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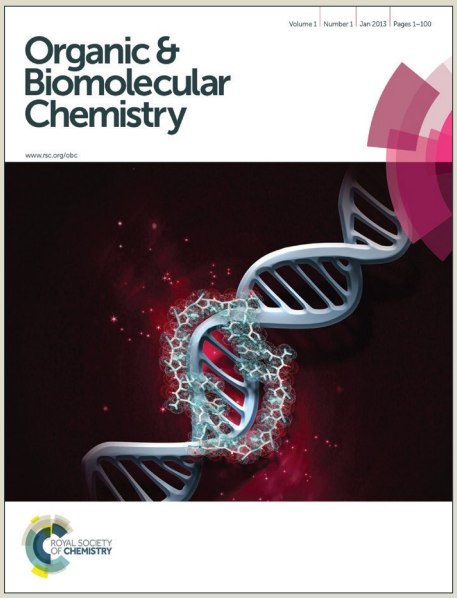

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ARTICLE

An Efficient Synthesis of Iminoquinones by Chemoselective Domino *ortho*-Hydroxylation/oxidation/imidation Sequence of 2-Aminoaryl Ketones

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An efficient chemoselective domino oxidative homocoupling of 2-aminoaryl ketone in presence of 2-iodoxybenzoic acid (IBX) for the synthesis of iminoquinone has been developed. The domino reaction proceeds *via* three consecutive steps, such as domino *ortho*-hydroxylation of 2-aminoaryl ketone, oxidation of phenol derivative to benzoquinone and dimerization through imine formation to yield iminoquinone. Importantly, this reaction allows the recycling of the oxidant IBX by recovering the by-product iodosobenzoic acid (IBA) and oxidizing it back to IBX. A four step domino strategy for the synthesis of iminoquinone through *in-situ* generation of 2-amino benzophenone from (2-amino phenyl)(phenyl)methanol was also developed.

Introduction

Iminoquinones are highly colored dye[1] and a core structure in several important natural products (Figure 1).[2] Iminoquinones are the key abiotic and biological components, which intercalate with DNA.[3] Many of these hybrid materials have provided new avenues for molecular sensor,[4] ligands[5] drug delivery,[6] and controlled material growth. Iminoquinone representing a new frontier for the design and generation of molecular complexity.[7] Their diverse biological activities and synthetic application have attracted the synthetic community to synthesize these important alkaloids.[8] In 2006, Francis *et al*. first reported an intramolecular oxidative coupling of *N*-acyl phenylenediamine in the presence of $NaIO_4$ as an oxidant.[9]

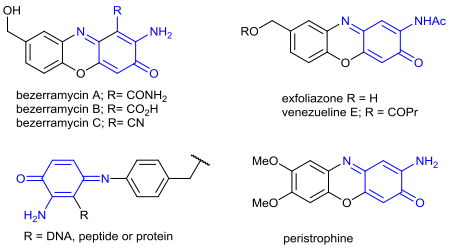
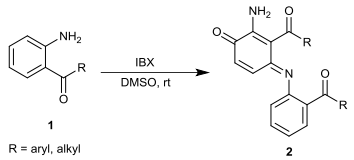


Fig. 1 some of the representative examples for iminoquinone containing biologically important compounds.

Recently, synthesis of iminoquinone with various oxidants such as $K_3[Fe(CN)_6]$,[10] $NaIO_4$[11] and photochemical reaction are reported.[12] Although, different methods were used for the preparation of iminoquinone,[13] the progress in the area has been limited with multistep synthesis.[14] There is no any general route to access iminoquinone from single substrate using environmental friendly methods.

Hypervalent iodine complexes are well-known as multifaceted oxidizing reagents and shown to promote many organic reactions for the formation of C-C, C-O and C-N bonds.[15] In view of their high reactivity, selectivity and environmentally benign nature, they have served as an economical useful synthetic oxidant in organic synthesis. These hypervalent iodines are highly welcome in both chemical industries and academic laboratories.

In continuation of our research towards metal free organic transformation.[16] herein, we report a new and viable domino strategy based on oxidative coupling of 2-amino benzophenone to synthesize iminoquinones using IBX (Scheme 1). Importantly, the reaction condition are mild enough to preserve the most of the reactive functional groups.



Scheme 1 Synthesis of IBX mediated iminoquinone through domino *ortho*-hydroxylation /oxidation /imidation sequence.

Results and discussion

Initially the reaction was carried out using 2-amino benzophenone **1a** in the presence of oxone in CH_3CN at 80 °C

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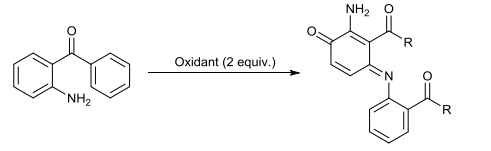
for 7 hours. Gratifyingly, highly stable dye molecule **2a** was isolated in 18 % yield (Table 1, entry 1). The structure of **2a** was unambiguously confirmed by ^{1}H NMR, ^{13}C NMR and single crystal X-ray crystallography analysis (Figure 2). The yield of the target molecule **2a** was improved to 40%.

