Studies with Enaminones: Synthesis and Chemical Reactivity of 2-(4-Dimethylamino-2-oxobut-3-enyl)-isoindole-1,3-dione and of 4-(4-Dimethylamino-2-oxobut-3-enyloxy)-2H-phthalazin-l-one

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The title compounds were synthesized *via* condensing acetonylphthalimide and 4-acetonyl-oxyphthalazine-l-one with dimethylformamide dimethylacetal (DMFDMA). The reaction of these enaminones with electrophiles and nucleophiles is reported as a route to polyfunctional heteroaromatics.

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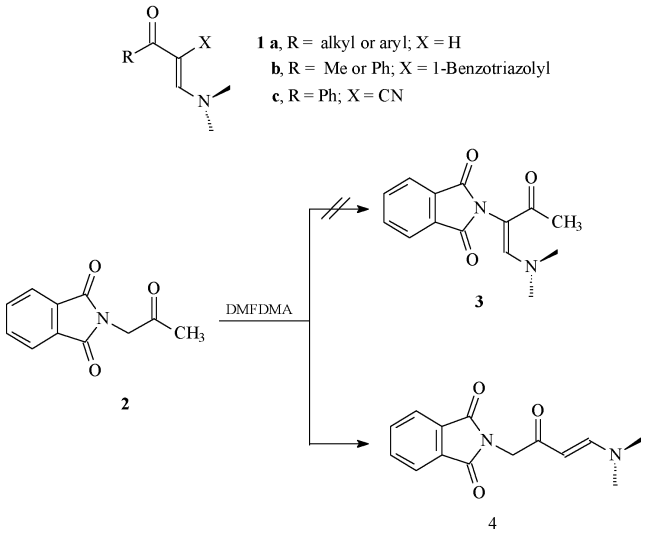
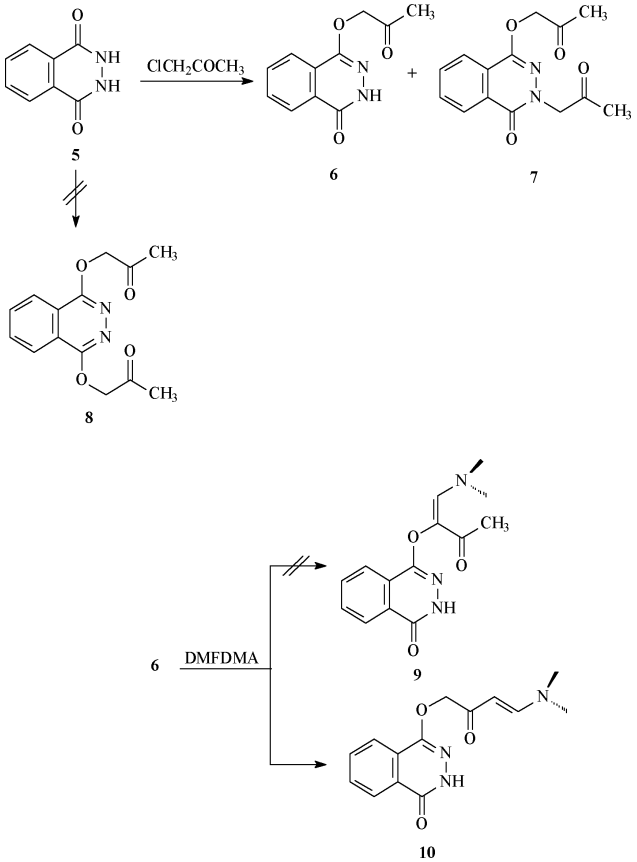
Certain functionally substituted pyridines are potential inhibitors of human immunodeficiency virus type 1(HIV-1) reverse transcriptase [1]. In addition, dihydropyridines are efficient calcium channel blockers [2]. Other pyridine derivatives are in use for treatment of congestive heart failure [3-5]. Previously, it has been shown that the readily obtainable enaminones, **1a-c**, are valuable starting materials for synthesis of polyfunctionally substituted pyridines [6-14], some of these are now being evaluated for potential biological activity. In light of this, we decided to develop syntheses for pyridines with other functional substituents. For this purpose, we attempted synthesizing enaminones **4** and **10** utilizing reaction of **2** and **6** with dimethylformamide dimethylacetal (DMFDMA). This is in analogy to previously reported activity of methylene moieties in 1-benzotriazolylacetone and 1-benzimidazolylacetone toward DMFDMA [12,15-16]. Therefore, **2** was synthesized utilizing literature procedure [6]. Compound **6** was obtained only in 20% yield together with **7** by reacting **5** with chloroacetone in basic solution. Although compound **6** may also be formulated as N-alkylation rather than O-alkylation product, structure **6** was confirmed based on Nuclear Overhauser Effect (NOE) difference experiments.

