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Unexpected and Efficient Photochemical Rearrangement of 6-Hydroxyethylpyran-2-ones to 4-Alkylidene-5,6-dihydropyrans

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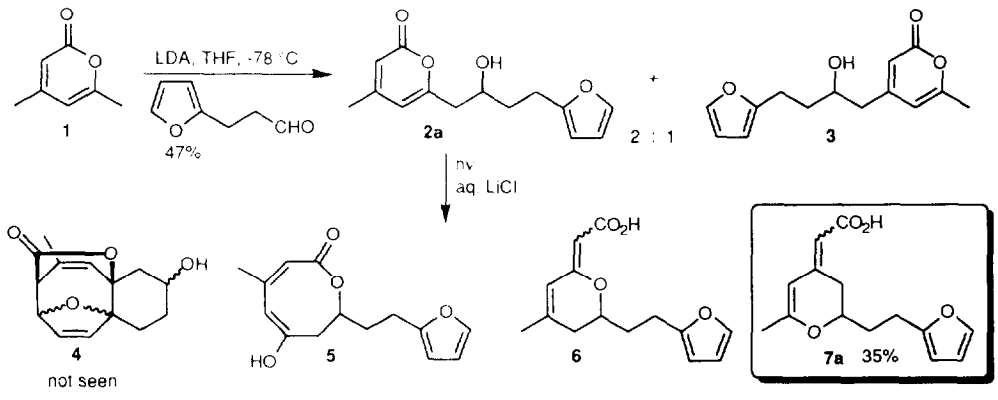
Abstract: *Pyran-2-ones* ***2a-e*** *bearing pendant alcohols underwent conversion to dihydropyrans* ***7*** *via irradiation in MeOH followed by stirring in the presence of catalytic HCl. This process requires the intervention of a prior skeletal rearrangement of the starting pyran-2-ones to place the hydroxyalkyl substituent at C-4, along with temporary incorporation of MeOH. Homologous substrates* ***2f-g*** *underwent intramolecular 1,6-addition exclusively to furnish spirolactones* ***9*** *in good yield.*

The photochemical behavior of pyran-2-ones has been the subject of extensive study. Photodimerizations in the [2+2], [4+2] and [4+4] modes have been reported by a number of labs.[2-4] In addition, there has been considerable mechanistic interest in the photochemical generation of ring-opened products which incorporate a molecule of solvent. Unsaturated ketenes,[5,6] bicyclic β-lactones[7] and solvent [1,6]-adducts[8] have all been identified as primary photoproducts, although only the latter two appear to lead to acyclic solvent adducts. In this letter, we report an unprecedented and highly efficient photoisomerization of 6-hydroxyalkylpyran-2-ones to 4-alkylidene-5,6-dihydropyrans, which occurs via an apparent skeletal reorganization involving transposition of C-4 and C-6 substituents of the starting pyran-2-one.

Our interest in pyran-2-ones has focused on cycloaddition chemistry, and we have previously reported that pyran-2-ones bearing pendant furan rings can undergo efficient intramolecular crossed [4+4]-photocycloadditions to furnish functionalized cyclooctadienes.[9] One example in this preliminary study showed significant levels of asymmetric induction by a stereogenic center in the tether connecting the two heterocyclic moieties. In an effort to further explore this phenomenon, we prepared compound **2a** (isolated as an inseparable mixture with isomer **3**) via condensation of the anion derived from 4,6-dimethylpyran-2-one **1** with 3-(2-furyl)propanal (Scheme 1). However, the expected [4+4]-cycloadducts **4** were not obtained upon irradiation of **2a**. Instead, a polar product in which the pendant hydroxyl moiety had apparently been incorporated into a new ring was isolated in modest yield. Assignment of a structure to the unexpected product proved to be difficult. Possible structures consistent with the spectral data included enolized 8-membered lactone **5**, which could arise

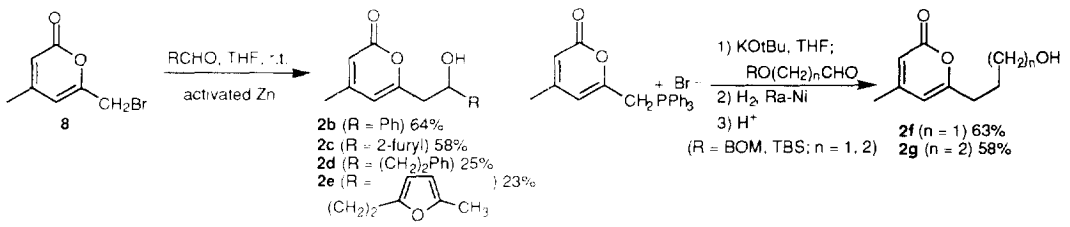
Scheme 1



from precedented pyran-2-one photorearrangements, along with isomeric dihydropyrans **6** and **7a**, whose formation would require a considerably more involved mechanism. Subsequent studies (*vide infra*) have revealed that **7a** is the correct structure.

