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Direct Amination of 9-Hydroxy-1-oxophenalene to Produce 9-Amino-1-oxophenalene and Related Compounds

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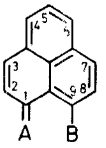
In connection with our studies of organo-non-metallic complexes of the 1,9-disubstituted phenalene unit **1** we required access to compounds possessing a total of just two ionizable hydrogen atoms in the A,B groups of **1**. The prototypical compound in this series, 9-amino-1-oxophenalene (**2**), is not known although 9-hydroxy-1-oxophenalene (**3**) was first prepared in 1941 and a number of derivatives of **1** possessing one or three ionizable hydrogen atoms in the A,B groups have recently become available. We have found that the high-pressure reaction between 9-hydroxy-1-oxophenalene (**3**) and aqueous ammonia affords the desired 9-amino-1-oxophenalene (**2**) in high yield and good purity under relatively mild conditions. In addition **2** may be alkylated to produce the 9-amino-1-ethoxyphenalenylium salt which serves as a precursor for the other derivatives in this series with two ionizable hydrogen atoms in the A,B groups of **1**.

In connection with our studies of organo-non-metallic complexes of the 1,9-disubstituted-phenalene unit **1**[1], we required access to compounds possessing a total of just two ionizable hydrogen atoms in the A,B groups (**1**). The prototypical compound in this series, 9-amino-1-oxo-phenalene (**2**), is not known although 9-hydroxy-1-oxo-phenalene (**3**) was first prepared in 1941[2,3,4] and a number of derivatives of **1** possessing one or three ionizable hydrogen atoms in the A,B groups have recently become available[5,6,7].



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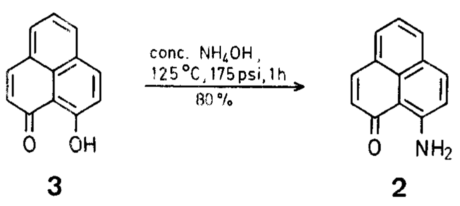
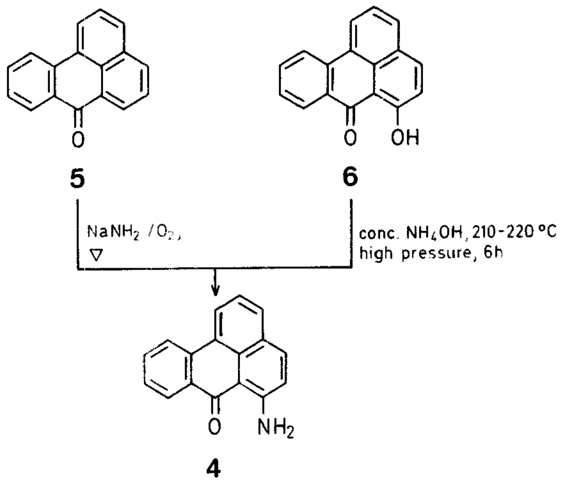
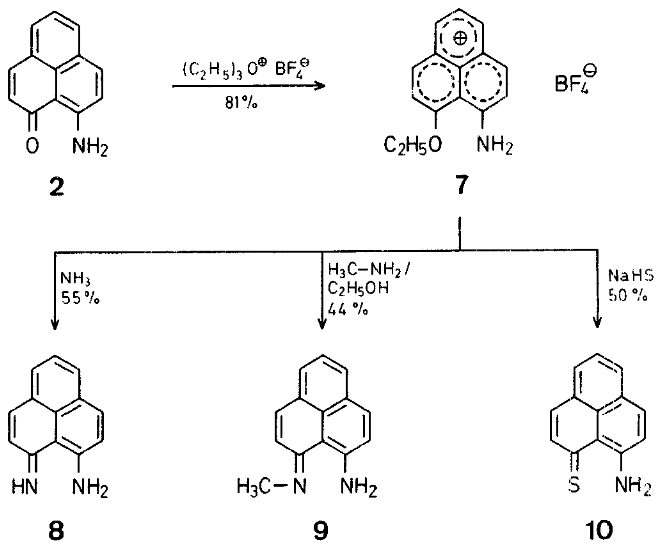


