

Synthesis of Bis(Indolyl) Methane and Some Devices Using Hydrogenous Catalysts (Acidic) in Ecofriendly Media

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Abstract

The organic reaction of indoles and benzaldehyde in the absence of organic solvents to obtain bis(Indolyl) Methanes (BIM) have been studied. The optimum reaction conditions were determined to produce (BIM). The optimal condition (catalysts, temperature and solvents) to get a high selective compounds and high yields have been studied. When use of heterogeneous catalyst (Amberlyst-15) (10%mol), tetrahydrofuran as a solvent and 65C getting a required selectivity and high yield (about 87%) in comparison to the homogeneous catalysts (H₂SO₄, PTSA, CH₃SO₃H), in addition to the low selectivity of the final product. The reaction followed by using thin layer chromatography (T.L.C), the molecular structures have determinate by spectroscopy methods :FT-IR, ¹H-NMR, ¹³C-NMR.

Keywords: BIM, Benzaldehyde, Amberlyst-15, Ecofriendly Media.

1. Introduction

In recent years, a large trend towards synthesis of bis(indolyl) methanes and their derivatives has attracted much attention due to their synthetic as well as biological applications [1]. Bis(indolyl) methanes as shown in figure.1 are most activecruciferous substances for promoting beneficial estrogen metabolism and inducing apoptosis in human cancer cells [2]. Because of their wide occurrence as natural products and various biological activities, synthesis of these bis(indolyl) methanes has attracted attention. Recently, oxidized bis(indolyl) methanes containing a conjugated bis(indolyl)skeleton have acted as colorimetricensorsand chromogenic sensors [3]. Solvent-free reactionshavebeen established an efficient technique for various organic reactions avoiding harmful solvents. The acid-catalyzed condensations of indole with carbonyl compounds have been of concern as a useful route for preparation of bis(indolyl) methanes. The protic acids and Lewis acids [4] have been used in excess and drastic conditions. To abate the environmental pollution of the disposal of excess acids with the improvement of reaction condition a number of catalytic systems were used, which were rare earth perfluorooctanoate [RE(PFO)₃] [5], trichloro-1,3,5-triazine [6], hexamethylenetetramine-bromine [7], ion-exchange resin [8]. Ionic liquids in conjugation with In(OTf)₃ or FeCl₃.6H₂O [9] were also found to promote this reaction. Recently, phosphate zirconia [10], heteropoly acids [11], fluoroboric acid [12], amberlyst, silica sulfuric acid [13], ZrOCl₂.2H₂O/SiO₂ [14], and protic solvents [15] were also reported to promote the synthesis of bis(indolyl) methanes.

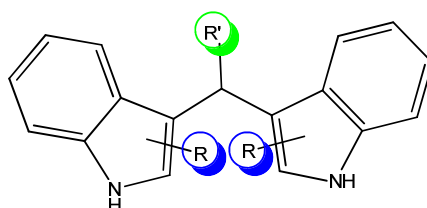


Figure 1. General formula of bis(indolyl) methane.

were also reported to promote the synthesis of bis(indolyl) methanes. However, many of these methods suffer from the drawback like use of expensive reagents [16-17-19], excess of catalyst [18], long reaction time [7-16-18] and low yield of products [20]. In order to develop a new method for the synthesis of bis(indolyl) methanes and to overcome all the problems on previous work of Posner et al., we use an Amberlyst-15 as an acidic catalyst. The role of Amberlyst-15 as a heterogeneous catalyst on several organic reactions, such as oxidation, reduction and displacement reactions is known from the previous work of Posner et al. [19], [20]. Keeping all these facts in mind, we go for synthesis of bis(indolyl) methanes using heterogeneous catalyst Amberlyst-15 which gives clean, efficient and fast reactions.

2. Experimental

2.1. Apparatus

spectrum NMR proton and carbon device 400 MHz model Bruker by Switzerland company, optical absorption

spectrum infrared device model FT-IR-4100 from the Japanese company Jasco, rotary evaporator 4.91 model from the German company Normschiff, thin layer chromatographic of aluminum coated by Silica Gel 60F254 measuring 20 X 20 from the German company Merck, thin layer chromatographic of preparatory glass coated by Silica Gel 60F254 measuring 20 X 20 from the German company Merck.