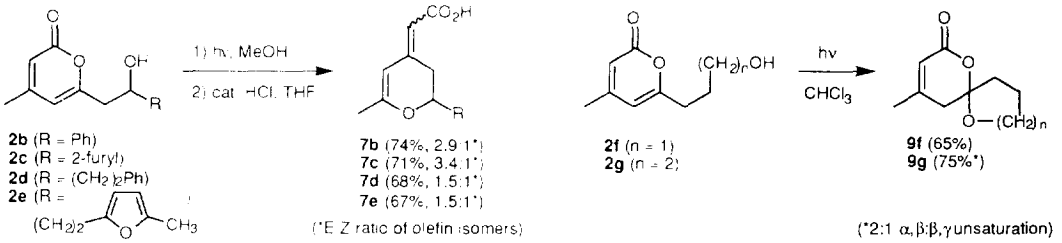
In an effort to better understand this transformation, we prepared several other substrates (Scheme 2). The lack of regioselectivity seen in the direct deprotonation **1** demanded the development of an alternative route to substituted hydroxyethyl 2-pyrones. Thus, selective bromination at the C-6 methyl group of **1** to give **8**,[9] followed by Reformatsky addition[10] to benzaldehyde, furfural, dihydrocinnamaldehyde, or 3-(5-methyl-2-furyl)propanal gave substrates **2b-e**, free of isomeric 4-hydroxyethyl derivatives. Homologous examples **2f-g** were prepared by Wittig olefination employing the phosphorane derived from **8** and protected hydroxyaldehydes, followed by hydrogenation and deprotection.

Scheme 2



Direct photochemical rearrangement of **2b-g** using the conditions employed for **2a** was inefficient and difficult to reproduce. However, careful optimization led to conditions which reproducibly furnished the products. Thus, irradiation of **2b-e** in methanol (1.0-1.5 x 10^{-2} M, r.t., ca. 4 h) resulted in a diastereomeric mixture of solvent adducts (Scheme 3). Removal of solvent and treatment of the crude residue with cat. HCl in THF (0.1 M, r.t.), in analogy to previously reported conditions for rearrangement of 1,6-adducts to acyclic esters,[8c] gave the corresponding dihydropyrans **7** in good yield as inseparable mixtures of exocyclic olefin geometrical isomers. In the case of **7b** and **c**, the major (E) isomer could be obtained in pure form (ca. 80% recovery) by trituration from dichloromethane. This permitted the unambiguous assignment of the structure of **7b** via X-ray diffraction analysis (Fig. 1). The structures of products **7a** and **7c-e** were assigned by their close spectral analogy to **7b**.

Scheme 3



In contrast to the hydroxyethyl cases, **2f-g** gave spirocyclic products **9f-g** under all conditions. This is presumably the result of irreversible 1,6-addition of the pendant alcohol in the photochemical step, a process which is disfavored for **2a-e** due to ring strain. Optimum yields of **9f-g** could be obtained by irradiation in chloroform, with **9g** isolated as a 2:1 mixture of olefin regioisomers. If proven to be general, this transformation may be useful in the construction of spiroketals.

Any mechanism for the formation of dihydropyran products **7** must address the transposition of the C-4 methyl and C-6 hydroxyethyl groups (Scheme 4). Although photochemical electrocyclic opening of pyran-2-ones to unsaturated acylketenes has been observed,[5] the short solution lifetime of these species would appear to preclude their involvement.[6,11] Closure to bicyclic β-lactones[7] and formation of 1,6-solvent adducts[8] have both

