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Silica Sulfuric Acid as an Inexpensive and Recyclable Solid Acid Catalyzed Efficient Synthesis of Quinolines

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Summary. Silica sulfuric acid as an inexpensive and recyclable solid acid efficiently catalyzes the *Friedländer* synthesis of quinolines through a condensation reaction of a 2-aminoaryl ketone with an activated α-CH acid compound under solvent-free conditions in high yields at 100°C.

Keywords. Silica sulfuric acid; Quinolines; Solvent-free.

Introduction

It is well known that quinolines exhibit a wide range of biological activities [1–3] and are valuable reagents for the synthesis of nano- and mesostructures with enhanced electronic and photonic properties [4].

The classic version of the *Friedländer* quinoline synthesis, which combines a 2-aminoaryl ketone and a carbonyl compound containing an activated α-CH acid under acidic or basic conditions by refluxing in an aqueous or alcoholic solution to give quinoline, has been extensively explored [5]. In a typical procedure, the catalyst is varied from strong protic inorganic liquid acids [6], such as HCl, H_2SO_4, and polyphosphoric acid, to *Lewis* acids [7], such as $ZnCl_2$, $NaAuCl_6$, and $AuCl_3 \cdot 3H_2O$, and transition-metals [8], such as ruthenium and palladium.

However, in spite of their potential utility, these homogeneous catalysts present limitations due to the use of toxic and corrosive reagents, the tedious work-up procedure, the necessity of neutralization of the strong acid media producing undesired washes, long reactions times, and high temperature. Moreover, the synthesis of these heterocycles has been usually carried out in a polar solvent such as *THF*, *DMF*, or *DMSO* leading to complex isolation and recovery procedures. Therefore, the discovery of a novel and inexpensive catalyst, which can be

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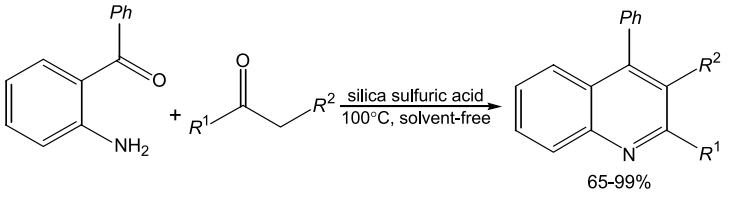


Scheme 1

easily separated, reused, and does not become contaminated by the products, is of prime importance.

In connection with our previous work using silica sulfuric acid and other solid acid catalysts in organic transformations [9], we wish to report the results of a study of the preparation of quinolines with silica sulfuric acid as an inexpensive and recyclable catalyst, which is easily separated from reaction mixture (Scheme 1).

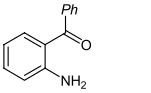
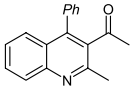
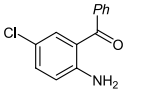
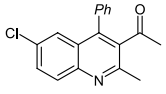
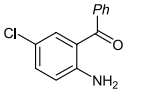
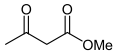
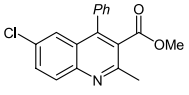
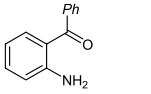
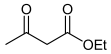
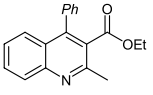
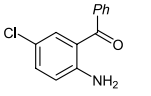
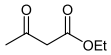
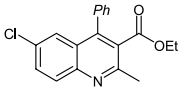
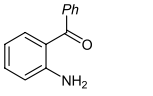
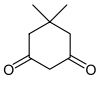
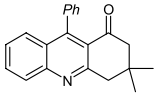
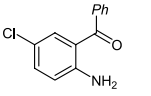
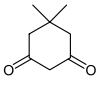
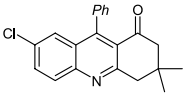
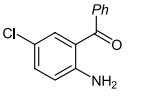
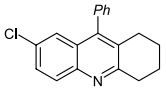
Results and Discussion

The procedure gives the product in high yields and avoids problems associated with solvent and liquid acids use (cost, handling, safety, pollution, corrosiveness, separation, and recovery). Decreased reaction times are also realized because of the increased reactivity of the reactant in the solid state and the fact that the other reaction product, water, evaporates at the reaction temperature of 100°C. The catalyst is simply prepared by the reaction of chlorosulfonic acid with commercially available silica and the by-product, HCl gas, is easily removed from the reaction vessel [10].

