

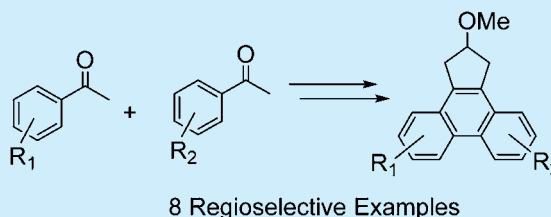
Regioselective Synthesis of Substituted Cyclopenta[*I*]phenanthrenes

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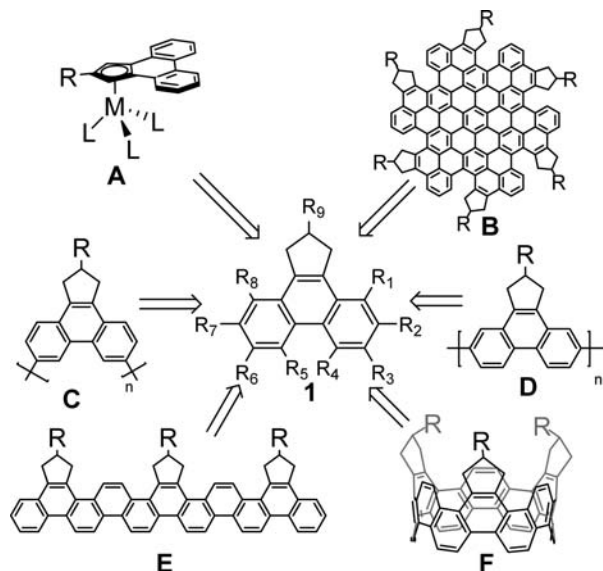
S Supporting Information

ABSTRACT: A simple and efficient synthesis of cyclopenta[*I*]phenanthrenes from substituted acetophenones provides access to polycyclic aromatics with a variety of substitution patterns. The synthesis requires only three steps from a silyl enol ether: a Mukaiyama aldol reaction followed by McMurry coupling and then Mallory photocyclooxidation to give the target phenanthrenes. Photocyclization conditions have been found that give regioselective formation of 2,7-phenanthrenes from bis(*meta*-substituted) stilbenes.



In efforts to make large, structurally well-defined aromatic molecules and conjugated polymers, phenanthrenes represent convenient intermediates: medium in size, easily characterized, stable, and potentially synthetically approachable. In particular, we have focused our efforts on cyclopenta[*I*]phenanthrenes (**1**, Scheme 1), because of the wide variety

Scheme 1. Current and Potential Uses of Cyclopenta[*I*]phenanthrenes

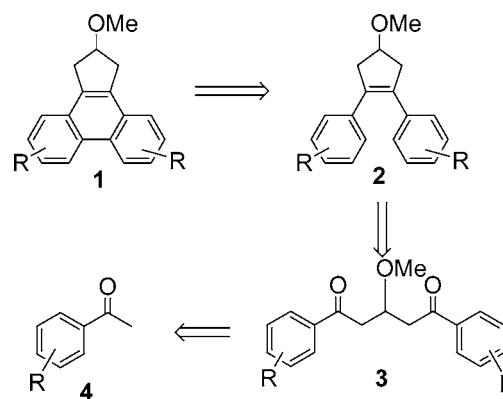


of compounds (A–F) that are accessible from this simple building block. Phenanthrenocyclopentadienes (A) serve as bulky metallocene ligands, increasing stereo- and regiocontrol in metallocene-catalyzed reactions.^{1–4} The cyclopentane ring could also allow the convenient attachment of solubilizing groups in the synthesis of structurally well-defined graphitic ribbons^{5–8} (B and E) and conjugated aromatic polymers (C and D).^{9,10} Poly(3,6-phenanthrenes) such as C have garnered interest because they allow a zigzag conformation and the

formation of helices in solution.¹¹ The cyclopentane ring also provides an attachment point for connecting phenanthrenes to a central scaffold as an approach to template-directed synthesis of three-dimensional aromatic compounds such as the elusive “buckybelts” (F).¹² While there have been numerous reports of phenanthrene synthesis in the literature,^{9,10,13–17} none provides the versatility needed to pursue these applications. Cyclopenta[*I*]phenanthrenes have been prepared by condensation of ethyl acetoacetate with phenanthroquinone¹⁸ and by intramolecular ring closure of a phenanthrene,¹⁹ biphenyl,²⁰ or tetrahydrophenanthrene.²¹ But there are no synthetic routes in the literature to cyclopenta[*I*]phenanthrenes with substituents on the phenanthrene (R₁–R₈, **1**). Here we report a new and efficient approach to prepare substituted cyclopenta[*I*]phenanthrenes regioselectively, starting from inexpensive starting materials.

