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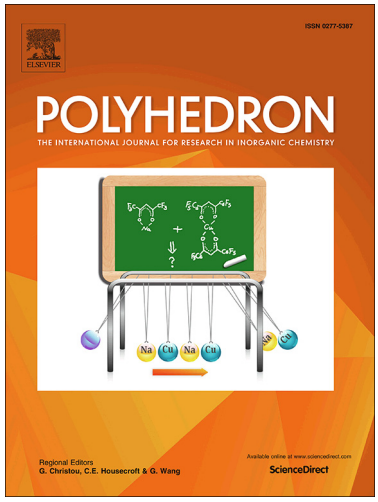

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S.S. Shapovalov, O.G. Tikhonova, A.V. Kolos, I.V. Skabitsky, S.G. Sakharov, V.A.Grinberg

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ORGANOMETALLIC PHTHALAZIN-1(2H)-ONES: ELECTROCHEMISTRY AND ADVANTAGE OF SOLVOTHERMAL SYNTHESIS

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Keywords
organometallic complex; ferrocene; phthalazin-1(2H)-one; azaheterocycle; solvothermal synthesis

Abstract

o-Ferrocenylcarbonylbenzoic acid (η^5-C_5H_5)Fe(η^5-$C_5H_4C(O)C_6H_4COOH$) (**I**) and *o*-cymantrenylcarbonylbenzoic acid (**II**) were obtained from ferrocene or (η^5-C_5H_5)$Mn(CO)_3$, respectively, by the Friedel-Crafts reaction with phthalic anhydride. Methyl *o*-ferrocenylcarbonylbenzoate (η^5-C_5H_5)Fe(η^5-$C_5H_4C(O)C_6H_4COOMe$ (**III**) and methyl *o*-cymantrenylcarbonylbenzoate $(CO)_3Mn(\eta^5$-$C_5H_4C(O)C_6H_4COOMe$) (**IV**) were synthesized from I and II, respectively using dimethyl carbonate (DMC) in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to promote the methylation reaction. 4-Ferrocenylphthalazin-1(2H)-one (**V**) and 4-cymantrenylphthalazin-1(2H)-one (**VI**) were obtained by the interaction of hydrazine hydrate with I and II, respectively, by the prolonged reflux or convenient solvothermal synthesis. Cyclic voltammetry measurements showed that compounds III and V undergo reversible one-electron oxidation, localized presumably at the ferrocene unit. For III the irreversible one-electron oxidation is apparently associated with the oxidation of the benzoate fragment. All new compounds were characterized by spectroscopic methods and the molecular structures of II and III were determined by X-ray diffraction analysis.

1. Introduction

In recent years, the oxygen atom substitution in carboxylate ligands of transition metal complexes draw active interest for the preparation of new structures. Reactions of trinuclear palladium (II) acetate with the formamidinate, triazine, and benzamidine ligands, produce mononuclear or binuclear compounds depending on the reaction conditions or the isolation procedure [[1]]. The O=C-NH fragment of heterocyclic compounds can be considered as an isolobal analogue of carboxylate and was used for complex formation with transition metals.
Phthalazin-1(2H)-one is a heterocyclic compound consisting of the benzene ring fused to the 1,2-diazine ring with two adjacent nitrogen atoms. It exhibits a tautomeric equilibrium between the

lactime and the lactam forms with the latter, which is predominant due to its minor aromaticity [[2]]. A variety of pharmacological effects, such as anticancer («Olaparib» is the type of targeted cancer drug), antidiabetic («Zopolrestat») (Fig. 1), antiasthmatic, antihistaminic, antihypertensive, antithrombotic, anti-inflammatory, analgesic, antidepressant or antimicrobial activities, are known for phthalazinones [[3]].

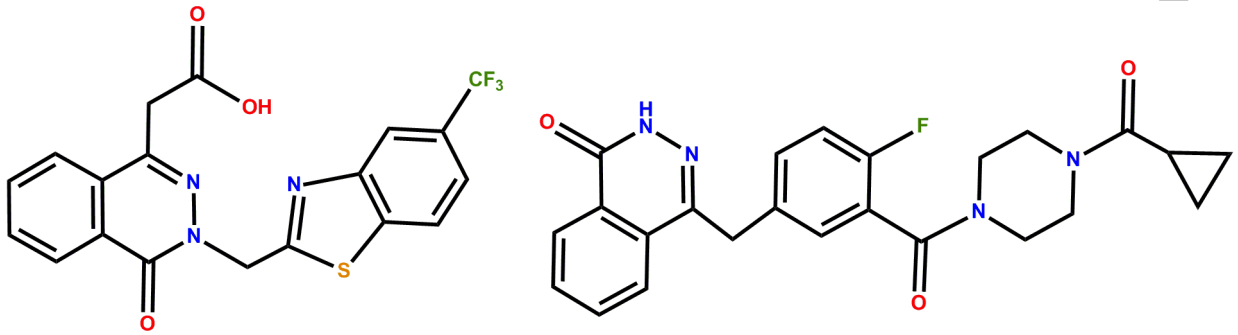


Fig. 1.

