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Condensation of Lactones with Primary Diamines

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The condensation of dehydroacetic acid and 4-hydroxy-6-methylpyran-2-one with primary diamine derivatives such as hydrazine, 1,2-diaminoethane and 1,6-diaminohexane yielded bispyrone and bispyridone derivatives has been reported. The condensation of 4-hydroxy-6-methylpyran-2-one with hydrazine in acetonitrile generated another bispyrazole product but in *n*-butanol, this reaction afforded the bispyridones. The structures of the synthesized bispyrazoles were examined by spectroscopy and X-ray diffraction analysis, while those of bispyridones were established by spectroscopy data (NMR, mass). Some new complexes were also synthesized in order to show the behaviour of ligands with suitable crystals for X-ray analysis.

Keywords: Pyrone, Diamine, Bispyrone, Bispyrazole, Bispyridone, X-ray diffraction.

INTRODUCTION

Heterocyclic compounds such as bispyrazoles are studied by numerous bioinorganic research teams [1-4]. Bispyrazoles and bispyridones are valuable multidentate ligands and were applied for coordination chemistry in many ways [5,6]. The mono- and polynuclear complexes derived from bispyrazoles and bispyridones were thoroughly studied due to their versatile applications [5-7]. These compounds exhibited remarkable physical, chemical and biological properties [8-20]. In particular, copper complexes derived from bispyrazoles are considered as especially stable and non-degradable upon exposure to air and moisture [5,21,22]. They were proposed as synthetic models for the type III active site of the copper proteins hemocyanin and tyrosinase and have successfully been applied as active agents for a large vary of human neoplastic cell lines [5,16-24].

In this context, we focus particularly on the condensation of dehydroacetic acid and 4-hydroxy-6-methyl-pyran-2-one with various primary diamines leading to the formation of bispyrone and bispyridone derivatives, where the bispyrone has been condensed with hydrazine. The structures of the obtained bispyrazoles were determined according to spectroscopic and X-ray diffraction data.

EXPERIMENTAL

Starting materials, reagents and solvents were purchased from Sigma-Aldrich and used without further purification. NMR spectra were measured on a BRUKER Avance 300 or a BRUKER ARX 200 spectrometer and the chemical shifts are given in parts per million (δ) downfield from internal tetramethylsilane standard. Mass spectra (EI) were measured on a Varian MAT 311A. IR spectra were recorded on an FT-IR spectrophotometer from Shimadzu. Melting points were measured on a Köfler apparatus and are uncorrected. X-ray structure analyses were carried out with a D8 Venture Bruker AXS diffractometer equipped with a (CMOS) Photon 100 detector.

Synthesis of bispyrone derivatives 3a-c: A mixture of dehydroacetic acid (**1**) (20 mmol) and diamines **2a-c** (10 mmol) was dissolved in *n*-butanol (30 mL) and heated under reflux. The reaction was followed by TLC. The formed precipitate was separated by filtration and recrystallized from $CHCl_3$ for several times.

3,3′-(1*E*,1′*E*)-Hydrazine-1,2-diylidenebis(ethan-1-yl-1-ylidene)*bis*(4-hydroxy-6-methyl-2*H*-pyran-2-one) (3a): Yield: 72%, m.p.: > 260 ºC; ^{1}H NMR (DMSO-d_6/TMS): 2.07 (3H, s, CH_3), 2.24 (3H, s, CH_3), 2.25 (3H, s,CH_3), 2.78 (3H, s, CH_3), 5.71 (1H, s, CH), 6.16 (1H, s, CH); ^{13}C NMR (DMSO-d_6/TMS): 17.09 (CH_3), 19.71 (CH_3), 20.07 (CH_3), 23.23 (CH_3), 100.39 (CH), 106.94 (CH), 95.24 (C), 96.31 (C), 157.90 (C-O), 161.12 (C-O), 163.47 (C=O), 164.98 (C=O), 168.38 (C=O), 171.02 (C=O); HRMS, *m/z*: 332(M), calcd. (found) for $C_{16}H_{16}N_2O_6$: 332.1008 (332.100). X-ray structural data [25]: m.f.: $C_{16}H_{16}N_2O_6$; m.w.: 332.31; crystal system, space group, monoclinic, C2/*c*; temperature (K), 296; a, b, c (Å), 27.797(3), 3.9750(4), 14.4569(15); β (°),110.642(4); V (Å^3), 1494.8(3); Z, 4. Density, 1.477 Mg m^{-3}; *F*(000), 696; Radiation type, Mo *K*α; μ (mm^{-1}), 0.12; Crystal size/mm^3, 0.32 × 0.25 × 0.19; θ range (data col), 3.0º to 27.1º; Index ranges, h = -34→34: Index ranges, k = -5→5; Index ranges, l = -18→18; T_{min}, T_{max}, 0.678, 0.746; No. of measured, independent and observed reflections with I > 2σ(I) 15395, 1627, 1221. $R_{int,}$ 0.043; $(\sin \theta/\lambda)_{max}$ (Å^{-1}), 0.641; $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S, 0.050, 0.148, 1.03; No. of reflections, 112; No. of parameters, 112; $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3}), 0.33, -0.23.