Thus, irradiating methylene moiety at δ 4.92 ppm enhanced aryl proton at δ 8.44 ppm, and *vice versa*, indicating that both are specially proximal, as required by structure **6**. Although compound **7** may also be formulated as **8**, structure **7** was established based on ^{13}C NMR (*cf.* experimental) which revealed the molecule to be unsymmetrical. Thus all six benzene moiety carbons are magnetically different, so are other carbons in the molecule, which is in contrast to what should be expected for structure **8**. Reacting **2** and **6** with DMFDMA afforded **4** and **10**

Scheme 1



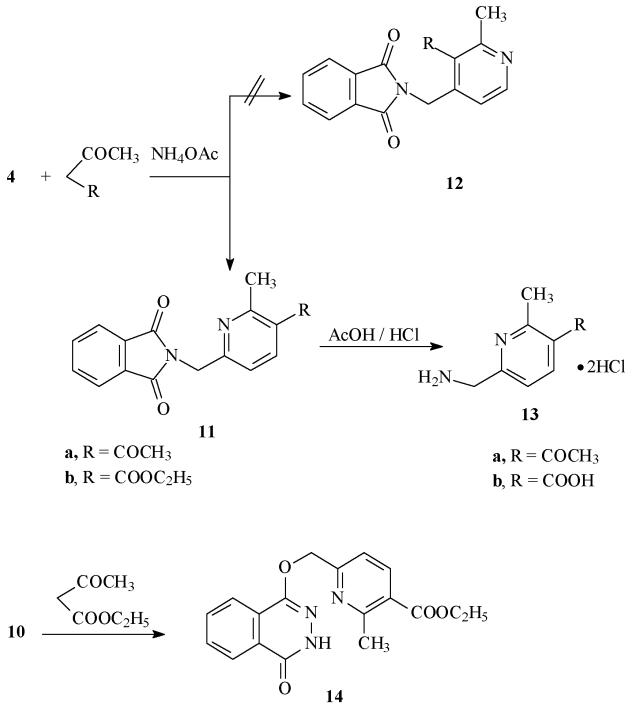
Scheme 2



respectively, rather than expected **3** and **9**. This could be realized readily *via* inspection of ^{1}H NMR which revealed absence of methyl signal and presence of a methylene signal at δ 4.76 ppm. Moreover, *trans* coupled olefenic protons at δ 5.07 ppm and δ 7.54 ppm are observed in both cases (J = 12.7 Hz). (Scheme 1 and 2).

Compound **4** reacted with acetylacetone and with ethyl acetoacetate, in refluxing acetic acid and in presence of ammonium acetate, to yield products that may be formulated as pyridines **11a,b** or isomeric **12a,b**. Structure **11** was readily established based on the fact that pyridine ring protons at δ 7.15 ppm and δ 8.12 ppm had J = 8 Hz, which is typical for H-3 and H-4 in pyridine system, and much larger than that for H-2 and H-3 (J = 3-4 Hz). Moreover, irradiating methyl function at δ 2.68 ppm (acetylmethyl) in **11a** enhanced both pyridine H-4 and methyl function at δ 2.56 ppm. If the reaction product was **12a**, only enhancement of methylene function at δ 5.03 ppm could have occurred. Compound **11a** was readily converted into the amine hydrochloride **13a** on reflux in acetic acid in presence of hydrochloric acid**.** Likewise, compound **11b** was converted into the carboxylic acid amine hydrochloride. Conversion of N-substituted phthalimides into substituted amines under similar conditions is widely used in the literature [12]. To our knowledge this is the first reported synthesis of methylaminopyridines *via* such a route. Methylaminopyridines are interesting as potential antitumor agents [18] and as immune response regulators [19] and as thrombin inhibitors [20].

