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LETTERS

Radical cyclisations to arenes for the synthesis of phenanthrenes

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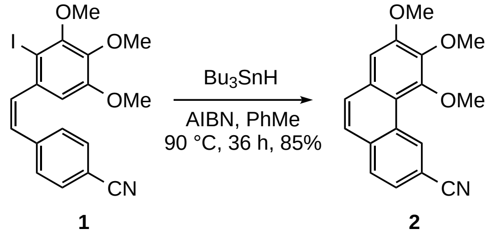
Abstract—6-*exo*/*endo*-Trig intramolecular additions of aryl radicals to electron-rich, unsubstituted and electron-deficient arenes have all been shown to proceed efficiently to give the corresponding phenanthrenes in high yield. © 2002 Elsevier Science Ltd. All rights reserved.

Phenanthrenes are commonly prepared by photocyclisation of stilbenes. When 3,3′-substituted stilbenes are employed, several regiochemical courses may be followed leading to as many as four regioisomeric products. The process is useful because electronic factors generally bias the outcome to favour one product over the other possibilities. However, little can be done to promote cyclisation via an unfavourable transition state, representing a severe limitation of the methodology.[1]

We recently faced such a problem during a total synthesis of the alkaloid toddaquinoline. Photolysis of a 3-aza-stilbene promoted cyclisation to C-4 of the pyridine moiety, whereas we required cyclisation to occur to C-2. Our means of biasing the reaction for the desired regiochemical course was to employ an intramolecular radical addition reaction mediated by cobalt.[2] Subsequently we have shown that all manner of radical cyclisation reactions to electron deficient nitrogen heteroaromatics are facile.[3] In this letter we report a further extension of the methodology to electron-rich, unsubstituted and electron-deficient arenes.[4,5]



Scheme 1.

The first cyclisation examined involved *cis*-4-cyano-2′-iodo-3′,4′,5′-trimethoxystilbene **1** which, on treatment with tributyltin hydride under standard radical forming conditions, was smoothly transformed into 3-cyano-5,6,7-trimethoxy-phenanthrene **2** in 85% yield (Scheme 1). Cyclisations were equally facile for the 2- and 3-cyano derivatives **3** (Scheme 2) and **5**, in the latter case giving rise to an easily separable 1:1 mixture of 2- and 4-cyano-5,6,7-trimethoxyphenanthrenes **6** and **7** (Scheme 3).

Our focus next turned to cyclisations involving the addition of an aryl radical to unsubstituted and electron-rich arenes. Pleasingly, cyclisation to a phenyl ring proved facile with *cis*-2′-iodo-3′,4′,5′-trimethoxystilbene **8** being transformed into the corresponding phenanthrene **9** in excellent yield (Scheme 4).[6]

Cyclisations to electron-rich arenes were equally efficient. Thus, when *cis*-2′-iodo-3,3′,4′,5′-tetramethoxystilbene **10** was treated with tributyltin hydride under standard radical forming conditions, a 1:1 mixture of 2,3,4,7-tetramethoxyphenanthrene **11** and 2,3,4,5-tetramethoxyphenanthrene **12** resulted (Scheme 5)[7] suggesting that substitution at C-3 plays only a minor role in determining the regiochemical course of such reactions.

In light of these experiments, it was curious to find that a combination of electron donating groups at C-3 and C-4 in the acceptor ring had a marked influence on the regiochemical course of the reaction. For example, when *cis*-2′-iodo-3,4-methylenedioxy-3′,4′,5′-

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Keywords: radicals and radical reactions; aromatic chemistry; phenanthrenes.