The coupling reactions of phthalazin-1(2H)-one with iodoferrocene are directed to the sterically more accessible lactam nitrogen atom, allowing the selected isolation of N-ferrocenyl derivatives [[4]]. Ferrocene was the first organometallic compound for which the antiproliferative properties were reported [[5], [6]]. The sodium salt of o-carboxybenzoylferrocene named as ferrocerone was patented by Nesmeyanov in 1971 [[7]] and it is now used to treat iron deficiency anemia. Nowadays, it is the single organometallic compound used as a drug. The organometallic drug "ferroquine", 7-chloro-4-[[[2-[(N,N-dimethylamino)methyl]-N-ferrocenyl]methyl]amino]quinoline), an analogue of the standard antimalarial drug “chloroquine” is currently undergoing clinical trial [[8]]. Ferroquine is active not only against the chloroquine-sensitive pathogenic plasmodium, but also against the chloroquine-resistant strains, such as *Plasmodium falciparum* causing malaria in humans. The specific cytotoxic properties of ferrocene compounds are also under active studies [[9], [10], [11]]. In this work we report the preparation of the organometallic phthalazinone ligands with the ferrocenyl and cymantrenyl fragments.

2.1. Materials

All reactions excluding autoclave synthesis were performed under dry argon using standard Schlenk technique. Solvents were purified, dried and distilled in an argon atmosphere. All chemicals and solvents were obtained from commercial sources and used without purification. Infrared spectra were recorded with a FTIR spectrometer «Bruker Alpha» with Platinum ATR. Elemental analyses were performed on a CHNS analyzer EA3000 «EuroVector». ^{1}H (300.13 MHz) and ^{13}C (75.4 MHz) NMR spectra were recorded on a Bruker “Avance 300” spectrometer,

all ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra being referenced to carbons or residual protons present in deuterated solvents ($CDCl_3$, d_6-acetone, d_6-dmso) with respect to TMS at $\delta = 0$.

2.2. Synthesis of *o*-ferrocenylcarbonylbenzoic acid $(\eta^5\text{-}C_5H_5)Fe(\eta^5\text{-}C_5H_4C(O)C_6H_4COOH)$ (I)

A mixture of phthalic anhydride (5.92 g, 40 mmol) and aluminum chloride (10.67 g, 80 mmol) in CH_2Cl_2 (80 ml) was stirred for 15 min at an ice bath. Then the solution of ferrocene (7.44 g, 40 mmol) in CH_2Cl_2 (80 ml) was added dropwise for 30 min. The mixture colour turned on blue. Then the mixture was refluxed for 4 h. The resulting mixture was poured into ice mixed with concentrated HCl (5 ml). After all ice melted, the orange organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. To the dark blue water layer in the beaker solution of $Na_2S_2O_4$ (4 g in 50 ml of water) was added in small portions till the colour was changed to yellow. The mixture was transferred to a separatory funnel and extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel, first using hexane and then CH_2Cl_2/EtOAc (1:1, v/v) as eluent. The orange product was precipitated from CH_2Cl_2/pentane at -25ºC.

Yield: orange powder, 4.54 g, 34 %.

IR (ν, cm^{-1}): 3078 (w), 2828 (sh), 2658 (sh), 2545 (sh), 1732 (w), 1676 (s), 1651 (vs), 1592 (m), 1571 (m), 1487 (w), 1449 (m), 1427 (m), 1375 (m), 1306 (s), 1282 (vs), 1257 (s), 1174 (m), 1147 (m), 1105 (m), 1086 (m), 1051 (m), 1023 (m), 1001 (m), 935 (m), 885 (m), 852 (m), 816 (s), 780 (m), 743 (vs), 707 (vs), 676 (s), 650 (m), 544 (m), 508 (s), 486 (vs), 455 (s), 425 (m).

^{1}H NMR ($CDCl_3$, δ, ppm): 4.21 (s, 5H, C_5H_5) 4.55 (s, 2H C_5H_4), 4.62 (s, 2H, C_5H_4), 7.69 – 7.53 (m, 3H, C_6H_4), 8.04 (d, J = 7,8 Hz, 1H, C_6H_4)

Elemental analysis for Mr = 334 g/mol

	%C	%H
Calculated:	64.69	4.22
Found:	64.41	4.85.

2.3. Synthesis of *o*-cymantrenylcarbonylbenzoic acid $(CO)_3Mn(\eta^5\text{-}C_5H_4C(O)C_6H_4COOH)$ (II).

A mixture of phthalic anhydride (5.92 g, 40 mmol) and aluminium chloride (10.67 g, 80 mmol) in dichloromethane (80 ml) was stirred for 30 min on an ice bath. Then the solution of $C_5H_5Mn(CO)_3$ (8.12 g, 40 mmol) in CH_2Cl_2 (80 ml) was added dropwise for 30 min and refluxed for 4 h. The resulting mixture was poured into ice mixed with concentrated HCl (5 ml). After all ice melted, the pale-yellow precipitate (insoluble in water and CH_2Cl_2) was separated with Buchner funnel and purified by recrystallization from boiling isopropyl alcohol.

Yield: yellow crystal, 6.78 g, 51 %

IR (ν, cm^{-1}): 2837 (w.), 2560 (w.), 2019 (s.), 1926 (vs.), 1665 (s.), 1593 (m.), 1571 (m.), 1490 (w.), 1459 (m.), 1430 (m.), 1376 (m.), 1305 (s.), 1289 (s.), 1262 (m.) 1180 (w.) 1149 (w), 1088 (w.), 1045 (m.), 1033 (m.), 935 (m.), 861 (m.), 848 (m.), 814 (w.), 776 (m.), 749 (m.), 709 (m.), 662 (s.), 628 (vs.), 580 (w.), 532 (s.), 491 (m.), 419 (w.).

