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STUDIES ON CATALYTIC PROPERTIES OF POLYMER-SUPPORTED REAGENTS

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ABSTRACT

This article presents a review summary of the materials commonly used in polymer -supported chemistry and their evolution. It begins Based on the extensive utility of these hypervalent iodine compounds in organic synthesis, polymer-supported reagents having (diacetoxy)iodo group (PSIBD), bis(trifluoroacetoxy)iodo groups (PS-BTI), [hydroxy(tosyloxy)iodo]group (PS-HTIB), (dichloro)iodo group (PS-DCIB) have recently been developed. Applications of polymer-supported hypervalent iodine reagents in organic synthesis have been widely studied and some of the key reactions of these are described herein.

***Keywords**:- Cross-linked polystyrene; thermogravimetry; stoichiometric; oxidation; spectroscopic techniques; benzimidazol heterocycles; heterocyclic compounds*

INTRODUCTION

Benzimidazole derivatives have received much attention due to wide variety of physiological activities and commercial applications. In particular 2-aminobenzimidazole has been recognized as useful building block for the synthesis of various substituted benzimidazoles and fused benzimidazole heterocycles of academic and industrial interest.

Imidazo [1, 2-a] benzimidazoles, a class of fused tricyclic heterocyclesderived from 2-aminobenzimidazole, are versatile compounds useful as analgesics, anxiolytic and anticonvulstant and as corticotrophin-releasing factor 1 receptor agonists. The dihydroimidazo [1,2-a] benzimidazole and tetrahydro imidazo[1,2-a] benzimidazole derivatives have been shown to exhibit antihypertensive, antihistamine, and antiproliferative activity. Hypervalent iodine compounds have gained much significance in view of their versatile applications and diverse chemical behaviour in organic synthesis. Among the various applications of these reagents, one area of recent interest is the oxidation studies of nitrogen containing compounds such as hydrazones, acid hydrazides and related compounds.1 Iodine (III) oxidation reactions of these compounds results in the formation of some interesting products. In particular, aryl and aroyl hydrazones results in the formation of products depending upon the nature as well as substituent on carbonyl moiety. The reaction involves the intermediacy of hydroxy azo compound which was further hydrolyzed to the parent carbonyl compound.

MATERIALS AND METHODS

The most common route involves the reaction of substituted 2-aminobenzimidazoles with □-bromoketone to generate N-alkylacyl benzimidazole intermediate which on subsequent cyclization afforded the fused imidazoles. Reaction of one and two equivalents of □-bromoketones with produced 2-amino-1-aroylbenzimidazole and 2-iminobis (1, 3-aroyl) benzimidazole, respectively. Cyclization of and was effected using NaOH/MeOH to give 2-substituted imidazo1, 2-a□ □benzimidazoles and 2,9 disubstituted imidazo□ 1,2-a□ benzimidazoles, respectively.

□-acetoxy, hydroxy, methoxy azo compounds were readily synthesized from phenyl and methyl hydrazones using or in dichloromethane or methanol can either be hydrolyzed to the corresponding □-hydroxy phenyl azo compounds or can be transformed into important compounds, such as indazoles and pyrazoles.

Mild oxidation of 2-nitrobenzaldehyde aryl hydrazones with either bromine-sodium acetate or lead (IV) acetate in dichloromethane resulted in overall loss of two hydrogen atoms and production of 2-aryl-1, 2, 3-benzotriazine-1, 4-dioxides.

Hydrazone of nitrogen heterocyclic ketones and aldehydes have been found to afford fused 1, 2, 3-triazolo compounds by intramolecular cyclization of hydrazone using IBD in dichloromethane.

A number of hetercocyclic ketones andaldehydes hydrazone of 2-acetylpyridine, 2-benzoylpyridine, pyridine 2-carbaldehyde and benzothiazole 2-carbaldehyde underwent smooth cyclization to the corresponding triazolo compounds.

A closely related transformation has described to involve oxidative dimerization of acid hydrazides with IBD. Further, diacyl hydrazine so obtained can be dehydrated in presence of thionyl chloride to 1, 3, 4-oxadiazoles.