3,3′-(1*E*,1′*E*)-Ethane-1,2-diylbis(azanylylidene)*bis*-(ethan-1-yl1-ylidene)*bis*(4-hydroxy-6-methyl-2*H*-pyran-2-one) (3b): Yield: 85%, m.p.: 256 ºC; ^{1}H NMR (DMSO-d_6/TMS) 2.03 (3H, d, ^4J = 0.83 Hz, CH_3), 2.57 (3H, s, CH_3), 2.97 (3H, s, CH_3), 3.81 (2H, t, ^3J = 2.7 Hz, CH_2), 5.58 (1H, d, ^4J = 0.87 Hz, CH=), 13.8 (1H, br, NH); ^{13}C NMR (DMSO-d_6/TMS): 16.99 (CH_3), 18.72 (CH_3), 42.01 (CH_2), 95.81 (Cq), 105.4 (CH=), 161.55 (Cq), 162.5 (Cq), 175.76 (C=O), 183.26 (C=O); HRMS, *m/z*: 360(M), calcd. (found) for $C_{18}H_{20}N_2O_6$: 360.1321, (360.132). X-ray structural data: m.f.: $C_{18}H_{24}N_2O_8$; extended formula, $C_{18}H_{20}N_2O_6{\cdot}2H_2O$; m.w.: 396.39; Crystal system, space group, monoclinic, P2$_1$/*c*; temperature (K), 150(2); a, b, c (Å), 14.0471(12), 4.4957(4), 14.3448(13); β (°), 91.376(4); V (Å^3), 905.64(14); Z, 2; Density, 1.454 Mg m^{-3}; *F*(000), 420; Radiation type, Mo*K*α; μ (mm^{-1}), 0.115; Crystal size/mm^{3,} 0.48 × 0.18 × 0.14; θ range (data col), 2.841° to 27.538°; Index ranges, h = -18→18; Index ranges, k = -5→5; Index ranges, l = -18 →18; T_{min}, $T_{max,}$ 0.796, 0.984; No. of measured, independent and observed reflections with $I > 2\sigma(I)$, 8567, 2066, 1797; $R_{int,}$ 0.0333; $(\sin \theta/\lambda)_{max}$ (Å^{-1}), 0.650; $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S, 0.0372, 0.1084, 0.890; No. of reflections, 2066; No. of parameters, 138; $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3}), 0.283, -0.243.

3,3′-(1*E*,1*E*′)-Hexane-1,6-diylbis(azanylylidene)*bis*-(ethan-1-yl-1-ylidene)*bis*(4-hydroxy-6-methyl-2*H*-pyran-2-one) (3c): Yield: 97%, m.p.: 174 ºC; ^{1}H NMR (DMSO-d_6/TMS) 1.50 (2H, m, CH_2), 1.77 (2H, m, CH_2), 2.10 (3H, s, CH_3), 2.61 (3H, s, CH_3), 5.65 (1H, s, CH), 6.90 (1H, m, 1H), 14.17 (1H, s, OH); ^{13}C NMR (DMSO-d_6/TMS): 18.07 (CH_3), 19.79 (CH_3), 20.42 (CH_3), 20.66 (CH_3), 26.21 (CH_2), 26.36 (CH_2), 26.46 (CH_2), 28.62 (CH_2), 28.83 (CH_2), 30.00 (CH_2), 43.81 (CH), 47.53 (CH), 96.53 (C), 101.43 (C), 107.34(C), 119.00 (C), 148.03 (C=N), 149.43 (C=N), 162.70 (C=O), 163.75 (C=O), 175.85 (C-O), 184.66 (C-O); HRMS, *m/z*: 416(M), calcd. (found) for $C_{22}H_{28}N_2O_6$: 416.1947 (416.194).

