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Efficient CeO_2 nanoparticles catalysed for Synthesis of heterocyclic Bis(Indolyl) methanes under mild conditions

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Abstract

There is need to develop simple, efficient & economically viable chemical pathways to synthesise biologically active & commercially important heterocyclic Bis(indolyl) methanes[1].The indole ring is an important constituent of many natural products, pharmaceuticals & other compounds of commercial importantance[2]. The literature survey shows that Bis(indolyl) methanes are known to increase estrogen metabolism in human beings and hence can be used for the treatment of breast cancer, also it exhibits antibacterial activities[3,4,5]. This wide range of applications has leaded the chemists to develop new methods to synthesise Bis (Indolyl) methanes.

Various methods have been developed for their synthesis using Lewis acid catalysts[6-12], ionicliquids[13], trichloro-1,3,5-triazine[14], and potassium hydrogen sulphate[15].However, many of these reported methods suffer from one or other disadvantages such as harsh reaction conditions and reagents that are expensive, moisture sensitive. A mild and efficient catalyst for the synthesis of bis(indolyl) methanes is highly desirable.

Key words: Bis(indolyl) methanes, CeO_2 nanoparticles, carbonyl compounds, indole, aldehydes

INTRODUCTION

Heterocyclic Bis(indolyl)methanes derivatives have been synthesized using a catalytic amount of ceria nanoparticals in $CHCl_3$ at room temperature, .CeO_2 nanoparticles were found to be an efficient catalyst in the reaction of indoles with carbonyl compounds to afford the corresponding bis(indolyl)methanes. .The significances of this method are mild reaction condition, excellent yield and simple work up procedure.

General Experimental Procedure for preparation of CeO_2 nanoparticles

Ceric Ammonium Nitrate (3.65 gm).as source of metal ion and 0.5 gm. of glycine along with L-Ascorbic Acid (1.117 gm.) has taken in given amount in de ionised water .It is heated on hot plate at 80^oC in order to get homogenised and gel

is formed after removal of excess of water transferent solution get formed. After removal of water gel get swallowed and then big bloom of gases comes out for 2-3 seconds .finally yellowish powder get formed this powder further heated at 600^{o}C in the muffle furnace for 30 minutes to get fine CeO_2 nanoparticles having size (70.5-82.3)nm

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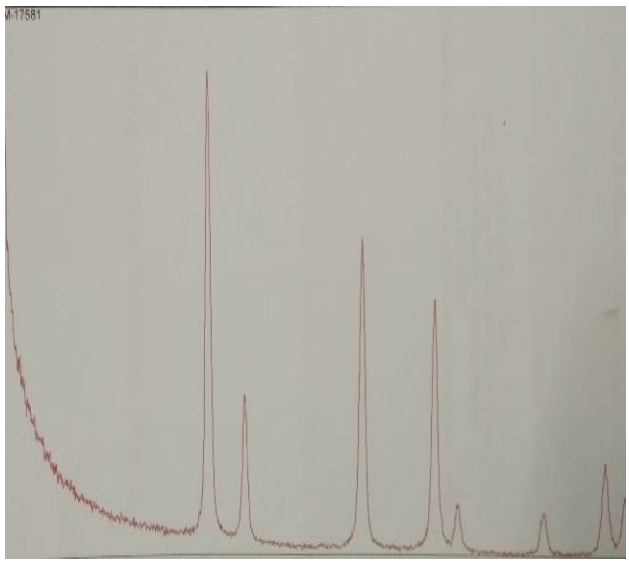
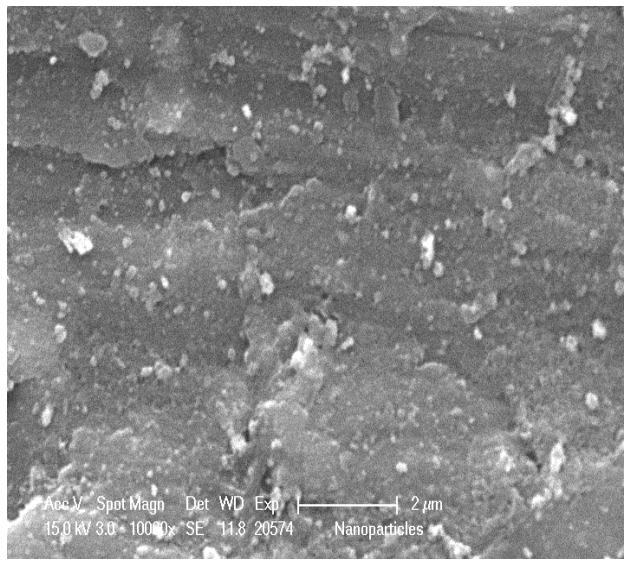


