SYNTHESES AND REACTIONS OF AMINO- AND AZIDOPHENALENONES [1]

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Abstract

3-Hydroxyphenalenones **3**, synthesized from 1,8-naphthalic anhydride **1** and malonates **2**, react by electrophilic halogenation to 2-chlorophenalenediones **4** or 2-iodophenalenone **5**. The chloro group of **4** was exchanged against azide by reaction with sodium azide to give 2-azidophenalenediones **6**. Nucleophilic chlorination of **3** furnishes 3-chlorophenalenones **7**, which were converted to 3-azidophenalenones **8**. *Staudinger* reaction of **8** with triphenylphosphane gave phosphazenes **9** which hydrolyzed to 3-aminophenalenones **10**. Amines **10** can also be obtained directly from 3-hydroxyphenalenones **3** and ammonium acetate, or by catalytic hydrogenolysis of azides **8**. Nitration of 3-hydroxyphenalenone **3a** with nitric acid forms 2-nitrophenalenone **11**, which was converted to 3-chloro-2-nitrophenalenone **12**. Attempts to introduce the 3-azido group in **12**, however, resulted in an exchange of both, the nitro group and the chloro group, to form 2,3-diazidophenalenone **13**.

2-Amino-3-hydroxyphenalenone **14** cyclizes with carboxylic acid derivatives to oxazolo-phenalenones **15**, which were also obtained from 3-azidophenalenone **8a** and a carboxylic acid involving an azirine intermediate **16**. This allows to move the position of the N-atom. Another cyclization reaction leads via the intermediate oxime **22** of 2-acetylphenalenone **21**, which gives an isomer mixture of isoxazolophenalenone **23** as main product and oxazolophenalenone **15** as by-product, because of a parallel reaction via a *Beckmann* rearrangement.

Introduction

Phenalenones are a class of compounds which can be found widespread in a series of natural products. One of the most interesting occurrence of this polyketides is that in different fungi [2] (e.g. from the soil fungus *Penicillum herquei* [2b]), and a series of antibiotic active derivatives were isolated (e.g. antimicrobial phenalenone derivatives from the marine-derived fungus *Coniothyrium cereale* [2e]). Phenalenone derivatives were produced by fermentation (e.g. for the manufacture of an agricultural phenalenone microbicide by fermentation) [3]. Also several plants contain phenalenones [4] (e.g. phenalenones from *Strelitzia reginae* [4d]) and especially pigments found great interest (e.g. phenalenone pigments of the root system of *Lachnanthes tinctoria*) [5]. Another application of phenalenones is their use as chemosensor (e.g. applications as fluorescent chemosensor for fluoride ions) [6] and their properties as a one-photon singlet oxygen sensitizer, described as tool for detecting DNA damages and receptor ligand activites [7].

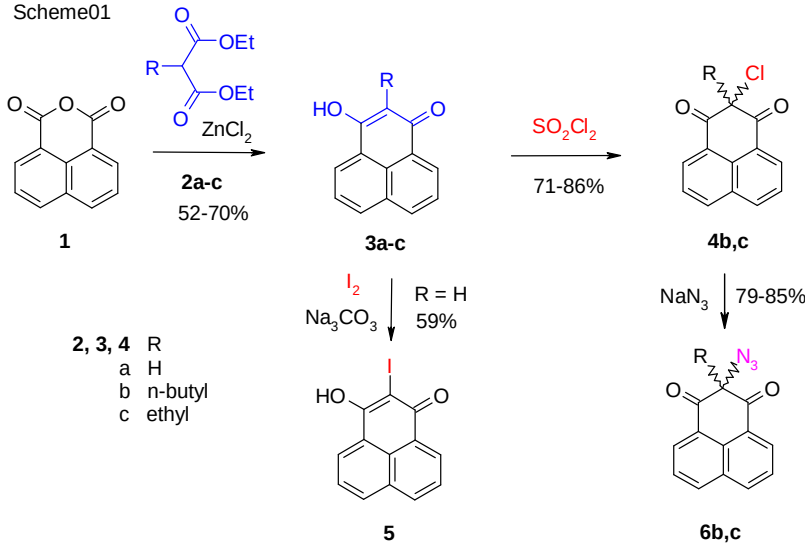
Results and Discussion

In the last years we studied the reaction of several phenalenediones or their tautomeric 3-hydroxyphenalen-1-ones as representatives of polycyclic aromatic systems, and used it as starting material for

cyclization reactions [8-11]. In this paper we investigate the synthesis of aminophenalenones and azidophenalenones, their reactivity against electrophilic and nucleophilic reactions and their ability for ring closure reactions to phenaleno-oxazoles and isoxazoles.

1. Synthesis of 3-hydroxyphenalenones 3. Electrophilic halogenation to 4 and 5. Azidation to azidophenalenediones 6.

Scheme01



The synthesis of 3-hydroxyphenalenone (**3a**) and its 2-alkylsubstituted derivatives **3b,c** was performed by acylation of 1,8-naphthalic anhydride (1*H*,3*H*-benzo[*de*]isochromene-1,3-dione) **1** with unsubstituted or 2-alkylsubstituted malonates **2a-c**. As condensation agent freshly melted anhydrous zinc chloride was applied. We have described this method earlier for 2-unsubstituted and 2-aryl derivatives [9,10] and adopted it now for 2-alkylsubstituted derivatives. Butyl and ethyl compounds **3b,c** were obtained in the this manner in good yields (Scheme 01).

Chlorination of 2-substituted phenalenones **3b,c** with sulfuryl chloride resulted in an electrophilic substitution at position 2 (which can be considered as the CH-acidic position of a cyclic 1,3-diketone in its tautomeric form) and furnished in good to excellent yields 2-chlorophenalene-1,3-diones **4b,c**, which possess a racemic stereo center at position 2. Further chlorination at the polycyclic aromatic system was not observed using these mild reaction conditions at 50 °C. The chloro substituent in position 2 of 2-chlorophenalene-1,3-diones **4** reacts with sodium azide and gives in excellent yields 2-azidophenalene-1,3-diones **6b,c**. Structure elucidation gave positive IR signals of the azido group at 2115-2125 cm^1.