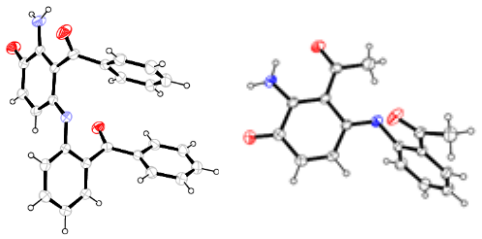
Table 1. Optimization of iminoquinone formation through domino reaction.[a]



1a 2a

Entry	Oxidant	Solvent	Tem (°C)	Time (h)	Yield (%)[b]
1	oxone	CH_3CN	80	7	18
2	m-CPBA	CH_3CN	80	10	40
3	IBX	CH_3CN	80	3	94
4	$PhI(OAc)_2$	CH_3CN	80	10 min	0[c]
5	$PhI(OCOCF_3)_2$	CH_3CN	80	10 min	0[c]
6	H_2O_2	CH_3CN	80	21	0[d]
7	DDQ	CH_3CN	80	21	0[d]
8	IBX	DCM	80	2	73
9	IBX	THF	80	7	43
10	IBX	$CHCl_3$	80	13	10
11	IBX	1,4-dioxane	80	13	18
12	IBX	DCE	80	6	66
13	IBX	DMSO	80	10 min	92
14	IBX	DMSO	60	10 min	95
15	IBX	DMSO	rt	25 min	96[e]
16	IBX	DMSO	rt	10 min	95[e]
17	IBX	DMSO	rt	10 min	95[e,f]
18	IBX	DMSO	rt	1	78[e,g]

[a]All the reactions were carried out using **1a** (0.5 mmol) with 2 equiv. of oxidant in 3 mL of solvent. [b]Isolated yield. [c]A complex inseparable reaction mixture was obtained.[d]No reaction. [e]Reaction was carried out at room temperature (27 °C-30 °C). [f]Reaction at open air atm. [g]1Equiv. of IBX was used.



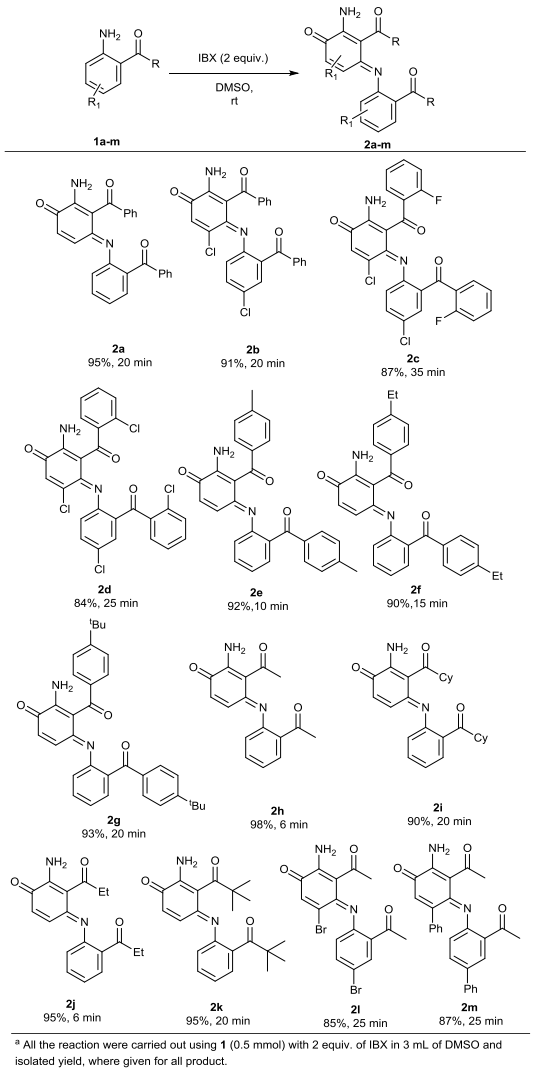
2a **2h**

Fig. 2 Single crystal X-ray structure of **2a** and **2h** (CCDC No: 1425851 and CCDC 1425852; 30% probability ellipsoid).

When 2 equiv. of *m-CPBA* was used (entry 2). To our delight, the yield of **2a** was significantly improved to 94% yield, when IBX was used as an oxidant (entry 3). Encouraged by this result, we further investigated the other oxidants such as (diacetoxyiodo)benzene,(bis(trifluoroacetoxy)iodo)benzene, hydrogen peroxide and DDQ but these reagents were not effective for this reaction (entries 4-7). Further to improve the efficiency of reaction we next tested the influence of solvent on the reaction. Aprotic and polar solvent, such as DCM, THF, $CHCl_3$, 1,4-dioxane, DCE etc. resulted in a very low yield of the corresponding product (entries 8-12).

However, when DMSO was used as a solvent at 80 °C, the desired product was obtained in 92% yield within 10 minutes (entry 13). At same time, when the reaction was carried out at 60 °C, it gave 95% yield (entry14). At room temperature, the yield of **2a** was increased to 96% (entry15). The domino reaction at an open air atmosphere gave 95% of yield in very short reaction time (entry 17). Decreasing the amount of IBX from 2 equiv. to 1 equiv., the yield of the product was also decreased to 78% (entry 18). This indicates that the reaction does not require any special conditions such as inert atmosphere, degassing, *etc*. Finally, the optimal reaction condition was found to be 2 equiv. of IBX in DMSO at room temperature for 10 minute.

Table 2. Substrate scope for the synthesis of different iminoquinones using IBX.[a]



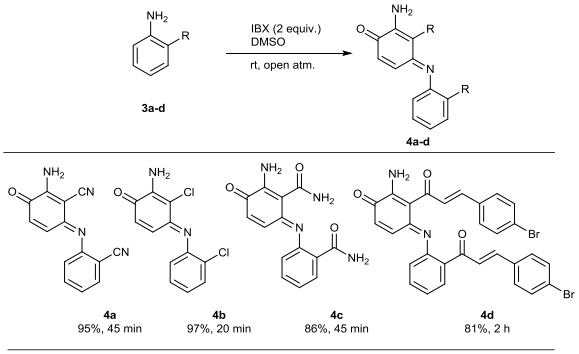
[a] All the reaction were carried out using **1** (0.5 mmol) with 2 equiv. of IBX in 3 mL of DMSO and isolated yield, where given for all product.

With this optimized reaction conditions in hand, the scope of the reaction was investigated (Table 2). The IBX catalyzed domino *ortho*-hydroxylation reaction followed by oxidative coupling of 2-amino benzophenone reaction displayed high functional group tolerance. 2-Amino benzophenone substituted with electron-withdrawing groups such as chloro, fluoro and dichloro or electron-donating groups, such as methyl, ethyl, and butyl groups gave the corresponding iminoquinone product in good to excellent yield (**2a**-**g**).

