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4,6-DIACETYLRESORCINOL IN HETEROCYCLIC SYNTHESIS PART II: SYNTHESIS OF SOME NOVEL 4,6-BIS(AZOLYL/AZINYL/ AZEPINYL)RESORCINOLS

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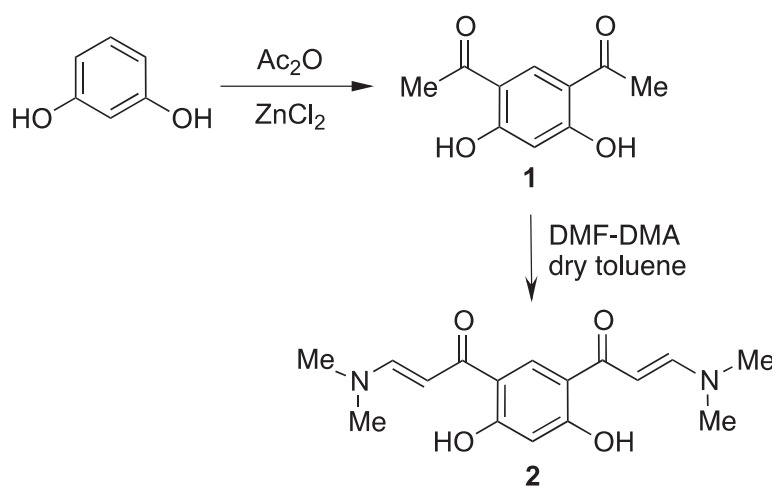
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Abstract – A series of new 4,6-bis(azolyl/azinyl/azepinyl)resorcinols was synthesized in a combinatorial manner besides, (2*E*,2'*E*)-4,6-bis[3-(aminophenyl-substituted)prop-2-en-1-oxo-1-yl]resorcinols were also obtained. Heterocyclization of (2*E*,2'*E*)-4,6-bis[3-(dimethylamino)prop-2-en-1-oxo-1-yl]resorcinol (**2**) with nitrogen-containing binucleophiles afforded the target compounds. All the newly synthesized compounds were characterized by spectral tools.

Resorcinol possesses unique structural characteristics for developing drug compounds exhibiting chemical structures and properties suitable for treating various human diseases.¹⁻³ Chemical compounds derived from the resorcinol derivatives can be potent and effective medicines. Resorcinol derivatives have been used by the major drug companies to develop new drugs, and also for the manufacture of existing therapeutic compounds.⁴⁻⁶ Enaminones are versatile reagents and their utilities in heterocyclic synthesis

have recently earned considerable attention.⁷⁻¹⁰ On the other hand, synthesis of nitrogen-containing heterocyclic systems occupies an important place in the realm of natural and synthetic organic chemistry, due to their therapeutic and pharmacological properties, including anti-inflammatory, antipyretic, analgesic, and antimicrobial activities.¹¹⁻¹⁷ The present research has been devoted to the development of new classes of *bis*-heterocyclic systems which incorporate the resorcinol moiety in the hope that they may be biologically active. Herein, we report the use of (*2E,2'E*)-4,6-*bis*[3-(dimethylamino)prop-2-en-1-oxo-1-yl]resorcinol (**2**) for the synthesis of some new 4,6-*bis*(azolyl/azinyl/azepinyl)resorcinols *via* its reactions with appropriate nitrogen-containing binucleophiles.

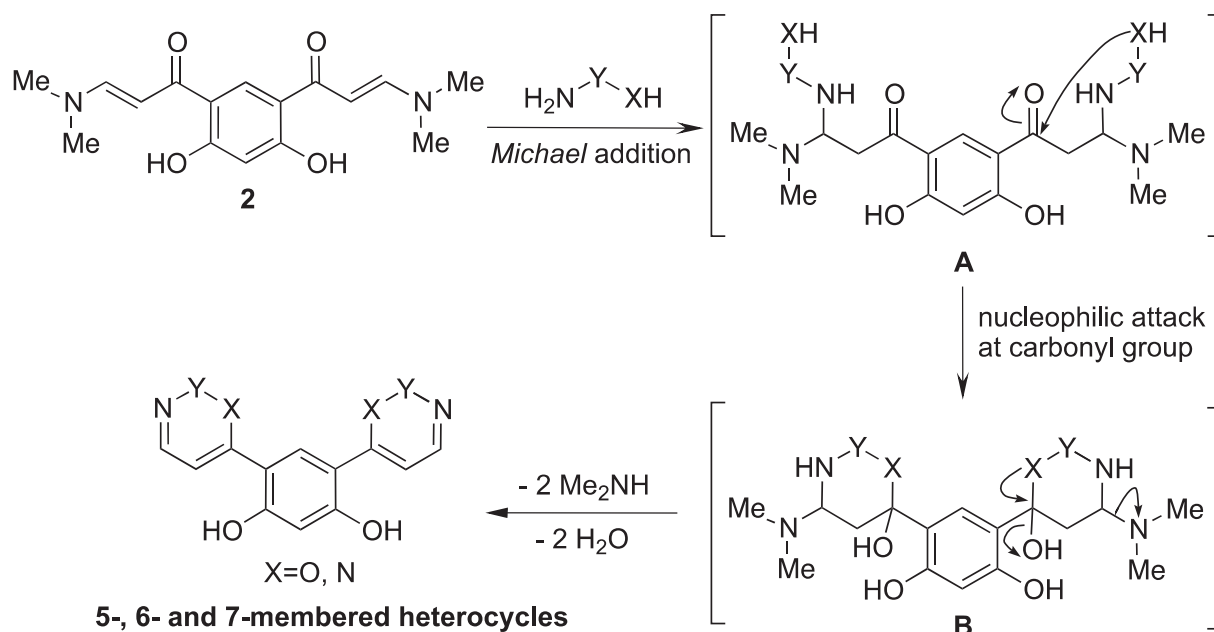
The starting material used in the synthesis, 4,6-diacetylresorcinol (**1**) was prepared *via* acetylation of resorcinol with acetic anhydride in the presence of freshly fused zinc chloride (Scheme 1).¹⁸ Condensation of compound **1** with dimethylformamide dimethyl acetal (DMF-DMA) in dry toluene under reflux for 6 hours furnished (*2E,2'E*)-4,6-*bis*[3-(dimethylamino)prop-2-en-1-oxo-1-yl]resorcinol (**2**) (Scheme 1). The IR spectrum of compound **2** showed the characteristic absorption band for carbonyl groups at 1629 cm⁻¹. Also, its ¹H-NMR spectrum displayed two singlets at δ 3.07 and 3.28 ppm due to the dimethyl groups and a broad singlet D₂O-exchangeable at δ 15.60 ppm due to the phenolic HO protons. Two doublets at δ 5.42 and 7.94 ppm with the same coupling constant 12 Hz were assigned to the vinylic protons which were existed in a *trans* configuration.¹⁹ The two aromatic protons H-2 and H-5 were appeared as singlets at δ 6.22 and 8.36 ppm, respectively. Furthermore, the mass spectrum of compound **2** recorded its molecular peak at *m/z* 304 (M⁺, 9%).