Synthesis of [Ni(3,3′-(1*E*,1′*E*)-ethane-1,2-diyl*bis*(azanylylidene)*bis*(ethan-1-yl1 ylidene)*bis*(4-hydroxy-6-methyl-2*H*-pyran-2-one))] (4): A mixture of (10 mL ethanol + bis-pyrone **2b** (0.2 mmol), was gently added while stirring at room temperature to 20 mL of a ethanolic solution of Ni(acac)$_2$ (0.1 mmol), after 30 min, the mixture was heated under reflux during 24 h. After 10 days of solvent evaporation. The orange crystals of complex have been isolated by filtration under vacuum, washed with ether. Yield: 68%; m.p.: > 260 °C. IR-ATR (cm^{-1}): 3593(w); 3513(w); 2919(w); 1684(s); 1654(s); 1611(w); 1560(s); 1463(s); 1425(s); 1364(w); 1346(s); 1281(w); 1243(w); 1222(w); 1172(w); 1104(w); 1063(w); 1033(w); 1004(s); 963(w); 918(w); 832(s); 770(s); 708(m); 652(m); 605(w); 588(w); 546(m). UV-vis [λ (nm), ε_{max} (M^{-1} cm^{-1})]: 234(28100). 242(16460); 248 (15790); 260(10870); 270(15330); 276(17680); 310(4500); 320(4090); 348(2280); 368(2290); 454(241); 540(191). X-ray structural data: m.f.: $C_{18}H_{20}N_2NiO_7$; extended formula, $C_{18}H_{18}N_2NiO_6{\cdot}H_2O$. m.w.: 435.07; Crystal system, space group, monoclinic, P2$_1$/*c*; temperature (K), 150(2); a, b, c (Å), a = 7.3129(8), b = 18.469(2), c = 13.6993(16); β (°), 111.523(4); V (Å^3), 1721.3(3); Z, 4; Density, 1.679 Mg m^{-3}; *F*(000), 904; Radiation type, Mo*K*α; μ (mm^{-1}), 1.175; Crystal size/mm^3, 0.55 × 0.18 × 0.12; θ range (data col), 2.724° to 27.544°; Index ranges, h = -9→9; Index ranges, k = -23→21; Index ranges, l = -17→17; T_{min}, T_{max}, 0.868, 0.700; 0.996; No. of measured, independent and observed reflections with $I > 2\sigma(I)$, 16775, 3956, 3442; $R_{int,}$ 0.0416; No. of reflections, 3956; No. of parameters, 264; $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3}), 0.466, -0.310.

Synthesis of [Fe(1-acetyl-4-hydroxy-6-methylpyran-2-one)$_3$)] (5): A mixture of (10 mL ethanol, 20 mL $CHCl_3$ and bispyrone **2c** (0.2 mmol), was gently added while stirring at room temperature to 20 mL of a ethanolic solution of $FeCl_3{\cdot}6H_2O$ (0.1 mmol), after 30 min, the mixture was heated under reflux during 24 h. After 10 days of solvent evaporation, the orange crystals of complex have been isolated by filtration under vacuum, washed with ether. Yield: 52%; m.p.: > 260 ºC. IR-ATR (cm^{-1}): 2961(w); 1714(s); 1644(s); 1556(s); 1474(s); 1437(w); 1417(s); 1383(s); 1345(s); 1265(m); 1233(m); 1161(m); 1094(w); 1067(m); 1029(m); 999(s); 972(s); 941(m); 860(w); 843(w); 777(s); 720(m); 663(m); 638(s); 609(w); 578(s); 534(s). UV-vis [λ (nm), ε_{max} (M^{-1} cm^{-1})]: 264(8470). X-ray structural data: m.f.: $C_{24}H_{21}O_{12}Fe$; extended formula, $C_{24}H_{21}FeO_{12}{\cdot}H_2O$; m.w.: 575.28; Crystal system, space group, trigonal, R3c; temperature (K), 296(2); a, b, c (Å), a = 15.2386(4), b = 15.2386(4), c = 37.3392(10); β (°), 90.376(4); V (Å^3), 7509.1(4); Z, 69; Density, 1.500 Mg m^{-3}; *F*(000), 3492; Radiation type, Mo*K*α; μ (mm^{-1}), 0.669; θ range (data coll.), 2.673° to 27.876°; Index ranges, h = -20→20; Index ranges, k = -20→19; Index ranges, l = -49→49; $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S, 0.0478, 0.1205, 1.033; No. of reflections, 2007; No. of parameters, 117.

Synthesis of 2-(5-methyl-1*H*-pyrazol-3-yl)-*N*-[2-(5-methyl-1*H*-pyrazol-3-yl)acetylboranyl]acetamide (7): A mixture of compound **6** (0.02 mol) and hydrazine **2a** (0.015 mol) was dissolved in acetonitrile (20 mL) and stirred under reflux. The reaction was followed by TLC. The solvent was removed in vacuum and the crude product was recrystallized from ethanol. Yield: 52%, m.p.: 240 ºC; ^{1}H NMR (DMSO-d_6/TMS): 2.15 (3H, s, CH$_3$), 3.38 (2H, s, CH$_2$), 5.89 (1H, s, CH), 9.95 (1H, s, NH), 11.92 (1H, s, NH); ^{13}C NMR (DMSO-d_6/TMS): 11.77 (s, CH$_3$), 33.38 (CH$_2$), 104.90 (CH), 142.70 (C), 144.27 (C=N), 169.97 (C=O); HRMS, *m/z*: 276(M), calcd. (found) for $C_{12}H_{16}N_6O_2$: 276.1335 (276.133).

