



## Electrochemical oxidation of substituted catechols in the presence of pyrazol-5-ones: characterization of products and reaction mechanism

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### ABSTRACT

The electrochemical oxidation of substituted catechol derivatives has been investigated in the presence of pyrazol-5-ones as C–H acid nucleophiles by using constant current technique in acetate buffer solution. The results indicate that different reaction mechanisms are involved and not only 1,4-Michael adducts but also 1,6-Michael adducts are formed, depending on the nature of the starting catechols and the nucleophiles, as well as the reaction conditions.

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## 1. Introduction

Catechols and their quinone derivatives have drawn considerable attention due to their abundance in nature and important roles in many biological systems. Moreover, most of compounds incorporating catechol moiety exhibit antioxidant,<sup>1</sup> anticarcinogenic,<sup>2,3</sup> antifungous,<sup>4</sup> and antibacterial activities<sup>5,6</sup> or are used as HIV integrase inhibitors.<sup>7–9</sup> For example, dopamine is a neurotransmitter in the central nervous system of human and other vertebrate animals,<sup>10</sup> whereas, dicaffeoyltartaric acid<sup>7</sup> and dicaffeoylquinic acid<sup>7,8</sup> exhibit HIV integrase inhibitory activity.

On the other hand, electroorganic synthesis<sup>11</sup> is regarded as an environmental friendly strategy for chemical transformation, wherein electrons are used as oxidants and thus the utilization of toxic metal-based reagents is avoid. Also, such transformation is generally performed under mild conditions. Indeed, catechols and their quinone derivatives can be achieved by the electrochemical synthesis of *o*-benzoquinones and their in situ transformation<sup>12–23</sup> since the electro-generated *o*-benzoquinones are active intermediates and readily undergo Michael addition reaction,<sup>12–15,18–23</sup> with nucleophiles or [4+2] cycloaddition with dienes<sup>16,17</sup> to form various

products. In this respect, electrochemical oxidation of catechols in the presence of nucleophiles (such as amines,<sup>13</sup> thiols<sup>14</sup> or sulfuric acids<sup>15</sup>) leads to the formation of substituted catechols or substituted *o*-benzoquinones.

C–H acids are common nucleophiles and therefore also are employed in the nucleophilic attack to the electro-generated *o*-benzoquinones.<sup>18–23</sup> However, most of the C–H acids employed are confined to acyclic and cyclic 1,3-dicarbonyl derivatives, such as barbituric acids,<sup>18</sup> acetylacetone,<sup>19</sup> cyclohexanediones,<sup>20</sup> acetoacetates,<sup>21</sup> 4-hydroxycoumarins<sup>12,22</sup> and Meldrum's acid,<sup>23</sup> and mainly lead to the formation of benzofurans and coumestans. Moreover, it is observed that only 1,4-Michael addition products are isolated in these electrochemical transformations.

As a continuous work toward the development of potential HIV-1 integrase inhibitors derived from polyhydroxylated aromatics, we have investigated the electrochemical synthesis of polyhydroxylated aromatics.<sup>24–29</sup> In the present work, we report the electrochemical oxidation of catechols **1** in the presence of pyrazol-5-ones **2** as C–H acids by constant current technique (Fig. 1). The outcomes indicate that different reaction mechanisms (not only 1,4-Michael addition, but also 1,6-addition) are involved, which demonstrates that a wide spectrum of products may be produced by simply tuning the natures of the starting catechols and nucleophiles, and reaction conditions.

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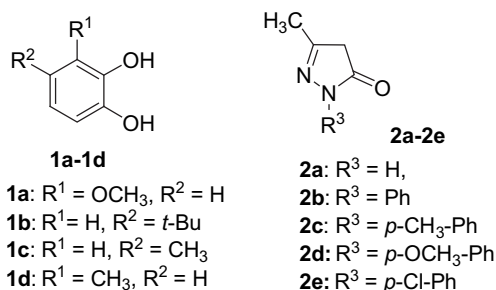


Fig. 1. Structures of starting substituted catechols **1** and pyrazol-5-ones **2**.

## 2. Results and discussion

### 2.1. Cyclic voltammetric studies

The electrochemical behavior of catechols **1** in the absence and presence of pyrazol-5-ones was examined at room temperature in water containing 0.2 M acetate buffer (pH 7.0) as the supporting electrolyte by cyclic voltammetry (CV).

Taking 4-methylcatechol (**1c**) as an example, as shown in Fig. 2, upon scanning anodically, 4-methylcatechol exhibits a well defined quasi-reversible oxidation wave (peak A) at +0.51 V versus Ag/AgCl (KCl 3 M) and its corresponding cathodic peak (C) at +0.30 V. Peak A is attributed to the oxidation of 4-methylcatechol to the corresponding 4-methyl *o*-benzoquinone and peak C to the reduction of the quinone. The ratio of the current amplitudes between the oxidation and reduction processes is equal to unity ( $I_p^{\text{ox}}/I_p^{\text{red}}$ ), indicating that the *o*-benzoquinone produced at the surface of the electrode is stable under pH 7 acetate buffer and that side-reactions, such as hydroxylation or dimerization reactions are too slow to be observed on the time scale of the cyclic voltammetry.<sup>13–23</sup>

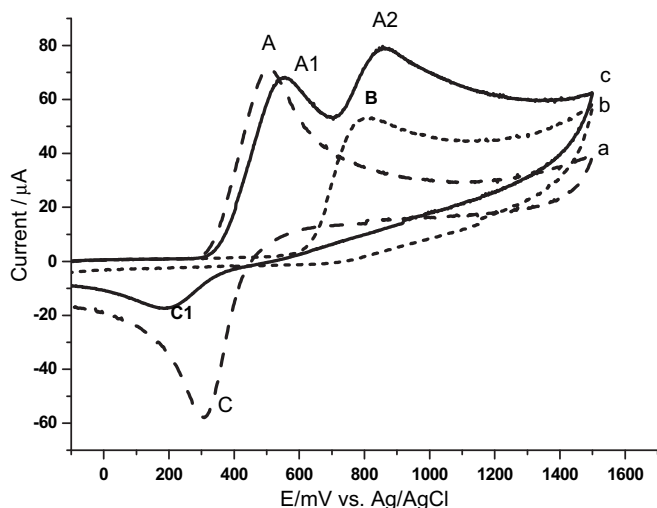


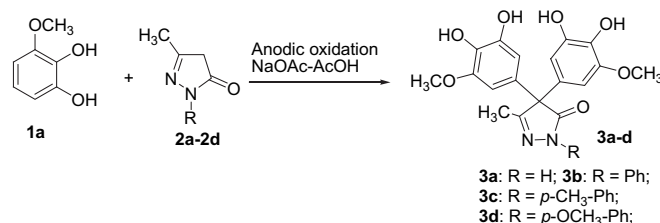
Fig. 2. Cyclic voltammograms of (a) 2 mM of 4-methylcatechol (**1c**), (b) 2 mM of 3-methyl-1H-pyrazol-5-one (**2a**), and (c) a mixture of 2 mM of **2a** and 2 mM of **1c**, at a glassy carbon working electrode, platinum wire counter, and Ag/AgCl reference electrodes, in acetate buffer (0.2 M, pH 7) solution; scan rate: 100 mV/s.

