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Silica gel supported $TaBr_5$: new catalyst for the facile and rapid cyclization of 2′-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones under solvent-free conditions

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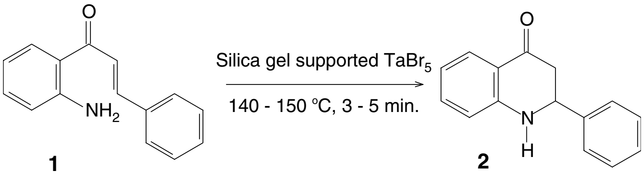
Abstract—Silica gel supported $TaBr_5$ (5–10 mol %) is a new solid-support catalyst that can be used under solvent-free conditions for the facile and efficient isomerization of 2′-aminochalcones to the corresponding 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones. The catalyst is easily prepared, stable and 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] which are often not readily accessible by other means.[2a,3] The formation of 2,3-dihydroquinolin-4(1*H*)-ones is generally accomplished by acid- or base-catalyzed isomerization of substituted 2′-aminochalcones.[4] Most of the procedures involve the use of corrosive reagents such as orthophosphoric acid, acetic acid or strong alkali. Furthermore, many of them are of limited synthetic scope due to low yields, long reaction times and the need for large amount of catalyst, specialized solvents[5] or microwave activation.[6] As a continuation of our interest in solid-support reactions,[7] we evaluated the synthesis of 2,3-dihydroquinolin-4(1*H*)-ones (**2**) from 2′-aminochalcones (**1**) using tantalum bromide ($TaBr_5$) under solvent-free conditions. The salient features of $TaBr_5$ impregnated on silica gel are rapid reaction rates, absence of unwanted products, improved and operational simplicity under conventional heating.

In recent years, TaX_5 ($X = Cl$, Br) have been used as Lewis acids in various organic syntheses.[8] In many cases, these metal halides are reported to be more efficient catalysts and easier to handle as compared to other metal halide catalysts such as TiX_4AlX_3, ZnX_2ZrX_4 and SnX_4.[9] It was also shown that metal bromides act as better Lewis acids in many organic syntheses as compared to their chloride counter part, for example, $InBr_3 > InCl_3$, $ZnBr_2 > ZnCl_2$.[7b] In-depth studies on the Lewis acid catalyzed reactions of tantalum halides revealed that $TaBr_5$ adsorbed on silica gel has better catalytic properties than $TaBr_5$ in solution, due to the increase in tantalum oxophilicity.[10] The high efficacy of this catalyst and ease of product isolation prompted us to investigate its use for the synthesis of the 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones (**2**). To our knowledge, no studies exploiting this catalyst for such cyclization reactions have previously been reported (Scheme 1).

Using a simple experimental procedure,[11] a wide range of substituted 2′-aminochalcones (**1**) adsorbed on silica gel supported $TaBr_5$ were heated for 3–5 min at 140–150 °C, which gave 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones



Scheme 1. Synthesis of 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones (**2**) using silica gel supported $TaBr_5$ under solvent-free conditions (overall yield 90–95%, vs 30–40% after 3 h in $TaBr_5$-solution).

Keywords: Silica gel supported $TaBr_5$; 2′-Aminochalcones; Michael addition reaction; 2-Aryl-2,3-dihydroquinolin-4(1*H*)-ones.

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Table 1. Silica gel supported $TaBr_5$ mediated oxidative cyclization of 2′-aminochalcones and 2′-hydroxychalcones

