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Synthesis of 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones Using Wet Cyanuric Chloride Under Solvent-Free Conditions

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A simple and facile synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones has been accomplished by isomerization of substituted 2'-aminochalcones under solvent-free conditions in the presence of wet-cyanuric chloride as a catalyst.

Key Words: 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones, Cyanuric chloride, 2'-Aminochalcones, Solvent-free.

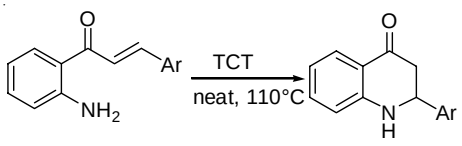
INTRODUCTION

2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones are important heterocycles that are known to possess multiple biological activities such as antitumor[1a], anthelmintic activities[1b]. In addition, these compounds are also useful synthetic intermediates for various pharmaceuticals and active compounds[2]. The formation of 2-aryl-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, *etc*.

Recently, 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride, TCT) has emerged as an inexpensive and easily available reagent in organic synthesis[4]. In this paper, we wish to report, a simple and facile synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones by isomerization of substituted 2'-aminochalcones under solvent-free conditions in the presence of wet-cyanuric chloride as catalyst (**Scheme-I**).

EXPERIMENTAL

NMR spectra were determined on Bruker AV-400 spectrometer at room temperature using TMS as internal standard, coupling constants (*J*) were measured in Hz; elemental analysis were performed by a Vario-III elemental analyzer; melting points were determined on a XT-4 binocular microscope and were uncorrected; commercially available reagents were used throughout without further purification unless otherwise stated.



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Scheme-I

General procedure for the preparation of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones: A mixture of 2'-aminochalcones (1 mmol), cyanuric chloride (0.1 mmol) and H_2O (3 drops) were mixed and stirred for 5 min at room temperature and then temperature was raised to 110 ºC and maintained for the appropriate time (Table-2). After completion of the reaction (monitored by TLC), the reaction mixture was diluted with water (15 mL) and stirred for 10 min in 80 ºC. The resulting mixture was extracted with diethyl ether (3 × 10 mL), filtered and the solvent evaporated *in vacuo*. Products were puried by silica gel column chromatography using hexane-diethyl acetate (10:1) as eluent. The spectral data of some new 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones are given below:

2-(2,6-Dibromophenyl)-2,3-dihydroquinolin-4(1*H*)-one (2i): Yellow semi-solid. IR (KBr, ν_{max}, cm^{-1}): 3309 (NH), 1612 (C=O). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.88 (dd, 1H, *J* = 2.0, 10.0 Hz), 7.42-7.02 (m, 4H), 6.84-6.80 (m, 1H), 6.68 (d, 1H, *J* = 8.0 Hz), 5.52 (dd, 1H, *J* = 4.0, 12.0 Hz), 4.42 (br s, 1H), 2.59-2.64 (m, 2H); MS m/z: 381 (M^+); Anal. calcd. (%) for $C_{15}H_{11}NOBr_2$: C 47.28, H 2.91, N 3.68; found (%): C 47.33, H 3.05, N 3.52.

2-(3,4-Dichlorophenyl)-2,3-dihydroquinolin-4(1*H*)-one (2j): Yellow semi-solid. IR (KBr, ν_{max}, cm^{-1}): 3312 (NH), 1662 (C=O). ^1H 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* = 4.4, 13.2 Hz), 4.58 (br s, 1H), 2.85-2.79 (m, 2H); MS m/z: 291 (M^+); Anal. calcd. (%) for $C_{15}H_{11}NOCl_2$: C 61.67, H 3.79, N 4.79; found (%): C 61.52, H 3.70, N 4.72.