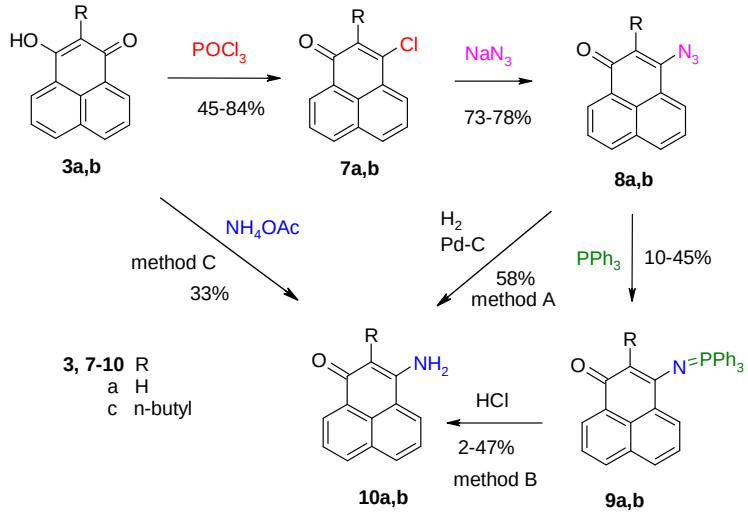
Iodination of 2-unsubstituted **3a** in alkaline solution at room temperature reveals 2-iodophenalenone **5** in good yields.

2. Nucleophilic chlorination of 3-hydroxyphenalenones 3. Formation of 3-azido- and 3-aminophenalenones 8 and 10.

The enolic 3-hydroxy substituent in phenalenones **3** was substituted in a nucleophilic reaction by a chloro atom which formed 3-chlorophenalenones **7** (Scheme 02). This chlorination could be carried out already at 15-20 °C using as reactive halogenation medium a mixture of phosphoryl chloride and dimethylformamide similar to a Vilsmeier reagent The exchange of chlorine against the azido group

proceeded in a smooth reaction with sodium azide at 50 °C, and 3-azidophenalenones **8** were obtained in very good yields. Structure elucidation of the azido derivative **8** showed again IR signals at 2110-2120 cm[1].

Scheme02

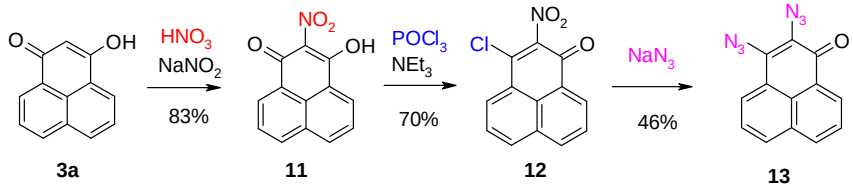


The conversion of azides **8** to 3-aminophenalenones **10** succeeded in two reaction pathways: in a one step reaction, the azido group could be reduced by hydrogenolysis with palladium as catalyst in good yields (method A). A 2-step reaction, involving an Aza-Wittig and a Staudinger reaction [12], gave from azides **8** with triphenylphosphane the iminophosphoranes **9**, which could then be hydrolyzed with hydrochloric acid and formed the corresponding 3-aminophenalenones **10** (method B). A simple and short amination reaction leads from 3-hydroxyphenalenones **3** with ammonium acetate in the melt without solvent in low yields to 3-aminophenalenones **10** (method C).

3. Introduction of azido substituents into 1-chloro-2-nitrophenalenone (12)

Cyclization reactions of azido compounds with ortho-nitro substituents are known to give interesting furoxane heterocycles [13], a reaction type we have investigated in the last years [14]. The reaction sequence to analog phenalenone derivatives started with the nitration of 3-hydroxyphenalenone **3a** with nitric acid. For this step we did not use the procedure with hot nitric acid which was described earlier [15]. We have adopted our recently developed method [14f] using sodium nitrite as catalyst. This method allowed to perform the reaction at room temperature with better yields and higher purity and we obtained **11** in excellent yields and purity (Scheme 03).

Scheme03



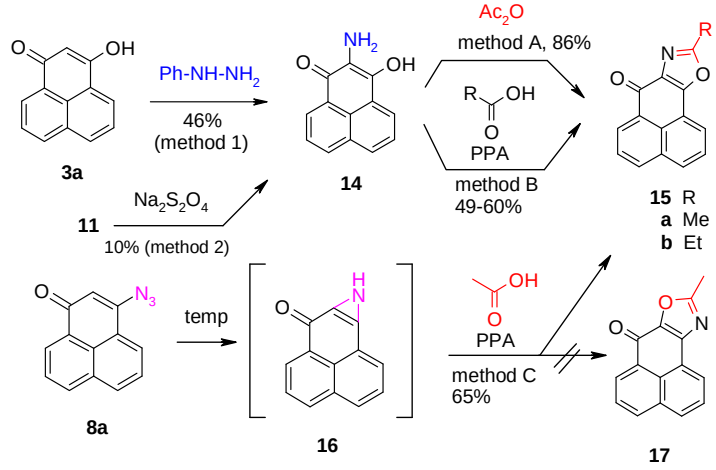
Removal of the hydroxy group of **11** and introduction of a chloro group for a reactive intermediate **12** did not work in the same manner as described for the synthesis of chlorophenalenones **7**, because the nitro group prevented a successful attack by hydrogen bondings between the 3-hydroxy group and the 2-nitro group. However, chlorination with excess phosphoryl chloride at reflux temperature, adding triethylamine as a base to break the hydrogen bondings, gave in very good yields 3-chloro-2-nitrophenalenone **12**. As the next step on the way to the furoxane derivative, the exchange of the chloro substituent against the azide in order to obtain 3-azido-2-nitrophenalenone was planned. The reaction was carried out similar as performed in the synthesis of azides **8**. Already at room temperature an azido compound was formed, which could be shown, however, to possess 2 azido substituents by loss of

both, the chloro and the nitro substituents. Analytical data verify the structure of 2,3-diazido-phenalenone **13**. An explanation for this phenomenon can be found in the HSAB principle, which shows that by hard nucleophils and borderline systems only the chloro atom should be exchanged, by soft nucleophils exclusively the nitro group. The 2-nitrophenalenone system with π-deficient properties seems to influence both the 2- and 3-positions in a manner that the nucleophilic substitution by the azide anion as borderline system takes place in a similar quick rate.

