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Phenanthrene type heterocycles via Rh(I) catalysed [2+2+2]-cycloaddition and Pd(0) catalysed arylation

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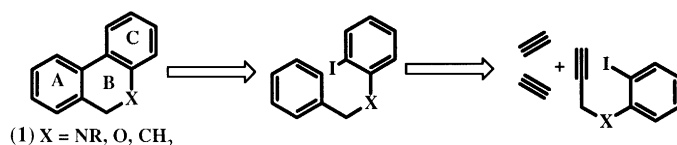
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Abstract

A simple procedure for the preparation of the phenanthrene type heterocycles is described, based on Rh(I) catalysed formation of benzene rings via a [2+2+2]-cycloaddition reaction followed by Pd(0) catalysed intramolecular arylation of the newly formed aromatic functionality. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: rhodium; cycloaddition; palladium; arylation; cyclisation; phenanthrene type heterocycles.

The phenanthrene type skeleton (**1**) is present in many natural products either in the carbocyclic¹ or heterocyclic form.² The *Amaryllidaceae* alkaloids² are a group of such natural products having in most cases a phenanthridine type (X=N) structure, whilst other natural products have oxygen (X=O) in place of nitrogen.² Ring A is almost always aromatic while the oxidation level of ring C varies. We reported earlier the synthesis of some of these alkaloids either by using intramolecular coupling of a bisaryl iodide in the presence of (Me₃Sn)₂ and a palladium catalyst^{3a} or by using the Heck reaction.^{3b} Our further interest in this area has resulted in the development of a simple procedure for the synthesis of type (**1**) structures based on Rh(I) catalysed [2+2+2]-cycloaddition⁴ and Pd(0) catalysed arylation⁵ of the newly formed aromatic functionality as shown in Scheme 1.

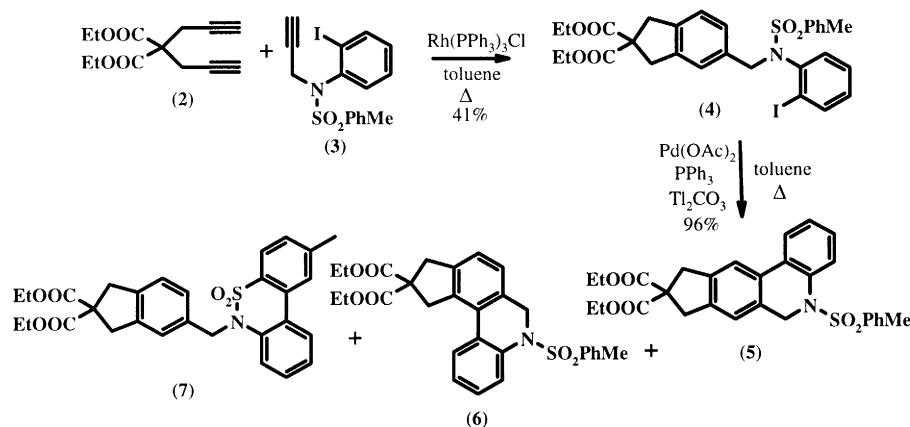


Scheme 1.

Thus, heating the diyne (**2**) and alkyne (**3**) in toluene at 80°C in the presence of Wilkinson's catalyst afforded (**4**) in 41% yield (Scheme 2). This product was further cyclised in the presence of Pd(OAc)₂ (10 mol%), PPh₃ (20 mol%) and Tl₂CO₃ (1.5 equiv.) in boiling toluene to produce a 1:5.7:8.3 mixture of (**5**),

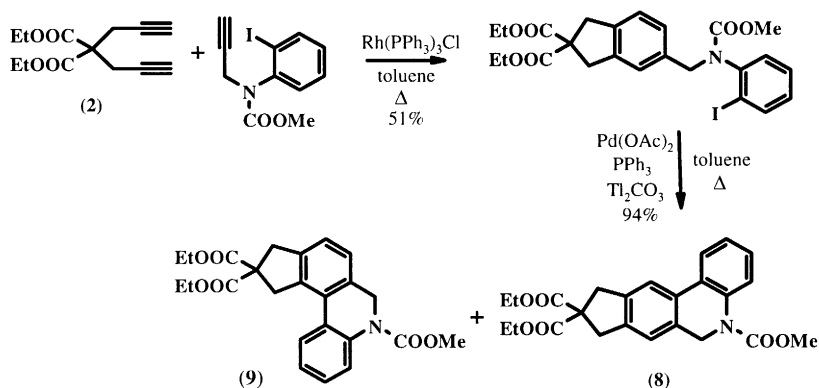
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(6) and (7) in almost quantitative yield. Products (5) and (6) arise by regioselective arylation of the *ortho* positions of the newly formed aromatic ring, while (7) arises by arylation of the tosyl group. The ratio of the products indicates slightly higher reactivity of the electron deficient tosyl ring but obviously the difference is not significant.



Scheme 2.

The carbomethoxy group was used as an *N*-protecting group instead of tosyl in order to minimise the number of products. Performing the same reaction sequence the two regioisomeric 5,6-dihydrophenanthridine derivatives (8) and (9) were obtained in good overall yield and in a 1 to 5.7 ratio, respectively (Scheme 3).

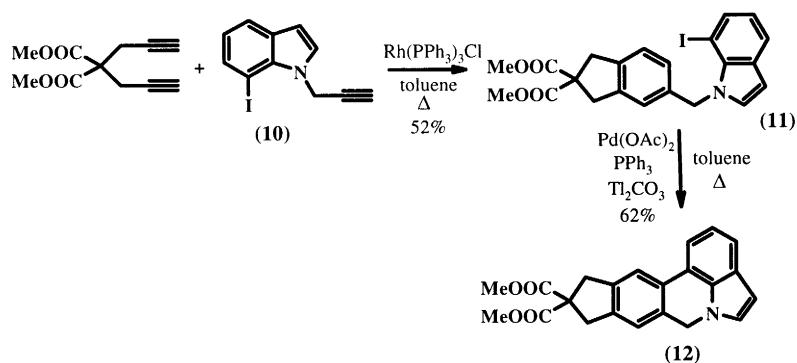


Scheme 3.

