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Catalytic Efficiency of Heteropoly 11-Tungsto-1-Vanadophosphoric Acid - Activated Clay in the Condensation Reaction of Thiourea with 4-Chlorobenzaldehyde

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Abstract: ***Catalytic efficiency of the heteropoly 11-tungsto-1-vanadophosphoric acid (HPV) supported on activated natural clay (HPVAC) towards condensation reaction of thiourea with 4-chlorobenzaldehyde to form (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea. The purification of organic products from crude products using chromatographic techniques. The product is analysed the nature of the product with the aid of FT-IR, 1H-NMR and 13C-NMR. Further, to estimate the optimum reaction condition for the catalytic ability of the HPV supported on activated clay using condensation reaction of thiourea with 4-chlorobenzaldehyde.***

Keywords: ***Heteropoly acid, Natural clay, Thiourea, (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea.***

I. INTRODUCTION

Heteropolyoxometalates (HPOM) having Keggin and Wells-Dawson-type structure has potential applications in various fields. They are used as homogeneous catalysts, heterogeneous catalysts, electro catalysts and photo catalysts for the synthesis of variety of organic compounds.[1-6] Heteropoly acids [HPV] were used in acid-catalysed reactions due to their strong Bronsted acidity. Clays form flat hexagonal sheets similar to the micas. Clay minerals are very common in fine grained sedimentary rocks such as shale, mudstone, and siltstone and in fine grained metamorphic slate and phyllite.[7, 8] The advantages of purified clay are natural availability, low cost and ease use in organic reactions. Efforts to prevent pollution in the development of new drug compounds paved the way for "Green chemistry", which produced an array of improved methodologies, including the use of clays as chemical catalysts.[9] Acidic properties of solid heteropolyacids (HPVs) made them useful versatile acid catalysts. They are usually solids that are insoluble in non-polar solvents but highly soluble in polar ones. They are more active than conventional inorganic and organic acids for various reactions in solution.[10, 11]

It was reported that urea and thiourea derivatives showed a broad spectrum of biological activities such as anti-HIV, antiviral, HDL- elevating antibacterial, analgesic properties.[12-15] 1, 3- disubstituted urea / thiourea derivatives are known for their antiproliferative activity against a panel of human tumor cell lines.[16] Many thiourea derivatives have been known to posses fungicidal and pesticidal action and several others have been reported to exhibit anti tubercular, anti-fungal, insecticidal and acaracidal activity.[17] Most of the derivatives of urea and thiourea are derived through condensation types of reactions with aromatic aldehydes and phenols / naphthols.[18] This work aims to utilize HPV supported activated natural clay as catalyst for the condensation reaction of thiourea and 4-chlorobenzaldehyde to form (1E, 3Z)-1,3-bis(4-chlorobenzylidene)thiourea.

II. EXPERIMENTAL

Materials and methods

Thiourea, 4-chlorobenzaldehyde and β-naphthol obtained from Sigma Aldrich were used as such. HPV supported activated natural clay catalysts (HPVAC) were prepared and characterized as reported earlier.[18] FT-IR spectra were recorded in IR Affinity-Fourier Transform Infra Red Spectrophotometer as KBr disks. ^{1}H-NMR and ^{13}C-NMR were recorded from Bruker NMR 300 MHz, instrument by dissolving the samples in $CDCl_3$.

Synthesis of (1E,3Z)-1,3-bis(4-chlorobenzylidene) thiourea

A mixture of 4-chlorobenzaldehyde (1 mmol), thiourea (1 mmol), HPVAC (0.08 g) and 1,2-dichloroethane (10 mL) was heated under reflux for 4 hours. The progress of the reaction was monitored by TLC (ethylacetate / dichloromethane in 7:3 ratio).

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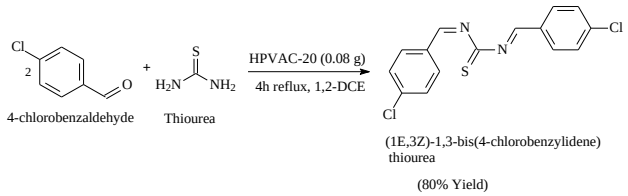
After the completion of the reaction the HPVAC was removed by filtration. The filtrate containing solvent was evaporated in water bath to get a yellow solid which was washed with water, for the removal of un-reacted thiourea. Further the product was purified by column chromatography (Petroleum ether / Ethylacetate 9:1 ratio). The catalyst was recovered by washing it thoroughly with dichloromethane and dried in an air oven at 120 ^{o}C for about an hour.

