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A Green One-Pot Protocol for Regioselective Synthesis of New Substituted 7,8-Dihydrocinnoline-5(6*H*)-ones

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A simple regioselective synthesis of cinnoline derivatives was achieved by a one-pot three component synthetic methodology. New substituted 7,8-dihydrocinnolin-5(6*H*)-ones are prepared *via* one-pot three component reaction of arylglyoxals with 1,3-cyclohexanedione and dimedone in the presence of hydrazine hydrate in moderate to good yields.

Key Words : Arylglyoxal, 1,3-Cyclohexanedione, Cinnoline, Dimedone, Regioselective

Introduction

In recent years, the key constraints for the synthetic chemists are the use of hazardous solvents, expensive, and toxic reagents, multistep protocols, and generation of unwanted side-products.[1] Now a days, green chemistry has attained the status of a major scientific discipline, and it now encompasses wide areas of chemical enterprise and is an alternative way to reduce drastic requirements for reactions.[2] To find new alternatives for simple and eco-compatible protocols, chemists have adopted water as the solvent of choice in organic synthesis.[3] Water offers several practical advantages over conventional organic solvents such as easy availability, cheap, non-toxic, non-corrosive, non-flammable, and environmentally acceptable.[4,5] Furthermore, besides having a unique reactivity and selectivity, water also offers an easy separation.[6] The above advantages have been attributed to many factors, including the hydrophobic effect, enhanced hydrogen bonding in the transition state and the high cohesive energy density of water.[7-10]

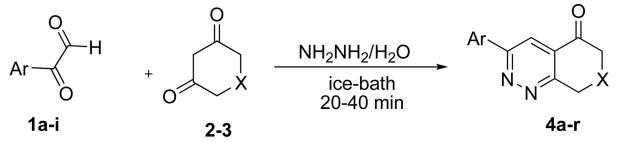
Due to growing environmental concerns, carrying out organic reactions in water has become highly desirable, and several reports of organic synthesis in water have appeared during the past decade.[11] Recently, a variety of organic transformations such as aldol reaction, allylation reaction, Diels-Alder reaction, Henry reaction, Michael reaction, Mannich reaction, and Pd-catalyzed coupling reactions have been reported in aqueous media.[12] Indeed, industry prefers to use water as a solvent rather than organic solvents. In the past decade there have been tremendous development in multi-component reactions and great efforts are being made to develop new multicomponent reactions (MCRs) in water.[13] They have become an increasingly powerful tool in organic, combinatorial, and medicinal chemistry because of their convergence, atomeconomy, multiple bond forming efficiency and other suitable characteristics from the green chemistry point of view.[14-16] These features make MCRs well-suited for the easy construction of diversified heterocyclic scaffolds.[17]

Cinnolines and their derivatives exhibit a broad range of biological activity, such as: anticancer, fungicidal, bactericidal, and anti-inflammatory properties.[18] Furthermore, compounds containing a cinnoline fragment demonstrate a series of interesting physical characteristics, such as luminescent and nonlinear optical properties.[19] Hence, the synthesis of cinnoline has been studied for many years.[20] Most syntheses of cinnolines involve arenediazonium salts,[21] arylhydrazones,[22] arylhydrazines,[23] and nitriles[24] as their starting materials. Recently, alkynyl-substituted aryltriazene was used as the precursor to prepare cinnoline,[25] however high temperatures or strong acidic conditions were still required. Palladium-catalyzed annulation of alkynes by functionally substituted aryl halides has been demonstrated to be a versatile methodology to construct a wide variety of complicated hetero- and carbocycles.[26] Cinnoline frameworks have been recently obtained *via* palladium catalyzed reaction of 2-iodotriazenes with internal alkynes.[27] These procedures often suffer from certain drawbacks such as multi step reactions, harsh reaction conditions and using expensive catalysts. Therefore, these reported annulation reactions prompted us to investigate a single green reaction to prepare cinnoline rings. Herein, we would like to introduce a novel and efficient one-pot protocol to regioselective synthesis of various substituted cinnoline derivatives by the reaction of arylglyoxals with 1,3-cyclohexanedione and dimedone in the presence of hydrazine hydrate in water.