Attempts were made to synthesize as reactive intermediate a 3-tosyloxy-derivative by tosylation of **11** as shown in other systems [16], which is known to be more reactive than the chloro derivative and could help to produce a mono-azido derivative. However, these experiments failed because no tosyloxy derivative could be obtained.

4. Cyclization reactions of 2-amino-3-hydroxyphenalenone 14 and 3-azidophenalenone 8a to phenaleno[2,1-*d*]oxazol-7-ones 15

Scheme04

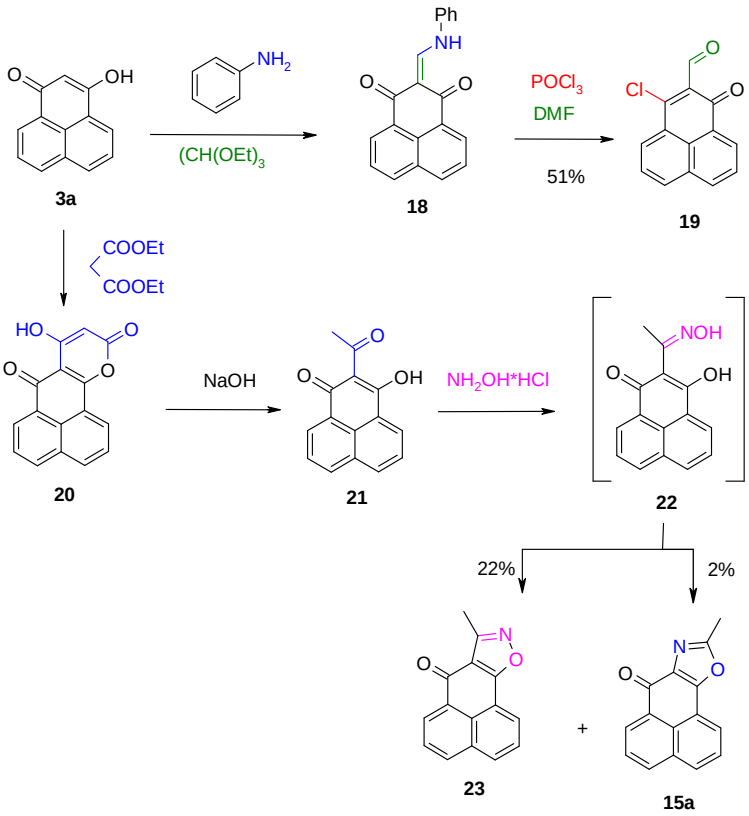


2-Amino-3-hydroxyphenalenone **14**, with a structure related to an ortho-aminophenol, was obtained either from 3-hydroxy-phenalenone **3a** in a *Neber* rearrangement reaction with phenylhydrazine under loss of aniline [17, 18] (method 1), or by reduction of 3-hydroxy-2-nitrophenalenone **11** with sodium dithionite similar to a reaction we applied in the quinoline series [19] (method 2). The latter reaction, however, gave only very low yields and insufficient purity, and was not used further (Scheme 04). Acylation of 2-amino-3-hydroxyphenalenone **14** with acetic anhydride (method A) did not stop at the N- or O-acetyl intermediate, but proceeded by cyclization in one step in excellent yields to phenaleno[2,1-*d*]oxazolone **15a**. A cyclization of the amine **14** with acetic or propanoic acid, using polyphosphoric acid as condensation agent, gave at temperatures of 150 °C in good yields phenaleno[2,1-*d*]oxazolones **15a** and **15b** (method B). Attempts with benzoic acid gave only mixtures of compounds which could not be separated.

Another approach to oxazoles and isoxazoles which we have investigated synthetically and mechanistically, starts from azido compounds and carboxylic acids similar as published recently [19, 20]. It involves the formation of an intermediate azirine and forms isoxazoles and oxazoles depending on the reactivity of the carboxylic acid reagent. Application of this reaction sequence on azido-phenalenone **8a** gave with acetic acid and polyphosphoric acid as reagents via the intermediate azirine **16** again phenaleno[2,1-*d*]oxazolones **15a** (method C), formed by the attack of oxygen of the acetic acid at the 8a-position of the phenaleno-azirine **16** (and not at the 7a-position). The isomer phenaleno[1,2-*d*]oxazolone **17** was not formed.

5. Cyclization reaction of 2-acetyl-3-hydroxyphenalenone 21 to phenaleno[2,1-*d*]oxazol-7-one 15 and phenaleno[2,1-*d*]isoxazol-7-one 23

Scheme05



Starting from 3-hydroxyphenalenone **3a**, 2-phenylaminomethylene-phenalen-dione **18** was obtained by reaction with aniline and triethyl orthoformate similar to phenylaminomethylene compounds described earlier [21]. Hydrolysis of **18** should give 3-hydroxy-1-oxo-1*H*-phenalene-2-carbaldehyde, which could serve as intermediate to form phenaleno-isoxazoles. However, this well known reaction [21] did not work in the phenalenone series. Attempts to perform a cleavage of the aniline and chlorination in a one-pot synthesis gave a completely other result, and a naph-tho[1,8-*bc*]acridinone was formed by cyclization [8].