Scheme 1

Enaminones are valuable intermediates in synthetic organic chemistry.^{20,21} They have reported a variety of syntheses of heteroaromatics developed using functionally substituted enaminones as readily

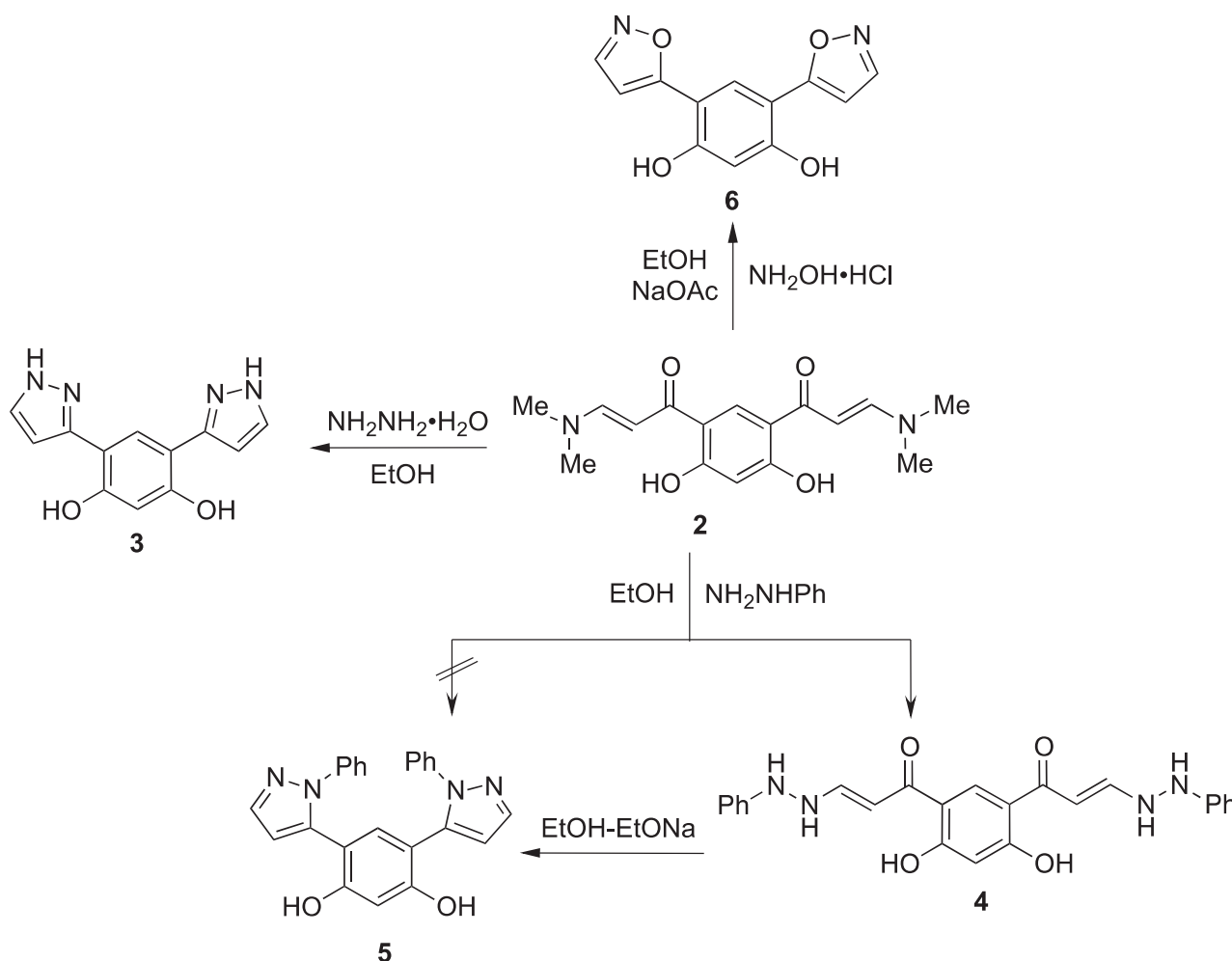
obtainable building blocks possessing multiple electrophilic and nucleophilic moieties.^{22,23} The reaction of the *bis*-enaminone **2** with nitrogen-containing 1,2-, 1,3- and 1,4-binucleophiles usually takes place *via* Michael addition on the position C- β , followed by an intramolecular cyclization *via* the loss of dimethylamine and water molecules (Scheme 2).



