New Method for Carbon–Carbon Bond Formation: Biogenetic-type Synthesis of Safranal

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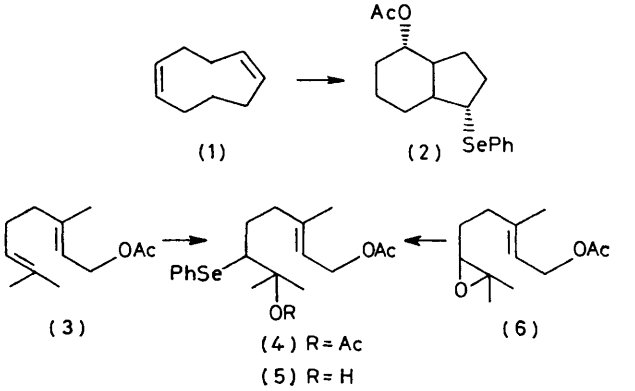
Summary Acid catalysed cyclisation of the olefinic β-hydroxy selenide (**5**) afforded the cyclic compound (**7**) which was converted into safranal (**16**) *via* the olefinic alcohol (**12**), diolefinic alcohol (**14**), and aldehyde (**15**).

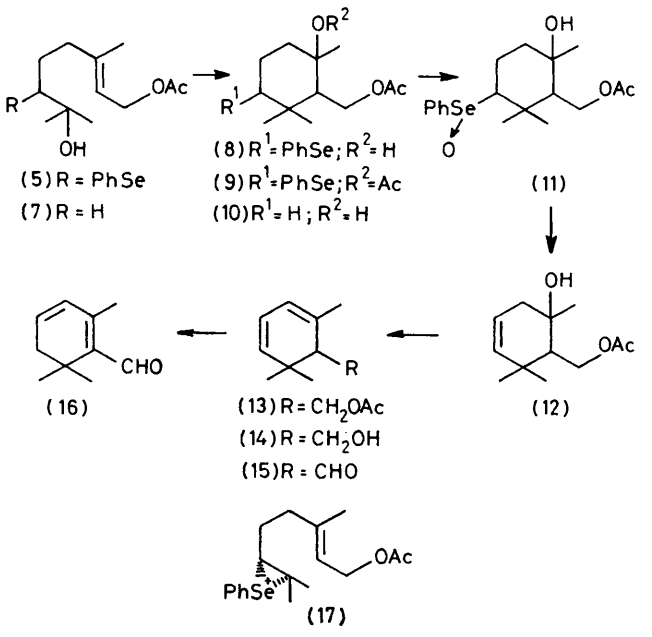
FUNCTIONAL group manipulation using organoselenium reagents has been thoroughly investigated and the chemistry of such reagents is of current interest.[1] In contrast to the well studied[2–4] synthesis of heterocycles by cyclisation reactions involving the use of organoselenium reagents, studies[5] concerned with carbon–carbon bond formation using selenium reagents are limited. Of prime importance to our study was that a cyclisation reaction be found which would provide a product suitably functionalised to further elaboration. Although a considerable amount of investigation in the area of polyolefin cyclisation has been reported,[6,7] we became interested in developing cyclisation reactions induced by organoselenium reagents because of the versatility of the selenyl functional groups.[1] We now report a new selenium-assisted cyclisation reaction resulting in carbon–carbon bond formation.

To determine whether the cyclisation (**1**) → (**2**) reported by Clive[3] is generally applicable for carbon–carbon bond formation, a preliminary experiment was carried out in which geranyl acetate (**3**) was treated with PhSeCl in AcOH in the presence of NaOAc under the same conditions.[3] However, the products isolated were shown to be (**4**) and (**5**) and not the expected cyclic compounds (**8**) or (**9**). Compound (**5**) was alternatively synthesised by epoxidation of (**3**) using *m*-chloroperbenzoic acid followed by treatment of the resulting epoxide (**6**) with phenylselenium anion.[8]



SCHEME 1

Since cyclisation of (**3**) could not be achieved under the conditions described, our interest turned to possible cyclisation of (**5**). The carbonium ion generated by acid treatment of (**5**) may be established by participation of the phenylselenyl group with *in situ* formation of the seleniranium ion (**17**).[9] Thus, treatment of (**5**) with



SCHEME 2

CF_3CO_2H in CH_2Cl_2 gave, in 65% yield, the cyclic compound (**8**)† [δ ($CDCl_4$) 0·97, 1·18, 1·30 (9H, each s, 3 × Me), 2·03 (3H, s, MeCO), 3·01 (1H, dd, *J* 2·5 and 5 Hz, PhSeC*H*), 4·1—4·7 (2H, m, C*H*$_2$OAc), and 7·2—7·7 (5H, m, PhSe)]. When the alcohol (**7**) was subjected to the same treatment, the product obtained, although uncharacterised, was shown not to be the corresponding cyclic compound (**10**). This remarkable difference in the reactivity of compounds (**5**) and (**7**) may be attributed to participation of the phenylselenyl group as already described. In order to demonstrate the easy manipulation of the functional groups thus introduced, the cyclic compound (**8**) was converted into safranal (**16**) as follows. Oxidation of (**8**) with 30% H_2O_2 gave the oxide (**11**), m.p. 139—140·5 °C, which on heating in CCl_4 afforded the olefin (**12**). The diene alcohol (**14**) was obtained by dehydration of (**12**) using $SOCl_2$ in pyridine, followed by hydrolysis of the resulting acetate (**13**) with 1 N KOH in MeOH. Oxidation of (**14**) with CrO_3 in pyridine yielded the aldehyde (**15**) which, on reflux in pyridine, furnished safranal (**16**) with identical n.m.r. spectra[10] to those of an authentic sample. All steps‡ in the reaction sequence from (**8**) to safranal (**16**) proceeded in moderate to high yield.

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† Although the stereochemistry of this compound (**7**) remains unknown, it was shown to be homogeneous, namely, it showed a single spot (R_f 0·46) on t.l.c. analysis using silica gel 60 F_{254} with benzene–ethyl acetate (4:1) as developer.

‡ The spectral data for the new compounds appearing in this paper are in agreement with the proposed structures.

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