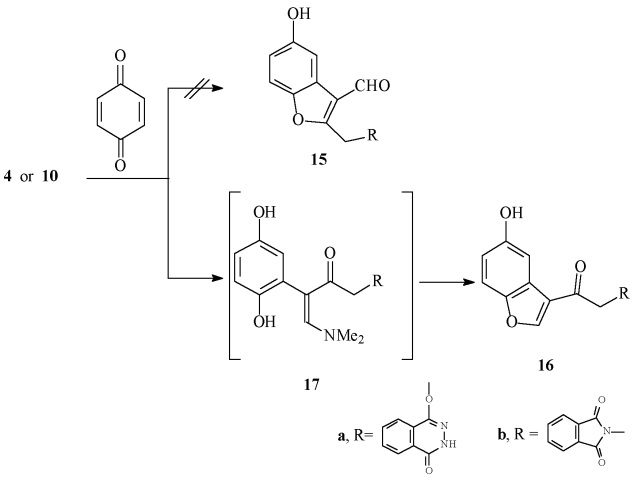
Scheme 3



Similar to the behavior of **4** toward ethyl acetoacetate, compound **10** also reacted with ethyl acetoacetate to yield the nicotinic acid derivative **14** (Scheme 3).

Compounds **4** and **10** reacted with *p*-benzoquinone to yield products that may be formulated as **15** or isomeric **16**. Heteronuclear Multiple Quantum Coherence spectroscopy (HMQC) indicated that carbonyl group at δ 188.9 ppm is not bonded to any hydrogen atoms. Thus structure **16** was established for the reaction product. It is believed that **16** is formed *via* initial addition of quinone to the electron rich C-3 of enaminone to yield **17**, which then affords **16**. Similar reaction of enaminones with naphthaquinones and benzoquinones has recently been reported from our laboratories but the exact structure of products in these reactions has not previously been firmly established [16,17] (Scheme 4).