RESULTS AND DISCUSSION

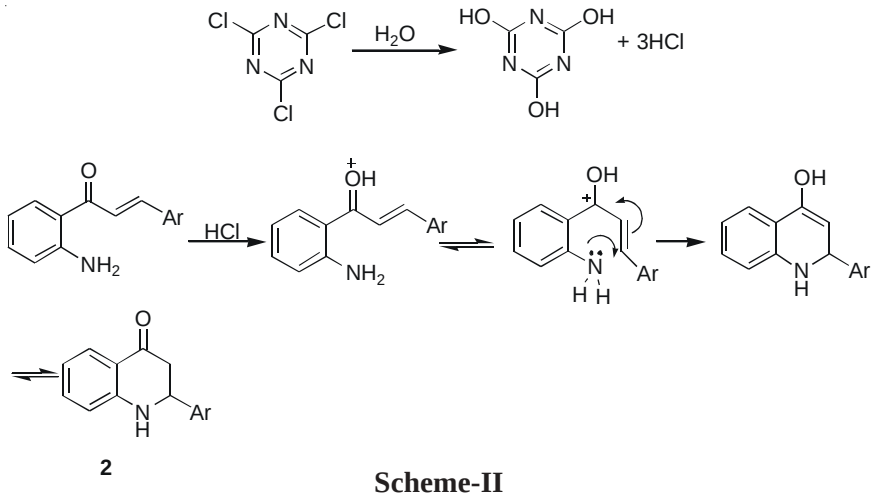
In order to optimize the reaction conditions, we first examined the amount of catalyst and the reaction temperature, the isomerization of (E)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one to the corresponding 2-phenyl-2,3-dihydroquinolin-4(1*H*)-one was studied under solvent-free conditions in the presence of wet-cyanuric chloride at different temperatures. The results are summarized in Table-1. As shown in Table-1, the reaction using 10 mol % cyanuric chloride at 110 °C proceeded in highest yield (Table-1).

Based on the optimized reaction conditions, a range of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones (**2**) was synthesized by the isomerization of 2'-aminochalcones (**1**). The reaction proceeded at 110 ºC within 1.5 h in excellent yields after the addition of 10 mol % cyanuric chloride (Table-2). The structures of the products were established from their spectral properties (IR, ^1H NMR, MS and elemental analysis) and also by comparison with available literature data.

TABLE-1
AMOUNTS OF CATALYST AND TEMPERATURE OPTIMIZATION FOR THE SYNTHESIS OF 2-PHENYL-2,3-DIHYDRO QUINOLIN-4(1*H*)-ONE*

Entry	TCT (mol %)	Temp. (ºC)	Time (min)	Yield (%)
1	0	110	150	0
2	5	100	90	62
3	5	110	90	67
4	5	120	60	66
5	10	25	150	26
6	10	50	120	48
7	10	80	90	55
8	10	90	90	64
9	10	100	60	73
10	10	110	60	89
11	10	120	60	88
12	10	130	60	88
13	15	100	60	82
14	15	110	60	86
15	15	120	60	84
16	20	110	60	87

*Reaction conditions: (E)-1-(2-aminophenyl)-3-phenylprop-2-en-1-one (1 mmol); solvent-free; H_2O (3 drops); TCT = Cyanuric chloride.



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Scheme-II

HCl generated *in situ*, from cyanuric chloride, efficiently catalyzes these reactions, a plausible mechanism is shown in **Scheme-II**. Accordingly, cyanuric chloride (10 mol %) reacts with 'incipient' moisture and releases 3 moles of HCl and cyanuric acid (removable by washing with water) as by-product. The in situ generated HCl acts as protic acid and activates the carbonyl oxygen and forms a carbocation. Intramolecular Michael addition of amino group to the the α,β-unsaturated ketone followed by subsequent cyclization to the corresponding products **2**.

TABLE-2
SYNTHESIS OF 2-ARYL-2,3-DIHYDROQUINOLIN-4(1*H*)-ONES

Entry	Ar	Time (h)	Product	Yield (%)
1	Ph	1.0	**2a**	89
2	4-$NO_2C_6H_4$	1.5	**2b**	86
3	4-ClC_6H_4	1.5	**2c**	83
4	4-$MeOC_6H_4$	1.0	**2d**	90
5	4-$N(Me)_2$ C_6H_4	1.0	**2e**	90
6	3-$NO_2C_6H_4$	1.5	**2f**	87
7	2-ClC_6H_4	1.5	**2g**	91
8	2,6-$(MeO)_2C_6H_3$	1.0	**2h**	85
9	2,6-$(Br)_2C_6H_3$	1.0	**2i**	92
10	3,4-$(Cl)_2C_6H_3$	1.0	**2j**	91

In summary, a novel and highly efficient methodology for the synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones by isomerization of substituted 2'-aminochalcones under solvent-free conditions in the presence of wet-cyanuric chloride as a catalyst is reported. In addition, this protocol describes a very fast, user friendly, 'green' and low cost procedure for the synthesis of these products. Furthermore, cyanuric chloride is a catalyst with cyanuric acid as by product that is removable by washing with water. This easy removal of the catalyst makes this method a better choice for chemical industries.

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