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PHOTOCHEMICAL ε-HYDROGEN ABSTRACTION AS A ROUTE TO TETRAHYDROPYRAN-3-OLS

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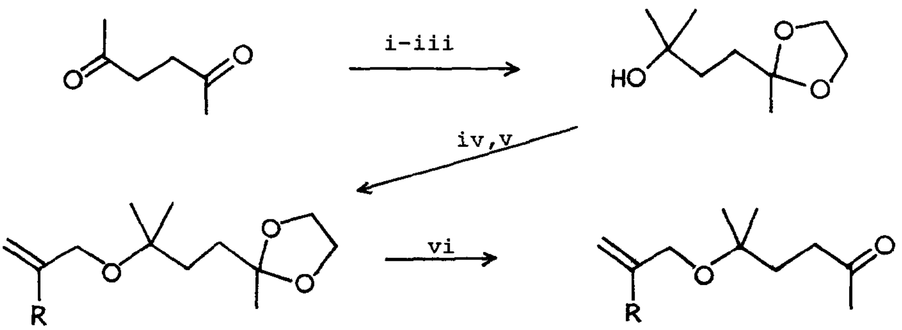
Abstract: Uv irradiation of γ-allyloxy-carbonyl compounds (1), (2) and (8) gives tetrahydropyran-3-ols in 45-61% isolated yields.

Formation of six-membered oxygen heterocycles is a reaction of continual synthetic interest. Recent work has shown that ring formation from straight-chain precursors can be induced by radical cyclisation, with carbon-carbon bond formation.[1,2] Cationic cyclisation is also feasible, *via* carbon-carbon[3] or *via* carbon-oxygen linking.[4,5] We now describe a photochemical synthesis of tetrahydropyran-3-ols which relies on intramolecular ε-hydrogen abstraction in acyclic compounds.

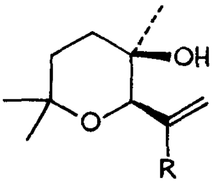
Hydrogen abstraction by photoexcited carbonyl compounds is a well-studied reaction. Intramolecular abstraction of hydrogen atoms attached at the position γ to the carbonyl group leads to the Norrish type II photoreaction.[6] When γ-hydrogens are unavailable to the oxygen atom of the carbonyl excited state, either by reason of substitution[7,8] or by reason of geometry,[9] alternative hydrogen abstractions may occur; such a reaction involving δ-hydrogen abstraction has been put to spectacular use in Paquette's synthesis of dodecahedrane.[10] Abstraction from more remote positions has occasionally proved useful.[11] Some imides, in particular, are able to undergo a remote cyclisation process possibly *via* an electron-transfer photochemical route.[12]

We have synthesised the γ-allyloxycarbonyl compounds, (1) and (2), by the route shown in Scheme 1. Uv irradiation of the ketone (1) in benzene solution[13] resulted in an efficient photochemical reaction in which the tetrahydropyranols (3) and (4) were formed in a 1:1 ratio, and 61% yield. Column chromatography allowed their separation, and the stereoisomeric structures were assigned on the basis of ^{1}H and ^{13}C data.[14] In particular, isomer (3) shows the more upfield ^{13}C signal for C-3, as expected on the basis of an axial hydroxyl arrangement at this carbon.[15] Likewise, irradiation of ketone (2) in

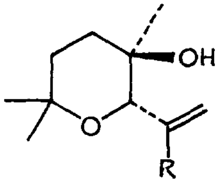


(1) R = H
(2) R = Me

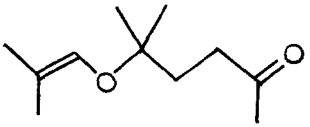
Scheme 1 Reagents: i, $HOCH_2CH_2OH$, H^+, C_6H_6; ii, MeMgI; iii, H_2O; iv, NaH, tetrahydrofuran; v, $CH_2{=}C(R)CH_2Br$; vi, CF_3CO_2H, H_2O, dioxane.



(3) R = H
(5) R = Me



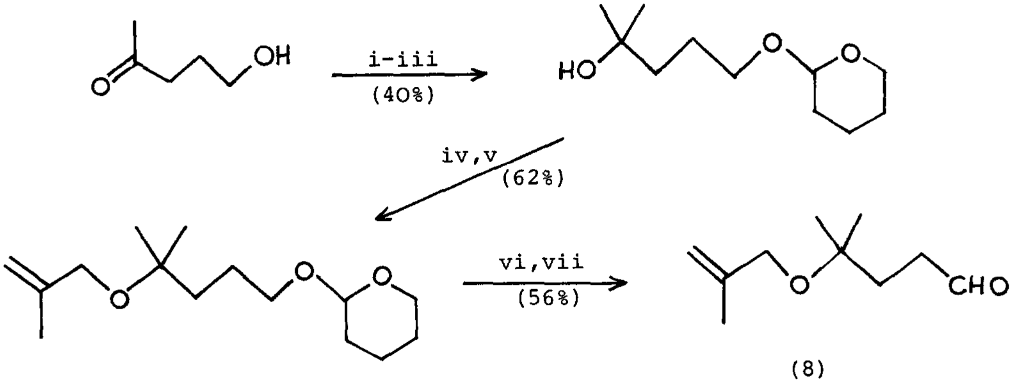
(4) R = H
(6) R = Me



(7)

