We are interested in the terminal functionalization of the isopropylidene terminus of easily accessible isoprenoids and recently reported a simple method for preparation of terminal *trans*-allylic alcohols.[1] We now report a terminal *trans*-oxidation and an internal allylic oxidation which proceed *via* the same intermediate adduct between benzenesulphenyl chloride and terpenoids containing an isopropylidene terminus.

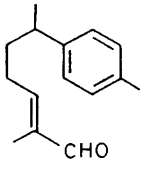
The overall sequence in the Scheme involves (i) quantitative and site-specific addition of benzenesulphenyl chloride to the isopropylidene terminus of the terpenoids (**1**), (ii) stereospecific formation of the terminal *trans*-allylic alcohols (**5**) *via* the terminal allylic sulphides (**3**) prepared by regiospecific dehydrochlorination of the adducts (**2**), followed by oxidation of sulphur and rearrangement, (iii) internal allylic oxygenation affording (**9**) *via* regiospecific acetoxylation of the adducts (**2**) followed by oxidation, thermal double bond formation, and finally allylic rearrangement illustrated by the sequence (**2**)→(**6**)→(**9**).



SCHEME

a; R = $CH_2CHMeC_6H_4Me$-*p*
b; R = $CH_2CMe{=}CHCH_2OCH_2Ph$ (*trans*)
c; R = $CH_2C(=CH_2)CH{=}CH_2$

Dropwise addition of benzenesulphenyl chloride (1 equiv.) into a solution of racemic α-curcumene (**1a**)[2] in CH_2Cl_2 at 0 °C gave a regioisomeric mixture of the adducts (**2a**)† quantitatively within 10 min. The crude product (**2a**) was warmed for 20 h at 60 °C with dimethylformamide and Et_3N to give regiospecifically the terminal allylic sulphide (**3a**) in 76% yield. Stereospecific transformation of (**3a**) into the terminal *trans*-allylic alcohol (**5a**) was carried out in 80% yield by oxidation with 30% H_2O_2 in AcOH at room temperature to provide the sulphoxide (**4a**) followed by treatment with trimethyl phosphite at room temperature. Oxidation with active MnO_2 of (**5a**) afforded easily and quantitatively racemic nuciferal (**11**).



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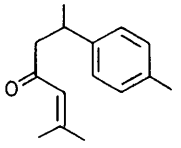

(12)

Alternatively, treatment of the adduct (**2a**) with AcONa in AcOH at room temperature for 1 h led to regiospecific formation of the tertiary acetoxy-sulphide (**6a**) in 94% yield. Compound (**6a**) was converted into the *trans*-allylic acetate (**8a**) (84%) by oxidation with 30% H_2O_2 in AcOH at room temperature followed by thermal elimination of sulphenic acid[3] in toluene in the presence of $NaHCO_3$ at 120 °C for 1·5 h. Allylic rearrangement to the internal allylic acetate (**9a**) was achieved in excellent yield (85%) with complete removal of the starting allylic acetate (**8a**) by treatment with a catalytic amount of toluene-*p*-sulphonic acid in AcOH–Et_2O (1 : 1) at 0 °C for 1 h.[4] Alkaline hydrolysis of the acetate (**9a**) gave the internal allylic alcohol (**10a**), which was oxidized with active MnO_2 to afford racemic ar-turmerone (**12**) in 73% overall yield from (**9a**).

The versatility of the method was demonstrated with benzyl geranyl ether (**1b**) which contains two isolated double bonds and myrcene (**1c**) which contains a 1,3-diene system as well as the isopropylidene terminus. Thus the terminal *trans*-allylic alcohols (**5b**) (76%) and (**5c**) (47%), the key intermediate for the synthesis of β-sinensal,[5] and the internal allylic alcohol (**10b**) (41%) and racemic ipsdienol (**10c**) (25%),[6] an active component of the pheromone of *Ips. confusus*, were obtained respectively *via* the site-specific adducts (**2b**) and (**2c**).

This extension of our previous work[1] thus enhances the synthetic utility of this sequence by providing the possibility of an easy synthesis of biologically active terpenes such as sirenin and dehydrojuvabione.

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† Separation of each regioisomer of the adducts (**2a**) was not necessary for transformation into (**3a**) and (**6a**) because of the easy interconversion between the regioisomers *via* an episulphonium ion in the reaction media; see ref. 1 and references cited therein.

[1] Y. Masaki, K. Hshimoto, and K. Kaji, *Tetrahedron Letters*, 1978, 4539, 5123.
[2] A. J. Birch and S. M. Mukherji, *J. Chem. Soc.*, 1949, 2531. This method was modified by the use of lithium in place of magnesium in C–C bond formation.
[3] For analogous elimination of sulphenic acid from β-hydroxysulphoxides providing allylic alcohols see: J. Nokami, K. Ueta, and R. Okawara, *Tetrahedron Letters*, 1978, 4903.
[4] Analogous conditions were used in the rearrangement of non-substituted vinyl carbinols; J. H. Babler, D. O. Olsen, and W. H. Arnold, *J. Org. Chem.*, 1974, **39**, 1656; J. H. Babler and D. O. Olsen, *Tetrahedron Letters*, 1974, 351.
[5] A. F. Thomas, *J. Amer. Chem. Soc.*, 1969, **91**, 3281, and references cited therein.
[6] A direct synthesis of racemic ipsdienol from myrcene has been reported but poor regioselectivity in formal oxygenation at the requisite position resulted in low overall yield (*ca.* 10%); K. Mori, *Agric. and Biol. Chem.* (*Japan*), 1974, **38**, 2045.