When 1 equiv amount of 3-methyl-1H-pyrazol-5-one **2a** was added, the voltammogram of the mixture exhibits two anodic peaks A<sub>1</sub> (+0.55 V vs Ag/AgCl) and A<sub>2</sub> (+0.86 V vs Ag/AgCl), whereas the cathodic peak shift to 0.19 V versus Ag/AgCl and its cathodic current decreases dramatically (curve c, Fig. 2). Curve b in Fig. 2 is the CV of 3-methyl-1H-pyrazol-5-one **2a**, where one irreversible anodic wave at 0.80 V is observed. The observation that the cathodic current of the corresponding *o*-benzoquinone decrease

indicates that the electro-generated *o*-benzoquinone intermediate undergoes follow-up chemical reactions under these conditions.

### 2.2. Electrochemical oxidation of substituted catechols in the presence of 3-methylpyrazol-5-ones

After examining the electrochemical properties of substituted catechols in the absence and presence of pyrazol-5-one, preparative scale of electrolyzes were carried out. At the outset, 3-methoxy catechol **1a** was subjected to anodic oxidation in the presence of 3-methylpyrazol-5-ones. Thus, in a pilot experiment, a solution of an equimolar quantity of **1a** and **2a** was electrolyzed at constant current of 12 mA (~4 mA/cm<sup>2</sup>) at pH 7.0 acetate buffer. The reaction mixture afforded C,C-dicatechol pyrazol-5-one derivative **3a** in 42% yield (Scheme 1).



Scheme 1. Anodic oxidation of 3-substituted catechol **1a** in the presence of 3-methylpyrazol-5-ones **2a–d**.

Subsequently, phenyl-substituted 3-methylpyrazol-5-ones **2b–d** were employed as C–H acid nucleophiles to react with the electro-generated 3-methoxy *o*-benzoquinone (Scheme 1). Here, due to the low solubility of phenyl-substituted 3-methylpyrazol-5-ones, acetonitrile was added as a co-solvent. Accordingly, a mixed solvent of acetate buffer solution and acetonitrile (3:1 ratio of acetate buffer to acetonitrile, pH 7) was used as supporting electrolyte. It was found that analogous reaction pattern occurred with respect to these 3-methyl-pyrazol-5-ones. As shown in Scheme 1, when the nucleophiles were **2b–d**, corresponding **3b**, **3c**, and **3d** were isolated in 23%, 20%, and 29%, respectively. Interestingly, an unexpected compound **4** was also isolated in 11% yield (Fig. 3), along with **3b**, from the anodic oxidation of the mixture of **1a** and **2b**. It is noteworthy that, structurally, compounds **3** and **4** are 1,4-Michael addition products. For example, compounds **3** may stem from the 1,4-Michael addition of pyrazol-5-ones to two molecules of the electro-generated 3-methoxy *o*-benzoquinone.

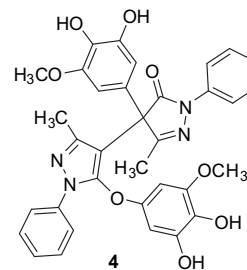
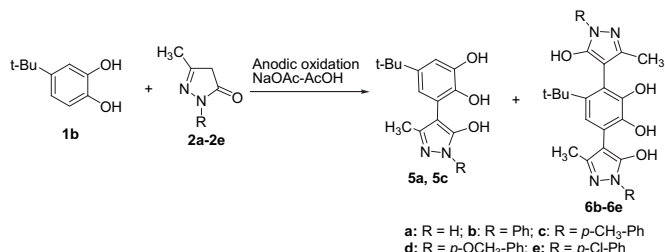


Fig. 3. Structure of compound **4**.

To investigate the limitation and scope of the anodic oxidation of substituted catechols in the presence of pyrazol-5-ones, next, 4-*tert*-butylcatechol (**1b**) was subjected to constant current electrolysis in the presence of 3-methylpyrazol-5-ones **2a–e** (Scheme 2). However, the benzoquinone generated from this catechol behaved in a way quite different from *o*-benzoquinone generated from 3-methoxy catechol: 1,6-addition occurred on the former instead of 1,4-addition on the later. It is noticed that the formation of the type of 1,6-addition has not been obtained in the oxidations of catechols

previously reported. For example, in the case of **2a**, mono adduct **5a** precipitated and was exclusively obtained in 34% yield. In a similar manner, **5c** was exclusively obtained in 44% yield from the anodic oxidation of **1b** and **2c** in 3:1 volume ratio of acetate buffer to acetonitrile as supporting electrolyte.



**Scheme 2.** Anodic oxidation of 4-*tert*-butylcatechol (**1b**) in the presence of 3-methylpyrazol-5-one **2a–e**.

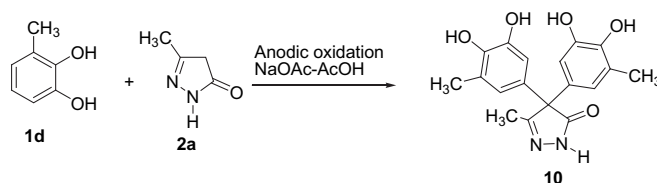
Interestingly, it was observed that the reaction condition affected the product composition. When the solvent-supporting electrolyte was a 2:1 volume ratio of acetate buffer to acetonitrile, anodic oxidation of **1b** in the presence of **2c** afforded exclusively compound **6c** in 17% yield, instead of **5c**. The plausible reason is that the initially formed **5c** can dissolve in this supporting electrolyte to an extent and thus underwent further oxidation followed by a second 1,6-Michael addition to generate bis(5-hydroxypyrazol-4-yl)catechols **6c**.

Similar to the anodic oxidation of the mixture of **1b** and **2c**, the anodic oxidation of **1b** in the presence of **2b**, **2d** or **2e**, in 2:1 volume ratio of acetate buffer to acetonitrile, gave **6b**, **6d** or **6e** in 29%, 25% or 21% yield, respectively, which was obtained by simple filtration of the reaction mixture.

Finally, we investigated the anodic oxidation of methyl-substituted catechols (**1c** and **1d**) in the presence of 3-methylpyrazol-5-ones. Again, different reaction pattern took place, where, not only 1,4-addition product, but also 1,6-addition product was detected. For instance, equimolar amount of **1c** and **2a** were electrolyzed at constant current to afford a mixture of compounds **7** and **8**, out of which only **7** was isolated in 20% yield after column chromatography (Scheme 3). It was observed that the pH of the solution obviously affected the composition of products. When the reaction was carried out in acidic condition (such as pH 4.0 buffer solution), compound **7** was selectively formed and isolated in 30% yield. However, compound **8** was isolated as the major product in 56% yield when the reaction was performed in basic condition (such as pH 9 buffer solution). The spectroscopic data of compound **7** demonstrated that it is stemmed from a 1,6-addition, whereas, compound **8** resulting from the 1,4-addition of 3-methyl-1*H*-pyrazol-5-one to two molecules of electro-generated 4-methyl *o*-benzoquinone.

