Monatsh Chem (2016) 147:425–428
DOI 10.1007/s00706-015-1607-4

ORIGINAL PAPER

The preparation of annulated 1,3-oxazoles from 1,3,2-oxazaphospholes and aldehydes

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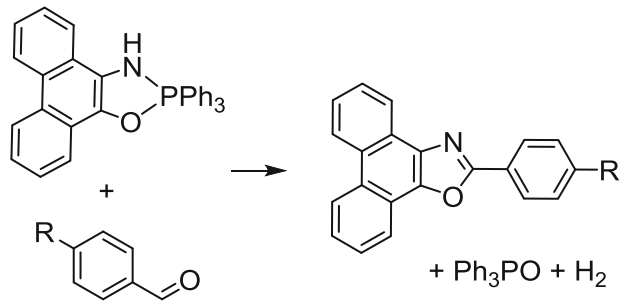
Received: 22 June 2015 / Accepted: 16 November 2015 / Published online: 25 November 2015

Abstract The reactions of 2,3-dihydro-2,2,2-triphenylphenanthro[9,10-*d*]-1,3,2-λ^5-oxazaphospholes with aromatic aldehydes lead to the corresponding 2-substituted phenanthro[9,10-*d*][1,3]oxazoles via an aza-Wittig reaction in good yields.

Graphical abstract



Keywords Annulated · Aldehydes · Heterocycles · aza-Wittig reaction

Introduction

1,3-Oxazole ring systems occur in nature [1] and their derivatives are important in pharmacology as antibacterial and antifungal agent [2]. Some of the 1,3-oxazole compounds show excellent scintillator properties [3], others are good fluorescent whitening agents [4]. One can find along other compounds, which are antiepileptic drugs, sedative muscle-relaxant, and useful against enteric infections [5]. Appetite depressants are also found among this type of compounds [6].

There are a fair number of methods for the preparation of 1,3-oxazoles [7]. However, we can find less papers concerning the preparation annulated phenanthro[9,10-*d*][1,3]oxazoles [8, 9, and references therein]. Recently, we studied the reactions of 2,3-dihydro-2,2,2-triphenylphenanthro[9,10-*d*]-1,3,2-λ^5-oxazaphosphole (**1**) with some small molecules such as triplet dioxygen [10] and carbon dioxide [11]. Surprisingly in the reaction of **1** with CO_2, we obtained 3*H*-phenanthro[9,10-*d*]oxazol-2-ones in good yield applying very mild conditions. As a continuation of this work, we extended the scope of the reaction of **1** with various carbonyl compounds. In this paper, we report these results.

Results and discussion

The starting 2,3-dihydro-2,2,2-triphenylphenanthro[9,10-*d*]-1,3,2-λ^5-oxazaphosphole (**1**) and 4,6-di-*tert*-butyl-2,2,2-triphenyl-2,3-dihydro-2λ^5-benzo[*d*][1,3,2]oxazaphosphole (**3**) as starting materials were prepared by a procedure described earlier [12]. Heating **1** with various 4-substituted aromatic aldehydes in acetonitrile at 85 °C for 12 h the corresponding 2-arylphenanthro[9,10-*d*][1,3]oxazoles **2** could be isolated in moderate or good yields (Scheme 1). Labeling of **2** is shown in Fig. 1. The reactions can be

Electronic supplementary material The online version of this article (doi:10.1007/s00706-015-1607-4) contains supplementary material, which is available to authorized users.

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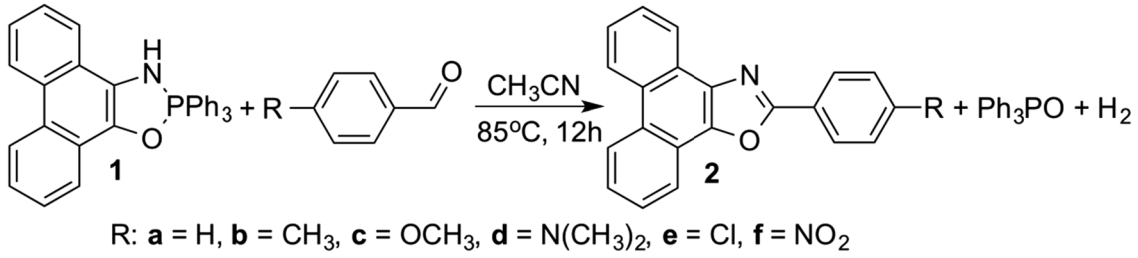
Scheme 1



