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# SELECTIVE PHOTOCYCLOADDITIONS OF BIACETYL TO ALLYL VINYL ETHERS: THE SYNTHESIS OF 2-ALKOXYOXETANES AS THROMBOXANE $A_2$ ANALOGUES.

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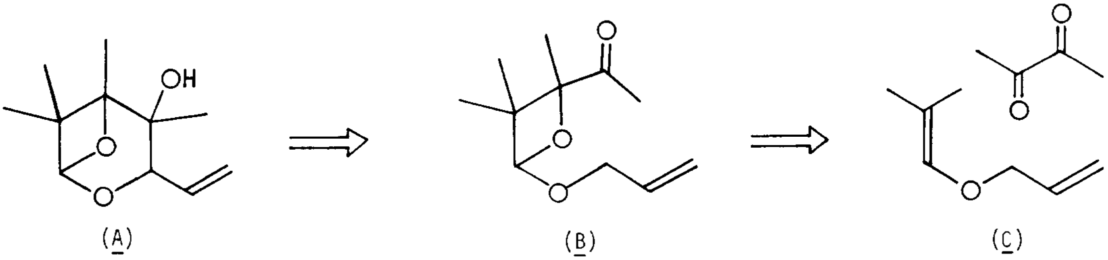
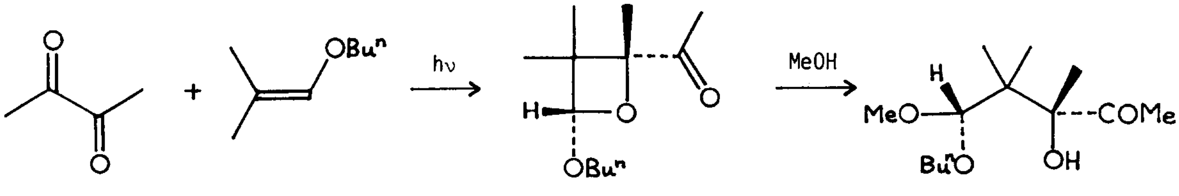
Abstract: Uv irradiation of biacetyl in the presence of the β,β-disubstituted vinyl ethers (2) and (9) gives reactive 2-alkoxyoxetanes (3) and (10), respectively; photoexcited biacetyl reacts chemoselectively with methallyl vinyl ethers (7) and (9) at the vinyl ether double bond.

The synthesis of the 2,6-dioxabicyclo[3.1.1]heptane system of thromboxane $A_2$ ($TXA_2$) has proved a challenging objective.[1,2] The high reactivity of the 2-alkoxyoxetane ring makes the molecule and its analogues exceptionally susceptible to nucleophiles in protic conditions. Thus, the majority of $TXA_2$ analogues so far produced have replaced one or both central oxygen atoms by carbon or sulphur.[3]

Retrosynthetic analysis suggested to us that a tandem photochemical approach based on cycloaddition[4] and hydrogen abstraction might be efficiently used for bicyclic ring construction (C→B→A). This route would involve selective oxetane formation between a dicarbonyl compound and a difunctional alkene, followed by intramolecular ε-hydrogen abstraction to give the required 2,6-dioxabicyclo[3.1.1]heptane nucleus. We now wish to describe an example of regioselective and stereoselective photocycloaddition of biacetyl to an allyl vinyl ether which achieves the first stage of this sequence (C→B).



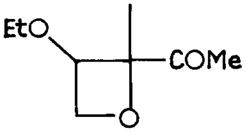
There are a few known examples of photocycloaddition of biacetyl to vinyl ethers.[5-8] We have confirmed that the photoreaction of biacetyl with ethyl vinyl ether generates the 3-alkoxyoxetane (1),[5,9] along with hydrogen-abstraction-type products. In contrast, irradiation of biacetyl in benzene solution in the presence of the β,β-disubstituted vinyl ether (2) yields a 2-alkoxyoxetane (3)(35% isolated yield) as a major photoproduct (Scheme 1).[10] Such a reversal in regioselectivity of cycloaddition might be expected, based on the photoreactivity of acetone towards vinyl ethers.[11] The stereochemistry of the oxetane (3) was assigned as shown, from $^1$H nOe n.m.r. studies at 400 MHz. As for $TXA_2$, the cyclic acetal structure of (3) proved to be exceptionally reactive towards nucleophiles such as methanol, giving a single major stereoisomer (6) from oxetane ring opening (72%).



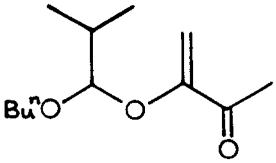
(2) (3) (6)

Scheme 1

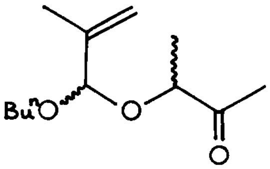
Lesser products from the photoreaction were identified as the vinyl ether (4) and two separable diastereoisomeric allyl ethers (5)(12%, 6% and 8% yields, respectively); these latter products are likely to be the result of alternative 1,5-hydrogen atom transfers in the intermediate 1,4-biradical.



