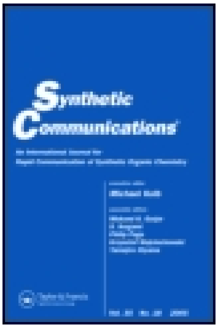

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Clay Catalysis: Stork's Alkylation and Acylation of Cyclohexanone Without Isolation of Enamine

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CLAY CATALYSIS: STORK'S ALKYLATION AND ACYLATION OF CYCLOHEXANONE WITHOUT ISOLATION OF ENAMINE

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Abstract:

Cyclohexanone and morpholine in the presence of KSF under azeotropic distillation gave 1-morpholinocyclohexene which is alkylated or acylated in situ without isolation of the enamine. The overall yield of these Stork's reactions are better or equivalent to those obtained by isolation of the enamine.

Clays are inexpensive, non-corrosive, strong Bronsted acids and are intensively used as acid catalyst in organic synthesis[1]. Reaction of the secondary amine with ketones under acidic conditions gave enamines which were extensively used as nucleophile [2] in organic synthesis (Stork's reaction) . Enamines are sensitive to water in presence of a trace of acid. The KSF clay was already used in a synthesis of enethioethers [3] and the clay K10 was also reported as a catalyst in a synthesis of some enamines [4] of cycloketones.

We report herein the use of Stork's alkylation or acylation without isolation of enamine, with the use of solid acid KSF clay (Scheme I).

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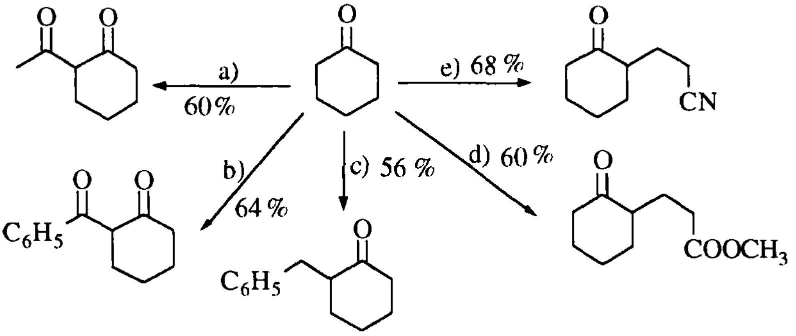
Scheme I: Stork's alkylation or acylation without isolation of the enamine



1°) morpholine, KSF reflux 24 h, 2°) then: a) CH_3COCl, *b)* C_6H_5COCl; *c)* $C_6H_5CH_2Cl$; *d)* $CH_2{=}CHCOOCH_3$; *e)* $CH_2{=}CHCN$

In a first step a solution of the enamine in toluene was prepared by reaction of cyclohexanone and morpholine with elimination of water by azeotropic distillation with a Dean-Stark apparatus. In a second step, the enamine was acylated or alkylated without separation of the enamine from the mixture containing the solvent (toluene), the catalyst (KSF), and unreacted cyclohexanone and morpholine. The overall yield is equal or superior to Stork's classical method [2]. Results were reported in table I.

Table I: Reaction of cyclohexanone without isolation of 1-morpholino-cyclohexene.

electrophile	procedure	product	yield (%)	Bp or *Mp* (°C)
acetyl chloride	a	2-acetyl-cyclohexanone	60	124 (18)
benzoyl chloride	a	2-benzoyl-cyclohexanone	64	*91-92*
benzyl chloride	a	2-benzyl-cyclohexanone	56	166 (18)
methylacrylate	b	methyl 3-(2-oxocyclohexyl)propionate	60	150 (18)
acrylonitrile	b	2-cyanoethyl-cyclohexanone	68	165 (18)

Experimental

General procedure

In a round bottom heated by an oil bath with a magnetic stirrer, cyclohexanone (50 mmol) and morpholine (50 mmol) were refluxed and stirred in toluene (50 ml) in presence of the KSF clay (2 g). Water formed was eliminated by a Dean-Stark apparatus under nitrogen. After 6 h, the mixture was allowed to room temperature.

According to the electrophile the following procedure was employed (see table I):

a) Acid chloride (50 mmol) was added, the mixture was stirred for 5 h at room temperature and was refluxed for 8 h and cooled

b) Acrylonitrile (50 mmol) or methyl acrylate was added and stirred for 5 h at room temperature. the mixture was refluxed for 36 h and then cooled.

An aqueous acetic acid solution (50 ml, 20%) was added and the mixture was refluxed for 30 mn. The mixture was filtered and extracted with ether (4 X 30 ml). The organic phase was washed with hydrochloric acid (10 %) and dried on magnesium sulfate. the solvent was distilled and the residue purified by Kugelrohr distillation.

All products are liquid and were identified by their physical [2] and spectroscopic data (IR, PMR, MS spectra).

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