When the derivatives of 2-amino acetophenone like 1-(2-aminophenyl)propan-1-one, 1-(2-aminophenyl)2-methylpropan-1-one and (2-aminophenyl)(cyclohexyl)methanone gave good yield of the desired product (Table 2, **2h**-**k**). Notably, when bromo and phenyl group substituted 2-amino acetophenones were used in this domino transformation, the corresponding iminoquinone was observed in good yield despite their electronic nature (**2l**, **2m**).

To verify the synthetic utility of this new strategy for compound containing sensitive functional groups such as amide, chloro and nitrile, were subjected to the reaction conditions. All of them were transformed into corresponding product with excellent yields (**4a**-**c**). We examined long chain containing starting material like 2-amino chalcone and it was converted to corresponding product in excellent yield (**4d**).[17,18]

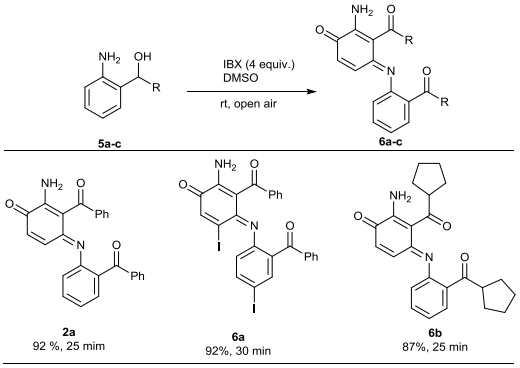
Table 3. Substrate scope different functional group domino *ortho*-hydroxylation/oxidation/imine formation for the synthesis of iminoquinone.[a]



[a]All the reaction were carried out using **3** (0.5 mmol) with 2 equiv. of IBX in 3 mL of DMSO and isolated yield, where given for all product. [b]1mmol scale of **4a**

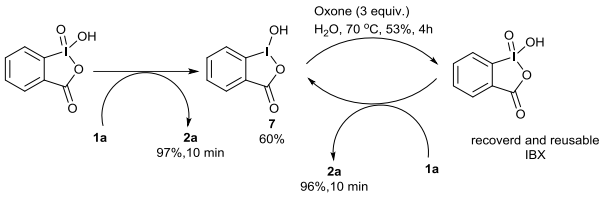
After successful development of this new method for the synthesis iminoquinones from 2-aminoaryl ketone, we extended the application of this strategy to alcohol containing compound like (2-aminophenyl)phenyl methanol, (2-amino-4-iodophenyl)phenyl methanol and (2-aminophenyl)(cyclopentyl)methanol. All of them gave good yield through four steps domino alcohol oxidation, *ortho*-hydroxylation, oxidation of phenol and imidation sequence with excellent yield (Table 4, **6a**, **6b**).

Table 4. Substrates scope for alcohol oxidation and oxidative coupling.[a]



[a] All of them are isolated yields.

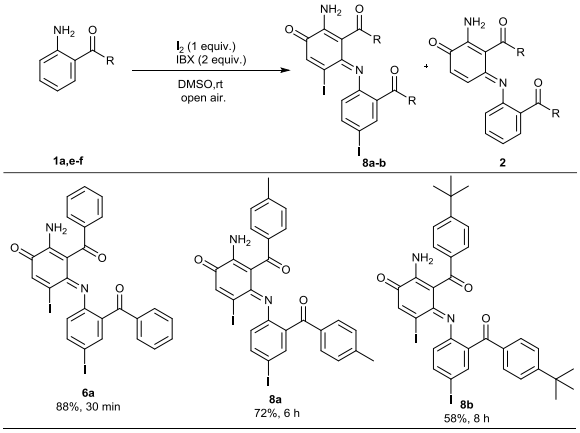
To show the reusability of IBX, the IBX by-product iodosobenzoic acid (IBA) **7** was filtered off after completion of reaction in 60% yield. The recovered iodosobenzoic acid was oxidized back to IBX in 53% yield. The IBX which was made by reoxidising the recovered IBA **7** was successfully used in the domino reaction and 96% of yield was obtained for the iminoquinone.



Scheme 2. Recycling of IBX.

Further, the application of newly developed domino reaction was extended to synthesis of iodide containing iminoquinones, which are beneficial for further derivatization, the optimized reaction condition was carried out with addition of 1 equivalent of I2. This reaction provided 72% of diiodoiminoquinone 8a. When 1g was used, it gave 58% of 8b in 8 hours (Scheme 2). The iodide incorporated to iminoquinone *in-situ* during reaction by addition of iodide with optimized reaction condition.

Table 5. Substrate scope for iodination/ domino oxidative homo coupling.[a]



[a]In all the reaction, simple homo coupling product **2** was isolated ranging from 7-12 % yield.

To prove practical utility of this domino reaction in mulitgram scale synthesis, the reaction was performed in 5 gram-scale under the optimized reaction conditions. This transformation proceeded smoothly and afforeded **2a** in 93% yield (Scheme 3).

Scheme 3. Gram-scale synthesis of iminoquinone.