Synthesis of [Cu$_2$(*N,N′-bis*(2-(5-methyl-1*H*-pyrazol-3-yl)acetylcarboxamide))](NO$_3^-$)$_2$(H$_2$O)$_2$ (8): To a suspension of bispyrazole **7** (0.108 mmol) dissolved in ethanol (15 mL), Cu(NO$_3^-$)$_2$·3H$_2$O (0.216 mmol, dissolved in 10 mL ethanol) was gently added while stirring at room temperature. After 15 min stirring at room temperature, the reaction mixture was refluxed for 24 h. After 40 days of slow evaporation of ethanol, blue crystals of the product were isolated by vacuum filtration, washed with diethyl ether and air-dried. Yield: 62%, m.p.: > 260 ºC, IR-ATR (cm^{-1}): 3621 (w), 3144 (br, m), 1581 (m), 1568 (s), 1487 (w), 1379 (s), 1295 (s), 1238 (s), 1187 (m), 1064 (m), 1040 (w), 1025 (w), 926 (w), 821 (m), 788 (s), 721 (s), 666 (s), 626 (m), 546 (w), 531 (w); UV-vis [λ (nm), ε$_{max}$ (M^{-1} cm^{-1})]: 230 (24520), 236 (21410), 248 (17610), 640 (240). X-ray structural data: m.f.: $C_6H_{11}CuN_4O_6$; m.w.: 298.73; Crystal system, space group, monoclinic, $P2_1/c$; temperature (K), 296; a, b, c (Å), 8.9633(11), 8.1400(9), 14.5577(17); β (º),91.890 (2); V (Å^3), 1061.6(2); Z, 4; Density, 1.869 Mg m^{-3}; *F*(000), 608; Radiation type, Mo*K*α: μ (mm^{-1}), 2.08; Crystal size/mm^{3,} 0.32 × 0.25 × 0.19; θ range (data coll.), 2.8º to 27.1º; Index ranges, *h* = -11→11; Index ranges, *k* = -10→10; Index ranges, *l* = -18 →18; T_{min}, $T_{max,}$ 0.641, 0.747; No. of measured, independent and observed reflections with $I > 2\sigma(I)$, 31717, 2348, 2039; $R_{int,}$ 0.055; $(\sin\theta/\lambda)_{max}$ (Å^{-1}), 0.641; $R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*, 0.025, 0.066, 1.06; No. of reflections, 2348; No. of parameters, 164; $\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3}), 0.39, -0.30.

Synthesis of 1,1′-*bis*[4-hydroxy-6-methyl-2(1*H*)-pyridinone] (9) and *N,N′-bis*[2-(5-methyl-1*H*-pyrazol-3-yl)-acetylcarboxamide] (7): 4-Hydroxy-6-methyl-2-pyrone (**6**, 0.042 mol) in 20 mL of *n*-butanol and hydrazine monohydrate (0.021 mol) was mixed. The mixture was heated under reflux for 48 h. The solvent was evaporated under vacuum and the obtained products **10** and **11** were separated by chromatography of the residue on the silica gel column (hexane/THF: 70/30). The products were recrystallized in CH$_3$CN.

***N,N′-Bis*[2-(5-methyl-1H-pyrazol-3-yl)acetylcarboxamide] (7):** Yield: 29%; m.p.: 240-242 ºC (ethanol).

1,1′-*Bis*[4-hydroxy-6-methyl-2(1*H*)-pyridinone] (9): Yield: 61%; m.p.: > 266 ºC (ethanol). ^{1}H NMR (DMSO-d_6): 1.95 (s, 3H, CH$_3$); 5.62 (d, ^4J = 2.73 Hz, 1H, CH=); 5.95 (dd, ^4J = 2.7 Hz, ^4J = 2.67 Hz, 1H, CH=); 11.03 (s, 1H, OH). ^{13}C NMR (DMSO-d_6): 17.71 (CH$_3$); 96.15 (CH=); 100.46 (CH=); 147.81(Cq); 160.75 (C=O); 167.04 (C-OH). IR (ATR) cm$^{-1:}$ 2605; 1654; 1559; 1466; 1432. *m/z*: 249.08 [M$^+$]. HRMS, *m/z*: 248(M), calcd. (found) for $C_{12}H_{12}N_2O_4$: 248.0797 (248.080).