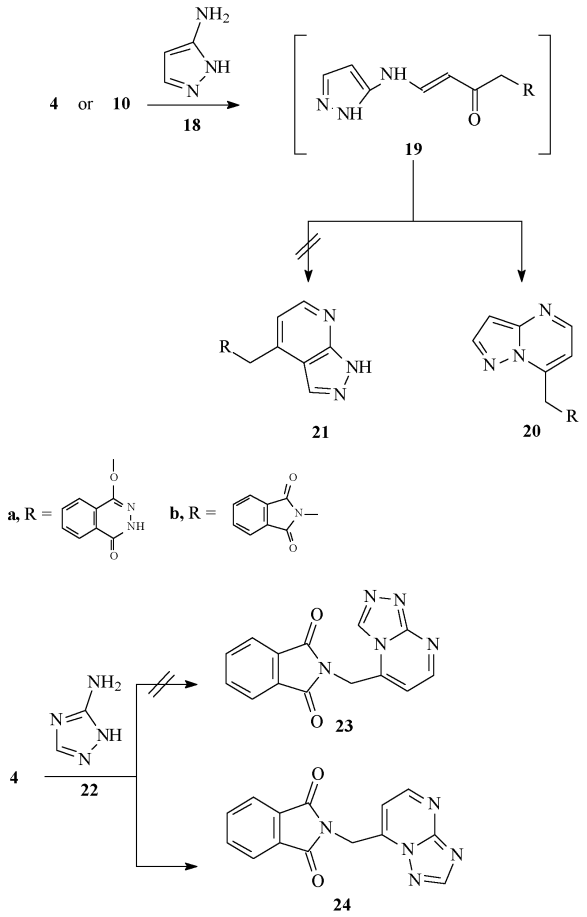
Scheme 4



Compounds **4** and **10** also reacted with 3-(1*H*)-aminopyrazole (**18**) in refluxing pyridine to yield products that can be formulated as pyrazolopyrimidines. Structures **20a,b** were established based on ^{1}H NMR which revealed absence of signal corresponding to NH and the presence of signals corresponding to H-2 and H-3 protons. Acyclic intermediate **19a,b** could be isolated and were cyclised to **20a,b** on reflux in pyridine in presence of hydrochloric acid.

Compound **4** also reacted with 5-amino-1*H*-[1,2,4] triazole **22** to yield the azolopyrimidine **24**. Although compound **24** can also be formulated as **23**, structure **24** was assigned. This was based on analogy to earlier reported behavior of enaminones toward **22** under similar conditions [21-22], and also NOE difference experiments, which indicated that triazole and methylene protons are specially proximal. Thus irradiating the methylene-H at δ 5.30 ppm has enhanced only the pyrimidyl-H at δ 7.48 ppm (Scheme 5).

Scheme 5



EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Shimadzu IR-740 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC-400 spectrometer with DMSO-d_6 as solvent (unless stated otherwise) and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on GS/MS INCOS XL Finnigan MAT. Microanalysis were performed on LECO CHNS-932 analyzer.

General Procedure for Preparation of Compounds **6** and **7**.

A mixture of **5** (1.62 g, 10 mmol), chloroacetone (0.9 ml, 10 mmol) and triethylamine (0.1 ml, 10 mmol) in toluene/acetone (50 ml) was refluxed for 24 h. The solvent was evaporated and the solid obtained was washed with water. A mixture of mono- and di-derivative was obtained and was separated using column chromatography with dichloromethane, methanol, ammonia as eluent in the ratio 75:15:10.

4-(2-Oxopropoxy)-2*H*-phthalazin-1-one (**6**).

This compound was obtained as white crystals from ethanol, in yield (20%, 0.4 g); mp 192°C; ir (KBr): ν max/cm^{-1}: 1664, 1722 (CO), 3163 (NH); ms: m/z = 218 (M$^+$); ^{1}H nmr (deuteriochloroform): δ (ppm) = 2.29 (s, 3H, CH_3), 4.92 (s, 2H, CH_2), 7.85-8.44 (m, 4H, Ar-H), 9.63 (br s, 1H, NH). ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 203.9 (CO), 159.6, 159.5, 149.5, 134.5, 133.3, 127.1, 124.9, 124.2 (aromatic carbons), 71.3 (CH_2), 26.96 (CH_3).

Anal. Calcd. for $C_{11}H_{10}N_2O_3$ (218.27): C, 60.55; H, 4.58; N, 12.85. Found: C, 60.79; H, 4.58; N, 12.84.

4-(2-0xopropoxy)-2-Oxopropyl)-2*H*-phthalazin-l-one (**7**).

This compound was obtained as white crystals from ethanol, in yield (10%, 0.27 g); mp 120 °C; ir (KBr): ν max/cm^{-1}: 1654, 1726 (CO); ms: m/z = 274 (M$^+$); ^{1}H nmr (deuteriochloroform): δ (ppm) = 2.23 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 4.85 (s, 2H, CH_2), 4.86 (s, 2H, CH_2), 7.84-8.44 (m, 4H, Ar-H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 203.8, 203.1 (2CO), 158.7, 149.1, 134.9, 133.9, 129.1, 127.6, 124.9, 124.5 (aromatic carbons), 71.5 (CH_2), 60.9 (CH_2), 28.1 (CH_3), 27.2 (CH_3).

Anal. Calcd. for $C_{14}H_{14}N_2O_4$ (274.27): C, 61.31; H, 5.10; N, 10.21. Found: C, 61.02; H, 5.08; N, 10.42.

General Procedure for Preparation of Compounds **4** and **10**.