It is expected that first *ortho*-hydroxylation takes place when **1a** is treated with IBX to give intermediate **9**. This is confirmed

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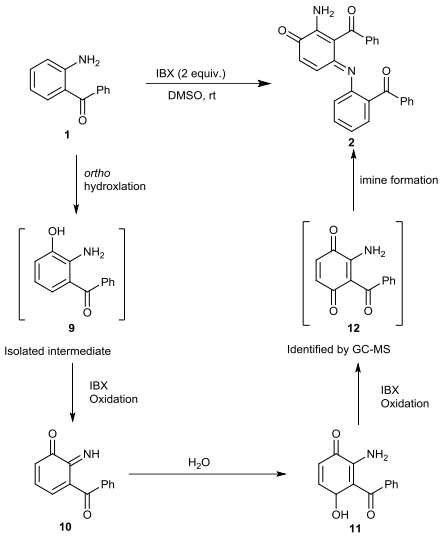
by isolation of **9** in 14% yield from the reaction mixture. In the conversion of **9** to **12,** the oxidation of **9** takes place in the presence of IBX to give **10**.[13d] Then water adds to **10** to give 2-amino-1,4-hydroquinone **11**. Then the IBX-mediated oxidation of **11** will give **12**, which will yield final product **12** through imine formation.**12** which was supported by GCMS analysis of reaction mixture.[19] another molecule of **1a** may react with **12** to give the product **2a.**



Scheme 4. The plausible reaction path for domino oxidative homo coupling of 2-amino benzophenone.

Conclusions

In conclusion, we have developed a highly chemoselective intramolecular domino oxidative homo coupling of 2-aminoaryl ketone to give iminoquinones in moderate to excellent yield. The reaction proceeds *via* three consecutive steps, such as domino *ortho*-hydroxylation of 2-aminoaryl ketone, oxidation of phenol derivative to benzoquinone and imine formation to yield iminoquinones. In the course of IBX-mediated consecutive reaction, the IBX by-product IBA was isolated and reoxidized back to IBX and reused in the reaction. The domino oxidative coupling was carried out from corresponding alcohol as well through four step domino sequence such as *ortho*-hydroxylation of 2-amino benzophenone, oxidation of phenol derivative to benzoquinone and dimerization through imine formation

Experimental Section

General considerations

Commercially available chemicals were purchased from Alfa Aesar or Sigma-Aldrich chemical and used as received. All the starting materials were synthesized according to the reported procedures. Thin-layer chromatography (TLC) was performed using Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV lamp for monitoring reaction. Silica gel for column chromatography (particle size 100–200 mesh) was purchased from SRL India. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz instrument. Chemical shifts were recorded in parts per million (ppm) relative to tetramethylsilane (δ 0.00), chloroform (7.26 ppm) or DMSO (2.50 ppm). ^{1}H NMR splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), m (multiplet), and etc. ^{13}C NMR spectral values were reported relative to $CDCl_3$ (77.16 ppm) and DMSO-d6 (39.52 ppm). FT–IR spectra were recorded on a JASCO spectrometer and are reported in frequency of absorption (cm^{-1}). High resolution mass spectra were recorded on Q-Tof Micro mass spectrometer for all the compounds. IBX was prepared from *o*-iodobenzoic acid and Oxone according to the literature procedure[20]

General procedure for the synthesis of iminoquinones derivatives:

A reaction tube equipped with a magnetic stir bar was charged with 2-amino benzophenones **1a–m** (0.5 mmol) and IBX (2 equiv.) under open atmosphere at then the solvent DMSO (3 mL) was added. The resulting mixture was stirred at room temperature (27 ^{o}C-30 ^{o}C) and the progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the reaction mixture was quenched by slow addition of $NaHCO_3$ and extracted with EtOAc (3×5mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc-10:2) to give the corresponding product **2a–m** as a red soilds.

(***E*)-2-Amino-3-benzoyl-4-((2-benzoyl)imino)cyclohexa-2,5-dien-1-one (2a):** Dark red colour soild; mp 150-152 ^{o}C, R_f 0.67; (hexanes : ethyl acetate, 70:30 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (t, *J* = 7.2 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 2H), 7.42-7.48 (m, 3H), 7.29-7.42 (m, 4H), 7.12-27 (m, 3H), 6.95 (d, *J* = 10 Hz, 1H), 6.90 (s, 2H) 6.67 (d, *J* = 2 Hz, 1H), 6.65 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.7, 195.5, 182.6, 156.7, 148.4, 143.6, 138.7, 136.6, 133.0, 131.8, 130.9, 130.3, 130.0, 129.3, 128.7, 128.5, 128.4, 127.9, 127.4, 123.9, 120.4, 110.4; IR (neat) 3456, 1963, 1585, 1403, 1262, 931, 702 cm^{-1}; HRMS (*m*/*z*): $[M+H]^+$calcd for $C_{26}H_{18}O_3N_2Na$: 429.1202; found: 429.1210

***(Z)*-2-Amino-3-benzoyl-4-((2-benzoyl-4-chloro phenyl) imino)-5-chlorocyclohexa-2,5-dien-1-one (2b):** Dark red colour soild; mp 140-142 ^{o}C, R_f 0.72; (hexanes : ethyl acetate, 70:30 v/v): ^{1}H NMR (400 MHz, CDCL3) δ 8.13(s 2H), 7.49-7.56 (m, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.32-7.37 (m, 4H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.25 (t, *J* = 7.6 Hz, 2H) 7.13 (dd, *J* = 2.4 Hz, J_2 = 8 Hz, 1H), 7.00 (d, *J* = 7.2 Hz, 2H), 6.84 (s, 1H), 6.10 (d, *J* = 8.4 Hz, 1H); ^{13}C

NMR (100 MHz, DMSO-d_6) δ 192.1, 191.7, 179.3, 155.1, 148.8, 146.5, 138.3, 136.1, 132.7, 132.2, 131.6, 129.6, 129.0, 128.7, 128.2, 128.1, 127.9, 127.4, 127.1, 125.7, 123.9, 102.5; IR (neat) 3392, 3061, 2925, 1654, 1592, 1277, 702, cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{16}Cl_2O_3N_2$: 475.3250; found: 475.0609.