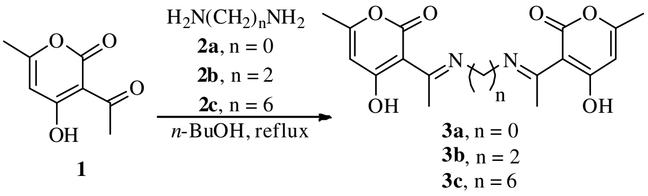
Synthesis of 1,1′-(1,2-ethanediyl)*bis*[4-hydroxy-6-methyl-2(1*H*)-pyridinone] (10): 4-hydroxy-6-methyl-2-pyrone (**6**, 0.03 mol) in 20 mL of *n*-butanol and (0.015 mol) of 1,2-diaminoethane was mixed. The mixture was heated under reflux for 18 h. The obtained precipitate was filtered under vacuum, washed by *n*-butanol. The products was recrystallized in ethanol.

1,1′-(1,2-Ethanediyl)*bis*[4-hydroxy-6-methyl-2(1*H*)-pyridinone] (10): Yield: 74 %; m.p.: > 266 ºC (ethanol). ^{1}H NMR (DMSO-d_6): 1.05, 1.07(d, 2CH$_3$); 2.16 (s, CH$_2$); 2.24 (s, CH$_2$); 2.3 (s, OH); 4 (s, OH); 5.52, 5.53 (d, 2H, 2CH=); 5.75, 5.76 (d, 2H, 2CH=). ^{13}C NMR (DMSO-d_6): 19.42 (CH$_3$); 41.4 (CH$_2$); 95.81 (CH=); 100.44 (CH=); 147.29 (Cq); 163.9 (C=O); 166.09 (C-OH). IR (ATR) cm$^{-1:}$ 3555; 3367; 2984; 1979; 1645; 1531; 1487; 1436. HRMS, *m/z*: 276(M), calcd. (found) for $C_{14}H_{16}N_2O_4$: 276.1110 (276.111).

Crystal structure analysis: Single crystals diffraction data have been collected at low temperature (T = 150 K) using Mo-Kα radiation (λ = 0.71073 Å, multilayer monochromator). Crystal structure was solved by dual-space algorithm using the SHELXT program and then refined with full-matrix least-squares method based on F^2 (SHELXL) [26,27]. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters except for compound **6** where hydrogen atom linked to oxygen atom was introduced in the structural model through Fourier difference maps analysis, all hydrogen atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters.

RESULTS AND DISCUSSION

The condensation of primary amines with several lactones was reported, ammonia and primary amines react with 2-pyrones to afford the corresponding 2-pyridones [28-32]. Other workers have investigated the condensation of bisnucleophiles with 4-hydroxy-6-methylpyran-2-one and dehydroacetic acid (3-acetyl-4-hydroxy-6-methyl-2-pyrone) and postulated a ring opening of these pyrones to explain their experimental results [26,33,34]. Some bispyrone derivatives have been reported as excellent ligands for complexation of ruthenium centers [34]. The present work deals with the synthesis of bispyrone derivatives from the condensation of aliphatic diamines **2a-c** with dehydroacetic acid (**1**) (**Scheme-I**).



Scheme-I: Synthesis of bispyrones **3a-c**

The obtained NMR and mass spectra were insufficient in order to clearly confirm the structures of the obtained products (either bispyrone or bispyridone). Thus, in order to establish the structures of products **3**, single crystals were synthesized for X-ray diffraction analysis of **3a** and **3b**. For compound **3a**, three fused rings and their symmetry, part of the molecule, $C_{16}H_{16}N_2O_6$, are almost coplanar, the maximum deviation from the mean plane is 0.082 (2) Å at C1 atom [35,36]. Two strong intramolecular hydrogen bonds complete two cycles of the molecule. The inter-centroids distance is being 3.975(2) Å. In case of compound **3b**, the additional ethyl linker prevents the formation of any intramolecular hydrogen bonding (Fig. 1).

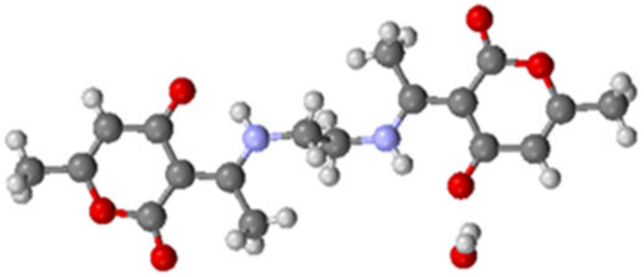


Fig. 1. ORTEP plot of **3b** (bottom). Displacement ellipsoids are drawn at the 50% probability level. H atoms are represented as small circles

In an other hand, the reaction of these bispyrones with several metals has been realized, for bispyrone **3b** with Ni, complex **4** was obtained (**Scheme-II**). While for bispyrone **3c** with Fe, the hydrolysis of the ligand lead to the formation of complex **5**, which is three dehydoacetic acid bonded to iron metal (**Scheme-III**). The structure of compounds **4** and **5** has been established, in particular, by X-ray diffraction (Fig. 2).