Results and Discussion

Following our recent reports on the arylglyoxals mediated one-pot three component synthesis of pyridazine derivatives,[28] at this stage the synthesis of new substituted 7,8-dihydrocinnolin-5(6*H*)-one derivatives were reported.

Hence, arylglyoxals **1a-i** were reacted with 1,3-cyclohexanedione **2** and 7,7-dimethyl-1,3-cyclohexanedione (dimedone) **3** in the presence of hydrazine hydrate in water at



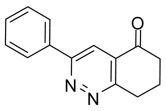
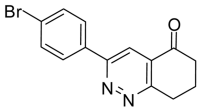
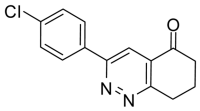
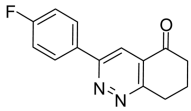
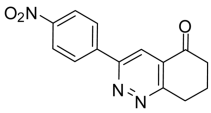
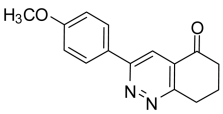
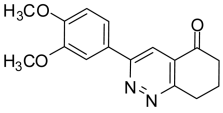
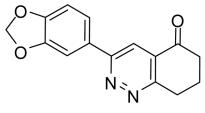
Ar=C_6H_5, 4-F-C_6H_4, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-CH_3O-C_6H_4, 4-NO_2-C_6H_4, 3,4-$(CH_3O)_2$-C_6H_3, 3,4-(OCH_2O)-C_6H_3, 4-OH-3-CH_3O-C_6H_3
X = CH_2 , $C(CH_3)_2$

Scheme 1. Synthesis of substituted 7,8-dihydrocinnoline-5(6*H*)-ones.

5-8 ºC (ice-bath) which led to form favor 3-aryl cinnoline products **4a-r** as sole regioisomers (Scheme 1).

All obtained cinnolines are listed in Table 1.

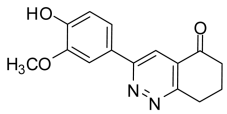
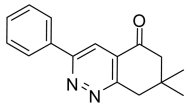
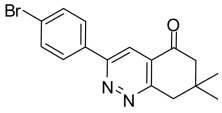
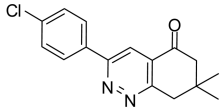
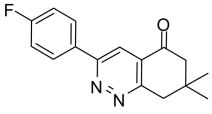
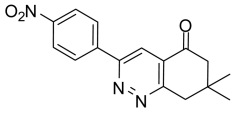
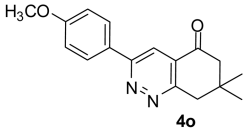
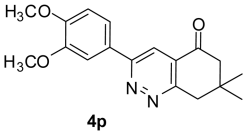
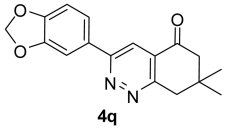
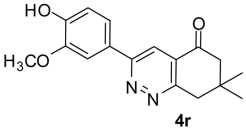
Table 1. List of substituted cinnolines

Entry	Cinnolone	Yield (%)
1	 **4a**	81
2	 **4b**	79
3	 **4c**	86
4	 **4d**	75
5	 **4e**	93
6	 **4f**	56
7	 **4g**	69
8	 **4h**	75

The structures of all synthesized cinnolines were characterized *via* ^{1}H-NMR, ^{13}C-NMR, FT-IR and Mass spectroscopies. In the ^{1}H-NMR spectra of these compounds, the CH on pyridazine ring is very deshielded and resonates at low field. In all compounds, the corresponding proton occurs at $\delta > 8$ ppm.