Scheme 2

Thus, when compound **2** was treated with nitrogen-containing 1,2-binucleophiles such as hydrazine hydrate and phenylhydrazine in refluxing ethanol resulted the novel *bis*-azolyl resorcinol **3** and **4**, respectively (Scheme 3). The reaction pathway was stopped at loss of dimethylamine during the formation of product **4** and there is no any traces of the *bis*-pyrazole derivative **5** was isolated (Scheme 3). The compound **5** was obtained *via* boiling of the product **3** in ethanolic sodium ethoxide. The structures of the latter products were deduced from their elemental analyses and spectral data. The IR spectra of the *bis*-pyrazole derivatives **3** and **5** showed disappearance of the carbonyl groups, while the IR spectrum of the *bis*-enaminone **4** recorded the carbonyl group at 1623 cm^{-1} . The $^1\text{H-NMR}$ spectra of compounds **3** and **5** revealed two characteristic signals for the protons of pyrazole rings at regions δ 6.88, 7.01 (H-4) and 7.82, 7.95 [(H-5 (3)) ppm. Their phenolic OH protons were also displayed at regions δ 14.01 and 13.00 ppm, respectively, as D_2O -exchangeable signals. The $^1\text{H-NMR}$ spectrum of compound **4** displayed two doublets at δ 5.95 and 7.87 ppm with the same coupling constant 12 Hz which were assignable to the vinylic protons which were existed in a *trans* configuration. In addition, its NH protons were recorded as D_2O -exchangeable singlets at δ 9.39 and 13.71 ppm. Furthermore, the molecular ion peaks of compounds **3–5** appeared at m/z 242 (M^+ , 39%), m/z 430 (M^+ , 52%), and m/z 394 (M^+ , 8%), respectively. Next,

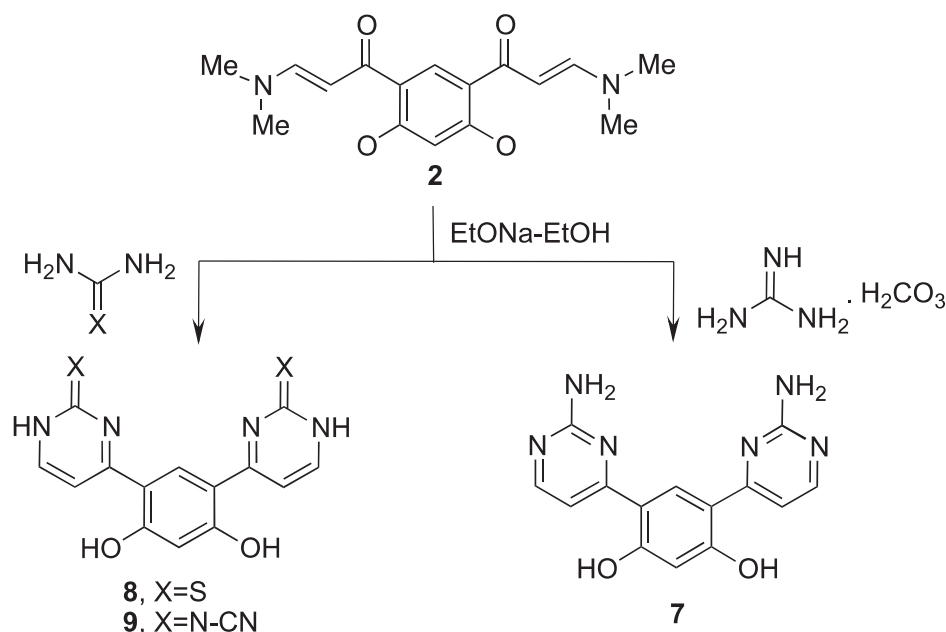
reaction of the *bis*-enaminone **2** with hydroxylamine hydrochloride in refluxing ethanol containing freshly fused sodium acetate afforded the corresponding 4,6-*bis*(isoxazol-5-yl)resorcinol (**6**) (Scheme 3). The $^1\text{H-NMR}$ spectrum of compound **6** revealed two characteristic doublets at δ 6.77 and 8.59 ppm with coupling constant 5.7 Hz which were readily assigned to the H-4 and H-3, respectively, of the isoxazole rings. The molecular ion peak of compound **6** appeared in its mass spectrum at m/z 244 (M^+ , 23%).



