SYNTHESIS OF2-AMINOBENZOPHENONE FROM ISATOICANHYDERIDE USING DIACETOXY IODO BENZENE AS A GREEN CATALYST

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ABSTRACT :

As an alternative reagent to $AlCl_3$, DIB is stable, non-hazardous. DIB is acidic and has been successfully used for Friedel Crafts reaction for the conversion of substituted isatoic anhydride to 2-aminobenzophenone under microwave condition.

Herein we report a new and efficient route for the one-pot synthesis of 2-aminobenzophenone from substituted isatoic anhydride under microwave.Substituted isatoic anhydride were prepared from isatin.

Keywords: 1,4-benzodiazepines,DIB, isatoic anhydride, 2-aminobenzophenone

INTRODUCTION:

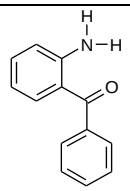
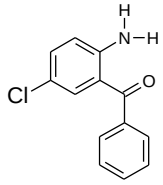
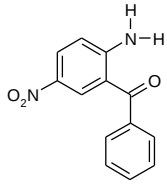
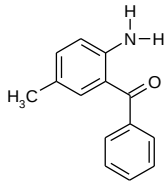
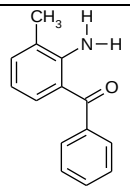
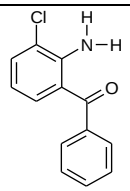
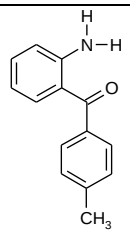
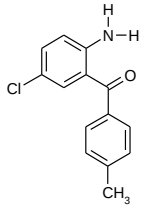
2-aminobenzophenone derivatives are important compounds in organic chemistry because of their application in heterocyclic synthesis and medicines.[1] 2-Amino-benzophenones have been used as starting material for the synthesis of a wide variety of heterocyclic systems, such as fluorenones, acridines, acridones, cinnolines, quinazolines, imidazoles,[1-2] and 3-arylindoles.[3-4]4-arylquinazolones,[6-7]4-arylquinolines,[8-10] 4-aryl-quinoline-2-ones,[11] polyphenylquinolines,[12-16] have been prepared from 2-aminobenzo-phenones. The pharmacological activity of 1,4-benzodiazepines[17-22] is the most important focus in the study of the preparation of 2-aminobenzophenone derivatives. In the past decade, the organic chemistry of iodine has experienced a rapid development. This growing interest in iodine compounds is mainly due to the mild and highly selective oxidizing properties of hypervalent iodine reagents, combined with their benign environmental character and commercial availability.

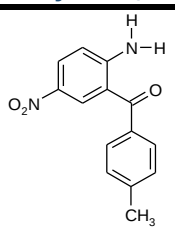
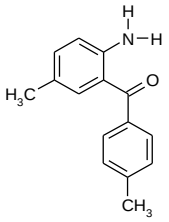
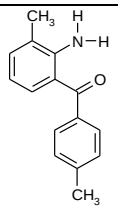
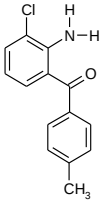
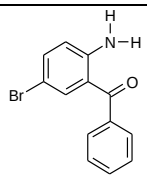
(Diacetoxyiodo)benzene has been used as an efficient catalyst for an improved and rapid one-pot synthesis of biscoumarin derivatives in excellent yield under reflux condition using water as an environmentally benign reaction medium. This aqua mediated Knoevenagel condensation of various aromatic and hetero-aromatic aldehydes with 4-hydroxycoumarin using catalytic amount of (diacetoxyiodo)benzene devoid the route of expensive, corrosive reagents and toxic solvents. Along with the routine aldehydes, the aldehydes like aryl-sulphonyloxybenzaldehyde, aryl-carbonyloxybenzaldehyde also leads to the product under the reaction

conditions. High yields, shorter reaction times, one pot condensation, operational simplicity, easy work-up, and purification of products by non-chromatographic methods are some additional features of this method.

