Synthesis of 2-Alkyl/ Aryl-6-Amino-*1H*-Benzimidazoles

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Abstract:

The novel 2-alkyl/ aryl-6-amino-*1H*-benzimidazoles compounds were synthesized by hydrogenation of 2-alkyl/ aryl-6-nitro-*1H*-benzimidazoles using Raney Nickel in presence of hydrogen atmosphere at room temperature. The synthesized compounds were fully characterized using Elemental, chemicaland spectroscopic analytical method.

Keywords: Benzimidazole, Hydrogenation, Raney Nickel

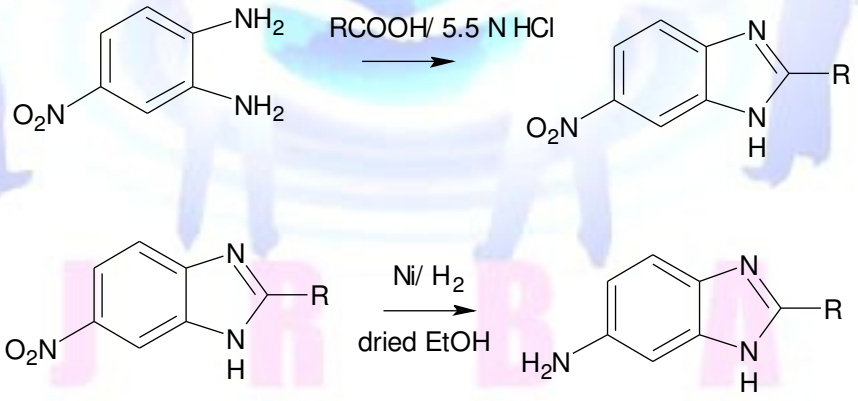
Introduction:

Aminoarene moiety is a ubiquitous structural element. It is commonly encountered in natural products, ligand for metal complexes, pharmaceutical, agrochemicals, xerographics, pigments, electronic materials, photographic materials as well as conducting polymers. Despite the simplicity of aryl amine moiety, preparation of this class of is often difficult. Many synthetic methods are available for preparation of aminoarene. One of the simplestand widely used preparative methods for the aminoarene is reduction which is a crucial step in many multistep synthesis of the benzene derivative and it is synthetically important transformation, both in the laboratory and in industry. Therefore the development of selective, mild, rapidand effective reduction of nitro compounds is still an area of considerable synthetic interest particularly when a molecule has several other reducible moieties like unsaturation, ketone, halides. Various hydrogen donors[1-14] such as hydrazine, formic acid, propan-2-ol, ammonium formate, triethyl ammonium formate, and hydraziniummonoformate, AlH_3-$AlCl_3$, hydrazine and Raney nickel,$TiCl_3$, and Pd-C, sodiumdihydro(trithio)-borate $NaBH_2S_3$, $iCl_2(PPh_3)_2$,sulphides such as NaSH, $(NH_4)_2S$ or polysulphides(zinin reduction); catalytic hydrogenationincludePd or Pt or Ni in presence of hydrogen gas; metallic reductionconsists of zinc, iron or tin in the presence of acid and stannous chloride in the presence of hydrochloric acid have been used for the reduction of nitroarene to corresponding aromatic amines. In view of these observations, herein our present work, we report a mild simple and selective reduction of 2-substtuted-6-nitro-1*H*-benzimidazoles to corresponding amino benzimidazoles using Raney Nickel catalyst, a stable hydrogen donor in conjugation with nickel metal in presence of hydrogen gas in super dried ethyl alcohol medium. This method is safer, highly selective, cost effective,mild and proceeds under ambient condition of temperature and pressure without need for any elaborate experimental set up and superior than the other methods because of the high yield and economy. It is worth noting that the presently used hydrogenation process selectively reduced 2-substituted-6-nitro-1*H*-benzimidazole to the corresponding amines in presence of other sensitive functional group such as halogens, carboxylic group. The reduction time is varying from half to one hr. The yields were virtually quantitativeand analytically pure. The major advantage of this method includes