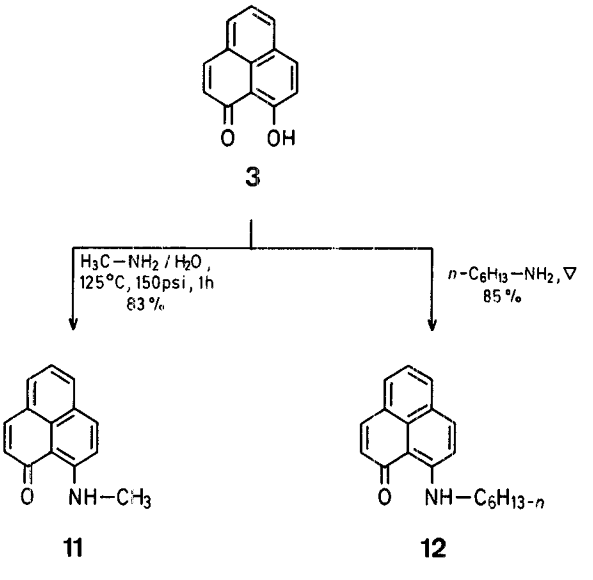
The related 6-amino-7-oxobenz[*d,e*]anthracene (**4**) was first prepared[8] by heating 7-oxobenz[*d,e*]anthracene (**5**) with sodium amide in the presence of oxygen while a subsequent synthesis utilized the high-pressure reaction between 6-hydroxy-7-oxobenz[*d,e*]anthracene (**6**) and aqueous ammonia at 210–220 °C over a period of six hours[9]. While these reactions did not prove particularly satisfactory in our hands, the analogous reaction between 9-hydroxy-1-oxophenalene (**3**) and aqueous ammonia affords the desired 9-amino-1-oxophenalene (**2**) in high yield and good purity under relatively mild conditions (125 °C, 1 h). This reaction provides a particularly convenient entry into this series of compounds as previous general syntheses of derivatives **1** have first required the generation of a 9-alkoxy-1-oxophenalene[5,10] via the use of silver oxide and an alkyl iodide to disrupt the hydrogen bond in **3**.



9-Amino-1-oxophenalene (**2**) is smoothly alkylated with triethyloxonium tetrafluoroborate to produce the 9-amino-1-ethoxyphenalenylium salt **7** (cf. Refs.[5–8]) which serves as precursor for the other derivatives in this series with two ionisable hydrogen atoms in the A,B groups of **1**. Thus **7** gives rise to 9-amino-1-methyliminophenalene (**9**) on treatment with methylamine while reaction with sodium hydrogen sulfide produces 9-amino-1-thioxophenalene (**10**). Reaction of ammonia with the salt **7** is also the best source of 9-amino-1-iminophenalene (**8**)[5,6].



The direct amination of 9-hydroxy-1-oxophenalene (**3**) is not restricted to the reaction with aqueous ammonia. Thus, aqueous methylamine reacts with **3** under the same conditions as were employed in the preparation of **2**. In this way it is possible to prepare 9-alkylamino-1-oxophenalenes (e.g. **11**) directly from **3** in high yield and good purity. In the case of high boiling primary amines (b.p. > 130 °C), high-pressure techniques are not required and overnight reflux of **3** in the neat amine effects a virtually quantitative conversion to the desired compound, as exemplified by the preparation of **12** with *n*-hexylamine (b.p. 131–132 °C).



Although it seems clear that the amination of **3** depends on a nucleophilic attack by the amine, we found other nucleophiles to be ineffective in this regard. Aqueous sodium sulfide and anhydrous hydrogen sulfide both failed to produce 9-hydroxy-1-thioxophenalene and compound **3** was recovered unchanged. Likewise the action of methanol did not bring about the formation of 9-methoxy-1-oxophenalene. Under particularly forcing conditions this reaction gave rise to dark needles containing copper and nickel – presumably in the form of complexes[11] generated by reaction of **3** with the Monel bomb.