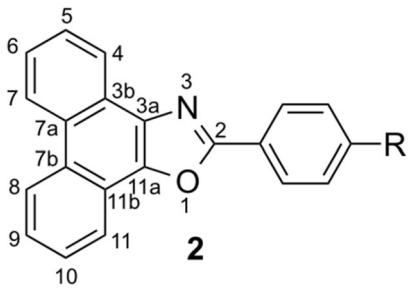


Fig. 1 The structure and numbering of 2-arylphenanthro[9,10-*d*][1,3]oxazole **2**

Table 1 Synthesis of 2-substituted phenanthro[9,10-*d*][1,3]oxazoles **2a–2f**

Product	R	Yield/%[a]	M.p./°C
2a	H	78	192–199
2b	Me	56	241–243
2c	OMe	37	219–223
2d	$N(Me)_2$	19	220–222
2e	Cl	52	258–260
2f	NO_2	62	252–254

[a] Isolated yield

carried out also in a Schlenk vessel melted the reactants together or in pressure vessel at 130 °C. The yields varied from 52 to 60 and 42 %.

Unfortunately, aliphatic aldehydes (propanal, paraformaldehyde, 2-ethylhexanal) and ketones (cyclohexanone, acetophenone) did not react under the condition used. So, the scope of the reaction could not be broadened. The same situation was observed when we applied *o*-quinones (9,10-phenanthrenequinone, acenaphthoquinone) 1,2-diketones (benzil) with benzaldehyde in the presence of ammonia and triphenylphosphine under the same conditions, preparing the starting compound **1** "in situ." A summary of compounds prepared is tabulated in Table 1.

The same reaction was also carried out with the starting compound 4,6-di-*tert*-butyl-2,3-dihydro-2,2,2-triphenyl[1,3,2-λ^5]-benzoxaphosphole (**3**). It was interesting to note that in these reactions we always obtained mixtures of *N*-benzylidene-3,5-di-*tert*-butylaminophenols **4** as main products and the corresponding [1,3]oxazoles **5** as minor products. In this case, the dehydrogenation steps seem to be more difficult.

Kinetic studies of the reactions between 2,3-dihydro-2,2,2-triphenylphenanthro[9,10-*d*]-1,3,2-λ^5-oxazaphosphole and benzaldehyde at 65 °C by measuring the formed triphenylphosphine oxide by GC revealed an overall second-order rate equation (Eq. 1).

$$\mathrm{d[Ph_3PO]}/\mathrm{d}t = k_2[\text{benzaldehyde}][1,3,2\text{-oxazaphosphole}]. \quad (1)$$

The k_2 value is 2.68×10^{-3} M^{-1} s^{-1}. The mechanistic findings are in agreement with theoretical calculation where a tandem [2 + 2] cycloaddition has been proposed [13, 14]. In order to obtain the Hammett plot, we determined also the reaction rates with various 4-substituted benzaldehydes. The Hammett plot is shown in Fig. 2, where it is obvious that electron-withdrawing substituents enhance the reaction rate, and the reaction constant (ρ) is 0.58. According to the kinetic data, we