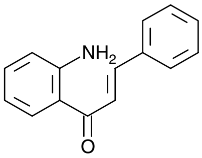
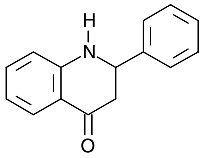
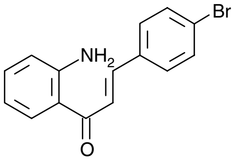
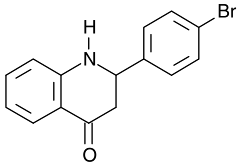
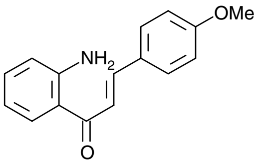
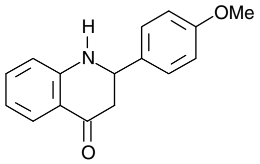
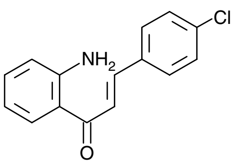
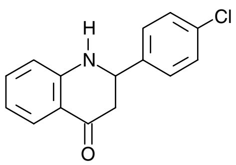
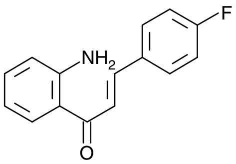
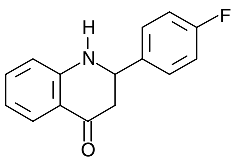
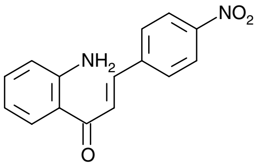
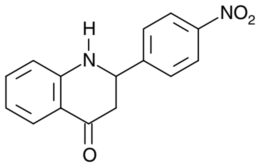
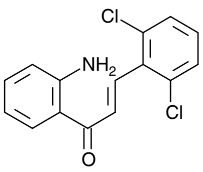
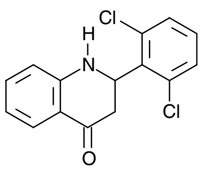
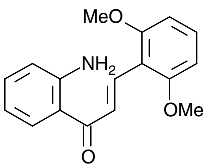
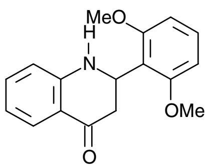
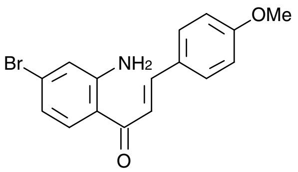
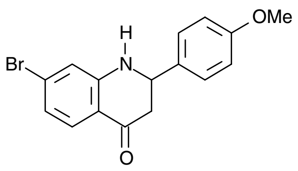
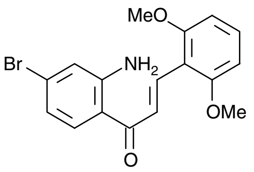
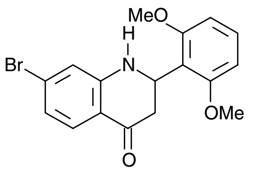
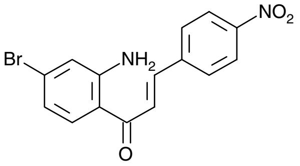
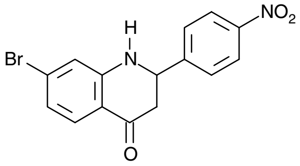
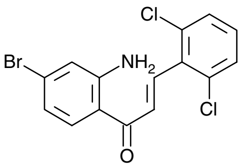
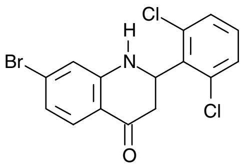
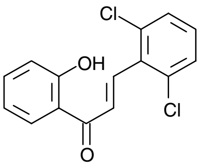
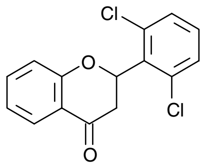
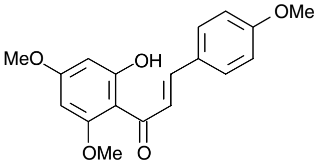
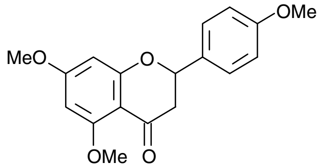
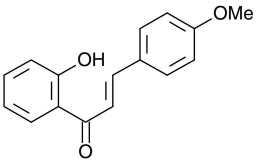
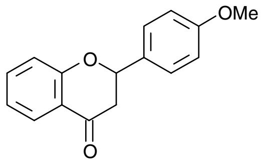
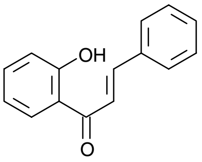
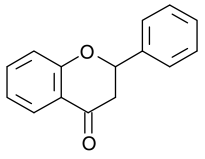
Entry	Substrate	Product	Yield (%)[a,b,c]
a			92
b			86
c			80
d			80
e			83
f			75
g			82
h			70
i			75