Subsequently, phenyl-substituted 3-methylpyrazol-5-ones **2b** were employed to react with the electro-generated 4-methyl *o*-benzoquinone (Scheme 3). After the consumption of starting 4-methylcatechol, compound **9b** precipitated and was obtained in 37% yield after recrystallization from methanol. In a similar manner, compounds **9c**, **9d**, and **9e** were obtained in 55%, 32%, and 62% yield, respectively. The <sup>1</sup>H NMR spectra of these compounds indicate that **9** are 1,4-Michael addition products and exist as a mixture of pyrazol **9b–e** and their corresponding isomers 1,2-dihydropyrazol-3-one **9b'–e'**.<sup>31</sup>

In addition, in the case of 3-methylcatechol (**1d**), C,C-diccatechol pyrazol-5-one **10** was isolated in 38% yield, which is from the 1,4-addition of 3-methyl-1*H*-pyrazol-5-one to two molecules of electro-generated 3-methyl *o*-benzoquinone (Scheme 4).

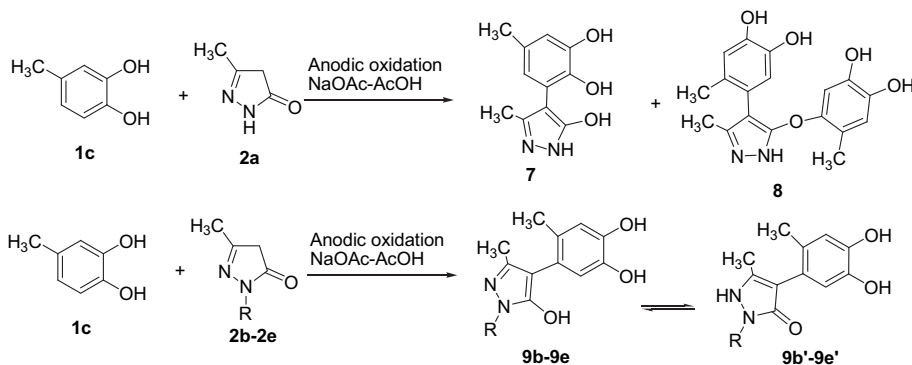


**Scheme 4.** Anodic oxidation of 3-methylcatechol (**1d**) in the presence of 3-methylpyrazol-5-one **2a**.

### 2.3. Spectroscopic characterization

All the synthesized products **3–10** were characterized by ESI-MS, <sup>1</sup>H NMR, and <sup>13</sup>C NMR. Firstly, the ESI-MS data of compounds **3** show that it is a double adduct of 3-methyl-1*H*-pyrazol-5-one with two 3-methoxy *o*-benzoquinone molecules. The <sup>1</sup>H NMR spectra of compounds **3** and **10** show that the two-catechol moieties are in the same chemical environment. Therefore, it is elucidated that both catechol moieties are bound to C(4) of 3-methyl-1*H*-pyrazol-5-one scaffold and compounds **3** and **10** are C,C-diccatechol pyrazol-5-ones. The assignment of the structure of compounds **3** and **10** is further demonstrated by <sup>13</sup>C NMR spectrum where a quaternary sp<sup>3</sup> carbon atom at about 65 Hz is observed for each C,C-diccatechol pyrazol-5-one derivative **3** and **10**. In addition, the split pattern of the two aromatic protons (doublet, *J*=2.0 Hz) of each catechol moiety indicates that 1,4-addition reaction occurred and C(4) atom of 3-methyl-1*H*-pyrazol-5-one moiety is bound to each C(5) atom (*para*-position to one of the two OH groups) of the catechol subunits.

The structure of compounds **3** and **10** are quite different from compound **8**. Although the ESI-MS data of compound **8** also show that it is a double adduct of 3-methyl-1*H*-pyrazol-5-one with two 4-methyl *o*-benzoquinone molecules, its <sup>1</sup>H NMR spectrum shows 4 singlets in the aromatic region (6.52, 6.61, 6.62, and 6.67 ppm),



**Scheme 3.** Anodic oxidation of 4-methylcatechol (**1c**) in the presence of 3-methylpyrazol-5-one **2a–e**.

along with 4 singlets at 8.58, 8.67, 9.03, and 9.12 ppm, attributed to the OH groups. These results indicate that the two-catechol moieties are in a quite different chemical environment. Therefore, it is elucidated that the two catechol moieties are bound, respectively, to C(4) and O atom of 3-methyl-1H-pyrazol-5-one scaffold. In addition, the split pattern of the two aromatic protons (singlet) of each catechol moiety indicates that it is a 1,4-addition product.

Regarding the structures of compound **4**, it was characterized firstly by ESI-MS as an adduct of two 3-methyl-1-phenyl-1H-pyrazol-5-one molecules with two 3-methoxy *o*-benzoquinone molecules (*m/e*: 620.9,  $M^- - 1$ ). The  $^1\text{H}$  NMR spectrum of **4** further shows that the two-catechol moieties are in different chemical environment. Therefore, it is elucidated that the two catechol moieties are bound, respectively, to C(4) and O atom of the two 3-methyl-1-phenyl-1H-pyrazol-5-one molecules, which are coupled through C(4)–C(4) bond.

## 2.4. Reaction mechanism

As to the mechanism, it is well documented<sup>12–23,32–36</sup> that the anodic oxidation of catechol and its derivatives in aqueous medium leads to the formation of the corresponding *o*-benzoquinone intermediates. In the presence of a nucleophile (or solvent), these intermediates are converted to other intermediates or products, following a pattern of an EC or an ECEC mechanism. Therefore, plausible mechanisms for the reaction between catechols and pyrazol-5-one derivatives under electrochemical oxidation conditions are proposed in Figs. 4 and 5 on the basis of the CV analysis and structures of products.

As shown in Fig. 4, when the starting catechol is 3-methoxy catechol **1a**, its anodic oxidation leads to the corresponding 3-methoxy *o*-benzoquinone **1a'**, in which, the electronic factor, lone electronic pair delocalized onto the benzene ring, is quite important and it deactivates the 1,6-addition. In addition, the methoxy group is less bulky than a methyl or a *tert*-butyl group. Consequently, nucleophiles **2** selectively attack the more electropositive C(5) position of the *o*-benzoquinone ring to form corresponding 1,4-addition mono adducts (Fig. 4), no product of 1,6-addition was obtained with 3-methoxy catechol (**1a**).

