



Synthesis of benzofuran-containing spiro lactones from diarylcyclopropenones



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ABSTRACT

Several novel benzofuran-containing spiro lactones were synthesized and characterized using copper-catalyzed heterodimerization of 1,2-diarylcyclopropenones, and followed by sequential intramolecular cyclopropene ring opening and oxidative cyclization.

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Introduction

Ever since the synthesis of diphenylcyclopropenone was reported half a century ago,¹ the chemistry and properties of cyclopropenone and its related cyclopropenyl derivatives² have inspired substantial research on account of the unusual aromaticity associated with this two- π -electron motif. Even today, this smallest Huckel aromatic continues to attract researchers' attention for its unique aromatic cation properties. For instances, Peart and Tovar³ have incorporated the cyclopropenium moiety into π -conjugated polymers and found that the increased contributions of cyclopropenium cation aromaticity restrict the quinoidal charge carriers. Kelly and Lambert have recently reported the use of diphenylcyclopropenone as a catalyst to catalyze cyclodehydration of diols⁴ and to activate the substitution of alcohols with mesylate ion.⁵ Our group was attracted by one of the unique properties of diphenylcyclopropenone, that is, its ease of dimerization to the corresponding cyclopropene spiro lactone under the influence of transition metal catalysts.⁶ We envision the resulting spiro lactone, in the presence of an intramolecular nucleophile, is prone to undergo cyclopropene ring opening reaction due to its intrinsic strained structure. The proposed ring-opened product is presumably susceptible to oxidative cyclization to afford the benzofuran-containing spiro lactone. Since spiro lactones are well-known heterocycles that exhibit various biological⁷ and functional properties,⁸ the design and synthesis of spiro lactones with novel molecular skeletons remain desirable. Here, we describe our effort toward

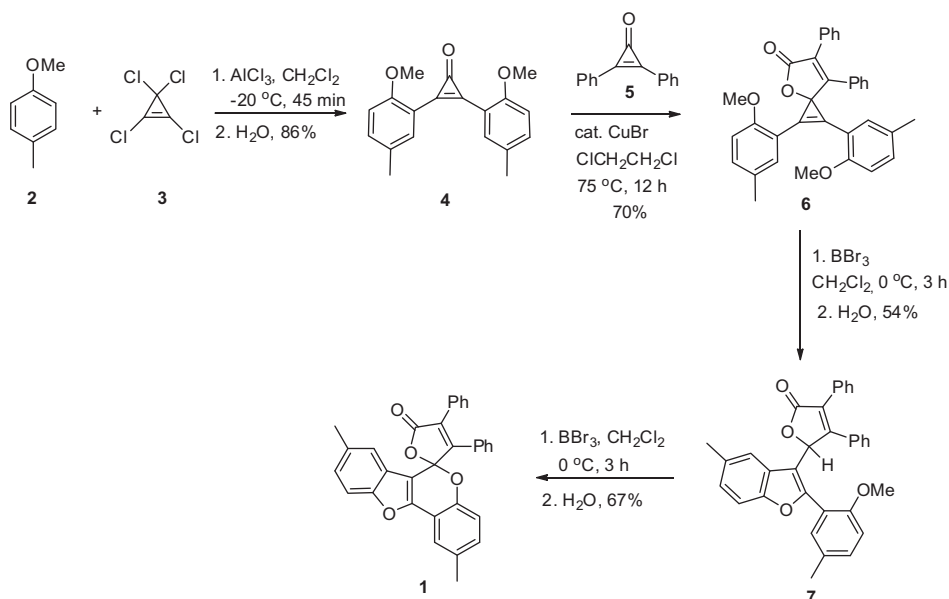
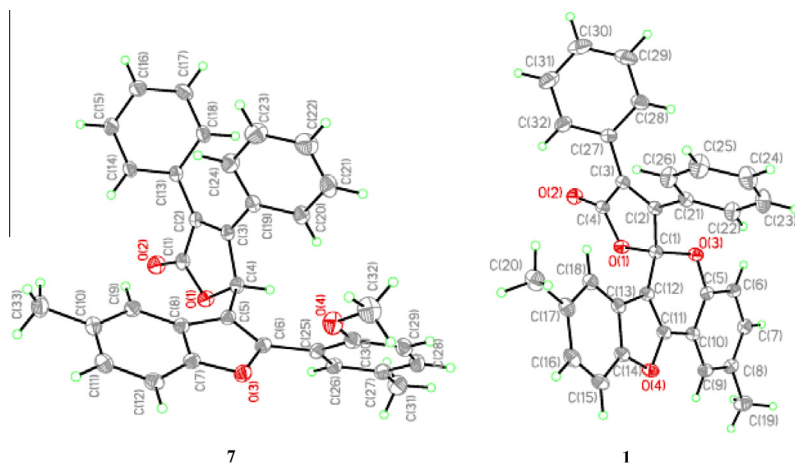
the synthesis and characterization of three *o*-hydroxyphenylcyclopropenone-derived, benzofuran-containing spiro lactones from 1,2-diarylcyclopropenones.