When the chlorination of the phenyl-aminomethylene compound **18** was car-ried out with a mixture of phosphoryl chloride and dimethylformamide (known as Vilsmeier reagent), product **19** was obtained, which contains the desired 2-formyl group and in addition the hydroxy group was already exchanged against a chloro group (Scheme 05). Attempts to introduce the azido group by reaction with sodium azide were not successful: at temperatures of 50 °C no reaction took place, and at 70 °C, a mixture of compounds was obtained, some of them showing a blue fluorescence giving a hint that already cyclization has taken place.

2-Acetylphenalenone **21**, which is available in a 2-step synthesis from hydroxyphenalenone **3a** via the formation of 8-hydroxypyrano[2,3-*b*]phenalene-7,10-dione (**20**) [10] and alkaline degradation, reacts with hydroxylamine to a mixture of two fluorescent reaction products in a ratio of 90:10. The planned ketoxime, 3-hydroxy-2-(N-hydroxyethanimidoyl)-1H-phenalen-1-one **22**, could not be isola-ted, and chromatographic separation furnished 2 cyclization products. The main product with the lar-ger R_f-value and a blue fluorescence was assigned to the structure of 8-methyl-7H-phenaleno[2,1-*d*]isoxazol-7-one (**23**), which was formed by dehydration of oxime **22** in 22% yield. The other product with a smaller R_f-value and a blue-yellow fluorescence was identical with phenaleno[2,1-*d*]oxazolone **15a** and obtained in 2% yield. The formation of **15a** can be explained by a *Beckmann* rearrangement.

Conclusion

It could be shown that 3-hydroxyphenalenones **3** give in an electrophilic halogenation at position 2 2-chlorophenalenones **4**, and in a nucleophilic halogenation at position 3 3-chlorophenalenones **7**, **12** and **19**. In both cases, chloro substituents can be exchanged against an azido group to form 2-azides **6** and 3-azides **8**. Azidation of 3-chloro-2-nitrophenalenone **12** gave 2,3-diazidophenalenone **13** by exchange of both the nitro group and the chloro group.

3-Aminophenalenones **10** are formed either directly from **3**, or from 3-azidophenalenones **8** by catalytic hydrogenolysis, or by a *Staudinger* reaction via phosphazenes **9**.

2-Amino-3-hydroxyphenalenone **14** cyclizes with carboxylic acid derivatives to oxazolo-phenalenones **15**, which were also obtained from 3-azidophenalenone **8a** and a carboxylic acid involving an azirine intermediate **16**. Another way for the cyclization to isoxazolo- and oxazolo-phenalenones leads via the intermediate oxime **22** of 2-acetylphenalenone **21**, which gives an isomer mixture: main product was the isoxazole **23**, as a by-product the isomer oxazole **15** is formed via a *Beckmann* rearrangement.

Methods and Experimental

General

Melting points were determined using a Stuart SMP3 Melting Point Apparatus (Bibby Scientific Limited, Stone, Staffordshire, UK) in open capillary tubes.

IR spectra were recorded with a Bruker Alpha-P instrument (Bruker GmbH, Karlsruhe, Germany) with Attenuated Total Reflectance (ATR) measurement, using a reflection method.

NMR spectra were recorded on a Bruker Avance III instrument (Bruker GmbH) (300 MHz ^{1}H). Chemical shifts are given in ppm (δ) from the internal TMS standard.

Elemental analyses were performed at the Microanalytical Laboratory of the University of Vienna, Austria.

Analytical HPLC was performed on a Shimadzu LC 20 system equipped with a diode array detector (215 and 254 nm) on a Pathfinder AS reversed phase (4.6150 mm, 5 µm) column, running in acetonitrile/water gradient (30-100% acetonitrile).

Dry column flash chromatography [22] was carried out on silica gel 60 H (5-40 µm) (Merck, Darmstadt, Germany).

All reactions were monitored by thin layer chromatography on 0.2 mm silica gel F 254 plates (Merck, Darmstadt, Germany) using UV light (254 and 366 nm) for detection.

Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

EXPERIMENTAL

3-Hydroxyphenalen-1-one (3a) was prepared as described in ref. [10, 17, 23].

2-n-Butyl-3-hydroxyphenalen-1-one (3b): A mixture of 1*H*,3*H*-benzo[*de*]isochromene-1,3-dione (**1**, 1,8-naphthalic anhydride) (30.0 g, 0.15 mol), diethyl n-butylmalonate (**2b**) (32.7 g, 0.15 mol) and freshly melted anhydrous zinc chloride (20.6 g, 0.15 g) was heated for about 5 hours to 240 °C. During this time the formation of ethanol and carbon dioxide was observed. The black solid obtained was cooled to 100 °C and treated with

water (60 mL), crushed and filtered. The crude product was stirred with hot 1 N aq. sodium hydroxide solution (300 mL) for 15 minutes, filtered and the filtrate acidified with diluted hydrochloric acid. The formed yellow precipitate was kept 2 hours at room temperature, filtered by suction, washed with water, dried and recrystallized from cyclohexane. The yield was 26.96 (70%), yellow prisms, mp 173-176 °C (ethanol). IR: 3303-3002 m, 2961-2919 m, 2881 w, 1631 m, 1609 m, 1551 s, 1506 w cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.85-1.02 (t, J=5 Hz, 3 H, Bu-CH_3), 1.31-1.56 (m, 4 H, 2 Bu-CH_2), 2.59-2.76 (t, J = 5 Hz, 2 H, 1-Bu-CH_2), 7.72-7.87 (m, 2 H, 5-H, 8-H), 8.21-8.42 (m, 4 H, aryl-H). Anal. calcd for $C_{17}H_{16}O_2$ (252.32): C, 80.93; H, 6.39. Found: C, 80.79; H, 6.32.