As shown in the retrosynthetic analysis in Scheme 2, diphenylcyclopentene **2** provides access to phenanthrene **1** via the Mallory photocyclization reaction.^{22–24} Stilbene **2** is synthesized from a 1,5-diketone (**3**) via McMurry cou-

Scheme 2. Retrosynthesis of Cyclopenta[*I*]phenanthrenes

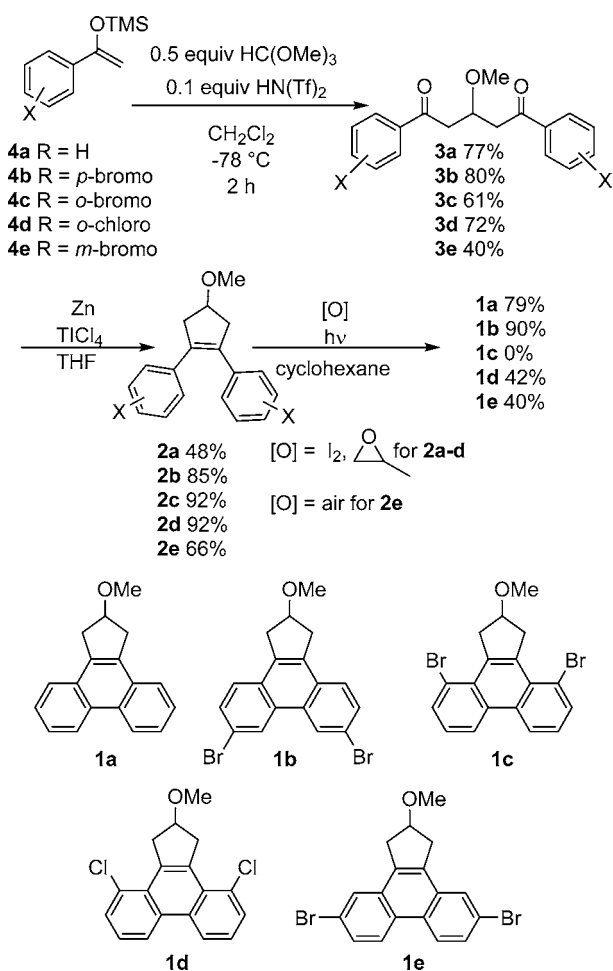


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pling.^{25,26} The desired diketone (**3**) can be generated via Mukaiyama aldol²⁷ reaction from an acetophenone (**4**) and trimethyl orthoformate. As shown in Scheme 3, this route to

Scheme 3. Synthesis of Symmetric Phenanthrenes **1a–e**

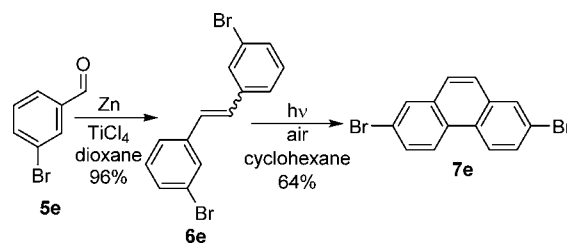


symmetric phenanthrenes is straightforward, starting from an acetophenone with the desired substituents. The Mukaiyama aldol reaction is performed in the presence of bis-(trifluoromethane)sulfonimide as an acid catalyst²⁷ with yields between 40% and 80%. The resulting diketones (**3a–e**) are then cyclized, with yields between 48% and 95%, via McMurry coupling under Mukaiyama's conditions, using Zn and TiCl₄.²⁶ Photocyclization of diarylcyclopentenes **2a** and **2b**, in the presence of iodine and excess propylene oxide, produces phenanthrenes **1a** and **1b**, respectively, in high yield.

Unfortunately, in the case of *o*-bromoacetophenone, the photocyclization reaction to give phenanthrene **1c** was unsuccessful. Reaction under irradiation at 300 nm returned only starting material. Using a shorter wavelength for irradiation did lead to cyclization to a phenanthrene but also to loss of one or both of the bromines. The steric hindrance of the *o*-bromine substituents slows the photocyclization to where the rate of photodehalogenation is competitive. Nevertheless, *o*-chloroacetophenone gives access to phenanthrene **1d**, one of only a few successful examples of the Mallory reaction on a stilbene with this substitution pattern.²⁸

In the Mallory reaction, *meta* substituents on the stilbene can end up either at the 2 or 4 position of the final phenanthrene; in most circumstances, the dihydrophenanthrene intermediates form in similar amounts, leading to a mixture of products.²⁹ However, Laarhoven and co-workers have worked out photocyclization conditions that, for stilbenes with one *meta* substituent, give selective formation of the phenanthrene with the substituent at the 2 position.³⁰ Under these conditions, when air is used as the oxidant in place of iodine, the irreversible oxidation of the dihydrophenanthrene intermediate is much slower. Because of this change in rate-determining step, and with the reaction carried out at elevated temperature, the initial photocyclization reaction becomes reversible, favoring formation of the intermediate dihydrophenanthrene that leads to product **1e**. Under these conditions, phenanthrene **1e** is formed selectively in 40% yield. These photocyclization conditions also allowed us to synthesize 2,7-dibromophenanthrene (**7e**) in two steps (Scheme 4). To our knowledge, these reactions are the first reported examples of regioselective photocyclization to a 2,7-phenanthrene.³¹