^{1}H NMR (d_6-acetone, δ, ppm): 3.79 (s, 1H), 5.10 (s, 2H, C_5H_5), 5.36 (s, 2H, C_5H_5), 7.46 (m, H, C_6H_4), 7.61-7.85 (m, 2H, C_6H_4), 8.04-8.15(m, H, C_6H_4)

Elemental analysis for Mr = 352 g/mol

	%C	%H
Calculated:	54.57	2.58
Found:	54.74	2.67

2.4 Synthesis of methyl *o*-ferrocenylcarbonylbenzoate (η^5-C_5H_5)Fe(η^5-$C_5H_4C(O)C_6H_4COOMe$ (III)

DBU (0.30 ml, 1.80 mmol) was added to the dark orange solution of **I** (0.60 g, 1.80 mmol) in DMC (10 ml), and the mixture was refluxed for 13 h. The reaction was monitored with TLC (silica, toluene - ethyl acetate 4 : 1 v/v). Then the solvent was removed under reduced pressure. The residue produced was extracted by EtOAc (17 ml). The solution obtained was purified with column chromatography (eluent: EtOAc) to produce the orange solid.

Yield: orange crystals, 0.37 g, 60 %

IR (ν, cm^{-1}): 3080 (w.), 2949 (w.), 1718 (s.) 1647 (s.), 1594 (m.), 1571 (m.), 1482 (w.), 1452 (m.), 1439 (m.), 1431 (m.), 1372 (m.), 1344 (w.), 1277 (vs.), 1257 (s.), 1195 (m.), 1166 (m.), 1137 (s.), 1105 (m.), 1085 (s.), 1050 (m.), 1023 (m.), 1002 (m.), 955 (m.), 855 (m.), 821 (s.), 781 (s.), 748 (s.), 711 (s.), 683 (m.), 651 (m.), 503 (s.), 477 (vs.), 451 (s.), 424 (m.).

^{1}H NMR (d_6-dmso, δ, ppm): 3.29 (s, HDO), 3.32 (s, H_2O), 3.58(s, 3H, Me), 4.25 (s, 5H, C_5H_5), 4.49 (m, 2H, C_5H_4), 4.61 (m, 2H, C_5H_4), 7.63-7.69 (m, 1H, C_6H_4), 7.74- 7.82 (m, 2H, C_6H_4), 7.84-7.89 (m, 1H, C_6H_4).

Elemental analysis for Mr = 348 g/mol

	%C	%H
Calculated:	65.54	4.63
Found:	65.76	5.20

2.5 Synthesis of methyl *o*-cymantrenylcarbonylbenzoate $(CO)_3Mn(\eta^5$-$C_5H_4C(O)C_6H_4COOMe)$ (IV)

The synthesis is similar to compound **III**.

Yield: light yellow powder, 81%

IR (ν, cm^{-1}): 3124(w.), 2957(w), 2024(s.), 1939(vs.), 1714(s.), 1665(s.), 1597(w.), 1573(m.), 1461(m) 1434(m.), 1413(w.), 1375(m.), 1290(s.), 1264(m) 1195(m.), 1181(w.), 1135(m.), 1090(m.), 1037(m.), 956(m.), 864(w.), 827(m.), 772(m.), 759(m.), 709(s.), 663(s.), 628(vs.), 584(m.), 531(s.), 504(m.), 486(w.), 406(m.).

^1H NMR ($CDCl_3$, δ, ppm): 1.53 (s, H_2O), 3.82 (s, 3H, Me), 4.83 (s, 2H, C_5H_4), 5.24 (s, 2H, C_5H_4), 7.44-7.71 (m, 3H, C_6H_4), 8.03 (m, H, C_6H_4)

Elemental analysis for Mr = 366 g/mol

	%C	%H
Calculated:	55.75	3.02
Found:	55.57	3.12

2.6 Synthesis of 4-ferrocenylphthalazin-1(2H)-one (V)

Protocol 1

$N_2H_4 \times H_2O$ (0.40 ml, 8.20 mmol) was added to orange solution of **I** (0.28 g, 0.85 mmol) in *i*-PrOH (15 ml), and the mixture was refluxed for 12 h. The reaction was monitored with TLC (acetone - EtOAc 4 : 1 v/v) until the disappearance of the starting acid was complete. Than the reaction mixture was cooled to -4 °C to form an orange precipitate. The solution was filtered off, and the precipitate was washed with cold *i*-PrOH (2×5 ml). The resulting product was further purified by recrystallization from boiling MeOH.

A single crystal suitable for XRD was obtained by slowly cooling a solution of **V** in MeOH in a sealed ampoule.

Yield: orange crystals, 0.21 g, 75%

Protocol 2

$N_2H_4 \times H_2O$ (0.14 ml, 2.87 mmol) was added to the orange solution of **III** (0.10 g, 0.287 mmol) in *i*-PrOH (6 ml) and the mixture was refluxed for 6 h. The reaction was monitored with TLC (Acetone - EtOAc 4 : 1 v/v) until complete disappearance of the starting ether. Then the reaction mixture was cooled at a room temperature. The solvent was removed under reduced pressure. The orange precipitate obtained was washed with cold *i*-PrOH.

Yield: orange powder, 0.08 g, 86 %,

Protocol 3

$N_2H_4 \times H_2O$ (2 ml, 42.60 mmol) was added to the orange solution of **I** (1.50 g, 4.50 mmol) in *i*-PrOH (62 ml). The reaction mixture was heated in an autoclave for 18 h at 95°C. Then the autoclave was slowly cooled to room temperature. The dark-red mother liquor was separated. The black precipitate was extracted with *i*-PrOH (2×5 ml), and the orange solution obtained was

combined with the mother liquor. The solvent was removed under reduced pressure. The brown oil obtained was washed with Et_2O (3×10 ml). The product was crystallized from hot MeOH.