2-Ethyl-3-hydroxy-phenalen-1-one (3c): Obtained from 1*H*,3*H*-benzo[*de*]isochromene-1,3-dione (**1**) (30.0 g, 0.15 mol), diethyl ethylmalonate (**2c**) (28.2 g, 0.15 mol) and zinc chloride (20.6 g, 0.15 g) according to the procedure described for **3b**. The yield was 17.46 g (52%), yellow prisms, mp 205 °C (ethanol). IR: 3044 w, 2908 m, 2852 w, 1666 m, 1604 m, 1571 sh, 1512 s cm^{-1}. ^1H NMR (DMSO-d_6): δ 0.91-1.02 (t, J = 5 Hz, 3 H, CH_3), 2.65-2.81 (t, J = 5 Hz, 2 H, CH_2), 7.74-7.86 (m, 2 H, 5-H, 8-H), 8.15-8.42 (m, 4 H, aryl-H). Anal. calcd for $C_{15}H_{12}O_2$ (224.26): C, 80.34; H, 5.39. Found: C, 80.51; H, 5.32.

2-Butyl-2-chlorophenalene-1,3-dione (4b): To a solution of 3-hydroxy-2-butylphenalen-1-one **(3b)** (2.00 g, 8 mmol) in dioxane (30 mL) and sulfuryl chloride (2.4 g, 18 mmol) was added dropwise, keeping the temperature at 50 °C. The mixture was heated to reflux for a few minutes and poured onto ice/water (100 mL). The oily residue was decanted, and fresh water added subsequently under stirring to remove sulfuric acid until the oily product solidified. The product was filtered by suction, washed with water and dried. The yield was 1.39 g (61%), grey-white crystals, mp 69-71 °C (methanol/water). IR: 2964-2923 m, 2861 w, 1702 s, 1679 s, 1582 s cm^{-1}. Anal. calcd for $C_{17}H_{15}ClO_2$ (286.76): C, 71.21; H, 5.27; Cl, 12.36. Found: C, 71.10; H, 5.35; Cl, 12.31.

2-Chloro-2-ethylphenalen-1,3-dione (4c): To a solution of 3-hydroxy-2-ethylphenalen-1-one **(3c)** (5.00 g, 22 mmol) in dioxane (50 mL) and sulfuryl chloride (5.0 g, 37 mmol) was added dropwise, keeping the temperature at 50 °C. The mixture was heated to reflux for a few minutes and poured onto ice/water (150 mL). The precipitate was filtered by suction, washed with water (50 mL) and dried under reduced pressure at 40 °C. The yield was 4.9 g (86%), light-gray prisms, mp 220 °C (ethanol/water). IR: 2954-2903 m, 2881 w, 1705 s, 1689 s, 1593 s cm^{-1}. Anal. calcd for $C_{15}H_{11}ClO_2$ (258.71): C, 69.64; H, 4.29; Cl, 13.70. Found: C, 69.32; H, 4.45; Cl, 13.95.

3-Hydroxy-2-iodophenalen-1-one (5): To a solution of 3-hydroxyphenalen-1-one **(3a)** (2.43 g, 12.4 mmol) and sodium carbonate (2.50 g, 23.6 mmol) in water (50 mL), a solution of iodine (3.5 g, 27.6 mmol) in 2-propanol (100 mL) was added dropwise at room temperature. The mixture was cooled to 5 °C, acidified with glacial acetic acid and then water was added, which gave a yellow precipitate. The solid was filtered by suction and dried at 40 °C. The yield was 2.34 g (59%), yellow prisms, mp 167-170 °C (cyclohexane). IR: 3113-2902 m, 2849 w, 1689 s, 1611 s, 1582 s cm^{-1}. Anal. calcd for $C_{13}H_7IO_2$ (322.10): C, 48.48; H, 2.19. Found: C, 48.23; H, 2.32.

2-Azido-2-butyl-phenalene-1,3-dione (6b): A mixture of 2-butyl-2-chlorophenalene-1,3-dione (**4b**) (2. 87 g, 10 mmol) and sodium azide (0.65 g, 10 mmol) in dimethylformamide (50 mL) was heated to 50 °C for 60 minutes, then cooled to room temperature and poured onto ice/water (100 mL). The solid mixture was stirred for 2 hours at room temperature and filtered by suction. The yield was 2.31 g (79%) yellowish powder, mp 155 °C (ethanol). IR: 3500-2905, 2116 s, 1711 s, 1684 s, 1600 s cm^{-1}. Anal. calcd for $C_{17}H_{15}N_3O_2$ (293.33): C, 69.61; H, 5.15; N,14.33. Found: C, 69.72; H, 5.47; N, 14.01.

2-Azido-2-ethylphenalene-1,3-dione (6c): Obtained from 2-ethyl-2-chlorophenalene-1,3-dione (**4c**) (2.58 g, 10 mmol) and sodium azide (0.65 g, 10 mmol) as described for **6b**. The yield was 2.25 g (85%), yellow crystals, mp 136 °C (ethanol). IR: 3503-2902 m, 2126 s, 1722 s, 1689 s, 1600 s cm^{-1}. Anal. calcd $C_{15}H_{11}N_3O_2$ (265.27): C, 67.92; H, 4.18; N, 15.84. Found: C, 68.25; H, 4.35; N, 15.51.

3-Chlorophenalen-1-one (7a): A solution of phosphoryl chloride (5.0 g, 30 mmol) in dimethylformamide (3 mL) was stirred for 20 minutes and then added dropwise to a solution of 3-hydroxy-phenalen-1-one **(3a)** (7.84 g, 40 mmol) in dimethylformamide (120 mL) at 15-20 °C. The mixture was stirred for 5 hours at room tempera-

ture, poured onto ice/water (300 mL) and brought to pH=5 with 2 M aq. sodium hydroxide solution. The precipitate was washed with water, filtered by suction and dried at 40 °C. The yield was 4.2 g (45%), brownish prisms, mp 172-173 °C (ethanol/water); lit mp 180-181 °C [24]. IR: 1641 s, 1575 s, 1502 w cm^{-1}. Anal. calcd for $C_{13}H_7ClO$ (214.65): C, 72.74; H, 3.29. Found: C, 72.59; H, 3.60.