Scheme 4. Synthesis of 2,7-Dibromophenanthrene

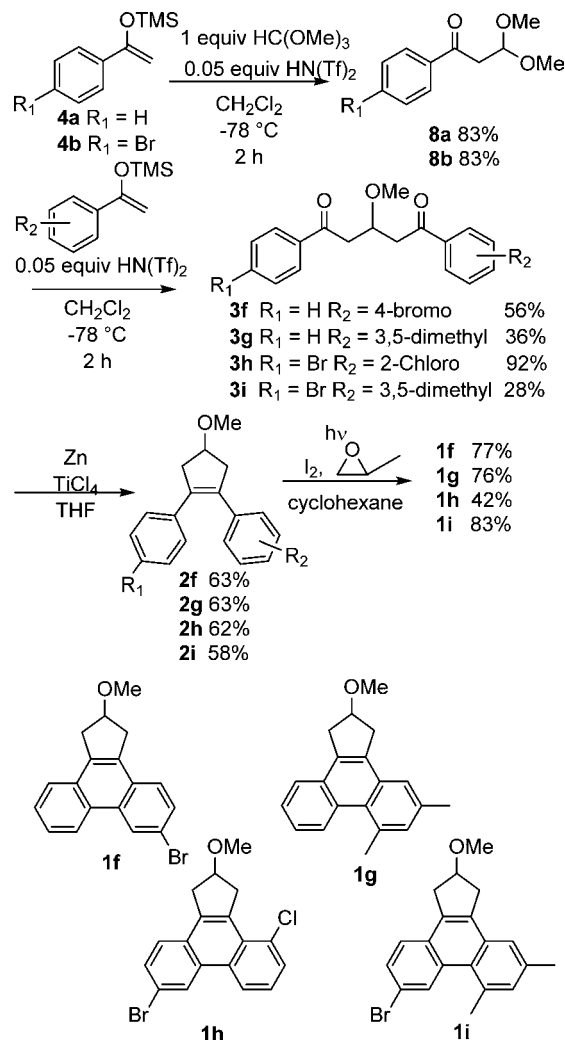


The approach described here can also be used to prepare unsymmetric cyclopenta[*l*]phenanthrenes (Scheme 5), by using 1 equiv of silyl enol ether in the initial reaction with trimethyl orthoformate and then allowing the resulting dimethyl acetal (e.g., **8a** or **8b**) to react with a different silyl enol ether in a second, analogous step. The succeeding two steps remain unchanged, so the unsymmetric phenanthrenes can each be synthesized in four linear steps from the silyl enol ether. Phenanthrenes **1f–i** were each synthesized by this method. Phenanthrenes **1g** and **1i**, with substituents in the bay region, particularly demonstrate the versatility of this method. Further functionalization at the halide substituents provides a route to additional phenanthrenes.

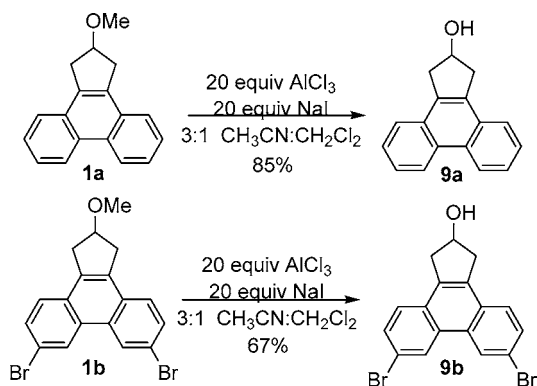
This approach provides each cyclopenta[*l*]phenanthrene as a methyl ether. Hydrolysis of the ether with sodium iodide and aluminum chloride generates the free alcohol.³² We have demonstrated this hydrolysis for phenanthrenes **1a** and **1b**, preparing alcohols **9a** and **9b** (Scheme 6). The hydrolysis of the methyl ether can also be performed at the stilbene stage if preferred for solubility reasons.

In conclusion, we have developed a versatile regioselective route to cyclopenta[*l*]phenanthrenes. A wide range of commercially available and inexpensive acetophenones can act as starting materials. This approach allows access to either symmetric or unsymmetric phenanthrenes with control over the substituents at the outer rings. The reactions tolerate chloride and methyl substituents, and *m*- or *p*-bromide substituents, with no major change in yields. We have also demonstrated conditions that selectively transform *meta*-substituted stilbenes into 2,7-phenanthrenes. The new

Scheme 5. Synthesis of Unsymmetric Phenanthrenes 1f–i



Scheme 6. Hydrolysis of the Methyl Ether



phenanthrene derivatives described here have potential use as starting materials for polymerization and as precursors to new cyclopentadienyl ligands.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs-orglett.6b02008.

Experimental details, compound characterization, and NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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