The regioselective formation of 3-aryl substituted cinnolines **4a-r** was unambiguously secured by X-ray crystal

Table 1. Continued

Entry	Cinnolone	Yield (%)
9	 **4i**	56
10	 **4j**	69
11	 **4k**	77
12	 **4l**	80
13	 **4m**	45
14	 **4n**	84
15	 **4o**	48
16	 **4p**	72
17	 **4q**	67
18	 **4r**	50

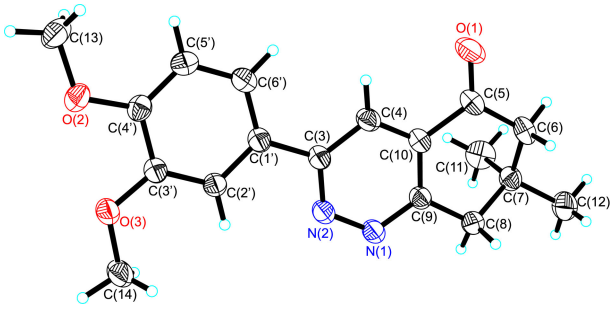


Figure 1. ORTEP representation of compound **4p**.

structure analysis of compound **4p** (Figure 1).[29]

A total plausible mechanism for regiselective formation of 3-arylcinnoline framework involves an initially Knoevenagel condensation between the more electrophilic formyl group of the arylglyoxals **1a-i** and the enolic form of cyclohexanedione **5** (path a) leading to form 1,4-dicarbonyl intermediate **6** followed by its dehydration reaction with hydrazine as shown in Scheme 2. Clearly the selectivity is driven by the enolization of the highly acidic dione by the hydrazine base, which competes with hydrazone formation, leading to the alternate 4-aryl isomers.

According to Carroti's report on the MAO inhibitory effect of cinnolones,[30] these new substituted cinnolones should be evaluated as new potential Monoamine Oxidase inhibitors MAOIs).

In conclusion, a green, efficient and convenient method for the regioselective preparation of new 3-aryl substituted 7,8-dihydrocinnolin-5(6*H*)-ones in water is reported. To the best of our knowledge, there is no reports in the literature about the synthesis of cinnoline rings *via* arylglyoxals. Additionally, this new protocol provides an opportunity to use water and avoid environmentally harmful conventional organic solvents, easy work up and reduced waste production by the lack of catalyst or additive agent.

Experimental

Melting Points were measured on an Electrothermal 9200 apparatus and are uncorrected.

^{1}H (300 MHz) and ^{13}C (75.5 MHz) NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer in $CDCl_3$ using TMS as the internal reference. FT-IR spectra were recorded *via* a Thermonicolet (Nexus 670) spectrometer using KBr discs. Mass spectra were recorded on a Varian Matt 311 spectrometer and relative abundances of fragments are quoted in parentheses after the *m/z* values. The chemicals used in this work were obtained from Acros and Merck companies and were used without purification.

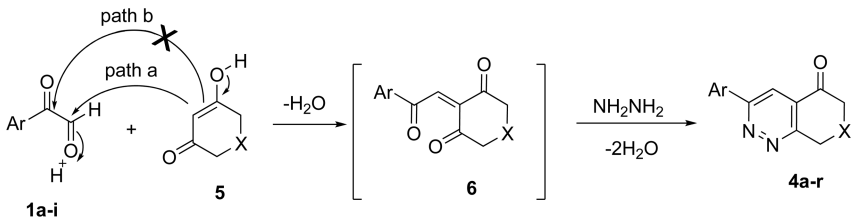
General Procedure for the Synthesis of 3-Aryl-7,8-dihydrocinnolin-5(6*H*)-ones (4a-i). To a mixture of 1,3-cyclohexanedione (1 mmol) and arylglyoxal (1 mmol) in water (5 mL), was successively added hydrazine hydrate 100% (3 mmol) at 5-8 °C (ice-bath). The reaction mixture was stirred for 20-40 minutes. The resulting solid was filtered then recrystallized from ethanol to obtain pure products in moderate to excellent yields (56-93%).