The reaction of 4-hydroxy-6-methylpyran-2-one (**6**) with hydrated hydrazine in acetonitrile formed the hydrazide-linked bispyrazole (**7**) (**Scheme-IV**). NMR and mass spectroscopic data of compound **7** were measured. The proposed mechanism of the formation of bispyrazole (**7**) is shown in **Scheme-V**. Initially, hydrazine opens the pyrone ring forming a *bis*-hydrazide followed by condensation of two additional hydrazine molecules with the β-diketone systems leading to bispyrazole (**7**).

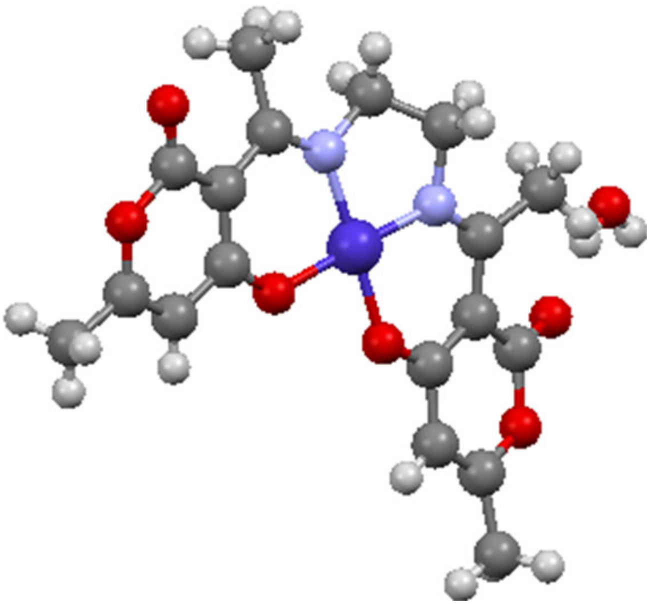
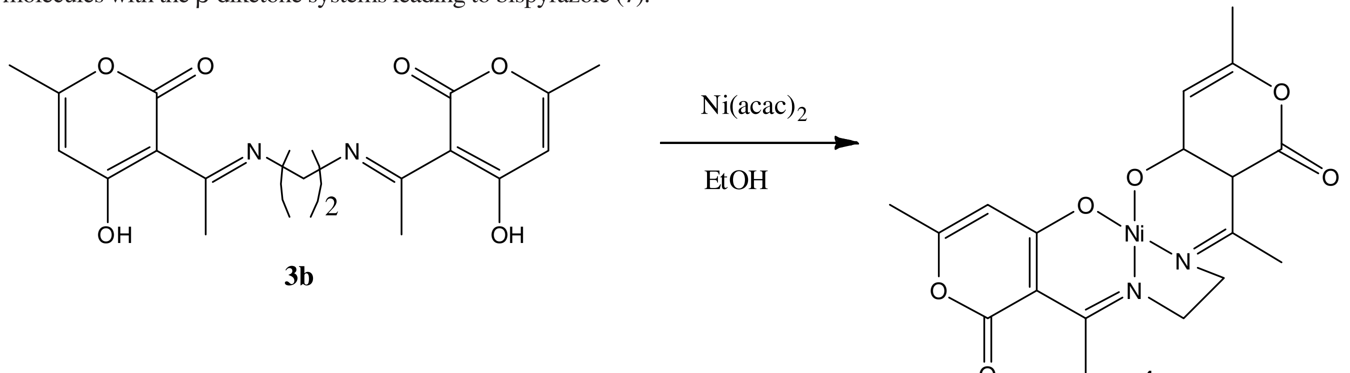