Once the 1,4-addition mono adducts were produced in the solvent, then two different pathways may involve, in parallel or in competitive, depending on the nature of the nucleophiles and the reaction conditions. One pathway is that the initially formed 1,4-addition mono adducts tautomerize to the corresponding ketone-type isomers and subsequently its methyne C atom functions as nucleophilic site to attack a second intermediate **1a'** in the 1,4-Michael addition manner, followed by an aromatization process, to form C,C-diccatechol pyrazol-5-ones **3a–d** (pathway I, Fig. 4). To the best of our knowledge, this type of reaction is known. For example, in the presence of barbituric acids, the electrooxidation of 4-*tert*-butylcatechol leads to the formation of spiropyrimidine derivatives.<sup>18</sup>

The formation of compound **4** is unique because it is a 'tetramer' comprised of two catechols subunits and two pyrazol subunits. Its formation may follow a second pathway, that is, in parallel to or in competitive with the pathway I, the 1,4-addition mono adduct was oxidized to mono adduct quinone derivative, which undergoes isomerization to the mono adduct quinone methide and was attacked by a second **2b** molecule. The formed 'trimer' intermediate further reacts with a second active **1a'** (1,4-addition) to finally form compound **4** (pathway II, Fig. 4). The hypothesis for the formation of compound **4** is reasonable, because previously it was reported that *para*-alkyl *o*-benzoquinones can isomerize to the corresponding *p*-benzoquinone methides at rates, which depend on the type of the substituent at the *para*-position. In addition, the *p*-benzoquinone methides are much more electrophilic than the

*o*-benzoquinone tautomers and thus nucleophilic addition takes place readily.<sup>37,38</sup>

In the cases of 4-methylcatechol (**1c**) and 3-methylcatechol (**1d**), the methyl group could also deactivate the 1,6-addition by electronic effects, but such electronic effect (hyperconjugation) is rather weak. Also, the methyl group is less bulky than a *tert*-butyl group. Therefore, both products of 1,4-addition (see compounds **8**, **9b–e** in Scheme 3 and compound **10** in Scheme 4) and 1,6-addition (see 7, Scheme 3 and Fig. 4) have been obtained and the former are the main products. As shown in Fig. 4, the anodic oxidation of 4-methylcatechol (**1c**) leads to the corresponding 4-methyl *o*-benzoquinone **1c'**. When **2a** is used as nucleophile, 1,6-addition mono adduct **7** and 1,4-addition mono adduct intermediate are formed. The latter further undergoes 1,4-Michael addition with a second *o*-benzoquinone **1c'** to afford compound **8** (C,O-double adduct) through the hydroxyl group in the pyrazol subunit. Interestingly, when phenyl-substituted pyrazoles **2b–e** were treated with **1c'**, only 1,4-addition mono adducts **9b–e** are produced.

Similarly, anodic oxidation of 3-methylcatechol (**1d**) generates the corresponding 3-methyl *o*-benzoquinone (**1d'**), which is attacked by nucleophile **2a** to form 1,4-addition mono adduct. Upon ketone-type isomerization and one more 1,4-Michael addition to a second intermediate **1d'**, C,C-diccatechol pyrazol-5-ones **10** was finally formed.

Different from that with **1a**, **1c**, and **1d**, in the case of 4-*tert*-butylcatechol **1b**, catechol derivatives resulting from a 1,6-addition of the nucleophile to the electro-generated *o*-benzoquinone are the main products. This is not surprising because the carbon *meta* to the *tert*-butyl group (1,6-addition) is much less hindered than the carbon at the *ortho*-position (1,4-addition). Once the *meta*-position is blocked (see **5'** in Fig. 5), then the nucleophile does add at the *ortho*-position, necessarily in a 1,6-fashion (there is no other possibility), to give catechols **6b–e** (Scheme 2).

Accordingly, the bulky *tert*-butyl group at C(4) position of the *o*-benzoquinone caused the preferential 1,6-addition (rather than 1,4-addition behaving as **1a**) of pyrazol-5-one moiety, followed by aromatization to form mono adduct **5**. Compounds **5** are by themselves catechols and then can be in situ oxidized to the corresponding quinones **5'**, followed by a second 1,6-Michael addition of **2** to form final compounds **6**. Such result is consistent with previous report in which high regioselective 1,6-addition product was obtained from reaction of 4-*tert*-butyl *o*-benzoquinone and silyl enol ethers.<sup>39</sup>

In addition, this regioselective 1,6-addition hypothesis can be demonstrated by the reaction of **1b** and **2c**. As mentioned above, when the electrochemical reaction was performed in 3: 1 volume ratio of acetate buffer to acetonitrile as supporting electrolyte, the reaction stopped at the mono-adduct step and **5c** precipitated from the solution due to its low solubility. However, if the volume of acetonitrile increased to 2:1 volume ratio of acetate buffer to acetonitrile, the initially-generated **5c** could dissolve and was further oxidized, followed by a 1,6-addition, to generate **6c** exclusively.

## 3. Conclusion

In summary, the electrochemical oxidation of substituted catechols in the presence of pyrazol-5-ones has been carried out by constant current technique in acetate buffer solution. The results indicate that the reaction is not selective. Depending on the nature of the nucleophiles, structures of the starting catechols and reaction conditions, different reaction pathways are involved and thus lead to a wide spectrum of products. The anodic oxidation of 3-methoxy catechol **1a** mainly led to the formation of 1,4-addition mono adducts, which underwent different pathway to form C,C-diccatechol pyrazol-5-ones **3a–d** and unexpected 'tetramer' **4**. In the case of 4-*tert*-butylcatechol **1b**, steric factor plays predominant role

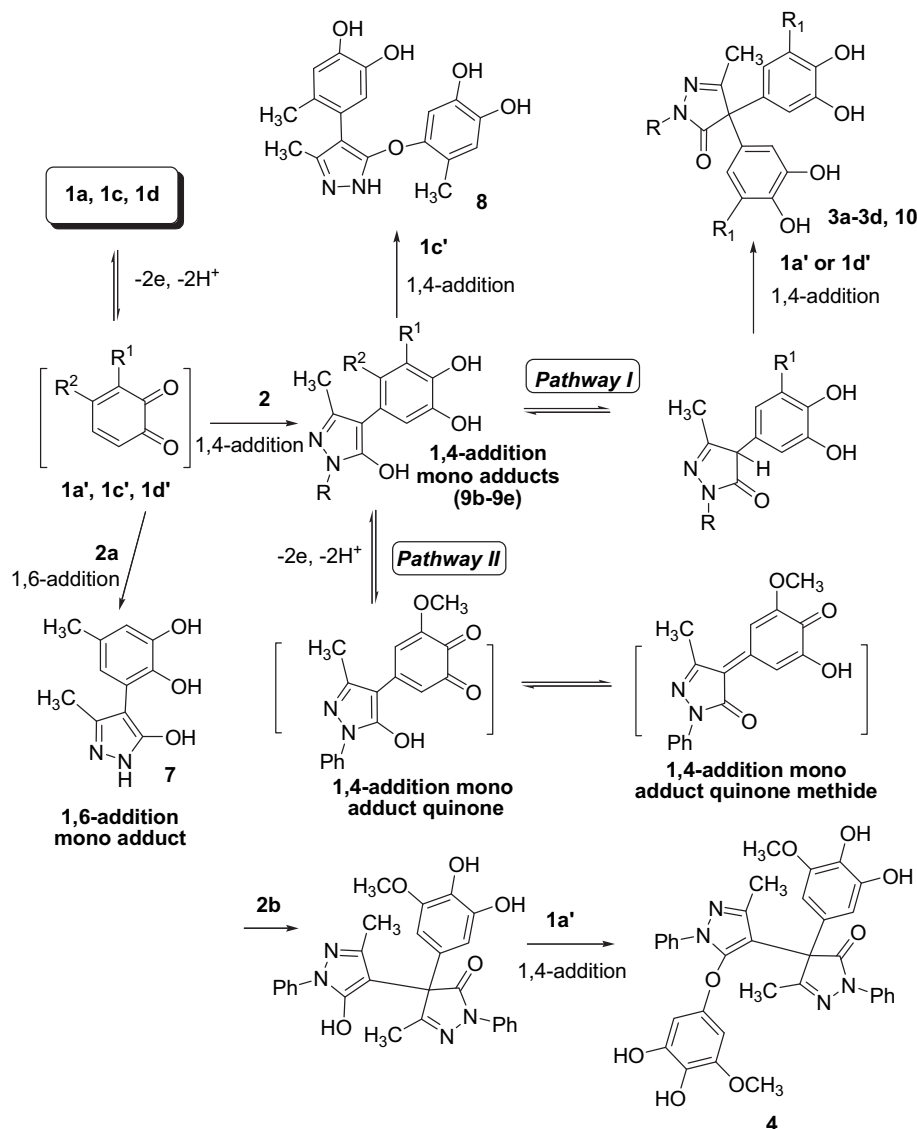


Fig. 4. Plausible electrochemical reaction mechanism of substituted catechols **1a**, **1c**, and **1d** in the presence of pyrazol-5-one derivatives **2**.