The amination reaction itself must be regarded as unusual as juglone (5-hydroxy-1,4-naphthoquinone) is known to undergo amination at the 2- and 3-positions without replacement of the hydroxy functionality[12,13]. Particularly remarkable is the ease with which **3** undergoes the amination reaction – in marked contrast to the behavior of **6**. This result is the inverse of the normal reactivity order for these two compounds. Thus, the alkoxy[14] and acetyl[15] derivatives of **6** were prepared over 50 years ago, but it is only recently that the same derivatives of **3** have become available[5,16].

9-Amino-1-oxophenalene (2):
A mixture of 9-hydroxy-1-oxophenalene[2,3,4] (**3**; 9.8 g, 0.05 mol) and concentrated ammonium hydroxide solution (200 ml, specific gravity 0.9) is placed in a Monel bomb. The contents are stirred vigorously at an internal temperature of 125 °C for 1 h during which the pressure in the bomb is about 175 psi. The mixture is allowed to cool, the bomb vented, opened, and the contents poured into distilled water (200 ml), and the mixture separated by filtration. The crude yield is virtually quantitative and the material quite pure (m.p. 159 °C). Sublimation gives rise to an orange-yellow solid; yield: 7.8 g (80 %); leaflets from benzene; m.p. 159.2–159.9 °C.

$C_{13}H_9NO$	calc.	C 79.98	H 4.65	N 7.18
(195.2)	found	79.93	4.95	7.14

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 6.8–7.9$ (m, 7 H); 6.9 ppm (br. s, 2 H).

I.R. (CsJ): $\nu = 3290$ (s, br), 3140 (m, br), 3030 (w), 1632 (vs), 1587 (s), 1560 (s), 1525 (s), 1462 (w), 1423 (m), 1346 (s), 1323 (m), 1281 (m), 1235 (m), 1210 (w), 1170 (m), 1146 (w), 1121 (m), 965 (w), 944 (m), 830 (vs), 739 (s), 730 (m), 696 (w), 670 (w), 580 (m), 524 (m), 460 (w), 428 (m), 400 (w), 335 cm^{-1} (w).

U.V. (CH_2Cl_2): $\lambda_{max} = 248$ ($\varepsilon = 38{,}000$); 265 (17,000); 277 (16,000); 334 (14,000); 349 (27,000); 405 (6,100); 429 (14,000); 455 nm (18,000).

9-Amino-1-ethoxyphenalenylium Tetrafluroborate (7):
Triethyloxonium tetrafluoroborate (1.9 g, 0.01 mol) is added to a solution of 9-amino-1-oxo-phenalene (**2**; 1.95 g, 0.01 mol) in dry 1,2-dichloroethane (50 ml) under argon. The resulting wine-red solution gives rise to a yellow precipitate. After stirring overnight a bright yellow solid is separated by filtration and vacuum dried; yield 2.51 g (81 %). This material is suitable for use in subsequent reactions, but can be further purified by recrystallization from ethanol to give yellow needles; m.p. 232 °C.

$C_{15}H_{14}BF_4NO$	calc.	C 57.92	H 4.50	N 4.50
(311.1)	found	57.75	4.53	4.46

^{1}H-N.M.R. (CD_3CN/TMS): $\delta = 1.62$ (t, 3 H, $J = 7$ Hz); 4.62 (q, 2 H, $J = 7$ Hz); 6.9–8.4 (m, 7 H); 8.5 (br. s, 1 H); 8.9 ppm (br. s, 1 H).

U.V. (CH_3CN): $\lambda_{max} = 240$ ($\varepsilon = 30{,}000$); 265 (16,900); 332 (7,300); 350 (11,400); 372 (23,600); 410 (7,100); 432 (11,800); 456 nm (12,300).