2.2. Reagents and materials

1*H*-indole, 1-methyl-1*H*-indole, 2-methyl-1*H*-indole (99.5% C Pure), Benzaldehyde (Acros Organics, Belgium), and Amberlyst-15 (99% by sigma aldrech), Methan Selfonic Acid, *p*-toluenesulfonic acid, Sulforic Acid and some Solvents (99% by Merck).

3. Experimental Procedure

We added different catalysts of benzaldehyde to indoles (1*H*-indole, 1-methyl-1*H*-indole, 2-methyl-1*H*-indole) and different solvents (tetrahydrofuran, acetonitrile, dimethylsulfoxed, ethanol, water) into a tow-necked flask equipped with a thermometer thorn fractionating column and cooler reflex as shown in figure-2.

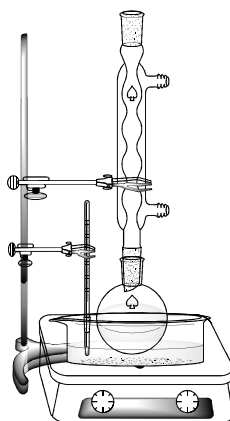
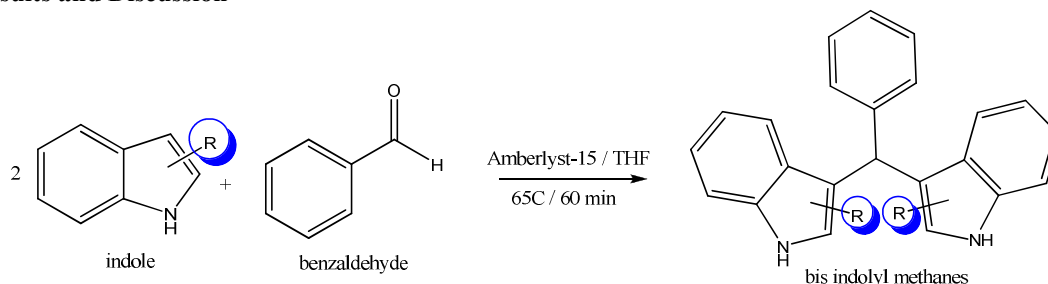


Figure 2. a tow-necked flask equipped with athermo meter.

Different kinds of catalysts (sulfuric acid, methane sulfonic acid, *p*-toluenesulfonic acid, and amberlyst-15) were added, respectively, to a tow-necked flask equipped with athermo meter thorn fractionating column, using cooler reflex, we then added benzaldehyde, indoles and catalyst (the best catalyst is amberlyst-15). All of these reactions were performed at about 65°C° under stirring and reflowing. After the optimum conditions obtained, we used different indoles to synthesized BIMs like 1-methyl-1*H*-indole, 2-methyl-1*H*-indole.

4. Results and Discussion



Scheme 1. Synthesis route of the main reaction.

Table 1. different aromatic carboxylic acid to the Product.

Entry	Indoles	Bis indolyl methanes
1	1 <i>H</i> -indole	3,3'-(phenylmethylene)bis(1 <i>H</i> -indole)
2	1-methyl-1 <i>H</i> -indole	3,3'-(phenylmethylene)bis(1-methyl-1 <i>H</i> -indole)
3	2-methyl-1 <i>H</i> -indole	3,3'-(phenylmethylene)bis(2-methyl-1 <i>H</i> -indole)

