

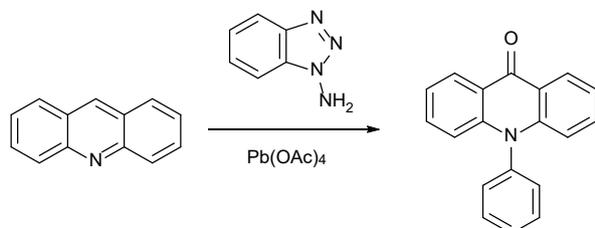
The reaction of benzyne with acridine

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Key words: 1-aminobenzotriazole, benzyne, lead tetraacetate, acridine, phenazine

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Abstract

Treatment of acridine with 1-aminobenzotriazole and lead tetraacetate gives N-phenylacridone via a non-concerted benzyne reaction. A mechanism is proposed by which an initial adduct is converted into this product.

Introduction

The oxidation of 1-aminobenzotriazole **1** with lead tetraacetate by the method of Rees and Campbell allows the rapid generation of benzyne **2** under mild conditions (Figure 1).¹⁻³

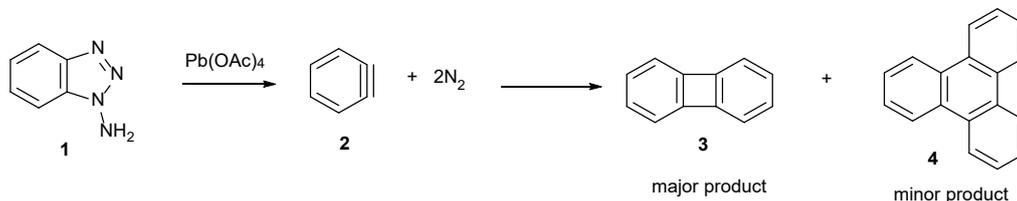


Figure 1 The oxidation of 1-aminobenzotriazole **1** with lead tetraacetate.

In the absence of other intercepting reagents biphenylene **3** is formed with a minor amount of triphenylene **4**. Of interest to us was the failed attempts to react benzyne **2** with either acridine **5** or phenazine **7** to give azatriptycene **6** and diazatriptycene **8** respectively (Figure 2)² Adducts **6** and **8** are interesting targets for synthesis² because of their triptycene derived shape and the basic nitrogens arising from their orthogonality to the three benzene rings.

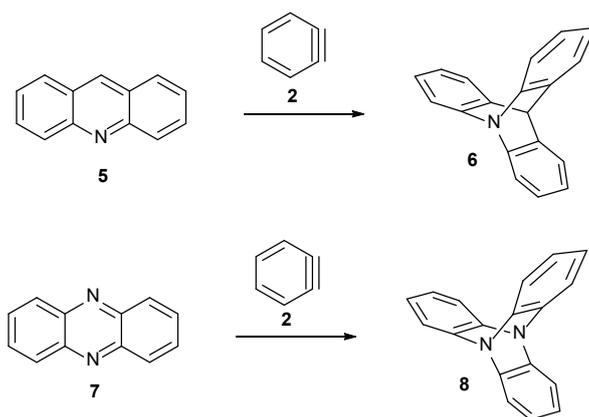


Figure 2 A failed attempt to react benzyne **2** with acridine **5** or phenazine **7**.²

Benzyne **2** has a high reactivity and so we thought that these reactions should work by a concerted or a non-concerted reaction mechanism. Rees did report an unknown compound from the lead tetraacetate oxidation of 1-aminobenzotriazole **1** in the presence of acridine **5** but it was not characterised, only given a mp of 270-271 °C.² This is above the mp of acridine **5** of 107-110 °C. The reaction with phenazine **7** was reported to give a complex mixture of red, blue, and purple crystals.² Azatriptycene **6** has been prepared by a tandem benzyne method.⁴ The oxidation of 1-aminobenzotriazole **1** with lead tetraacetate has been widely studied for the generation of benzyne intermediates.⁵⁻⁸

Discussion

The experimental method is straightforward but the chromatographic purification is not. Biphenylene **3** is easily separated from the reaction but care must be taken to isolate a low yield of a product and separate it from an excess of acridine **5**. With care though this can be done to give a pure product which has two IR stretches, 1633 and 1598 cm⁻¹, rather than a typical carbonyl group stretch at 1700 cm⁻¹. The spectroscopic data suggested structure **9** and this was confirmed by an X-ray single crystal structure determination.⁹ Structure **9** has been reported previously but was prepared by a different method.⁹ Data on related compounds is also available.¹⁰⁻¹² The two low IR stretches are presumably because of strong resonance conjugation from the amine lone pair to the carbonyl group. The mp of 268-269 °C is similar to the mp of 270-271 °C reported by Rees² suggesting these compounds are the same.

