SHORT PAPER

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An improved procedure for the isomerisation of 2′-hydroxysubstituted chalcones to flavanones using silica supported-$BiCl_3$ under dry conditions[†]

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The isomerisation of 2'-hydroxychalcones to their corresponding flavanones, in good to excellent yield using silica supported-Bi(III) chloride as a catalyst under dry conditions at 70-80°C is reported.

Keywords: 2-hydroxychalcones, silica gel, isomerisation, flavanones

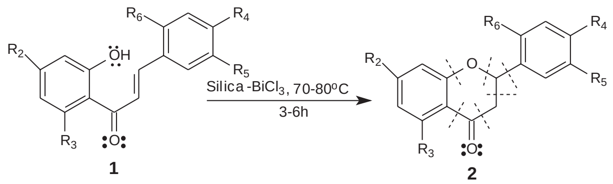
Flavanones (2,3-dihydroflavones) are physiologically active compounds with a diverse spectrum of biological activities, including acting as cholagogues, antioxidants, hepatoprotectors and antiphlogistics, to name a few. They are important intermediates in the biogenesis of flavonoids[1] and they also are used as synthons for the preparation of other organic compounds.

Generally, flavanones are obtained by the isomerisation of 2'-hydroxychalcones in acidic or basic conditions, but other methods have also been reported.[2] However, these methods give low to moderate yields due to the equilibrium between 2'-hydroxychalcones and the corresponding flavanones.[1f] The conditions that displace the equilibrium in favour of flavanones are difficult to predict.

Recently, solid support chemistry has been used as an efficient method for many syntheses. In most cases, the reactions proceed smoothly and work-up procedures are more convenient than those for synthesis in solution. The oxidative dimerisation of 2'-hydroxychalcones on $FeCl_3$-supported silica gel was reported, giving two secondary products.[2d] Bismuth (a heavier p-block element) has potential for both covalent and coordinate bonding due to weak shielding of the 4f-shell (lanthanide contraction). The stabilisation of the 6s-orbital (inert-pair effect) confers to Bi(III) a potential Lewis acidity and its use as a catalyst has only recently been advanced.[3] This prompted us to investigate the isomerization of 2'-hydroxychalcones on silica supported-$BiCl_3$ under dry conditions.

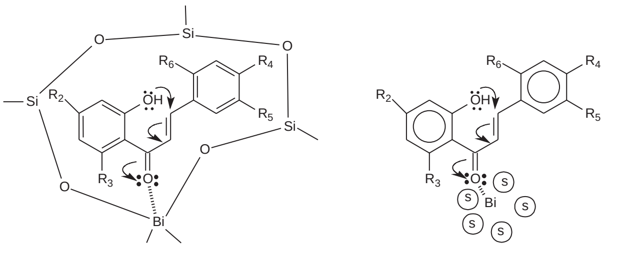
In a typical procedure, $BiCl_3$ (2 mmol, dissolved in a minimum amount of water) was adsorbed on silica gel (3 g, 60–120 mesh) and brought to dryness. 2'-Hydroxychalcones (2 mmol) dissolved in a minimum amount of ethyl acetate was then added, the solvent was removed and the dry mixture was heated at 70–80°C for 3–6 h with occasional shaking. The progress of reaction was monitored by thin layer chromatography (TLC). The reaction mixture was recovered with ethyl acetate and purified by column chromatography on silica gel, using a mixture of petroleum ether and ethyl acetate, which gave the desired product in 94% yield (entry 1) (Scheme 1).

The reaction proceeds efficiently, with good yields and convenient reaction times, particularly as compared to those reported in the literature.[2c,f] To confirm the role of the catalyst the reaction was attempted on alumina (neutral, basic and acidic), silica alone and $BiCl_3$ in solution at different temperatures and concentrations. However, none of these conditions gave any significant product. The reason why the solid surface is so efficient is not known. This might be related to the silica structure, which has a complex surface with cavities of different shapes and sizes.[4] The reaction is likely to take place inside the silica-cavities, which hold the bismuth in the appropriate conformation for Lewis acid activation. This lowers the activation energy of the reaction, rendering it faster than in solution. Bi(III) chloride in solution is surrounded by solvent molecules, which interfere with the activation for the intramolecular cyclisation, leading to a comparatively high activation energy (Scheme 2). In the case of products **2e** and **2f** yields are low, likely due to the delocalisation of electrons through the resonance of the electron-donating group (*i.e.* OH) on the B-ring.



	R_2	R_3	R_4	R_5	R_6
a.	OMe	OMe	OMe	H	H
b.	H	H	OMe	H	H
c.	H	H	H	H	H
d.	OMe	H	OMe	OMe	H
e.	H	H	OH	H	H
f.	OMe	OMe	H	H	OH

Scheme 1 Mass spectral fragmentations of **2a** are indicated by dotted lines.



Constrained environment will lower the activation energy

In solution phase Bi is surrounded by solvent molecules

Scheme 2

In conclusion, we have shown that silica supported-Bi(III) chloride is a new and efficient catalyst for the isomerisation of 2’-hydroxychalcones to their corresponding flavanones under dry conditions, providing a significant improvement over currently available procedures.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Experimental

Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer 621 spectrophotometer. ^{1}H NMR in CDCl$_3$ on a Bruker Avone DPX-300 (300MHz) using TMS as an internal standard and mass spectra on JEOL-D-300 spectrometer at 70eV.