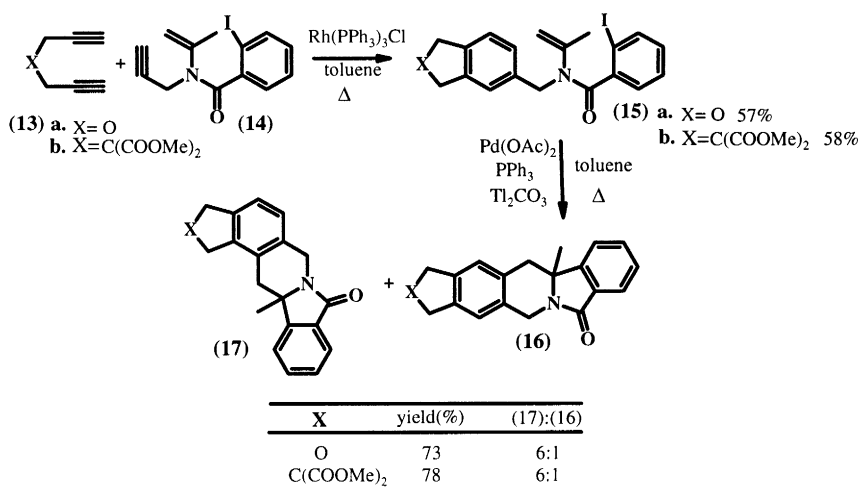
When 1-propargyl-7-iodoindole (**10**)⁶ was used as the alkyne component the [2+2+2]-cycloaddition afforded (11) in 52% yield. In this case the Pd(0) catalysed cyclisation produced only regioisomer (12) in 62% yield (Scheme 4).

It was also demonstrated that this methodology could be equally efficient when applied to the preparation of polycyclic products (Scheme 5). Thus (15), obtained from diene (13) and alkyne (14), underwent biscyclisation in the presence of a Pd-catalyst to afford (16) and (17) in good yield.

The scope of this synthetic procedure was further investigated by using functionalised *O*-analogs (Scheme 6). Thus, heating (13a) and vanillin derivative (19) under the conditions used for [2+2+2]-cycloaddition afforded (20) in 64% yield. The intramolecular Pd(0) catalysed arylation of (20) produced a 1:6 mixture of (21) and (22) in 82% yield. The use of pyridine derivative (23) proved to be equally



Scheme 4.



Scheme 5.

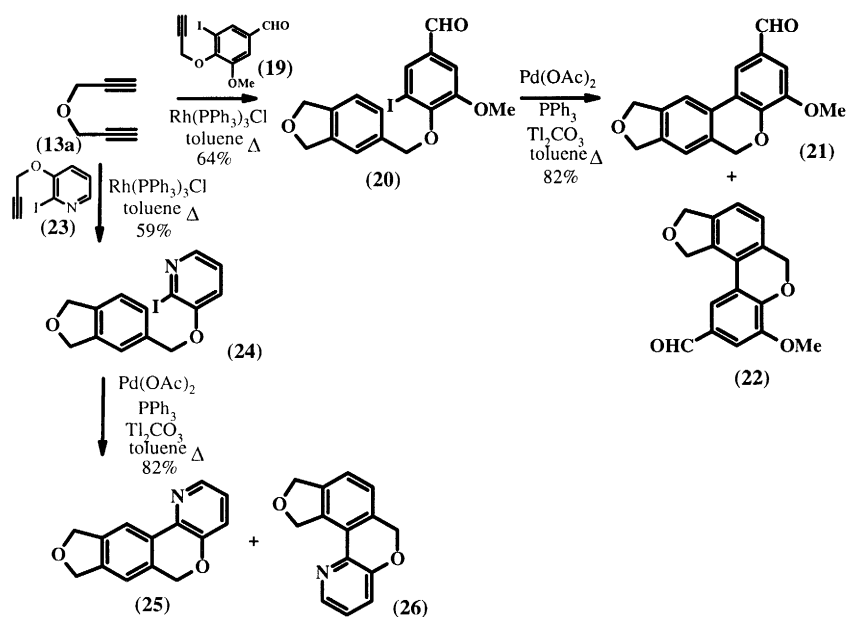
efficient producing first (**24**) in 59% yield and then after cyclisation affording a 1:1 mixture of (**25**) and (**26**) in 82% yield.

The palladium catalysed arylation step can be rationalised by two possible mechanistic pathways involving formation of either Pd(IV) or Pd(II) species. Pd(IV)⁷ would be formed via the oxidative addition of initially obtained ArPd(II)I into the aromatic C–H bond, while Pd(II) would result from nucleophilic displacement at palladium.⁸ Reductive elimination from either of these produces the expected product. Very small difference in reactivity of two electronically different rings, as shown in Scheme 2, suggest the intermediate formation of Pd(IV).

In conclusion, we have demonstrated a simple synthetic procedure for the preparation of phenanthrene type heterocycles. The two step procedure, involving sequential Rh(I) catalysed [2+2+2]-cycloaddition and Pd(0) catalysed arylation, produces polycyclic products in acceptable yields, showing tolerance towards a range of functional groups. The Pd(0) catalysed arylation shows a certain degree of substrate dependant regioselectivity.

Acknowledgements

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Scheme 6.

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