SOLVENT FREE SYNTHESIS OF BIS (INDOLYL) METHANES USING GRINDING TECHNIQUE

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ABSTRACT: Tartaric acid was found to be a mild, efficient acid catalyst in electrophilicsubstitution reaction of indoles with carbonyl compounds to afford the correspondingbis(indolyl)alkanes in excellent yields. In the present work, variouselectrophilic substitutionreactions of indoles with several aldehydes were carried out using grinding technique. the products were characterized by FT-IR, 1H-NMR

KEYWORDS: Grinding technique Tartaric acid, Indole, Aromatic Aldehyde, bis (indolyl) methanes, Spectralanalysis.

INTRODUCTION:

The design and developmentof sequences allowing highly selective access to complexmolecular skeleton while combining structural diversity withthe use of eco-friendly and environmentally benign catalystsand reagents are great challenges for organic chemists.The bis(indolyl)methanes have been gaining increasing importance in recent years and known as an important class of heterocyclic compounds. Indole fragments are featured wide variety of pharmacologically and biologically active compounds [1]. Among the various indole analogues, bis-indolylmethane derivatives display versatile biological and pharmacological activities [2,3]. These types of compounds are also known to promote the estrogen metabolism in both women and men and are expected to have an application in prevention of breast cancer [4,5,6].

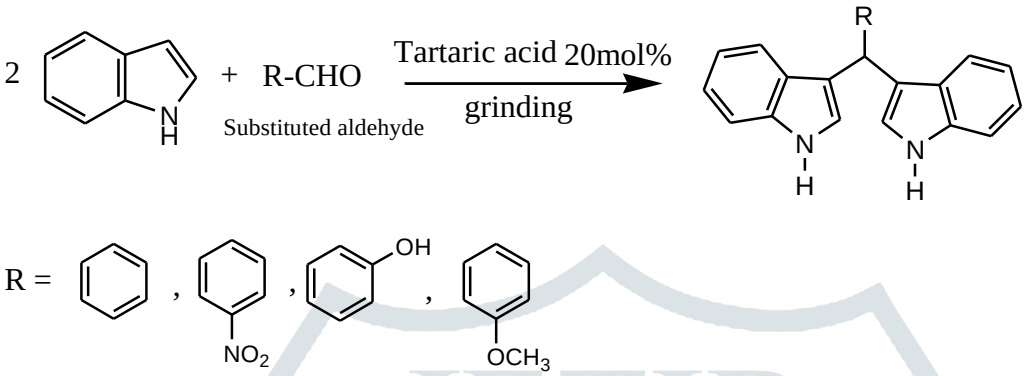
Bis(indolyl)methanes (BIMs) alsoexhibit a range of biological activities such as antimicrobial and antifungal, antibacterial,analgesic and anti-inflammatory, growth promoting ,antitumor activities[7].A wide range ofpharmaceutical applications of bis(indolyl)methane derivatives has grown interest amongchemist to develop their easy synthetic methods. A simple, standard and common method forthe synthesis of bis(indolyl)methanes is the Friedel–Crafts reaction between indoles andcarbonyl compounds in the presence of protic acids or lewis acids. Varieties of catalyticreagents used in the synthesis of BIMs have been reviewed. Researchers are competing fordeveloping the economic, ecofriendly, easily accessible methodologies for the synthesis of bis(indolyl) methane by using various catalytic systems and reaction conditions like citrus lemonjuice[8], grapejuice[9],phenylphosphonicacid[10],triethylborane [11], poly (4vinylpyridinium)hydrogensulfate [12],tetrabutyl ammonium hydrogen sulphate [13]. Most of these reported methods sufferfrom one or several drawbacks, including the requirement of large or stoichiometric amountof catalysts, low yields, prolonged reaction times, involving harsh reaction conditions,tediousworkup procedure, and difficulty in recovery, expensive catalysts. In this report we haveinvestigated the synthesis of various bis (indolyl) methanes catalyzed by tartaric acid using grinding technique.

