The Mechanism of Allylic Oxidation by Selenium Dioxide

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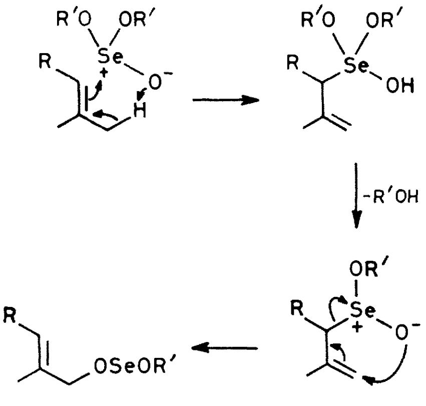
Summary In the course of the SeO_2-oxidation of 5-cyclopentyl-2-methyl[1-^{13}C]pent-2-ene and its isotopomer (**2**), which stereoselectively yields the *E*-products (**7**)—(**10**), the ^{13}C label is distributed between C-1 and the C-2 substituent, indicating that two separate steps in the sequence determine the stereochemical features of the products the ene-reaction proceeds in favour of the *trans*-methyl-group of the olefin by a factor of 7 : 3 and the

following [2,3] sigmatropic rearrangement generates the *E*-configuration of the resulting alcohols.

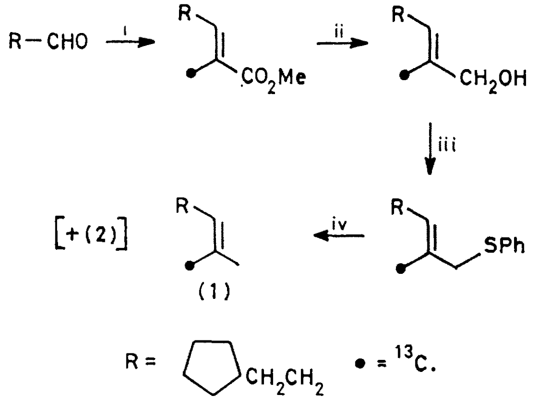
THE importance of SeO_2 as a reagent in organic synthesis[1,2] relies mainly on the regio- and stereo-selective oxidation of allylic C-atoms at trisubstituted double bonds in the order of preference $CH_2 > CH_3 > CH$.[3,4] Wiberg and Nielsen[5] were the first to consider Se–C bond formation during the attack by SeO_2 which was later supported experimentally by Sharpless and Lauer.[6] Further insight into the mechanism stems from the isolation of seleninolactones[7] as trapped representatives of allylseleninic esters, which have been postulated to be reaction intermediates.[5,6] In agreement with these observations is the mechanism[6] in Scheme 1, which involves an ene-addition of a $>\overset{+}{\mathrm{Se}}\text{-O}^-$ moiety across the double bond and a [2,3] sigmatropic rearrangement of an allylseleninic ester to a selenium(II) ester, which hydrolyses to the *E*-alcohol.