The presence of 2, 3-dihydroindole moiety in a variety of natural products and potential physiological activity associated with them resulted in the development of several strategies for their synthesis.

Reduction of indoles to indoline i.e. 2,3-dihydroindole has been one of the most common route employed for its synthesis.NaBH4 in neat carboxylic acid reduced the indole double bond but simultaneously alkylate the nitrogen atom to afford N-alkyl-2,3-dihydroindoles. However, the use of NaCN-BH3 under similar conditions avoids N-alkylation thereby permitting selective reduction of indoles to 2, 3-dihydroindoles

METHODOLOGY

There are many procedures for the preparation Chemical modifications of preformed polymers, Polymer-supported iodobenzene diacetate (PS-IBD), Polymer-supported [hydroxy(tosyloxy)]iodobenzene (PS-HTIB); The polymer-supported hypervalent iodine reagents were synthesized using commercially available 2% divinylbenzene cross-linked polystyrene. Its main advantages are:

(a) Good mechanical stability and well defined physical characteristics,
(b) The aliphatic backbone of the polymer is un-reactive and thus the polymer is not susceptiveto degradative chain scission and
(c) The aromatic rings are very reactive that can be easily functionalized.

The synthesized polymer-supported hypervalent iodine reagents were characterized using physical methods as well as IR and thermal studies [differential scanning calorimetry (DSC) and thermogravimetry (TG)]. However, NMR spectra could not be recorded due to solubility problem. All the polymer supported hypervalent iodine reagents (PS-IBD, PS-BTI, PS-HTIB and PSHMIB) showed the presence of C-H stretching and aromatic ring stretching bands (vide experimental). The carbonyl stretching bands in PS-IBD and PS-BTI were observed respectively at 1650 and 1659 cm-1.Thermal behavior of hypervalent iodine reagents and polymer-supported hypervalent iodine reagents (PS-IBD, PS-BTI, PS-HTIB and PS-HMIB) including that of polystyrene and iodopolystyrene was investigated by TG and DSC.

Reactions:-

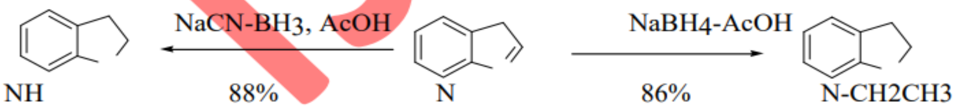
These results suggest that polymer-supported hypervalent iodine reagents may be utilized in high boiling solvent without decomposition upto 398° C. TG data are presented in Table. TG analysis of hypervalent iodine reagent andpolymer-supported hypervalent iodine reagents

Entry	**IDT(°C)**	**T_{max}(°C)**	**HDT(°C)**	**Wt. loss at 300/600°C (%)**
PS	310	375	420	97
PS-I	305	372	410	95
IBD	154	178	205	97
PS-IBD	337	380	398	95
BTI	132	175	194	98
PS-BTI	355	381	402	94
HTIB	160	180	243	98
PS-HTIB	361	380	407	96
HMIB	136	174	221	94
PS-HMIB	330	372	398	98

DSC study indicated that there was appearance of an endotherm at the melting temperature of hypervalent iodine reagents followed by an exotherm. The enthalpy change along with peak temperature and onset temperature are gathered in Table. DSC analysis of hypervalent iodine reagent and polymer-supported hypervalent iodine reagents.

Entry	**Peak Temp. (°C)**	**Onset (°C)**	**Enthalpy ΔH J/g**
PS	262.86	229.13	155.1
	401.04	337.88	301.4
PS-I	307.73	286.93	62.86
	388.17	369.74	143.0
IBD	161.14	153.14	85.75
	188.94	174.58	266.7
PS-IBD	157.99	123.27	136.5
	390.42	371.33	164.2
BTI	115.87	104.62	60.44
	171.70	150.65	228.9
PS-BTI	331.08	303.65	50.11
	393.25	376.38	64.54
HTIB	131.54	111.68	92.60
	153.85	147.79	144.2
PS-HTIB	324.78	296.91	121.0
	398.67	381.89	153.8

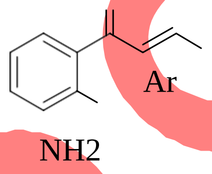
The use of NaCN-BH3 under similar conditions avoids N-alkylation thereby permitting selective reduction of indoles to 2, 3-dihydroindoles.