(*Z*)-2-Amino-5-chloro-4-((4-chloro-2-(2-fluoro benzoyl) phenyl)imino)-3-(2-fluorobenzoyl)cyclohexa-2,5-dien-1-one (2c): Dark red colour soild; mp 161-163 °C, R_f 0.67; (hexanes : ethyl acetate, 70:30 v/v): ^1H NMR (400 MHz, DMSO-d_6) δ 8.38 (s 2H), 7.55 (q, *J* = 6.8 Hz, 1H), 7.46 (q, *J* = 6.3 Hz, 1H), 7.23-7.37 (m, 3H), 7.09-7.22 (m, 3H), 7.00-7.09 (m, 2H), 6.81 (t, *J* = 7.2 Hz, 1H), 6.43 (d, *J* = 8Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 189.0, 187.1, 179.5, 159.9 (d, $^1J_{C-F}$ = 252 Hz), 158.8 (d, $^1J_{C-F}$ = 251 Hz), 154.9, 148.8, 146.6, 134.1(d, $^3J_{C-F}$ = 9.3 Hz,2C), 132.2, 130.3, 129.5, 129.4, 129.1, 128.9, 128.2, 127.4, 127.2, 125.7, 124.6, 124.4, 122.4, 116.4(d, $^2J_{C-F}$ = 10.8 Hz), 116.2(d, ^2J = 21.1 Hz), 104; IR (neat) 3435, 2924, 2359, 1663, 1581, 1291, 758, cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{14}Cl_2O_3F_2N_2Na$: 533.0242; found: 533.0242.

(*Z*)-2-Amino-5-chloro-4-((4-chloro-2-(2-chloro benzoyl))imino)-3-(2-chlorobenzoyl)cyclohexa-2,5-dien-1-one (2d): Dark red colour soild; mp 148-150 °C, R_f 0.47; (hexanes :ethyl acetate, 70:30 v/v): ^1H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 2H), 7.41-7.50 (m, 2H), 7.30-7.41 (m, 3H), 7.23-7.31 (m, 2H), 7.09-7.24 (m, 3H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.45 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.7, 190.3, 179.6, 149.3, 146.9, 138.4, 137.8, 132.9, 132.1, 131.9, 130.4, 130.12, 130.03, 130.00, 129.9, 129.6, 129.3, 128.6, 128.4, 127.3, 127.1, 121.2, 105.3; IR (neat) 3423, 2255, 1645, 1240, 1026, 1001, 826, 765, cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{26}H_{14}Cl_4O_3N_2Na$: 564.9657 ; found: 564.9651

***(E)*-2-Amino-3-(4-methylbenzoyl)-4-((2-(4-methyl benzoyl)phenyl)imino)cyclohexa-2,5-dien-1-one (2e):** Dark red colour soild; mp 118-120 °C, R_f 0.5; (hexanes : ethyl acetate, 80:20 v/v): ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 5.4 Hz, *J* = 27.2 Hz, 3H), 7.12-7.28 (m, 2H), 6.91-7.12 (m, 2H), 6.87 (d, *J* = 9.6 Hz, 1H), 6.70 (d, *J* = 5.6 Hz, 2H), 6.46 (d, *J* = 7.6 Hz, 1H), 6.27 (s, 1H), 2.31 (s, 3H) 2.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 196.0, 182.6, 156.8, 149.1, 144.5, 143.7, 142.0, 136.9, 134.6, 130.8, 130.6, 130.2, 129.7, 128.9, 128.8, 128.4, 123.3, 120.2, 111.4, 42.5, 40.7, 21.6, 21.3; IR (neat) 3362, 2925, 2856, 1658, 1605, 1267, 794 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{28}H_{22}O_3N_2$: 434.1630; found: 435.1699.

***(E)*-2-Amino-3-(4-ethylbenzoyl)-4-((2-(4-ethyl benzoyl) phenyl)imino)cyclohexa-2,5-dien-1-one (2f):** Dark red colour soild; mp 119-121 °C, R_f 0.47; (hexanes : ethyl acetate, 80:20 v/v): ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8 Hz, *J* = 27.6 Hz, 4H), 7.27 (t, *J* = 7.6Hz, 1H), 7.21 (t, *J* = 9.6 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 10.4 Hz, 1H), 6.74 (d, *J* = 8 Hz, 2H), 6.43-6.53 (m, 2H), 6.26 (s, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 2.30 (q, *J* = 7.6 Hz, 2H), 1.20 (t, *J* = 7.6 Hz, 3H), 0.95(t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9, 196.1, 182.8, 157.0, 150.0, 149.6, 148.4, 144.8, 137.3, 135.0, 131.2, 130.8, 130.5, 129.7, 129.4, 129.3, 129.3, 127.8, 127.3, 123.4, 120.4, 111.6, 29.1, 28.8, 15.3, 15.0; IR (neat) 3490, 2925, 2857, 1620, 1456, 757cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{30}H_{26}O_3N_2Na$: 485.1837; found: 485.1836.

***(E)*-2-Amino-3-(4-(tert-butyl)benzoyl)-4-((2-(4-(tert-butyl)benzoyl)phenyl)imino)cyclohexa-2,5-dien-1-one (2g):** Dark red colour soild; mp 120-122°C, R_f 0.52; (hexanes : ethyl acetate, 80:20 v/v): ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 8.4 Hz, 4H), 7.19-7.35 (m, 5H), 6.82-7.03 (m, 5H), 6.41-6.52 (m, 2H), 6.29 (s, 2H), 1.27 (s, 9H); 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 195.6, 182.7, 157.1, 156.6, 155.3, 150.1, 144.7, 136.7, 134.5, 131.2, 131.0, 130.1, 129.8, 129.6, 129.4, 128.7, 125.3, 124.6, 123.1, 120.5, 111.6, 35.1, 34.7, 31.1, 31.0; IR (neat) 3434, 2250, 2123, 1659, 1027, 824, 763, 625, cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{34}H_{34}O_3N_2$: 518.6570; found: 518.6469.