the ability to obtain amino benzimidazoles in pure form with no laborious work-up. The separation of products from the reaction mixture is simpleand involves direct removal of the catalyst by filtration and evaporation of the solvent under vacuum. The reduction process used in present work over other methods are system being readily available and easy to h and le, produces the product in good yield with high purities without requiring further purification. The superiority of reduction in our present work over the previous reduction methods are: selective reduction of nitro group of benzimidazole ring in presence of other reducible groups, rapid reaction, high yield, reduction takes place at room temperature, cast effective, no delicate apparatus is needed, easy way to isolate final product, recovery of dried ethyl alcohol (solvent), no strong acidic media, no pressure apparatus is required. Therefore present method is used to reduce nitro benzimidazoles to corresponding amino benzimidazoles.All the products were characterized by chemical, functional group test, melting pointand spectral analysis like IR and ^{1}HNMR spectroscopy. All amino benzimidazoles showed positive orange red dye testand negativemulliken barker test. In FT IR they showed two medium intensity b and s at 3400-3500 cm^{-1} due to symmetricand asymmetric stretching. In ^{1}HNMR they showed singlet at 4.5-5.7 tfor two proton of amine (NH_2-C)

Resultand Discussion:

The condensation of 4-nitro-o-phenylene diamineand different carboxylic acids in 5.5 N HCl acid gives desired benzimidazole in good yield (**Scheme 1**). The role of hydrochloric acid in the preparation of benzimidazole is to activate carboxyl group of



Scheme 1

carboxylic acid by protonation of oxygen forming carbonium ion. The intermediate is the addition product formed by attack of unshared pair of electron of one of nitrogen of o-phenylenediamine into the carbonium ion of the acid. The addition product finally loses two water molecules producing benzimidazole**.** The nitro benzimidazoles are yellow crystalline solid, soluble in dilHCl, dilNaOH, but insoluble in benzeneand water. They offers positive Mulliken-Barkers test for nitro group. In FT-IR (KBr) the infra red spectrum of the product exhibited characteristic band at 3102 cm^{-1} (br, -NH peak of benzimidazole), 1590 cm^{-1} (C-NO_2 group str). The melting point, elements test, functional group test, elemental analysis dataand spectral evidences confirms the formation of 6-nitro-1*H*-benzimidazole (Table **1**).

All the 2-alkyl-6-nitro-1*H*-benzimidazoles described and synthesized in preceding **Table 1** were subjected to Raney nickel reduction to produce corresponding 6-amino-1*H*-benzimidazoles.They have been prepared by the Raney nickel induced reduction in the atmosphere of hydrogen gas at room temperature in excellent yield. The completion of reduction is checked r and omly by dipping cotton ribbon. The ribbon acquires disappearance of yellow color shadeand appearance of brown to red colored shade ensures the complete reduction of nitro benzimidazoles to amino benzimidazoles. After completion of reaction, the reaction mixture was made free from metallic residue by filtrationand the product 2-substituted-6-amino-1*H*-benzimidazoles has been isolated in high yield by concentrating filtrate under vacuum. This hydrogenation is probably proceeds via the different intermediates shown in following generalized mechanism (**Figure. 1**).

On the characterization they are deep red to brown colored crystalline solids, soluble in dil. HCl, and insoluble in waterand benzene. These compounds gave positive orange red dye test when coupled with alkaline solution of β-napthol. Their infrared spectrum of the product exhibited the band in the region of 3460 cm^{-1} is due to the presence of -NH_2 str. The C, Hand N elemental analysis, physical constants and spectral data are in consistent with the assigned structure, which confirmed the product (Table **2**).

Experimental

2-alkyl-6-Nitro-1*H*-benzimidazole: The mixture of 4-nitro-o-phenylenediamine (0.02 mole), different aliphatic carboxylic acid (0.03mole)and HCl acid (5.5 N, 50 mL) was boiled for 3 hour in round bottom flask under reflux. The reaction mixture was then cooled to room temperature, diluted with waterand neutralized with dilNaOH. The solid separated was filtered, washed with water, driedand crystallized from alcohol.

2-alkyl/aryl-6-amino-1*H*-benzimidazole: To a solution of 2-substituted-6-nitro-1*H*-benzimidazole (0.02 mole) in super dried ethyl alcohol freshly prepared Raney Nickel (0.02 mole) was added into three necked hydrogenation flask. The hydrogen gas was bubbled through this solution with constant stirring at room temperature for one hour. Filtered the reaction mixtureand washed metal residue twice with dried ethyl alcohol. Collect all washingand concentrated in vacuo to obtained titled compound.