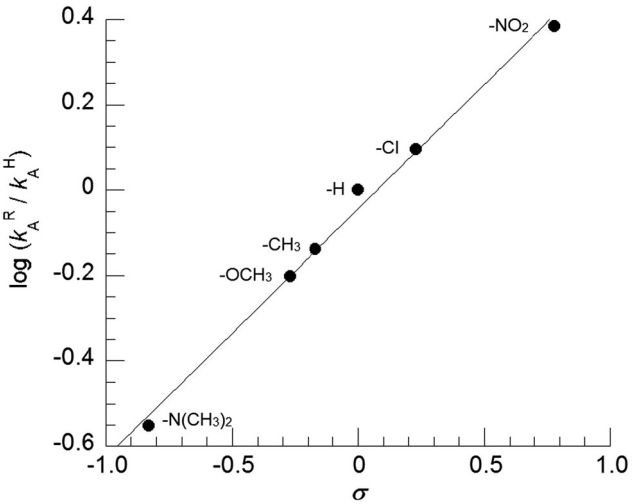
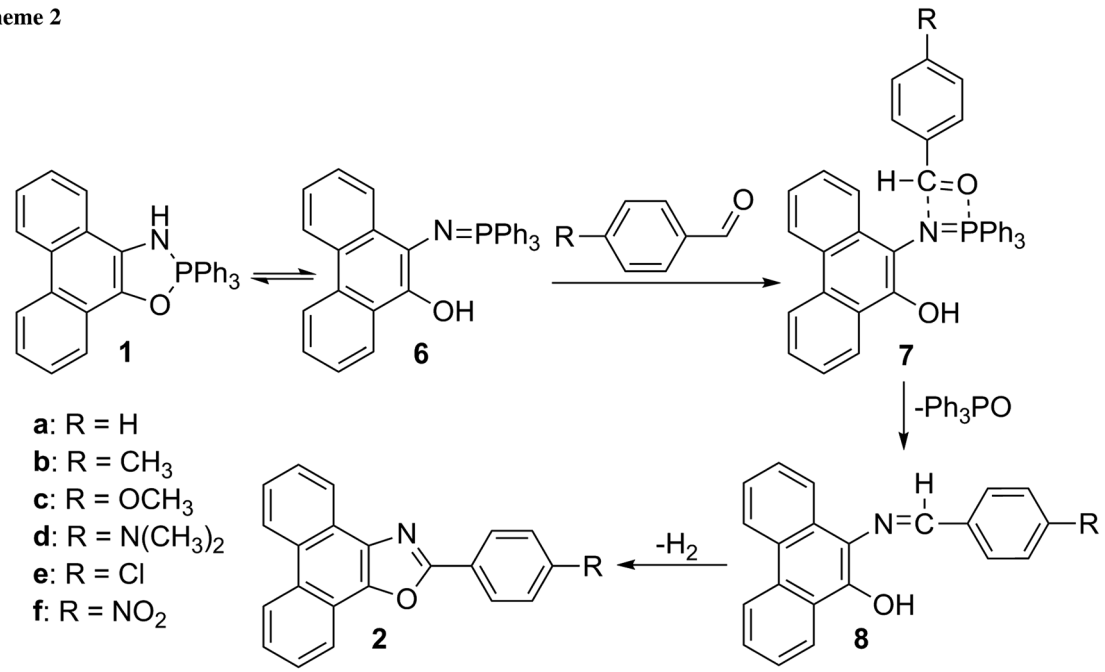


Fig. 2 The Hammett plot of the reactions of **2** with various 4-substituted benzaldehydes

Scheme 2



propose a mechanism for the reaction as depicted in Scheme 2.

Conclusions

1,3,2-oxazaphosphole **1** undergoes valence tautomerism resulting also in the ring-opened iminophosphorane form **6**. This reacts then in an aza-Wittig reaction (**7**) to the *N*-benzylidene-9,10-phenantrenaminophenol **8** and triphenylphosphine oxide. The latter spontaneously is dehydrogenated to the end product **2**. This dehydrogenation step has been observed earlier in other *N*-benzylidene compounds, which showed instant dihydrogen evolution. It was, however, unexpected, that if we carried out the reaction using 4,6-di-*tert*-butyl-2,2,2-triphenyl-2,3-dihydro-2λ^5-benzo[*d*][1,3,2]oxazaphosphole (**3**) as starting materials, slow H_2 formation was observed and only a mixture of *N*-benzylidene-3,5-di-*tert*-butylaminophenol **4** and [1,3]oxazole **5** could be isolated. Neither **4** nor **5** could be obtained as a pure compound (NMR).

Experimental

Benzaldehyde and its derivatives were obtained commercially and used without further purification. We have prepared 2,3-dihydro-2,2,2-triphenylphenanatro[9,10-*d*]-1,3,2-λ^5-oxazaphosphole (**1**) and 4,6-di-*tert*-butyl-2,3-dihydro-2,2,2-triphenyl[1,3,2-λ^5]-benzoxaphosphole (**3**) according to the literature [12].

Melting points were obtained by using a calibrated melting point microscope. Gas chromatographic (GC) analyses were carried out on a HP 4890D instrument with flame ionization detector equipped with an HP-5 capillary column. NMR spectra: ^{1}H and ^{13}C NMR spectra were collected on 400 MHz NMR spectrometers (Bruker Avance) using $CDCl_3$ as solvent. Chemical shifts are reported in parts per million (ppm). Chemical shifts for protons are reported in parts per million downfield and are referenced to residual protium in the NMR solvent ($CDCl_3$: $\delta = 7.27$ ppm). Chemical shifts for carbon are reported in parts per million downfield and are referenced to the carbon resonances of the solvent ($CDCl_3$: $\delta = 77.0$ ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, and m = multiplet), and coupling constants in Hertz (Hz). Gas chromatographic–mass spectrometric (GC–MS) analyses were carried out on a GCMS-QP2010 SE instrument with secondary electron multiplier detector.