(XRD of Ceria Nanoparticle).Sample No. M- 17581(CIRCOT)



SEM of Ceria nanoparticle

RESULT AND DISSCUSSION

We selected the reaction between Benzaldehyde and Indole in the presence of synthesis of Bis(indolyl) emethane. The effect of solvent was studied. The reaction were performed in polar solvent like $CHCl_3$the yield of the corresponding products were found to be maximum (Table 1, Entry 1.)

Table 1. Investigation of solvent effects for the synthesis of Bis(Indolyl)methanes

Entry	Solvent	Bis(Indolyl)methanes (1b)*	
		Time (min.)	Yield[b] (%)
1	$CHCl_3$	20	95
2	CH_2Cl_2	40	78
3	CH_3CN	35	82
4	C_2H_5OH	25	71

[a]Isolated Yields

Therefore, $CHCl_3$ was selected as the most appropriate solvent for the Scheme .

The catalytic activity of CeO_2 nanoparticles was studied with respect to the loadings. It was observed that 0.1 mmole catalyst gave excellent yield (Table 2)

Table 2 Catalytic effect of CeO_2 nanoparticles on synthesis of Bis(Indolyl) methanes

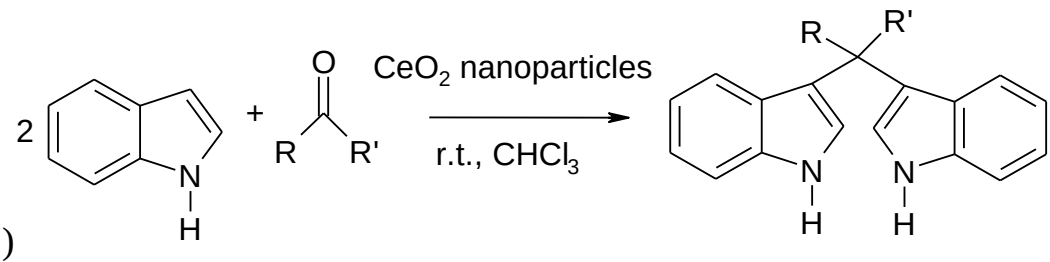
Entry	CeO_2 nanoparticles (mmol)	Bis(Indolyl) methanes (1b)	
		Time (min.)	Yield[b] (%)
1	0.01	30	70
2	0.05	30	85
3	0.10	20	95
4	0.20	20	95

[b]Isolated Yield of product in Scheme

Experimental Procedure for Bis(Indolyl) methanes:

A mixture of Benzaldehyde (2 mmol), Indole(4mmol) and CeO_2nanoparticles (0.1 mmol) with one ml of $CHCl_3$was stirred magnetically at room temperature, and the progress of the reaction was monitored by thin-layer chromatography. After completion of reaction, the reaction mixture was centrifuged to separate the catalyst and evaporated to get product. The product was dried over anhydrous Na_2SO_4 and further purified by column chromatography.

In this communication, we report a synthesis of Bis(indolyl) Methanes by using CeO_2 nanoparticles in a wide variety of compounds that were applied to the optimal reaction Conditions to prepare a wide range of bis(indolyl) methane



(Scheme-1)

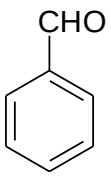
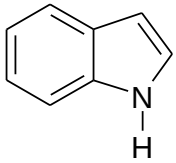
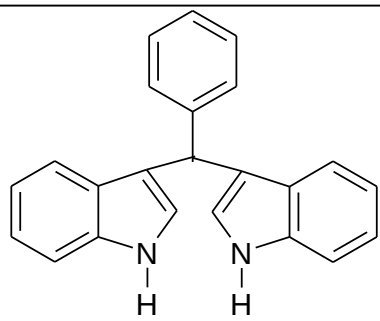
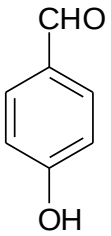
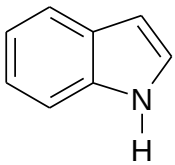
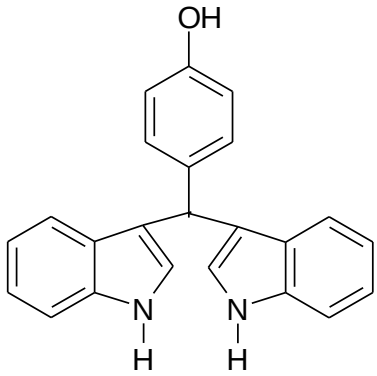
R: Phenyl, Alkyl; R': H, Phenyl, Alkyl