Scheme 3

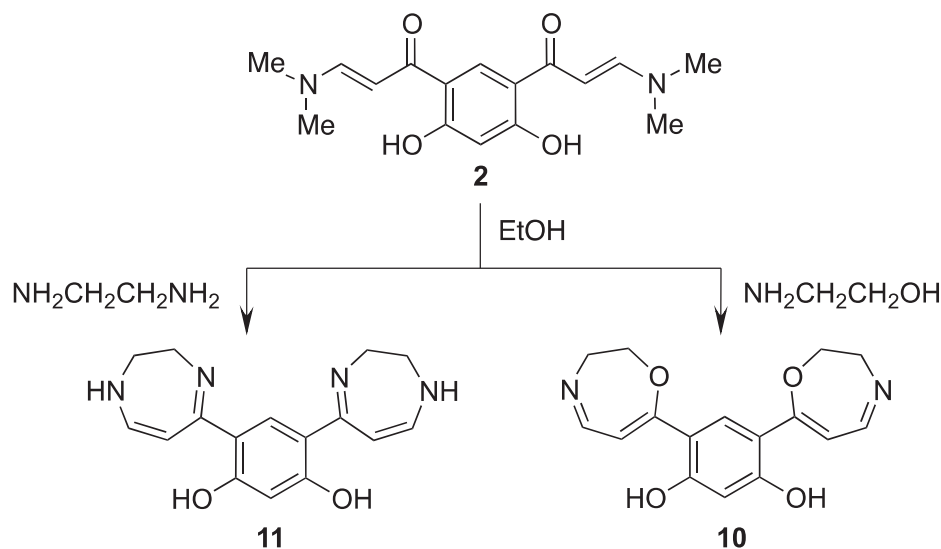
When compound **2** was treated with nitrogen-containing 1,3-binucleophiles such as guanidinium carbonate, thiourea and cyanoguanidine in refluxing ethanolic sodium ethoxide solution, the expected 1,3-*bis*(pyrimidinyl)resorcinol derivatives **7–9** were obtained, respectively (Scheme 4). The IR spectra of compounds **7–9** confirmed the absence of carbonyl groups and revealed the appearance of absorption bands in the region $3446\text{--}3193\text{ cm}^{-1}$ due to NH_2 and NH groups. In case of compound **9**, the nitrile groups were appeared at 2177 cm^{-1} . The structures of products **7–9** were confirmed by the $^1\text{H-NMR}$ spectra, which displayed new pairs of doublets at δ 7.38, 8.33 ($J = 5.4\text{ Hz}$), 7.72, 8.26 ($J = 7.5\text{ Hz}$), and 7.66, 8.22

($J = 6.6$ Hz), respectively, attributed to H-5 and H-6 protons of pyrimidine rings.^{24,25} The $^1\text{H-NMR}$ spectra also revealed two broad singlets corresponding to NH protons at δ 12.74 and 12.80 ppm for compounds **8** and **9**, respectively, in addition to the NH_2 protons at δ 7.20 ppm for compound **7**. Furthermore, the mass spectral data of compounds **7–9** support the suggested structures.



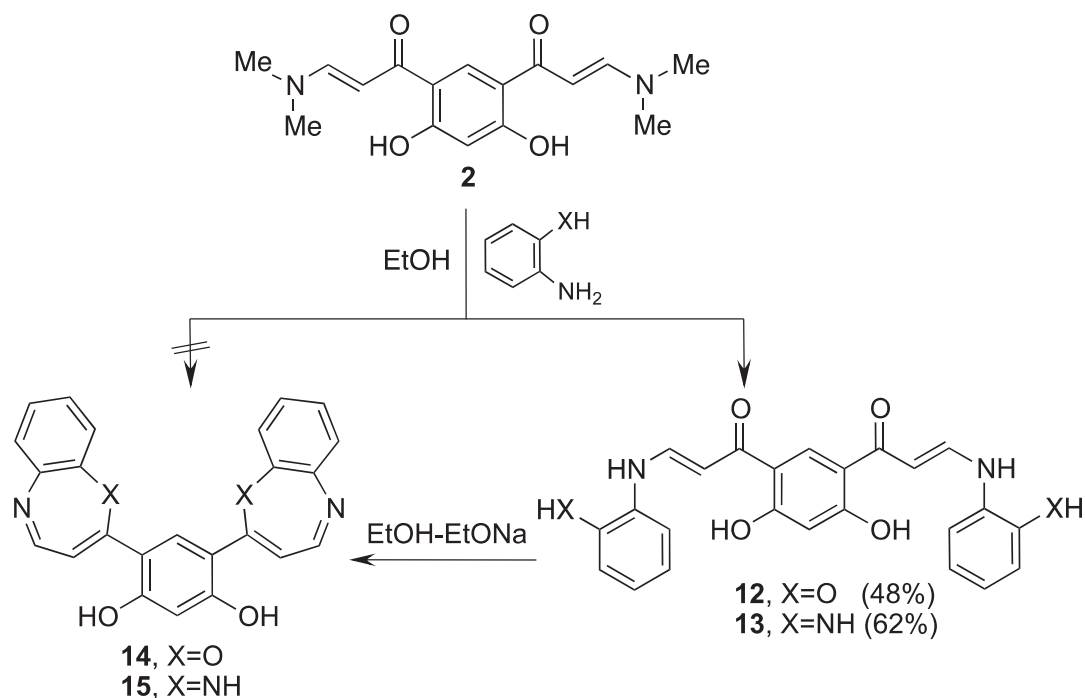
Scheme 4

The utility of the *bis*-enaminone **2** in the synthesis of seven-membered heterocycles was further explored *via* its reactions with different nitrogen-containing 1,4-binucleophiles. Thus, reaction of the *bis*-enaminone **2** with aliphatic 1,4-*bi*-nucleophiles such as ethanolamine and ethylenediamine in absolute ethanol furnished the corresponding 4,6-*bis*(2,3-dihydro-1,4-oxazepin-7-yl)resorcinol (**10**) and 4,6-*bis*(2,3-dihydro-1*H*-1,4-diazepin-5-yl)resorcinol (**11**), respectively, in good yields (Scheme 5). Spectral data (IR, $^1\text{H-NMR}$ and MS) and elemental analysis were consistent with the isolated products **10** and **11**. For example, the $^1\text{H-NMR}$ spectra of compounds **10** and **11** displayed a characteristic pair of doublets at δ 5.80, 8.32 ($J = 4.2$ Hz) and 5.90, 8.18 ($J = 9.6$ Hz), respectively, ppm assigned to the hydrogen at C-6, and C-5 (7) of the oxazepine and diazepine rings, respectively. Other important signals are displayed at δ 3.66 and 4.98 ppm for CH_2CH_2 groups in compound **10**, while that of compound **11** appeared at δ 3.85–4.01 ppm.