3-Phenyl-7,8-dihydrocinnolin-5(6*H*)-one (4a): Yellow crystals, 81%, mp 109-110 °C. ^{1}H-NMR ($CDCl_3$) δ 8.29 (s, 1H, Ar), 8.15 (dd, J_1 = 7.8 Hz, J_2 = 2.1 Hz, 2H, Ar), 7.52-7.58 (m, 3H, Ar), 3.47 (t, J = 6 Hz, 2H, CH_2), 2.82 (t, J = 6 Hz, 2H, CH_2), 2.31 (quin, J = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 197.0, 160.3, 159.8, 135.3, 130.5, 129.1, 128.1, 127.0, 120.2, 38.7, 29.1, 21.3. FT-IR ν_{max} 3068, 2949, 2881, 1697, 1582, 1402, 1369, 1329, 1203, 1179, 1138, 1106, 1032, 1016, 909, 870, 780, 697, 671, 551 cm^{-1}. Mass *m/z* (%): 224 [M$^+$, (24)], 167 (33), 153 (23), 139 (100), 115 (20), 102 (24), 87 (18), 77 (33), 63 (43), 51 (54).[30]

3-(4-Bromophenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4b): Yellow crystals, 79%, mp 198 °C. ^{1}H-NMR ($CDCl_3$) δ 8.24 (s, 1H, Ar), 8.02 (d, J = 8.4 Hz, 2H, Ar), 7.67 (d, J = 8.4 Hz, 2H, Ar), 3.45 (t, J = 6 Hz, 2H, CH_2), 2.81 (t, J = 6 Hz, 2H, CH_2), 2.30 (quin, J = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 197.2, 160.6, 158.6, 134.5, 132.3, 128.6, 128.4, 125.1, 119.1, 38.7, 29.4, 21.3. FT-IR ν_{max} 3091, 3057, 2949, 2882, 1704, 1587, 1489, 1398, 1329, 1203, 1180, 1068, 1002, 855, 828, 724, 556 cm^{-1}. Mass *m/z* (%): 304 [M$^+$+2, (24)], 302 [M$^+$, (53)], 220 (26), 165 (86), 152 (100), 139 (57), 113 (64), 102 (34), 83 (52), 75 (75), 69 (55), 63 (83), 55 (75).

3-(4-Chlorophenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4c): Yellow crystals, 86%, mp 196 °C. ^{1}H-NMR ($CDCl_3$) δ 8.22 (s, 1H, Ar), 8.08 (d, J = 8.4 Hz, 2H, Ar), 7.51 (d, J = 8.4 Hz, 2H, Ar), 3.44 (t, J = 6 Hz, 2H, CH_2), 2.80 (t, J = 6 Hz, 2H, CH_2), 2.30 (quin, J = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 197.2, 160.6, 158.5, 136.7, 134.0, 129.3, 128.5, 128.2, 119.1, 38.7, 29.4, 21.3. FT-IR ν_{max} 3093, 3054, 2950, 1704, 1589, 1491, 1399, 1328, 1202, 1180, 1084, 1004, 856, 832, 731, 555 cm^{-1}. Mass *m/z* (%): 260 [M$^+$+2, (20)], 258 [M$^+$, (64)], 229 (16), 202 (19), 188 (18), 174 (35), 165 (52), 152 (30), 139 (100), 113 (20), 75 (26), 57 (33), 43 (36).

3-(4-Fluorophenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4d): Pale yellow crystals, 75%, mp 170 °C. ^{1}H-NMR (CD_2Cl_2) δ 8.23 (s, 1H, Ar), 8.14-8.20 (m, 2H, Ar), 7.23-7.30 (m, 2H, Ar), 3.42 (t, J = 5.7 Hz, 2H, CH_2), 2.80 (t, J = 5.7 Hz, 2H, CH_2), 2.30 (quin, J = 5.7 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ



Scheme 2. Proposed mechanism for the synthesis of 3-aryl substituted cinnolines.

197.4, 165.8, 162.5, 160.6, 158.5, 132.3, 128.9, 128.8, 128.4, 118.7, 116.1, 115.8, 38.7, 29.5, 21.4. FT-IR ν_{max} 3061, 2947, 2889, 1699, 1602, 1509, 1400, 1365, 1329, 1237, 1222, 1160, 1180, 1138, 1105, 903, 847, 811, 728, 559 cm^{-1}. Mass *m/z* (%): 242 [M^+, (35)], 185 (34), 171 (17), 165 (42), 157 (100), 132 (24), 120 (23), 107 (16), 95 (24), 75 (42), 63 (24), 51 (27).