Yield: orange crystals, 0.82 g, 58 %

Protocol 4

The synthesis was similar to that in Protocol 3, with the exception of reaction time (48 h).

Yield: orange crystals, 1.38 g, 93 %

IR (ν, cm^{-1}): 3291(w.), 3199(w.), 3154(w.), 3136(w.), 3092(w.), 3018(w.), 2980(m.), 2928(w.), 2916(w.), 2877(w.), 2842(w.), 1638(vs.), 1608(s.), 1575(s.), 1496(m.), 1472(m.), 1409(m.), 1383(m.), 1351(s.), 1327(m.), 1307(m.), 1268(m.), 1225(m.), 1171(m.), 1153(m.), 1123(m.), 1105(m.), 1056(m.), 1024(m.), 1000(m.), 903(m.), 887(m.), 872(m.), 775(vs.), 726(m.), 686(vs.), 645(s.), 632(m.), 584(m.), 481(vs.), 453(s.), 405(m.).

^{1}H NMR (d_6-dmso, δ, ppm): 4.22 (s, 5H, C_5H_5), 4.50 (m, 2H, C_5H_4), 4.76 (m, 2H, C_5H_4), 7.88 (m, 1H, C_6H_4), 8.04 (m, 1H, C_6H_4), 8.31 (m, 1H, C_6H_4), 8.69 (m, 1H, C_6H_4).

^{13}C NMR (d_6- dmso, ppm): 159.06, 143.96, 133.20, 131.22, 129.03, 127.52, 126.71, 126.04, 81.33, 69.48, 69.14, 69.01, 48.55.

Elemental analysis for Mr = 330g/mol

	%C	%H	%N
Calculated:	65.48	4.27	8.48
Found:	65.01	4.50	8.75

2.7 Synthesis of 4-cymantrenylphthalazin-1(2H)-one (VI)

Method 1

$N_2H_4×H_2O$ (0.4 ml, 8.20 mmol) was added to a light-yellow solution of **II** (0.30 g, 0.85 mmol) in *i*-PrOH (15 ml), and the mixture was refluxed for 9 h. The reaction was monitored with TLC (acetone - EtOAc 4 : 1 v/v) until disappearance of the starting acid was complete. The reaction mixture was cooled to -4 °C to form a pale-yellow precipitate. The solution was filtered off, and the precipitate was washed with cold *i*-PrOH (2×5 ml).

A single crystal suitable for XRD was obtained by recrystallization of the product from hot MeCN.

Yield: light-yellow powder, 0.22 g, 73 %,

Method 2

$N_2H_4×H_2O$ (0.4 ml, 8.20mmol) was added to the yellow solution **IV** (0.30 g, 0.82 mmol) in *i*-PrOH (20 ml) and the mixture was refluxed for 1 h. The reaction was monitored with TLC (acetone - EtOAc 4 : 1 v/v) until the disappearance of the starting ether was complete. Then the

reaction mixture was cooled at room temperature. The mother liquor is filtered off. The light-yellow precipitate obtained was washed with cold *i*-PrOH.

Yield: light-yellow powder, 0.23 g, 82 %,

Protocol 3

$N_2H_4 \times H_2O$ (2 ml, 42.60 mmol) was added to the yellow solution of **II** (1.50 g, 4.26 mmol) in *i*-PrOH (62 ml). The reaction mixture was heated in an autoclave for 18 hours at 95°C. Then the autoclave was slowly cooled to room temperature. The colorless mother liquor was separated by decantation. The crystal precipitate was washed with cold *i*-PrOH, and dried under reduced pressure.

Yield: light-yellow crystals, 1.05 g, 70 %

Method 4

The synthesis is similar to that in Protocol 3 with the exception of the reaction time (48 h).

Yield: light-yellow crystals, 1.33 g, 90 %

IR (ν, cm^{-1}): 2997(m.), 2932(m.), 2897(m.), 2164(w.), 2033(s.), 1953(vs.), 1932(vs.), 1739(w.), 1666(s.), 1607(w.), 1553(w.), 1477(w.), 1344(m.), 1231(w.), 1157(w.), 1029(w.), 986(w.), 869(w.), 851(w.),842(w.), 785(m.), 729(w.), 684(w.), 664(m.), 633(s.), 590(w.), 536(m.), 428(w.),

^1H NMR (d_6-dmso, δ, ppm): 5.20 (m, 2H, Cp), 5.67 (m, 2H, Cp), 7.84-7.95 (m, 1H, C_6H_4), 7.98 (m, 2H, C_6H_4), 8.31(m, 1H, C_6H_4)

^{13}C NMR (d_6-dmso, δ, ppm): 224.97, 159.07, 138.86, 133.72, 131.83, 128.58, 127.21, 126.18, 125.68, 99.00, 86.26, 83.16, 48.58

Elemental analysis for Mr = 342 g/mol

	%C	%H	%N
Calculated:	55.19	2.61	8.05
Found:	55.58	2.79	8.45

2.5. X-ray crystallography

X-ray diffraction data were collected using a Bruker SMART CCD diffractometer. Crystallographic data and structure refinement details for structures **V** and **VI** are listed in Table 1. Absorption correction was applied using the program SADAB [[12]]. Using Olex2 [[13]], the structures were solved with ShelXS program [[14]] by direct methods and refined with ShelXL [[15]] program using Least Squares refinement on F^2. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were positioned geometrically using a riding model with fixed isotropic thermal factors on carbon atoms. Hydrogen atoms of NH groups were refined with isotropic thermal parameters.

Table 1. Crystal data and structure refinement for compounds **V** and **VI**.

