ISSN 1070-3632, Russian Journal of General Chemistry, 2015, Vol. 85, No. 8, pp. 1862–1865. © Pleiades Publishing, Ltd., 2015.
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Synthesis and Reactivity of 2-(2-Thienyl)phenanthro[9,10-*d*]oxazole

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Received April 14, 2015

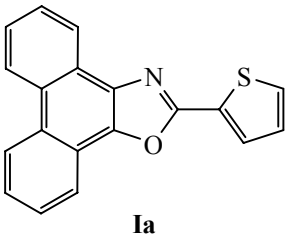
Abstract—2-(2-Thienyl)phenanthro[9,10-*d*]oxazole has been synthesized via reaction of 9,10-phenanthrene quinone imine with thiophene-2-carbaldehyde in ethanol. The product interaction with electrophilic reagents (nitration, bromination, sulfonation, formylation, acylation) has been studied. Electrophilic attack takes place at the thiophene ring or at phenanthrene moiety, depending on the reaction conditions.

Keywords: 9,10-phenanthrene quinone, thiophene-2-carbaldehyde, 2-(2-thienyl)phenanthro[9,10-*d*]imidazole, electrophilic substitution, thiophene, phenanthrene

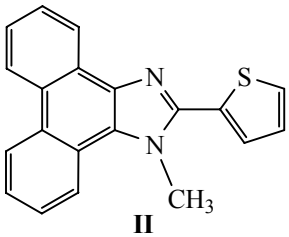
DOI: 10.1134/S1070363215080125

Synthesis and spectral study of fluorescent organic substances is an important aspect of development of new laser dyes and biomedical probes. The fluorescent dye molecule should combine a fluorophore polycyclic moiety providing high quantum yield of fluorescence and groups sensitive to the polarity or proton-donor activity of the medium. We have failed to find any information on preparation and properties of phenanthro[9,10-*d*]oxazole containing thiophene moiety in the literature. However, bisheterocyclic compounds of this type are of interest as potential bioactive substance [1] and organic phosphors [2].

In this work we aimed to elaborate a convenient method for synthesis of 2-(2-thienyl)phenanthro-[9,10-*d*]oxazole **Ia** and to study its reactivity in comparison with the imidazole analog **II** [3].



Ia



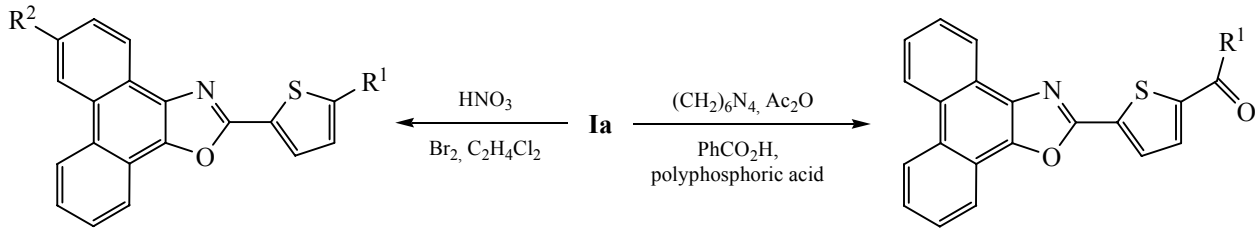
II

Reactions of 9,10-phenanthrene quinone with aromatic aldehydes in ammonia medium have been previously studied [4]. According to the available data, the reactions exclusively afford oxazoles at low temperature, whereas imidazoles or a mixture of the both are formed at higher temperature. 4-Nitro-, 4-hydroxy- and 4-methoxybenzaldehydes have given only imidazoles at both low and high temperatures in ammonia medium. However, we failed to obtain (2-thienyl)phenanthro[9,10-*d*]oxazole **Ia** via that procedure. Therefore, we adopted the method described in [5]: condensation of imine 9,10-phenanthrene quinone with thiophene-2-carbaldehyde in ethanol. In that case the yield of oxazole **Ia** was of 72%.

The so prepared 2-(2-thienyl)phenanthro[9,10-*d*]-oxazole **Ia** was further introduced in the reactions with electrophilic reagents: acetyl nitrate, bromine in dichloroethane, sulfuric acid, polyphosphoric acid, hexamine and carboxylic acids in polyphosphoric acid, and diluted nitric acid (d = 1.42 g cm^{-3}) as a radical reactant (Scheme 1).