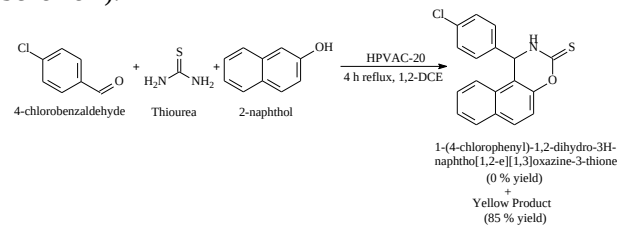


Scheme 1. Synthesis of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea.

III. RESULTS AND DISCUSSION

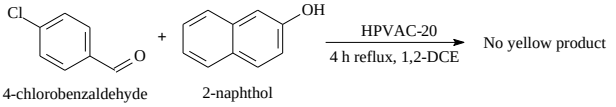
Catalytic efficiency of HPVAC

One-pot three-component condensation of 4-chlorobenzaldehyde, β-naphthol and thiourea in the presence of HPVAC-20 catalyst using 1,2-dichloroethane as solvent was carried out. 1 mmol of each of the reactants were mixed with 0.08 g of HPVAC-20 in 10 mL of 1,2-dichloroethane (1,2-DCE). The mixture was heated under reflex for about 4 h. According to reported literature,[19] the product of the reaction was assumed to be 1-(4-chlorophenyl)-1,2-Dihydro-3H-naphtho[1,2-e] [1,3]oxazine-3-thione. But in the present attempt instead of that, a yellow colour product was obtained with 85 % yield (Scheme 2).



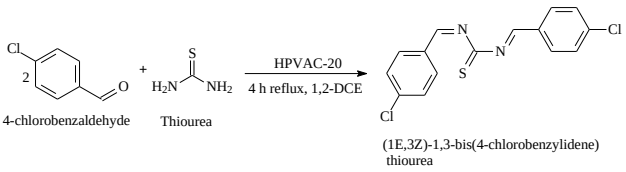
Scheme 2. Condensation of 4-chlorobenzaldehyde, β-naphthol and thiourea

Next, the reaction was carried out under the same condition in the absence of thiourea (Scheme 3). After 4 hours of reaction, no more change of colour of the reaction mixture was noted. TLC analysis (Ethyl acetate / Dichloromethane, 7:3) of the reaction mixture also gave only two spots characteristics of the reactants 4-chlorobenzaldehyde and β-naphthol (Scheme 2). Therefore it is concluded that there is no reaction between 4-chlorobenzaldehyde and β-naphthol under the present experimental conditions.



Scheme 3. Condensation of 4-chlorobenzaldehyde and β-naphthol

Further the reaction was carried out under the same condition. This time β-naphthol was removed. After 4 hours of reaction, a yellow colour product was obtained. TLC analysis (Ethyl acetate / Dichloromethane, 7:3) of the reaction mixture showed one spots characteristics of the new yellow product (Scheme 4). Therefore it is concluded that under the present experimental condition both 4-chlorobenzaldehyde and thiourea condensed together to give a yellow colour product.

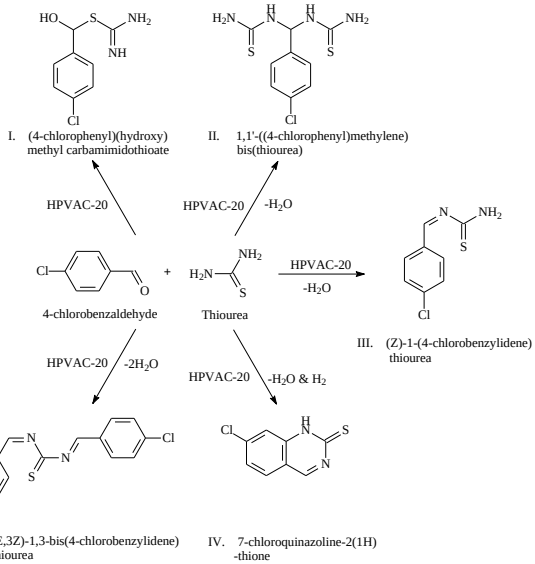


Scheme 4. Condensation of 4-chlorobenzaldehyde and thiourea

The yellow product analysis

There are five possible products during the course of the reaction. The possible reactions for the present case are explained with the help of Scheme 5. According to this the possible products are

I. (4-chlorophenyl)(hydroxyl) methyl carbamimidothiate
II. 1,1'-((4-chlorophenyl)methylene)bis(thiourea)
III. (Z)-1-(4-chlorobenzylidene)thiourea
IV. 7-chloroquinazoline-2(1H)-thione
V.(1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea



Scheme 5. Possible products during the course of the reaction.

Compound I was formed when 4-chlorobenzaldehyde, thiourea and *para*-toluenesulphonic acid were refluxed in toluene for 24 h.[20] Compound I contains free -OH group. Therefore one can expect band around 3650-3590 cm^{-1} in the FT-IR spectrum of the product. In this case the FT-IR (Fig. 1) of the yellow product did not show the characteristic band and therefore this product is ruled out.