***(E)*-3-Acetyl-4-((2-acetylphenyl)imino)-2-amino cyclo hexa-2,5-dien-1-one (2h):** Dark red colour soild; mp 121-123 °C, R_f 0.53; (hexanes : ethyl acetate, 70:30 v/v): ^1H NMR (400 MHz, DMSO-d_6) δ 8.46 (s, 2H), 7.86 (dd, *J* = 7.6 Hz, *J* = 1.2 Hz, 1H), 7.54 (td, *J* = 1.2 Hz, *J* = 7.2 Hz,1H), 7.24 (td, *J* = 1.2 Hz, *J* = 7.6 Hz, 1H), 6.85 (d, *J* = 10 Hz, 1H), 6.74 (dd, *J* = 7.8 Hz, *J* = 0.8Hz, 1H), 6.63 (d, *J* = 10 Hz, 1H), 2.55 (s, 3H), 2.44 (s , 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 200.7, 198.9, 182.6, 155.1, 149.2, 147.9, 132.6, 131.9, 129.9, 128.9, 123.9, 121.1, 107.9, 33.2, 29.9; IR (neat) 3455, 2252, 2125, 1658, 1025, 824, 764, 625 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{14}O_3N_2Na$: 305.0897; found: 305.0897.

***(E)*-2-Amino-3-(cyclohexanecarbonyl)-4-((2-(cyclo hexanecarbonyl)phenyl)imino)cyclohexa-2,5-dien-1-one (2i):** Red colour soild; mp 128-130 °C, R_f 0.5; (hexanes : ethyl acetate, 90:10 v/v): ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.62 (d, *J* = 0.8 Hz, 1H), 7.37 (td, *J* = 1.2Hz, *J* = 7.4 Hz,1H), 7.12 (td, *J* = 1.2 Hz, *J* = 4 Hz, 1H), 6.83 (d, *J* = 10 Hz, 1H), 6.57 (d, *J* = 7.2 Hz, 1H), 6.43 (d, *J* = 10 Hz, 1H), 3.68 (t , *J* = 11.2 Hz,1H), 3.01 (t , J = 11.2 Hz,1H), 1.5-1.92 (m , 10H) 1.0-1.42 (m , 10H); 13C NMR (100 MHz, CDCl3) δ 208.2, 205.8, 182.6, 155.6, 149.3, 147.0, 131.8, 131.6, 129.5, 129.2, 128.9, 123.9, 120.5, 108.8, 49.6, 48.4, 29.4, 28.9, 26.1, 25.9, 25.8, 25.7; IR (neat) 3405, 1655, 1579, 1269, 1118, cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{14}O_3N_2Na$: 305.0897; found: 305.0897.

***(E)*-2-Amino-3-propionyl-4-((2-propionylphenyl) imino)cyclohexa-2,5-dien-1-one (2j):** Dark red colour soild; mp 123.5-124.5 °C, R_f 0.6; (hexanes : ethyl acetate, 75:25 v/v): ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 2H), 7.75 (dd, *J* = 1.2 Hz, *J* = 7.6Hz, 1H), 7.44 (td, *J* = 1.2 Hz, *J* = 7.6 Hz,1H), 7.19 (td, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 10 Hz, 1H), 6.61 (d, *J* = 8Hz, 1H), 6.50(d, *J* = 10 Hz, 1H), 2.55 (s, 3H), 1.07-1.15 (m, 6H), 2.44 (s , 3H);; ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.3,202.7, 182.8, 155.4, 149.3, 147.6, 132.1, 129.5, 129.3, 129.3, 124.1, 120.8, 108.9, 38.2, 35.1, 9.0, 8.5; IR (neat) 3441, 2976, 2365, 1633, 1585 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{18}H_{118}O_3N_2$: 310.3530; found: 310.3170.

***(E)*-2-Amino-3-isobutyryl-4-((2- isobutyrylphenyl) imino) cyclohexa-2,5-dien-1-one (2k):** Dark red colour soild; mp 126-128 °C, R_f 0.35; (hexanes : ethyl acetate, 80:20 v/v): ^1H NMR (400 MHz, DMSO-d_6) δ 8.15(s, 2H), 7.98 (dd, *J* = 0.8 Hz, *J* = 7.8 Hz, 1H), 7.74 (dd, *J* = 1.6 Hz, *J* = 7.6 Hz, 1H), 7.70 (dd, *J* = 1.2 Hz, *J* = 8 Hz,1H), 7.44-7.60 (m, 2H), 7.23 (td, *J* = 1.2 Hz, *J* = 7.6Hz, 1H), 7.21 (t, *J* =

0.8 Hz, 1H), 7.91 (d, *J* = 10 Hz, 1H), 6.70 (d, *J* = 0.8 Hz, 1H), 6.64 (d, *J* = 10 Hz, 1H), 3.76-3.89 (sep , 1H) 3.28-3.41 (sep , 1H) 1.01 (t, *J* = 6.8 Hz, 12H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ 208.0, 206.1, 182.6, 155.5, 148.5, 146.7, 132.3, 131.5, 130.1, 129.8, 128.4, 128.1, 123.9, 108.3, 38.5, 37.9, 19.0, 18.2; IR (neat) 3434, 2972, 2364, 1671, 1636, 1580, 975, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{20}H_{22}O_3N_2$: 338.4070; found: 338.1630.

(*Z*)-3-Acetyl-4-((2-acetyl-4-bromophenyl)imino)-2-amino-5-bromocyclohexa-2,5-dien-1-one (2l): Dark red colour soild; mp 125-127 °C, R_f 0.4; (hexanes : ethyl acetate, 80:20 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (s, 2H), 7.92 (d, *J* = 2 Hz, 1H), 7.43 (dd, *J* = 2 Hz, *J* = 8.4 Hz,1H), 7.39 (s, 1H), 6.75 (d, *J* = 8.8 Hz, 1H), 2.63 (s, 3H), 1.53 (s , 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 198.4, 196.9, 179.9, 153.9, 147.3, 135.0, 133.3, 133.1, 132.0, 128.2, 122.3, 117.2, 106.1, 30.3, 29.3; IR (neat) 3421, 2254, 1651, 1025, 1003, 826, 765, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{16}H_{12}O_3N_2$ Br_2Na: 460.9112; found: 460.9107.