(1)

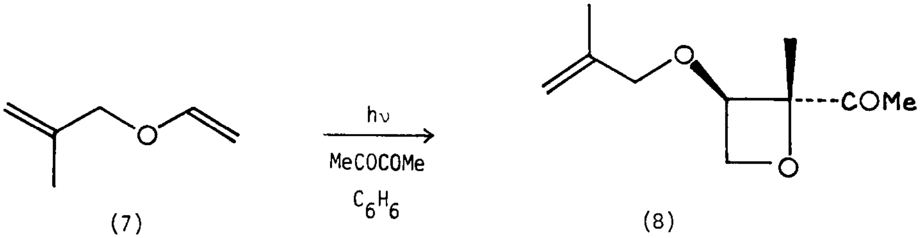


(4)



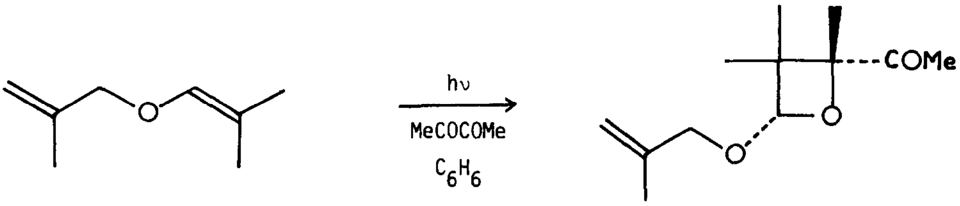
(5)

Methallyl vinyl ether (7)[12] reacted regioselectively at its vinyl ether grouping with biacetyl to generate a 3-alkoxyoxetane (8)(30%), analogous to (1). The stereochemistry of the major adduct was again assigned with the help of nOe experiments.



(7) (8)

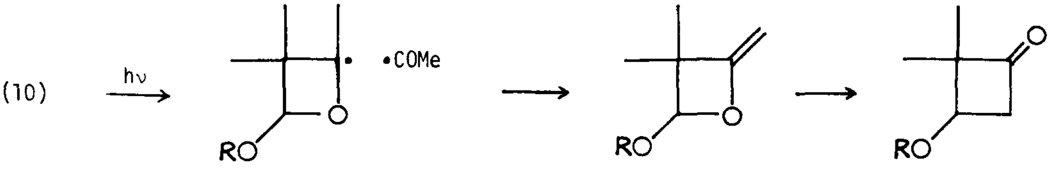
Biacetyl also gave a photochemical reaction with the substituted allyl vinyl ether (9),[13] yielding 2-alkoxyoxetanes (26%) of which the major stereoisomer (4:1) could be assigned the structure (10) shown, with stereochemistry identical to that of (3). Minor products (totalling 11%) which were isolated were the vinyl and allyl ethers analogous to (4) and (5). The high reactivity of (10) was shown by its complete reaction with neutral methanol on standing at 20°C for 3 days.



(9) (10)

We believe that the chemoselective attack by triplet biacetyl on the ethers (7) and (9) arises because of the lower ionisation potential of the vinyl ether (rather than alkenyl) functional group, encouraging exciplex formation and photocycloaddition towards that site.[14] Although ionisation potentials for the ethers (7) and (9) have not been measured, those for the model compounds ethyl vinyl ether (9.07 eV), and 2-methylpropenyl ethyl ether (8.2 eV) are available.[15] (cf. 2-methylpropene, 9.23 eV).[16]

If the molecule (10) can adopt a suitable conformation, the cis- relationship of the 2-acetyl and 4-methallyloxy groups should allow bond formation to occur between them, via intramolecular hydrogen abstraction and radical combinations. When photochemical intramolecular γ- and δ-hydrogen abstraction are not possible for reasons of geometry and/or substitution pattern, ε-abstraction can be a surprisingly efficient process.[17,18] However, attempts to cause intramolecular abstraction of the reactive allyloxy hydrogens[19] in (10) by irradiation in acetonitrile solution at -20°C gave only methyleneoxetane (11) in low yield (10%); this compound is probably derived from Norrish type I photoreaction, and subsequent radical reactions as suggested in Scheme 2. The methyleneoxetane (11) itself underwent an interesting rearrangement on prolonged contact with silica gel, to afford the cyclobutanone (12).[20]



Scheme 2

$R = H_2C{=}C(Me)CH_2-$

Other reactions to bring about intramolecular bond formation in (10) and analogous compounds are being investigated.

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