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Insight into Friedel-Crafts acylation of 1,4-dimethoxybenzene to 2,5-dimethoxyacetophenone catalysed by solid acids—mechanism, kinetics and remedies for deactivation

Ganapati D. Yadav *, Ketan P. Pimparkar

Department of Chemical Engineering, University Institute of Chemical Technology, University of Mumbai, Matunga, Mumbai 400 019, India

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Abstract

Friedel-Crafts acylation of aromatic ethers is challenging, which frequently encounters rapid catalyst deactivation by the ether. Although H-Y and H-β are known to perform better, there is still deactivation due to both the ether and the acylated ether. In the current work, the synthesis of 2,5-dimethoxyacetophenone, an intermediate used in the production of fine chemicals, was carried out via acylation of 1,4-dimethoxybenzene with acetic anhydride over various solid acid catalysts such as sulfated zirconia, UDCaT-1, UDCaT-5, 20% w/w $H_3P_{12}W_{40}$/K10, 20% w/w $Cs_{2.5}H_{0.5}P_{12}W_{40}$/K10, Amberlyst-15 and Indion-125. The cation exchange resins, Amberlyst-15 and Indion-125, were superior to other inorganic solid acids. A systematic study was undertaken to understand the reaction mechanism and catalyst functioning with Indion-125. The catalyst gets deactivated slowly over repeated use and this was studied independently. The adsorption of reactants and products was studied from pure component solutions and mixtures. The experimental data so generated were used to develop a model, incorporating deactivation. The model fits the experimental data very well. The current work gives an insight into choice of catalyst, kinetic modeling, studies in catalyst deactivation and methods to avoid deactivation.

Keywords: Friedel-Crafts acylation; 1,4-Dimethoxybenzene; 2,5-Dimethoxyacetophenone; Acetic anhydride; Sulfated zirconia; Heteropoly acids; $H_3P_{12}W_{40}$; $Cs_{2.5}H_{0.5}P_{12}W_{40}$; Acid treated clay; Montmorillonite clay; Mesoporous solid superacids; UDCaT-1; UDCaT-5; Amberlyst-15; Indion-125; Deactivation; Dynamic adsorption; Kinetics; Mechanism

1. Introduction

Acid catalyzed Friedel-Crafts acylation constitutes a major route to synthesize aromatic ketones, which are valuable precursors in dyestuff, agrochemicals, fine chemicals and pharmaceuticals industries. Traditionally homogeneous catalysts are used including Bronsted acids (sulphuric acid, polyphosphoric acid, hydrofluoric acid) or Lewis acids ($AlCl_3$, $ZnCl_2$ and BF_3 in nitrobenzene, carbon disulfide and dichloromethane) [1,2]. These catalysts are often required in little over stoichiometric amounts for acylations and selectivity to the desired ketone is poor. Besides, the post treatment of the reaction mass leads to generation of huge quantities of deleterious waste. Additionally the corrosive nature of acids leads to increasing costs due to premature ageing of the processing equipment and pipe lines. The acylating agents used in most of the traditional processes are the expensive and polluting acyl halides that require special care in handling and work up. With the increasing emphasis on green chemistry and technology, efforts have been made to develop environmentally friendly yet cost efficient processes for the synthesis of aromatic ketones. A plethora of solid acids has been tested to replace homogeneous acid catalysts by several researchers all over the world, and obviously zeolites are the most widely studied owing to their ease of preparation and/or availability, robustness and commercial success in refinery technologies. Solid acid catalysts are easy to recover and reuse, produce no salts, overcome corrosion problems thereby allowing use of cheaper materials of construction; they permit the use of cheaper and non polluting carboxylic acids and anhydrides as acylating agents, and offer several different reactor config-

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* Corresponding author. Tel.: +91 22 2410 2121; fax: +91 22 2414 5614.
E-mail addresses: gdyadav@yahoo.com, gdyadav@udct.org (G.D. Yadav).