(*E*)-5-Acetyl-6-((3-acetyl-[1,1'-biphenyl]-4-yl)imino)-4-amino-[1,1'-biphenyl]-3(6H)-one (2m): Dark red colour soild; mp 122-124 °C, R_f 0.4; (hexanes : ethyl acetate, 80:20 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (s, 2H), 8.00 (s 2H), 7.63-7.78 (m,5H), 7.46 (t, *J* = 8 Hz, 2H), 7.33-7.42 (m,4H), 6.85 (s, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 1.85 (s, 3H) 1.17 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 199.8, 197.1, 181.9, 157.7, 154.4, 147.8, 147.4, 138.4, 135.9, 135.8, 130.0, 129.8, 129.5, 128.9, 128.1, 127.8, 127.6, 127.3, 126.3, 125.2, 121.2, 107.5, 29.4, 13.0; IR (neat) 3434, 2370, 1636, 1036, 768, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{28}H_{23}O_3N_2$: 435.1699 ; found: 435.1703.

(*E*)-2-((3-Amino-2-cyano-4-oxocyclohexa-2,5-dien-1-ylidene)amino)benzonitrile (4a): Red colour soild; mp 117-119 °C, R_f 0.44; (hexanes : ethyl acetate, 60:40 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (s, 2H), 7.85 (dd, *J* = 0.8 Hz, *J* = 7.8 Hz 1H), 7.68 (td, *J* = 1.2 Hz, *J* = 7.6 Hz 1H), 7.33 (td, *J* = 0.8 Hz, *J* = 8 Hz 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 10.4 Hz, 1H), 6.71 (d, *J* = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 180.8, 153.9, 146.9, 141.0, 130.1, 129.7, 129.2, 127.2, 126.0, 124.9, 121.7, 112.1; IR (neat) 3479, 3369, 2369, 1662, 1627, 1340, 1230, 770 cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{14}H_8ON_4Na$: 271.0587; found: 271.0590.

(*E*)-2-Amino-3-chloro-4-((2-chlorophenyl) imino) cyclohexa-2,5-dien-1-one (4b): Red colour soild; mp 130-132 °C, R_f 0.47; (hexanes : ethyl acetate, 75:25 v/v): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 1H), 6.70 (t, *J* = 10.8 Hz, 2H), 6.36 (d, *J* = 10 Hz, 1H), 5.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 153.9, 146.9, 141.0, 130.1, 129.7, 129.2, 127.2, 126.0, 124.9, 121.7, 112.1; IR (neat) 3479, 3369, 2369, 1662, 1627, 1340, 1230, 770 cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{12}H_9ON_2Cl_2Na$: 267.0087; found: 267.0086.

(*E*)-2-((3-Amino-2-carbamoyl-4-oxocyclohexa-2,5-dien-1-ylidene)amino)benzamide (4c): Red colour soild; mp 136-138 °C, R_f 0.48; (hexanes : ethyl acetate, 65:35 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (s, 1H), 7.48-7.70 (m, 2H), 7.26-7.48 (m, 4H), 7.22 (t, *J* = 7.2 Hz 2H), 6.90 (d, *J* = 10 Hz 1H), 6.73 (d, *J* = 7.6 Hz 1H), 6.61 (d, *J* = 10 .4Hz 1H);^{13}CNMR (100MHz,DMSO-d_6); 182.2, 170.2, 168.7, 155.5, 149.0, 146.4, 132.0, 130.2, 129.4, 128.4, 128.3, 124.3, 121.6, 96.6;. IR (neat) 3434, 2250, 2124, 1659, 1028, 823, 763, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{14}H_{12}O_3N_4Na$: 307.0801; found: 307.0802. IR (neat) 3434, 2250, 2124, 1659, 1028, 823, 763, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{14}H_{12}O_3N_4Na$: 307.0801; found: 307.0802.

(*E*)-2-Amino-3-((E)-3-(4-bromophenyl)acryloyl)-4-((2-((E)-3-(4-bromophenyl)acryloyl)phenyl) imino) cyclohexa-2,5-dien-1-one (4d): Red colour soild; mp 138-140 °C R_f 0.56; (hexanes : ethyl acetate, 75:25 v/v): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 15.6 Hz, 1H), 7.67 (d, *J* = 7.2 Hz, 1H), 7.35-7.55 (m, 5H), 7.14-7.35 (m, 8H), 7.11 (d, *J* = 15.6 Hz, 2H), 6.92 (d, *J* = 10 Hz, 1H), 6.63 (d, *J* = 8 Hz, 2H), 6.5 (d, *J* = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.8, 192.0, 182.6, 156.1, 149.7, 147.5, 143.7, 138.3, 134.7, 134.0, 132.4, 132.2, 132.0, 130.4, 129.9, 129.8, 129.7, 129.6, 126.1, 125.2, 124.5, 123.8, 121.7, 110; IR (neat) 3435, 1738, 1578, 1241, 1044 cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{30}H_{20}O_3N_2$ Br_2Na: 636.9737; found: 636.9733.

(*Z*)-2-Amino-3-benzoyl-4-((2-benzoyl-4-iodophenyl) imino)-5-iodocyclohexa-2,5-dien-1-one (6a): Red colour soild; mp 125-127 °C, R_f 0.7; (hexanes : ethyl acetate, 75:25 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 (s, 2H), 7.57 (d, *J* = 2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.28-7.40 (m, 6H), 7.25 (t, *J* = 7.6 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 5.82 (d, *J* = 8.4 Hz, 1H) ; ^{13}C NMR (100 MHz, DMSO-d_6) δ 191.8, 191.3, 178.3, 157.2, 149.3, 147.4, 140.3, 140.2, 138.4, 138.2, 135.8, 132.8, 132.0, 129.0, 128.7, 128.4, 128.3, 128.0, 127.1, 124.9, 101.4, 88.7; IR (neat) 3410, 1590, 1268, 1120, 1039, cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{26}H_{17}O_3N_2I_2$: 658.2339; found: 658.9323.