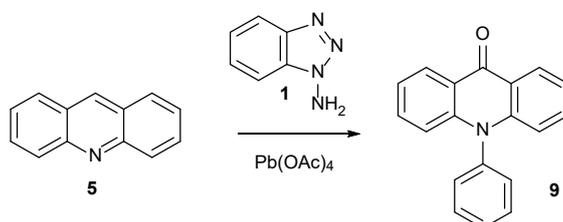


Figure 3 The reaction of benzyne **2** with acridine **5** to give N-phenylacridone **9**.

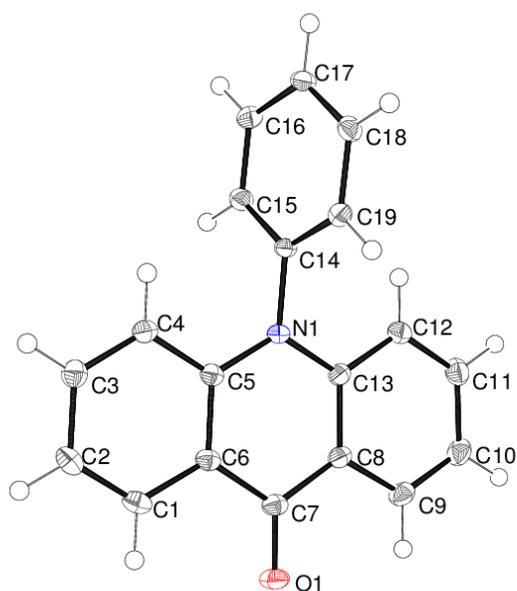


Figure 4 Crystallographic drawing of N-phenylacridone **9**

The acridone ring system in **9** shows a small, but significant, pucker [dihedral angle between the C1 and C7 rings = 2.22 (5) $^{\circ}$; dihedral angle between the C7 and C9 rings = 5.32 (5) $^{\circ}$]. The dihedral angle between the tricyclic ring system and the pendant phenyl group is 75.92 (4) $^{\circ}$. In the crystal, inversion dimers are linked by pairs of C15–H15 \cdots O1 (H \cdots O = 2.38 Å) hydrogen bonds.

Figure 5 shows a proposal for how this unusual compound might have formed. Benzyne **2** appears not to have undergone a concerted cycloaddition with acridine **5**. Instead a non-concerted reaction has occurred because the acridine nitrogen is nucleophilic leading to ylide **10** then to salt **11** because there is acetic acid present in lead tetraacetate. The counter-ion must be acetate and might add as a nucleophile to the N-phenylacridinium salt **11** to give acetate **12**. If acetate **12** hydrolyses to alcohol **13** the secondary alcohol could be oxidised by more lead tetraacetate to the final product N-phenylacridone **9**.

