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INTRAMOLECULAR [2+2] PHOTOCYCLOADDITION OF ENONE-ACETALS

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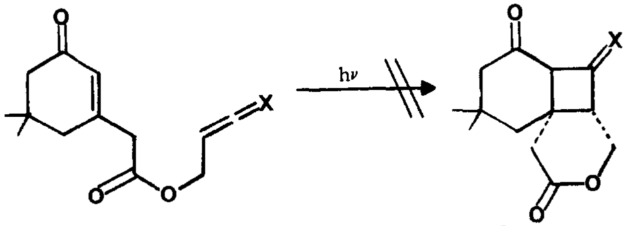
Abstract: Lewis acid catalyzed condensation of unsaturated orthoformates with dienol ethers gives enone-acetals suitable for intramolecular photocycloadditions, yielding heterocyclic precursors to sesquiterpene lactones.

As part of a projected sesquiterpene lactone synthesis, the transformation of Eq.1 was planned. Unfortunately, under a variety of conditions with a variety of X groups, no photocyclization is observable.[1]

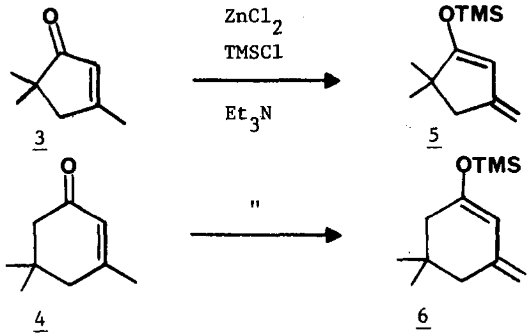


1 2

X= H_2; CH_2; H, CO_2R

These results are similar to observations by Boeckman concerning the intramolecular Diels-Alder reaction.[2] While the exact reason for this result is unclear, it is obvious that esters are in some cases poor linking units for intramolecular cycloadditions. Based on Boeckman's precedent, it was thought that an acetal might be more suitable. This Letter concerns the preparation of such acetals and their intramolecular photocyclizations.

The Lewis-acid catalyzed condensation of an orthoformate and dienyl silyl ether[3] was chosen as a suitable route to the desired substrates. While Holton has provided a route to the ether 6 from the enone using specially activated iron powder as a base,[4] a simpler procedure involves

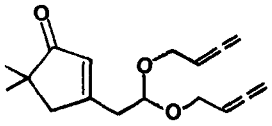
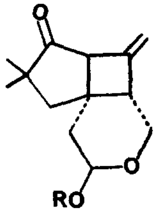
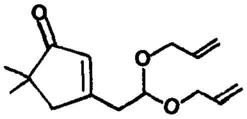
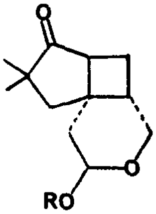
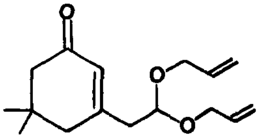
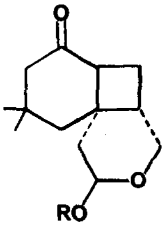
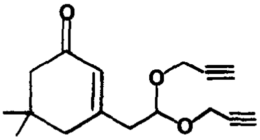
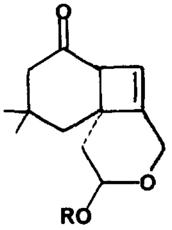


treatment under Danishefsky's conditions.[5] With isophorone and another 5,5-disubstituted enone 3[6], enolization occurs exclusively toward the methyl group to provide 5 and 6 in 72% and 70% yields, respectively. This result may be due to steric hindrance to deprotonation at the methylene. The required orthoformates were prepared by exchanging propargyl alcohol with trimethyl orthoformate (cat.TsOH, 10 h, 56%, bp 90°C @ 0.5 mm Hg) and treatment under Crabbe' conditions[7] for allene formation (CH_2O, CuI, iPr_2NH, reflux 8 h, 50%, bp 125°C @ 1.5 mm Hg). Triallyl orthoformate is commercially available or readily prepared from allyl alcohol and chloroform[8].

The condensation of the dienyl ethers and orthoformates occurs at -78° under the influence of $EtAlCl_2$ to provide enones 7-10 in good yields (Table). Exclusive condensation at the gamma-carbon occurs. The enones could be purified by bulb-to-bulb distillation (9) or flash chromatography (7,8,10). While fairly stable compounds, they were treated with care, as earlier work had shown that the corresponding vinyl ether-enones are more stable than the acetals.[9]

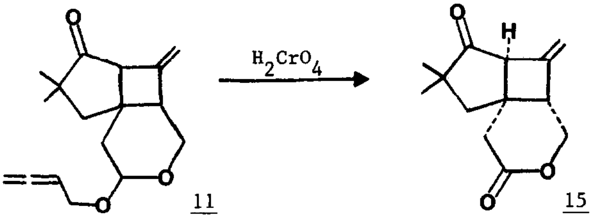
The cycloaddition of these enones occurs readily under the influence of Pyrex filtered irradiation to provide tricyclic acetals 11-14 as diastereomeric mixtures. With the allenic substrate, only 2,3-head-to-head addition to the allene unit is observed. In some recent work on intramolecular allene[2+2] cycloadditions, both 1,2- and 2,3-addition were observed.[10] The acetylenic substrate provides 14, an example of a rarely used route to cyclobutenes.[11] While these acetals are stable to chromatography, they are readily transformed by Jones reagent into the corresponding tricyclic lactones. Lactone 15 can be obtained in 55% overall yield from 7.

TABLE

ENOL ETHER	R	ENONE [a]		CYCLOADDUCT [b]	
5	$CH_2CH{=}C{=}CH_2$	 7	(65%)	 11	(70%)
5	$CH_2-CH{=}CH_2$	 8	(78%)	 12	(81%)
6	$CH_2-CH{=}CH_2$	 9	(85%)	 13	(75%)
6	$CH_2-C{\equiv}CH$	 10	(42%)	 14	(58%)

[a] Prepared by adding a solution of orthoformate (10 mmol) in CH_2Cl_2 to a solution of $EtAlCl_2$ (10 mmol) in 40 mL CH_2Cl_2 cooled to -78°. After 10 min, a solution of enol ether (10 mmol) in CH_2Cl_2 was added. After 2 h at -78°, the solution was warmed to room temperature, quenched with aq. Na_2CO_3, and the product isolated.

[b] A 0.07 M solution of enone in CH_2Cl_2 was degassed and irradiated with a 450 W Hanovia lamp filtered by Pyrex for 6-36 h, depending on substrate.



Applications of these techniques to sesquiterpene synthesis will be reported separately.

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