Parameter	**V**	**VI**
M	330.16	348.19
Radiation (λ, Å)	MoKα (λ = 0.71073)	
Temperature, K	150	150
Space group	$P2_1/n$	P-1
a, (Å)	9.8419(2)	6.8627(2)
b, (Å)	10.4329(2)	7.4687(2)
c, (Å)	14.6051(3)	14.7430(4)
α, (°)	90	85.9450(10)
β, (°)	107.4770(10)	78.8932(10)
γ, (°)	90	71.3360(9)
V, Å^3	1430.42(5)	702.48(3)
Z	4	2
ρ_{calc}, g/cm^{-3}	1.533	1.646
μ, mm^{-1}	1.056	0.962
F(000)	680.0	352.0
2Θ range for data collection (°)	4.878 to 70.332	5.632 to 55.712
Measurement method	ω	
Number of independent reflections, (N_1)	6087 [R_{int} = 0.0302, R_{sigma} = 0.0253]	3289 [R_{int} = 0.0204, R_{sigma} = 0.0245]
Number of reflections $I > 2\sigma(I)$ (N_2)	5236	3.072
Parameters	203	212
GOOF (F^2)	1.048	1.068
R_1 for N_2	0.0338	0.0287
wR_2 for N_1	0.0846	0.0723
$\Delta\rho_{max}/\Delta\rho_{min}$, *e* Å^{-3}	0.49/-0.35	0.41/-0.24

2.6. Electrochemical study of complexes III and V.

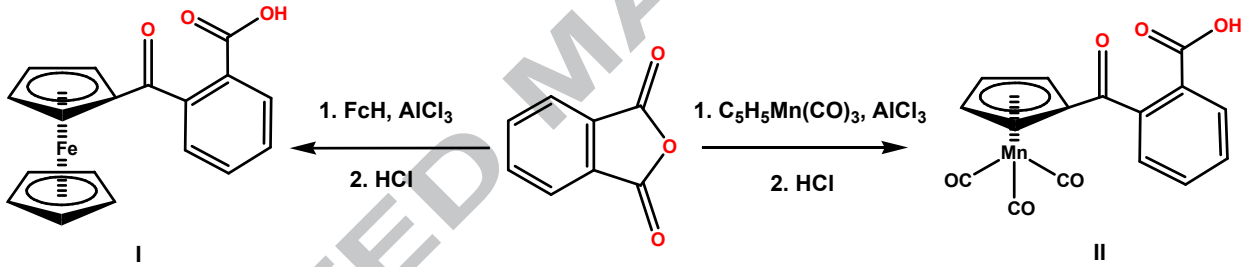
Cyclic voltammograms (CVs) of complexes **III** and **V** were recorded on a PAR 273 potentiostat/galvanostat (Princeton Applied Research) with a standard software. The

measurements were carried out in a thermostatically controlled three-electrode electrochemical cell in a high-purity argon atmosphere. A SU-2000 (0.0078 cm^2) glassy carbon disk pressed in Teflon served as working electrode and a platinum plate (1 cm^2) was auxiliary electrode. The potentials were measured versus an Ag quasi-reference electrode in the same solution. The potential of the Fc/Fc^+ couple versus Ag in the same solution is ~ 0.20 V [[16]].

The measurements were carried out in dichloromethane with 0.2 M Bu_4NPF_6 as supporting electrolyte. The CVs were recorded in the range of the potentials (1.7 ÷ -1.9) V. Reversible waves on cyclic voltammograms were recorded with a different sweep rates in the interval 0.1 to 1.0 Vs^{-1}.

3. Results and discussion

o-Ferrocenylcarbonylbenzoic acid (I) and *o*-cymantrenylcarbonylbenzoic acid (II) were obtained by the Friedel-Crafts reaction from ferrocene or manganese cyclopentadienyl tricarbonyl (cymantrene) with phthalic anhydride (Scheme 1).



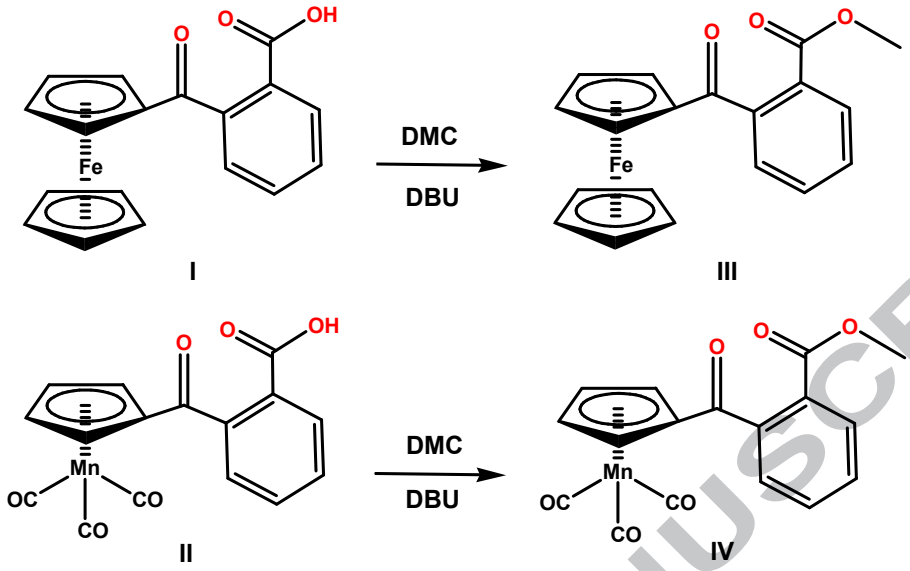
I II

Scheme 1.