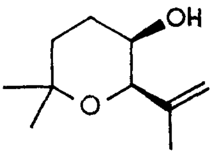
benzene solution gave tetrahydropyranols (5) and (6) (22% and 23% isolated yields, respectively). In this latter experiment, an additional minor product was isolated and shown to be the vinyloxyketone (7) (2.3%), identical with a sample prepared by palladium-catalysed isomerisation of (2).[16]

The versatility of this method would be increased if it could also be applied to aldehydes, although aldehydes are more prone than ketones to photoinitiated free-radical chain reactions.[17] The resulting tetrahydropyranols could then be oxidised to tetrahydropyran-3-ones, producing a carbonyl group as a convenient site for further transformations. We therefore investigated the photochemistry of the γ-methallyloxyaldehyde (8), prepared as shown in Scheme 2. Irradiation of (8) in benzene solution gave an easily separable 2:1 mixture of the two tetrahydropyranols (9) and (10) (33% and 22%). The relative stereochemistry as shown was established from the presence of large ^1H diaxial couplings on H-2 and H-3 in isomer (10). Oxidation of either isomer by pyridinium chlorochromate gave the tetrahydropyranone (11) (75%-80%) having a substitution pattern related to that of the monoterpene-derived cineolic and cinenic acids.



(8)

Scheme 2 Reagents: i, H^+, 2,3-dihydropyran; ii, MeMgI; iii, H_2O; iv, NaH; v, CH_2=C(Me)CH_2Cl; vi, H^+, H_2O, dioxane, chromatography; vii, pyridinium chlorochromate.



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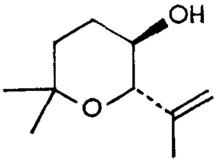
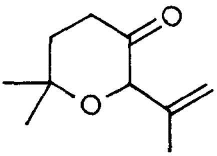
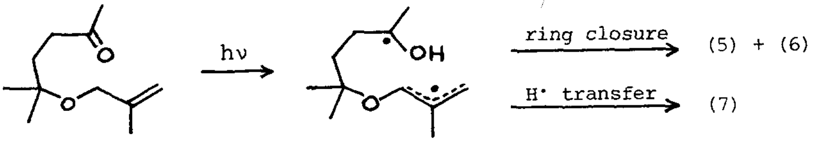


(10)



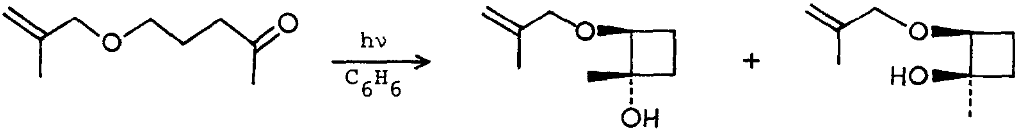
(11)

The above carbonyl compounds do not possess γ- or δ-hydrogen atoms, but do have highly activated allyloxy-hydrogens.[8] We believe that hydrogen abstraction by the excited carbonyl group from this methylene position gives the 1,6-biradical [*e.g.* (12), from ketone (2)]. Subsequent ring closure yields tetrahydropyranols such as (5) and (6). Alternatively, hydrogen atom transfer provides a minor pathway for conversion of the biradical to the vinyl ether (7). Such hydrogen transfer would represent a 1,7- or 1,9-hydrogen shift if intramolecular, but a series of *inter*molecular hydrogen transfers seems a more likely route to the observed product.



(2) (12)

In order to obtain these cyclisation products, it is necessary to maintain substituents at the γ-carbon atom. Thus, irradiation of the ketone (13) leads mainly to γ-hydrogen abstraction to give volatile fragmentation products



(13) (14) (15)

+ fragmentation products

(methallyl vinyl ether and acetone) of the Norrish type II photoreaction,[6] and the stereoisomeric cyclobutanols (14) and (15) (10% and 5%, respectively) as the only isolated photoproducts. This is in contrast to the photochemistry of alkylthio-substituted imides, where ε-abstraction is apparently preferred over γ-abstraction.[18]

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