In a blank experiment no desired product was observed under similar reaction conditions in the absence of catalyst within 24 h. Catalyst reuse studies were carried out by recycling the catalyst for the reaction of 2-amino-5-chlorobenzophenone with ethyl acetoacetate on a 3 mmol scale. This was done by washing the reactants and product with *Et*OH and charging the reaction vessel with fresh substrate and then repeating the experiment. Interestingly, the recycled catalyst could be used for at least four reaction cycles, corresponding to an overall turnover number of 345 (Table 1, Entry 5). These results clearly show the practical reusability of the silica sulfuric acid catalyst under the described reaction conditions. To explore the scope and limitations of this catalyst further, we have extended it to various β-dicarbonyl compounds and cyclohexanone. As indicated in Table 1, the reaction proceeds efficiently with various kinds of β-dicarbonyl compounds, but the yield of the reaction with cyclohexanone was lower.

In conclusion, we have shown that the silica based solid acid catalyst, which can be easily prepared from commercially available starting materials efficiently catalyzes the *Fridedländer* synthesis of quinolines through the condensation of 2-aminoaryl ketone with activated α-CH acid compounds. Because solid acids are environmentally friendly with respect to corrosiveness, safety, waste, and ease of separation and recovery, replacement of liquid acids with solid acids is desirable in the chemical industry.

Table 1. Silica sulfuric acid catalyzed *Fridedländer* synthesis of quinolines under solvent-free conditions at 100°C

Entry	2-Aminoaryl ketone	CH-acid	Product	Yield/% (Time/min)	MP/°C Found (Reported)
1				99 (45)	111–112 (115)[a]
2				99 (45)	154 (151)[b]
3				85 (30)	133–135
4				87 (55)	99–100 (98)[a]
5				83 (60) 84 (120) 87 (360) 79 (360)[c]	102–105 (108)[b]
6				86 (120)	191 (195)[a]
7				99 (120)	209–211
8				65 (60)	162–164 (163)[b]

[a] Ref. [11]; [b] Ref. [12]; [c] the same catalyst was used for each of the four runs

Experimental

Melting points were measured on an Electrothermal 9100 apparatus. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. ^{1}H and ^{13}C NMR spectra were recorded on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz. ^{1}H and ^{13}C NMR spectra were obtained on solutions in $CDCl_3$. 2-Aminoaryl ketones and ketones were obtained from Fluka and Merck and were used without purification.

General Procedure

A mixture of 1.0 mmol 2-aminoaryl ketone, 1.2 mmol α-CH acid, and 0.16 g silica sulfuric acid [10] (0.4 mmol) was heated under solvent-free conditions with stirring at 100°C. After completion of the reaction as indicated by TLC, the reaction mixture was washed with hot ethanol ($2\times10\,cm^3$), the filtrate was concentrated, and the solid product was recrystallised from ethanol.

All products (except entries 3 and 7) are known compounds, which were characterized by IR and ^{1}H NMR spectral data and their mp values were compared with literature reports.

6-Chloro-2-methyl-4-phenyl-quinoline-3-carboxylic acid methylester (**3**, $C_{18}H_{14}ClNO_2$)
White solid, mp 133–135°C; IR (KBr): $\bar{\nu} = 3070$, 2925, 1715 cm^{-1}; MS: m/z (%) = 311 (M^+, 85), 279 (87), 252 (45), 217 (100), 176 (60), 150 (20), 108 (25), 87 (35), 50 (25); ^1H NMR ($CDCl_3$): $\delta = 2.69$ (s, CH_3), 3.51 (s, O–CH_3), 7.2–7.96 (m, 8H-arom) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 23.77$ (CH_3), 52.31 (O–CH_3), 125.26, 125.87, 128.05, 128.52, 128.84, 129.14, 130.54, 131.23, 132.41, 134.93, 145.57, 146.13, 154.93 (arom), 168.66 (C=O) ppm.

7-Chloro-3,3-dimethyl-9-phenyl-3,4-dihydro-2H-acridin-1-one (**7**, $C_{21}H_{18}ClNO$)
Yellow solid, mp 209–211°C; IR (KBr): $\bar{\nu} = 3065$, 2945, 1692 cm^{-1}; MS: m/z (%) = 335 (M^+, 55), 334 (100), 306 (40), 279 (35), 251 (20), 216 (75), 189 (30), 151 (15), 121 (25), 39 (50); ^1H NMR ($CDCl_3$): $\delta = 1.09$ (s, $2CH_3$), 2.5, 3.19 (2s, $2CH_2$), 7.08–7.95 (m, 8H-arom) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 28.34$ (CH_3), 32.27 (C), 48.29, 54.18 ($2CH_2$), 123.30, 126.79, 127.91, 127.99, 128.22, 128.37, 130.18, 132.45, 132.54, 136.80, 147.36, 150.14, 161.45, 154.93 (arom), 197.73 (C=O) ppm.

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