Scheme 5

Subsequently, we planned to examine the reactions of aromatic nitrogen-containing 1,4-binucleophiles, such as 2-aminophenol and 1,2-phenylenediamine with compound **2**. However, when the reactions were carried out in absolute ethanol, the products isolated in 48–62% yields were found to be the novel *bis*-enaminones **12** and **13**, respectively (Scheme 6).²⁶ The structures of *bis*-enaminones **12** and **13** were well established with help of the spectral and analytical data. Thus, the $^1\text{H-NMR}$ spectra of compounds **12** and **13** showed doublets at δ 5.99 ppm ($J = 12$ Hz) and δ 6.00 ppm ($J = 12$ Hz) for the vinylic protons at C- α whereas the vinylic protons at C- β , appeared at δ 7.94 ppm ($J = 12$ Hz) and δ 7.94 ppm ($J = 12$ Hz), respectively. Other aromatic protons resonated in their usual range. The NH protons in both compounds **12** and **13** appeared as broad signals δ 11.70 and 11.40 ppm, respectively. Moreover, the *bis*-enaminone **13** displayed the free NH_2 protons at δ 4.80 ppm as a broad signal, while the OH protons in the *bis*-enaminone **12** appeared at δ 10.25 ppm as a broad signal. The high coupling constants of vinylic protons confirmed *E*-configuration of the *bis*-enaminones **12** and **13**. The boiling of the *bis*-enaminones **12** and **13** in ethanolic sodium ethoxide led to the formation of the benzoxazepines of type **14** and **15**, respectively, in moderate yields (Scheme 6). The IR spectra of the benzoxazepine **14** and benzodiazepine **15** showed disappearances of the carbonyl groups which supported the cyclization process. The $^1\text{H-NMR}$ spectra of compounds **14** and **15** revealed two characteristic signals for the H-3 and H-4 protons of seven-membered rings at regions δ 7.22, 8.11 and 7.01, 7.92 ppm. Their phenolic OH protons were also displayed at regions δ 12.81 and 12.5 ppm, respectively, as D_2O -exchangeable signals. Furthermore, the molecular ion peaks of compounds **14** and **15** appeared at m/z 396 (M^+ , 5%) and m/z 394 (M^+ , 11%), respectively. The prepared compounds are still under evaluation for their antioxidant, anticancer and antitumor properties in *vitro* and in *vivo* methods and their results will be published in individual article.



Scheme 6

EXPERIMENTAL

The melting points were determined in an open capillary tube on a digital Stuart SMP-3 apparatus. Infrared spectra were measured on FTIR Nicolet IS10 spectrophotometer (cm^{-1}), using KBr disks. The $^1\text{H-NMR}$ spectra were measured on Mercury-300BB (300 MHz), using $\text{DMSO-}d_6$ as a solvent and the chemical shifts δ downfield from TMS as an internal standard. Mass spectra recorded on a Gas Chromatographic DI analysis Shimadzu instrument Q-2010 Plus at 70 eV. Elemental analyses were performed on Perkin-Elmer 2400II at the Chemical War department, Ministry of Defense, Cairo, Egypt. The purity of the synthesized compounds was checked by thin layer chromatography (TLC).

Synthesis of (2E,2'E)-4,6-bis[3-(dimethylamino)prop-2-en-1-oxo-1-yl]resorcinol (2).

A mixture of (1.94 g, 10 mmol) of 4,6-diacetylresorcinol (**1**) and (2.37 mL, 20 mmol) of dimethylformamide dimethyl acetal (DMF-DMA) in 50 mL of dry toluene, was heated under reflux for 6 h. After cooling, the formed precipitate was filtered off and crystallized from toluene to give the product **2** as orange crystals. Yield 80%; mp 198–200 °C. IR (KBr, cm^{-1}): 3423 (br, OH), 3058 (C-H_{arom}), 2915, 2808 ($\text{C-H}_{\text{aliph}}$), 1629 (C=O), 1532 (C=C). $^1\text{H-NMR}$ (δ ppm, $\text{DMSO-}d_6$): 3.07 (s, 6 H, 2 CH_3), 3.28 (s, 6 H, 2 CH_3), 5.42 (d, 2 H, $J = 12$ Hz, CH_α), 6.22 (s, 1 H, $\text{C}_2\text{-H}_{\text{resorcinol}}$), 7.94 (d, 2 H, $J = 12$ Hz, CH_β), 8.36 (s, 1 H, $\text{C}_5\text{-H}_{\text{resorcinol}}$), 15.60 (brs, 2 H, 2 OH exchangeable with D_2O). MS (m/z , I %): 304 (M^+ , 9%), 283 (31), 249 (30), 205 (83), 189 (42), 179 (52), 161 (28), 98 (49), 71 (100), 55 (45). Anal. Calcd for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_4$: C, 63.14; H, 6.62; N, 9.20. Found: C, 62.82; H, 6.34; N, 8.93.

General procedure for reaction of bis-enaminone 2 with nitrogen-containing 1,2-binucleophiles:

A mixture of (0.5 g, 1.65 mmol) of *bis*-enaminone **2** and (3.3 mmol) of each one from 1,2-binucleophiles, namely hydrazine hydrate, phenylhydrazine and hydroxylamine hydrochloride in absolute EtOH (15 mL, containing 0.5 g of sodium acetate in case of hydroxylamine hydrochloride), was heated under reflux for 6 h. After cooling, the formed precipitates were filtered off and crystallized from the proper solvents to give the product **3**, **4** and **6**, respectively.