(*E*)-3-Acetyl-4-((2-acetylphenyl)imino)-2-amino cyclo hexa-2,5-dien-1-one (6b): Red colour soild; mp 122-124 °C, R_f 0.42; (hexanes : ethyl acetate, 75:25 v/v): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.68 (dd, *J* = 0.8 Hz, *J* = 8 Hz, 1H), 7.43 (td, *J* = 1.2Hz, *J* = 7.6 Hz,1H), 7.18 (t, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 10 Hz, 1H), 6.59 (d, *J* = 8 Hz, 1H), 6.50 (d, *J* = 10 Hz, 1H), 4.11 (quin , *J* = 7.6 Hz,1H), 3.56 (quin, *J* = 8 Hz,1H), 1.79 (q , 6.8, 8H) 1.51-1.68 (m , 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.4, 205.5, 183.0, 155.7, 149.4, 147.1, 132.1, 131.8, 130.4, 129.4, 129.2, 124.1, 120.9, 109.6, 51.1, 49.4, 30.7, 29.9, 26.6, 26.3; IR (neat) 3435, 2944, 1632, 1582 cm^{-1}; HRMS (*m/z*): [M+H]$^+$ calcd for $C_{24}H_{26}O_3N_2Na$: 390.4830; found: 413.1834.

General procedure for the synthesis of iodo iminoquinones derivatives.

A reaction tube equipped with a magnetic stir bar was charged with 2-amino benzophenones **1e,1g** (0.5 mmol), IBX (2 equiv.) with I_2 (1equiv.) under open atmosphere at

room temperature then the solvent DMSO (3 mL) was added. The resulting mixture vigorous stirring (1000 rpm) and the progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the reaction mixture was quenched by slow addition of $NaHCO_3$ and combined organic layer was washed with $Na_2S_2O_3$ solution extracted with EtOAc (3×5mL). The combined organic layer dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel (hexanes/EtOAc = 10:1) to give the corresponding product (**8a, 8b)** as a red.

(*Z*)-2-Amino-5-iodo-4-((4-iodo-2-(4-methylbenzoyl) phenyl)imino)-3-(4-methylbenzoyl)cyclohexa-2,5-dien-1-one (8a): Red colour soild; mp 128-130 °C, R_f 0.48; (hexanes : ethyl acetate, 75:25 v/v): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.30-7.38 (m, 1H), 7.10 (d, *J* =8 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.90 (d, *J* = 8 Hz 2H), 5.96 (t, *J* = 7.6 Hz, 1H), 6.91; ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.5, 192.3, 178.4, 149.7, 148.4, 147.8, 143.7, 143.2, 140.7, 140.4, 139.4, 139.2, 135.9, 133.7, 129.7, 129.6, 129.2, 129.0, 127.6, 124.9, 103.3, 89.2, 21.8, 21.7; IR (neat) 3413, 2958, 1600, 1590, 1580, 1270, 1118 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{28}H_{21}O_3N_2I_2$: 686.2879; found: 686.9644.

(*Z*)-2-Amino-3-(4-(tert-butyl)benzoyl)-4-((2-(4-(tert-butyl)benzoyl)-4-iodophenyl)imino)-5-iodocyclohexa-2,5-dien-1-one (8b): Red colour soild; mp 131-133 °C, R_f 0.52; (hexanes : ethyl acetate, 70:30 v/v): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 2H), 7.57 (d, *J* = 2 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H), 7.28-7.40 (m, 6H), 7.25 (t, *J* = 7.6 Hz, 2H), 6.91 (d, *J* = 7.6 Hz, 2H), 5.82 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.8, 191.3, 178.3, 157.2, 149.3, 147.4, 140.3, 140.2, 138.4, 138.2, 135.8, 132.8, 132.0, 129.0, 128.7, 128.4, 128.3, 128.0, 127.1, 124.9, 101.4, 88; IR (neat) 3406, 2923, 1598, 1578, 1169 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{34}H_{33}O_3N_2I_2$: 770.4499; found: 771.0579.

(2-Amino-3-hydroxyphenyl)(phenyl)methanone (9): white soild; mp 148-150 °C, R_f 0.6; (hexanes : ethyl acetate, 60:40 v/v): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.64 (s, 2H), 7.59-7.66 (m,3H), 7.46-7.50 (m, 2H), 7.24 (d, *J* = 8.4 Hz), 6.95 (dd, *J* = 2.8 Hz, *J* = 8.8 Hz, 1H), 6.76 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 192.0, 150.9, 134.2, 130.0, 129.5, 126.5, 125.1, 124.7, 123.1, 115.3, 112.6 ; IR (neat) 3479, 3369, 2369, 1662, 1627, 1340, 1230, 770 cm^{-1}; HRMS (*m/z*): $[M+H]^+$ calcd for $C_{14}H_8ON_4Na$: 213.0587; found: 213.0590.

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17 When this reaction was carried out with different ketone in optimized condition, it gave only homo coupling products. For example, when we reacted **1a** with **1e** or **1b** with **1e,** both the reactions gave only homocoupling product.

18 When the domino reaction of **1a** was carried out with aliphatic amines (n-$BuNH_2$, methyl amine or *tert*-butylamine) under the optimized reaction condition, a series of inseparable mixture was observed in all reactions.

19 When the reaction mixture was analysed by GCMS (shimadzu GC-2010 plus-GCMS QP2010 ultra) one peak at 28 min, gave the M^+ peak at 227, which is corresponding to molecular weight of benzoquinone intermediate **10** molecular weight 227.

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