MATERIALS AND METHODS:

Aldehydes, Indole, Tartaric acid, were all commercial products purchased from Avra Synthesis Pvt Ltd. used without further purification. They were chemically and analytically pure.Melting points were determined in open capillaries using ThermocalAnalabapparatus and are uncorrected. The progress of the reactions as well as purity ofcompounds was monitored by thin layer chromatography with F254 silica-gel precoatedsheets usinghexane, ethyl acetate (9:1) as eluent; UV lightvapours were used for detection. IRspectra were recorded on Agilent Cary 630FTIRInstrument, and valuesare expressed in cm−1.H1 NMR spectra were recordedwith Bruker 400MHz spectrometer and chemical shifts areexpressed in ppm

General Procedure for Synthesis of bis(indolyl)methanes

In Mortar 0.02mole Indole was taken add to it 20mol % Tartaric acid followed bydrop by drop additionof 0.01mol Aryl aldehyde. The mixture vigorously grind till the completion of the reaction as indicated by TLC, The solid mass was pouredon crushed ice and additionally stirred for several minutes. The resulting solid was filtered and recrystallized from ethanol. All these products were characterized by their melting points.



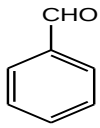
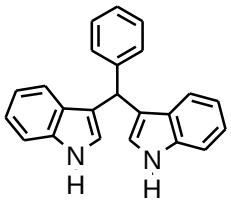
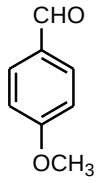
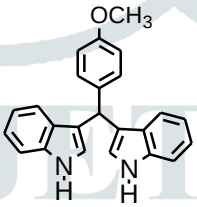
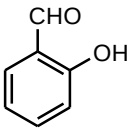
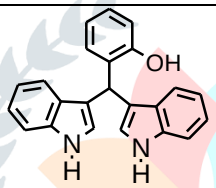
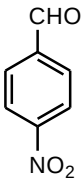
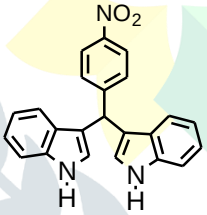
RESULTS AND DISCUSSION:

We have report here a simple approach for synthesis bis(indolyl)methaneswhich involved condensation of substituted benzaldehyde ,Indole and using the inexpensive, non-toxic and easily availableTartaric acid as a catalyst under solvent free condition using grinding technique.To determine the appropriate concentration of the catalyst, we investigated themodel reaction at different concentrations of catalyst. It is observed that Tartaric acid (20 mole %) acts as the effective catalyst by activating the carbonyl group of thealdehydes in this reaction.

Substrates with an electron-withdrawing substituent gave excellent yields in comparison with those carrying an electron-donating group, the time required was also less for electron withdrawing substituents. Para substituted aromatic aldehydes gave high yields.

The condensation between indoles and different substituted aldehydes takes place smoothly in presence of tartaricacid catalyst under grinding condensation.

Table No.1.Tartaric acid catalyzed synthesis of bis(indolyl) methanes using grinding technique

Code No.	Aldehyde	Product	Time (hour)	yield	Melting point (^{0}c)	
					Found	Reported
a			2.10	81.22	88	86-87 [7]
b			3.50	75.73	140	140-141 [6]
c			2.35	72.47	186	120-121 [5]
d			1.51	84.70	222	220-223 [5]

