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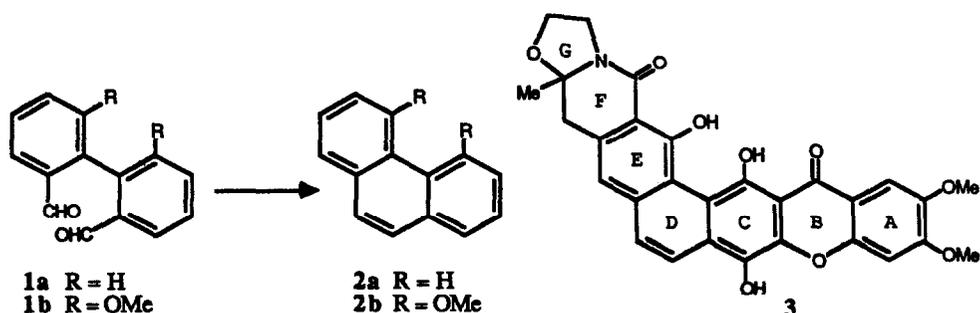
NEW ALKENE-FORMING REACTION: PHENANTHRENES FROM 2-(2-FORMYLPHENYL)BENZALDEHYDE BIS-TOSYLHYDRAZONE DECOMPOSITION

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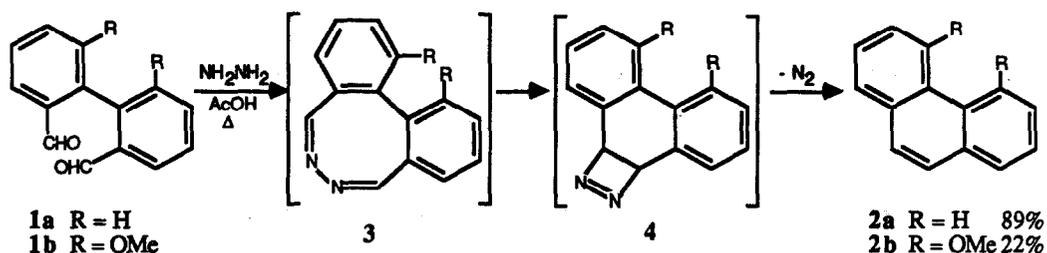
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Abstract: Heating the dilithium or disodium salts of the bistosylhydrazones **5ab** of the 2-(2-formylphenyl)benzaldehydes **1ab** affords the phenanthrenes **2ab** in fair to good yields.

There are several procedures known for the conversion of a dicarbonyl compound into an alkene, often a useful synthetic process. Best known among these is the treatment of the dicarbonyl compound with low-valent metals to produce the pinacol and from it the alkene, often in the same step. For example, a procedure involving low-valent titanium was developed simultaneously and independently by McMurry,² Mukaiyama,³ and Wolochowicz⁴ and has been used by many others.⁵ Recently we had need of such a transformation in the conversion of a 2-(2-formylphenyl)benzaldehyde **1** into the corresponding phenanthrene **2**, especially in the more sterically demanding case **1b** when two *ortho*-methoxy group were present to give the 4,5-dimethoxyphenanthrene **2b**, as a model study for the preparation of the CDE ring system in cervinomycin **3**, a novel antibiotic discovered recently.^{6,7} We report here the development of a new method for this transformation.