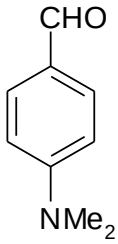
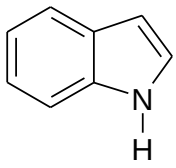
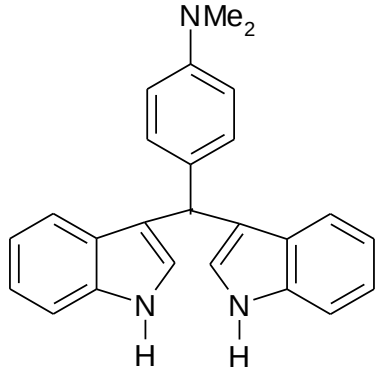
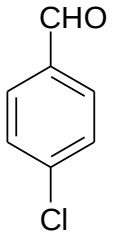
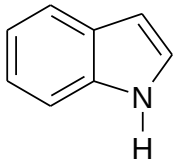
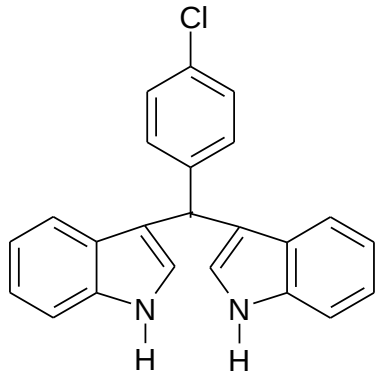
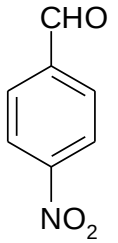
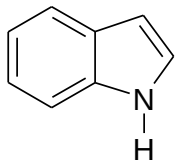
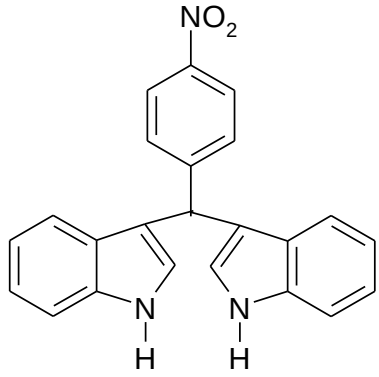
RESULT AND DISCUSSION

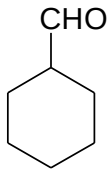
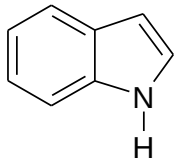
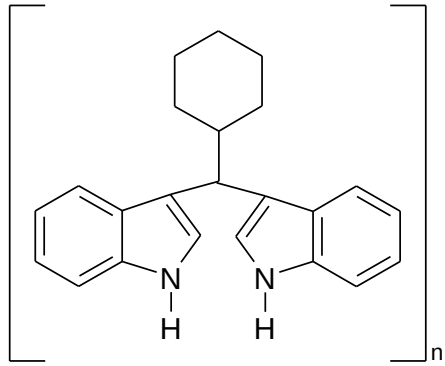
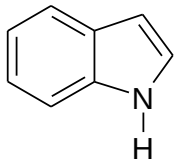
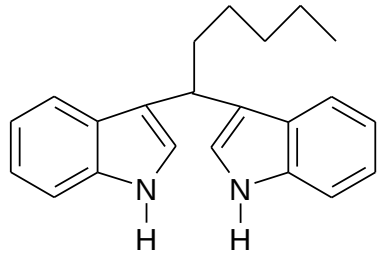
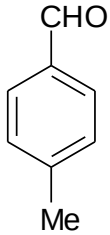
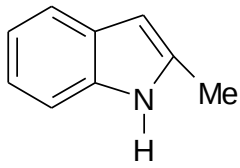
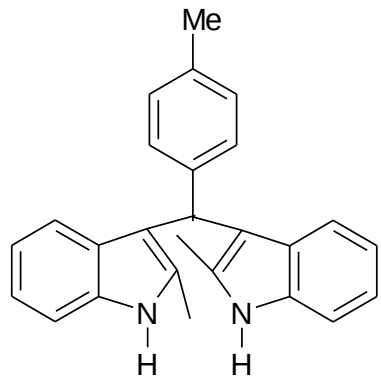
The reaction proceed efficiently and smoothly at room temperature in presence of CeO_2 nanoparticles as a catalyst in $CHCl_3$, In order to show generality of this method various aldehydes & ketones were made to react with two equivalents of indole under same reaction conditions. It is found that reaction