TABLE NO. 1

ANALYTICAL DATA OF SUBSTITUTED 2-AMINO BENZOPHENONES

Sr. No.	Product	M.P. (^{0}C)	Time		Yield	
			C.M.	M.W.	C.M.	M.W.
1		121	6 hrs	5 min	70%	82%
2		114	6 hrs	4.5 min	72%	84%
3		120	7 hrs	5.5 min	64%	72%
4		122	6.5 hr	5 min	78%	84%
5		111	6 hrs	5 min	78%	82%
6		110	6.5 hrs	5.5 min	72%	80%
7		108	6 hrs	5 min	75%	80%
8		120	6 hrs	5 min	70%	78%

9		112	6.5 hrs	5.5 min	65%	76%
10		118	5.5 hrs	5 min	76%	82%
11		115	5 hrs	4.5 min	78%	86%
12		110	5.5 hrs	5 min	70%	78%
13		105	5 hrs	5 min	70%	82%

EXPETIMENTAL:

All the chemicals used were of S.D. Fine chemicals. All the solvent used were distilled previously.

Melting points were measured in open glass capillaries on a Perfit Electro-thermal melting-point apparatus and are uncorrected. ^{1}H-NMR spectra were recorded at room temperature on a 300 MHz. Varian Inova Spectrometer in $CDCl_3$ using TMS as internal standard. A LG domestic microwave oven was used at 400W power level for all the experiments. A LG domestic microwave oven was used at 400W power level for all the experiments. The reactions were monitored by TLC using pre-coated plates (Merck). Column chromatography was performed using Acme silica gel (100–200 mesh). The products were also characterized by comparison of their melting point with literature values.

A) REPRESENTATIVE EXPERIMENTAL PROCEDURE FOR THE SYNTHESIS OF ISATINS :

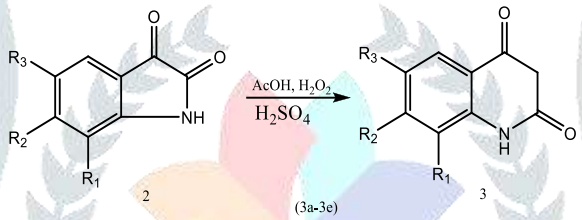
In a round bottomed flask (0.04 moles) of chloral hydrate and 120 cc. of water were placed. To this solution were then added, 130g. of sodium sulphate; a solution of (0.05mole) of aromatic amine in 30cc. of water to which (0.052mole) of hydrochloric acid, in order. Then a solution of (0.158moles) of hydroxyl amine hydrochloride in 50cc. of water was added. The flask was heated over a wire gauze by a Meker burner so that vigorous boiling begins in about forty to forty-five minutes. After one to two minutes of vigorous boiling the reaction was complete. During the heating period, some crystals of isonitrosoanilide separated. On cooling the

solution in running water the remainder crystalisesed, was filtered with suction, and air-dried.60 grams (32.6cc.) of concentrated sulfuric acid was warmed to 500 in a round-bottomed flask fitted with an efficient mechanical stirrer, and to this (0.046mole) of dry isonitrosoanilide was added at such a rate as to keep the temperature between 60 and 70^0C but not higher. External cooling should be applied at this stage.

After the addition of isonitrosoanilide compound, the solution was heated to 800 and kept at this temperature for about ten minutes to complete the reaction. Then the reaction mixture was cooled to room temperature and poured upon ten to twelve times its volume of cracked ice. After standing for about one-half hour, the isatin was filtered with suction,washed several times with cold water to remove the sulfuric acid, and then dried in the air. (Scheme 01)

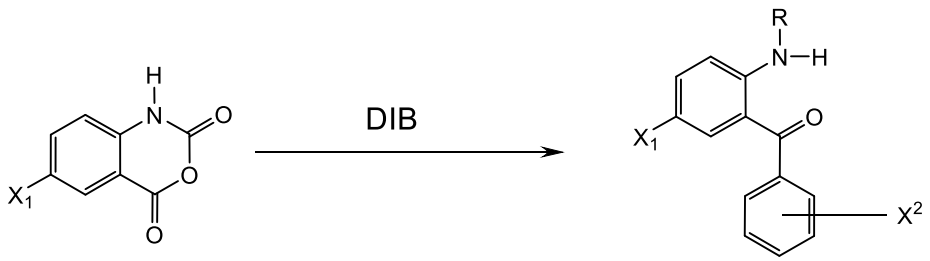
B) REPRESENTATIVE PROCEDURE FOR THE SYNTHESIS OF ISATOIC ANHYDRIDES:

Isatin was dissolved or suspended in acetic acid/formic acid and an aqueous hydrogen peroxide solution was added dropwise. The hydrogen peroxide solution was of 30 percent strength aqueous solution. The reaction was carried out at room temperature, or slightly above this (25-65^0C). The addition of sulfuric acid accelerated the reaction. The reaction mixture was stirred for 1-2 hours. The desired isatoic anhydrides were obtained in a crystalline form during the reaction and were isolated by filtering or centrifuging.



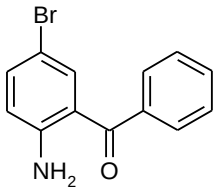
REPRESENTATIVE PROCEDURE FOR THE SYNTHESIS OF SUBSTITUTED 2-AMINOBENZOPHENONES:

A well stirred mixture of DIB(5Mole%) and dry benzene (0.1 m mol) in CH_2Cl_2 was added isatoic anhydride chloride (0.1 m mol) at room temperature. The mixture was then heated in microwave for a range of5 to 6 min. The progress of reaction was followed by TLC. Resultant mixture was treated with 1 : 1 HCl and extracted with chloroform. The organic layer was dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator.



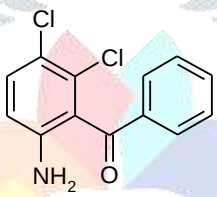
SPECTRAL ANALYSIS :

The structures of the products were confirmed from NMR, IR and LCMS. The representative spectral analysis for few of the products is given below. The observed values are in accordance with the literature values.



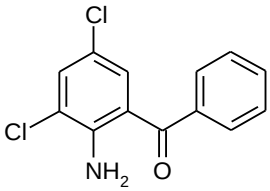
2-amino-5-bromo-benzophenone

Nature	Yellow crystals
Mp	106^0C
^{1}H-NMR (500 MHz, $CDCl_3$)	δ 5.90 (s,2H), 6.52 (d,J = 9.2 Hz, 1H), 7.30 (dd, J = 9.2, 2 Hz,1H), 7.45 (m, 2H), 7.50 (m, 2H), 7.61 (d, J = 8.7 Hz, 2H)
^{13}C-NMR (125 MHz,$CD Cl_3$)	112.8, 117.0, 126.6, 128.2, 130.1, 132.2, 134.2, 136.3, 137.8, 147.3, 190.1.
IR (KBr)	3411, 3314, 1613, 1585, 1532, 1400, 1314,1142.
LCMS	(M+1) = 277



2-Amino- 5,6-dichloro-benzophenone

Nature	Yellow crystals
Mp	108 ◦C,
^{1}H-NMR (500 MHz, $CDCl_3$)	δ (500 MHz, CDCl3): 4.5 (s,2H),6. 70 (d,J = 8.7 Hz,1H),7. 35 (d,J = 8.7 Hz,1H),7. 5 (m,2H), 7.6 (t, J = 7.37 Hz,1H) (d, J = 8.7 Hz,2H)
^{13}C-NMR (125 MHz,$CD Cl_3$)	117, 122, 125, 129, 130, 130. 3, 132,134. 5,137,145
IR (KBr)	3462,3365,1665,1619,1460,1403,1314
LCMS	(M+1) = 267



2-Amino-3,5-dichloro-benzophenone

Nature	Yellow crystals
Mp	94^0C
^{1}H-NMR (500 MHz, $CDCl_3$)	δ 6.58 (s, 2H), 7. 42 (s, 1H), 7. 48 (s, 1H), 7. 53 (m, 2H), 7. 62 (m, 1H), 7. 67 (d, J = 7.3 Hz, 2H)
^{13}C-NMR (125 MHz,$CD Cl_3$)	119.57, 119.72,121. 5,128. 8, 129.6,132. 3,132. 56, 133.8,139. 3,146, 198
IR (KBr)	3462,3344,1608,1573,1439, 1314,1153
Mass	(M+1) = 267