3-(4-Nitrophenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4e): Orange crystals, 93%, mp 236 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.40 (d, *J* = 8.7 Hz, 2H, Ar), 8.34 (d, *J* = 8.7 Hz, 2H, Ar), 8.35 (s, 1H, Ar), 3.50 (t, *J* = 6 Hz, 2H, CH_2), 2.84 (t, *J* = 6 Hz, 2H, CH_2), 2.34 (quin, *J* = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 196.9, 161.6, 157.5, 149.0, 141.5, 128.5, 127.8, 124.3, 119.8, 38.6, 29.5, 21.3. FT-IR ν_{max} 3062, 2924, 2853, 1701, 1597, 1511, 1400, 1340, 1251, 1203, 1180, 1103, 872, 846, 756, 723, 696, 554 cm^{-1}. Mass *m/z* (%): 269 [M^+, (100)], 240 (28), 195 (29), 185 (35), 165 (76), 152 (57), 139 (61), 127 (30), 89 (23), 63 (30).

3-(4-Methoxyphenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4f): Pale yellow crystals, 56%, mp 121 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.20 (s, 1H, Ar), 8.11 (d, *J* = 8.4 Hz, 2H, Ar), 7.05 (d, *J* = 8.4 Hz, 2H, Ar), 3.89 (s, 3H, OCH_3), 3.42 (t, *J* = 6 Hz, 2H, CH_2), 2.79 (t, *J* = 6 Hz, 2H, CH_2), 2.29 (quin, *J* = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 197.6, 161.5, 159.6, 159.2, 128.5, 128.3, 128.1, 118.6, 114.5, 55.4, 38.7, 29.4, 21.4. FT-IR ν_{max} 3060, 2957, 2839, 1700, 1606, 1583, 1510, 1405, 1251, 1176, 1038, 1019, 832, 556 cm^{-1}. Mass *m/z* (%): 254 [M^+, (15)], 170 (23), 155 (47), 139 (28), 127 (79), 115 (33), 101 (34), 89 (64), 77 (89), 63 (100), 51 (96).

3-(3,4-Dimethoxyphenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4g): Yellow crystals, 69%, mp 191 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.24 (s, 1H, Ar), 7.88 (s, 1H, Ar), 7.62 (d, *J* = 8.4 Hz, 1H, Ar), 7.00 (d, *J* = 8.4 Hz, 1H, Ar), 4.01 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 3.44 (t, *J* = 6 Hz, 2H, CH_2), 2.81 (t, *J* = 6 Hz, 2H, CH_2), 2.30 (quin, *J* = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 196.8, 159.6, 159.2, 151.5, 149.7, 129.4, 127.5, 120.1, 120.0, 111.2, 109.6, 56.1, 56.0, 38.7, 29.0, 21.2. FT-IR ν_{max} 3060, 2945, 2894, 2835, 1700, 1596, 1517, 1458, 1404, 1340, 1259, 1219, 1142, 1019, 916, 848, 763, 556 cm^{-1}. Mass *m/z* (%): 284 [M^+, (81)], 269 (13), 255 (10), 238 (15), 200 (13), 185 (16), 165 (16), 148 (25), 128 (37), 115 (45), 107 (100), 91 (25), 77 (42), 55 (52), 43 (54).

