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An efficient synthesis of N-(*tert*-butylsulfinyl) imines devoid of catalyst

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Abstract

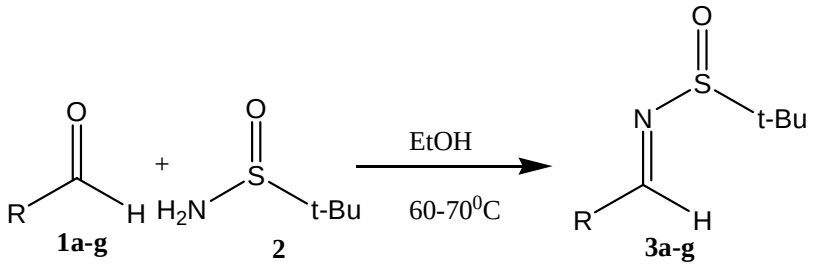
Neat non-volatile amines react efficiently with various aromatic aldehydes in the absence of any catalyst, to give imines. The reactions did not require any additives and were effective for a wide range of amines.

Introduction

Imines are one of the important substrates in organic and medicinal chemistry, as various type of amines can be prepared from this sort of substrates directly. Imines have been discovered to have a wide spectrum of biological activities such as lipoxygenase inhibition, anti-inflammatory[1] and anti-cancer behavior.[2] Furthermore, they are used as versatile components in the formation of optically active α-alkyl aldehydes,[3] in the preparation of secondary amines by hydrogenation,[4] in nucleophilic addition with organometallic reagents[5] and in cycloaddition reactions.[6]

In most of the reports, titanium (Ti(IV)) based reagents[7] has been mentioned for the preparation of N-(*tert*-butylsulfinyl) imines. Other reagents, such as copper (II) sulphate,[7,8] magnesium sulphate/pyridinium *p*-toluenesulfonate,[9] cesium carbonate,[10] yeterbium(III) triflate,[11] and potassium hydrogen sulphate[12] are also shown in literature to accomplish this conversion. Although, several reagents are reported to achieve this transformation, different methods are needed to develop the process in order to overcome the current difficulties reported in literature.

Scheme-I



R = 3-methoxyphenyl, 2,4,6-trimethoxyphenyl, 4-tert-butylphenyl, 1*H*-indole-3-yl, 4-trifluoromethylphenyl, phenyl, 4-methoxyphenyl

Experimental

Nuclear Magnetic Resonance spectra were recorded on Varian 300 and 75 instruments respectively. All H NMR experiments are reported in δ units, parts per million (ppm) and were measured relative to the signals for residual chloroform (δ 7.26 ppm) in the deuterated solvents. LCMS were recorded using a Micromas-Quattro microTM API instrument. Infrared spectra were recorded using a Perkin-Elmer Spectrum 100 FTIR spectrometer. All new compounds were characterized by IR, NMR and mass spectroscopic analysis.

General procedure for the synthesis of N-(tertbutylsulfinyl)imines (3):

To a stirred solution of aldehyde **1** (1 mmol) in EtOH (1 mL) was added 2-methyl-2-propanesulfinamide **2** (1.5 mmol) under N_2 atmosphere and the reaction mixture was heated to 60-70°C. After, it was cooled to room temperature and washed with EtOAc. The solvent was evaporated under reduced pressure to obtain a crude mass which was purified by chromatography over silica gel (Hexanes-Ethyl acetate system) to afford compound **3**.

N-(3-methoxybenzylidene)-2-methylpropane-2-sulfinamide (3a)

IR (neat, cm^{-1}): 2956, 1610, 1534, 1268, 1227, 1170,; ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.24 (s, 9H), 3.81 (s, 3H), 7.02-7.05 (m, 1H), 7.24-7.38 (m, 3H), 8.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22, 55, 57, 113, 118, 122, 129, 135, 159, 162; MS (*m/z*) [M^++H]: 240.

2-methyl-N-(2,4,6-trimethoxybenzylidene)propane-2-sulfinamide (3b)

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.26 (s, 9H), 3.86 (s, 9H), 7.07 (s, 2H), 8.53 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22, 56, 57, 106, 129, 141, 153, 162; MS (*m/z*) [M^++H]: 300.

N-(4-tert-butylbenzylidene)-2-methylpropane-2-sulfinamide (3c)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.28

(s, 9H), 1.40 (s, 9H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.78 (d, *J* = 8.4 Hz, 2H), 8.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22, 31, 35, 57, 125, 129, 131, 156, 162; MS (*m/z*) [M^++H]: 266.

N-((1H-indol-3-yl)methylene)-2-methylpropane-2-sulfinamide (3d)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (s, 9H), 7.34-7.38 (m, 2H), 7.41-7.42 (m, 1H), 7.54 (d, *J* = 2.7 Hz, 1H), 8.26 (dd, *J* = 2.7, 8.7 Hz, 1H), 8.65 (s, 1H), 9.67 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22, 57, 111, 115, 122, 122, 123, 124, 133, 137, 156; MS (*m/z*) [M^++H]: 248.

2-methyl-N-(4-(trifluoromethyl) benzylidene)propane-2-sulfinamide (3e)

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.25 (s, 9H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.89 (d, *J* = 9.0 Hz, 2H), 8.62 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 22, 57, 120, 120, 130, 132, 151, 161.

N-benzylidene-2-methylpropane-2-sulfinamide (3f)

^{1}H NMR ($CDCl_3$, 300 MHz): δ= 1.09 (s, 9H), 7.19-7.28 (m, 3H), 7.58-7.73 (m, 2H), 8.54 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21, 57, 128, 128, 131, 133, 162.

N-(4-methoxybenzylidene)-2-methylpropane-2-sulfinamide (3g)

^{1}H NMR ($CDCl_3$, 400 MHz): δ= 1.11 (s, 9H), 3.71 (s, 3H), 6.78 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.8 Hz, 2H), 8.42 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22, 54, 57, 113, 126, 130, 161, 162.

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