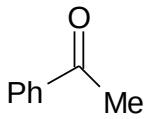
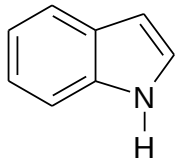
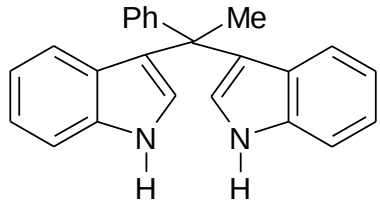
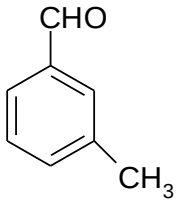
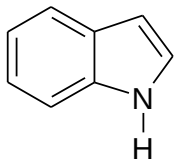
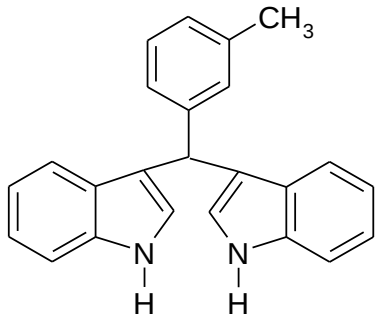
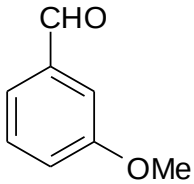
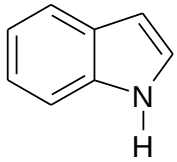
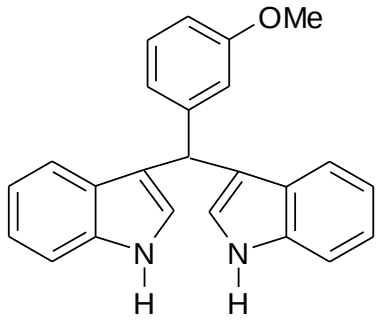
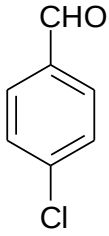
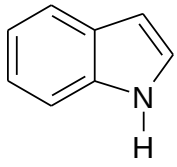
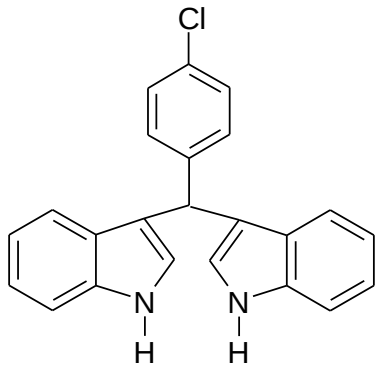
proceeds smoothly giving excellent yields with compounds having electrone withdrawing groups (Table-3, Entries-5, 14, 15) while electrone donating group gives corresponding yields. (Table-3, Entries-2, 3 .,8,, 11, 12).. Alicyclic aldehydes(6,7) and ketones gives affordable products,(Table-3, Entries-9)