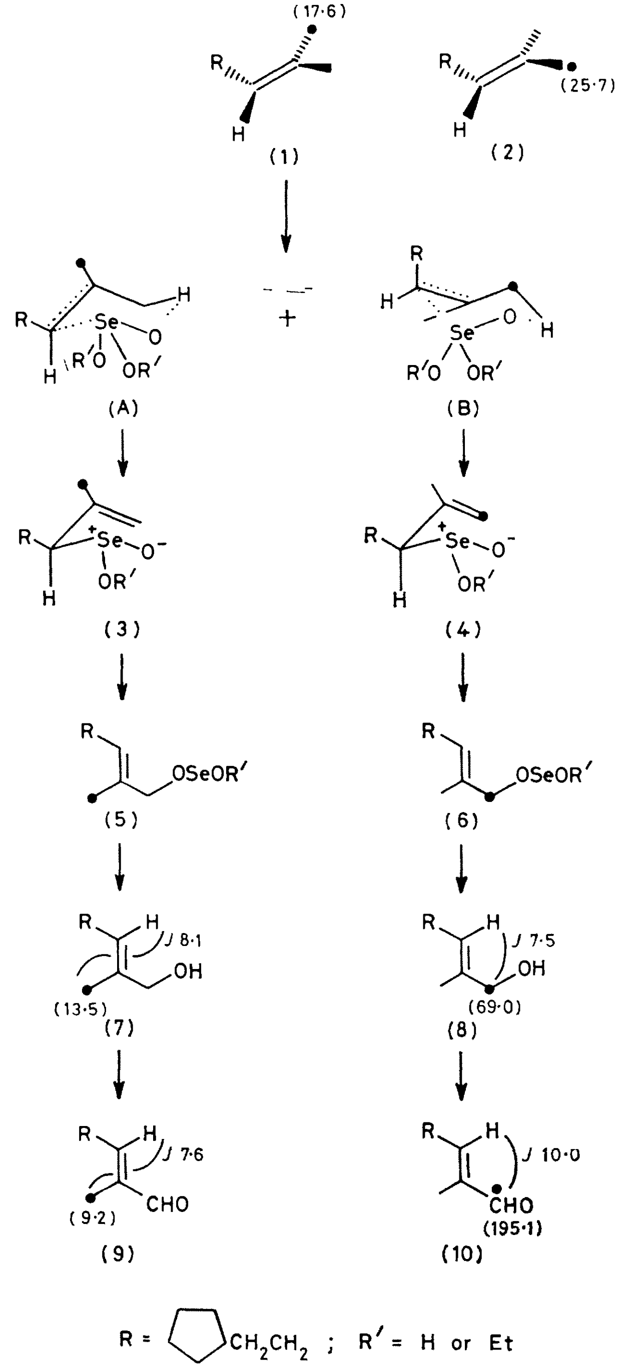
SCHEME 1.

In connection with our studies on the biosynthesis of insect pheromones we have been confronted with the analytical problem of distinguishing between geminal allylic methyl-groups. We wished to ascertain whether an SeO_2 reaction proceeds without randomisation of a specific label in a methyl-group of a trisubstituted olefin.[4] In order to investigate this, the ^{13}C-labelled olefin (**1**) and its isotopomer (**2**) were synthesized according to Scheme 2.†

A 0·2 molar solution of the isotopomers (**1**) and (**2**) (ratio 4 : 1) in 95% ethanol was heated under reflux for 90 min in the presence of an equimolar amount of freshly



SCHEME 2. Conditions: i, $\mathrm{Ph_3\overset{+}{P}{-}CH(^{13}CH_3)CO_2MeI^-}$, oxiranbenzene; ii, di-isobutylaluminium hydride–ether; iii, MeLi, *p*-$\mathrm{MeC_6H_4SO_2Cl}$, PhSLi, hexamethylphosphoric triamide–ether; iv, Li, $\mathrm{EtNH_2}$–tetrahydrofuran.



SCHEME 3. ● = ^{13}C. Figures in parentheses are ^{13}C n.m.r. resonances in p.p.m. *J* values are in Hz.

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† Satisfactory spectroscopic data were obtained for all compounds in this synthesis (part of the Diploma Thesis of F.R., Universität Zürich, 1978); details will be described elsewhere.

sublimed SeO_2 After the usual work up, the oxidation products (Scheme 3) (**7**)—(**10**)† were obtained in 27% yield (isomeric purity 96 1%), ^{13}C n m r analysis showed that the methyl-groups as well as the carbonyl- and hydroxymethyl-groups were ^{13}C labelled The chemical shifts of the ^{13}C labelled C-atoms and the vicinal coupling constants were in agreement with published data[8,9] concerning γ-effects For a quantitative measurement of the ^{13}C-distribution at C-1 and the C-2 substituent the ^1H n m r spectra of the products were analysed and a ratio of 1 5 : 1 established for the isotopomers (**7**) : (**8**) and (**9**) : (**10**), respectively To explain the observed partial randomisation the following reasons can be suggested (i) Selenous acid-catalysed double bond isomerisation of (**1**) and (**2**) (ii) Reversible double bond protonation of the intermediates (**3**) and (**4**) (iii) A limited stereoselectivity of the ene-reaction