3-(3,4-Methylenedioxyphenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4h): Yellow crystals, 75%, mp 150 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.25 (s, 1H, Ar), 7.71 (s, 1H, Ar), 7.62 (dd, J_1 = 8.1 Hz, J_2 = 1.8 Hz, 1H, Ar), 6.96 (d, *J* = 8.1 Hz, 1H, Ar), 6.07 (s, 2H, CH_2), 3.49 (t, *J* = 6 Hz, 2H, CH_2), 2.82 (t, *J* = 6 Hz, 2H, CH_2), 2.31 (quin, *J* = 6 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 196.7, 159.7, 159.2, 150.0, 148.8, 129.3, 129.2, 121.6, 120.1, 108.8, 107.2, 101.7, 38.6, 28.9, 21.2. FT-IR ν_{max} 2956, 2900, 1697, 1636, 1596, 1501, 1443, 1406, 1347, 1245, 1211, 1104, 1037, 936, 871, 825, 555 cm^{-1}. Mass *m/z* (%): 268 [M^+, (100)], 239 (32), 211 (75), 198 (72), 186 (50), 153 (62), 126 (66), 76 (27), 63 (32).

3-(4-Hydroxy-3-methoxyphenyl)-7,8-dihydrocinnolin-5(6*H*)-one (4i): Yellow crystals, 56%, mp 200 (dec) ºC. ^{1}H-NMR ($CDCl_3$) δ 8.33 (s, 1H, Ar), 7.92 (s, 1H, Ar), 7.56 (d, *J* = 8.1 Hz, 1H, Ar), 7.06 (d, *J* = 8.1 Hz, 1H, Ar), 5.96 (bs, 1H, OH), 4.03 (s, 3H, OCH_3), 3.50 (t, *J* = 5.7 Hz, 2H, CH_2), 2.82 (t, *J* = 5.7 Hz, 2H, CH_2), 2.31 (quin, *J* = 5.7 Hz, 2H, CH_2). ^{13}C-NMR ($CDCl_3$) δ 197.4, 159.7, 159.1, 148.1, 147.2, 128.7, 127.6, 120.5, 119.0, 114.8, 109.2, 56.2, 38.7, 29.3, 21.3. FT-IR ν_{max} 3422, 3106, 3033, 2949, 2830, 1699, 1591, 1534, 1413, 1353, 1299, 1269, 1206, 1167, 1137, 1051, 863, 813, 785, 555 cm^{-1}. Mass *m/z* (%): 270 [M^+, (100)], 200 (28), 186 (29), 171 (40), 151 (62), 128 (28), 115 (68), 89 (27), 77 (31), 63 (46), 55 (56).

General Procedure for the Synthesis of 3-Aryl-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one Derivatives (4j-r). A mixture of dimedone (1 mmol), arylglyoxal (1 mmol) and hydrazine hydrate 100% (3 mmol) in water (5 mmol) was stirred at 5-8 ºC (ice-bath) for 20-40 minutes. After the appropriate time, the solids were filtered and recrystallized from ethanol to obtain pure products in moderate to excellent yields (45-84%).

3-Phenyl-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4j): Yellow crystals, 69%, mp 112-114 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.32 (s, 1H, Ar), 8.12-8.18 (m, 2H, Ar), 7.53-7.58 (m, 3H, Ar), 3.38 (s, 2H, CH_2), 2.67 (s, 2H, CH_2), 1.18 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 195.7, 160.1, 158.8, 155.5, 136.6, 131.4, 129.4, 127.2, 122.4, 52.0, 41.4, 33.1, 28.2. FT-IR ν_{max} 3067, 2958, 2883, 1702, 1590, 1455, 1401, 1228, 1106, 914, 770, 689, 594 cm^{-1}. Mass *m/z* (%): 252 [M^+, (87)], 209 (31), 181 (51), 167 (36), 152 (26), 139 (100), 114 (34), 102 (34), 89 (34), 77 (33), 63 (26), 51 (50).

3-(4-Bromophenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4k): Yellow crystals, 77%, mp 166-167 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.24 (s, 1H, Ar), 8.03 (d, *J* = 8.4 Hz, 2H, Ar), 7.68 (d, *J* = 8.4 Hz, 2H, Ar), 3.34 (s, 2H, CH_2), 2.66 (s, 2H, CH_2), 1.17 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 197.3, 159.4, 158.6, 134.4, 132.3, 128.4, 128.0, 125.2, 119.0, 52.1, 43.0, 33.1, 28.2. FT-IR ν_{max} 3059, 2957, 2929, 2870, 1702, 1586, 1398, 1366, 1220, 1066, 1002, 849, 829, 727 cm^{-1}. Mass *m/z* (%): 332 [M^++2, (5)], 330 [M^+, (5)], 165 (24), 152 (24), 139 (100), 113 (42), 101 (39), 87 (60), 75 (79), 63 (82), 55 (87).