Analysis of ^{1}H NMR spectra of compound **Ia** and 2-(2-thienyl)phenanthro[9,10-*d*]imidazole **II** [3] revealed a clear correlation between the low-field shift of the H^3 thiophene ring protons (7.98 and 7.52 ppm) (caused primarily by the induction effect) and the influence of the electron-withdrawing phenanthro-oxazole and imidazole substituents, weaker in the latter case. The apparent reason was that the pyrrole heteroatom in phenanthrooxazole **Ia** was an acceptor, in contrast to imidazole **II**; therefore the decreased in reactivity of the thiophene core in compound **Ia** could be expected.

Scheme 1.



Ib–Id **Ie–Ig**

$R^1 = NO_2$, R^2 = H (**b**); R^1 = Br, R^2 = H (**c**); $R^1 = R^2$ = Br (**d**); R^1 = H (**e**), Me (**f**), Ph (**g**).

We performed several test reactions that confirmed the assumption. In particular, nitration of **Ia** with a mixture of $Cu(NO_3)_2$ with acetic anhydride (under conditions of smooth nitration of compound **II**) took place with very low yield. Therefore, we carried out radical nitration via heating in diluted nitric acid (d = 1.42 g cm^{-3}). In that case, 5-nitro derivative **Ib** was obtained with yield of 62%. It was also obtained independently via *ipso*-substitution of the bromine atom of 2-(5-bromo-2-thienyl)phenanthro[9,10-*d*]oxazole **Ic** with nitro group.

Similar result was obtained in the reaction of phenanthrooxazole **Ia** bromination with an equivalent amount of bromine in dichloroethane under reflux. Yield of 2-(5-bromo-2-thienyl)phenanthro[9,10-*d*]-oxazole **Ic** was of 64%. However, the dibromo derivative **Id** was produced via further substitution at position 6 of the phenanthrene ring in an excess of bromine, as confirmed by the spectral data. In detail, the signal of H^7 atom (doublet at 8.74 ppm, J = 8.0 Hz) was not observed in ^{1}H NMR spectrum of compound **Id,** and a new signal appeared at 8.80 ppm (J = 1.5 Hz) owing to deshielding with the adjacent bromine atom. Furthermore, the H^6 signal disappeared from the four-proton multiplet at 7.65–7.75 ppm, the latter being transformed into a three-proton multiplet at 7.70–7.77 ppm.

Compound **II** formed the similar dibromide at temperature as low as –5°C [3], whereas compound **Ia** was regenerated under those conditions.

Similarly to imidazole **II**, compound **Ia** was inert to the Vilsmeier's reagent, even under severe conditions. Therefore, we took advantage of formylation of hindered phenols with urotropin in polyphosphoric acid at 70–80°C. Aldehyde **Ie** was obtained in 41% yield. Compound **II** reacted under the same conditions at lower temperature of 60°C to form 5-formylthiophene derivative (52%).

Due to the strong suppression of reactivity of the thiophene ring with the phenanthrooxazole fragment, acetylation of compound **Ia** was only possible under the action of acetic anhydride in polyphosphoric acid at 110–120°C. The reaction selectivity was poor; a large amount of unidentified side products was generated, their fraction increasing as the temperature was raised. Therefore, ketone **If** was obtained in yield of below 37%, whereas compounds **II** under the same conditions afforded the corresponding ketone in 55% yield. Acylation of compound **Ia** with benzoic acid was carried out similarly, but occurred at higher temperature (150–160°C). Unlike acetylation, it was smooth to yield phenyl ketone **Ig** in yield of 46%.

In summary, we designed preparative method for synthesis of 2-(2-thienyl)phenanthro[9,10-*d*]oxazole **Ia** and studied its reactivity towards various electrophiles. Electron-withdrawing effect of oxazole moiety was found to be more pronounced than that in the case of compound **II**, which was consistent with the more electron-excessive thiophene ring in this compound.

EXPERIMENTAL

Structure of compounds **Ia**–**Ig** was elucidated using equipment installed in the Center for Collective Use of the Platov South-Russian State Polytechnic University.

