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Oxidative conversion of δ -sultones to γ -lactones

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Abstract

Delta-sultones, prepared by C-H insertion, can be oxidatively converted to gamma-lactones by treatment with *t*-BuOK/*t*-BuOOH. An intermediate in the synthesis of (–)-eburnamonin was prepared using this approach.

Sultones are cyclic sulfonates, sulfonic ester analogs of lactones.¹ δ -Sultones, particularly, can be conveniently prepared by C-H insertion from alkyl diazosulfonates.^{2,3} This reaction effectively permits functionalization of alcohols at the γ -position relative to the hydroxyl group, contrasted with β -functionalization that occurs with a more common ester tether (Scheme 1).⁴

Since the discovery of this reaction we have been working on development of synthetically useful transformation of the obtained δ -sultones. Earlier, we reported a conversion of these compounds to δ -lactones via reductive desulfonation by treatment with samarium(II) iodide/DMPU in THF.⁵ After obtaining this result, we contemplated developing a method for conversion of δ -sultones to γ -lactones, a common structural fragment in many natural compounds. This transformation would require an oxidative conversion of the C2 carbon of the sultone to a carboxylate, along with removal of the ester carbon, possibly via a sort of oxidative decarboxylation process.

Du Bois has earlier demonstrated C2 oxidation of potassium anions of δ -sultones by Davis oxaziridine.³ Guided by this finding, we surveyed several oxidizing agents. We found that treatment of δ -sultones by *t*-butyl hydroperoxide in presence of potassium *t*-butoxide produced the desired γ -lactones.¹⁰ Good to excellent yields of the lactones were obtained for a range of δ -sultones (Table 1). The structures of lactones 2a and 2b, obtained from sultones 1a and 1b, were confirmed by comparison of their spectral data to the literature reports.⁶

We propose the following mechanism for this transformation (Scheme 2). Deprotonation of the sultone would produce enolate **3**. This would be followed by an oxidation of the

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/>.

carbanion by *t*-butyl hydroperoxide anion, as known in some examples.⁷ The collapse of the produced alkoxide would produce α -ketoester **5**, the product that was observed by Du Bois in the Davis oxaziridine oxidation.³ In presence of *t*-butylhydroperoxide, however, further oxidation may occur. *t*-Butylhydroperoxide anion could add to the ketone carbonyl, producing tetrahedral intermediate **6**, then 3-membered intermediate **7** via an intramolecular attack on the ester carbonyl. The resulting intermediate would fragment with the expulsion of *t*-butoxide to form anhydride **8**. Alternatively, **6** could form directly from **8** via a Bayer-Villiger type acyl shift. Extrusion of SO₂ (either in the course of the reaction or during the work-up) would liberate the alcohol functionality that would close onto the anhydride to form the γ -lactone ring.

Using the sequence of sulfonate C-H insertion and this oxidative conversion to γ -lactone we prepared a key intermediate in the synthesis of (–)-eburnamonin. For this purpose enantiomerically enriched alcohol **10** was prepared via enantioselective addition of ethylmagnesium cuprate to α,β -unsaturated ester **9**, catalyzed by tol-BINAP,⁸ followed by LAH reduction of the obtained ester. This alcohol was converted to diazosulfonate **11** using previously developed methods.² C-H insertion of this diazosulfonate proceeded as expected under Rh₂(esp)₂ catalysis to produce δ -sultone **12** in good yield (Scheme 3).

Oxidative desulfonation of this sultone to lactone **13** proceeded in a 75% yield using the general procedure, effectively achieving a “remote carboxylation” of alcohol **10** at the tertiary position. Removal of the benzyl protecting group produced from lactone **13** provided intermediate **14** that was previously diastereoselectively converted to (–)-eburnamonin.⁹

Thus, a δ -sultones can be converted to γ -lactones by treatment with *t*-butylhydroperoxide and potassium *t*-butoxide. In combination with C-H insertion to prepare δ -sultones this provides a method for “remote carboxylation” of alcohols at C3, leading to γ -lactones. An intermediate in the synthesis of (–)-eburnamonin was prepared using this approach.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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10. General procedure for oxidative conversion of sultones to lactones: To a solution of the corresponding δ -sultone (1 equiv) in THF (2.5 mL) at rt was added a solution of *tert*-butyl hydroperoxide in decane (5M, 5 equiv), followed by a dropwise addition of a solution potassium *tert*-butoxide in THF (1M, 6 equiv). After stirring at rt for 16 h, sodium sulfite was added and the resulting suspension stirred for 15 min. 20 mL of 1N hydrochloric acid solution was added and the resulting mixture was extracted with diethyl ether, washed with brine, dried over anhydrous magnesium sulfate and evaporated to afford a crude product, which was purified by flash chromatography.

Scheme 1.
C-H insertion of diazosulfonates

Scheme 2.
Proposed mechanism of the transformation

Scheme 3.
Synthesis of the key intermediate for (–)-eburnamonin

Table 1Oxidative preparation of γ -lactones from δ -sultones

Substrate	Product	Yield
1a	2a	54%
1b	2b	60%
1c	2c	93%
1d	2d	90%
1e	2e	72%
1f	2f	70%