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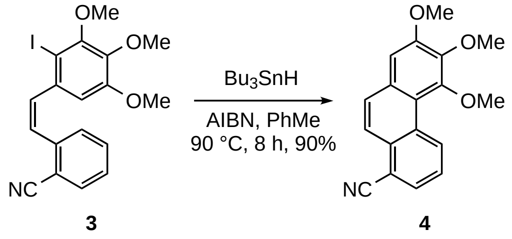
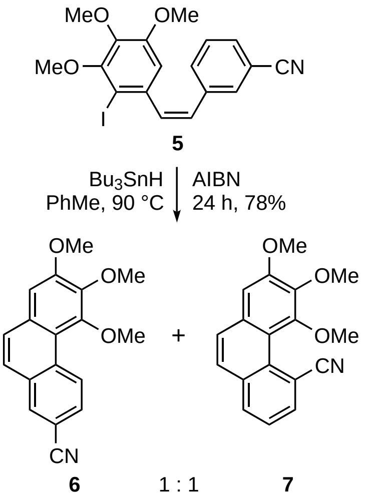
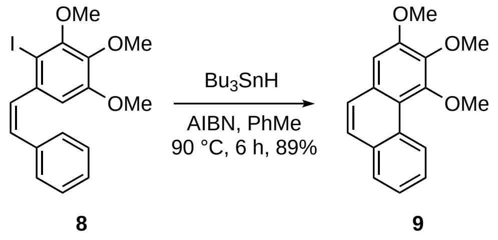


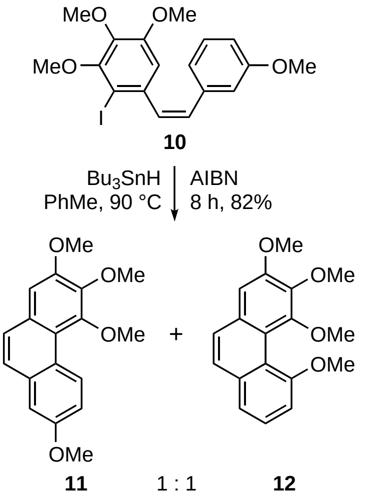
Scheme 2.



Scheme 3.



Scheme 4.

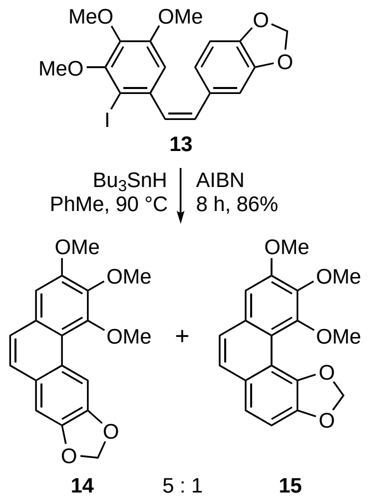


Scheme 5.

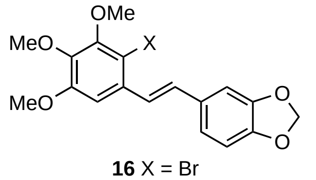
trimethoxystilbene **13** was subjected to standard tin mediated radical cyclisation conditions, the dominant product, formed in 72% yield, was 2,3-methylenedioxy-3′,4′,5′-trimethoxyphenanthrene **14** with 3,4-methylenedioxy-3′,4′,5′-trimethoxyphenanthrene **15** accounting for just 14% of the total mass balance (Scheme 6).

At this juncture it is worth noting that Aidhen and Narasimhan reported the conversion of *trans*-bromostilbene **16** into phenanthrene **14** in 32% yield by reaction with tributyltin hydride.[8] This is in stark contrast to the reaction of *trans*-iodostilbene **17** which gave **14** in less than 5% yield and *trans*-stilbene **18** in 68% yield. The dichotomy suggests that for 2-halostilbenes carbon to iodine bond homolysis outpaces addition of the tributyltin radical to the alkene, which in turn outpaces carbon to bromine bond homolysis.[3,9]

In conclusion, we have shown that intramolecular 6-*exo*/*endo*-trig radical cyclisations of *cis*-2-iodostilbenes are facile processes providing a rapid and predictable method for the synthesis of phenanthrenes in high yield. Cyclisations follow the non-reducing radical cyclisation pathway, with aromaticity in the radical acceptor being re-established through overall loss of a hydrogen atom.[5] The radical acceptor may be electron-rich, unsubstituted or electron-deficient and when this is substituted at C-2, cyclisation occurs to C-6 exclusively. By contrast, substitution at C-3 appears to have little influence on the regiochemical course of the reaction unless a substituent is also present at C-4. We are presently exploring further facets of this chemistry in the hope of delineating the origin of that effect and are seeking to apply the methodology in target oriented synthesis.



Scheme 6.



16 X = Br
17 X = I
18 X = H

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