Results and discussion

Scheme 1 outlines the synthesis of the spiro lactone **1**. It started with the coupling of *p*-methylanisole (**2**) with perchlorocycloprop-1-ene (**3**) in the presence of aluminum chloride at low temperature to give 2,3-bis(2-methoxy-5-methylphenyl)cycloprop-2-enone (**4**).⁹ Compound **4** was then coupled with commercially available 1,2-diphenylcyclopropenone (**5**) under the influence of a catalytic amount of copper bromide in 1,2-dichloroethane at 75 °C to obtain the spiro lactone **6**.⁶ Selective demethylation of one of the two methoxy groups on **6** with 1.2 equiv of tribromoborane followed by in situ cyclopropene ring opening afforded the benzofuran **7**. The subsequent demethylation of the second methoxy group of **7** with tribromoborane induced the oxidative cyclization of the lactone and phenol moiety to furnish the target spiro lactone **1**. The molecular structures of **7**, **1**, and **6** were all elucidated by the X-ray crystallography as shown in **Figures 1 and 2**.¹⁰

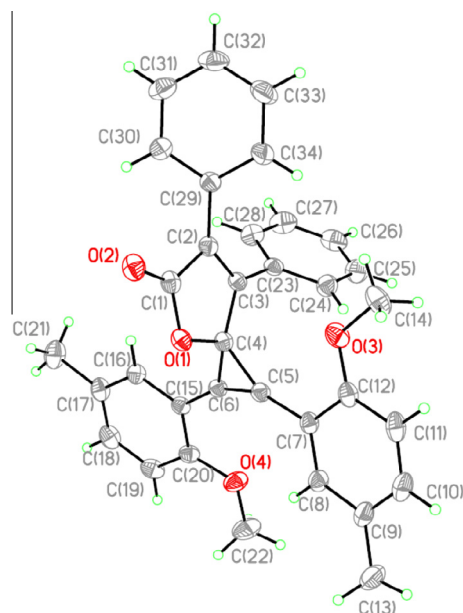
In the coupling reaction between **4** and **5**, four possible regioisomers were expected. To our delight, the desired product **6** was the major isomer with the ratio of the major product to other combined three regioisomers to be approximately 7 to 1. The X-ray crystal structure of the major coupling product **6** (**Fig. 2**) unambiguously revealed that the two methoxyphenyl groups were attached to the cyclopropene ring. **Scheme 2** depicts the proposed mechanism for the Cu(I)-catalyzed heterodimerization of **4** and **5** to **6**. We envisioned that the first step involves the preferred

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Scheme 1. Synthesis of the spiro lactone **1**.Figure 1. X-ray crystal structures of **7** and **1**.

chelation of copper(I) with **4** rather than **5**, since the former contains two potential chelating sites, that is, the *o*-methoxy and carbonyl oxygens; the latter, however, contains only one. The resulting **8** then undergoes single-electron transfer from copper(I) to the attached carbonyl oxygen to yield the radical anion **9**. The negatively charged oxygen of **9** selectively attacks the carbonyl carbon of **5**, which is more electrophilic than that of **4**, to yield the radical anion **10**. The subsequent back electron transfer from the cyclopropane radical moiety of **10** to copper(II) affords the zwitterion **11**. Final ring opening of the dioxygen-substituted cyclopropane ring of **11** and subsequent neutralization of the positive charge on the other cyclopropane ring furnish the product **6**, along with the regenerated copper(I) catalyst. Presumably, the high chemoselectivity of this heterodimerization can be attributed to the combination of chelate¹¹ and electronic effects.

In the first demethylation step, the isolation of the benzofuran **7**, rather than the corresponding demethylated phenol derivative, suggests that the cyclopropane spiro lactone moiety is highly susceptible to ring opening via an intramolecular nucleophilic attack to release the ring strain.¹² Scheme 3 depicts the proposed mechanism for the formation of **7** from **6**. After BBr₃-mediated demethylation of **6**, the boron-complexed phenoxide

Figure 2. X-ray crystal structure of the spiro lactone **6**.

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