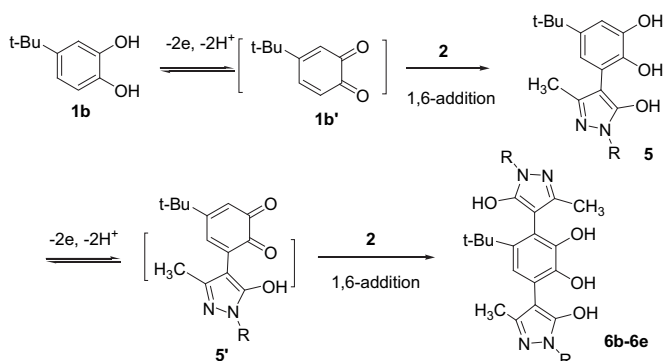


Fig. 5. Plausible electrochemical reaction mechanism of substituted catechol **1b** in the presence of pyrazol-5-one derivatives **2**.

and 1,6-addition is preferential, hence 1,6-addition mono adducts **5** or bis-(5-hydroxypyrazolyl)-substituted catechols **6** were produced. Finally, both 1,6-addition product **7** and 1,4-addition products **8** (C,O-double adduct), **9** and **10** (C,C-double C-double adduct) were obtained from anodic oxidation of methyl-substituted catechol in the presence of pyrazol-5-one.

## 4. Experimental section

### 4.1. Instruments and reagents

Cyclic voltammograms were measured by a 273 A Potentiostat/Galvanostat equipped with an electrochemical analysis software, using a conventional three-electrode cell. The working electrode was a glassy carbon disk electrode (ca.  $\phi=3$  mm). The auxiliary and reference electrodes in these studies were Pt wire and saturated Ag/AgCl, respectively. Glassy carbon was polished with polishing cloth before each measurement. All electrodes for CV experiments were from CH Instruments, Inc. USA. Acetate buffer solution was prepared by NaAc and HAc monitored by a digital pH meter. Scan rate was 100 mV/s. The concentration of **1** and **2** were 2 mmol L<sup>-1</sup>, while that of the supporting electrolyte was 0.2 mol L<sup>-1</sup>.

All melting points were measured with a XT4A Electrothermal melting point apparatus and are uncorrected. IR spectra were recorded as KBr pellets. <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded with an AV 400M Bruker spectrometer (400 MHz <sup>1</sup>H frequency, 100 MHz <sup>13</sup>C frequency). Chemical shifts are given as  $\delta$  values (internal standard: TMS). The MS spectra (ESI) were recorded on a Bruker esquire 6000 mass spectrometer.



Catechols **1**, **2a**, and **2b** were reagent-grade from Alfa Aesar China (Tianjin Co., Ltd.), whereas compounds **2c–e** were prepared according to known procedure<sup>30</sup> Other chemicals and solvents were from Beijing Chemicals Co. and used without further purification. Doubly distilled de-ionized water was used for preparation of aqueous acetate buffer. All experiments were performed at room temperature and ambient pressure.

## 4.2. General procedure for the synthesis of compounds 3–10

A 100 mL of H-type cell was equipped with a medium glass frit as a membrane. The anode compartment contained an assembly of seven graphite rods as the anode, whose upper rims were wrapped by a copper wire, and a platinum wire as the counter electrode was immersed in the cathode compartment. The current throughout electrolysis was controlled by a DC regulated power. During electrolysis, a magnetic stirrer stirred the mixture.

To the anode compartment, which is kept in water at room temperature was added 50 mL acetate buffer solution. Subsequently, catechols **1** (1 mmol) and **2** (1 mmol) were added to the anodic compartment and electrolyzed at constant current of 12 mA ( $\sim 4 \text{ mA/cm}^2$ ). The electrolysis was terminated when the starting **1** was consumed as determined by TLC. After electrolysis, the anolyte was worked up by one of the methods shown below.

In the cases of starting catechols **1** and phenyl-substituted pyrazol-5-ones **2b–e**, a mixed solvent of acetate buffer solution and acetonitrile (3:1 or 2:1 ratio of acetate buffer to acetonitrile) was used as supporting electrolyte due to the low solubility of **2b–e**.

Method A: the anolyte was acidified to pH=1 with 1 mol/L aqueous HCl and a precipitate was generated, which were filtered and washed with water. Pure compounds were finally obtained after recrystallization from methanol.

Method B: the anolyte was acidified to pH=1 with 1 mol/L aqueous HCl, extracted with ethyl acetate ( $3 \times 20 \text{ mL}$ ), and the organic layer was washed with water (20 mL). The separated organic layer was dried over  $\text{MgSO}_4$ , filtered and evaporated. The crude product was purified by column chromatography on silica gel, eluted with a mixture of petroleum ether and ethyl acetate ( $v:v=1:1$ ).

**4.2.1. 4,4-Bis(3,4-dihydroxy-5-methoxyphenyl)-3-methyl-1H-pyrazol-5(4H)-one (3a).** Yield: 42%; mp: 173 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.93 (s, 3H,  $\text{CH}_3$ ), 3.66 (s, 6H,  $\text{OCH}_3$ ), 6.13 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 6.23 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 8.34 (s, 2H, OH), 9.02 (s, 2H, OH), 11.14 (s, 1H, NH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  15.7, 56.4, 65.3, 104.1, 109.7, 127.4, 134.4, 146.2, 148.7, 161.8, 178.2; IR (KBr):  $\nu$  3430, 1674, 1621, 1530; ESI-MS:  $m/z$  372.6 ( $\text{M}^- - 1$ ), 396.8 ( $\text{M}^+ + \text{Na}$ ), 770.9 ( $2\text{M}^+ + \text{Na}$ ), 746.8 ( $2\text{M}^- - 1$ ).