Earlier, bis-*o*-carboxybenzoylferrocene was obtained and characterized as its dimethyl ester [[17]]. The reaction of ferrocene with phthalic anhydride was also mentioned by Nesmeyanov [[18]] and described by Qi Shuai [[19]]. Compound II was reported earlier [[20]] without experimental data. Similar reaction of $C_5H_5Mn(CO)_3$ with succinic anhydride results in cyclopentadien-1-yl-(3-carboxylato-1-oxopropyl) manganese tricarbonyl [[21]]. It was conjugated to cell-penetrating peptides (CPPs) for diagnostic imaging and therapeutic applications in human medicine. *o*-Cymantrenylcarbonylbenzoic acid is worse soluble in CH_2Cl_2 compared to the ferrocene analogue and can be easily separated from the reaction mixture without column chromatography. IR spectra of both corresponding acids showed a strong absorbance band at ~1665 cm^{-1} due to the carbonyl stretching vibration of C=O group between benzene and cyclopentadienyl rings.

The esterification reactions of organometallic acids I and II were carried out using dimethyl carbonate (DMC) as a "green" methylating agent in the presence of DBU as a strong non-nucleophilic base (Scheme 2). The main advantage of DMC compared to other methylating

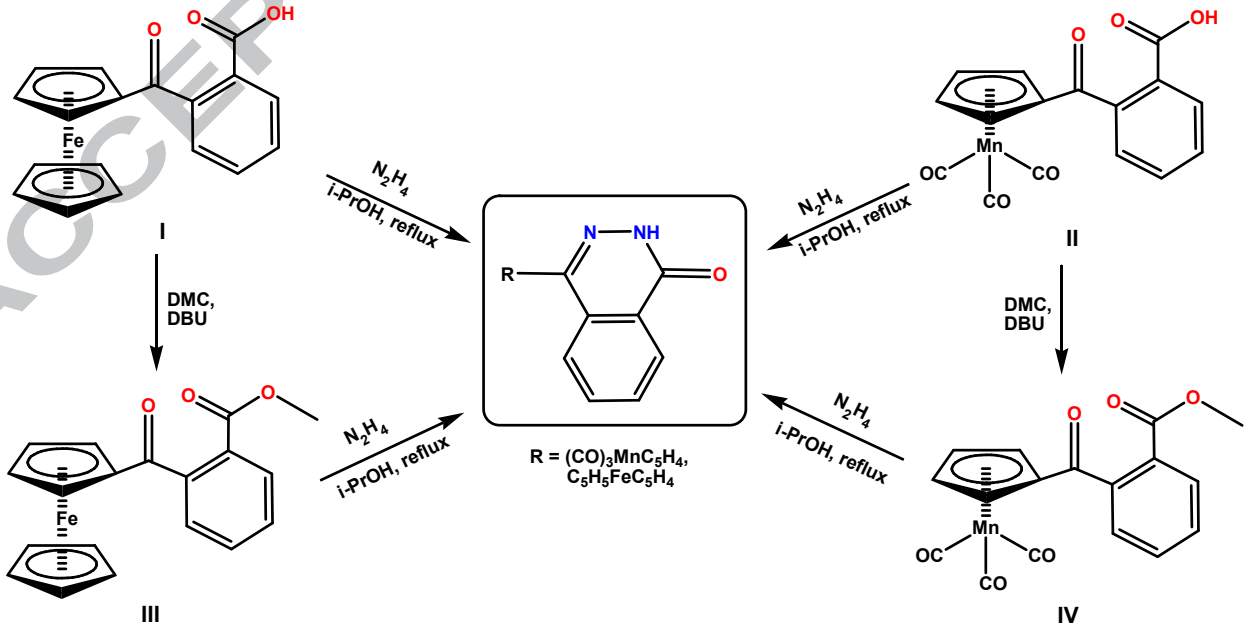
reagents such as methyl iodide and dimethyl sulfate is its low toxicity and biodegradability [[22]].



Scheme 2.

The IR spectra of methyl *o*-ferrocenylcarbonylbenzoate $FcC(O)C_6H_4COOMe$ (**III**) contains two bands of carbonyl stretching vibration C=O (1714 and 1665 cm^{-1}), as well as manganese analogue methyl *o*-cymantrenylcarbonylbenzoate $(CO)_3MnC_5H_4C(O)C_6H_4COOMe$ (**IV**) (1714 and 1665 cm^{-1}).

Different routes can be used for the preparation of the organometallic phthalazin-1(2H)-ones, such as 4-ferrocenylphthalazin-1(2H)-one (V) and 4-cymantrenylphthalazin-1(2H)-one) (VI) (Scheme 3).



Scheme 3.

Firstly, compounds V and VI can be obtained by prolonged reflux of acids I and II with hydrazine hydrate (Protocol 1). The corresponding methyl ester reactions (Protocol 2) with

hydrazine hydrate also result in the same compounds with higher yields and rates, because -OCH_3 is the better leaving group than –OH (Table 2). However, the organometallic phtalazinone synthesis via ester is a two-stage reaction, so the total yield is lower than that in the first Protocol.

If the interaction of I and II with hydrazine hydrate is carried out in an autoclave, compounds V and VI can be obtained in high yield (method 3). When the reaction time reaches 48 hours, yields increase to more than 90 % (Protocol 4).