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Nomenclature

a	activity of the catalyst
a_p	external surface area per unit liquid volume (cm^2/cm^3)
A	1,4-dimethoxybenzene
B	acetic anhydride
C	acetic acid
C_s	concentration of active sites on the catalyst surface (mol/g)
C_t	total concentration of active sites (mol/g)
C_A	concentration of A in the liquid phase (mol/cm^3)
C_{AL}	concentration of species A in the liquid phase at any time t (mol/cm^3)
C_{BS}	concentration of acetic anhydride on the catalyst surface
C_{CS}	concentration of acetic acid on the catalyst surface
C_{ALi}	initial concentration of species A in the liquid (mol/cm^3)
C_{ALf}	final concentration of species A in the liquid phase at infinite time
C_{MS}	concentration of 2,5-dimethoxybenzene on the catalyst surface
D	2,5-dimethoxyacetophenone
k_{ad}	adsorption constant (cm^3/(g cat/s))
k_A	adsorption constant per unit active site of catalyst
k_A	adsorption constant ($k_{ad}C_t$)
k_{DE}	deactivation rate constant
k_{SL}	solid–liquid mass transfer coefficient (cm/s)
k_{SR}	reaction rate constant assuming only forward reaction
k_{D1}	desorption constant for D_1
k_{D2}	desorption constant for D_2
k'_{D1}	desorption constant for D_1
k'_{D2}	desorption constant for D_2
K_A	adsorption equilibrium constant for A
K'_A	adsorption equilibrium constant for A, cm^3/gm ($=K_A C_t$)
K_{A1}	adsorption equilibrium constant for D
K_{A2}	adsorption equilibrium constant for C
K_{D1}	desorption equilibrium constant for D ($K_{D1} = k_{D1}/k'_{D1}$)
K_{D2}	desorption equilibrium constant for $C = k_{D2}/k'_{D2}$
M	2,5-dimethoxyacetophenone
M	initial mole ratio of acetic anhydride to 1,4-dimethoxybenzene (in Table 1) and Eq. (37) onwards
S_A	surface concentration of adsorbed A (mol/g)
w	catalyst loading, g/cm^3 of liquid

urations. Thus, solid acid catalysts can advantageously replace conventional catalysts.

Acylations are very difficult to accomplish with substituted benzenes using solid acids. In the case of acylation of aromatic ethers, indeed it is a formidable task, due to rapid deactivation of the catalysts, related to strong adsorption of reactants or products and intra-particle diffusion limitation. Zeolite HY and Hβ in chlorobenzene have been used for acylation of aromatic ethers at higher temperatures but still deactivation of the catalyst occurs rapidly due to the saturation of the active sites by the products acetic acid and/or the acylated product [3–7]. As an alternative to zeolites, several acylations of substituted benzenes were investigated with a variety of catalysts in our laboratory, including sulfated zirconia, UDCaT-1, UDCaT-5, dodecatungostophosphoric acid (DTP) supported on K10 clay (20% w/w DTP/K10), dodecatungostophosphoric acid (DTP), partially substituted with Cs ($Cs_{2.5}H_{0.5}P_{12}W_{40}$) and supported on K10 clay (20% w/w Cs-DTP/K10) and ion exchange resins [8–20]. UDCaT-1 and UDCaT-5 are mesoporous solid superacids developed by us. In the case of acylation of ethers, 20% DTP/hexagonal mesoporous silica (HMS) and cation exchange resins were more active but deactivation was still a problem [18]. There is a dearth of systematic studies on acylation of aromatic ethers which deactivate solid acids in liquid phase reactions. For instance, synthesis of 2,5-dimethoxyacetophenone is achieved by the acylation of 1,4-dimethoxybenzene with $AlCl_3$ as catalyst [21–23]. It is used as a precursor for the CNS stimulant 2,5-dimethoxy-4-ethylphenethylamine (also called 2C-E). No report has so far appeared on the synthesis of 2,5-dimethoxyacetophenone using solid acid catalysts. The current work gives an insight into the acylation of 1,4-dimethoxybenzene with acetic anhydride as the acylating agent to get 2,5-dimethoxyacetophenone as the sole product including choice of catalyst, kinetic modeling and studies in catalyst deactivation and methods to avoid deactivation.

Table 1
Best fit values for Eq. (38) using nonlinear regression in Polymath 5.1

T (°C)	$k_{SR\times10^2}$	K_A	k_{DE}	K_{A1}	K_{A2}	R^2
90	3.60	1400	0.01	1000	1000	0.9795
95	5.00	1250	0.0105	800	833.33	0.9939
100	14.0	985.6	0.02	684.931	657.89	0.9716
105	16.0	755	0.0203	546.44	537.63	0.9844
$M=1$	9.50	1056	0.019	724.63	675.67	0.9866

$M=1$ implies reaction at molar ratio of reactants equal to unity. Where A: 1,4-dimethoxybenzene, B: acetic anhydride, C: acetic acid, D: 2,5-dimethoxyacetophenone, k_{SR} is reaction rate constant assuming only forward reaction, K_A is the adsorption equilibrium constant for B, k_{DE} is the deactivation rate constant, K_{A1} is the adsorption equilibrium constant for D, K_{A2} is the adsorption equilibrium constant for C.

2. Experimental section

2.1. Chemicals and catalysts

All chemicals were A.R. grade and procured from reputed firms: 1,4-dimethoxybenzene (hydroquinone dimethyl ether) (Loba Chemie, Mumbai, India); acetic anhydride (Thomas Baker Chemicals Ltd., Mumbai); dodecatungstophoshporic acid (DTP), cesium chloride, zirconium oxychloride, ammonia solution (s.d. Fine Chemicals Pvt Ltd., Mumbai).