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Environmentally Benign Process for Acylation of Arenes Using Carboxylic Acidanhydrides as Acylating Agents in Presence of Solid Acid Catalysts under Solvent-Free Condition.

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Abstract

Friedel–Crafts reaction is one of the oldest carbon–carbon bond forming processes and is still an attractive method to introduce substituent on aromatic rings. This article is focused on Friedel–Crafts Acylation Reaction especially given by electron-rich arenes under solvent free condition in presence of different solid acid catalysts. The catalyst can be easily separated and recycled making the process environmentally friendly.

Keywords: Friedel-craft acylation, Solid acid catalyst, Solvent free, Heterogeneous catalyst.

Introduction

For ages, the basic problem facing the synthetic chemists is to come out with newer and better methods for introducing a carbon side chain onto an organic compound i.e. to create a C-C bond [1-3].The discovery of a new aromatic C-C bond formation reaction by Charles Friedel and James Crafts brought about a revolution in organic chemistry. Considered in its various modifications, Friedel-Crafts reaction is by far the most important method for attaching a side chain to an aromatic ring. The reaction can be classified into alkylation and acylation. In Friedel-Crafts acylation, an aromatic ketone is formed by the reaction of an aromatic compound with an acylating agent such as an acyl halide, an acid, an acid anhydride or an ester in the presence of an acidic catalyst [4,5].

Friedel–Crafts acylation of aromatic compounds is widely used in the synthesisof aromatic ketones, which are important intermediates for the production of pharmaceuticals,dyes, agrochemicals, and fragrances.[6-10] Conventionally, the Acylationis catalyzed by Lewis acids such as AlCl3,BF3, TiCl4, ZnCl2, SbCl5[10] andso forth or Brønsted acids, such as methane sulfonic acid,Nafion-H,trifluoromethanesulfonic acid,polyphosphoric acid, and HF[11]. In particular,the use of metal halides causes problems associated with strong complexationbetween the product and catalyst, which necessitates the use of more than a stoichiometricamount of the catalyst. The workup commonly requires hydrolysis of thecomplex, leading to the loss of the catalyst and a large corrosive waste stream.For these reasons, the development of more ecofriendly Friedel–Crafts Acylation has become important.

Experimental Work:

Material and Methods

Materials

Chemicals: The chemicals were of LR or sometimes AR grade and procured from M/s s.d fine chemicals, Mumbai; LOBA Chemie, Mumbai; Fluka Chemicals, A. G, Switzerland; E. Merk (India) Ltd., Mumbai; Aldrich Chemical Company, Inc., and Lancaster, USA and used as such. The solvents used were of LR grade and were purified and dried by known procedures before their use.

Catalysts

Zeolite Hβ: It was procured from M/s Sud-Chemie (India), (Al_2O_3:/SiO_2 = 15), and had the following specifications: Surface area: 510 ± 20m^2/g, Total pore volume: 0.38cm^3/g, Volume of micropores: 0.11 m^3/g.

Analysis

GC: Gas chromatographic analysis was carried out on a Chemito 8610 gas chromatograph using SS column (OV 17, ½ in. x 2 m) equipped with Flame Ionization Detector.

GC-MS: GC-MS spectra were recorded on Shimatzu GCMS QP 2010 (RTX-WAX, capillary column, 30m, 0.25 mm) equipped with electron capture detector.

IR: IR spectra were recorded on a Perkin-Elmer Spectrum-100 FT-IR spectrophotometer and peak positions were recorded in wavenumber (cm^{-1}).

NMR: ^{1}H-NMR spectra were recorded in $CDCl_3$ on a JEOL 60 or 300 MHz (A1-300) spectrometer with TMS as internal standard.

Thin layer chromatography: TLC was performed on MERCK TLC silica gel 60 F254 aluminum sheets (20 x 20cm). Spot visualization on TLC was carried out in an iodine or UV chamber.

Column chromatography: The adsorbent (stationary phase) for column chromatography was silica gel (60-120 mesh) procured from s. d. fine chemicals Ltd.