Table 1 (*continued*)

Entry	Substrate	Product	Yield (%)[a,b,c]
j			70
k			72
l			75
m			12[d]
n			10[d]
o			20[d]
p			30[d]

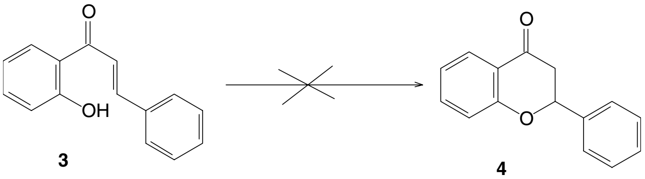
[a] Substrate (1.0 mmol), silica gel (200 mg) and $TaBr_5$ (10 mg, 5–10 mol %) were stirred for 3–5 min with heating at 140–150 °C.

[b] Isolated and non-optimized yield.

[c] Identification of the products was ascertained by ^1H and ^{13}C NMR, mass spectroscopy and by comparison with available physical and spectroscopic data.

[d] Based on reactant recovered after >72 h.

(**2**) in high yields (Table 1). The structures of the products were established from their spectral properties (IR, ^1H and ^{13}C NMR, and MS) and also by comparison with available literature data. These reactions did not occur in the presence of silica gel alone, while $TaBr_5$ in solution in the absence of silica gel gave the products in low yield (30–40%), even after prolonged reaction times of 3 h. Similarly, it has been reported that silica gel or other solid supports such as neutral alumina, coated with *p*-toluenesulfonic acid also catalyzed these reactions in relative low yields, whereas basic alumina completely destroyed the substrates.[12] Recently reported methods using microwave irradiation on montmorillonite K10 clay[6b] or silica gel impregnated $InCl_3$[6a] as solid support gave good yields. Again, these supports were found less efficient under conventional thermal heating. This confirms that $TaBr_5$ plays an important Lewis acid role in our silica gel supported cyclization reaction.



3

4

Scheme 2. Attempted cyclization of **3** to **4**, using silica gel supported $TaBr_5$ under solvent-free conditions (3–4 min, 140–150 °C), resulted in substrate decomposition. Prolonged heating at lower temperature (72 h, 60–70 °C) gave **4** in 10–30% yield.

We also tried to cyclize 2′-hydroxychalcones (**3**) to their corresponding flavanones (**4**) using $TaBr_5$ on silica gel support under similar reaction conditions (Scheme 2).

The reaction gave a mixture of flavanone and flavone together with other unidentified products. However, the same reaction mixture when kept at 60–70 °C in dichloromethane for 72 h gave **4** in 10–30% yields, depending on the substituants present on the aromatic rings (Table 1). It has been reported that 2′-hydroxychalcones **3** on silica gel supported $BiCl_3$ gave the corresponding flavonones **4** in good yield at lower temperature (60–70 °C).[7a] Accordingly, $TaBr_5$ on silica gel is less efficient for the isomerization of 2′-hydroxychalcones **3** as compared to the cyclization of 2′-aminochalcones **1**. Presumably, the mechanism of the latter reaction involves the heat-facilitated intramolecular Michael addition[6a] of the amino group to the α,β-unsaturated ketone, whereby the essential configuration of both the $TaBr_5$ catalyst and the substrate is secured by their attachment to the silica gel matrix.

In conclusion, we have shown that 2-aryl-2,3-dihydroquinolin-4(1*H*)-ones **2** can easily be prepared from 2′-aminochalcones **1** in high yield under solvent-free condition using commercially available tantalum salt and silica gel. The advantages of this procedure over earlier reported processes include simplicity, fast and clean reactions, high yield, and the absence of organic solvent.