2-Butyl-3-chlorophenalen-1-one (7b): 2-Butyl-3-hydroxyphenalen-1-one (**3b**) (5.00 g, 20 mmol) in dimethylformamide (80 mL) and phosphoryl chloride (9.2 g, 60 mmol) in dimethylformamide (1.5 mL) was brought to reaction and worked up as described for **7a**. The oily residue was decanted, then ethanol was added and with water precipitated and kept for 12 hours at 5 °C. The solid was filtered by suction, washed and dried at 40 °C. The yield was 4.52 g (84%), brown prisms, mp 62-64 °C. IR: 2958 m, 2921 m, 2873 w, 2862 m, 1632 s, 1615 s, 1571 s, 1502 m cm^{-1}. Anal. calcd for $C_{17}H_{15}ClO$ (270.76): C, 74.41; H, 5.58; Cl, 13.09. C, 75.12; H, 5.42; Cl, 13.05.

3-Azidophenalen-1-one (8a): To a solution of 3-chloro-phenalen-1-one (**7a**) (5.0 g, 23.3 mmol) in dimethylformamide (150 mL), sodium azide (4.60 g, 71 mmol) was added slowly at room temperature. The mixture was warmed to 50-55 °C and stirred for 5 hours and then poured onto ice/water (300 mL). The formed precipitate was kept for 3-4 hours at 5 °C, then filtered by suction and dried at 20 °C at reduced pressure. The yield was 4.0 g (78%), light yellow prisms, mp 161-162 °C (ethanol/water). IR: 2183 w, 2121 s, 1635 s, 1582 s cm^{-1}. Anal. calcd for $C_{13}H_7N_3O$ (221.22): C, 70.58; H, 3.19; N, 18.99. Found: C, 70.63; H, 3.36; N, 18.63.

3-Azido-2-butylphenalen-1-one (8b): To a solution of 2-butyl-3-chlorophenalen-1-one (**7b**) (2.60 g, 9.6 mmol) in dimethylformamide (100 mL), sodium azide (3.12 g, 48 mmol) in dimethylformamide was added slowly at room temperature. The mixture was warmed to 50 °C and stirred for 12 hours and then poured onto ice/water (250 mL). A brown oil was formed which was kept for 12 hours at 5 °C under stirring. The formed precipitate was filtered by suction and dried at 20 °C at reduced pressure. The yield was 1.95 g (73%), brown platelets, mp 44-45 °C. IR: 2962 w, 2924 w, 2861 w, 2112 s, 1635 s, 1575 s cm^{-1}. Anal. calcd for $C_{17}H_{15}N_3O$ (277.33): C, 73.63; H, 5.45; N, 15.15. Found: C, 73.34; H, 5.48; N, 14.78.

3-Triphenylphosphoranylideneaminophenalen-1-one (9a): To a suspension of 3-azidophenalen-1-one (**8a**) (1.47 g, 6.7 mmol) in toluene (35 mL), triphenylphosphane (1.90 g, 7.2 mmol) was added and the mixture heated under reflux for 2.5 hours. After cooling, the solvent was removed under reduced pressure and the residue digested with cyclohexane to remove unreacted triphenylphosphane. The solid product was recrystallized from ethanol/water, filtered by suction and dried at 40 °C. The yield was 1.67 g (55%), yellowish prisms, mp 224.8 °C (ethanol/water). IR: 3051 w, 1633 s, 1605 m, 1562 s cm^{-1}. Anal. calcd for $C_{31}H_{22}NOP$ (455.50): C, 81.74; H, 4.87; N, 3.08. C, 81.40; H, 5.00; N, 2.69.

2-Butyl-3-triphenylphosphoranylideneaminophenalen-1-one (9b): To a solution of 3-azido-2-butylphenalen-1-one (**8b**) (1.95 g, 7 mmol) in toluene (35 mL), triphenylphosphane (2.0 g, 7.6 mmol) was added and the mixture heated to 80 °C for 45 min. After cooling, the solvent was removed under reduced pressure and the oily black residue digested several times with cyclohexane to remove unreacted triphenylphosphane. The orange product was dissolved in toluene (50 mL) and precipitated with hexane (200 mL). The yield was 0.36 g (10%) brown prisms, mp 35-40 °C. For further reactions, the orange raw material was used. IR: 3051 w, 2963-2922 m, 2863 w, 1711 m, 1682 m, 1625 m, 1601 w, 1582 m cm^{-1}. Anal. calcd for $C_{35}H_{30}NOP$ (511.61): C, 82.17; H, 5.91; N, 2.74. C, 81.92; H, 5.55; N, 2.41.

3-Aminophenalen-1-one (10a): Method A: A solution of 3-azido-phenalen-1-one (**8a**) (0.90 g, 41 mmol) in dimethylformamide was diluted with ethanol (50 mL), then palladium/charcoal (0.20 g) was added and the mixture hydrogenated under stirring at room temperature and standard pressure. The catalyst was filtered off and the solution diluted with water (100 mL). The formed precipitate was filtered by suction and dried. The yield was 0.48 g (58%), light yellowish prisms, mp 236 °C (water).

Method B: A suspension of 3-triphenylphosphoranylideneaminophenalen-1-one (**9a**) (2.50 g, 5 mmol), 5 *M* hydrochloric acid (55 mL) and methanol (3.3 mL) was heated under reflux for 5 minutes. The formed triphenylphosphane oxide was filtered and the filtrate brought to pH=10 with 2 *M* sodium hydroxide solution. A

yellow precipitate was formed, which was filtered by suction after stirring for 12 hours at 5 °C. The yield was 0.50 g (47%), yellow prisms, mp 235 °C (water).