A suspension of each of **2** (2 g, 10 mmol) or **6** (2.18 g, 10 mmol) in xylene (10 ml) was treated with DMFDMA (1.46 g, 11 mmol) and refluxed for 1.5 to 5 h. The solid product obtained upon cooling was filtered and recrystallized from ethanol.

2-(4-Dimethylamino-2-oxobut-3-enyl)-isoindole-l,3-dione (**4**).

This compound was obtained as yellow crystals from ethanol, in yield (70%, 1.8 g); mp 153 °C; ir (KBr): ν max/cm^{-1}: 1709, 1767 (CO); ms: m/z = 258 (M$^+$); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 2.79 (s, 3H, CH_3), 3.09 (s, 3H, CH_3), 4.40 (s, 2H, CH_2), 5.05 (d, 1H, *J* = 12.58 Hz, CH), 7.62 (d, 1H, *J* = 12.54 Hz, CH), 7.85-7.91 (m, 4H, Ar-H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 187.41 (CO), 168.81 (CO), 154.30, 135.80, 135.57, 132.73, 124.50, 124.16 (aromatic carbons), 45.28 (CH_2), 37.72 (NMe).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$ (258.27): C, 65.10; H, 5.46; N, 10.85. Found: C, 65.12; H, 5.48; N, 10.90.

4-(4-Dimethylamino-2-oxobut-3-enyloxy)-2*H*-phthalazin-l-one (**10**).

This compound was obtained as brown crystals in yield (70%, 1.91 g); mp 227 °C; ir (KBr): ν max/cm^{-1}: 1667 (CO), 3172 (NH); ms: m/z = 273 (M$^+$); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 2.69 (s, 3H, CH_3), 3.01 (s, 3H, CH_3), 4.76 (s, 2H, CH_2), 5.08 (d, 1H, *J* =12.68 Hz, CH), 7.54 (d, 1H, *J* =12.71 Hz, CH), 7.56-8.24 (m, 4H, Ar-H), 11.78 (s, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 189.71 (CO), 159.6 (CO), 153.91, 150.01, 134.39, 133.22, 129.54, 127.03, 125.28, 124.32 (aromatic carbons), 69.93 (*C*HCO), 55.79 (CH_2), 45.13 (CH_3), 37.59 (CH_3).

Anal. Calcd. for $C_{14}H_{15}N_3O_3$ (273.28): C, 61.53; H, 5.53; N, 15.38. Found: C, 61.44; H, 5.49; N, 15.27.

General Procedure for Preparation of Compounds **11a,b** and **14**.

To a stirred suspension of each of **4** (2.6 g, 10 mmol) or **10** (2.7 g, 10 mmol) with ammonium acetate (0.77 g, 10 mmol) and acetic acid (5 ml), each of ethyl acetoacetate (1.3 g, 10 mmo1) or acetylacetone (1.12 g, 10 mmol) was added. The reaction mixture was heated under reflux for 10 minutes-2 h. The solid product obtained on cooling was collected by filtration and recrystallized from proper solvent.

2-(5-Acetyl-6-pyridin-2-ylmethyl)-isoindole-1,3-dione (**11a**).

This compound was obtained as yellow crystals from dioxane in yield (60%, 1.76 g); mp 173 °C; ir (KBr): ν max/cm^{-1}: 1678, 1713, 1768 (CO); ms: m/z = 294 (M^+); ^{1}H nmr (deuteriochloroform): δ (ppm) = 2.56 (s, 3H, CH_3), 2.68 (s, 3H, $COCH_3$), 5.03 (s, 2H, CH_2), 7.15 (d, 1H, *J* = 8 Hz, pyridyl-H), 7.76-7.94 (m, 5H, Ar-H); ^{13}C nmr (deuteriochloroform): δ (ppm) = 200.50 (CO), 168.64 (CO), 159.01, 157.79, 138.25, 134.75, 132.69, 132.05, 124.12, 118.55 (pyridyl and isoindolyl carbons), 43.48 (CH_2), 29.93 (CH_3), 25.53 (CH_3CO).