3-(4-Chlorophenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4l): Yellow crystals, 80%, mp 148 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.34 (s, 1H, Ar), 8.11 (d, *J* = 8.4 Hz, 2H, Ar), 7.54 (d, *J* = 8.4 Hz, 2H, Ar), 3.41 (s, 2H, CH_2), 2.68 (s, 2H, CH_2), 1.19 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 196.1, 159.1, 158.9, 137.6, 132.9, 130.6, 129.6, 128.4, 121.1, 52.0, 41.9, 33.1, 28.2. FT-IR ν_{max} 3061, 2958, 2931, 1702, 1592, 1401, 1222, 1086, 1007, 847, 832 cm^{-1}. Mass *m/z* (%): 288 [M^++2, (63)], 286 [M^+, (100)], 271 (8), 257 (94), 243 (29), 230 (8), 215 (28), 180 (20), 174 (94), 165 (31), 139 (92).

3-(4-Fluorophenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4m): Pale yellow crystals, 45%, mp 174-175 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.26 (s, 1H, Ar), 8.10-8.20 (m, 2H, Ar), 7.19-7.27 (m, 2H, Ar), 3.36 (s, 2H, CH_2), 2.66 (s, 2H, CH_2), 1.18 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 196.1, 166.4, 163.0, 159.0, 158.9, 130.6, 129.6, 129.3, 129.2, 121.0, 116.6, 116.3, 52.0, 41.9, 33.1, 28.2. FT-IR ν_{max} 3066, 2961, 2930, 2870, 1731, 1588, 1488, 1384, 1240, 1097, 1077,

1037, 1006, 824, 786, 494 cm^{-1}. Mass *m/z* (%): 270 [M^+, (38)], 199 (16), 183 (20), 157 (100), 133 (20), 120 (24), 95 (17), 75 (20), 63 (17), 55 (23).

3-(4-Nitrophenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4n): Orange crystals, 84%, mp 222-223 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.41 (d, *J* = 8.7 Hz, 2H, Ar), 8.35 (d, *J* = 8.7 Hz, 2H, Ar), 8.33 (s, 1H, Ar), 3.38 (s, 2H, CH_2), 2.68 (s, 2H, CH_2), 1.19 (s, 6H, 2×CH_3). ^{13}C-NMR (DMSO-d_6) δ 197.9, 161.1, 157.4, 142.0, 128.7, 128.1, 125.2, 124.5, 120.1, 51.6, 42.8, 33.1, 28.1. FT-IR ν_{max} 3076, 2956, 2873, 1706, 1593, 1511, 1475, 1405, 1341, 1252, 1169, 1108, 906, 852, 693 cm^{-1}. Mass *m/z* (%): 297 [M^+, (100)], 280 (30), 251 (53), 185 (70), 165 (40), 149 (82), 139 (57), 69 (34), 57 (59), 43 (65).

3-(4-Methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4o): Pale yellow crystals, 48%, mp 147 ºC. ^{1}H-NMR (CD_2Cl_2) δ 8.20 (s, 1H, Ar), 8.13 (d, *J* = 8.7 Hz, 2H, Ar), 7.09 (d, *J* = 8.7 Hz, 2H, Ar), 3.91 (s, 3H, OCH_3), 3.30 (s, 2H, CH_2), 2.64 (s, 2H, CH_2), 1.17 (s, 6H, 2×CH_3). ^{13}C-NMR (CD_2Cl_2) δ 197.8, 161.4, 159.0, 158.6, 128.4, 128.2, 127.5, 117.8, 114.3, 55.3, 52.0, 43.1, 32.8, 27.9. FT-IR ν_{max} 3055, 3009, 2955, 2932, 2871, 1701, 1605, 1510, 1403, 1305, 1249, 1229, 1173, 1022, 833, 771, 584 cm^{-1}. Mass *m/z* (%): 282 [M^+, (100)], 253 (9), 239 (26), 226 (23), 211 (48), 197 (23), 170 (32), 155 (27), 135 (23), 127 (23).