Cyclisation of 2'-hydroxysubstituted chalcones **(1 a, b, c, d, e, f)** *on Silica supported-BiCl$_3$; general procedure:* An aqueous solution of bismuth(III) chloride (BiCl$_3$, 0.6 g, 2 mmol in a minimum amount of water) was adsorbed on silica gel (3 g, 60–120 mesh) and evaporated to dryness. 2'-Hydroxysubstituted chalcones (2 mmol) dissolved in a minimum amount of ethyl acetate solvent was then added, the solvent removed. The dry mixture was heated at 70–80^{o}C for 3–6 h with occasional shaking. The progress of reaction was monitored by tlc. The reaction mixture was recovered with ethyl acetate and purified by column chromatography on silica gel (60–120 mesh) using a mixture of petroleum ether : ethyl acetate (98:2, v/v) as eluent to afford the corresponding product (**2 a, b, c, d, e, f**) respectively.

2a (*5,7,4'-Trimethoxyflavanone*): Yield: 93.6%; R$_f$-value: 0.62 (P.E.: E.A, 2:1 v/v); M.p.: 125–126^{o}C (acetone – MeOH) (Lit.^{5} 123–125^{o}C); UV (λ_{max}, nm): 289, 325 and 327; IR (KBr-plate, ν_{max}, cm^{-1}) : 2956, 2923 (CH, CH$_2$, aromatic), 1680 (C=O), 1630, 1600, 1590 (C=C, phenyl), 1320, 1300, 1225, 964, 951 (flavanone skeleton); ^{1}H NMR (δ) : 8.06 (d, 2H, *H*-2', *H*-6', *J*= 8.4Hz), 6.95 (d, 2H, *H*-3, *H*-5', *J*= 8.8Hz), 6.66 (d, 1H, *H*-6, *J*= 2.5Hz), 6.78 (d, 1H, *H*-8, *J*= 2.5Hz), 5.32 (dd, 1H, C-2*H*, *J*= 13.5, 2.0Hz), 3.88 (s, 9H, 3 × OC*H*$_3$), 2.70 (dd, 1H, C-3*H*$_{eq-3}$, *J*= 13.5, 2.0Hz), 2.98 (dd, 1H, C-3*H*$_{ax-3}$, *J*= 16.8, 13.0Hz); EIMS (70eV) *m/z*: M$^{+\bullet}$ 314 (3.4), 286(28.5), 179(1.8), 152(100), 135(80.6), 121(6.5), 119(12.6), 107(27.8), 105(16.5), 93 (2.1), 77 (62.6), 65 (10.2).

2b (*4'-Methoxyflavanone*): Yield: 92%; R$_f$-value: 0.61 (P.E.: E.A, 2:1 v/v); M.p.: 96–97^{o}C (Lit.^{6} 97^{o}C); UV (λ_{max}, nm): 316, 320, 328, 350 and 413; IR (KBr-plate, ν_{max}, cm^{-1}): 2956, 2865 (CH, CH$_2$, aromatic), 1682 (C=O), 1630, 1600, 1586 (C=C, phenyl), 1335, 1298, 1224, 970, 949 (flavanone skeleton); ^{1}H NMR (δ): 7.60 (d, 2H, *H*-2', *H*-6', *J*= 8.6Hz), 7.40–7.24 (m, 4H, *H*-5, *H*-6, *H*-7, *H*-8), 6.93 (d, 2H, *H*-3', *H*-5', *J*= 8.6Hz), 5.37 (dd, 1H, C-2*H*, *J*= 14.0, 2.5Hz), 3.75 (s, 3H, 1 × OC*H*$_3$), 2.71 (dd, 1H, C-3*H*$_{eq-3}$, *J*= 14.0, 2.5Hz), 3.0 (dd, 1H, C-3*H*$_{ax-3}$, *J*= 14.0, 12.4Hz).

2c (*Flavanone*): Yield: 92%; R$_f$- value: 0.56 (P.E.: E.A, 2:1 v/v); M.p.: 76–77^{o}C (Lit.^{6} 75–76^{o}C); UV (λ_{max}, nm): 310, 357 and 378; IR (KBr-plate, ν_{max}, cm^{-1}): 2965, 2932 (CH, CH$_2$, aromatic), 1690 (C=O), 1625, 1605, 1580 (C=C, phenyl), 1325, 1298, 1205, 954 (flavanone skeleton); ^{1}H NMR (δ): 8.26 (d, 2H, *H*-2', *H*-6', *J*= 7.4Hz), 7.45–7.36 (m, 3H, *H*-5', *H*-3', *H*-4'), 7.60 (dd, 1H, *H*-5, *J*= 8.4, 3.0Hz), 7.20–7.0 (m, 2H, *H*-6, *H*-7), 6.91 (m, 1H, *H*-8), 5.3 (dd, 1H, C-2*H*, *J*= 13.7, 2.3Hz), 2.73 (dd, 1H, C-3*H*$_{eq-3}$, *J*= 14.0, 2.3Hz), 2.97 (dd, 1H, C-3*H*$_{ax-3}$, *J*= 17.0, 14.0Hz).

2d (*3', 4', 7-Trimethoxyflavanone*): Yield: 92%; R$_f$- value: 0.56 (P.E.: E.A, 2:1 v/v); M.p.: 119–120^{o}C (Lit.^{7} 120–121^{o}C).

2e (*4'-hydroxyflavanone*): Yield: 25–30%; M.p.: 186–188^{o}C (P.E.- MeoH) (Lit.^{8} 186–187^{o}C).

2f (*2'-Hydroxy-5, 7-dimethoxyflavanone*): Yield: 40%; M.p.: 85^{o}C (P.E.-EtOH)(Lit.^{9} 86^{o}C).

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