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Synthesis of Some Functionalized Pyridazino[4,5-*d*]pyridazine Derivatives

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The condensation reactions between ninhydrin and 1,3-dione compounds are one of the type extended reactions in various conditions. Compounds **1-3** were synthesized *via* the condensation of ninhydrin with barbituric acid, 1,3-dimethyl barbituric acid and 4-cyclopenten-1,3-dione in presence of sodium hydroxide and in Et-OH/H_2O as solvent (in good yield). Compounds **4-6** as functionalized pyridazino[4,5-d]pyridazine derivatives could be made by simple reaction of **1-3** with hydrazine in very good yields. These compounds **1-3** and **4-6** show fluorescent properties.

Key Words: Heterocycles, Ninhydrin, 1,3-Diones, Pyridazino-[4,5-*d*] pyridazine, Fluorescent compounds.

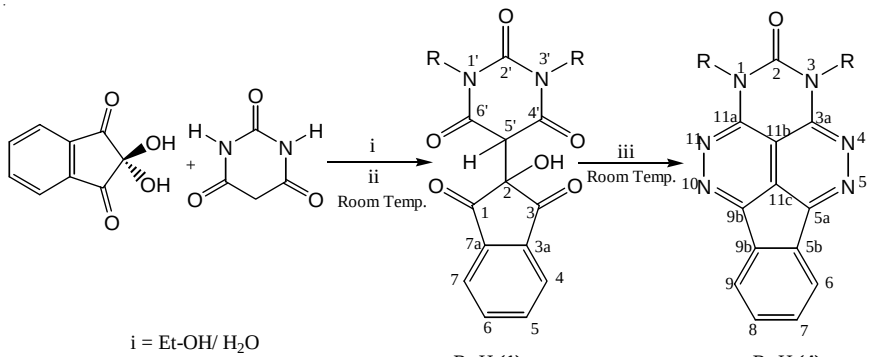
INTRODUCTION

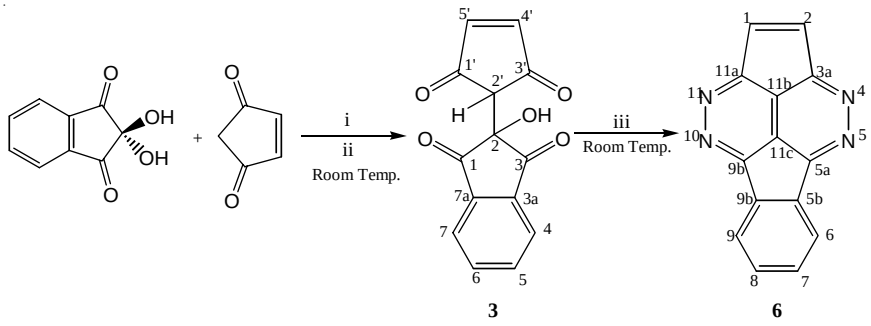
The reactions of ninhydrin and 1,3-dione compounds are one of the condensation types extended process in various conditions. The reactions of solid-solid, gas-solid, and solution states of ninhydrin with some of the 1,3-diones such as dimedone have already been investigated[1-4].

Here we report the synthesis of compounds **1-3**. These compounds **1-3** were produced by condensation of ninhydrin with barbituric acid, 1,3-dimethyl barbituric acid and 4-cyclopenten-1,3-dione (in good yields).

The standard method of synthesis of the pyridazine ring is the action of hydrazine on compounds 1,4-dicarbonyl or their equivalent. Saturated 1,4-diketones give dihydropyridazines which are easily oxidized to the aromatic compounds, but 2,3-unsaturated-1,4-diketones give the aromatic ring system directly[5,6].

It is reported that, first, pyridazino[4,5-*d*]pyridazine was obtained by Gault *et al.*[7] Entire data about the synthesis and reactivity of this heterocyclic system are due to Singermann and Castle[8]. Several studies were reported earlier regarding the reaction of ninhydrin and barbituric acid derivatives[9,10].





