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Triptycenediols by Rhodium-Catalyzed [2 + 2 + 2] Cycloaddition

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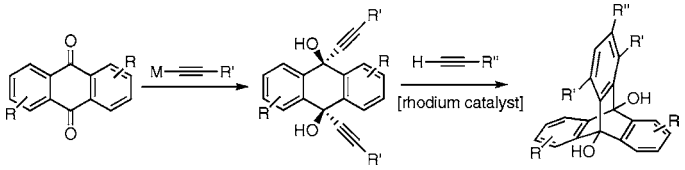
ABSTRACT

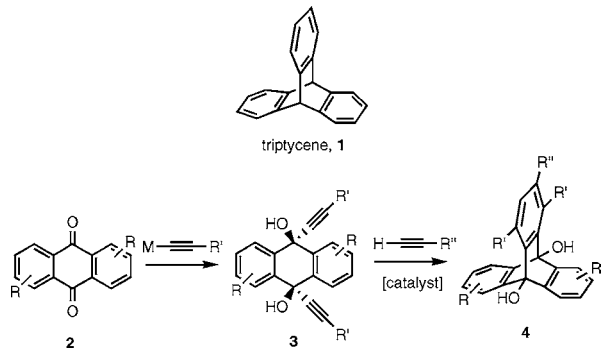


An efficient, modular synthesis of triptycene derivatives is presented, in which the triptycene ring system is constructed from readily available anthraquinone and alkyne starting materials. A rhodium-catalyzed alkyne cyclotrimerization reaction serves as the key step in this new method for the preparation of these useful unnatural products.

The rigid hydrocarbon triptycene (**1**, Scheme 1) was first prepared in 1942, in order to test the hypothesis that a radical at the bridgehead position of this ring system would be significantly less stable than the geometrically unconstrained triphenylmethyl radical.[1] Since these initial studies, the triptycene scaffold has been applied creatively in a number of settings, including studies of atropisomerism[2] and host−guest chemistry,[3] ligand design, and as a component of "molecular machines".[4] Synthetic studies have expanded this family of unnatural products to include a wide range of related structures, known collectively as iptycenes.[5] Our group has demonstrated that the "free volume" of iptycenes can be exploited to increase the thin-film quantum yield of fluorescent polymers,[6] to improve the porosity[7] and mechanical properties[8] of polymers, and to favor the alignment of fluorophores in liquid crystalline matrices.[9]

Diels−Alder reactions of anthracene with benzyne or with *p*-benzoquinone (followed by aromatization) have served as the dominant synthetic strategy for the preparation of iptycenes, both historically and in recent applications. While

Scheme 1. Structure of Triptycene and [2 + 2 + 2] Approach to Substituted Triptycenediols



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(4) (a) Godinez, C. E.; Zepeda, G.; Mortko, C. J.; Dang, H.; Garcia-Garibay, M. A. *J. Org. Chem.* **2004**, *69*, 1652−1662. (b) Kelly, T. R.; Cai, X.; Damkaci, F.; Panicker, S. B.; Tu, B.; Bushell, S. M.; Cornella, I.; Pigott, M. J.; Salives, R.; Cavero, M.; Zhao, Y.; Jasmin, S. *J. Am. Chem. Soc.* **2007**, *129*, 376−386 and references therein.
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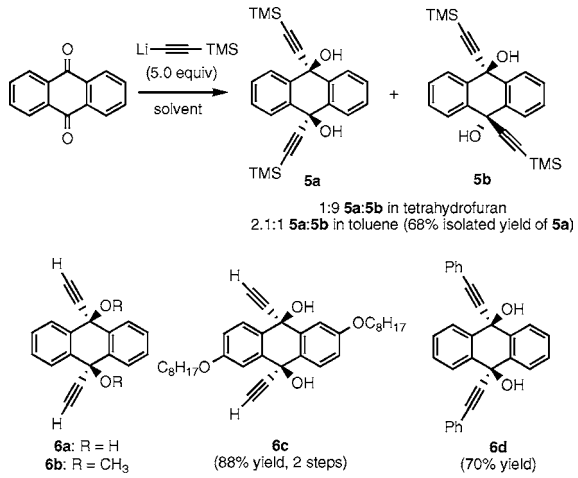
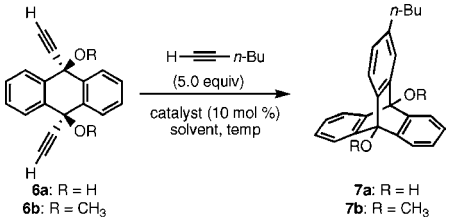
Scheme 2. *Cis*-Selective Acetylide Additions to Anthraquinones



these reactions are clearly well suited to this class of targets, limitations of this approach have become evident. In particular, the preparation of iptycenes bearing multiple side chains at defined positions often necessitates multistep, moderate-yielding syntheses. Since the presence of such substituents improves the solubility of iptycene-based polymers,[10] and may provide "handles" for the introduction of new functional components to iptycene derivatives, we have become interested in developing new, modular methods for the construction of substituted iptycenes. Herein, we describe a new application of metal-catalyzed alkyne cyclotrimerization reactions ([2 + 2 + 2] cycloadditions) that provides access to substituted 9,10-triptycenediols in 2−3 steps from readily available anthraquinones and alkynes.