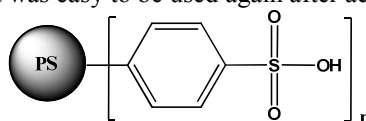
The optimal conditions for preparations of Bis indolyl methanes by reacted of aldehydes and 1*H*-indole to produce Bis indolyl methanes (BIM). The catalytic effects of several catalytic systems were inspected in the reaction of aldehydes and 1*H*-indole, these catalytic systems included sulfuric acid, methanesulfonic acid, *p*-toluenesulfonic acid and amberlyst-15 as shown in table(2), sulfuric acid did a remarkably bad job on this reaction in reverse, while methanesulfonic acid, *p*-toluenesulfonic acid and amberlyst-15 had good catalytic activities. However, it was easy to remove amberlyst-15 after the reaction, because it was a heterogeneous catalyst. There for, amberlyst-15 was determined to be optimal catalyst for the reaction of the 1*H*-indole. The

several acidic catalysts homo and heterogeneous has used table (2):

Table 2. effect of different catalysts to the Product yield% (BIM).

Entry	H ₂ SO ₄	<i>p</i> -toluenesulfonic acid	CH ₃ SO ₃ H	Amberlyst-15	Time (min)
1	18	29	25	20	10
2	32	38	48	35	20
3	39	52	57	50	30
4	36	78	66	87	60
5	33	68	51	60	120

The last figer shown that the best one has an Amberlyst-15 "acid heterogeneous catalyst" and the best time (60 min), because after that secondary products was formed, so the yield of Bis indolyl methanes will beging decline, as it shows when using ather catalysts "H₂SO₄, CH₃SO₃H, *p*-toluenesulfonic acid ". besides an environmental perspective It was found that the best acid catalyst is an Amberlyst-15, because it was an acidic heterogeneous catalyst figure(3): and it was easy to be used again after activated.



Amberlyst-15 (4.7meq/g)

Figure 3. Catalytic formula (amberlyst-15).

The specific impacts of different molar amount of catalyst on the yield did not notice when encesses the amount of catalyst table(3).

Table 3. effect of different amount of catalyst (amberlyst-15).

Entry	amount of catalyst %mol	% yield
1	-----	traces
2	5	traces
3	10	87
4	20	87
5	30	87
6	40	87

So we conclude that when using large amounts of heterogeneous catalyst "Amberlyst-15" do not affect to the preparation BIM, so from an economic perspective preferred using the least possible result. After that the reaction between benzaldehyde and 1*H*-indole with different solvents had been studied as shown table (4).

Table 4. effect of different solvents.

Entry	solvent	% yield
1	Tetrahydrofuran	87
2	Dimethylsulfoxid	65
3	Acetonitrile	85
4	Ethanol	20
5	Methanol	30
6	Water	20

Different solvents used to studying effects to the yield reaction. However, polar solvents (Ethanol, Methanol, Water) was bad to the yield reaction, besides dimethylsulfoxyd was bad to remove it after reaction. while using Tetrahydrofuran was the best choice (Tetrahydrofuran is a moderately polar). So in this case the moderately polar solvents working to increase the yields interactions.

Then and studying the effect of temperature, synthesis of BIM was carried out at the temperature range of 40°C – 100°C (Table 5):

Table 5. Effect of different temperature to the reaction yield.

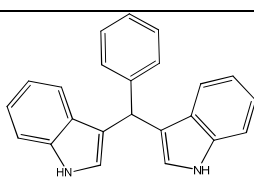
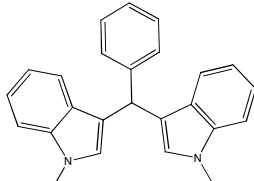
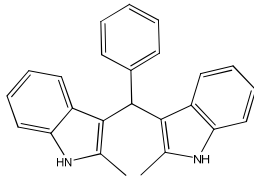
Entry	temperature	% yield
1	40	45
2	65	87
3	75	80
4	85	55
5	100	30

We found that when using a tetrahydrofuran as a solvent, Amberlyst-15(10%mol) as a hydrogenous catalyst, temperature is 65°C, and time 65 min the yield reaction was the best (87%).

Finally, when applying the previous conditions to prepare BIM on the reaction of preparing some products, we had synthesized successfully which had used in the many applications in industry and food as

shown in table(6).

Table 6. different products to the esterification.