Method C: A mixture of 3-hydroxyphenalen-1-one (**3a**) (6.50 g, 31 mmol) and ammonium acetate (65 g, 840 mmol) was heated slowly to 140-145 °C. Melting of the mixture started at 140 °C, and an exothermic reaction was observed. The mixture was kept for several hours at 140-145 °C until the evolution of ammonia stopped. Then the reaction mixture was poured still hot in a solution of concentrated nitric acid (30 mL) in water (500 mL). The formed precipitate was filtered and the filtrate neutralized with sodium carbonate. An oily product was separated, which solidified after stirring for 12 hours at 20 °C to give a yellow precipitate which was filtered by suction. The yield was 2.15 g (33%), yellow prisms, mp 234 °C (water); lit. mp 235-238°C [24, 25]. IR: 3382-3204 m, 1631 s, 1602 w, 1589 s cm^{-1}.

3-Amino-2-butylphenalen-1-one (10b): Method B: A suspension of orange, raw 2-butyl-3-triphenylphosphoranylideneaminophenalen-1-one (**9b**) (1.00 g, 2 mmol), 5 *M* hydrochloric acid (20 mL) and methanol (1.5 mL) was heated under reflux for 1 hour. The formed triphenylphosphane oxide was filtered and the filtrate brought to pH=10 with 2 *M* sodium hydroxide solution to give an oily product. Methanol was evaporated under reduced pressure and the residue extracted with diethylether until the ether phase did not show a yellow color. The ether phase was dried with calcium chloride, filtered and taken to dryness. The yield was 0.01 g (2%), orange crystals, mp 30-35 °C. IR: 2922 s, 2853 m, 1661 m, 1612 w, 1589 m cm^{-1}. Anal. calcd for $C_{17}H_{17}NO$ (251.33): C, 81.24; H, 6.82; N, 5.57. Found: C, 80.89; H, 6.52; N, 5.91.

3-Hydroxy-2-nitrophenalen-1-one (11): To a suspension of 3-hydroxyphenalen-1-one (**3a**) (16.0 g, 82 mmol) in glacial acetic acid (400 mL), nitric acid (40 mL) was added and the mixture stirred at room temperature. Then sodium nitrite (0.42 g, 6.1 mmol) was added to start the slightly exothermic reaction. A clear solution was obtained, which was stirred at room temperature for 30 minutes. The mixture was poured onto ice/water (600 mL) and stirred for 2 hours at room temperature. The formed precipitate was filtered by suction and dried at 40 °C. The yield was 16.35 g (83%), yellow prisms, mp 159 °C (ethanol); lit. mp 160 °C [15, 26]. IR: 3603-3201 m, br, 1662 s, 1631 w, 1589 s cm^{-1}. Anal. calcd for $C_{13}H_7NO_4$ (241.21): C, 64.74; H, 2.93; N, 5.81. Found: C, 64.62; H, 3.11; N, 5.47.

3-Chloro-2-nitrophenalen-1-one (12): A mixture of 3-hydroxy-2-nitrophenalen-1-one (**11**) (2.08 g, 8.3 mmol), phosphoryl chloride (30 mL) and triethylamine (1.26 mL, 9 mmol) was heated for 1 hour under reflux, cooled to room temperature and poured onto ice/water (150 mL) under stirring. A greenish precipitate was formed, which was stirred for 1 hour at 20 °C and then filtered by suction. The yield was 1.57 g (70%), greenish prisms, mp 227.9-231.6 °C (cyclohexane). IR: 1722 w, 1653 s, 1611 sh, 1595 sh, 1559 s cm^{-1}. Anal. calcd for $C_{13}H_6ClNO_3$ (259.65): C, 60.14; H, 2.33; N, 4.48. Found: C, 59.86; H, 2.43; N, 4.47.

2,3-Diazidophenalen-1-one (13): A suspension of 3-chloro-1-nitrophenalen-1-one (**12**) (3.89 g, 15 mmol), dimethylformamide (100 mL) and sodium azide (2.92 g, 45 mmol) was stirred for 48 hours at room temperature. Then the mixture was poured onto ice/water, the formed brown precipitate stirred for 1 hour at 20 °C and then filtered by suction and dried. The yield was 1.87 g (46%), yellow prisms, mp 142 °C dec. (acetone). IR (KBr): 2161 s, 1765 s, 1622 m, 1583 m, 1509 w cm^{-1}. Anal. calcd for $C_{13}H_6N_6O$ (262.23): C, 59.54; H, 2.31; N, 32.05. Found: C, 59.94; H, 2.57; N, 31.65.

2-Amino-3-hydroxyphenalen-1-one (14): Method 1: To a suspension of 3-hydroxyphenalen-1-one (**3a**) (3.35 g, 17 mmol) in glacial acetic acid (20 mL), phenylhydrazine (6.55 mL) was added under stirring to start an exothermic reaction. The mixture was slowly heated to 105-110 °C for 1 hour, then cooled to room temperature and kept at this temperature for 12 hours. The solid was filtered by suction, washed subsequently with glacial acetic acid, ethanol and acetone, and then dried at 40 °C. The yield was 1.66 g (46%) brownish prisms, mp 302-303 °C; lit. mp 260-265 °C [17]. IR: 3041 m, 2955 s, 2581 m, 1710 sh, 1701 w, 1682 s, 1589 m, 1578 m, 1570 m cm^{-1}.

Method 2: To a solution of 3-hydroxy-2-nitrophenalen-1-one (**11**) (10 mmol, 2.41 g) in 2 *M* sodium hydroxide solution (50 mL), sodium dithionite (10 g) was added in small portions under stirring at room temperature, until the color of the mixture did not further change. The reaction mixture was then cooled down to O °C and brought

to pH = 1 with hydrochloric acid. The resulting precipitate was filtered by suction and dried at room temperature. The yield was 0.24 g (10%) dark black powder of **14.HCl**. It was used for further reactions without purification.