Methods

Preparation of the catalysts:

Preparation of silica sulfuric acid:

Silica sulfuric acid was prepared according to the reported method. Silica gel (20g) was soaked with a 50% sulfuric acid (25 mL), water was evaporated under reduced pressure to afford a white free flowing powder. The powder was stored in an air tight vessel until used.

Heat treatment: Silica- sulfuric acid was activated at 120°C for a period of 5h to obtain SiO_2-H_2SO_4-120. The catalysts were preserved in a vacuum dessicator and used after activation.

Procedure

General Experimental procedure

A mixture of aromatic ether (10mmol), acetic anhydride (12mmol), catalyst (40wt % wrtwt of substrate) were stirred in a round-bottomed flask equipped with a reflux condenser; under nitrogen atmosphere at 120°C for 3h. The zeolite was filtered off, and washed with diethyl ether (3x15 mL). The filtrate and washing were treated with saturated bicarbonate solution and extracted with diethyl ether. After evaporated of solvents products were subjected to column chromatography (silica gel, mesh size 60-120, eluent: ethyl acetate and hexane) to obtain pure products.

Spectral analysis

***p*-phenoxyacetophenone:** solid; m.p. 48-50 °C.

FT-IR spectrum (KBr) of*p*-phenoxyacetophenone: 3085(=C-H), 2924(aliphatic C-H)**,** 1600 (C=O), 1586 (C=C), 1239 (C-O).

^{1}H NMR spectrum ($CDCl_3$, 60 MHz) of *p*-phenoxyacetophenone: 2.3 (s, 3H, $COCH_3$), 6.9-7.4 (m, 9H, Ar-H).

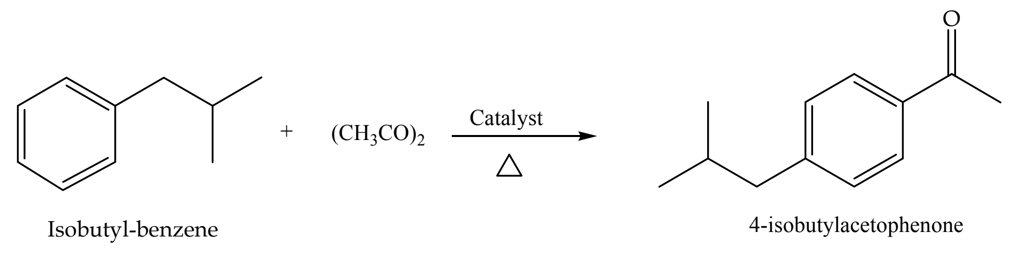
MS of *p*-phenoxyacetophenone:*m/z* (EI)212 (M+), 197 (base peak), 141, 115, 77.

Results and Discussions

We were interested in the development of a method for Friedel-Crafts Acylationthat:

a) circumvents chromatographic purification, b) avoids the use of acidanhydrides or toxic acid chlorides, c) is easy to perform, d) is economical forapplication to large scale preparation, and e) allows to use solvent-free conditions.

The acylation of isobutylbenzene with hydrogen fluoride is currently used in thesynthesis of ibuprofen[12]. Because of the current environmental restrictions,replacement of hazardous conventional homogeneous catalysts with solid acidcatalyst has great industrial importance. Zeolite Hβ has been found to be a goodsolid acid catalyst for aromatic acylation reaction. To start with, the acetylation of isobutylbenzene with acetic anhydride wascarried out in the presence of different solid acid catalysts in the presence andabsence of solvent (1,2-dichloroethane) (Scheme I). The reactions were carriedout at different temperature, i.e. 80, 100, 120°C (**Table 1**).