Acknowledgements

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11. General procedure: $TaBr_5$ (5–10 mol %) was added to a stirred solution of 2′-aminochalcones[13] (1.0 mmol) in dichloromethane (1–1.5 mL) under argon and further stirred for 10 min to complete dissolution. Then, dried silica gel[14] (200 mg) was added and solvent was evaporated. The reaction mixture was heated with stirring for 3–5 min at 140–150 °C. After cooling, the silica gel was extracted with diethyl ether, filtered and the solvent evaporated in vacuo. Products were purified by silica gel column chromatography using hexane–diethyl acetate (9:1 to 4:1) as eluent. (entry g). *(2-(2,6-Dichlorophenyl)-2,3-dihydroquinolin-4(1H)-one)*: yellow semi-solid; IR ($CHCl_3$): 3310 (NH), 1640 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.90 (dd, $J = 9.6$, 1.6 Hz, 1H), 7.45–7.10 (m, 4H), 6.79 (t, $J = 8.0$, 1.0 Hz, 1H), 6.68 (d, $J = 8.1$ Hz, 1H), 5.78 (dd, $J = 4.0$, 12.2 Hz, 1H), 4.67 (br s, 1H, NH), 2.66 (dd, 12.2, 4.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.46 MHz): 193.0, 151.7, 138.4, 135.5, 132.8, 130.0, 129.4, 127.6, 127.5, 119.0, 118.6, 116.2, 54.2, 44.1; EIMS: *m*/*z* 371 (M^+). *(2-(2,6-Dimethoxyphenyl)-2,3-dihydroquinolin-4(1H)-one, entry* h): yellow semi-solid; IR ($CHCl_3$): 3280 (NH), 1630 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.89 (dd, $J = 9.4$, 1.5 Hz, 1H), 7.69 (dd, $J = 9.4$, 1.5 Hz, 1H), 7.31–7.11 (m, 2H), 6.68–6.58 (m, 3H), 5.45 (dd, $J = 4.0$, 12.6 Hz, 1H), 4.57 (br s, 1H, NH), 3.81 (s, 2 × OMe, 6H), 2.69 (dd, $J = 4.0$, 12.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.46 MHz): 193.5, 152.0, 149.0, 148.6, 136.4, 134.5, 132.8, 128.0, 119.4, 118.64, 116.5, 113.0, 108.6, 56.8, 56.2, 54.2, 46.1; EIMS: *m*/*z* 383 (M^+). *(7-Bromo-2-(4-nitrophenyl)-2,3-dihydroquinolin-4(1H)-one, entry* k): yellow solid; mp >250 °C; IR ($CHCl_3$): 3210 (NH), 1628 cm^{-1} (C=O); ^1H NMR ($CDCl_3$, 300 MHz): δ 8.29 (dd, $J = 9.7$, 1.2 Hz, 2H), 7.98 (dd, $J = 9.6$, 1.2 Hz, 1H), 7.64–7.48 (m, 2H), 7.42 (dd, $J = 9.6$, 1.6 Hz, 1H), 6.88 (d, $J = 1.6$ Hz, 1H), 4.88 (dd, $J = 4.3$, 12.9 Hz, 1H), 4.57 (br s, 1H, NH), 2.86 (dd, $J = 4.3$, 12.9 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75.46 MHz): 193.5, 152.7, 148.4, 145.5, 135.8, 133.4, 132.6, 131.5, 124.5, 122.0, 119.8, 118.6, 58.2, 48.1; EIMS: *m*/*z* 347/345 (M^+).

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13. 2′-aminochalcones were prepared following the reported method in Murphy, W. S.; Watanasin, S. *Synthesis* **1980**, 647.
14. Silica gel (60A, 70–230 mesh, EM Science, Germany) dried for 24 h in the oven (i.e., 120–130 °C) prior to use. If not dried, a mixture of products or decomposed products is obtained.