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2-Oxobenzo[*h*]chromene: a novel entry for the concise and efficient synthesis of indeno[1,2-*c*]phenanthrenes☆

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This Letter is dedicated to Professor R. P. Rastogi, on the occasion of his 81st birthday

Abstract—An efficient and concise synthesis of 7-*sec*-amino-5,13-dihydro-6*H*-indeno[1,2-*c*]phenanthrene-8-carbonitriles is described through base catalyzed ring transformation of 4-*sec*-amino-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles with 1-indanone in moderate to good yields.

Polycyclic aromatic hydrocarbons (PAHs) are environmental pollutants and can be introduced into the atmosphere through incomplete combustion of organic matters,[1] fossil fuels,[2] and also from tobacco smoke.[2] Most PAHs are potent carcinogens and are metabolized by cytochrome P-450 and epoxide hydrolase to bay region epoxides responsible for carcinogenicity.[3–5] These metabolites covalently bind to cellular DNA through a C–N linkage, resulting in mutations, leading to tumor induction.

The steric constraints in the bay region are believed to enhance the carcinogenicity.[6,7] More polar metabolites play a significant role in carcinogenesis, particularly those which have more than one bay or fjord region.

Through an extensive literature survey it is evident that the chemistry of 9*H*-indeno[2,1-*c*]phenanthrene (**I**) is little developed[8] in comparison to 13*H*-indeno[1,2-*c*]-phenanthrene (**II**). The derivatives of 9*H*-indeno[2,1-*c*]-phenanthrene (**I**) are mostly noncarcinogenic but the mutagenic properties of 13*H*-indeno[1,2-*c*]phenanthrenes has not been explored enough due to the non-availability of compounds of this ring system. Through extensive study of the carcinogenic properties of various polycyclic aromatic hydrocarbons, it was found that the planarity of the ring is one of the factors behind their mutagenic property. We decided to prepare partially reduced indeno[1,2-*c*]phenanthrenes (**III**) to distort the planarity and to reduce the binding affinity of their metabolites with cellular DNA in order to diminish the mutagenic properties (Fig. 1). Thus, we planned to prepare 7-*sec*-amino-5,13-dihydro-6*H*-indeno[1,2-*c*]phenanthrene-8-carbonitriles (**III**). Reduction of the olefinic bond between C5–C6 in **II** would result in compound **III**. Partial catalytic reduction of **II** is not easy and may lead to a complex mixture. Thus, we planned our synthetic strategy to start with a precursor having a reduced olefinic bond. We contemplated achieving our objective by using 4-*sec*-amino-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **4** as precursors for the ring transformation reactions. The precursors were prepared in two steps through base induced condensation–cyclization of 1-tetralone **2** and methyl 2-cyano-3,3-dimethylthioacrylate **1** followed by amination of

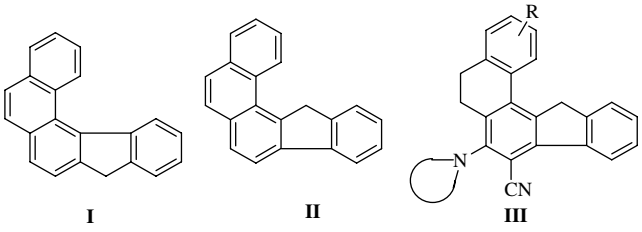

Figure 1. 9*H*-Indeno[2,1-*c*]phenanthrene (**I**), 13*H*-indeno[1,2-*c*]phenanthrene (**II**), 5,13-dihydro-6*H*-[1,2-*c*]phenanthrenes (**III**).

Keywords: Indeno[1,2-*c*]phenanthrenes; 2-Oxobenzo[*h*]chromenes; Ring transformation.
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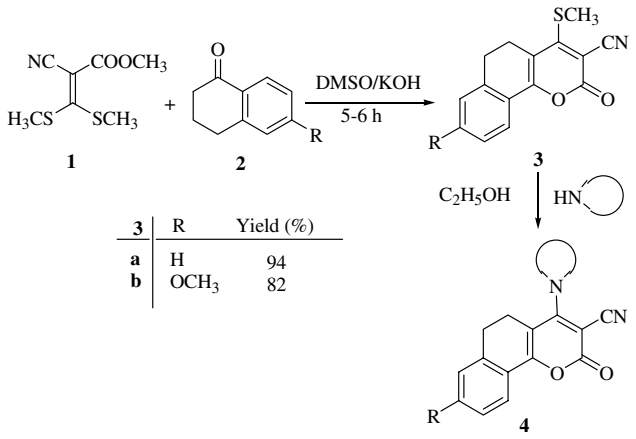
the resulting 4-methylsulfanyl-2-oxo-5,6-dihydro-2*H*-benzo[*h*]chromene-3-carbonitriles **3** with a secondary amine in refluxing ethanol in excellent yields (Scheme 1, Table 1).[9]