If a water molecule is removed by the condensation [21] of two molecules of thiourea with a molecule 4-chlorobenzaldehyde the possible product is compound II. This compound has free NH_2 group and therefore one can expect characteristic FT-IR band at 3367 cm^{-1} and ^{1}H-NMR peak (Fig. 15) at 6.34δ (S, 1H). Absence of these features for the present product ruled out compound II as the possible product.

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Currently, there is no report [22] on the successful synthesis of compound III and IV using aromatic aldehyde and thiourea as substrates. Therefore, compound III and IV are ruled out as possible products. Further the FT-IR, ^{1}H-NMR and ^{13}C-NMR data are favorable for the compound V as product of the present condensation.
(1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea is formed by the condensation of 4-chlorobenzaldehyde with thiourea. It is a Schiff base. Structural elucidation of the compound using spectral technique is explained as follows.

FT-IR analysis of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea

The FT-IR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea is given as Fig.1. The spectral features are analysed with the help of reported literature.[17, 23] The FT-IR spectral bands at 2926 cm^{-1} and 1620 cm^{-1} respectively are attributed to υ(C-H) and υ(C=N) stretching vibrations. The bands at 1591 cm^{-1}, 1544 cm^{-1} and 1255 cm^{-1} are attributed due to υ(Aromatic C-C) and υ(C=S) stretching vibrations. The FT-IR spectral data of compound V along with the same for thiourea and 4-chlorobenzaldehyd are collected in Table 1 for the sake of comparison.

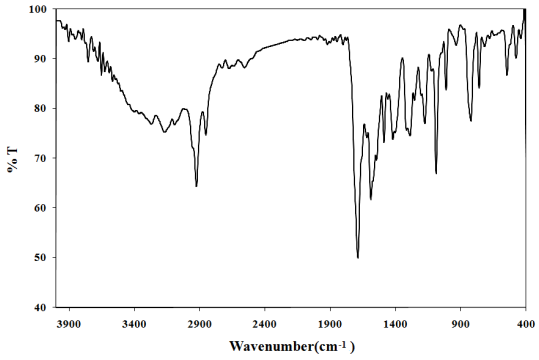

Fig. 1. The FT-IR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea recorded as KBr pellet

Table 1. The FT-IR spectrum data of 4-chlorobenzaldehyde, thiourea and (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea

S. No.	Functional groups	4-chloro-benzaldehyde (cm^{-1})	Thiourea (cm^{-1})	(1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea (cm^{-1})
1.	-NH$_2$ group	---	3367	---
2.	-C-H group	---	---	2926
3.	Aldehyde (C=O) group	1695	---	---
4.	Aromatic C-C group	1590	---	1591, 1544
5.	>C=S group	---	1195	1255
6.	>C=N group	---	---	1620

^{1}H-NMR analysis

The proton NMR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea is given Fig. 2. The chemical shift values are collected in Table 2 along with possible assignment.

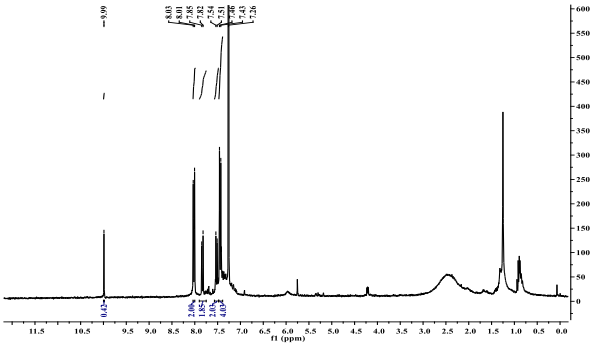

Fig. 2. ^{1}H-NMR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea in CDCl$_3$

Table 2. ^{1}H-NMR data for (1E,3Z)-1,3-bis(4-chlorobenzylidene) thiourea

S. No	Multiplicity	Chemical shift (δ) (ppm)	No. of Hydrogen
1.	Doublet (HC=N)	8.02	2H
2.	Doublet	7.84	2H
3.	Doublet	7.53	2H
4.	Doublet	7.45	4H

^{13}C-NMR analysis

^{13}C-NMR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea recorded in CDCl$_3$ solvent is given in Fig. 3. The NMR data are collected in Table 3.