2-Aminoacetophenone was added to a solution of appropriate aldehyde in 15 mL of ethanol containing 2-3 pellets of NaOH and the resulting solution was stirred for 8-10 h at 5- 10 ° C. The resulting orange solid formed was filtered and dried. TLC confirmed the purity of orange crystals.

Physical data of 2-aminochalcones

Entry	**Ar**	**m. p. (□C)**	**Lit. m.p. (□C)**	**Yield (%)**	**Ref.**
210a	C6H5	71	71-72	65	37
b	4-ClC6H4	110		71	
c	4-BrC6H4	114-15		70	
d	4-	90-91	91-92	72	37
e	4-NO2C6H4	145-46		74	



2-aminochalcones

Procedure

FTIR spectra were obtained in KBr on Shimadzu FTIR 8201 PC spectrophotometer and are reported in cm-1. Polystyrene with 2% cross linked with divinylbenzene, (MW = 2,50,000, 200-400 mesh) was purchased from Aldrich. All solvents were of reagent grade and were used without further purification.

Melting points were determined in open capillaries and are uncorrected. FTIR spectra were obtained in KBr on either Shimadzu FTIR 8210 PC or Perkin Elmer Spectrum RX1 instruments and are reported in cm-1. 1H and 13C NMR spectra were determined on a Bruker Avance II NMR spectrometer operating at 400 MHz and 100 MHz, respectively in CDCl3 or CDCl3+DMSO-d6 and are expressed as ppm with respect to TMS. Elemental analysis was carried out on Perkin Elmer 2400 instrument. HRMS were recorded on VG 70 EB mass spectrometer.

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Synthesis of 2-aminochalcones

2-Aminoacetophenone was added to a solution of appropriate aldehyde in 15 mL of ethanol containing 2-3 pellets of NaOH and the resulting solution was stirred for 8-10 h at 5-10° C. The resulting orange solid formed was filtered and dried. TLC confirmed the purity of orange crystals.

Synthesis of PS-I

Mixture of 2% cross-linked polystyrene iodine iodine pentoxide in 25 mL of carbon tetrachloride and 20 mL of 50% sulfuric acid in 100 mL of nitrobenzene in a round bottomed flask was stirred at 90° C in an oil bath for 72 h. The reaction mixture was diluted with 50mL of chloroform followed by the addition of methanol to precipitate out iodopolystyrene that was collected by filtration and dried.
IR (KBr, cm-1): 3024 (CH), 3001 (CH), 2922, 2850, 1598, 1583, 1523, 1477, 1444, 1402, 1344, 1180, 1153, 1001, 812, 744, 680.

Synthesis of PS-IBD

Hydrogen peroxide was added drop wise to acetic anhydride in a round bottom flask at 0° C. The solution was slowly warmed to room temperature and stirred overnight followed by addition of iodopolystyrene. Then the reaction mixture was stirred overnight. After completion of the reaction, diethyl ether was added to cause precipitation. PS-IBD so precipitated was collected by filtration and dried.
IR (KBr, cm-1): 3010 (CH), 2920 (CH), 2852, 1650 (CO), 1492, 1361, 1234,
1153, 1000, 770.

Synthesis of PS-BTI

A mixture of PS-IBD in 10 mL of trifluoroacetic acid was refluxed for 5 h. The solvent was removed at reduced pressure. Addition of diethyl ether precipitated PS-BTI which was filtered, washed with diethyl 24ether and dried.
IR (KBr, cm-1): 3001 (CH), 2966 (CH), 2802, 1689 (CO), 1514, 1401, 1322,
1204, 1148, 987, 835.

Synthesis of 1, 2-diaminobenzimidazole

Hydroxylamine-O-sulfonic acid was added to a solution of 2-aminobenzimidazole and potassium hydroxide in 80 mL of water at room temperature. The resulting solution was stirred at ambient temperature for 30 min. The solid so formed was collected at suction and recrystallized from ethanol to afford 1, 2-diaminobenzimidazole.Yield: 54%; m.p. 257 ◦C (Lit.5 m.p. 256-259 ◦C).