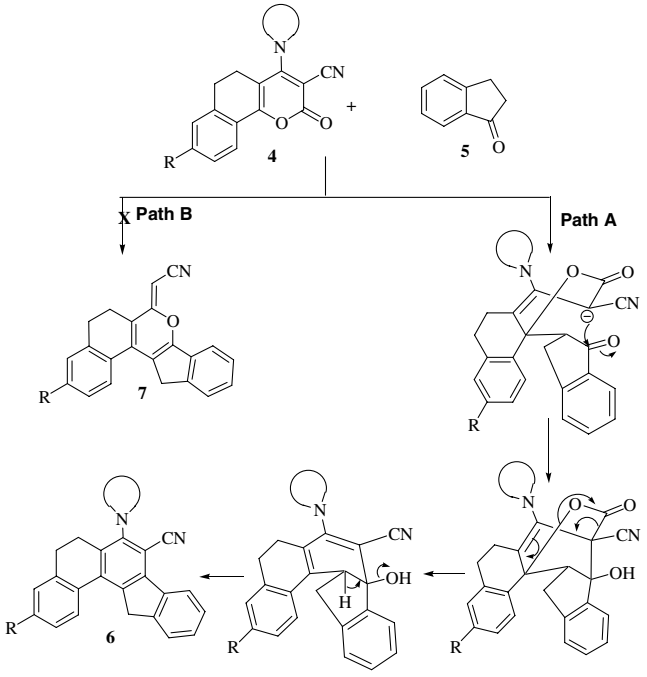


3	R	Yield (%)
a	H	94
b	OCH_3	82

Scheme 1.

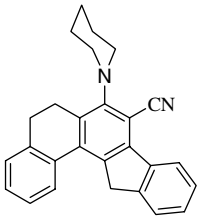
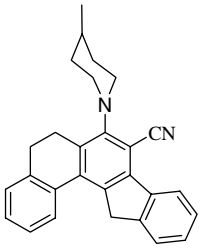
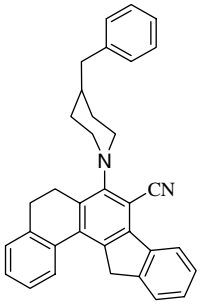
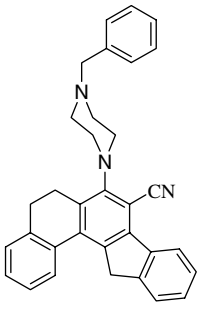
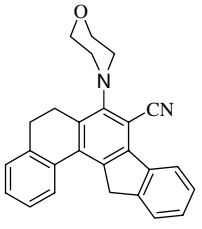
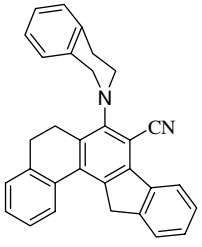
Table 1. Yields of the different 4-*sec*-amino-2-oxo-5,6-dihydrobenzo[*h*]-chromenes **4**

4		R	Yields (%)
a	Piperidin-1-yl	H	96
b	4-Methylpiperidin-1-yl	H	91
c	4-Benzylpiperidin-1-yl	H	81
d	4-Benzylpiperazin-1-yl	H	79
e	4-Morpholin-1-yl	H	88
f	Tetrahydroisoquinolin-2-yl	H	82
g	Piperidin-1-yl	OCH_3	85
h	4-Methylpiperidin-1-yl	OCH_3	71



Scheme 2. Mechanism involved in the formation of **6** and alternative product **7**.

Table 2. Yields of 7-*sec*-amino-5,13-dihydro-6*H*-indeno[1,2-*c*]phenanthrene-8-carbonitriles **6**

6	Product	Yield (%)
a		68
b		71
c		66
d		75
e		64
f		60