**4.2.2. 4,4-Bis(3,4-dihydroxy-5-methoxyphenyl)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (3b).** Yield: 23%; mp: 123–124 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  2.11 (s, 3H,  $\text{CH}_3$ ), 3.67 (s, 6H,  $\text{OCH}_3$ ), 6.21 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 6.29 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 7.23 (t, 1H,  $J=7.6 \text{ Hz}$ , Ar–H), 7.46 (t, 2H,  $J=7.6 \text{ Hz}$ , Ar–H), 7.88 (d, 2H,  $J=7.6 \text{ Hz}$ , Ar–H), 8.43 (s, 2H, OH), 9.09 (s, 2H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  15.7, 56.5, 67.9, 104.3, 109.7, 119.0, 125.5, 126.8, 129.5, 134.9, 138.3, 146.4, 148.9, 163.2, 174.1; IR (KBr):  $\nu$  3435, 1689, 1517; ESI-MS:  $m/z$  448.8 ( $\text{M}^- - 1$ ), 450.9 ( $\text{M}^- + 1$ ), 4773.0 ( $\text{M}^+ + \text{Na}$ ).

**4.2.3. 4,4-Bis(3,4-dihydroxy-5-methoxyphenyl)-3-methyl-1-p-tolyl-1H-pyrazol-5(4H)-one (3c).** Yield: 20%; mp: 117 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  2.10 (s, 3H,  $\text{CH}_3$ ), 2.31 (s, 3H,  $\text{CH}_3$ ), 3.67 (s, 6H,  $\text{OCH}_3$ ), 6.19 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 6.28 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 7.26 (d, 2H,  $J=8.8 \text{ Hz}$ , Ar–H), 7.75 (d, 2H,  $J=8.4 \text{ Hz}$ , Ar–H), 8.45 (s, 2H, OH), 9.11 (s, 2H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  15.7, 21.0, 56.5, 67.9, 104.2, 109.7, 119.0, 126.9, 129.9, 134.7, 134.8,

135.9, 146.4, 148.9, 163.0, 173.9; IR (KBr):  $\nu$  3432, 2927, 1697, 1620, 1514, 1457; ESI-MS:  $m/z$  462.9 ( $\text{M}^- - 1$ ), 486.9 ( $\text{M}^+ + \text{Na}$ ).

**4.2.4. 4,4-Bis(3,4-dihydroxy-5-methoxyphenyl)-3-methyl-1-methoxyphenyl-1H-pyrazol-5(4H)-one (3d).** Yield: 29%; mp: 242–243 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  2.09 (s, 3H,  $\text{CH}_3$ ), 3.66 (s, 6H,  $\text{OCH}_3$ ), 3.77 (s, 3H,  $\text{OCH}_3$ ), 6.19 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 6.28 (d, 2H,  $J=2.0 \text{ Hz}$ , Ar–H), 7.02 (d, 2H,  $J=7.2 \text{ Hz}$ , Ar–H), 7.75 (d, 2H,  $J=7.2 \text{ Hz}$ , Ar–H), 8.46 (s, 2H, OH), 9.12 (s, 2H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  15.6, 55.8, 56.5, 67.7, 104.3, 109.7, 114.6, 121.0, 126.9, 131.5, 134.8, 146.4, 148.9, 157.1, 162.9, 173.7; IR (KBr):  $\nu$  3484, 3394, 1686, 1618, 1510, 1368, 1241, 1205, 1099; ESI-MS:  $m/z$  479 ( $\text{M}^- - 1$ ), 503 ( $\text{M}^+ + \text{Na}$ ).

**4.2.5. 4-[5-(3,4-Dihydroxy-5-methoxyphenoxy)-3-methyl-1-phenyl-1H-pyrazol-4-yl]-4-(3,4-dihydroxy-5-methoxyphenyl)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one (4).** Yield: 11%; mp: 157 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.68 (s, 3H,  $\text{CH}_3$ ), 2.17 (s, 3H,  $\text{CH}_3$ ), 3.70 (s, 3H,  $\text{OCH}_3$ ), 3.74 (s, 3H,  $\text{OCH}_3$ ), 6.38 (d, 1H,  $J=2.4 \text{ Hz}$ , Ar–H), 6.43 (d, 1H,  $J=2.0 \text{ Hz}$ , Ar–H), 6.45 (d, 1H,  $J=2.4 \text{ Hz}$ , Ar–H), 6.57 (d, 1H,  $J=2.4 \text{ Hz}$ , Ar–H), 7.16–7.88 (m, 10H, Ph–H), 8.48 (s, 1H, OH), 8.60 (s, 1H, OH), 9.15 (s, 1H, OH), 9.21 (s, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.9, 16.2, 56.6, 56.6, 61.2, 103.5, 105.2, 108.0, 108.4, 118.7, 124.4, 125.1, 125.6, 126.6, 129.0, 129.4, 134.9, 135.0, 135.8, 138.6, 146.3, 146.7, 148.8, 149.3, 156.6, 161.7, 163.4, 173.5; IR (KBr):  $\nu$  3435, 1702, 1622; ESI-MS:  $m/z$  620.9 ( $\text{M}^- - 1$ ), 645.3 ( $\text{M}^+ + \text{Na}$ ).

**4.2.6. 3-(5-Hydroxy-3-methyl-1H-pyrazol-4-yl)-5-tert-butylbenzene-1,2-diol (5a).** Yield: 34%; mp: 247 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.22 (s, 9H,  $\text{C}(\text{CH}_3)_3$ ), 2.22 (s, 3H,  $\text{CH}_3$ ), 6.59 (d,  $J=2.4 \text{ Hz}$ , 1H, Ar–H), 6.65 (d,  $J=2.4 \text{ Hz}$ , 1H, Ar–H), 8.42 (br s, 1H, OH), 11.43 (br s, 3H, 2OH, and NH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  12.5, 31.9, 34.1, 103.1, 110.7, 116.1, 116.7, 120.0, 141.1, 141.6, 143.2, 146.4; IR (KBr):  $\nu$  3435, 1591, 1530, 1453; ESI-MS:  $m/z$  260.5 ( $\text{M}^- - 1$ ), 284.7 ( $\text{M}^+ + \text{Na}$ ), 546.9 ( $2\text{M}^+ + \text{Na}$ ).

**4.2.7. 3-(5-Hydroxy-3-methyl-1-p-tolyl-1H-pyrazol-4-yl)-5-tert-butylbenzene-1,2-diol (5c).** Yield: 44%; mp: 222–223 °C;  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.25 (s, 9H,  $\text{CH}_3$ ), 2.32 (s, 3H,  $\text{CH}_3$ ), 2.35 (s, 3H,  $\text{CH}_3$ ), 6.66 (d, 1H,  $J=2.4 \text{ Hz}$ , Ar–H), 6.72 (d, 1H,  $J=2.0 \text{ Hz}$ , Ar–H), 7.32 (d, 2H,  $J=8.4 \text{ Hz}$ , Ar–H), 7.62 (s, 2H,  $J=7.2 \text{ Hz}$ , Ar–H), 8.45 (br s, 1H, OH), 10.25 (br s, 1H, OH), 12.39 (br s, 1H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.1, 21.0, 32.0, 34.2, 105.0, 111.4, 116.6, 119.4, 121.0, 129.6, 130.0, 134.2, 135.8, 141.2, 142.0, 145.6, 146.8; IR (KBr):  $\nu$  3435, 2961, 1632, 1548, 1513, 1485, 1410; ESI-MS:  $m/z$  353.1 ( $\text{M}^+ + 1$ ), 350.7 ( $\text{M}^- - 1$ ), 375.0 ( $\text{M}^+ + \text{Na}$ ), 727.2 ( $2\text{M}^+ + \text{Na}$ ), 702.8 ( $2\text{M}^- - 1$ ).