Fig. 2. ORTEP structure of the nickel complex **4**

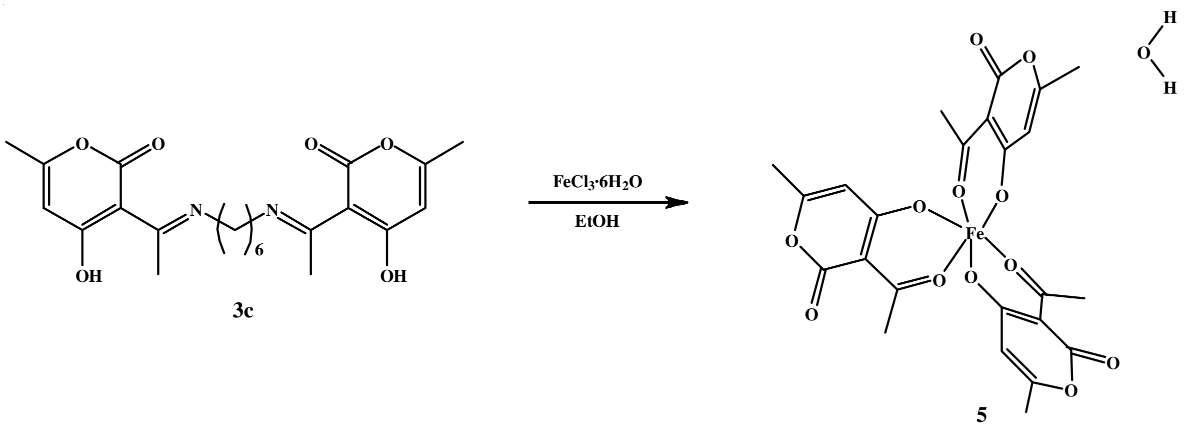
In order to confirm the proposed structure of compound **7**, compound **7** was treated with $Cu(NO_3)_2(H_2O)_3$ and crystals of the formed bis-copper complex **8** were prepared for X-ray diffraction analysis. The obtained data confirmed that compound **7** is a bispyrazole derivative with metal chelating properties (two copper ions per ligand **7**). The crystal structure of the copper complex **8** is shown in Fig. 4. Two Cu(II) centers were chelated by one bispyrazole molecule **9** *via* the nitrogens



3b

4

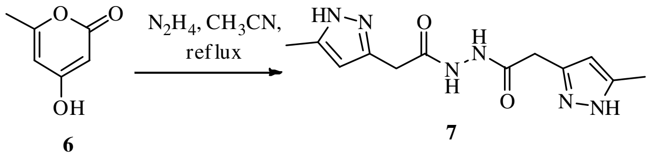
Scheme-II: Synthesis of the nickel complex **4**