IR spectra were recorded using a Specord 75IR spectrometer in paraffin oil. ^{1}H NMR spectra were registered with a Varian Unity 300 spectrometer (300 MHz, $CDCl_3$) relative to internal TMS. The reaction progress was monitored by TLC on the plates coated with Al_2O_3 (Brockmann II type) eluting with CH_2Cl_2 or $CHCl_3$ and detecting with iodine vapor. Elemental analysis was performed using a Perkin Elmer 2400 analyzer. Melting points were determined via the capillary method on a PTP apparatus. Physico-

Table 1. Yields, melting points, and elemental analysis data for compounds **Ia**–**Ig**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
Ia	72	264–265	75.93	3.47	4.88	$C_{19}H_{11}NOS$	75.72	3.68	4.65
Ib	62	245–246	66.13	2.77	8.21	$C_{19}H_{10}N_2O_3S$	65.89	2.91	8.09
Ic	64	233–234	59.77	2.86	3.45	$C_{19}H_{10}BrNOS$	60.01	2.65	3.68
Id	55	199–200	49.56	2.17	–	$C_{19}H_9Br_2NOS$	49.70	1.98	–
Ie	41	228–229	73.15	3.49	4.48	$C_{20}H_{11}NO_2S$	72.93	3.37	4.25
If	37	232–233	73.17	4.07	3.79	$C_{21}H_{13}NO_2S$	73.45	3.82	4.08
Ig	46	166–167	76.73	3.55	3.67	$C_{26}H_{15}NO_2S$	77.02	3.73	3.45

Table 2. IR and ^{1}H NMR spectroscopy data for compounds **Ia**–**Ig**

Comp. no.	ν, cm^{-1}	δ, ppm (*J*, Hz, $CDCl_3$)
Ia	–	7.22 t (1H, H^4, Ht, *J* 3.8), 7.54 d (1H, H^5, Ht, *J* 5.1), 7.65–7.75 m (4H, $H^{5,6,9,10}$, Ar), 7.98 d (1H, H^3, Ht, *J* 3.9), 8.32 d (1H, H^{11}, Ar, *J* 7.8), 8.59 d (1H, H^4, Ar, *J* 7.8), 8.72 d (1H, H^8, Ar, *J* 8.1), 8.74 d (1H, H^7, Ar, *J* 8.0)
Ib	1370 s (NO_2) 1530 as (NO_2)	7.73–7.88 m (4H, $H^{5,6,9,10}$, Ar), 7.92 d (1H, H^3, Ht, *J* 4.2), 8.02 d (1H, H^4, Ht, *J* 4.2), 8.39 d (1H, H^{11}, Ar, *J* 7.8), 8.52 d (1H, H^4, Ar, *J* 7.8), 8.62 d (1H, H^8, Ar, *J* 8.1), 8.77 d (1H, H^7, Ar, *J* 8.0)
Ic	–	7.15 d (1H, H^4, Ht, *J* 3.9), 7.65–7.73 m (4H, $H^{5,6,9,10}$, Ar), 7.68 d (1H, H^3, Ht, *J* 3.9), 8.26 d (1H, H^{11}, Ar, *J* 7.8), 8.55 d (1H, H^4, Ar, *J* 7.8), 8.69 d (1H, H^8, Ar, *J* 8.2), 8.73 d (1H, H^7, Ar, *J* 8.0)
Id	–	7.17 d (1H, H^4, Ht, *J* 4.2), 7.68 d (1H, H^3, Ht, *J* 4.2), 7.70–7.77 m (3H, $H^{5,9,10}$, Ar), 8.07 d (1H, H^{11}, Ar, *J* 8.1), 8.50 d (1H, H^4, Ar, *J* 7.8), 8.57 d (1H, H^8, Ar, *J* 7.8), 8.80 d (1H, H^7, Ar, *J* 1.5)
Ie	1640 (C=O)	7.65–7.75 m (4H, $H^{5,6,9,10}$, Ar), 7.83 d (1H, H^3, Ht, *J* 3.9), 8.01 d (1H, H^4, Ht, *J* 3.9), 8.30 d (1H, H^{11}, Ar, *J* 8.1), 8.58 d (1H, H^4, Ar, *J* 8.1), 8.71 d (1H, H^8, Ar, *J* 6.3), 8.74 d (1H, H^7, Ar, *J* 7.8), 10.00 s (1H, CHO)
If	1670 (C=O)	2.64 s (3H, CH_3), 7.71 d (1H, H^3, Ht, *J* 3.9), 7.68–7.75 m (4H, $H^{5,6,9,10}$, Ar), 8.01 d (1H, H^4, Ht, *J* 3.9), 8.30 d (1H, H^{11}, Ar, *J* 7.9), 8.59 d (1H, H^4, Ar, *J* 8.1), 8.72 d (1H, H^8, Ar, *J* 7.2), 8.74 d (1H, H^7, Ar, *J* 7.2)
Ig	1680 (C=O)	7.55 t (3H, H^{3-5}, Ar, *J* 7.8), 7.69 d (1H, H^3, Ht, J 4.0), 7.68–7.73 m (4H, $H^{5,6,9,10}$, Ar), 7.98 d (1H, H^4, Ht, *J* 4.0), 8.12 d (2H, $H^{2,6}$, Ar, *J* 7.8), 8.25 d (1H, H^{11}, Ar, *J* 7.8), 8.53 d (1H, H^4, Ar, *J* 8.1), 8.70 d (1H, H^8, Ar, *J* 7.2), 8.72 d (1H, H^7, Ar, *J* 7.2)