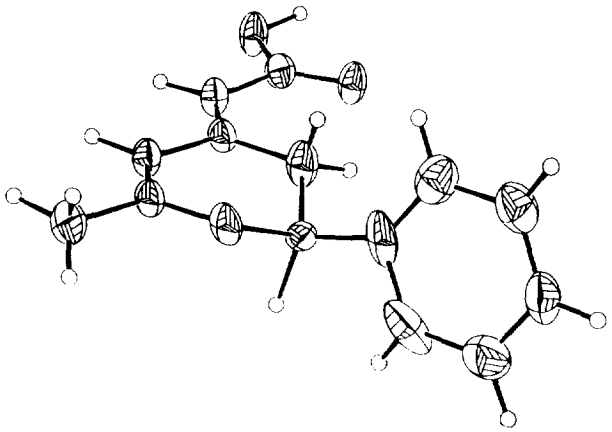
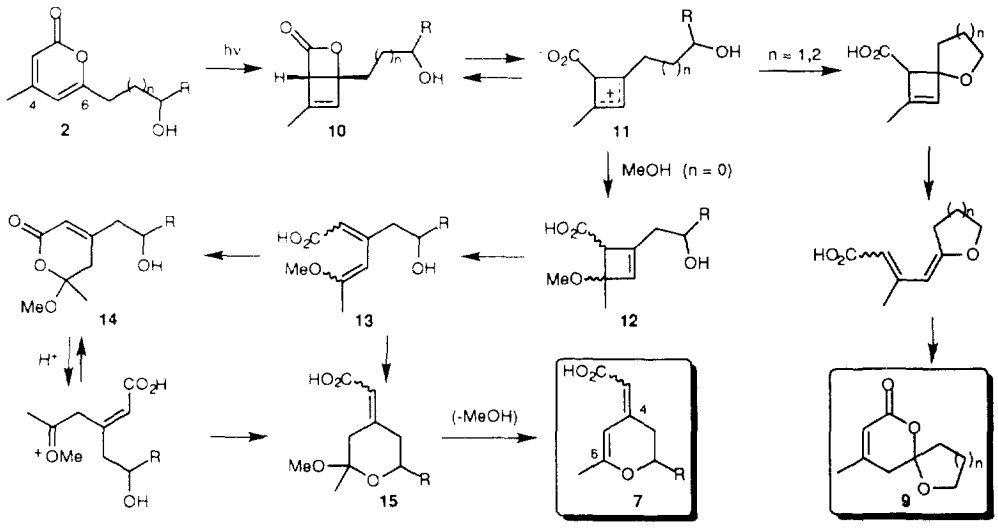


Figure 1. ORTEP representation of 7b (major isomer).

been implicated in the production of acyclic solvent adducts. The mechanism by which the 1,6-adducts are formed is not well understood, although solvolytic capture of ionized β-lactone, followed by electrocyclic opening of the resulting cyclobutene and reclosure of the lactone appears reasonable.[12] With pyran-2-ones **2**, ionization of β-lactone **10** to unsymmetrical cyclobutenium carboxylate **11** would permit two regioisomeric solvent trapping routes. Capture by methanol at the less hindered methyl-substituted terminus[13] would furnish **12**, and subsequent cyclobutene opening to dienoic acid **13** could allow lactone closure to give ring-isomerized 1,6-methanol adducts **14**. Subsequent treatment with catalytic acid would lead to rearranged dihydropyrans **7**. Alternatively, **13** may cyclize directly to intermediate **15** as a mixture of exocyclic olefin isomers.[14] For the homologous substrates **2f,g**, the pathway would diverge from the process described above at the point of **11**, with intramolecular capture by the pendant hydroxyl occurring in preference to methanol trapping.

Scheme 4



In summary, we have reported a novel photochemical process employing pyran-2-ones bearing pendant alcohols. The overall transformation, involving skeletal reorganization and incorporation of the nucleophilic

side-chain, furnishes functionalized dihydropyrans from readily available 6-hydroxyethyl pyran-2-ones in two steps. The spirocyclization process observed with longer tethers suggests that the ring transposition process can be diverted if pendant nucleophiles can intercept the putative cyclobutenium intermediate, and may be useful for the construction of a variety of spirocyclic products. Extrapolation of these reactions to other nucleophilic traps and further efforts to fully elucidate their mechanisms will be reported elsewhere.

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[†]All questions regarding X-ray crystallographic data should be directed to this author.

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13. In addition to steric effects, diminished charge density at the hydroxyethyl substituted terminus due to inductive electron withdrawal by the side-chain oxygen may disfavor attack at that position.

14. Following irradiation, a complex, inseparable mixture of polar methanol adducts was obtained which may include **13**, **14** and/or **15**. Upon treatment with acid, these components converged upon **7**. To the extent that the process occurs via **14**, product **7** should be initially formed as the Z isomer exclusively, although subsequent acid-catalyzed isomerization is possible.

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