Anal. Calcd. for $C_{17}H_{14}N_2O_3$ (294.30): C, 69.37; H, 4.80; N, 9.52. Found: C, 69.27; H, 4.84; N, 9.53.

6-(l,3-Dioxo-l,3-dihydroisoindol-2-ylmethyl)-2-methylnicotinic Acid Ethyl Ester (**11b**).

This compound was obtained as yellow crystals from ethanol in yield (67%, 2.17 g); mp 115 °C; ir (KBr): ν max/cm^{-1}: 1711, 1721 (CO), 1767 ($COOC_2H_5$); ms: m/z = 324 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 1.30 (t, 3H, CH_3), 2.59 (s, 3H, CH_3), 4.29 (q, 2H, CH_2), 4.91 (s, 2H, CH_2), 7.34 (d, 1H, *J* = 8 Hz, pyridyl-H), 7.82-7.98 (m, 4H, Ar-H), 8.12 (d, 1H, *J* = 8 Hz, pyridyl-H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 168.77 (CO), 166.87 (CO), 159.26, 158.94, 139.99, 135.68, 132.67, 125.03, 124.35, 119.59 (aromatic carbons), 62.03 (CH_2), 45.26 (CH_2), 25.47 (CH_3), 15.04 (CH_3).

Anal. Calcd. for $C_{18}H_{16}N_2O_4$ (324.32): C, 66.66; H, 4.97; N, 8.64. Found: C, 66.52; H, 4.95; N, 8.89.

2-Methyl-6-(4-oxo-3,4-dihydrophthalazin-l-yloxymethyl)nicotinic Acid Ethyl Ester (**14**).

This compound was obtained as white crystals from dioxane; in yield (60%, 2.03 g); mp 251°C; ir (KBr): ν max/cm^{-1}: 1659, 1722 (CO), 3171 (NH); ms: m/z = 339 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 1.32 (t, 3H, *J* = 8 Hz, CH_3), 2.72 (s, 3H, CH_3), 4.32 (q, 2H, *J* = 8 Hz, CH_2), 5.45 (s, 2H, CH_2), 7.52 (d, 1H, *J* = 8.08 Hz, pyridyl-H), 7.90-8.25 (m, 5H, Ar-H), 11.92 (br s, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 166.91 (CO), 160.10 (CO), 159.79, 159.19, 150.07, 146.06, 140.08, 134.71, 133.48, 129.81, 127.30, 125.31, 124.50, 119.24 (aromatic carbons), 69.12 (CH_2), 62.06 (CH_2), 25.32 (CH_3), 15.08 (CH_3).

Anal. Calcd for $C_{18}H_{17}N_3O_4$ (339.34): C, 63.71; H, 5.05; N, 12.38. Found: C, 63.63; H, 5.05; N, 12.46.

General Procedure for Preparation of Compounds (**13a,b**).

A mixture of compound **11a,b** (10 mmol) acetic acid/hydrochloric acid (1:1, 8 ml) was refluxed for 7 h. The reaction mixture was allowed to cool and the solid obtained was collected by filtration and recrystallised from dioxane.

1-(6-Aminomethyl-2-methylpyridin-3-yl)-ethanone Dihydrochloride (**13a**).

This compound was obtained as grey crystals in yield (56%, 1.32 g); mp 183 °C; ir (KBr): ν max/cm^{-1}: 1711 (CO), 3400-3427 (chelated NH); ms: m/z = 237 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 2.59 (s, 3H, CH_3), 2.66 (s, 3H, CH_3), 4.18-4.22 (m, 2H, CH_2), 7.49 (d, 1H, *J* = 8 Hz, pyridyl-H), 8.30 (d, 1H, *J* = 8 Hz, pyridyl-H), 8.47 (br s, 2H, NH_2); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 201.62 (CO), 157.53, 155.78, 146.66, 139.45, 120.86 (aromatic carbons), 45.62 (CH_2), 30.63 (CH_2), 25.17 (CH_3).

