1,12-Hydrogen atom abstraction reactions of α-keto esters

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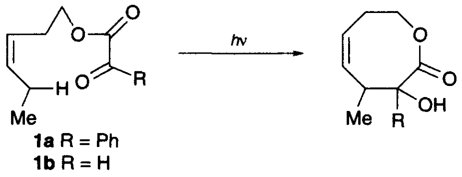
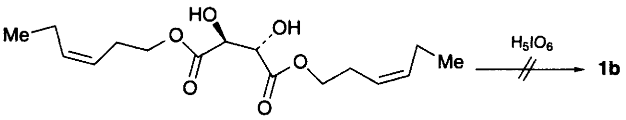
Eleven-membered ring lactones are made by 1,12-hydrogen atom abstraction.

Photochemical hydrogen atom abstraction reactions proceeding *via* six-atom transition states are well known in organic chemistry. Such reactions include the Norrish Type II reaction and the photoenolization reaction.[1] Hydrogen atom abstraction reactions proceeding *via* many-atom transition states have also been extensively studied. Examples include the remote functionalization reactions developed by Breslow and others.[2] In contrast, hydrogen atom abstraction reactions which proceed by medium-ring transition states are comparatively rare. Wagner recently reported a number of examples.[3]



Scheme 1



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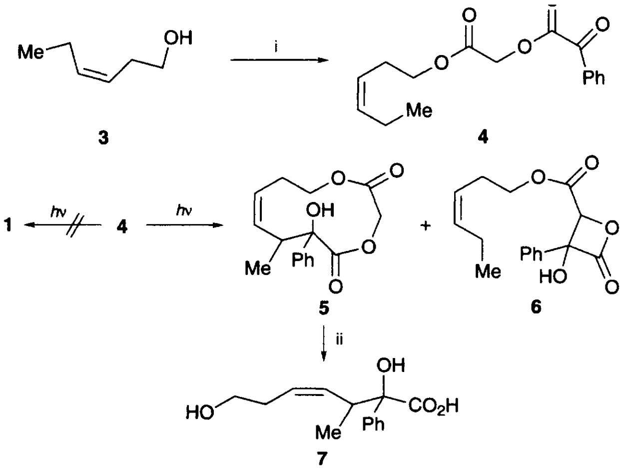
Scheme 2

In the course of examining photochemical strategies for the initiation of radical cyclizations, we recently discovered several novel 1,9-hydrogen atom abstraction reactions.[4] An example is shown in Scheme 1. Our hypothesis is that the more stable *syn* conformation of the ester is the key control element that favours the 1,9-hydrogen atom abstraction, leading to the eight-membered ring lactone.

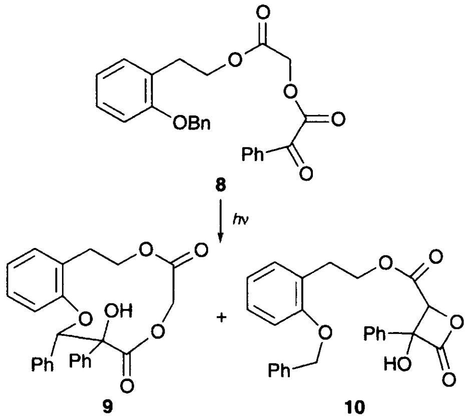
The hydroxy lactones produced in this reaction are potential intermediates for the preparation of natural products containing the oxocene ring system.[5] In order for our photochemical methodology to be more directly applicable, we decided to prepare aldehyde **1b**. When diol **2** was subjected to anhydrous periodate,[6] only hex-3-en-1-ol was isolated (Scheme 2).

We next devised a photochemical method for the production of **1b**. Binkley has shown that the photolysis of α-keto esters affords labile aldehydes.[7] The plan was to produce **1b** under conditions where it could be irradiated without isolation. Alcohol **3** was acylated with bromoacetyl bromide and diisopropylethylamine in THF at 0 °C and was converted into diester **4** by displacement of the bromide with 1.5 equiv. of the potassium salt of phenylglyoxylic acid in DMF at 25 °C (Scheme 3). Irradiation in benzene using a Rayonet apparatus (350 nm bulbs) for 18 h afforded products **5** and **6** in 24 and 37% yield, respectively. The structure of **5** was assigned based on double irradiation experiments and infrared absorptions at 1735 and 1752 cm^{-1}.† Hydrolysis of **5** with LiOH at 25 °C afforded acid **7**. β-Lactone **6** was characterized by its infrared spectrum showing absorptions at 1846 and 1735 cm^{-1} and its NMR spectra. Compound **5** could be derived from a 1,12-hydrogen atom abstraction followed by cyclization. Interestingly, only one ring size was produced, even though an allylic radical was involved. Although a few 1,12-hydrogen atom abstraction reactions have been observed, these reactions involve ω-aminophthalimides, where charge transfer reactions can be operative.[8]

Additionally, **8** was prepared by the same pathway and was irradiated in the Rayonet reactor (Scheme 4). Lactone **9** was obtained in 28% yield.‡



Scheme 3 *Reagents*: i, $BrCH_2COBr$, Pr^i_2NEt, $PhCOCO_2H$, K_2CO_3, DMF; ii, LiOH



Scheme 4

Footnotes

† *Selected data* for **5**: 400 MHz ^{1}H NMR (CDCl$_3$) δ 0.75–0.80 (m, 3 H), 2.00–2.20 (m, 1 H), 2.60-2.75 (m, 1 H), 3.41–3.55 (m, 1 H), 3.69 (s, 1 H), 4.10–4.18 (m, 2 H), 4.25 (d, *J* 15 Hz, 1 H), 5.07 (d, *J* 15 Hz, 1 H), 5.40–5.50 (m, 1 H), 5.75 (t, *J* 9 Hz, 1 H), 7.25–7.40 (m, 3 H), 7.60–7.72 (m, 2 H); IR (KBr): 3522, 3016, 2926, 1752, 1735, 1286, 752 cm^{-1}. HRMS for $C_{16}H_{18}O_5$: found, 290.1152. Calc., 290.1154.

‡ *Selected data* for **9**: 300 MHz ^{1}H NMR (CDCl$_3$) δ 3.72 (br s, 1 H), 5.07 (s, 1 H), 5.12 (s, 2 H), 5.42 (dd, *J* 5, 10 Hz, 2 H), 6.98 (d, *J* 6 Hz, 2 H), 7.26–7.60 (m, 12 H); IR (KBr) 3446, 3063, 1734, 1719, 1246, 754 cm^{-1}. HRMS for $C_{24}H_{20}O_6$: found, 404.1251. Calc., 290.1259.

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Received, 2nd July 1996; Com. 6/04666E