Molecular Iodine: A Versatile Catalyst for the Synthesis of 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones

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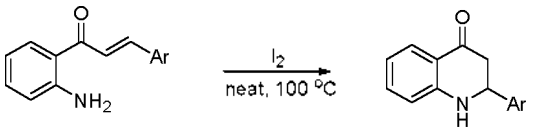
2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones are of considerable interest as they possess a wide range of pharmacological and therapeutic properties such as antitumor,[1a] anthelmintic activities.[1b] In addition, they are also useful synthetic intermediates for various pharmaceuticals and active compounds.[2] The formation of 2,3-dihydroquinolin-4(1*H*)-ones is generally accomplished by isomerization of substituted 2'-aminochalcones in the presence of NaOEt,[3a] H_3PO_4,[3b] montmorillonite,[3c] $InCl_3$,[3d] silica gel supported $TaBr_5$,[3e] silica gel supported $NaHSO_4$,[3f] $ZnCl_2$,[3g] Silica-supported $Yb(OTf)_3$,[3h] PEG-400,[3i] alumina supported-$CeCl_3{\cdot}7H_2O$-NaI.[3j] However, most of these procedures have signicant drawbacks such as long reaction times, low yields, harsh reaction conditions, tedious workup procedures, use of environmentally toxic reagents or media. Thus, there is still need of a simple and general procedure for synthesis of 2,3-dihydroquinolin-4(1*H*)-ones under mild conditions.

In recent years, the use of molecular iodine in organic synthesis has received considerable attention. Because of numerous advantages associated with this eco-friendly element, iodine has been explored as a powerful catalyst for various organic transformations.[4] We now report a highly efficient procedure for the preparation of 2,3-dihydroquinolin-4(1*H*)-ones using I_2 as an efficient and versatile catalyst under solvent-free conditions (Scheme 1).



1 2

Scheme 1

Table 1. Temperature optimization for the synthesis of 2-phenyl-2,3-dihydroquinolin-4(1*H*)-one[a]

Entry	Temp./°C	Time/h	Yield/%[b]
1	60	6	61
2	70	6	66
3	80	5	72
4	90	4	84
5	100	3	92
6	110	3	91
7	120	3	92

[a]Reaction conditions: (*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one (1 mmol); I_2 (0.1 mmol); solvent-free. [b]Isolated yield.

Initially, to optimize the reaction temperature, the isomerization of (*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one to the corresponding 2-phenyl-2,3-dihydroquinolin-4(1*H*)-ones was studied under solvent-free conditions in the presence of 10 mol% I_2 at different temperatures. The results were summarized in Table 1. As shown in Table 1, the reaction at 100 °C proceeded in highest yield.

The effect of amount of catalyst on the conversion and rate of the reaction was studied by varying the amount of I_2 under solvent-free conditions at 100 °C (Table 2). It was found that 10 mol% of I_2 was sufficient to carry out this reaction smoothly. An increase in the amount of I_2 to more than 10 mol% showed no substantial improvement in the yield, whereas the yield was reduced by decreasing the amount of I_2 to 5 mol%.

Based on the optimized reaction conditions, a range of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones (**2**) was synthesized

Table 2. The amounts of catalyst optimization for the synthesis of 2-phenyl-2,3-dihydroquinolin-4(1*H*)-one[a]

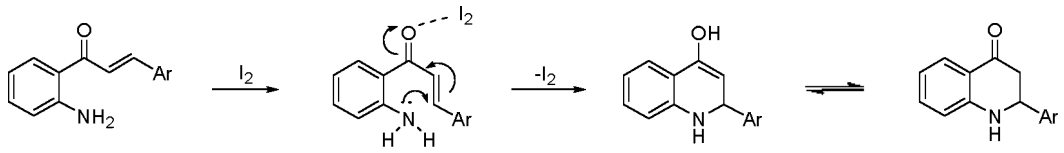
Entry	Amounts of I_2/mol%	Time/h	Yield/%[b]
1	0	10	0
2	5	5	71
3	10	3	92
4	15	3	92
5	20	2	89
6	25	2	92

[a]Reaction conditions: (*E*)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one (1 mmol); I_2 (0.1 mmol); solvent-free; 100 °C. [b]Isolated yield.

Table 3. Synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones

Entry	Ar	Time/h	Product	Yield /%[a]
1	Ph	3	**2a**	92
2	4-$NO_2C_6H_4$	4	**2b**	86
3	4-ClC_6H_4	4	**2c**	85
4	4-$MeOC_6H_4$	3	**2d**	92
5	4-$N(Me)_2C_6H_4$	3	**2e**	93
6	3-$NO_2C_6H_4$	4	**2f**	89
7	2-ClC_6H_4	4	**2g**	95
8	2,6-$(MeO)_2C_6H_3$	3	**2h**	88
9	2,4-$(Cl)_2C_6H_3$	3	**2i**	93
10	3,4-$(Cl)_2C_6H_3$	3	**2j**	91

[a]Isolated yield.



Scheme 2

by the isomerization of 2'-aminochalcones (**1**). The reaction proceeded at 100 °C within 4 hour in excellent yields after the addition of 10 mol% I_2. (Table 3). The structures of the products were established from their spectral properties (IR, ^{1}H NMR, MS and elemental analysis) and also by comparison with available literature data.

In conclusion, we have described a convenient route to 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones from 2'-aminochalcones under solvent-free conditions in the presence of I_2 (10 mol%) at 100 °C. The simple experimental procedure, solvent-free reaction conditions, utilization of an inexpensive and readily available catalyst, short period of conversion and excellent yields are the advantages of the present method.

Experimental Section

A mixture of 2'-aminochalcones (1 mmol) and I_2 (0.1 mmol) was heated at 100 °C for the appropriate time (see Table 3). The reaction was monitored by TLC. After completion, the mixture was treated with aqueous $Na_2S_2O_3$ solution, extracted with diethyl ether (3 × 10 mL), filtered and the solvent evaporated in vacuo. Products **2** were puried by silica gel column chromatography using hexane-diethyl acetate (10:1) as eluent.

2-(2,4-dichlorophenyl)-2,3-dihydroquinolin-4(1*H*)-one (2i). Yellow semi-solid. IR (cm^{-1}): 3341 (NH), 1650 (C=O). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, 1H, *J* = 1.4 Hz), 7.81 (dd, 1H, *J* = 1.0, 7.6 Hz), 7.62-7.50 (m, 2H), 7.26 (dd, 1H, *J* = 1.4, 8.0 Hz), 6.80-6.65 (m, 2H), 4.65 (br s, 1H), 5.14 (dd, 1H, *J* = 4.4, 13.6 Hz), 2.88-2.82 (m, 2H); MS *m/z*: 291 (M^+); Anal. calcd for $C_{15}H_{11}Cl_2NO$: C 61.67, H 3.79, N 4.79; found: C 61.47, H 3.88, N 4.85.

2-(3,4-dichlorophenyl)-2,3-dihydroquinolin-4(1H)-one (2j). Yellow semi-solid. IR (cm^{-1}): 3312 (NH), 1662 (C=O). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (dd, 1H, *J* = 1.0, 7.6 Hz), 7.55-7.42 (m, 2H), 7.23-7.02 (m, 2H), 6.75-6.58 (m, 2H), 5.08 (dd, 1H, *J* = 4.6, 13.2 Hz), 4.58 (br s, 1H), 2.85-2.79 (m, 2H); MS *m/z*: 291 (M^+); Anal. calcd for $C_{15}H_{11}Cl_2NO$: C 61.67, H 3.79, N 4.79; found: C 61.52, H 3.70, N 4.72.

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