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Synthesis of Phenanthropyrroles and Phenanthrolinopyrroles from Isocyanoacetates: An Extension of the Barton-Zard Pyrrole Condensation

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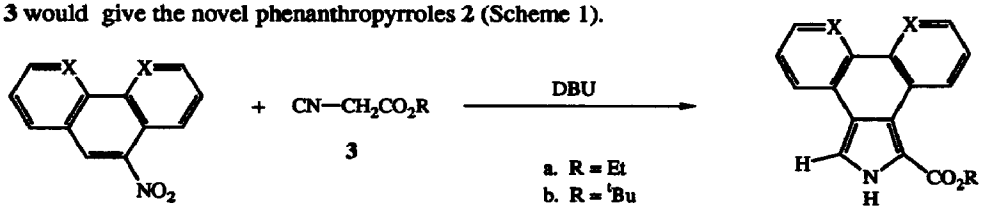
Abstract: *9-Nitrophenanthrene (1) and 5-nitro-1,10-phenanthroline (4) condensed with esters of isocyanoacetic acid in the presence of one equivalent of DBU to give the corresponding phenanthropyrroles 2 and phenantholinopyrroles 5, respectively, in excellent yields.*

Esters of pyrrole-2-carboxylic acids have been extensively utilized as intermediates in the total synthesis of porphyrins.[1] These valuable intermediates are commonly prepared by variations on the Knorr pyrrole condensation,[1,2] although several other routes to these systems have been developed.[3,4] A particularly exciting new method for preparing 5-unsubstituted pyrrole-2-carboxylates from nitroalkenes and esters of isocyanoacetic acid (the Barton-Zard pyrrole condensation) has been described[4] and this methodology has been extensively used in the porphyrin area.[5-10] We have been investigating the synthesis and properties of porphyrins fused to polycyclic aromatic systems,[8,11] and speculated that the Barton-Zard approach might be extended to the reaction of certain nitroaromatic compounds. In particular, 9-nitrophenanthrene (**1**) would be expected to exhibit extensive nitroalkene character and it was anticipated that base catalyzed condensation of **1** with isocyanoacetate esters **3** would give the novel phenanthropyrroles **2** (Scheme 1).



1 X = CH
4 X = N

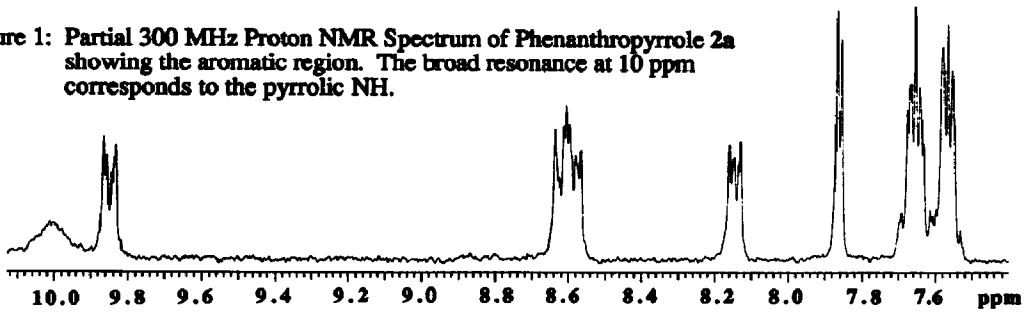
SCHEME 1

2 X = CH
5 X = N

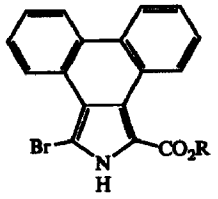
9-Nitrophenanthrene (**1**)[12] was reacted with 1 equivalent of ethyl isocyanoacetate (**3a**)[13] in the presence of the non-nucleophilic base DBU in 50% isopropyl alcohol/THF at room temperature for 24 hrs. The expected phenanthropyrrole **2a** was formed in excellent yield together with some of the corresponding isopropyl ester. When the reaction was repeated in the absence of isopropyl alcohol, the required ethyl ester **2a** was isolated after crystallization from toluene as an off-white powder in 86% yield, mp 143-144°C. The 300 MHz proton NMR spectrum of **2a** showed the presence of 9 aromatic protons (Figure 1), and the pyrrole CH appeared as a doublet (J = 3.4 Hz) at 7.82 ppm. *tert*-Butyl isocyanoacetate (**3b**)[14,15] was similarly reacted with **1** and the related *tert*-butyl ester **2b** (mp 178-179°C) was obtained, following crystallization from carbon tetrachloride, in 65% yield.

1,10-Phenanthrolines exhibit a rich coordination chemistry and the formation of phenanthrolinopyrroles was also of great interest. 5-Nitro-1,10-phenanthroline (**4**)[16] was reacted with ethyl isocyanoacetate in the presence

Figure 1: Partial 300 MHz Proton NMR Spectrum of Phenanthropyrrole **2a** showing the aromatic region. The broad resonance at 10 ppm corresponds to the pyrrolic NH.



of DBU and gave the required phenanthrolinopyrrole **5a** in 53% yield, mp 290°C dec. ^{1}H NMR ($CDCl_3$): δ 1.52 (3H, t, CH_2CH_3), 4.53 (2H, q, OCH_2), 7.59 (1H, dd), 7.69 (1H, dd), 7.86 (1H, d, J = 3.3 Hz, pyrrole-CH), 8.40 (1H, dd), 9.07 (1H, dd), 9.16 (1H, dd), 10.18 (1H, dd), 10.3 (1H, br, NH). The *tert*-butyl ester **5b** was also obtained in excellent yield (83%) from the reaction of **4** with **3b**. Benzyl ester **5c** has also been prepared from benzyl isocyanoacetate (**3c**),[9] but in this case more vigorous conditions were required. However, **4** reacted with 1.8 equiv. of **3c** and DBU in refluxing isopropyl alcohol/THF to give the benzyl ester **5c** in 73% yield.



6 X = CH

The phenanthropyrroles **2a,b** and the phenanthrolinopyrroles **5a-c** are stable crystalline compounds and, as expected, these systems undergo electrophilic substitution at the pyrrolic CH. For instance, reaction of **2a** with one equivalent of bromine in acetic acid/chloroform gave the corresponding bromo compound **6** in excellent yield.

The results in this study demonstrate that the Barton-Zard approach can be applied to the synthesis of polycyclic heterocycles from suitably reactive nitroaromatic compounds and these structures may have value in porphyrin synthesis.

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