Anal. Calcd. for $C_9H_{14}N_2OCl_2$ (237): C, 45.56; H, 5.90; N, 11.81. Found: C, 45.66; H, 5.68; N, 11.51.

1-(6-Aminomethyl-2-methyl)nicotinic Acid Dihydrochloride (**13b**).

This compound was obtained as grey crystals in yield (70%, 1.67 g); mp 226 °C; ir (KBr): ν max/cm^{-1}: 1722 (CO), 2348-3002 (OH dimer), 3385-3447 (chelated NH); ms: m/z = 239 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 2.77 (s, 3H, CH_3), 4.22 (s, 2H, CH_2), 7.51 (d, 1H, *J* = 7.9 Hz, pyridyl-H), 8.27 (d, 1H, *J* = 7.9 Hz, pyridyl-H), 8.62 (br s, 2H, NH_2), 11.20 (br s, 1H, OH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 168.10 (CO), 158.91, 155.89, 141.05, 126.90, 121.54 (aromatic carbons), 43.06 (CH_2), 24.72 (CH_3).

Anal. Calcd. for $C_8H_{12}N_2O_2Cl_2$ (239): C, 40.16; H, 5.02; N, 11.71. Found: C, 40.01; H, 5.07; N, 11.71.

General Procedure for Preparation of Compounds (**16a,b**).

A mixture of each of **4** (2.6 g, 10 mmol) or **10** (2.7 g, 10 mmol) and *p*-benzoquinone (1.08 g, 10 mmol) in acetic acid (10 ml) was stirred overnight at room temperature. The solution was poured in water containing two drops conc. HC1. The solid formed was collected by filtration and crystallised from ethanol/dioxane.

4-[2-(5-Hydroxybenzofuran-3-yl)-2-oxoethoxy]-2*H*-phthalazin-1-one (**16a**).

This compound was obtained as white crystals in yield (60%, 2.01 g); mp >350 °C; ir (KBr): ν max/cm^{-1}: 1644 (CO), 3290 (NH); ms: m/z = 336 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 5.50 (s, 2H, CH_2), 6.76-8.25 (m, 7H, Ar-H), 8.1 (s, 1H, benzofuryl-H), 9.44 (br s, 1H, OH), 11.81 (s, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 203.94 (CO), 190.46 (CO), 159.66, 155.74, 154.76, 149.64, 134.61, 133.37, 129.54, 127.33, 125.32, 124.96, 124.35, 119.09, 115.37, 113.08, 107.03 (aromatic carbons), 67.20 (CH_2).

Anal. Calcd for $C_{18}H_{12}N_2O_5$ (336.29): C, 64.28; H, 3.6; N, 8.33. Found: C, 63.98; H, 4.01; N, 8.24.

2-[2-(5-Hydroxybenzofuran-3-yl)-2-oxoethyl]-isoindole-1,3-dione (**16b**).

This compound was obtained as brown crystals in yield (55%, 1.76 g); mp 252 °C; ir (KBr): ν max/cm^{-1}: 1709, 1776 (CO); ms: m/z = 321 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 5.11 (s, 2H, CH_2), 6.86 (d, 1H, *J* = 8.2 Hz, Ar-H), 7.36 (d, 1H, J = 7.8 Hz, Ar-H), 7.54 (d, 1H, J = 8.3 Hz, Ar-H), 7.90-7.98 (m, 4H, Ar-H), 9.19 (s, 1H, benzofuryl-H), 9.53 (br s, 1H, OH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 188.92 (CO), 168.57 (CO), 156.18, 156.02, 149.92, 135.86, 132.55, 125.28, 124.45, 119.53, 115.65, 113.29, 107.11 (aromatic carbons), 45.61 (CH_2).

Anal. Calcd. for $C_{18}H_{11}NO_5$ (321.28): C, 67.29; H, 3.45; N, 4.36. Found: C, 67.04; H, 3.60; N, 4.58.

General Procedure for Preparation of Compounds (**20a,b**).