These reports described the preparation of a number of pyridazino[4,5-*d*]pyridazine derivatives[11-14]. Compounds **4-6** as functionalized heterocyclic compounds, were produced by a simple synthesis of the reaction between **1-3** and hydrazine monohydrate (in very good yields). Both groups of compounds **1-3** and **4-6** show fluorecent properties. The fluorescent dyestuffs are used in making daylight products[15].

EXPERIMENTAL

Melting points were measured on Electrothermal apparatus. Elemental analyses were performed by using a Metler Toledo HR73 CHN analyser. The FT-IR spectra were recorded on a Shimadzu FT-IR 8000 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured with Brüker 500 MHz spectrometer at 500 and 125.7 MHz, respectively. Mass spectra were recorded on a GC-MS QP-1100EX Shimadzu mass spectrometer operating at an ionization potential of 70 eV.

Typical procedure

The synthesis and purification of 5-(2-hydroxy-1,3-dioxo-indan-2yl)-pyrimidine-2,4,6-trione (compound **1**) and 1,3-dihydro-1,3,4,5,10,11-hexaaza-benzo[cd]fluoranthen-2-one (compound **2**) as typical procedures were explained.

Preparation and Purification of 5-(2-hydroxy-1,3-dioxo-indan-2-yl)-pyrimidine-2,4,6-trione (compound 1): A solution of sodium hydroxide (3 mL, 1 N) was added dropwise to a magnetically stirred solution of ninhydrin (0.01 mol) in H_2O (15 mL) and barbituric acid (0.01 mol) in ethanol (15 mL), at room tempreature for 2 h. A yellow solid was collected by filtration after evaporation of the solvent. Recrystallization from water yielded compound **1** as yellow crystals yield 90 %, m.p. = 168-170ºC; ν_{max} (KBr, cm^{-1}): 3645 ν(O–H, Free); 3429 ν(N–H); 3020, 3217 ν(Ar-H); 1751, 1716, 1689 ν(C=O groups) and 1639, 1547, 1458 ν(C=C). ν_{max}/nm (in H_2O): 235.5 (2.6). MS (m/z, %): 289 (M+1, 2), 288 (M, 10), 270 (M-18, 4.5), 147 (85), 128 (12.5), 104 (22), 76 (27.5), 44 (100), 43 (86.25). Elemental analysis $C_{13}H_8N_2O_6$ calcd. (%): C (54.17), H (2.78), N (9.72), O (33.33); Found: C (54.25), H (2.55), N (9.9) and O (33.40). $\delta_H(D_2O)$: 4.70-4.73 (2H), 7.8-7.9 (4H, Ar-H, AA'BB' system). $\delta_C(D_2O)$: 77.2 (C_5'), 84 (C_2), 124, 137.6, 140.5 (C_{Ar}), 153.4 (C_2'), 166.4 (C_4',C_6') and 202.6 (C_1, C_3), yield 90 %.

Preparation and Purification of 1,3-dihydro-1,3,4,5,10,11-hexaaza-benzo[cd]fluoranthen-2-one (compound 4): Add hydrazine (0.02 mol) to compound **1** (0.01 mol) in a 50 mL beaker and stir for 1 h at room temperature. A red-orange solid was collected by filtration. Recrystallization from DMF yielded compound 4 as red-orange crystals (yield 92%, m.p. = 280-281ºC, degraded in 285ºC). ν_{max} (KBr, cm^{-1}): 3549_{asym}, $3425_{sym.}$ ν(N–H); 3186 ν(Ar–H); 1728 ν(C=O); 1675 ν(C=N); 1659 ν(C=C); 1512 ν(C=C, Ar); 1404 ν(NH, bending); 1370 ν(N–C–N, asym.); 1203 ν(N–C–N, Sym.); 810 ν(C–H, bending or N–H wagging). ν_{max}/nm (in Et-OH): 466.73 (1.35). MS (m/z, %): 262 (M-1, 3.75), 260 (M-2, 22.5), 259 (100), 258 (67.5), 215 (18.75), 144 (15.5), 76 (3.25), 44 (8.25), 43 (5) and 42 (10). For $C_{13}H_6N_6O$ the calculated percentage of elements (%) is: C (59.55), H (2.31), N (32.05), O (6.10); Found: C (59.67), H (2.20), N (31.99) and O (6.30). δ_H (^{6}d-DMSO): 6.70, 6.80, 8.40, 8.50 (4H, Ar-H, AX system), 10.9, 11.04 (2H, NH); δ_C (d_6-DMSO): 109.5 (C_{11b}), 111.2 (C_{11c}), 119.9, 139.1, 150.3 (C_{Ar}), 154.6 (C_{5a}, C_{9b}), 155.3 (C_{3a}, C_{11a}), 164.59 (C_2), yield 92%.

