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## A Novel Tandem Bicyclization to Form An Indenopyran Ring System

Manisha Chakraborty, David B. McConville, Takeshi Saito, Huihan Meng

Peter L. Rinaldi, Claire A. Tessier and Wiley J. Youngs\*

Department of Chemistry, University of Akron, Akron, Ohio 44325-3601 Received 18 June 1998; revised 29 July 1998; accepted 12 August 1998 Abstract: A new palladium-copper catalyzed intramolecular acetylene-zipper type bicyclization between alkyne and hydroxy functionality of an alkynyl hydroquinone has been observed to give a highly conjugated ring system. © 1998 Elsevier Science Ltd. All rights reserved.

Cuprous acetylides,<sup>1</sup> cuprous oxide<sup>2</sup> and palladium catalysts<sup>3</sup> have been shown to promote the formation of 5-membered heterocyclic rings by the intramolecular additions of alcohols, amines and carboxylic acids to adjacent acetylenes. Pd/Cu catalyzed coupling<sup>4</sup> between substituted *o*-iodophenols and terminal alkynes has been found to give substituted benzo[*b*]furans, without isolation of the (*o*-hydroxyaryl)acetylene intermediates,<sup>5</sup> while in similar cases a stronger base is needed for furan ring formation.<sup>6</sup>



Tandem reaction processes are a rapidly growing area of chemistry and have been found to be extremely useful for synthetic organic chemistry. These reactions, also called cascade, iterative or zipper reactions, are generally a combination of several transformations in a one-pot synthesis.<sup>7</sup>

In the course of investigating various cyclynes<sup>8</sup> and cyclodiynes<sup>9</sup> with differently substituted benzene rings we became interested in studying the hydroquinone derivatives of cyclynes and cyclodiynes, their metal chemistry and their packing patterns. We recently reported a convenient, novel, high yield synthesis of substituted isoindolequinones from diethynylhydroquinones and primary amines.<sup>10</sup> Here we report a new zippertype bicyclization in attempting to form 5 by Pd/Cu catalysis as shown in Scheme 2. Compounds  $2^{11}$  and  $3^{20}$  were synthesized by Pd/Cu catalyzed coupling of 2,3-diiodo 5,6-dimethyl hydroquinone, 1, and trimethylsilylacetylene in 30% and 50% yield, respectively. No furan formation was observed at rt. Prolonged heating with catalyst gave low yields of furanoid and quinonoid byproducts. Treatment of o-diethynylbenzene 4a<sup>12</sup> with two equivalents of 2, 3-iodo-5,6-dimethyl-2-(2-(trimethylsilyl)ethynyl)hydroquinone, in the presence of the Pd/Cu catalyst in diisopropylamine-toluene as solvent under reflux (10h, 90°) afforded compound 6a (1,4-benzenediol, 2-(trimethylsilyl)ethynyl-3-(1-(trimethylsilyl)ethynyl-2 hydroxy-3,4-dimethylbenz[b]indeno [2,1-d] pyran-6-y])-5,6-dimethyl) as a yellow solid in 45% isolated yield.<sup>13</sup> The presumed intermediate 5a was not observed. At lower temperatures, coupling between 4a and 2 did not proceed. This unusual product was structurally characterized by a series of HMQC<sup>14</sup> and HMBC<sup>15</sup> NMR experiments. Desilylation of 6a with KF provides 7a. Crystallization of 7a from methylene chloride gave crystals suitable for X-ray crystallography. The thermal ellipsoid plot of 7a is shown below.<sup>16</sup> Compound 4b, 2,3-diethynyl-5,6-dimethylbenzene,<sup>17</sup> coupled with 2 in toluene with a trace of diethylether present to give 40% yield of 6b at 50 °C for 10 h. The presumed intermediate 5b was not isolated. At lower temperatures, and/or in the absence of a trace amount of ether coupling of 4a or 4b with 2 did not proceed.



As part of our study of the mechanism and generality of this novel zipper like bicyclization, 2,3diethynyl-5,6-dimethyl hydroquinone **8**, formed by desilylation of **3**, was subjected to Pd/Cu catalysis with two equivalents of *o*-iodophenyl trimethylsilyl acetylene **9**. In addition to isolating the linear compound (**10**) in 40% yield, we isolated two cyclized products, mono-furanoid compound (**11**, 12%) and di-furanoid compound (**12**, 10%), and the quinonoid linear trimer (**13**, 10%). Compounds **10** and **11** have been structurally characterized by NMR (<sup>1</sup>H, <sup>13</sup>C, HMQC, HMBC, and DEPT), IR, elemental analysis, and mass spectra. <sup>18</sup> The formation of an indeno-pyran ring system was not observed.

Mechanistically it can be proposed that the one-pot synthesis of the conjugated compounds 7a and 7b having the indeno-pyran nucleus is a result of a tandem reaction beginning with Sonogashira/Hagihara coupling<sup>4</sup> to form intermediate 5. Intermediate 5 is likely to undergo base catalyzed tautomerization of one of the hydroquinones to a ketylallene intermediate such as 14. A 4 + 2 intramolecular cycloaddition of 14 would result in the formation of the observed product 7. Intermediate 14 may be held in conformation 14b in preference to conformation 14a by hydrogen bonding between the OH of the hydroquinone and the oxygen of the ketylallene moiety. This proximity effect would promote the 4 + 2 cycloaddition. This postulate is consistent with the observation that 10 does not form the indeno-pyran ring system. If 10 where to undergo a hydroquinone to

ketylallene tautomerization there would be no OH group present to hold it in the conformation, 10a, that would lead to the indeno-pyran ring system.









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- <sup>1</sup>H (CDCl<sub>3</sub>, ref. at δ7.24, 300 MHz) δ -0.13 (SiMe<sub>3</sub>), 0.42 (SiMe<sub>3</sub>), 2.29, 2.31, 2.32, 2.42 (4 CH<sub>3</sub>'s) 5.23, 5.84, 6.36 (3 OH's), 7.18, 7.28, 7.38, 7.60 (4 m, for 4 aromatic H's), 8.00 (s, vinyl H).
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- 16. Crystal data for compound 7(C<sub>30</sub>H<sub>22</sub>O<sub>4</sub>). FW=446.48, monoclinic, space group P2<sub>1</sub>/c, μ = 0.088 mm<sup>1</sup>, a=8.346(2), b=14.966(3), c=17.893(4)Å, β=95.79(2)<sup>0</sup>, Z=4, V=2223.5(9)Å<sup>3</sup>, D=1.334 mg/m<sup>3</sup>, λ=0.71073Å, T=130K. Syntex P2<sub>1</sub> diffractometer. 3891 reflections were collected of which 2895 were unique (R<sub>int</sub>=0.0625). Full-matrix least squares refinement on F<sup>2</sup> of 308 parameters on all unique data yields R1=7.66% for I >2σ(I) with goodness of fit=1.083. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.
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- 18. <sup>1</sup>H (CDCl<sub>3</sub> ref. at δ 7.27, 300 MHz) δ 0.33 (s, 9H, Si(CH<sub>3</sub>)<sub>3</sub>), 2.26 (s, 3H, aromatic CH<sub>3</sub>), 7.58 (m, aromatic H), 7.31, 7.34, 7.37, 7.39 (m, all aromatic H).