A mixture of each of **4** (2.6 g, 10 mmol) or **10** (2.7 g, 10 mmol) with 3-aminopyrazole (0.84 g, 10 mmol) was refluxed in pyridine (10 ml) for 1.5 to 2 h. The solid product, so formed, was collected by filtration and crystallized from ethanol and dioxane.

4-(Pyrazolo[1,5-*d*]pyrimidin-7-ylmethoxy)-2*H*-phthalazin-1-one (**20a**).

This compound was obtained as white crystals from ethanol in yield (65%, 1.9 g); mp 284 °C; ir (KBr): ν max/cm^{-1}: 1662, 1700

(CO), 3182 (NH); ms: m/z = 293 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 5.89 (s, 2H, CH_2), 6.84-6.85 (d, 1H, *J* = 2.24 Hz, pyrazolyl-H), 7.30-7.31 (d, 1 H, *J* = *5* Hz, pyrimidyl-H), 7.95-8.27 (m, 4H, Ar-H), 8.31 (d, 1H, *J* = 2.3Hz, pyrazolyl-H), 8.59-8.60 (d, 1H, *J* = 5 Hz, pyrimidyl-H), 12.02 (s, 1H, NH); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 159.68 (CO), 150.32, 149.58, 149.09, 145.62, 144.85, 134.59, 133.45, 129.68, 127.17, 124.91, 124.38, 105.74, 97.36 (aromatic carbons), 62.42 (CH_2).

Anal. Calcd. for $C_{15}H_{11}N_5O_2$ (293.28): C, 61.43; H, 3.78; N, 23.88. Found: C, 61.50; H, 3.78; N, 23.58.

2-Pyrazolo[1,5-*a*]pyrimidin-7-ylmethyl-isoindole-1,3-dione (**20b**).

This compound was obtained as white crystals from ethanol in yield (77%, 2.14 g); mp 293 °C; ir (KBr): ν max/cm^{-1}: 1710, 1775 (CO); ms: m/z = 278 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 5.25 (s, 2H, CH_2), 6.84 (d, 1H, *J* = 2 Hz, pyrazolyl-H), 7.10 (d, 1H, *J* = 5 Hz, pyrimidyl-H), 7.90-7.98 (m, 4H, Ar-H), 8.32 (d, 1H, *J* = 2 Hz, pyrazolyl-H), 8.48 (d, 1H, *J* = 5 Hz, pyrimidyl-H).

Anal. Calcd. for $C_{15}H_{10}N_4O_2$ (278.26): C, 64.74; H, 3.62; N, 20.14. Found: C, 64.51; H, 3.71; N, 19.8.

2-[1,2,4]Triazolo[1,5-*a*]pyrimidin-7-ylmethylisoindole-l,3-dione (**24**).

A mixture of **4** (2.6 g, 10 mmol) and 5-amino-1*H*-[l,2,4]-triazole (0.84 g, 10 mmol) was refluxed in pyridine (10 ml) for 1.5 h. The solid product, so formed, was collected by filtration and crystallized from ethanol/dioxane. This compound was obtained as white crystals in yield (60%; 1.67 g); mp 262 °C; ir (KBr): ν max/cm^{-1}: 1712 (CO); ms: m/z = 279 (M^+); ^{1}H nmr (dimethyl sulfoxide-d_6): δ (ppm) = 5.30 (s, 2H, CH_2), 7.40 (d, 1H, *J* = 5 Hz, pyrimidyl-H), 7.89-7.97 (m, 4H, Ar-H), 8.76 (s, 1H, triazolyl-H), 8.83 (d, 1H, *J* = 5 Hz, pyrimidyl-H); ^{13}C nmr (dimethyl sulfoxide-d_6): δ (ppm) = 168.41, 156.84, 156.06, 155.91, 146.49, 135.77, 132.72, 124.51, 109.41 (aromatic carbons), 37.58 (CH_2).

Anal. Calcd for $C_{14}H_9N_5O_2$ (279.25): C, 60.21; H, 3.25; N, 25.08. Found: C, 60.05; H, 3.34; N, 24.80.

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