RESULTS AND DISCUSSION

The structures of compounds **1-3** and **4-6** were deduced from their elemental analyses and their ^{1}H and ^{13}C NMR spectra as well as from IR spectra which exhibited strong C=O signals. The molecular ion peak is very weak in the mass spectra of compound **1**. The ion peak at m/z = 270 shows the omission of one H_2O molecule from compound **1**. The base peak of this compound was appeared in m/z = 44. The molecular ion peak of **4** is very weak. The base peak of **4** was appeared in m/z = 259.

TABLE-1
SELECTED DATA OF **1-6** (FT IR (cm^{-1}), NMR (δ), λ_{max} (nm) AND MELTING POINT IN ºC)

Compounds **1-3**		Compounds **4-6**	
1	m.p. =168-170 λ_{max} = 235.5 FT-IR: 3645 (O-H, Free); 3429 (N-H); 3020, 3217 (Ar-H); 1751, 1716, 1689 (C=O groups) and 1639, 1547, 1458 (C=C). ^{1}H NMR : 4.70-4.73 (2H), 7.8-7.9 (4H, Ar-H, AA'BB' system). ^{13}C NMR : 77.2 (C_5'), 84 (C_2), 124, 137.6, 140.5 (C_{Ar}), 153.4 (C_2'), 166.4 (C_4',C_6') and 202.6 (C_1, C_3). Yield =90%.	**4**	m.p. = 280-281 λ_{max} = 466.7 FT-IR : 3549_{Asym}, 3425_{sym}. (N-H); 3186 (Ar-H); 1728 (C=O); 1675 (C=N); 1659 (C=C); 1512 ($Ar_{C=C}$); 1404 (NH, bending); 1370 (N-C-N, Asym.); 1203 (N-C-N, Sym.);810 (C-H, bending or N-H wagging). ^{1}H NMR : 6.70, 6.80, 8.40, 8.50 (4H, Ar-H, AX system), 10.9, 11.04 (2H, NH). ^{13}C NMR : 109.5 (C_{11b}), 111.2 (C_{11c}), 119.9, 139.1, 150.3 (C_{Ar}), 154.6 (C_{5a}, C_{9b}), 155.3 (C_{3a}, C_{11a}), 164.59 (C_2). Yield =92%.
2	m.p. = 168-170 λ_{max} = 247.0 FT-IR : 3610 (O-H, Free); 3050, 3200 (Ar-H); 2850-2950 (C-H, alipha.); 1745, 1715, 1691 (C=O groups) & 1620, 1550, 1455 ($Ar_{C=C}$) ^{1}H NMR : 2.8 (6H), 1.8 (1H); 7.8-7.9 (4H, Ar-H, AA'BB' system). ^{13}C NMR : 50 (CH_3); 77.0 (C_5'); 84 (C_2); 124, 138, 141(C_{Ar}); 152 (C_2'); 165 (C_4',C_6') and 201 (C_1, C_3). Yield =90%.	**5**	m.p. = 277-279 λ_{max} = 478.0 FT-IR : 3150 (Ar-H); 1730 (C=O); 1680 (C=N); 1650 (C=C); 1512 (C=C, Ar); 1490, 1600 ($Ar_{C=C}$); 1390 (N-C-N, Asym.); 1198 (N-C-N, Sym.); ^{1}H NMR : 3.0 (6H, 2Me); 6.7, 6.8, 8.4, 8.5 (4H,Ar-H, AX system). ^{13}C NMR: 55 (CH_3); 108 (C_{11b}); 110 (C_{11c}); 119, 139, 150 (C_{Ar}), 153 (C_{5a}, C_{9b}), 155 (C_{3a}, C_{11a}), 163.0(C_2). Yield =94%.
3	m.p. = 128-130 λ_{max} = 215.5 FT-IR: 3600 (O-H, Free); 3150-3200 (Ar-H); 3050 (=C-H); 1710, 1688 (C=O groups); 1610 (C=C); 1570, 1475 ($Ar_{C=C}$). ^{1}H NMR : 6(2H); 7.5-7.6 (4H, Ar-H, AA'BB' system). ^{13}C NMR : 70.0 (C_2'); 82 (C_2); 126, 133, 137(C_{Ar}); 122 (C_4',C_5'); 160 ($C_{1'}$, C_3'); 202 (C_1, C_3). Yield =92%.	**6**	m.p. = 207-209 λ_{max} = 495.0 FT-IR : 3125 (Ar-H); 3075 (=C-H); 1650 (C=N); 1615(C=C); 1475, 1600 ($Ar_{C=C}$). ^{1}H NMR : 6.5 (2H,s); 6.8, 6.9, 8.0, 8.1 (4H, Ar-H, AX system). ^{13}C NMR: 110 (C_{11b}); 111 (C_{11c}); 123, 138, 147 (C_{Ar}); 152 (C_{5a}, C_{9b}); 150 (C_{3a}, C_{11a}); 127(C_1,C_2). Yield =90%.