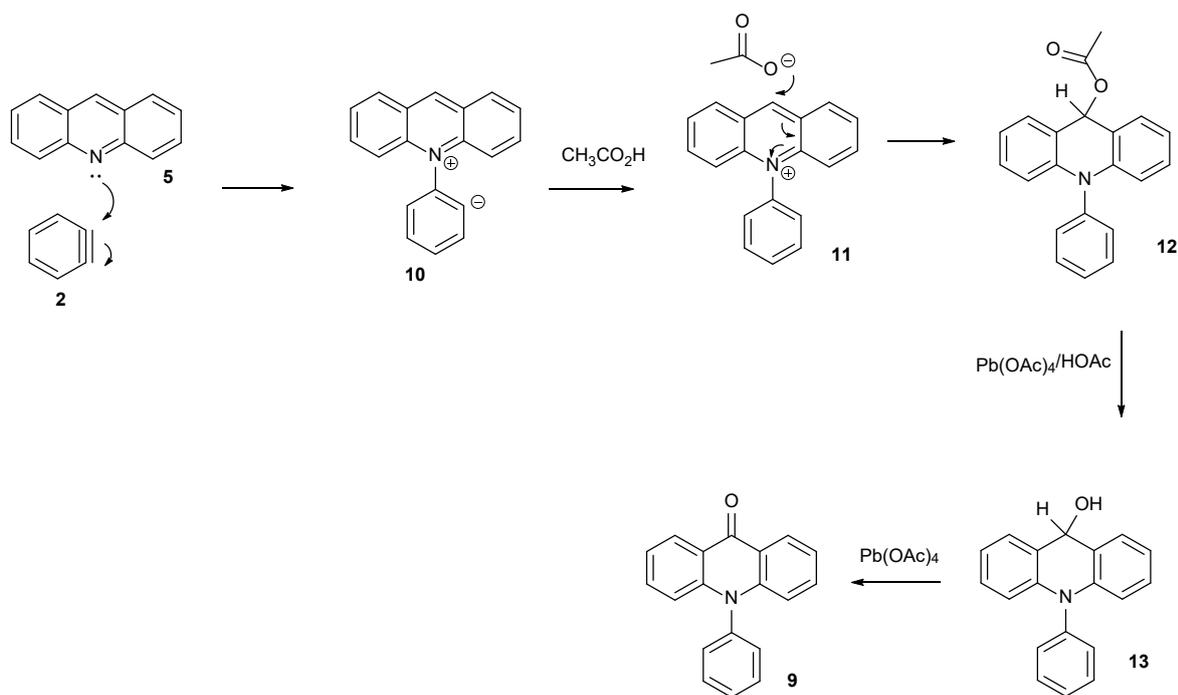


Figure 5 A possible route for the formation of N-phenylacridone **9**.

No products were obtained from reacting benzyne **2** with phenazine **7** with or without the addition of NaBH₄ to reduce an intermediate phenazinium salt so this reaction remains elusive.

Summary

A study of the reaction of benzyne **2** with acridine **5** has revealed that the mystery product formed is N-phenylacridone **9**. The benzyne **2** reacts by a non-concerted mechanism rather than by a concerted mechanism owing to the nucleophilic nitrogen of acridine **5** and its poor reactivity as an inverse electron demand diene. The mp of 268-269 °C for compound **9** is close to that reported by Rees (270-271 °C) suggesting that this is the same compound which has now been identified.

Experimental

IR spectra were recorded on an ATI Mattson FTIR spectrometer using KBr discs. UV spectra were recorded using a Perkin-Elmer Lambda 25 UV-Vis spectrometer with CH₂Cl₂ as the solvent. ¹H and ¹³C NMR spectra were recorded at 400 MHz and 100.5 MHz, respectively, using a Varian 400 spectrometer. Chemical shifts, δ are given in ppm and measured by comparison with the residual solvent. Coupling constants, J are given in Hz. Low resolution and high resolution mass spectra were obtained at the University of Wales, Swansea using electron impact ionisation and chemical ionisation. Melting points were determined on a Kofler hot-stage microscope.

Synthesis of N-phenylacridone **9**

1-Aminobenzotriazole **1** (50 mg, 0.37 mmol) and acridine **5** (67 mg, 0.37 mmol) were stirred in dichloromethane (50 ml) and treated with Pb(OAc)₄ (165 mg, 0.37 mmol) for 24 h. The mixture was poured directly onto a flash silica column (12 inches x 1 inch) and eluted with dichloromethane to remove biphenylene **3**. Elution with ether : dichloromethane (10:90) and careful fraction collection from the excess acridine **5** gave the *title compound* (5.0 mg, 5.0 %) as a yellow solid, mp 268-269 °C (from dichloromethane:light petroleum ether 40-60). λ_{max}

(EtOH)/nm 395 (log ϵ 3.5), 380 (3.4), and 250 (4.1); ν_{\max} (KBr)/cm⁻¹ 3047w, 1633s, 1598s, 1489s, 1458s, 1359s, 1305s, 1162m, 1038w, 942w, 934w, 778m, 748s, 705s, 672s, 620s, 558s and 514 ; δ_{H} (400 MHz; CDCl₃) 6.69 (2H, d, J = 8.0), 7.21 (2H, t, J = 6.0 and 8.0), 7.30 (2H, d, J = 8.0), 7.43 (2H, t, J = 6.0 and 8.0), 7.64 (1H, t, J = 4.0 and 8.0), 7.64 (2H, t, J = 8.0 and 8.0) and 8.52 (2H, d, J = 8.0) ; δ_{C} (100.1 MHz; CDCl₃) 116.9, 121.6, 121.8, 127.3, 129.6, 130.1, 131.1, 133.3, 138.9, 143.2 and 178.2; m/z (orbitrap ASAP) 272.1062 (M⁺ + H, 100%) C₁₉H₁₄NO requires 272.1070.

Crystal structure

Colourless plates of **9** were recrystallized from DCM/light petroleum ether solution. Intensity data were collected at $T = 100$ K using a Rigaku Mercury CCD diffractometer (Mo K α radiation, $\lambda = 0.71073$ Å): C₁₉H₁₃NO, $M_r = 271.30$, triclinic, space group $P\bar{1}$ (No. 2), $a = 8.5687$ (5), $b = 9.0551$ (4), $c = 9.3238$ (4) Å, $\alpha = 68.028$ (4), $\beta = 78.202$ (5), $\gamma = 76.553$ (5)°, $V = 646.94$ (6) Å³, $Z = 2$, $R(F) = 0.036$, $wR(F^2) = 0.106$, CCDC deposition number 1883546.

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