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Alumina supported-$CeCl_3 \cdot 7H_2O$–NaI: an efficient catalyst for the cyclization of 2′-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones under solvent free conditions

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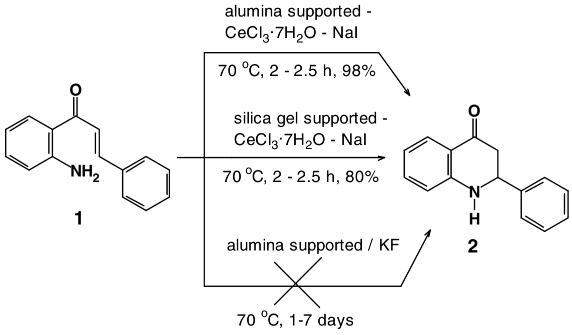
Abstract—We recently advanced silica gel supported-$TaBr_5$ as an efficient catalyst for the isomerization of 2′-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones under solvent free conditions (*Tetrahedron Lett.* **2006**, *47*, 2725–2729). This conversion can be further improved through the use of more economic alumina supported-$CeCl_3 \cdot 7H_2O$–NaI, providing high yields of up to 98% at lower reaction temperatures. This stable catalyst is easily prepared, active under solvent-free conditions and employed under environmentally friendly conditions.

2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones substituted on the aromatic rings are valuable precursors[1] for the synthesis of medicinally important compounds.[2] Generally, their synthesis is carried out using acid or base catalyzed isomerization of substituted 2′-aminochalcones via the aza-Michael reaction.[3] Many of the existing procedures are of limited synthetic scope due to low yields, long reaction times and the need for large amount of catalyst, specialized solvents[4] or microwave activation.[5] The Michael addition reaction has found many applications for carbon–carbon and carbon–heteroatoms bond formation in the presence of acid or base catalysts.[6] To avoid typical disadvantages like polymerization of enones (Michael acceptors) resulting from the presence of acid and base catalysts, a number of alternative procedures have been developed including various Lewis acid-induced reactions.[7] Particularly, the conjugate addition of nitrogen nucleophiles (Michael donors through intermolecular or intramolecular attack) to the α,β-unsaturated carbonyl compounds (aza-Michael reaction) is noteworthy due to its simplicity, economy, and atom efficiency.[8] With the aim to further improve the reaction's efficiency, several heterogeneous catalysts have also been evaluated and excellent results have been achieved.[9]

We recently reported that silica gel supported-$TaBr_5$ is an efficient catalyst for the isomerization of 2′-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones under solvent free conditions.[10] In a search for a more economic catalyst showing high activity under mild reaction conditions, we evaluated alumina supported-KF (Aldrich–Fluka) as well as silica and alumina supported-$CeCl_3 \cdot 7H_2O$–NaI. Particularly the latter provided high yields at low reaction temperatures for the intramolecular aza-Michael cyclization of aminochalcones to flavonones. This stable catalyst is



Scheme 1.

Keywords: Alumina and silica gel supported-$CeCl_3 \cdot 7H_2O$–NaI; 2′-Aminochalcones; Aza-Michael reaction; 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones.

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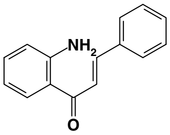
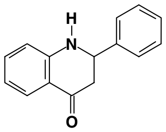
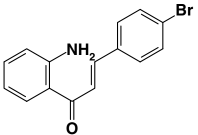
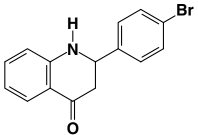
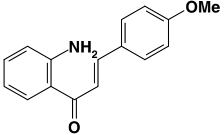
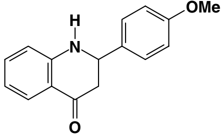
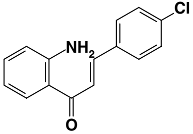
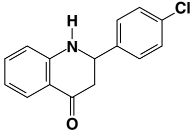
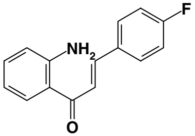
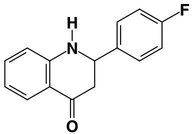
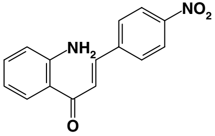
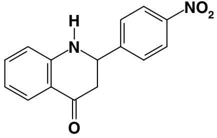
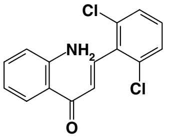
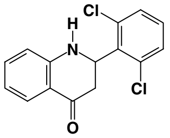
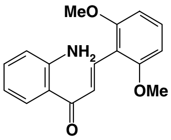
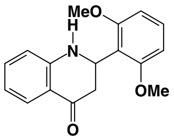
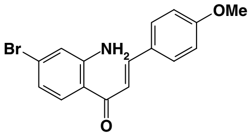
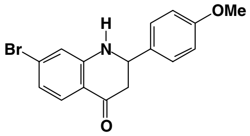
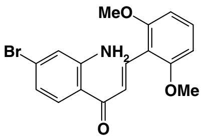
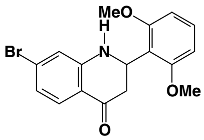
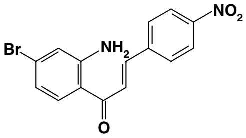
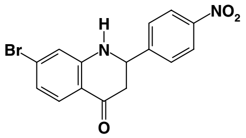
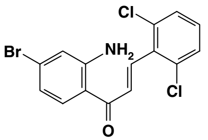
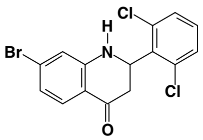
Table 1. Oxidative cyclization of 2′-aminochalcones catalyzed by alumina supported-$CeCl_3{\cdot}7H_2O$–NaI[a]

Entry	Substrate	Product[b]	Yield[c] (%)
a			98
b			98
c			92
d			96
e			96
f			94
g			90
h			86
i			85
j			84
k			84
l			83

[a] Reaction conditions: Substrate (1.0 mmol) and alumina supported-$CeCl_3{\cdot}7H_2O$–NaI (300–400 mg) were kept at 70 °C for 2–2.5 h.