4,6-Bis(1H-pyrazol-3-yl)resorcinol (3): Yellow crystals from EtOH; yield 73%; mp > 300 °C. IR (KBr, cm^{-1}): 3134 (br, OH, NH), 3049 (C–H_{arom}), 1636 (C=N), 1558 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.39 (s, 1 H, C₂–H_{resorcinol}), 6.88 (br, 2 H, C₄–H_{pyrazole}), 7.82 (br, 2 H, C₅–H_{pyrazole}), 7.97 (s, 1 H, C₅–H_{resorcinol}), 11.10 (br, 2 H, 2 NH exchangeable with D₂O), 14.01 (s, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 242 (M⁺, 39%), 213 (18), 186 (18), 147 (15), 117 (18), 95 (39), 71 (53), 57 (100), 55 (87). Anal. Calcd for C₁₂H₁₀N₄O₂: C, 59.50; H, 4.16; N, 23.13. Found: C, 59.23; H, 3.85; N, 22.86.

(2E,2'E)-4,6-Bis[3-(phenylhydrazinyl)prop-2-en-1-oxo-1-yl]resorcinol (4): Yellow crystals from DMF-EtOH; yield 69%; mp 266–268 °C. IR (KBr, cm^{-1}): 3289 (br, OH, NH), 3052 (C–H_{arom}), 1623 (C=O), 1600 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 5.95 (d, 2 H, *J* = 12 Hz, CH_α), 6.23 (s, 1 H, C₂–H_{resorcinol}), 6.82 (t, 2 H, *J* = 7.5 Hz, Ph–H), 7.02 (d, 4 H, *J* = 7.8 Hz, Ph–H), 7.28 (t, 4 H, *J* = 7.5 Hz, Ph–H), 7.87 (d, 2 H, *J* = 12 Hz, CH_β), 7.95 (s, 1 H, C₅–H_{resorcinol}), 9.39 (s, 2 H, 2 NH exchangeable with D₂O), 13.71 (s, 2 H, NH exchangeable with D₂O), 15.18 (s, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 430 (M⁺, 52%), 399 (62), 389 (48), 356 (52), 311 (63), 257 (72), 239 (78), 190 (54), 151 (50), 128 (95), 72 (78), 57 (100), 55 (74). Anal. Calcd for C₂₄H₂₂N₄O₄: C, 66.97; H, 5.15; N, 13.02. Found: C, 66.74; H, 4.86; N, 12.83.

4,6-Bis(isoxazol-5-yl)resorcinol (6): Yellow crystals from EtOH, yield 56%; mp 220–222 °C. IR (KBr, cm^{-1}): 3405 (br, OH), 1632 (C=N), 1574 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.51 (s, 1 H, C₂–H_{resorcinol}), 6.77 (d, 2 H, *J* = 5.7 Hz, C₄–H_{isoxazole}), 7.83 (s, 1 H, C₅–H_{resorcinol}), 8.59 (d, 2 H, *J* = 5.7 Hz, C₃–H_{isoxazole}), 12.07 (s, 1 H, OH exchangeable with D₂O), 12.52 (s, 1 H, OH exchangeable with D₂O). MS (*m/z*, I %): 244 (M⁺, 23%), 234 (100), 204 (32), 163 (20), 133 (13), 119 (15), 105 (15), 91 (17), 69 (25), 53 (16). Anal. Calcd for C₁₂H₈N₂O₄: C, 59.02; H, 3.30; N, 11.47. Found: C, 58.89; H, 3.05; N, 11.13.

4,6-Bis(1-phenylpyrazol-5-yl)resorcinol (5):

A solution of 0.5 g (1.16 mmol) of *bis*-enaminone **4** in ethanolic sodium ethoxide solution (0.2 g of Na in 20 mL of absolute EtOH) was heated under reflux for 15 h. The reaction mixture was cooled, poured into ice and acidified with diluted hydrochloric acid. The resulting precipitate was filtered off, washed with water several times and crystallized from EtOH to give the product **5** as yellow crystals. Yield 63%; mp 296–297 °C. IR (KBr, cm^{-1}): 3310 (br, OH, NH), 3045 (C–H_{arom}), 1605 (C=N), 1592 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.48 (s, 1 H, C₂–H_{resorcinol}), 7.01 (d, 2 H, C₄–H_{pyrazole}), 7.11–7.42 (m, 10 H, Ph–H), 7.95

(d, 2 H, C₃-H_{pyrazole}), 7.78 (s, 1 H, C₅-H_{resorcinol}), 13.00 (s, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 394 (M⁺, 8%). Anal. Calcd for C₂₄H₁₈N₄O₂: C, 73.08; H, 4.60; N, 14.20. Found: C, 72.73; H, 4.36; N, 13.95.

General procedure for reaction of bis-enaminone 2 with nitrogen-containing 1,3-binucleophiles:

A mixture of (0.5 g, 1.65 mmol) of bis-enaminone 2 and (3.3 mmol) of each one from 1,3-binucleophiles, namely guanidinium carbonate, thiourea and cyanoguanidine, in ethanolic sodium ethoxide solution (0.2 g of Na in 20 mL of absolute EtOH) was heated under reflux for 10 h. The reaction mixture was cooled, poured into ice and acidified with diluted hydrochloric acid. The resulting precipitates were filtered off, washed with water several times and crystallized from the proper solvents to give the products 7–9, respectively.