REFERENCES :

1. D.A. Walsh, *Synthesis*, 677-88 **(1980).**
2. J.C.E. Simpson, C.M. Atkinson, K. Schofield and O. Tephenson, *J. Chem. Soc.*646-57 **(1945).**
3. A. Walser and G. Silverman, *J. Heterocycl. Chem.* 10, 883-4 **(1973).**
4. Y. Nakamura and T. Ukita, *Org. Lett.* 4, 2317-20 **(2002).**
5. O.A. Raevskii, A.M. Sapegin, I.I. Kitova, T.A. Voronina, S.B. Seredenin, and S.A. Andronati Translated from *Khimiko-farmatsevticheskii Zhurnal*, Vol. 23, No. 1, pp. 62–66, January, **1989**.
6. A.I. Rachlin, *U. S. Patent* 3261870 **(1962).**
7. G. Gamboni, W. Schmid and A. Sutter, *U.S. Patent* 4236006, **(1980).**
8. E.A. Fehnel, *J. Org. Chem.* 31, 2899-2902 **(1966).**
9. H. Matsumoto and T. Horiuchi, *U.S. Patent* 6310249 B1 **(2001).**
10. A. Capelli, G.P.Mohr, A. Gallelli, M. Rizzo, M. Anzini, S. Vomero, L.Mennumi, F. Ferrari, F. Makovec, M.C. Menziani, P.G.D. Benedetti and G. Giorgi, *J. Med. Chem.* 47, 2574-86 **(2004).**
11. P. Hewawasam, W. Fan, M. Ding, K. Flint, D. Cook, G.D. Goggins, R.A. Myers, V.K. Gribkoff, C.G. Bassard, S.I. Dworetzky, J.E. Starrett and N.J. Lodge, *J. Med. Chem.* 46, 2819-22 **(2003).**
12. H. Ma, A.K.Y. Jen, J. Wu, X. Wu and S. Li u, *Chem. Matter.* 11, 2218-25 **(1999).**
13. J.L. Kim, J.K. Kim, H.N. Cho, D.Y. Kim, C.Y. Kim and S.I. Hong, *Macromolecules*, 33, 5880-85 **(2000).**
14. X.L. Chen and S.A. Jenekhe, *Macromolecules*, 33, 4610-12 **(2000).**
15. Liangde Lu and S.A. Jenekhe, *Macromolecules*, 34, 6249-54 **(2001).**
16. T.W. Kwon, M.M. Alam and S.A. Jenekhe, *Chem. Matter.* 16, 4657-66 **(2004).**
17. L.H. Sternbach, *Angew.Chem. Internat. Edit.* 10, 34-43 **(1971).**
18. G. Semple, H. Ryder, D.P. Rooker, A.R. Batt, D.A. Kendri ck, M. Szelke, M. Ohta, M. Satoh, A. Ni shi ha, S. Akuzawa and K. Miyata, *J. Med. Chem.* 40, 331-41 **(1997).**
19. F. Mauriand S.P.A. Ravizza, *U.S. Patent 4511510***(1985).**

20. N. Micale, R. Vairagoundar, A.G. Yakovlev and A.P. Kozikowski, *J. Med. Chem.* 47, 6455-58 **(2004).**

21. M.H. Bolli, J. Marfurt, C. Grisostomi, C. Boss, C. Binkert, P. Hess, A. Treiber, E. Thorin, K. Morrison, S. Buchmann, D. Bur, H. Ramuz, M. Clozel, W. Fischli and T. Weller, *J. Med. Chem.* 47, 2776-95 **(2004).**

22. I.M. Buck, J.W. Black, T. Cooke, D.J. Dunstone, J.D. Gaffen, E.A. Harper, R.A.D. Hull, S.B. Kalindjian, E.J. Lilley, I.D. Linney, C.M.R. Low, K.I.M. Steel, D.A. Sykes, M.J. Tozer and G.F. Watt, *J. Med. Chem.* 48, 6803-12 **(2005).**