**4.2.8. 4-tert-Butyl-3,6-bis(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)benzene-1,2-diol (6b).** Yield: 29%; mp: 263 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.25 (s, 9H,  $\text{CH}_3$ ), 1.91 (s, 3H,  $\text{CH}_3$ ), 2.44 (s, 3H,  $\text{CH}_3$ ), 6.81 (s, 1H, Ar–H), 7.18 (t, 1H,  $J=7.2 \text{ Hz}$ , Ar–H), 7.33 (t, 1H,  $J=7.2 \text{ Hz}$ , Ar–H), 7.43 (t, 2H,  $J=7.6 \text{ Hz}$ , Ar–H), 7.54 (t, 2H,  $J=8.0 \text{ Hz}$ , Ar–H), 7.72 (br s, 2H, OH), 7.78 (d, 2H,  $J=7.6 \text{ Hz}$ , Ar–H), 7.80 (d, 2H,  $J=7.6 \text{ Hz}$ , Ar–H), 10.89 (br s, 2H, OH);  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  13.3, 32.0, 36.0, 105.1, 115.9, 116.7, 118.2, 121.0, 124.8, 126.6, 129.3, 129.7, 136.4, 140.8, 142.1, 145.7, 147.4, 160.1; IR (KBr):  $\nu$  3515, 3435, 2967, 1602, 1558, 1532, 1498, 1482, 1458; ESI-MS:  $m/z$  511.1 ( $\text{M}^+ + 1$ ), 533.1 ( $\text{M}^+ + \text{Na}$ ), 508.8 ( $\text{M}^- - 1$ ).

**4.2.9. 4-tert-Butyl-3,6-bis(5-hydroxy-3-methyl-1-p-tolyl-1H-pyrazol-4-yl)benzene-1,2-diol (6c).** Yield: 32%; mp: 312 °C (dec);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ ):  $\delta$  1.25 (s, 9H,  $\text{CH}_3$ ), 1.89 (s, 3H,  $\text{CH}_3$ ), 2.32 (s, 3H,  $\text{CH}_3$ ), 2.36 (s, 3H,  $\text{CH}_3$ ), 2.44 (s, 3H,  $\text{CH}_3$ ), 6.80 (s, 1H, Ar–H), 7.24 (d, 1H,  $J=8.0 \text{ Hz}$ , Ar–H), 7.35 (d, 1H,  $J=8.0 \text{ Hz}$ , Ar–H), 7.63–7.68 (m, 4H, Ar–H), 10.87 (br s, 1.5H, OH), 12.70 (br s, 0.5H, OH);  $^{13}\text{C}$  NMR

(100 MHz, DMSO- $d_6$ ):  $\delta$  13.1, 21.0, 21.0, 32.0, 36.0, 116.0, 116.5, 118.1, 121.1, 129.6, 130.0, 133.8, 134.9, 136.2, 140.8, 142.0; IR (KBr):  $\nu$  3435, 3188, 2959, 2922, 2804, 1628, 1603, 1513, 1482, 1404; ESI-MS:  $m/z$  539.0 ( $M^+ + 1$ ), 561.0 ( $M^+ + Na$ ), 537.0 ( $M^- - 1$ ).

**4.2.10.** 4-*tert*-Butyl-3,6-bis(5-hydroxy-1-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl)benzene-1,2-diol (**6d**). Yield: 21%; mp: 323 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.24 (s, 9H, CH<sub>3</sub>), 1.87 (s, 3H, CH<sub>3</sub>), 2.43 (s, 3H, CH<sub>3</sub>), 3.78 (s, 3H, OCH<sub>3</sub>), 3.81 (s, 3H, OCH<sub>3</sub>), 6.79 (s, 1H, Ar-H), 7.01 (d, 2H,  $J=8.8$  Hz, Ar-H), 7.10 (d, 2H,  $J=8.8$  Hz, Ar-H), 7.63 (d, 4H,  $J=8.8$  Hz, Ar-H), 10.45 (br s, 0.5H, OH), 10.45 (br s, 1H, OH), 10.86 (br s, 0.5H, OH), 11.07 (br s, 0.5H, OH), 12.73 (br s, 0.5H, OH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  32.0, 55.8, 55.9, 114.4, 114.9, 123.6; IR (KBr):  $\nu$  3437, 2961, 2928, 2029, 1630, 1513, 1465, 1441; ESI-MS:  $m/z$  571.5 ( $M^+ + 1$ ), 593.4 ( $M^+ + Na$ ), 569.0 ( $M^- - 1$ ).

**4.2.11.** 4-*tert*-Butyl-3,6-bis(1-(4-chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)benzene-1,2-diol (**6e**). Yield: 25%; mp: 237–238 °C;  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.24 (s, 9H, CH<sub>3</sub>), 1.90 (s, 3H, CH<sub>3</sub>), 2.42 (s, 3H, CH<sub>3</sub>), 6.80 (s, 1H, Ar-H), 7.49 (d, 2H,  $J=9.2$  Hz, Ar-H), 7.61 (d, 2H,  $J=8.8$  Hz, Ar-H), 7.82 (d, 2H,  $J=8.4$  Hz, Ar-H), 7.84 (d, 2H,  $J=8.8$  Hz, Ar-H), 10.63–12.7 (br s, 2H, OH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  13.3, 32.0, 36.0, 115.9, 117.0, 118.1, 118.5, 119.6, 121.1, 122.2, 128.6, 129.2, 129.5, 129.6, 129.9, 130.4, 140.8, 142.1, 146.6, 147.4, 156.8; IR (KBr):  $\nu$  3436, 2962, 1626, 1601, 1493; ESI-MS:  $m/z$  577 ( $M^- - 1$ ).

**4.2.12.** 3-(5-Hydroxy-3-methyl-1H-pyrazol-4-yl)-5-methylbenzene-1,2-diol (**7**). Yield: 30%; mp: 238 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  2.15 (s, 3H, CH<sub>3</sub>), 2.20 (s, 3H, CH<sub>3</sub>), 6.42 (d, 1H,  $J=1.6$  Hz, Ar-H), 6.45 (d, 1H,  $J=1.6$  Hz, Ar-H), 8.45 (br s, 1H, OH), 11.17 (br s, 3H, 2OH, and NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  12.4, 21.0, 102.5, 114.2, 120.4, 120.6, 127.8, 141.0, 141.1, 146.7, 161.9; IR (KBr):  $\nu$  3376, 3204, 1625, 1582, 1496, 1450; ESI-MS:  $m/z$  220.7 ( $M^+ + 1$ ), 218.4 ( $M^- - 1$ ), 242.7 ( $M^+ + Na$ ).