3-(3,4-Dimethoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4p): Yellow crystals, 72%, mp 172 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.27 (s, 1H, Ar), 7.89 (s, 1H, Ar), 7.63 (d, *J* = 8.1 Hz, 1H, Ar), 7.01 (d, *J* = 8.1 Hz, 1H, Ar), 4.01 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 3.35 (s, 2H, CH_2), 2.66 (s, 2H, CH_2), 1.18 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 195.8, 159.4, 158.2, 152.2, 149.9, 130.3, 126.2, 122.0, 120.5, 111.2, 109.7, 56.3, 56.1, 52.0, 41.5, 33.1, 28.2. FT-IR ν_{max} 3082, 2991, 2939, 2868, 2834, 1703, 1602, 1516, 1451, 1423, 1403, 1263, 1229, 1214, 1144, 1023, 869 cm^{-1}. Mass *m/z* (%): 312 [M^+, (100)], 297 (22), 280 (16), 266 (16), 251 (35), 241 (21), 200 (14), 185 (17), 165 (19), 152 (12), 139 (16), 128 (20), 43 (26).

3-(3,4-Methylenedioxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4q): Yellow crystals, 67%, mp 168 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.39 (s, 1H, Ar), 7.72 (s, 1H, Ar), 7.65 (d, *J* = 8.4 Hz, 1H, Ar), 6.98 (d, *J* = 8.4 Hz, 1H, Ar), 6.09 (s, 2H, CH_2), 3.47 (s, 2H, CH_2), 2.69 (s, 2H, CH_2), 1.19 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 197.0, 159.2, 158.5, 150.0, 148.7, 129.2, 124.2, 123.5, 121.7, 108.8, 107.2, 101.6, 52.1, 42.6, 33.0, 28.2. FT-IR ν_{max} 2955, 2924, 1700, 1635, 1598, 1503, 1448, 1402, 1245, 1105, 1033, 929, 808 cm^{-1}. Mass *m/z* (%): 296 [M^+, (98)], 253 (12), 225 (24), 191 (44), 184 (33), 167 (12), 149 (100), 126 (40), 91 (14), 63 (44), 43 (30).

3-(4-Hydroxy-3-methoxyphenyl)-7,7-dimethyl-7,8-dihydrocinnolin-5(6*H*)-one (4r): Yellow crystals, 50%, mp 127 ºC. ^{1}H-NMR ($CDCl_3$) δ 8.24 (s, 1H, Ar), 7.91 (s, 1H, Ar), 7.57 (d, *J* = 8.4 Hz, 1H, Ar), 7.06 (d, *J* = 8.4 Hz, 1H, Ar), 5.96 (bs, 1H, OH), 4.02 (s, 3H, OCH_3), 3.32 (s, 2H, CH_2), 2.65 (s, 2H, CH_2), 1.17 (s, 6H, 2×CH_3). ^{13}C-NMR ($CDCl_3$) δ 197.9, 159.0, 158.5, 148.0, 147.2, 127.9, 127.6, 120.4, 118.2, 114.8, 109.2, 56.1, 52.2, 43.2, 33.0, 28.2. FT-IR ν_{max} 3390, 3063, 3008, 2951, 2865, 2631, 1703, 1589, 1514, 1460, 1408, 1335, 1275, 1208, 1128, 1029, 872, 796 cm^{-1}. Mass *m/z* (%): 298 [M^+, (7)], 297 (8), 280 (17), 265 (13), 251 (32), 237 (12), 202 (11), 167 (18), 149 (49), 115 (16), 97 (24), 83 (37), 69 (73), 57 (83), 43 (100).

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