4,6-Bis(2-aminopyrimidin-4-yl)resorcinol (7): Green crystals from EtOH; yield 66%; mp 298–300 °C. IR (KBr, cm⁻¹): 3405 (OH), 3331, 3193 (NH₂), 1647 (C=N), 1574 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.34 (s, 1 H, C₂-H_{resorcinol}), 7.20 (s, 4 H, 2 NH₂ exchangeable with D₂O), 7.38 (d, 2 H, *J* = 5.4 Hz, C₅-H_{pyrimidine}), 8.33 (d, 2 H, *J* = 5.4 Hz, C₆-H_{pyrimidine}), 8.42 (s, 1 H, C₅-H_{resorcinol}), 12.80 (s, 1 H, OH exchangeable with D₂O), 15.12 (s, 1 H, OH exchangeable with D₂O). MS (*m/z*, I %): 296 (M⁺, 39%), 230 (95), 203 (29), 179 (39), 110 (9), 105 (35), 93 (12), 77 (31), 66 (12), 64 (100), 55 (50). Anal. Calcd for C₁₄H₁₂N₆O₂: C, 56.75; H, 4.08; N, 28.36. Found: C, 56.43; H, 3.88; N, 28.10.

4,6-Bis[2(1H)thioxopyrimidin-4-yl]resorcinol (8): Brick red crystals from EtOH; yield 57%; mp >300 °C. IR (KBr, cm⁻¹): 3420 (br, OH, NH), 1648 (C=N), 1600 (C=C), 1168 (C=S). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.37 (s, 1 H, C₂-H_{resorcinol}), 7.72 (d, 2 H, *J* = 7.5 Hz, C₅-H_{pyrimidine}), 8.26 (d, 2 H, *J* = 7.5 Hz, C₆-H_{pyrimidine}), 8.57 (s, 1 H, C₅-H_{resorcinol}), 12.74 (s, 2 H, 2 NH exchangeable with D₂O), 13.92 (s, 2 H, OH exchangeable with D₂O). MS (*m/z*, I %): 330 (M⁺, 16%), 278 (18), 216 (14), 194 (21), 161 (24), 111 (55), 85 (75), 71 (90), 57 (100). Anal. Calcd for C₁₄H₁₀N₄O₂S₂: C, 50.90; H, 3.05; N, 16.96; S, 19.41. Found: C, 50.63; H, 2.86; N, 16.68; S, 19.11.

4,6-Bis[(pyrimidin-2(1H)-ylidene-4-yl)cyanamido]resorcinol (9): Brown crystals from EtOH; yield 54%; mp >300 °C. IR (KBr, cm⁻¹): 3446 (br, OH, NH), 2177 (C≡N), 1629 (C=N), 1580 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.23 (s, 1 H, C₂-H_{resorcinol}), 7.66 (d, 2 H, *J* = 6.6 Hz, C₅-H_{pyrimidine}), 8.22 (d, 2 H, *J* = 6.6 Hz, C₆-H_{pyrimidine}), 8.37 (s, 1 H, C₅-H_{resorcinol}), 12.80 (s, 2 H, 2 NH exchangeable with D₂O), 16.04 (brs, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 346 (M⁺, 1%), 295 (1), 267 (2), 205 (100), 189 (35), 161 (16), 125 (16), 97 (40), 71 (99), 57 (71). Anal. Calcd for C₁₆H₁₀N₈O₂: C, 55.49; H, 2.91; N, 32.36. Found: C, 55.11; H, 2.65; N, 32.02.

General procedure for reaction of bis-enaminone 2 with nitrogen-containing 1,4-binucleophiles:

A mixture of (0.5 g, 1.65 mmol) of bis-enaminone 2 and (3.3 mmol) of each one from 1,4-binucleophiles, namely ethanolamine, ethylenediamine, 2-aminophenol and 1,2-phenylenediamine in absolute EtOH (25

mL), was heated under reflux for 10 h. After cooling, the resulting precipitates were filtered off and crystallized from the proper solvents to give the products **10–13**, respectively.

4,6-Bis(2,3-dihydro-1,4-oxazepin-7-yl)resorcinol (10): Pale green crystals from EtOH; yield 77%; mp 208–210 °C. IR (KBr, cm^{-1}): 3315 (br, OH), 3050 (C–H_{arom}), 2924 (C–H_{aliph}), 1607 (C=N), 1537 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 3.66 (s, 4 H, 2 CH₂N), 4.98 (brs, 4 H, 2 CH₂O), 5.80 (d, 2 H, *J* = 4.2 Hz, C₆–H_{oxazepine}), 6.21 (s, 1 H, C₂–H_{resorcinol}), 8.00 (s, 1 H, C₅–H_{resorcinol}), 8.32 (d, 2 H, *J* = 4.2 Hz, C₅–H_{oxazepine}), 17.20 (brs, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 300 (M⁺, 60%), 285 (82), 274 (63), 256 (84), 227 (100), 185 (66), 150 (85), 118 (78), 99 (90), 88 (94), 68 (77), 54 (16). Anal. Calcd for C₁₆H₁₆N₂O₄: C, 63.99; H, 5.37; N, 9.33. Found: C, 63.69; H, 4.12; N, 9.09.

4,6-Bis(2,3-dihydro-1H-1,4-diazepin-5-yl)resorcinol (11): Yellow crystals from DMF-EtOH; yield 79%; mp >300 °C. IR (KBr, cm^{-1}): 3384 (br, OH, NH), 3055 (C–H_{arom}), 2950 (C–H_{aliph}), 1609 (C=N), 1533 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 3.85–4.01 (br, 8 H, 2 CH₂CH₂), 5.90 (d, 2 H, *J* = 9.6 Hz, C₆–H_{diazepine}), 6.20 (s, 1 H, C₂–H_{resorcinol}), 7.34 (s, 1 H, C₅–H_{resorcinol}), 8.18 (d, 2 H, *J* = 9.6 Hz, C₇–H_{diazepine}), 9.60 (brs, 2 H, NH exchangeable with D₂O), 17.00 (br, 2 H, OH exchangeable with D₂O). MS (*m/z*, I %): 298 (M⁺, 63%), 285 (66), 265 (75), 220 (69), 197 (69), 182 (68), 133 (75), 121 (74), 97 (100), 60 (47). Anal. Calcd for C₁₆H₁₈N₄O₂: C, 64.41; H, 6.08; N, 18.78. Found: C, 64.12; H, 5.87; N, 18.62.