**4.2.13.** 3-Methyl-4-(4,5-dihydroxy-2-methylphenyl)-5-(4,5-dihydroxy-2-methylphenoxy)-1H-pyrazole (**8**). Yield: 56%; mp: 203 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.75 (s, 3H, CH<sub>3</sub>), 1.83 (s, 3H, CH<sub>3</sub>), 2.00 (s, 3H, CH<sub>3</sub>), 6.52 (s, 1H, Ar-H), 6.61 (s, 1H, Ar-H), 6.62 (s, 1H, Ar-H), 6.67 (s, 1H, Ar-H), 8.58 (s, 1H, OH), 8.67 (s, 1H, OH), 9.03 (s, 1H, OH), 9.12 (s, 1H, OH), 9.53 (br s, 1H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  11.0, 16.4, 19.4, 104.9, 115.6, 117.3, 117.5, 118.9, 122.9, 126.7, 128.3, 130.2, 137.9, 143.0, 143.6, 144.5, 146.0, 158.7; IR (KBr):  $\nu$  3527, 3435, 2961, 1608, 1571, 1542, 1492, 1452; ESI-MS:  $m/z$  342.8 ( $M^+ + 1$ ), 340.6 ( $M^- - 1$ ), 364.8 ( $M^+ + Na$ ), 682.8 ( $2M^- - 1$ ).

**4.2.14.** 4-(5-Hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)-5-methylbenzene-1,2-diol (**9b**) and 4-(4,5-dihydroxy-2-methylphenyl)-5-methyl-2-phenyl-1,2-dihydropyrazol-3-one (**9b'**). Yield: 37%; mp: 235 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.97–2.06 (m, 6H, 2CH<sub>3</sub>), 6.52–6.65 (m, 2H, Ar-H), 7.20 (t, 1H,  $J=6.8$  Hz, Ar-H), 7.44 (t, 2H,  $J=8.0$  Hz, Ar-H), 7.65 (d, 2H,  $J=8.0$  Hz, Ar-H), 8.60–8.72 (m, 2H, OH), 10.57 (br s, 0.5H, OH), 10.96 (br s, 0.5H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  19.5, 117.6, 118.9, 120.3, 122.0, 125.1, 128.6, 129.3, 138.9, 143.1, 144.9, 147.6, 160.1; IR (KBr):  $\nu$  3507, 3437, 2922, 1603, 1553, 1527, 1497, 1458; ESI-MS:  $m/z$  296.9 ( $M^+ + 1$ ), 294.9 ( $M^- - 1$ ), 318.9 ( $M^+ + Na$ ).

**4.2.15.** 4-(5-Hydroxy-3-methyl-1-*p*-tolyl-1H-pyrazol-4-yl)-5-methylbenzene-1,2-diol (**9c**) and 4-(4,5-dihydroxy-2-methylphenyl)-5-methyl-2-*p*-tolyl-1,2-dihydropyrazol-3-one (**9c'**). Yield: 55%; mp: 243 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  2.01–2.1 (m, 6H, 2CH<sub>3</sub>), 2.32 (s, 3H, CH<sub>3</sub>), 6.54–6.64 (m, 2H, Ar-H), 7.24 (d, 2H,  $J=8.0$  Hz, Ar-H), 7.59 (d, 2H,  $J=8.4$  Hz, Ar-H), 8.60–8.71 (m, 2H,

2OH), 10.48 (br s, 0.5H, OH), 10.93 (br s, 0.5H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  19.5, 20.9, 117.6, 118.8, 121.4, 128.6, 129.7, 143.1, 144.8; IR (KBr):  $\nu$  3436, 2924, 1632, 1556, 1513, 1440, 1408; ESI-MS:  $m/z$  310.9 ( $M^+ + 1$ ), 308.7 ( $M^- - 1$ ), 332.9 ( $M^+ + Na$ ), 618.9 ( $2M^- - 1$ ).

**4.2.16.** 4-(5-Hydroxy-1-(4-methoxyphenyl)-3-methyl-1H-pyrazol-4-yl)-5-methylbenzene-1,2-diol (**9d**) and 4-(4,5-dihydroxy-2-methylphenyl)-5-methyl-2-*p*-methoxyphenyl-1,2-dihydropyrazol-3-one (**9d'**). Yield: 62%; mp: 279 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.95–2.07 (m, 6H, 2CH<sub>3</sub>), 3.78 (s, 3H, OCH<sub>3</sub>), 6.49–6.64 (m, 2H, Ar-H), 7.00 (d, 2H,  $J=8.4$  Hz, Ar-H), 7.55–7.62 (m, 2H, Ar-H), 8.62–8.70 (m, 2H, 2OH), 10.38 (br s, 0.5H, OH), 10.94 (br s, 0.5H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  13.5, 19.5, 55.8, 114.4, 114.5, 117.6, 119.0, 122.3, 123.1, 123.3, 128.6, 143.1, 144.8, 146.4, 157.1; IR (KBr):  $\nu$  3437, 2963, 2928, 1622, 1595, 1555, 1513, 1445, 1410; ESI-MS:  $m/z$  326.9 ( $M^+ + 1$ ), 324.7 ( $M^- - 1$ ), 650.8 ( $2M^- - 1$ ).

**4.2.17.** 4-(1-(4-Chlorophenyl)-5-hydroxy-3-methyl-1H-pyrazol-4-yl)-5-methylbenzene-1,2-diol (**9e**) and 4-(4,5-dihydroxy-2-methylphenyl)-5-methyl-2-*p*-chlorophenyl-1,2-dihydropyrazol-3-one (**9e'**). Yield: 32%; mp: 254 °C (dec);  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.92–2.17 (m, 6H, 2CH<sub>3</sub>), 6.53 (s, 1H, Ar-H), 6.64 (s, 1H, Ar-H), 7.50 (d, 2H,  $J=8.4$  Hz, Ar-H), 7.81 (d, 2H,  $J=8.0$  Hz, Ar-H), 8.64 (s, 1H, OH), 8.74 (s, 1H, OH), 10.82 (br s, 0.5H, OH), 11.01 (br s, 0.5H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  13.4, 19.5, 117.6, 118.9, 120.2, 121.8, 128.6, 129.3, 143.1, 145.0; IR (KBr):  $\nu$  3514, 3436, 1603, 1553, 1524, 1494, 1445, 1404; ESI-MS:  $m/z$  328.8 ( $M^- - 1$ ), 352.7 ( $M^+ + Na$ ), 658.8 ( $2M^- - 1$ ).

**4.2.18.** 4,4-Bis(3,4-dihydroxy-5-methylphenyl)-3-methyl-1H-pyrazol-5(4H)-one (**3e**). Yield: 38%; mp: 163–165 °C;  $^1H$  NMR (400 MHz, DMSO- $d_6$ ):  $\delta$  1.90 (s, 3H, CH<sub>3</sub>), 2.08 (s, 6H, CH<sub>3</sub>), 3.77 (s, 3H, OCH<sub>3</sub>), 6.25 (d, 2H,  $J=1.6$  Hz, Ar-H), 6.42 (d, 2H,  $J=2.0$  Hz, Ar-H), 8.24 (s, 2H, OH), 9.20 (s, 2H, OH), 11.05 (s, 1H, NH);  $^{13}C$  NMR (100 MHz, DMSO- $d_6$ ):  $\delta$  15.7, 16.6, 64.9, 113.7, 120.9, 124.8, 128.0, 143.3, 145.3, 161.9, 178.5; IR (KBr):  $\nu$  3420, 1668, 1601, 1501, 1300; ESI-MS:  $m/z$  341 ( $M^- - 1$ ), 365 ( $M^+ + Na$ ).

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