General procedure for the synthesis of 1,3-oxazoles ***2a–2f***

A solution of 0.47 g 2,3-dihydro-2,2,2-triphenylphenanthro[9,10-*d*]-1,3,2-λ^5-oxazaphosphole (1 mmol), benzaldehyde or its derivatives (2 mmol), and 20 cm^3 acetonitrile was refluxed under argon for 12 h. When the reaction was finished, the mixture was cooled to room temperature. The deposited pale yellow to brown crystals were filtered off and dried in vacuo.

*2-Phenylphenanthro[9,10-d][1,3]oxazole (**2a**, $C_{21}H_{13}NO$)*

Yellow crystals; 78 % yield; m.p.: 192–199 °C; $R_f = 0.58$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.73$ (app. t, $J = 16.4$ Hz, 2H), 8.63 (d, $J = 7.6$ Hz, 1H), 8.32–8.39 (m, 3H), 7.77–7.52 (m, 7H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 162.11$, 144.83, 135.51, 130.85, 129.25, 128.86, 127.55, 127.35, 127.20, 127.13, 126.33, 126.16, 126.07, 123.68, 123.36, 122.90, 121.04, 120.81 ppm; IR (KBr): $\bar{\nu} = 3055$, 2910, 1617, 1548, 1487, 1315, 1058, 755, 722, 692, 685, 539 cm^{-1}; MS (ESI): $m/z = 295$ (M^+, 100).

*2-(p-Tolyl)phenanthro[9,10-d][1,3]oxazole (**2b**, $C_{22}H_{15}NO$)*

Yellow crystals; 56 % yield; m.p.: 241–243 °C; $R_f = 0.66$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.73$ (app. t, $J = 17.6$ Hz, 2H), 8.64 (d, $J = 8.0$ Hz, 1H), 8.33 (d, $J = 7.6$ Hz, 1H), 8.27 (d, $J = 8.0$ Hz, 2H), 7.78–7.61 (m, 4H), 7.37 (d, $J = 8.0$ Hz, 2H), 2.47 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 162.42$, 141.16, 135.58, 129.50, 129.20, 128.88, 127.23, 127.11, 126.29, 126.10, 125.92, 124.96, 123.64, 123.29, 122.91, 121.16, 120.72, 21.45 ppm; IR (KBr): $\bar{\nu} = 3027$, 2912, 1613, 1496, 1311, 1061, 822, 755, 725, 691, 497 cm^{-1}; MS (ESI): $m/z = 309$ (M^+, 100).

*2-(4-Methoxyphenyl)phenanthro[9,10-d][1,3]oxazole (**2c**, $C_{22}H_{15}NO_2$)*

Yellow crystals; 37 % yield; m.p.: 219–223 °C; $R_f = 0.33$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.73$ (app. t, $J = 16.4$ Hz, 2H), 8.63 (d, $J = 9.2$ Hz, 1H), 8.32–8.29 (m, 3H), 7.76–7.64 (m, 4H), 7.07 (d, $J = 9.2$ Hz, 2H), 3.91 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 162.31$, 144.52, 135.60, 129.06, 128.84, 127.18, 127.05, 126.27, 125.97, 125.85, 123.63, 123.28, 122.88, 121.16, 120.62, 120.38, 114.33, 55.33 ppm; IR (KBr): $\bar{\nu} = 3064$, 2962, 1608, 1495,1451, 1302, 1247, 1170, 1032, 833, 754, 736, 721, 689, 518 cm^{-1}; MS (ESI): $m/z = 325$ (M^+, 100).

*N,N-Dimethyl-4-(phenanthro[9,10-d]][1,3]oxazol-2-yl)aniline (**2d**, $C_{23}H_{18}N_2O$)*

Brown crystals; 19 % yield; m.p.: 220–222 °C; $R_f = 0.21$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.75$ (app. t, $J = 14.8$ Hz, 2H), 8.64 (d, $J = 9.2$ Hz, 1H), 8.33 (d, $J = 8.8$ Hz, 1H), 8.24 (d, $J = 8.8$ Hz, 2H), 7.76–7.63 (m, 4H), 6.83 (d, $J = 9.2$ Hz, 2H), 3.09 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 163.56$, 152.11, 144.37, 129.02, 128.93, 127.46, 127.36, 126.36, 126.07, 123.92, 123.60, 123.25, 121.42, 120.85, 112.16, 40.55 ppm; IR (KBr): $\bar{\nu} = 3051$, 2896, 2851, 2794, 1611, 1502,1443, 1362, 1233, 1188, 1166, 1058, 814, 755, 737, 721 cm^{-1}; MS (ESI): $m/z = 338$ (M^+, 100).