Substrate	Condition	Time, h	Yield, %
o-Ferrocenylcarbonylbenzoic acid	reflux	12	75
o-Ferrocenylcarbonylbenzoic acid	solvothermal synthesis	18	58
o-Ferrocenylcarbonylbenzoic acid	solvothermal synthesis	48	93
Methyl *o*-ferrocenylcarbonylbenzoate	reflux	6	86
o-Cymantrenylcarbonylbenzoic acid	reflux	9	73
o-Cymantrenylcarbonylbenzoic acid	solvothermal synthesis	18	70
o-Cymantrenylcarbonylbenzoic acid	solvothermal synthesis	48	90
Methyl o-cymantrenylcarbonylbenzoic acid	reflux	1	82

Table 2. Preparation of organometallic phthalazin-1(2H)–ones.

The structures of 4-ferrocenylphthalazin-1(2H)-one and 4-cymantrenylphthalazin-1(2H)-one were established by X-ray diffraction. The structural data of the compounds obtained can be compared with the structure of the unsubstituted phthalazin-1(2H)-one [[23]].

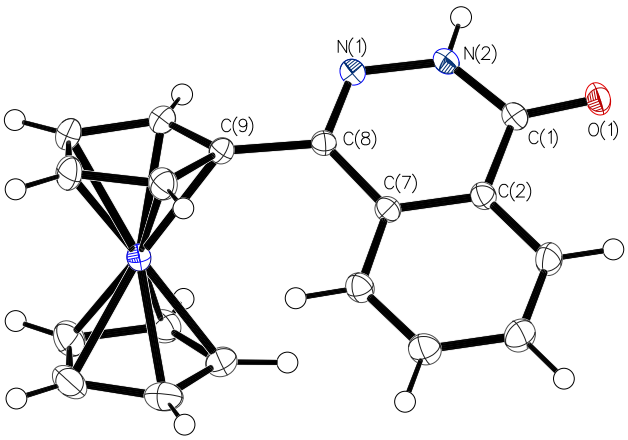


Fig. 2. Molecular structure of complex **V.** The most important bond length (Å): O1-C1 1.244(1), N2-N1 1.366(1), N2-C1 1.355(1), N1-C8 1.310(1), C7-C8 1.455(1), C7-C2 1.405(2), C8-C9 1.477(2) C2-C1 1.459(1).

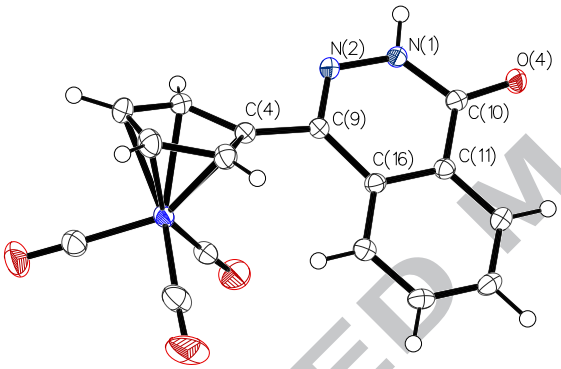


Fig. 3. Molecular structure of complex **VI.** The most important bond length (Å): O4-C10 1.245(2), N2-N1 1.364(2),N2-C9 1.300(2), N1-C10 1.363(2), C16-C9 1.457(2) C16-C11 1.409(2), C10-C11 1.456(2), C9-C4 1.479(2)

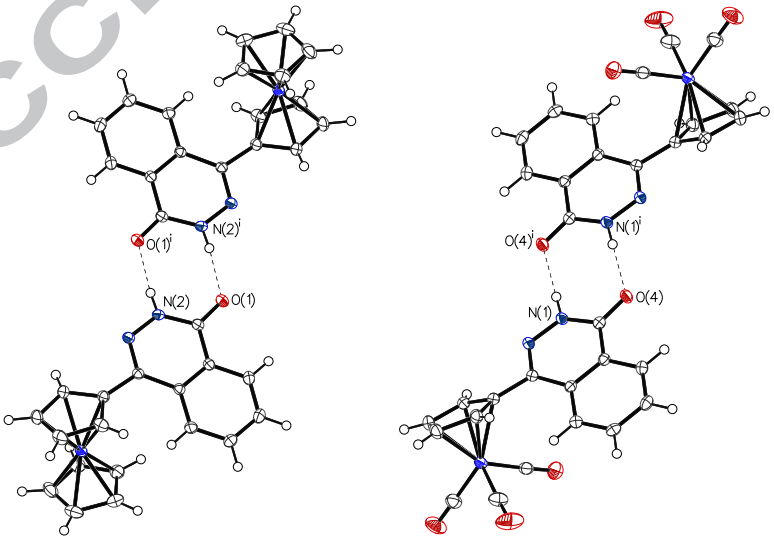


Fig. 4. Intermolecular double hydrogen bonds in phtalazinone dimers V (N(2)-O(1)^{i} 2.810(1) Å) and VI (N(1)-O(4)^{i} 2.820(2) Å).

Phthalazin-1(2H)-ones V and VI form dimers with intermolecular hydrogen bonds (N···O distances are 2.810(1) for ferrocenyl- and 2.820(2) for cymantrenyl derivatives), which are slightly shortened compared to the unsubstituted phthalazin-1 (2H) –one (N···O 2.842(2) Å) (Fig. 3). Angles between cyclopentadienyl and heterocyclic rings are 30° for V and 34° for VI. The IR spectra of V and VI contain characteristic bonds of carbonyl stretching vibration C=O (1638 cm^{-1} for V and 1666 cm^{-1} for VI). The characteristic νCO stretching vibrations observed for cymantrenyl fragment increase from 2019 and 1926 for II to 2033, 1953 and 1932 for VI.