[b] Isolated and non-optimized yield.

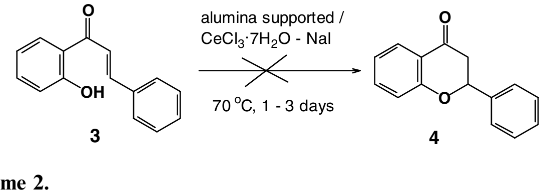
[c] Identification of the products was ascertained by ^{1}H- and ^{13}C NMR, mass spectroscopy and by comparison with published values.[10a]

easily prepared, active under solvent-free conditions and employed under environmentally friendly conditions.[11]

The experimental procedure[11c] consists of absorbing 2′-aminochalcone (**1**) on neutral alumina or silica gel supported-$CeCl_3{\cdot}7H_2O$–NaI catalysts (3.5 mol % $CeCl_3{\cdot}7H_2O$), heating the reaction mixture for 2–2.5 h at 70 °C followed by extraction to give the 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones (**2**) in high yield (Scheme 1). Using basic conditions, as in the case of alumina supported-KF, failed to give the desired product, which is likely due to complete decomposition of the substrate.[9a] To test the general applicability of neutral alumina supported-$CeCl_3{\cdot}7H_2O$–NaI as a catalyst for 2′-aminochalcone cyclization, a wide range of substrates were treated as described above.[11] The resulting 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones were obtained in excellent yields (Table 1); the assigned structures were confirmed by their spectral properties (IR, ^{1}H- and ^{13}C NMR, and MS) and by comparison with literature data.[10a] The relative long reaction time (2–2.5 h) likely reflects the low nucleophilicity of the aromatic amines and could not be improved upon by increasing the reaction temperature. Neither $CeCl_3{\cdot}7H_2O$ nor NaI alone could induce the reaction even after 7 days incubation. However, using $CeCl_3{\cdot}7H_2O$–NaI (3.5 mol %) in CH_2Cl_2 at reflux gave 20–25% of the desired product after a 3 day reaction period. Furthermore, omitting NaI in the alumina or silica gel–$CeCl_3{\cdot}7H_2O$ preparation resulted in complete loss of catalytic activity. NaI likely induces halide-exchange resulting in enhanced Lewis acid activity of $CeCl_3{\cdot}7H_2O$, which in turn is essential for its catalytic activity.[9b] Our data show that alumina supported-$CeCl_3{\cdot}7H_2O$–NaI is a more efficient catalyst for the intramolecular aza-Michael cyclization reaction as compared to recently reported methods using microwave irradiation on montmorillonite K 10 clay[5b] or silica gel impregnated $InCl_3$.[5a]

We also subjected 2′-hydroxychalcones (**3**) to the same reaction conditions but failed to detect the corresponding flavonones (**4**), even after prolonged reaction times of 3 days (Scheme 2). This lack of reactivity may be due to the low nucleophilicity of oxygen in **3** as compared to the amino nitrogen in **1**.

In conclusion, we have shown that different 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones can easily be prepared from their 2′-aminochalcone precursors in high yield under solvent free conditions, using neutral alumina supported-$CeCl_3{\cdot}7H_2O$–NaI as a catalyst. The advantage of this procedure over earlier reported processes includes simplicity, low reaction temperature, high yield, absence of secondary products, and organic solvent-free conditions.



Scheme 2.

Acknowledgment

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11. (a) *Preparation of neutral alumina supported* $CeCl_3{\cdot}7H_2O$*–NaI*: Neutral alumina (1.35 g) (BIO-RAD, Brockman activity, grade I, 2–44 μm) was added to a stirred mixture of $CeCl_3{\cdot}7H_2O$ (0.68 g, 1.82 mmol) and NaI (0.23 g, 1.55 mmol) in MeCN (10 mL) and further stirred overnight. The acetonitrile was evaporated on a rotary evaporator and the resulting powdered catalyst was stored under argon for future use. (b) *Preparation of silica gel supported-*$CeCl_3{\cdot}7H_2O$*–NaI*: Silica gel (1.26 g) (EM Science Germany, 60A, 70–230 mesh), $CeCl_3{\cdot}7H_2O$ (1.0 g, 2.72 mmol) and NaI (0.34 g, 2.32 mmol) in MeCN (10 mL), followed by the above procedures gave powdered catalyst that was stored under argon for further use. (c) *General procedure for cyclization of 2′-aminochalcones*: 2′-Aminochalcone (1.0 mmol) was dissolved in CH_2Cl_2 (1–1.5 mL) and alumina supported $CeCl_3{\cdot}7H_2O$–NaI (300–400 mg) or silica gel supported catalyst (300–400 mg) was added. The solvent was evaporated by heating and the resulting powdered reaction mixture was further heated for an additional 2–2.5 h at 70 °C. After completion of the reaction (by TLC monitoring), the mixture was cooled to rt and the product was recovered by washing with diethyl ether and solvent evaporation. Alternatively the reaction mixture was directly applied on a silica gel column and eluted with hexane:CH_2Cl_2 (1:9) to afford the pure products (Table 1).