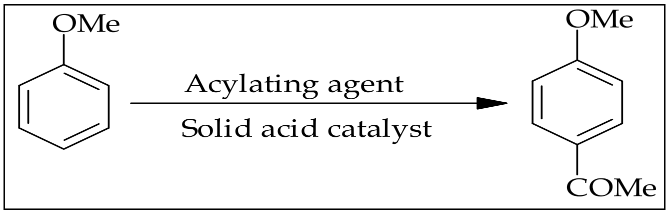
Scheme IAcetylaion of IBB using Ac_2O in presence of solid acid catalysts.

Table 1 Acetylaion of isobutylbenzene (IBB) using acetic anhydride (Ac_2O) as acylating agent in presence of solid acid catalyst.

Entry	Molar ratio IBB:Ac_2O	Solvent	Catalyst	Catalyst loading (mass %)	Reaction temp. (°C)	Remarks
1	1:1	EDC	SiO_2-H_2SO_4 120	20	80	No reaction
2	1:2	EDC	SiO_2-H_2SO_4 -120	20	80	No reaction
3	1:1.2	EDC	SiO_2-H_2SO_4 -120	100	80	No reaction
4	1:1.2	EDC	Zeolite Hβ - 120	100	80	No reaction
5	1:1.2	EDC	Zeolite Hβ -500	100	80	No reaction
6	1:2	--	Zeolite Hβ - 120	20	80	No reaction
7	1:2	--	Zeolite Hβ - 500	20	80	No reaction
8	1:2	--	Zeolite Hβ - 120	20	100	No reaction
9	1:2	--	Zeolite Hβ - 120	20	120	No reaction

Reaction conditions: Isobutylbenzene (10mmol). acetic anhydride, catalysts activated at 120°C or 500°C (5h), time 12h

Thus, SiO_2-H_2SO_4 and Hβ were not active for the acetylation of isobutylbenzene. Hence, it was decided to study the solventfree acylation of activated arenes in the presence of solid acid catalysts. To begin with acylation of anisole was attempted over Hβ in the absence of a solvent (**Scheme II**).



Scheme II Acylation of anisole over different solid acid catalysts.

We first examined the effect of various acylating agents on the acylation of anisole over Hβ (**Table 2)**
It was clear from the results that acetic anhydride was the most effective acylating reagent giving 42% yield of *p*-methoxyacetophenone at 80°C. A lower degree of acetylation occurred with acetyl chloride under the same conditions, while no reaction occurred with ethyl acetate or acetic acid. Thus, acetic

anhydride was selected for further study. The acetylation of anisole with acetic anhydride was next carried out over various solid acid catalysts (**Table 3**).

Table 2 Acetylaion of anisole using different acylating agents in the presence of Zeolite Hβ**.**

Entry	**Acylating agent**	**Yield of *p*-methoxyacetophenone (%)^b**
1	Acetic anhydride	42
2	Acetic acid	No reaction
3	Acetyl chloride	31
4	Ethyl acetate	No reaction

Reaction conditions: Anisole (10mmol), acylating agent (12mmol), temperature 80°C, catalyst (10 wt%), time 3h, ^{b} isolated yield.

Table 3 Acetylaion of anisole using acetic anhydride in the presence of different solid acid catalysts.

Entry	**Solid acid catalyst**	**Yield of *p*-methoxyacetophenone (%)^b**
1	Zeolite Hβ	42
2	Mont K10-120	15
3	Zeolite HY	35
4	Amberlyst-15	38

Reaction conditions: Anisole (10mmol), acetic anhydride (12mmol), temperature 80°C,
Catalyst (10 wt %), time 3h, ^{b} isolated yield

Among the catalysts, Zeolite Hβwas found to be more active. For the economic use, it would be beneficial to utilize minimum quantity of the catalyst which would give maximum yield hence a series of reactions was therefore carried out in which the amount of Hβwas varied (**Table 4**).