The CVs for complexes III and V are presented at Fig. 5 and 6. For complex III one can observe two one-electron oxidation waves. The first wave at the peak potential 0.38 V (A) is reversible with (ΔE_p = 60 mV) and the second wave at the peak potential 1.47 V (B) is irreversible, being associated with the oxidation of benzoate fragment. For complex V in the wide range of the potentials there is an only one-electron reversible wave at the peak potential 0.23 V (ΔE_p = 60 mV). For both complexes there are one-electron reversible oxidation waves connected with the ferrocene unit. Redox separation between reversible waves of complexes III and V is $\Delta E^{\circ\prime}$ = 150 mV. Such separation in redox processes of III and V may be due to the electron-acceptor properties of carbonylbenzoate fragment. In the cathodic range of the potentials one can not observe well-defined waves of the reduction for complexes III and V up to potential -1.9 V.

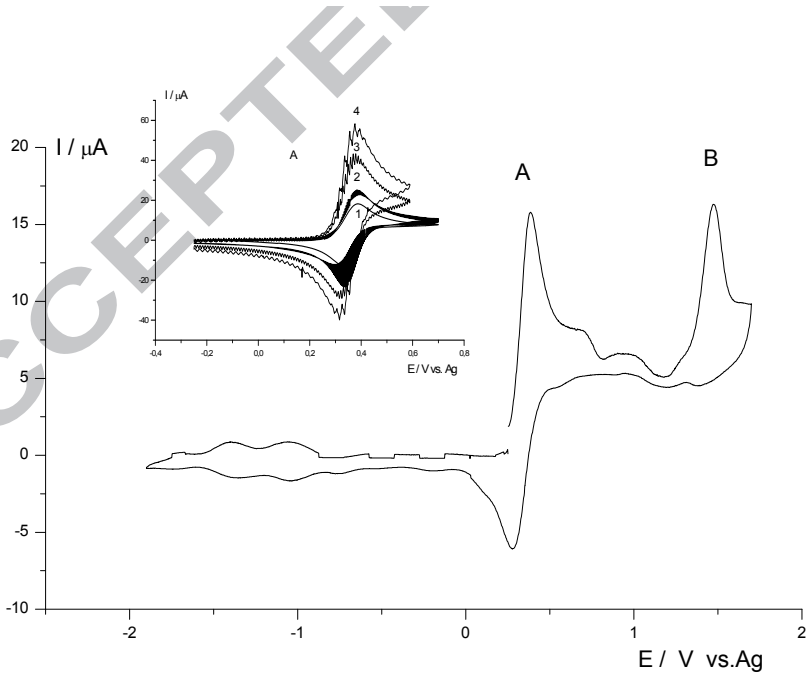


Fig. 5. CVs of complex **III** (C= 3.5 mM) recorded at the GC electrode SU –2000 (0.0078 cm^2) in dichloromethane deaerated by high-purity argon with 0.2 M Bu_4NPF_6 as the supporting electrolyte in the potential range (-1.9 ÷ 1.7) V at the potential sweep rate 0.1 V s^{-1} and the wave

(A) recorded in interval potentials (-0.25 ÷ 0.7) V with a different sweep rate, V s^{-1}: 1- 0.1; 2- 0.2; 3-0.5; 4- 1.0

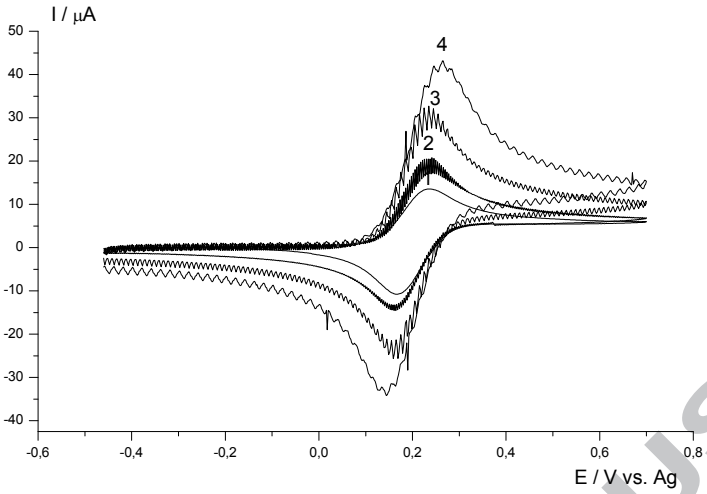


Fig. 6. CVs of complex **V** (C= 3.2 mM) recorded at the GC electrode SU –2000 (0.0078 cm^2) in dichloromethane deaerated by high-purity argon with 0.2 M Bu_4NPF_6 as the supporting electrolyte) in interval potentials (-0.45 ÷ 0.7) V with a different sweep rate, V s^{-1}: 1- 0.1; 2- 0.2; 3-0.5; 4- 1.0.

Conclusion

Hence, we synthesized *o*-cymantrenylcarbonylbenzoic and ferrocenylcarbonylbenzoic acid methyl esters. Cyclic voltammetric measurement of the latter revealed that irreversible one-electron oxidation is associated with the oxidation of benzoate fragment. Cymantrene- and ferrocene-containing phthalazin-1(2H)-ones were prepared from the corresponding carboxylic acids and their methyl esters. All ferrocene derivatives undergo a reversible one-electron oxidation localized presumably at the ferrocene unit. Solvothermal conditions of organometallic phthalazin-1(2H)-ones were optimized. All compounds were characterized by spectroscopic methods and the molecular structures of 4-ferrocenylphthalazin-1(2H)-one and 4-cymentrenylphthalazin-1(2H)-one were confirmed by X-ray structural analysis.

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Appendix A. Supplementary data

CCDC 1901244 and 1901245 contain the supplementary crystallographic data for compounds **V** and **VI**, correspondingly. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

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