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A novel stereoselective [8+2] double cycloaddition route to hydronaphthalene ring systems

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Abstract: Substituted hydronaphthalenes where each of the ten carbons of the two-ring system contains functionality were obtained through a tandem [8+2] cycloaddition and base-catalyzed rearrangement process using dienylfurans and electron-deficient alkynes. If the [8+2] process is conducted under solvent-free conditions the process could be conducted in a single reaction flask without isolation of the chromatographically sensitive [8+2] cycloadducts. A mechanism involving base catalysed alkene positional isomerization followed by disrotatory electrocyclic ring closure was proposed for the key reaction step that converts [8+2] cycloadducts to hydronaphthalenes. The products undergo selective ring opening-isomerization processes upon treatment with Lewis acids.

Introduction

Furan-bridged ten-membered ring systems (*e.g.* **3a**, Scheme 1) are readily accessed through [8+2]-cycloaddition of electron-deficient alkynes [*e.g.* dimethylacetylene dicarboxylate (DMAD), **2**] and dienylfurans[1] (*e.g.* **1a**) or their isobenzofuran analogs.[2] Although that process proceeds in relatively high yield, the products are somewhat acid-sensitive and require tremendous care in their purification. The preferred purification method was silica gel chromatography using triethylamine-treated silica gel. In some experimental runs, an unanticipated minor compound, assigned as the fused oxanorbornene **4a,** was obtained in addition to the [8+2]-cycloadduct **3a**. Compound **4a** was never observed in the crude reaction mixture, thus suggesting that its formation is an artifact of the chromatographic purification process. This product could be eliminated by performing the chromatography purification quickly and avoiding excess triethylamine in the column preparation. In this manuscript the scope, limit, and mechanism for the formation of compound **4a** in a single pot from the coupling of dienylfurans and electron-deficient alkynes is discussed. This process represents a novel and unconventional stereoselective construction of densely functionalized hydronaphthalenes in a formal [8+2]-double cycloaddition process. Densely functionalized cyclohexadiene and hydronaphthalene derivatives are highly useful building blocks for preparation of medicinally-important derivatives featuring these ring systems and their preparation has been the focus of numerous recent investigations.[3] This ring system is most