Entry	Product	amount of catalyst (10%mol)	amount of indoles	temperature	Time reaction	% yield
1		0.042gr:0.0002mol	0.234gr:0.002mol	65C°	60 min	87
2		0.042gr:0.0002mol	0.262gr:0.002mol	65C°	60 min	94
3		0.042gr:0.0002mol	0.262gr:0.002mol	65C°	60 min	93

5. Carectarization

product entry (1) gave yeild (87%).

IR spectrum (v, cm⁻¹): 1455, 1599, 2852 (-CH-), 2928 (-CH-), 3022 (Ar- H), 3055 (Ar-H), 3410 (-NH-).

¹H-NMR (δ, ppm): 5.88 (s, 1H, -CH), 6.63 (d, 2H, J= 2.4 Hz, -NH-CH=), 7.00 (dd, 2H, J = 7.9 Hz, -CH=), 7.17 (dd, 2H, J = 7.9 Hz, -CH=), 7.21 (m, 1H, -CH=), 7.27 (m, 2H, -CH=), 7.33 (d, 4H, J = 8.0 Hz, -CH=), 7.38 (d, 2H, J = 8.0 Hz, -CH=), 7.87 (br s, 2H, - NH).

¹³C-NMR (δ, ppm): 40.2 (-CH-), 111.0 (-CH=), 119.3 (-CH=), 119.7 (-C=), 119.9 (-CH=), 121.9 (-CH=), 123.6 (-CH=), 126.2 (-C=), 127.1 (-CH=), 128.2 (-CH=), 128.7 (-CH=), 136.9 (-C=), 144.0 (-C=).

product entry (2) gave yeild (94%).

IR spectrum (v, cm⁻¹): 1472, 1598, 2853 (-CH-), 2927 (-CH-), 3021 (Ar-H), 3054.

¹H-NMR (δ, ppm): 3.66 (s, 6H, -CH₃), 5.87 (s, 1H, -CH), 6.52 (s, 2H, -N-CH=), 6.98 (dd, 2H, J = 7.9 Hz, -CH=), 7.19 (dd, 3H, J = 7.9 Hz, -CH=), 7.29 (m, 4H, -CH=), 7.33 (d, 2H, J = 7.9 Hz, -CH=), 7.35 (d, 2H, J = 7.9 Hz, -CH=).

¹³C-NMR (δ, ppm): 32.7 (-CH₃), 40.1 (-CH-), 109.1 (-CH=), 118.3 (-C=), 118.7 (-CH=), 120.1 (-CH=), 121.4 (-CH=), 126.0 (-CH=), 127.5 (-C=), 128.2 (-CH=), 128.3 (-CH=), 128.7 (-CH=), 137.4 (-C=), 144.5 (-C=).

product entry (3) gave yeild (93%).

IR spectrum (v, cm⁻¹): 1584, 1623, 2925 (-CH-), 2960 (-CH-), 3314, 3391 (-NH-).

¹H-NMR (δ, ppm): 2.11 (s, 6H, -CH₃), 6.05 (s, 1H, -CH-), 6.71 (dd, 2H, J = 7.9 Hz, -CH=), 6.92 (m, 4H, -CH=), 7.26 (m 7H, -CH=), 9.85 (br s, 2H, -NH=).

¹³C-NMR (δ, ppm): 12.3 (-CH₃), 40.2 (-CH-), 111.1 (-CH=), 113.7 (-C=), 119.1 (-CH=), 119.8 (-CH=), 120.8 (-CH=), 126.6 (-C=), 128.8 (-CH=), 129.8 (-CH=), 129.9 (-CH=), 132.8 (-C=), 136.4 (-C=), 145.6 (-C=).

6. Conclusion

In summary, the condition of reaction was successfully studied by synthesis of BIM, When the molar ratio of benzaldehyde to indoles was (1:2), amberlyst-15 worked as a green catalyst, and the reaction time was around 60 min, the reaction yielded about (87%). Under these conditions most of products table(6) was successfully synthesized, With little difference in the yields of interaction. The results proved that the optimum conditions to obtain high selective compounds with high yields by studying the affect of different catalysts, temperatures and solvents have been investigated.

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