Table. 1- Characterization data of 2-alkyl/aryl-6-nitro-1H-benzimidazoles (1-9)

Compounds	R	M. F.	Yield	m. p. (°C)	Chemical analysis calcd (found)		
					C	H	N
1.	H	$C_7H_5N_3O_2$	70	203	51.54(51.86	3.09 3.52	25.76 25.81)
2.	CH_3	$C_8H_7N_3O_2$	62	225	54.24(54.65	3.98 4.15	23.72 23.86)
3.	CH_2CH_3	$C_9H_9N_3O_2$	68	185	56.54 (56.97	4.74 5.09	21.98 22.34)
4.	$(CH_2)_2CH_3$	$C_{10}H_{11}N_3O_2$	70	174	58.53	5.40	20.48

					(58.32	5.97	20.75)
5.	C $(CH_3)_3$	$C_{11}H_{13}N_3O_2$	56	105	60.26 (60.54	5.98 6.32	19.17 19.26
6.	$(CH_2)_3CH_3$	$C_{11}H_{13}N_3O_2$	55	165	60.26 (60.24	5.98 6.37	19.17 19.06)
7.	$CH_2C_6H_5$	$C_{14}H_{11}N_3O_2$	62	173	66.40 (66.51	4.38 4.42	16.59 16.81)
8.	$(CH_2)_2COOH$	$C_{10}H_{19}N_3O_4$	68	120	51.07 (51.24	3.86 3.75	17.87 17.92)
9.	C_6H_5	$C_{13}H_9N_3O_2$	53	169	65.27 (65.74	3.79 3.93	17.56 17.65
All the compounds are yellowin color							

Table. 2- Characterization data of 2-alkyl/aryl-6-amino-1H-benzimidazoles (1-9)

Sr. No.	**R**	**M. F.**	**Yield**	**Reaction Time (min)**	**m. p. (°C)**	**Chemical analysis calcd (found)**		
						C	H	N
1.	H	$C_7H_7N_3$	79	25	140	63.14 (63.26	5.30 5.52	31.56 31.81
2.	CH_3	$C_8H_9N_3$	89	25	95	65.29 (65.54	6.16 6.15	28.55 28.86
3.	CH_2CH_3	$C_9H_{11}N_3$	76	30	105	67.06 (66.97	6.88 6.79	26.07 26.34
4.	$(CH_2)_2CH_3$	$C_{10}H_{13}N_3$	70	45	175	68.54 (68.58	7.48 7.77	23.98 23.75
5.	C $(CH_3)_3$	$C_{11}H_{13}N_3$	68	40	105	69.81 (69.94	7.99 7.13	22.20 22.26
6.	$(CH_2)_3CH_3$	$C_{11}H_{13}N_3$	59	45	163	69.81 (69.87	7.99 8.14	22.20 12.56)
7.	$CH_2C_6H_5$	$C_{14}H_{13}N_3$	62	45	173	75.31 (75.51	5.87 5.97	18.88 18.81
8.	$(CH_2)_2COOH$	$C_{10}H_{11}N_3O_5$	64	40	160	58.53 (58.63	5.40 5.75	20.48 20.92
9.	C_6H_5	$C_{13}H_{11}N_3$	55	45	189	74.62 (74.74	5.30 5.53	20.08 20.17)
All the compounds are brown colored								

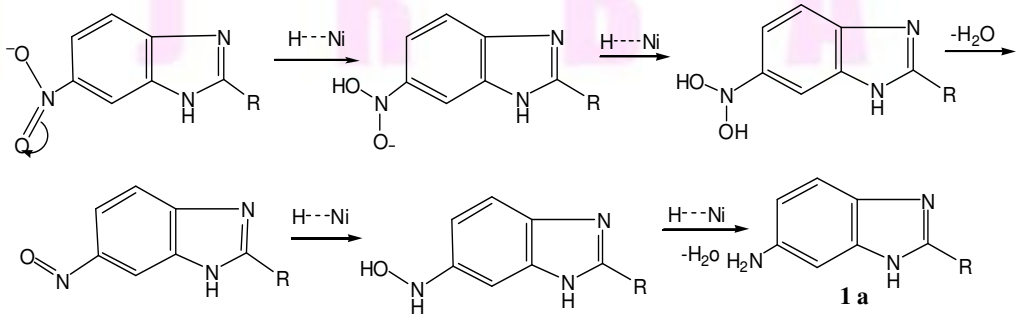


Figure. 1

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