chemical and spectral characteristics of the obtained compounds are shown in Tables 1, 2.

2-(2-Thienyl)phenanthro[9,10-*d*]oxazole (Ia). A mixture of 2.07 g (10 mmol) of 9,10-phenanthrene quinone imine, 1.34 g of thiophene-2-carbaldehyde (12 mmol), and 0.85 g (10 mmol) of piperidine in 10 mL of ethanol was refluxed during **II** h. The reaction mixture was then cooled down, and the precipitated 2-(2-thienyl)phenanthro[9,10-*d*]oxazole was separated. The product was crystallized from ethanol with addition of activated charcoal. Yield 2.17 g.

2-(5-Nitro-2-thienyl)phenanthro[9,10-*d*]oxazole (Ib). A suspension of 0.3 g (1 mmol) of compound **Ia** in 5 mL of diluted nitric acid (d = 1.42 g mL^{-1}) was heated during 1 h at 60–65°C upon stirring. The mixture was then poured into 25 mL of water and neutralized with 25% aqueous ammonia solution. The precipitate was separated and recrystallized from ethanol. Yield 0.21 g.

2-(5-Bromo-2-thienyl)phenanthro[9,10-*d*]oxazole (Ic). 0.16 g (1 mmol) of bromine was added to a solution of 0.3 g (1 mmol) of compound **Ia** in 5 mL of dichloroethane. The mixture was refluxed during 3 h. The solvent was then evaporated; the residue wad dissolved in methylene chloride and purified via chromatography on an alumina column eluting with methylene chloride. Yield 0.24 g.

2-(5-Bromo-2-thienyl)-6-bromphenanthro[9,10-*d*]-oxazole (Id). 0.48 g (3 mmol) of bromine was added to a solution of 0.3 g (1 mmol) of compound **Ia** in 5 mL

of dichloroethane. The mixture was refluxed during 4 h. The solvent was then evaporated; the residue was dissolved in methylene chloride and purified via chromatography on an alumina column eluting with methylene chloride. Yield 0.25 g.

2-(5-Formyl-2-thienyl)phenanthro[9,10-*d*]oxazole (Ie). A mixture of 0.3 g (1 mmol) of compound **Ia** and 0.42 g (3 mmol) of hexamethylenetetramine in 5 g of polyphosphoric acid was stirred at 70–80°C during 8 h. The reaction mixture was diluted with 10 mL of water and carefully neutralized with ammonia solution. The reaction product was extracted with 10 mL of chloroform and purified via chromatography on am alumina column (h = 10 cm, d = 2.5 cm) eluting with chloroform. Compound **Ie** was recrystallized from ethanol. Yield 0.19 g (41%), yellow crystals.

2-(5-Acetyl-2-thienyl)phenanthro[9,10-*d*]oxazole (If). A mixture of 0.3 g (1 mmol) of compound **Ia** and 0.31 g (3 mmol) of acetic anhydride in 5 g of polyphosphoric acid was stirred at 110–120°C during 8 h. The reaction mixture was diluted with 10 mL of water and neutralized with ammonia solution. Further isolation of the reaction product was carried out as described for compound **Ie**. Compound **If** was recrystallized from methanol. Yield 0.13 g (37%).

2-(5-Benzoyl-2-thienyl)phenanthro[9,10-*d*]oxazole (Ig). A mixture of 0.3 g (1 mmol) of compound **Ia** and 0.37 g (3 mmol) of benzoic acid in 5 g polyphosphoric acid was stirred for 15 h at 150–160°C. Isolation of the reaction product was carried out as described for compound **Ie**. Compound **Ig** was recrystallized from methanol. Yield 0.19 g (46%).

ACKNOWLEDGMENTS

This work was financially supported by the Russian Science Foundation (agreement no. 14-23-00078).

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