9-Methylphenaleno[2,1-*d*]oxazol-7-one (15a): Method A: A mixture of 2-amino-3-hydroxyphenalen-1-one (**14**) (0.48 g, 2.3 mmol) and anhydrous sodium acetate (0.08 g, 0.9 mmol) in acetic anhydride (20 mL) was heated under reflux for 2 hours. The solvent was removed under reduced pressure and the residue recrystallized from cyclohexane. The yield was 0.58 g (86%), mp 175.7-176.5 °C (cyclohexane).
Method B: A mixture of 2-amino-3-hydroxyphenalen-1-one (**14**) (2.11 g, 10 mmol), acetic acid (R = Me) (10 g, 0.17 mol) and polyphosphoric acid (20 g) was heated for 2 hours to 150 °C under stirring. The hot black mixture was poured onto ice/water (200 mL), stirred for 1 hour and then brought to pH=5-6 with 2 *M* sodium hydroxide solution. The formed green precipitate was filtered by suction and dried. The yield was 1.40 g (60%) greenish prisms, mp 178-180 °C (toluene/cyclohexane).
Method C: A mixture of 2-azido-3-hydroxyphenalen-1-one (**8a**) (2.21 g, 10 mmol), acetic acid (10 g, 0.17 mol) and polyphosphoric acid (20 g) was heated for 2 hours to 150 °C under stirring. The hot mixture was poured onto ice/water (200 mL), stirred for 1 hour and then brought to pH=5-6 with 2 *M* sodium hydroxide solution and then filtered by suction and dried. A second crop was obtained by extraction of the filtrate with dichloromethane (2x 100 mL), drying the organic phases with sodium sulfate and removing the solvent under reduced pressure. The combined solids were crystallized from toluene. The yield was 1.53 g (65%) greenish prisms, mp 178-180 °C (toluene/cyclohexane); lit. mp 184-185 °C [ex06]. IR: 1655 s, 1581 s, 1505 m cm^{-1}. ^1H NMR($CDCl_3$): δ 2.67 (s, Me), 7.61-8.29 (m, 5 H, aryl-H), 8.70-8.85 (d, J = 8 Hz, 1 H, 6-H). Anal. calcd for $C_{15}H_9NO_2$ (235.24): C, 76.59; H, 3.86; N, 5.95. Found: C, 76.57; H, 4.10; N, 5.86.

9-Ethylphenaleno[2,1-*d*]oxazol-7-one (15b): A mixture of 2-amino-3-hydroxy-phenalen-1-one (**14**) (2.11 g, 10 mmol), propanoic acid (R = Et) (10.0 g, 0.14 mol) and polyphosphoric acid (20 g) was heated for 2 hours to 150 °C (internal temperature) under stirring. The hot black mixture was poured onto ice/water (200 mL), stirred for 1 hour and then brought to pH=5-6 with 2 *M* sodium hydroxide solution. The formed green precipitate was filtered by suction, dried and purified using a heat extractor with cyclohexane. The yield was 1.20 g (49%), greenish prisms, mp 125.5 °C (toluene/cyclohexane); lit. mp 106-107 °C [27]. IR: 1652 s, 1588 w, 1580 m 1512 m cm^{-1}. ^1H NMR ($CDCl_3$): δ 1.51 (t, J = 8 Hz, Me), 3.02 (q, J = 8 Hz, CH_2), 7.61-8.15 (m, 5 H, ArH), 8.25-8.32 (d, J = 8 Hz, 1 H, 6-H). Anal. calcd for $C_{16}H_{11}NO_2$ (249.27): C, 77.10; H, 4.45; N, 5.62. Found: C, 76.97; H, 4.54; N, 5.62.

2-Phenylaminomethylenephenalene-1,3-dione (18) was prepared as described previously [8].

3-Chloro-1-oxo-1*H*-phenalene-2-carbaldehyde (19): A solution of phosphoryl chloride (2.1 g, 14 mmol) in dimethylformamide (1 mL) was stirred 1 hour at room temperature and then added dropwise to a solution of 2-phenylaminomethylenephenalene-1,3-dione (**18**) (3.0 g, 10 mmol) in dimethylformamide (60 mL), keeping the temperature between 15-20 °C. The reaction mixture was stirred for 3 days at room temperature and then poured onto ice/water (150 mL) which forms a yellow-greenish precipitate. The solid was stirred for 2 hours at room temperature and then filtered by suction and dried. The yield was 1.25 g (51%), mp 145-146.7 °C (cyclohexane). IR: 1695 s, 1642 s, 1615 w, 1575 s, 1535 m, 1502 m cm^{-1}. Anal. calcd for $C_{14}H_7ClO_2$ (242.66): C, 69.30; H, 2.91; Cl, 14.61. Found: C, 69.64; H, 3.37; Cl, 14.22.

8-Hydroxypyrano[2,3-*b*]phenalene-7,10-dione (20) and **2-acetyl-3-hydroxyphenalen-1-one (21)** were prepared as described previously [10].

8-Methyl-7*H*-phenaleno[2,1-*d*]isoxazol-7-one (23): A mixture of 2-acetyl-3-hydroxyphenalen-1-one (**21**) (2.38 g, 10 mmol), hydroxylamine hydrochloride (1.75 g, 50 mmol) and sodium hydrogencarbonate (3.0 g) in ethanol/water (100 mL : 50 mL) was heated under reflux for 90 minutes, cooled and stirred for 12 hours at 5 °C. The formed precipitate was filtered by suction and the mixture purified and separated by dry flash column chromatography (eluents hexane and ethyl acetate). First a blue fluorescent product (isoxazole **23**, yield: 0.52 g, 22%) was isolated, the second product was a yellow-blue fluorescent compound, identical with the oxazole **15a**

(yield: 0.05 g, 2%). Analytical data of **23**: mp: 184-185 °C. IR: 2952 w, 1655 s, 1585 w, 1571 m 1505 m cm^{-1}. Anal. calcd for $C_{15}H_9NO_2$ (235.24): C, 76.59; H, 3.86; N, 5.95. Found: C, 76.21; H, 4.19; N, 5.65.

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