*2-(4-Chlorophenyl)phenanthro[9,10-d][1,3]oxazole (**2e**, $C_{21}H_{12}ClNO$)*

Yellow crystals; 52 % yield; m.p.: 258–260 °C; $R_f = 0.57$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.74$ (app. t, $J = 18.8$ Hz, 2H), 8.62 (d, $J = 8.8$ Hz, 1H), 8.36–8.29 (m, 3H), 7.77–7.68 (m, 4H), 7.53 (d, $J = 8.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 161.14$, 144.98, 137.00, 135.59, 130.55, 129.43, 129.14, 128.96, 128.85, 128.33, 127.37, 127.19, 126.43, 126.14, 123.71, 123.34, 122.87, 121.11, 120.76 ppm; IR (KBr): $\bar{\nu} = 3055$, 2921, 1601, 1479,1451, 1308, 1235, 1094, 1084, 1030, 831, 757, 722, 683, 544 cm^{-1}; MS (ESI): $m/z = 329$ (M^+, 100).

*2-(4-Nitrophenyl)phenanthro[9,10-d][1,3]oxazole (**2f**, $C_{21}H_{12}N_2O_3$)*

Yellow crystals; 62 % yield; m.p.: 252–254 °C; $R_f = 0.52$ (hexan/diethyl ether 9/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.77$ (q, $J = 19.6$ Hz, 2H), 8.64 (m, $J = 10.0$ Hz, 1H), 8.55 (q, $J = 8.8$ Hz, 2H), 8.43 (q, $J = 9.2$ Hz, 2H), 8.38 (d, $J = 10$ Hz, 1H), 7.72–7.81 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 160.01$, 149.17, 133.29, 130.28, 129.39, 128.02, 127.80, 127.46, 126.95, 126.18, 124.55, 124.17, 123.81, 123.22, 121.39, 121.11, 121.02 ppm; IR (KBr): $\bar{\nu} = 3064$, 2962, 1606, 1511,1338, 1104, 853, 744, 710, 668 cm^{-1}; MS (ESI): $m/z = 340$ (M^+, 100).

Acknowledgments This work was supported by a grant from The Hungarian Research Fund (OTKA) #K108489 and COST Actions CM1205, CM1201, and CM1003.

References

1. Nicolaou KC, Junliang H, Reddy MV, Rao PB, Rassias G, Snyder SA, Xianhai H, Chen DYK, Brenzovich WE, Giuseppone N, Giannakakou P, O'Brate A (2004) J Am Chem Soc 126:12897
2. Pattenden G, González MA, Little PB, Millan DS, Plowright AT, Tornos JA, Ye T (2003) Org Biomol Chem 1:4173
3. Bransome ED (1970) The current status of liquid scintillation counting. Grune and Stratton, New York
4. Joussot-Dubien J (1975) Lasers in physical chemistry and biophysics. Elsevier, Amsterdam
5. Withrow CD (1980) Adv Neurol 27:577
6. Tubaro E (1965) Chem Pharm Bull 104:602
7. Boid GV (1984) The structure, reactions, synthesis and uses of heterocyclic compounds. In: Katritzky AR, Rees CW (eds) Comprehensive heterocyclic chemistry, vol 6, part 4B. Pergamon, Oxford, p 177
8. Ling R, Yoshida M, Mariano PS (1996) J Org Chem 61:4439
9. Khalafi-Nezhad A, Panahi F (2014) ACS Catal 4:1686
10. Bors I, Kaizer J, Speier G (2014) RSC Adv 4:16928
11. Bors I, Kaizer J, Speier G, Giorgi M (2014) RSC Adv 4:45969
12. Speier G, Tyeklár Z, Fülöp V, Párkányi L (1988) Chem Ber 121:1685
13. Palacios F, Alonso C, Aparicio D, Rubiales G, de los Santos JM (2007) Tetrahedron 63:523
14. Cossío FP, Alonso C, Lecea B, Ayerbe M, Rubiales G, Palacios FJ (2006) Org Chem 71:2839