9-Amino-1-iminophenalene (8):
Ammonia gas is bubbled through a slurry of 9-aminoethoxyphenalenylium tetrafluoroborate (**7**; 1.55 g, 0.005 mol) in ethanol (50 ml) until all of the solid has dissolved (~ 2 h) to give a dark green solution. The ethanol is removed by evaporation and the solid extracted with benzene. The benzene solution is washed with water, dried with magnesium sulfate, and taken down on a rotary evaporator to give a yellow solid (0.82 g). Recrystallization from heptane gives yellow plates; yield: 0.53 g (55 %); m.p. 186 °C (Ref.[5,6], m.p. 188 °C).

9-Amino-1-methyliminophenalene (9):
33 % Ethanolic methylamine (8.03 molar, 4 ml) is added to a slurry of 9-aminoethoxyphenalenylium tetrafluoroborate (**7**; 1.55 g, 0.005 mol) in ethanol (50 ml) and the mixture stirred overnight. The resulting yellow solid is separated by filtration and recrystallized from heptane to give brownish-yellow needles (0.40 g). A further quantity of product is obtained by taking the filtrate to dryness and extracting the solid with boiling heptane; total yield: 0.54 g (44 %); m.p. 148 °C.

$C_{14}H_{12}N_2$	calc.	C 80.77	H 5.77	N 13.46
(208.3)	found	80.77	5.83	13.45

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 3.30$ (s, 3 H); 6.6–8.0, 7.0–8.0 ppm (br, NH, m, 7 H).

U.V. (hexane): $\lambda_{max} = 268$ ($\varepsilon = 39{,}100$); 284 (19,900); 314 (5,900); 337 (3,600); 350 (7,400); 354 (6,300); 365 (12,900); 428 (6,600); 450 (12,300); 478 nm (12,300).

9-Amino-1-thioxophenalene (10):
Sodium hydrogen sulfide (1.40 g, 0.025 mol) is added to a slurry of 9-aminoethoxyphenalenylium tetrafluoroborate (**7**; 1.55 g, 0.005 mol) in methanol (50 ml) and the mixture stirred overnight. The solvent is removed and the residue extracted with benzene. The resulting solution is washed with water, the organic layer dried with magnesium sulfate, and then taken down on a rotary evaporator. The solid is recrystallized from benzene/heptane to give shiny, dark-red plates; yield: 0.52 g (50 %); m.p. 130–131 °C

$C_{13}H_9NS$	calc.	C 73.93	H 4.27	N 6.64
(211.3)	found	74.01	4.62	6.68

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 6.8–8.2$ (m); 6.0–8.6 ppm (br).

U.V. (hexane): λ_{max} = 230 (ε = 14,600); 250 (16,300); 269 (24,400); 330 (5,000); 345 (7,100); 372 (10,200); 390 (26,300); 426 (3,100); 442 (3,700); 452 (6,000); 495 (10,600); 517 (9,700); 528 nm (11,100).

9-Methylamino-1-oxophenalene (11):

A mixture of 9-hydroxy-1-oxophenalene (**3**; 0.98 g, 0.005 mol) and aqueous methylamine (10 ml; 40% solution) is placed in a Monel bomb. The contents are stirred vigorously at an internal temperature of 125 °C for 1 h during which the pressure in the bomb is about 150 psi. The mixture is allowed to cool, the bomb vented, opened, and the contents poured into distilled water (50 ml). The aqueous mixture is extracted with benzene, the organic layer is separated, dried with magnesium sulfate, and taken down on a rotary evaporator to give a yellow solid; yield: 0.88 g (83%); m.p. 110–111 °C (Ref.[5], m.p. 112 °C).

9-*n*-Hexylamino-1-oxo-phenalene (12):

A mixture of 9-hydroxy-1-oxophenalene (**3**; 0.98 g, 0.005 mol) and hexylamine (10 ml) is refluxed overnight. The excess amine is removed on a rotary evaporator to give a brownish-yellow oil which crystallizes on standing under a stream of nitrogen. Recrystallization from hexane gives yellow plates; yield: 1,2 g (85%); m.p. 72 °C.

$C_{19}H_{21}NO$	calc.	C 81.68	H 7.58	N 5.01
(279.4)	found	82.03	7.67	5.03

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