Table 4 Acetylaion of anisole using acetic anhydride as acylating agent in the presence of different loading of Zeolite Hβ

Entry	**Catalyst loading (wt%) wrtamt of anisole**	**Yieldof *p*-methoxyacetophenone (%)^b**
1	10	42
2	20	48
3	30	55
4	40	64

Reaction conditions: Anisole (10mmol), acetic anhydride (12mmol), temperature 80°C,
time 3h, ^{b} isolated yield

From the results it was clear that 10 wt% of the catalyst was capable of catalyzing the reaction although the yield of product increased with increasing amount of catalyst and 40 wt% of catalyst loading was used for further study.

The effect of temperature was studied (**Table 5**)

Table 5 Acetylaion of anisole using acetic anhydride as acylating agent in presence of zeolite Hβ at different temperatures

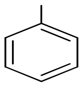
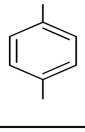
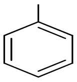
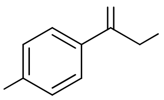
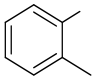
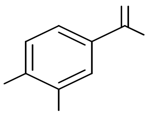
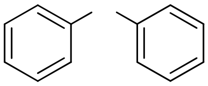
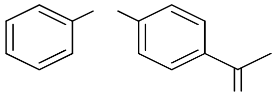
Entry	**Temperature (°C)**	**Yield of *p*-methoxyacetophenone (%)^b**
1	Room temperature (30)	Trace
2	60	28
3	80	64
4	100	71
5	120	78

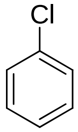
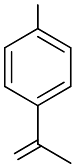
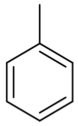
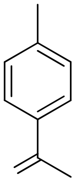
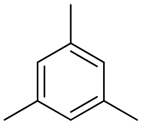
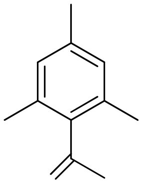
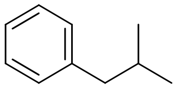
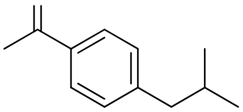
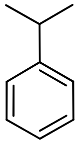
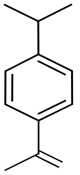
Reaction conditions: Anisole (10mmol), acetic anhydride (12mmol), Hβ(40 wt% wrt anisole), time 3h, ^{b} isolated yield

The reaction proceeded to some extent even at low temperatures; however maximum yield was obtained at 120°C.

Next the reaction of different arenes was carried under the optimized conditions (**Table 6**).

Table 6 Acetylaion of arenes using acid anhydrides in the presence of Hβ at 120°C

Entry	**Arene**	**Acid anhydride**	**Product**	**Yield *(%)^b***
1		Acetic anhydride		78
2		Propionic anhydride		73
3		Acetic anhydride		60
4		Acetic anhydride		46

5		Acetic anhydride		No reaction
6		Acetic anhydride		No reaction
7		Acetic anhydride		No reaction
8		Acetic anhydride		No reaction
9		Acetic anhydride		No reaction

Reaction conditions: Arene (10mmol), acetic anhydride (12mmol), time 3h,temperature 120°C, ^{b} isolated yield

It was observed that the reaction was successful only with activated arenes. The ring should preferably bear an alkoxyl group. Phenoxy group could not activate the ring much. Alkyl group was totally ineffective.

To check the recyclability of the catalyst, the spent catalyst was filtered, washed with dichloromethane to remove any impurities present, dried in an oven at 120°C for 3h, and reused for next run. The catalyst was found to be recyclable (**Table 7**).

Table7 Recyclability study of zeolite Hβ

Entry	Cycle	Yield of *p*-methoxyacetophenone (%)^b
1	1	78
2	2	77.5
3	3	74
4	4	71.2

Reaction condition: Anisole (10 mmol), acetic anhydride (12mmol), temperature 120°C, Hβ (40wt% wrt anisole), time 3h, ^{b} isolated yield

Conclusions

Zeolite Hβ is an efficient catalyst for acylation of activated arenes in the absence of any solvent. The catalyst can be easily filtered and can be reused. The methodology is applicable to only activated arenes. The process has advantage like simplicity, easier filtration of the catalyst, recyclability of catalyst and waste minimization.

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