In order to distinguish between these possibilities, the SeO_2 oxidation of (**1**) and (**2**) was carried out in an n m r tube using the solvent system 95% C_2H_5OD–5% D_2O Addition of only catalytic amounts (0 1 mol equiv) of SeO_2 gave no change in the isotopomeric ratio of (**1**) and (**2**) (4 1), either at 30 or 70 °C, during 2 h and virtually no oxidation products were visible After addition of 1 equiv of SeO_2 the noise-decoupled ^{13}C n m r spectrum was recorded 10 times during 90 min at 72 °C From these spectra it is obvious that the starting material is consumed within 90 min, following second-order kinetics, without a change of its isotopomeric ratio The first visible products were the alcohols (**7**) and (**8**) showing the same isotopomeric ratio of 1 5 : 1‡ as calculated from the isolated material unchanged over the whole reaction time (Figure) Only after an induction period of 30 min is aldehyde formation detectable, indicating that (**9**) and (**10**) are not directly derived from the selenium(II) esters (**5**) and (**6**), but from the alcohols (**7**) and (**8**) Neither the alcohol (**8**) nor the aldehyde (**10**) showed any deuterium incorporation from the solvent, providing evidence that reversible double bond protonation of (**3**) and (**4**) does not occur

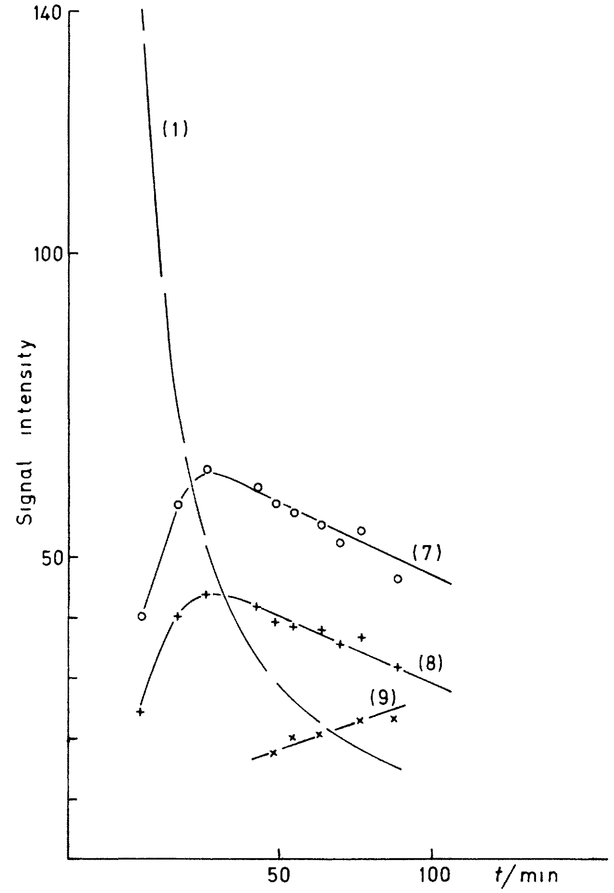

FIGURE ^{13}C N m r signal intensities of (**1**), (**7**), (**8**),‡ and (**9**) during the oxidation of (**1**) and (**2**) with SeO_2

These results demonstrate that the stereochemistry of the oxidation products and the distribution of the label are a consequence of two separate key steps in the SeO_2 oxidation The [2,3] sigmatropic rearrangement determines the *E* configuration of the products in agreement with earlier results[3,6] (however, see ref 10) and the ene-reaction proceeds with a stereoselectivity determined by different steric interactions in the transition states (A) and (B) (Scheme 3), which favour (A) (where R is in a pseudoequatorial position) over (B) by a ratio of 7 : 3

In contrast with this result Stephenson and Speth[4] claim that geminal allylic methyl-groups are equally reactive in the rate-determining[4,11] hydrogen-removal step, an interpretation based on an ineligible comparison between an inter- and an intra-molecular isotope effect

Using different compounds Prof D Arigoni, S Godtfredsen, and J P Obrecht (E T H -Zurich) have obtained results similar to ours

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‡ For a calculation of the ratio of the isotopomers from the ^{13}C n m r spectra a correction factor has been applied which is known from a comparison between the ^1H n m r and ^{13}C n m r spectra of compounds (**7**)—(**10**), isolated from preparative work

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