(2E,2'E)-4,6-Bis{3-[N²-(2-amino-1-hydroxyphenyl)]prop-2-en-1-oxo-1-yl}resorcinol (12): Yellow crystals from EtOH; yield 48%; mp >300 °C. IR (KBr, cm^{-1}): 3000 (br, OH, NH), 1625 (C=O), 1600 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 5.99 (d, 2 H, *J* = 12 Hz, CH_α), 6.22 (s, 1 H, C₂–H_{resorcinol}), 6.28–6.34 (m, 2 H, Ar–H), 6.89–6.96 (m, 4 H, Ar–H), 7.94 (d, 2 H, *J* = 12 Hz, CH_β), 8.36 (s, 1 H, C₅–H_{resorcinol}), 8.41 (d, 2 H, Ar–H), 10.25 (br, 2 H, 2 OH exchangeable with D₂O), 11.70 (d, 2 H, 2 NH exchangeable with D₂O), 15.80 (br, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 432 (M⁺, 86%), 397 (74), 372 (65), 312 (74), 263 (61), 207 (82), 165 (54), 125 (72), 80 (93), 52 (100). Anal. Calcd for C₂₄H₂₀N₂O₆: C, 66.66; H, 4.66; N, 6.48. Found: C, 66.42; H, 4.48; N, 6.15.

(2E,2'E)-4,6-Bis{3-[N¹-(1,2-diaminophenyl)]prop-2-en-1-oxo-1-yl}resorcinol (13): Brown crystals from EtOH; yield 62%; mp >300 °C. IR (KBr, cm^{-1}): 3361 (br, OH, NH₂, NH), 1624 (C=O), 1600 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 4.90 (br, 4 H, 2 NH₂ exchangeable with D₂O), 6.00 (d, 2 H, *J* = 12 Hz, CH_α), 6.25 (s, 1 H, C₂–H_{resorcinol}), 6.35–6.95 (m, 6 H, Ar–H), 7.94 (d, 2 H, *J* = 12 Hz, CH_β), 8.19 (s, 1 H, C₅–H_{resorcinol}), 8.40 (d, 2 H, Ar–H), 11.40 (br, 2 H, 2 NH exchangeable with D₂O), 14.10 (brs, 2 H, 2 OH exchangeable with D₂O). MS (*m/z*, I %): 430 (M⁺, 20%), 414 (14), 381 (25), 312 (23), 262 (25), 217 (19), 169 (18), 132 (16), 118 (27), 86 (23), 60 (23), 54 (100). Anal. Calcd for C₂₄H₂₂N₄O₄: C, 66.97; H, 5.15; N, 13.02. Found: C, 66.64; H, 4.89; N, 12.89.

General procedure for heterocyclization of bis-enaminone 12 and 13:

A solution of (1.15 mmol) of each *bis*-enaminone **12** and **13** in ethanolic sodium ethoxide solution (0.2 g of Na in 20 mL of absolute EtOH) was heated under reflux for 15 h. The reaction mixture was cooled, poured into ice and acidified with diluted hydrochloric acid. The resulting precipitates were filtered off, washed with water several times and crystallized from EtOH to give the product **14** and **15**, respectively.

4,6-Bis(1,5-benzoxazepin-2-yl)resorcinol (14): Yellow crystals; yield 58%; mp >300 °C. IR (KBr, cm⁻¹): 3321 (br, OH), 3021 (C–H_{arom}), 1595 (C=N), 1586 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.20 (s, 1 H, C₂-H_{resorcinol}), 6.41–7.00 (m, 6 H, Ar–H), 7.22 (d, 2 H, *J* = 6.0 Hz, C₃-H_{oxazepine}), 8.11 (d, 2 H, *J* = 5.8 Hz, C₄-H_{oxazepine}), 8.28 (s, 1 H, C₅-H_{resorcinol}), 8.47–8.51 (m, 2 H, Ar–H), 12.81 (br, 2 H, OH exchangeable with D₂O). MS (*m/z*, I %): 396 (M⁺, 5%). Anal. Calcd for C₂₄H₁₆N₂O₄: C, 72.72; H, 4.07; N, 7.07. Found: C, 72.49; H, 3.92; N, 6.85.

4,6-Bis(1H-1,5-benzodiazepin-2-yl)resorcinol (15): Pale brown crystals; yield 67%; mp >300 °C. IR (KBr, cm⁻¹): 3390–3186 (br, NH, OH), 3021 (C–H_{arom}), 1601 (C=N), 1589 (C=C). ¹H-NMR (δ ppm, DMSO-*d*₆): 6.23 (s, 1 H, C₂-H_{resorcinol}), 6.30–6.96 (m, 6 H, Ar–H), 7.01 (d, 2 H, *J* = 6 Hz, C₃-H_{diazepine}), 7.92 (d, 2 H, *J* = 5.8 Hz, C₄-H_{diazepine}), 8.17 (s, 1 H, C₅-H_{resorcinol}), 8.32–8.35 (m, 2 H, Ar–H), 10.50 (br, 2 H, NH exchangeable with D₂O), 12.50 (br, 2 H, OH exchangeable with D₂O). MS (*m/z*, I %): 394 (M⁺, 11%). Anal. Calcd for C₂₄H₁₈N₄O₂: C, 73.08; H, 4.60; N, 14.20. Found: C, 72.82; H, 4.32; N, 13.87.

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