RESULTS

Hypervalent iodine compounds have gained much significance in view of their versatile applications and diverse chemical behaviour in organic synthesis. Oxidative cyclization reactions using hypervalent iodine compounds have been emerged as versatile and leading tool in past few years in synthetic transformation owing to the mild reaction conditions and eco friendly nature required. Further oxidation of carbonyl hydrazones has been investigated with hypervalent iodine reagents and has been reported to afford useful products.

In order to extend the scope of this reaction, the oxidation of Naroyl/acetyl-2-nitrobenzaldehyde hydrazones with IBD or PS-IBD was also investigated. The hydrazones were synthesized by the reaction of 2-nitrobenzaldehyde and appropriate acid hydrazide on refluxing in ethanol in presence of 5-6 drops of glacial acetic acid in 70-80% yield.

The synthesized polymer-supported hypervalent iodine reagents were characterized using physical methods as well as IR and thermal studies [differential scanning calorimetry (DSC) and thermogravimetry (TG)].All the polymer supported hypervalent iodine reagents (PS-IBD, PS-BTI, PS-HTIB and PSHMIB)showed the presence of C-H stretching and aromatic ring stretching bands (vide experimental). The carbonyl stretching bands in PS-IBD and PS-BTI were observed respectively at 1650 and 1659 cm-1.

DISCUSSION

Hypervalent iodine reagents have been found to show broad applications in organic chemistry and now-a-days are frequently used in synthetic transformations. Because these are non metallic oxidation reagents, they avoid the issues of toxicity of many transition metals commonly involved in such processes. Hypervalent iodine compounds bear a high potential for the improvement of known reactions from environment and pharmaceutical point of view. The participation of 2- hydroxy- and 2-amino groups during the oxidation of hydrazones resulted in the synthesis of a variety of useful important products using hypervalent iodine reagents. The basic requirement for successful reaction generating and using hypervalent iodine compounds in catalytic amounts is ability of the stoichiometric oxidant that should selectively react only with the polymeric iodine (I) and transform it into the iodine (III) reagent in presence of a substrate. The oxidant must not react with the substrate, as the substrate must be oxidized by the polymer-supported hypervalent iodine species generated.

SUMMARY

Benzimidazoles are one of the longest known nitrogen heterocycles and have been recognized as useful building blocks for the synthesis of a wide variety of heterocycles of academic, pharmaceutical and industrial interest. Triazolo benzimidazoles derived from 1, 2- diamino benzimidazoles have been found to possess antifungal, anti-inflammatory and analgesic as well as antihistamine effects. Imidazo□ 1, 2-b□-[1, 2, 4] triazine were found as □ 2/□ 3 subtypeselective GABAagonists for the treatment of anxiety. Hypervalent iodine compounds have gained much significance in view of their versatile application and diverse chemical behavior in organic synthesis. Hypervalent iodine compounds have gained much significance in view of their versatile applications and diverse chemical behavior in organic synthesis. Oxidative cyclization reactions using hypervalent iodine compounds have been emerged as versatile and leading tool in past few years in synthetic transformation owing to the mild reaction conditions and eco friendly nature required. Further oxidation of carbonyl hydrazones has been investigated with hypervalent iodine reagents and has been reported to afford useful products. The participation of 2- hydroxy- and 2-amino groups during the oxidation of hydrazones resulted in the synthesis of a variety of useful important products using hypervalent iodine reagents. Therefore, in continuation of our interest in the use of these reagents led us to investigate the oxidation of 2-nitrobenzaldehyde hydrazones in order to observe the effect of nitro group. In animals, serotonin (5- hydroxytryptamine) is a crucial neurotransmitter in the central nervous system. The potent physiological properties of indole derivatives led to vast research for their use as medicine in the field of pharmaceutical chemistry. Indomethacin, a non -steroidal anti- inflammatory agent and pindolol, a □- adrenergic blocks, are clinically proven indole compounds. Several naturally occurring indoles are also of clinical relevance, vincristine, a dimerize indole alkaloid and related compounds were the first of antimitotic class of chemotheraptic agent for cancer.

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