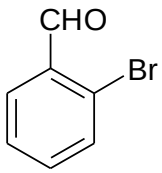
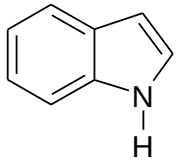
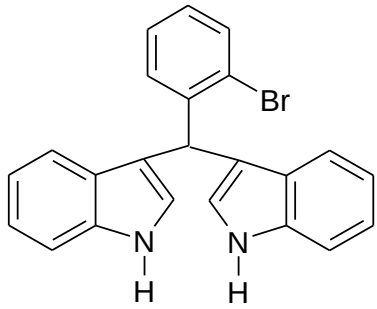
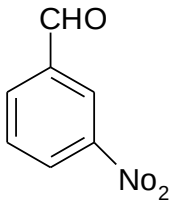
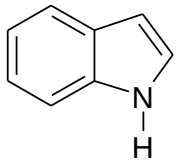
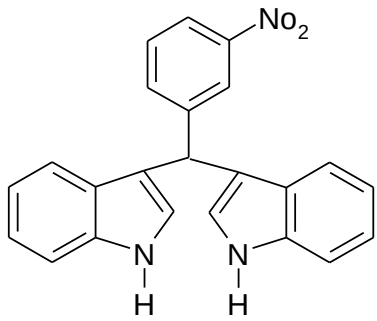
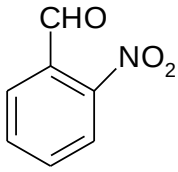
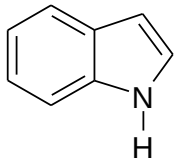
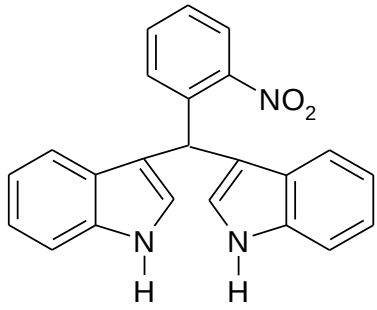
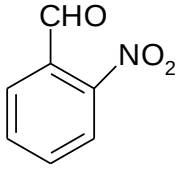
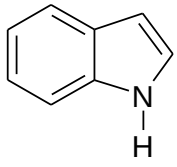
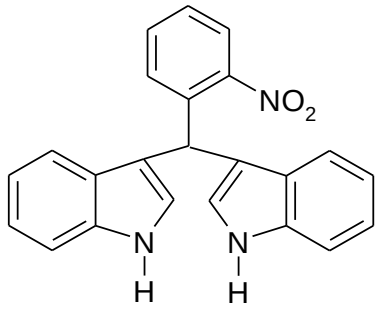
Table-3 . Synthesis of bis(indolyl) methanes

Entry	Aldehyde(a)	Indoles	Product (b)	)Time (min)	Yield[c] (%)
1.				20	95
2.				20	91

3.				40	89
4.				40	87
5.				20	95

6.				25	85
7.				25	85
8.				25	88

9.				60	90
10.				25	85
11.				25	86
12.				25	84

13.				25	80
14.				25	95
15.				25	92
16.				25	90

[a]The substrate was treated with Indole (2mmol) by stirring at room temperature with CeO_2 nanoparticles in presence $CHCl_3$assolvent; [b]All products were identified by their IR and ^1H NMR spectra;

[c]Isolated yields after column chromatography.

SPECTRAL DATA

3,3'-Bisindolyl phenyl methane (1b): Pale-red solid, yield 93%, m.p. 122-124^{0}C

IR (KBr): 738, 1010, 1175,1333, 1415, 1602, 2845, 3024, 3055, 3410 cm^{-1}

^{1}H NMR (300MHz, $CDCl_3$): δ = 7.7(s, 2H); 7.2-7.4(br m, 8H); 6.4-6.8(m, 5H); 4.2-4.4(s, 2NH); 2.3 (s, H): ^{13}C NMR ($CDCl_3$) : 144.2, 136.7, 128.5, 128.7, 127.3, 126.8, 123.5, 121.5, 119.9, 111.2,40.5. EIMS; m/z 322

3,3'-[(4-methylphenyl)methanediyl]bis(1H-indole) (8b)

IR (KBr) 3412, 3055 ,1610, 1457 cm-1, 1H NMR (CDCl3,300MHz) δ2.5 (s,3H,-CH3), 5.7(s,1H,-CH), 6.5 (s,2H,Ar-H), 6.96 (m,14H,ArH), 7.9(bs,2H), 13C NMR (CDCl3,300MHz) δ 22,38,112, 119.14, 119.95, 119.90, 123.57, 127.15, 128.59, 128.95,135.48, 136.72, 141

CONCLUSION

In summary, it can be concluded that CeO_2 nanoparticles is an efficient and excellent catalyst for the synthesis of the bis(indolyl)methanes from various aromatic aldehydes , ketones and indole in high yields under mild conditions in short reaction time.The mild reaction condition ,rapid reaction rate, simple work up procedure, excellent product yields.

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