The IR and H^{1}NMR study of the synthesised compounds is as given below

a) 3-((1H-indol-3-yl)(phenyl)methyl)-1H-indole: IR (Cm-1) 3384,3421,1092,13361503,1593,3060,740H^{1}NMR (400MHz, DMSO) : δ5.78(S, 1H,Ar-CH), 10.71 (brS, 2H,NH),7.30-7.35 (m,4H),7.28 7.29 (m,5H), 7.09-6.99 (m,2H),6.65-6.80(m,2H),6.5(d,2H),

b)3-((1H-indol-3-yl)(4-methoxyphenyl)methyl)-1H-indole : IR (Cm-1)3390,2825,1505.8 ,1612.1,1176,1243.1,1008.2,1092.1,800 H^{1}NMR (400MHz,DMSO) : δ5.77(S, 1H, Ar-CH),10.74(b,r S, 2H, NH), 7.35 (d,2H),7.28 (t,4H),7.05-7.009 (m,2H),6.87-6.80 (m,4H),6.77(d,2H),3.7 (s,3H),

c) 2-(di(1H-indol-3-yl)methyl)phenol :IR (Cm-1) 3401.2,3050,1416.4, 455.5,1584.1,1092.1,1220.7, 740 H^{1}NMR (400MHz, DMSO) : δ 6.1(S, 1H Ar-CH), 10.64(br S, 2H NH), 9.28(S,1H),7.33-7.27(m,4H),7.07-6.95(m,4H),6.71(d,2H),6.86-6.65(m,4H),

d)3-((1H-indol-3-yl)(4-nitrophenyl)methyl)-1H-indole: IR (Cm-1)3371,1602,1508,1339,841, H^{1}NMR (400MHz, DMSO) : δ5.99 (S,1HAr-CH) ,10.86 (br S 2H NH) ,8.13 (d, 2H), 7.59 (d,2H), 7.36(d,2H), 7.27(d,2H), 7.05 (t,2H), 6.88-6.84 (m,4H)

CONCLUSION:

We have developed an eco-friendly and economic process for the synthesis of bis(indolyl)methanes using mild, easily available Tartaric acid as a catalyst. This solvent free grinding approach is totally nonpolluting and there is no any use of toxic materials, quantifying it as a green approach to this reaction.

REFERENCES:

[1] Sundberg, R. J. *The chemistry of Indoles*; Academic Press: New York, **1996**.
[2] Pal, C.; Dey, S.; Mahato, S. K.; Vinayagam, J.; Pradhan, P. K.; Giri, V. S.; Jaisankar, P.; Hossain, T.; Baruri, S.; Ray, D.; Biswas, S. M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 4924.
[3] Hong, C.; Firestone, G. L.; Bjeldanes, L. F. *Biochem. Pharmacol.***2002**, *63*, 1085.
[4] Karthik, M.; Tripathi, A. K.; Gupta, N. M.; Palanichamy, M.; Murugesan, V. *Catal. Commun*.**2004**, *5*, 371.
[5] A.Rajendran, D.Raghupathy,andM.Priyadarshini International Journal of ChemTech Research Vol. 3, No.1, 298-302, (2011) and reference cited therein
[6] D. M. Pore ,Uday V. Desai, T. S. Thopate, and P. P. Wadgaonkar ARKIVOC75-80,(2006)and reference cited therein
[7]Rammohan Pal, International Journal of Chemtech Applications Vol. 2; Issue 3; Page26-40(2013) and reference cited therein.
[8] Rammohan Pal, International Journal of Organic Chemistry, 3,136-142 (2013)
[9]Abrar Sheikh and G. M. Nazeruddin, Journal of Chemical and PharmaceuticalResearch, 8(4):224-228 (2016)
[10] MahgolTajbakhsh and MonirehNadim, Iranian Journal of Organic Chemistry Vol. 5,No.2,1055-1059,(2013)
[11] J. Pablo GarciaMerinosa,b, HeraclioLopezRuiza, YlianaLopezb and Susana RojasLimaa Letters in Organic Chemistry, 12, 332-336(2015)
[12] JanardhanBanothu, RajithaGali, RavibabuVelpula, RajithaBavantula, and Peter A.Crooks, ISRN Organic Chemistry Volume 2013,Article ID 616932,5pages
[13] HarindranSuhana,Premkumar.G, International Journal of Advanced Chemical Scienceand Applications,Volume -2, Issue -2, 31-34, 2014