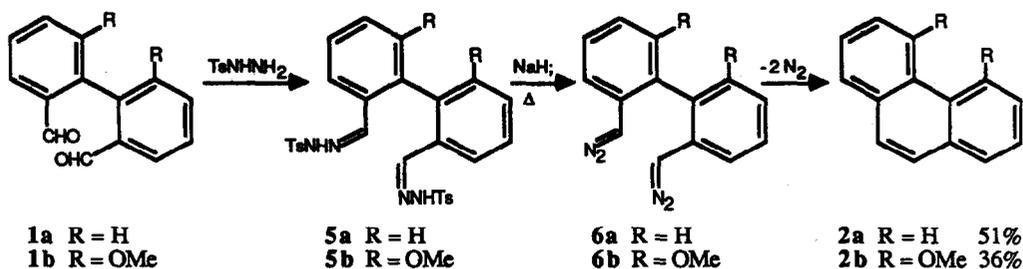


A little-used method for the formation of phenanthrene **2a** from the dialdehyde **1a** is due to Bacon,⁸ who heated a solution of **1a** and hydrazine in acetic acid to give **2a** in 95% yield. In our hands, slow addition over 1 h of the dialdehyde **1a** to the hydrazine/acetic acid solution afforded an 89% yield of **2a**. When applied to the dialdehyde **1b**¹⁰ (prepared in 47% yield by a Ullmann-Ziegler coupling⁹ of 2-iodo-3-methoxybenzaldehyde cyclohexylimine followed by hydrolysis), this method gave only 11% of the more sterically congested 4,5-dimethoxyphenanthrene **2b**.¹¹ Although the mechanism of this reaction is unknown, it probably involves formation of the cyclic azine **3** (in this case a dibenzo[*d,f*],[1,2]diazocine) which then cyclizes to give **4** and loses nitrogen to give the phenanthrene **2**. Since formation of this cyclic azine is hindered in this case due to the substituents at the 1 and 12 positions, we reasoned that even slower addition of the dialdehyde **1b** to the hydrazine/acetic acid solution would produce more of this cyclic azine and less bis-hydrazone from intermolecular reactions. Addition of **1b** over 4h raised the yield of the



desired phenanthrene **2b** to 22%. Even slower addition did not further improve the yield. We therefore turned to the titanium coupling as described by McMurry.^{2a} Addition of **1a** over 24h at 80°C to a suspension of $\text{TiCl}_3(\text{DME})_{1.5}$ and Zn/Cu couple (which had been heated in DME at 80°C for 4h) followed by refluxing at 120°C for 8 h gave a 23% yield of **2a**. However, similar treatment of **1b** (35h addition) gave none of the desired product **2b** but rather returned 75% of the starting material **1b** along with about 25% of a polymeric material.¹²

With the failure of these two routes to produce the desired phenanthrene **2b** in reasonable yield, we decided to investigate other routes from **1b** to **2b**. Since it is well known that the salts of aldehyde tosylhydrazones produce the diazoalkanes on heating, we reasoned that it might be possible to generate the bis-diazoalkane, e.g., **6a**, from the bis-tosylhydrazone, e.g., **5a**, which might then cyclize to the phenanthrene **2a** with loss of two moles of nitrogen. While this mechanistic analysis may well be incorrect, the process does work, as described below. The dialdehyde **1a** was treated with tosylhydrazine to give the bis-hydrazone **5a** in 64% yield along with 15% of phenanthrene **2a**. The hydrazone **5a** was then treated with sodium hydride in THF at 25°C for 3h and then the mixture heated to reflux for 3h to produce an additional 36% of phenanthrene **2a** (57% for conversion of **5a** into **2a**), bringing the overall yield of **2a** from **1a** up to 51%. Formation of the lithium anion (*n*BuLi, THF:Et₂O 1:1, -78°C) of **3a** followed by stirring at 25°C for 37h and heating at 70°C for 2h gave a 29% yield of **2a** (overall yield of **2a** from **1a** by this route is



34%). However, addition of an equivalent of $\text{CuI}\cdot\text{P}(\text{OEt})_3$ to the lithium anion of **5a** at -78°C followed by stirring at 25°C for 17h and heating at 70°C for 4h gave **2a** in 80% isolated yield (overall yield of 66% from **1a**). Thus this method compares favorably with the Bacon procedure⁸ for simple phenanthrene formation.

Application of this method to the more sterically encumbered phenanthrene **2b** was then studied. Treatment of the dialdehyde **1b** with tosylhydrazine gave the corresponding hydrazone **5b** which was then treated with sodium hydride in THF. The resulting bis-salt was stirred at 25°C for 4h and then heated to 85°C for 12h to produce the desired 4,5-dimethoxyphenanthrene **2b** in 36% yield. This represents the best overall yield we have achieved to date for the conversion of **1b** to **2b**. Preparation of the lithium salt of **5b**, addition of one equivalent of $\text{CuI}\cdot\text{P}(\text{OEt})_3$, followed by stirring at 25°C for 9h and heating at 80°C for 1h gave **2b** in only 21% yield. Thus in this case, the sodium salt gives better results.

Thus we have developed a new method for alkene formation from dialdehydes which is at present the method of choice for the preparation of sterically hindered phenanthrenes such as **2b**.

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- On leave from Japan Tobacco Company, Inc.
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