Metal-catalyzed [2 + 2 + 2] cycloadditions have become a powerful synthetic tool for the construction of benzene rings, advancing at a rapid pace since the pioneering studies of Vollhardt and co-workers.[11] A range of transition metal catalysts have been identified for these reactions, including

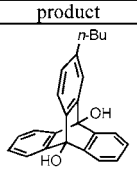
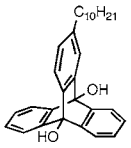
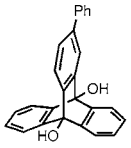
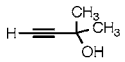
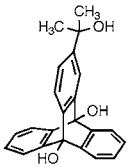
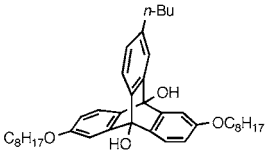
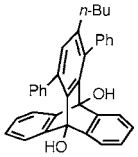
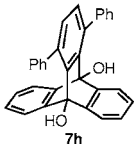
Table 1. Optimization of [2 + 2 + 2] Cycloaddition Reaction



entry	substrate	catalyst	yield[c] (%)
1	**6a**	Cp*Ru(cod)Cl[a]	10
2	**6b**	Cp*Ru(cod)Cl[a]	40
3	**6a**	$Rh(PPh_3)_3Cl$[b]	90
4	**6b**	$Rh(PPh_3)_3Cl$[b]	40

[a] Conditions: 70 °C in 1,2-dichloroethane, 14 h. [b] Conditions: 100 °C in toluene, 14 h. [c] Isolated yield on 0.1 mmol scale.

Table 2. Preparation of Substituted Triptycenediols by Rhodium-Catalyzed [2 + 2 + 2] Cycloaddition[a]

diyne	alkyne	product	yield[b]
6a	H—n-Bu	 **7a**	95%
6a	H—$C_{10}H_{21}$	 **7c**	86%
6a	H—Ph	 **7d**	73%
6a		 **7e**	95%
6c	H—n-Bu	 **7f**	81%
6d	H—n-Bu	 **7g**	99%
6d	norbornadiene[c]	 **7h**	91%

[a] General conditions: 5 mol % of $Rh(PPh_3)_3Cl$, 2.5 equiv of alkyne, toluene, 100 °C. [b] Isolated yield, 0.25 mmol scale. [c] 2.5 mol % of $[Rh(cod)Cl]_2$, 5 equiv of norbornadiene, toluene, 100 °C.

complexes of cobalt, nickel, ruthenium, rhodium and palladium.[12] We envisioned that a [2 + 2 + 2] cycloaddition of diyne **3** with substituted alkynes could generate the triptycene ring system (Scheme 1). In turn, diyne **3** would be prepared by a cis-selective addition of two equivalents of metal acetylide to an anthraquinone (**2**), an attractive starting point since many anthracene derivatives employed in Diels−Alder preparations of triptycenes are themselves derived from anthraquinones. The identification of a suitable catalyst for the proposed [2 + 2 + 2] cycloaddition, and of reaction conditions for the diastereoselective preparation of

cis-diol **3** were challenges to be addressed in order to implement this synthetic plan.

We studied the addition of lithium (trimethysilyl)acetylide to anthraquinone (Scheme 2) and found that the diastereoselectivity of this reaction is solvent dependent. Whereas the addition is highly trans-selective (>9:1 trans/cis) when carried out in tetrahydrofuran, moderate selectivity for the cis isomer was observed when toluene was used as solvent. Separation of the diastereomers was achieved by column chromatography, resulting in the isolation of diastereomerically pure **5** in 64% yield.[13] Desilylation (KOH, THF/CH_3OH, 80%) provided terminal diyne **6a**, which served as the test substrate for the optimization of conditions for the metal-catalyzed [2 + 2 + 2] cyloaddition, along with methyl ether **6b**. Alkoxy-substituted **6c** and internal alkyne **6d** were prepared by similar protocols.

Ruthenium- and rhodium-based catalysts were evaluated for the reaction of **6a** and **6b** with 1-hexyne (Table 1). Although reactions of **6b** were sluggish, presumably a result of the steric influence of the methyl ether groups, **6a** reacted smoothly in the presence of Wilkinson's catalyst, yielding triptycenediol **7a** in 90% yield. The catalytic activity of Ru(Cp*)(cod)Cl (cod = cyclooctadiene) was significantly lower than that of Wilkinson's catalyst for this combination of substrates.

The scope of the rhodium-catalyzed [2 + 2 + 2] cycloaddition was evaluated with respect to both the alkyne and the diyne components. A variety of terminal alkynes, including aliphatic, aromatic, and functionalized derivatives, reacted smoothly with **6a**, yielding triptycenediols **7a**−**h** (Table 2). Alkoxy-substituted **7f** was obtained in 81% yield by reaction of **6c** with 1-hexyne. Internal alkynes, such as 4-octyne, diphenylacetylene, and bis(trimethylsilyl)acetylene, did not react with **6a** under the optimized conditions. In contrast, phenylacetylene adduct **6d** readily underwent [2 + 2 + 2] cycloaddition with 1-hexyne to provide the desired product **7g**. Furthermore, **7h**, the product of formal cycloaddition of acetylene with **6d**, was obtained by reaction with norbornadiene in the presence of $[Rh(cod)Cl]_2$, a precedented reaction that is postulated to proceed by [2 + 2 + 2] cycloaddition followed by retro-Diels−Alder reaction and expulsion of cyclopentadiene.[14]

The synthetic approach to triptycenediols presented herein thus represents an attractive alternative to Diels−Alder-based approaches, rapidly providing access to multi-substituted derivatives suitable for further functionalization. Continued investigations of the scope of this method, and applications in materials science, are attractive avenues for future studies.

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Supporting Information Available: Experimental procedures and characterization data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) X-ray crystallography of **6b** served to elucidate the configuration of **6a** and **6b**. Diols **6c** and **6d** are assigned by analogy, an assignment that is supported by diagnostic chemical shifts in the ^1H NMR spectrum (see the Supporting Information).

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