The ^{1}H NMR spectrum of **1-3** displayed a multiplet readily recognizable as arising from the aromatic region (4H, δ = 7.8-7.9 ppm). The ^{13}C NMR spectrum of compounds **1-3** showed distinct resonances in agreement with the structure. The ^{1}H NMR spectrum of compounds **4-6** exhibited the doublet of doublet pattern at δ = 6.7, 6.8 and 8.4, 8.5 ppm readily recognizable as arising from the aromatic protons (AX system).

The ^{13}C NMR spectrum of compounds **4** and **6** displayed eight signals in agreement with the symmetric structure of this compound. The compound **5** has nine signals in ^{13}C NMR spectrum according to its symmetric form. Some information related to these results are illustrated in the experimental section and Table-1.

The structural information obtained on the base of the NMR spectra of the groups compounds **1-3** and **4-6** were supported by the measurements of their IR and UV spectra applied in interpreating the carbonyl absorption (1750-1690 cm^{-1}) in this compounds. The conjugation with the aromatic ring and functional groups, such as N–H in **1** and **4**, N–CH_3 in **2** and **5**, and C=C for **3** and **6**, appears to be a plausible factor in the reduction of the wave numbers of the carbonyl absorption bands[16]. Each of the λ_{max} in UV spectra of compounds **1-3** and **4-6** exhibited UV spectral bands (λ_{max}) at 235 (**1**), 247 (**2**), 260 (**3**), 467 (**4**), 478 (**5**) and 495 (**6**) and 467 nm.

Conclusion

The reactions described here are the simple and efficient synthesis of **1-3** compounds as a condensation product of ninhydrin with some of the 1,3-diones such as barbituric acid, 1,3-dimethyl barbituric acid and 4-cyclopenten-1,3-dione, also **4-6** are some fuctionalized derivatives of pyridazino[4,5-*d*]pyridazine. These compounds exhibit the fluorecent properties. It is shown that the compounds (**1-3**) are useful precursor for synthesis of compounds **4-6** with hydrazine. The one-pot synthesis and simple nature of the present procedures make an effective method to synthesize type **2** derivatives of **4-6**. The compounds **4-6** are insoluble in water insolubility of the compounds is an effective property in fluorecent dyes.

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