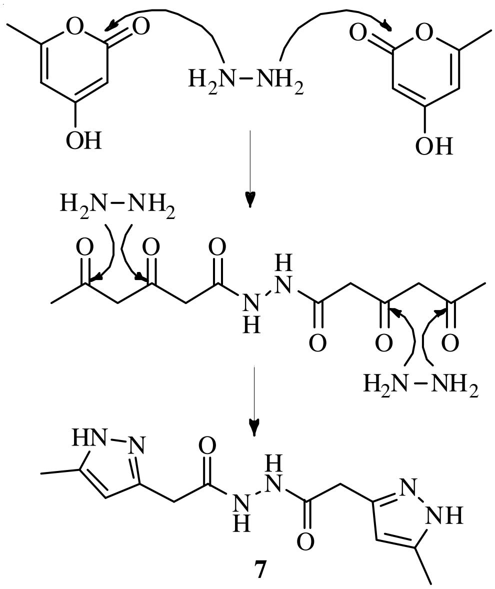
3c

5

Scheme-III: Synthesis of the iron complex **5**



Scheme-IV: Synthesis of bispyrazole **7**



Scheme-V: Proposed mechanism of the formation of bispyrazole **7**

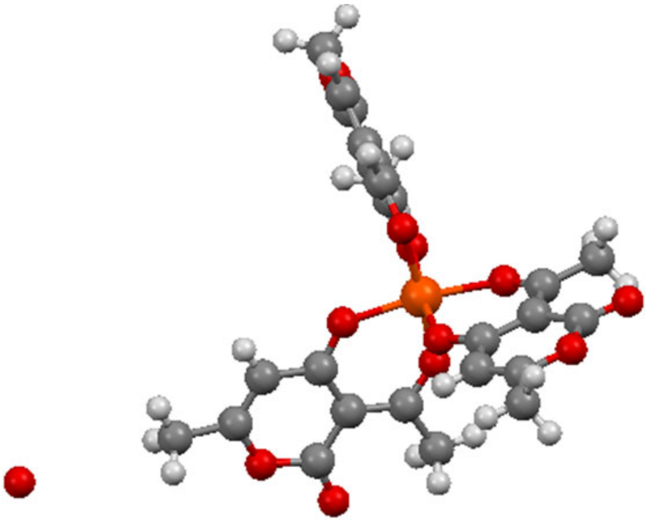


Fig. 3. ORTEP structure of the iron complex **5**

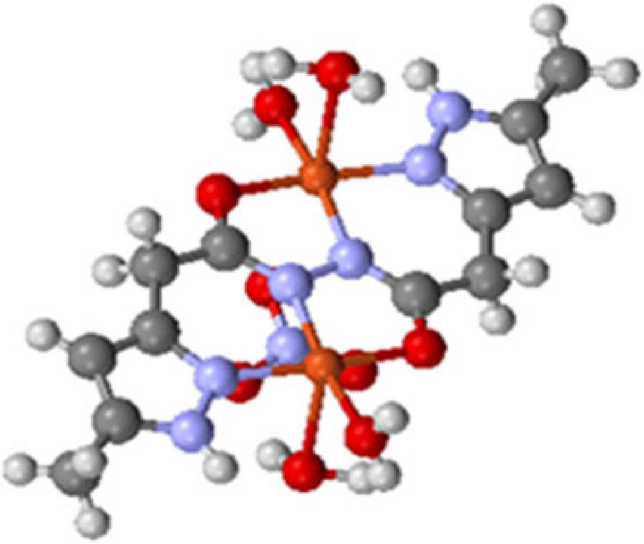


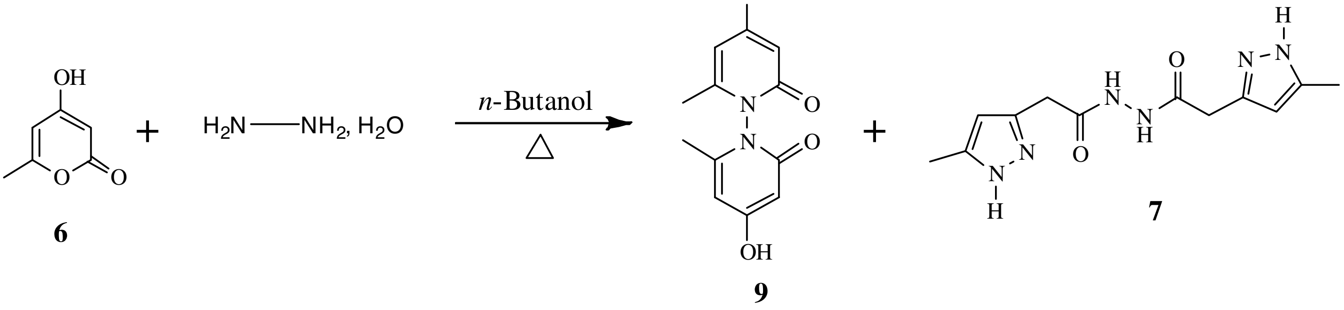
Fig. 4. ORTEP structure of the *bis*-copper complex **8**

of one pyrazole ring and the hydrazide bridge and by one hydrazide carbonyl oxygen. However, the reaction of 4-hydroxy-6-methylpyran-2-one (**6**) with primary diamines in *n*-butanol instead of acetonitrile lead to the formation of bispyridone compound. The condensation of 4-hydroxy-6-methylpyran-2-one (**6**) with hydrazine in *n*-butanol give two products, the bispyridone (**9**) as major compound and the bispyrazole (**7**) (**Scheme-VI**).

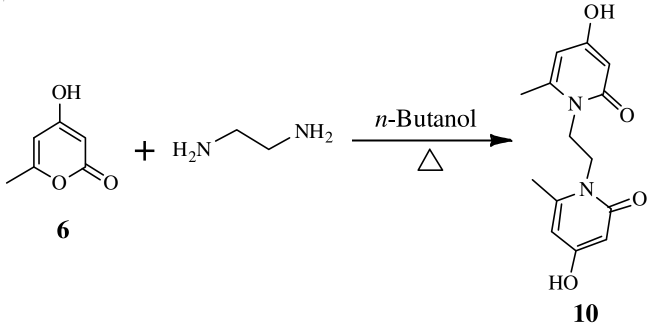
The reaction of 4-hydroxy-6-methylpyran-2-one with 1,2-diaminoethane in *n*-butanol lead to the bispyridone **10** (**Scheme-VII**). The structure of the bispyridone derivatives **9** and **10** has been established based on their spectroscopic data (NMR and mass).The NMR of proton of these bispyridones shows, in particular, a singlet of the proton in position 3 and a doublet of the proton in position 5 coupling with the proton of methyl group.

Conclusion

This work describes straightforward procedures for the synthesis of several bisheterocyles as bispyrones, bispyrazoles and bispyridones. The presented condensation reactions of lactone derivatives with hydrazine led to unexpected results and new bispyrazole, bispyridone derivatives were obtained. These findings suggest the formation of reactive intermediates which can easily undergo pyrazole and pyridone ring formation reactions.



Scheme-VI: Synthesis of bispyridone **9**



Scheme-VII: Synthesis of bispyridone **10**

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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