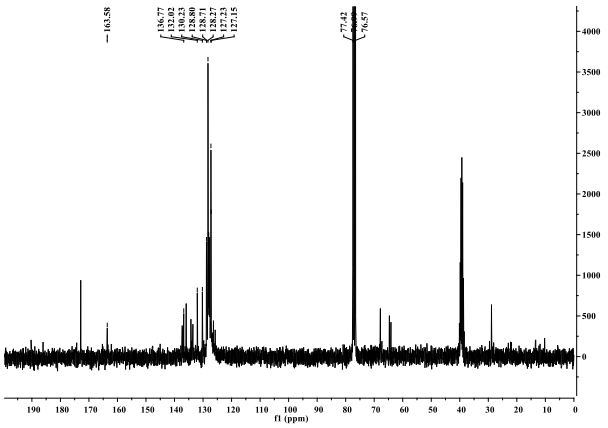

Fig. 3. ^{13}C-NMR spectrum of (1E,3Z)-1,3-bis(4-chlorobenzylidene) thiourea in CDCl$_3$

Table 3. ^{13}CNMR data for (1E,3Z)-1,3-bis(4-chlorobenzylidene) thiourea

S. No	Chemical shift (δ) (ppm)	Carbon
1.	163.58	(-HC=N)
2.	136.77	Aromatic C
3.	132.02	Aromatic C
4.	130.23	Aromatic C
5.	128.80	Aromatic C

Influence of different catalysts and different solvents

Two-component condensation of 4-chlorobenzaldehyde and thiourea under reflux conditions for 4 h using different acid catalysts in various solvent systems such as 1,2-dichloroethane, dichloromethane and toluene was carried out. The results are depicted in Table 4.

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Table 4. Effect of different catalysts and solvents

S. No	Catalyst	Solvent	Reaction time (reflex) (h)	% of yield
1.	No catalyst	1,2-dichloroethane	4	0
2.	Acetic acid	1,2-dichloroethane	4	40
3.	Acetic acid	Dichloromethane	4	32
4.	Acetic acid	Toluene	4	45
5.	$H_3[PW_{12}O_{40}]$	1,2-dichloroethane	4	26
6.	$H_3[PW_{12}O_{40}]$	Dichloromethane	4	29
7.	$H_3[PW_{12}O_{40}]$	Toluene	4	31
8.	$H_4[PVW_{11}O_{40}]$	1,2-dichloroethane	4	65
9.	$H_4[PVW_{11}O_{40}]$	Dichloromethane	4	52
10.	$H_4[PVW_{11}O_{40}]$	Toluene	4	59
11.	HPVAC-10	1,2-dichloroethane	4	**80**
12.	HPVAC-10	Dichloromethane	4	**70**
13.	HPVAC-10	Toluene	4	**73**
14.	Activated clay	1,2-dichloroethane	4	0
15.	$H_5[PV_2W_{10}O_{40}]$	1,2-dichloroethane	4	52
16.	$H_5[PV_2W_{10}O_{40}]$	Dichloromethane	4	41
17.	$H_5[PV_2W_{10}O_{40}]$	Toluene	4	48
18.	$K_7H_2[BCoW_{11}O_{40}]$	1,2-dichloroethane	4	25
19.	$K_7H_2[BCoW_{11}O_{40}]$	Dichloromethane	4	20
20.	$K_7H_2[BCoW_{11}O_{40}]$	Toluene	4	24

It clearly indicates that the catalyst HPVAC-10 in the presence of 1, 2-dichloroethane gave maximum yield among the given combination.

Effect of catalyst loading

Under the above optimized reaction solvent system the reaction was tried with catalyst with different loadings of HPV say 10 %, 20 % and 30 %. The catalysts are respectively denoted as HPVAC-10, HPVAC-20 and HPVAC-30 (Table 5).

Table 5. Variation of percentage of HPV loading clay catalyst

S. No	% of HPV loading in clay catalyst (%)	Weight of catalyst (g)	Reaction time (reflex) (h)	% of yield
1.	10	0.08	4	80
2.	20	0.08	4	**85**
3.	30	0.08	4	86

Activated clay with 20% HPV loading was found to be more efficient than the other two combinations. The optimization studies with varying amount of HPVAC-20 from 0.02 to 0.12 g was performed. In these trials 0.08 g of HPVAC-20 gave maximum yield of the product. Further the optimum time required for the completion of the reaction was also evolved and it is found to be 4 h.

Optimization studies recommends 0.08 g HPVAC-20 as catalyst in the presence of 1,2-dichloroethane medium under reflux condition for 4 h in order to get the maximum yield for the condensation of 4-chlorobenzaldehyde and thiourea to get (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea (Scheme 1).

IV. CONCLUSION

Synthesis of (1E, 3Z)-1,3-bis(4-chlorobenzylidene)thiourea by the condensation reaction of thiourea and 4-chlorobenzaldehyde in the presence of HPVAC catalyst produced high yield under heterogeneous condition. The product was identified as (1E,3Z)-1,3-bis(4-chlorobenzylidene)thiourea by FTIR and ^{1}H and ^{13}C-NMR . Further the optimum conditions for the catalytic reaction were reported.

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