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A Novel route of dehydrogenation of substituted 6-aryl 5,6- dihydrobenzimidazole [1,2-C]Quinazolines to substituted 6-aryl benzimidazo[1,2-c] quinazolines by dehydrogenation using DIB catalyst.

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ABSTRACT : In the last years, there has been considerable attention on hypervalent iodine compounds in organic synthesis. A lot of contributors36,37 have reviewed a wide range of applications of these powerful and selective oxidising agents. Although numerous reagents are mentioned for related studies, (DIB) is one of the first reagent of this family to be investigated, and is the synthetic precursor to several related compounds; among these derivatives, [Bis(trifluoroacetoxy)iodo] benzene (BTI) plays a key role by offering several interesting applications in modern organic synthesis

INTRODUCTION :

Benzimidazoles and quinazolines are of the most extensively studied classesof heterocyclic compounds, and have received much attention from synthetic organic as well as medicinal chemists, because of the diverse range of their biological activities[1,2] and their applications in several areas of electrochemistry as anticorrosive agents, as polymers and fluorescent tags in DNA sequencing.[3-5] In general, quinazoline compounds have been well-recognized for their pharmacological properties, such as anti-inflammatory,[6,7] antihypertensive,[8] anti-HIV,[9] z roncodilatory, [10] anti-allergic,[11] anti-cancer,[12-14] anticonvulsant,[15,16] antihelmintic,[17] analgesic,[18] antimalarial[19] and antimicrobial [20] activities

. Literature survey reveals that,benzimidazo [1,2-c] quinazoline derivatives also show various biological activities,[16,21-23] such as anticancer, antiviral, antimicrobial, anti-inflammatory and anticonvulsants. However, search is continuously on to identify a more potent lead molecule as these molecules are developing resistance over a period. Based on the importance of these molecules, our attention was attracted towards synthesis of novel quinazoline derivatives in order to find more potent biologically active molecules.

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KEYWORDS :

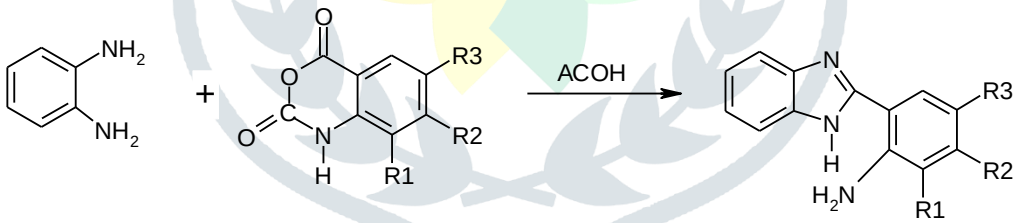
substituted 6-aryl 5,6- dihydrobenzimidazole [1,2-C], substituted 6-aryl benzimidazo[1,2-c],DIB

RESULT AND DISCUSSION:

The major disadvantages encountered in the use of dehydrogenating reagentsinclude corrosion, unfriendliness to the environment and stoichiometric requirementof it thereby generating large amount of waste. The last two decades have witnessedan exponential growth in the applications of hypervalent iodine reagents in organicsynthesis.43 (Diacetoxyiodo)benzene (DIB) is the most extensively utilized parenthypervalent iodine (III) reagent.44 It is easy to handle, nontoxic, commerciallyavailable and is similar in reactivity to heavy metal reagents. 6-aryl 5,6-dihydrobenzimidazo [1,2-c] quinazoline was dehydrogenated using Diacetoxy Iodo Benzeneto give 6-aryl benzimidazo [1,2-c] quinazolines. In comparison with theof dehydrogenation this methodology is ecofriendly is and the product was obtained in high yield oxidation45.

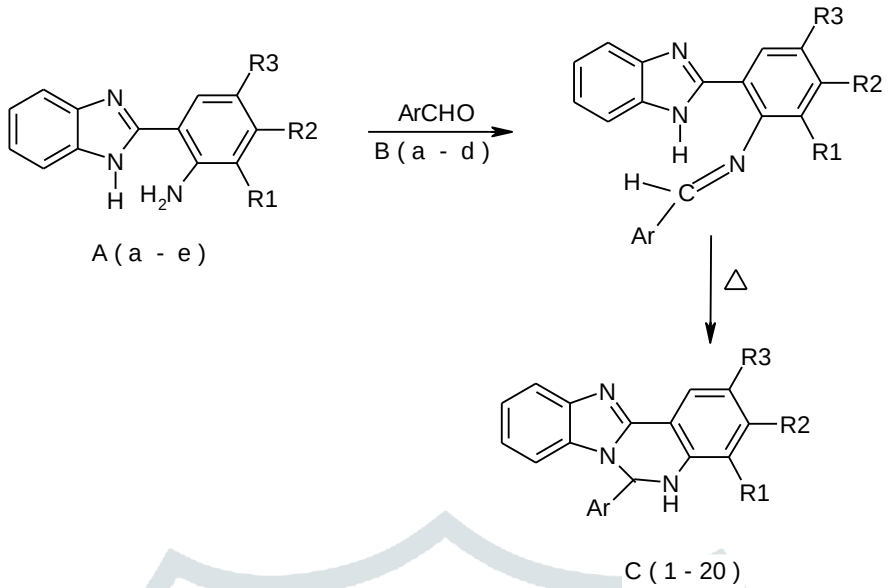
A) SYNTHESIS OF SUBSTITUTED 2-(2-AMINOPHENYL) BENZIMIDAZOLE :

To a solution of isatoic anhydride (1mmol) in acetic acid (2ml) is added the appropriate o-phenylene diamine (1mmol), the reaction mixture heated on a steam bath for 2hr. and left aside overnight. The reaction mixture isolated in each case was separated into substituted 2-(2-aminophenyl) benzimidazole (Scheme-01) and substituted benzimidazo(1,1c) quinazolin-6(5H)-one by preparative TLC using benzenz-methanol mixture.



B) SYNTHESIS OF SUBSTITUTED 6-ARYL 5,6-DIHYDRO BENZIMIDAZO [1,2-C]QUINAZOLINES :

2-(2-aminophenyl) benzimidazole (0.05 m) dissolved in 200 ml alcohol. To this 0.05 m of aldehyde is added and refluxed for 5 hrs. The resulted solution is concentrated under vacuum to obtain 6-aryl 5,6-dihydro benzimidazo[1,2-c]quinazolines (Scheme - 02). It was filtered and recrystalised from alcohol.



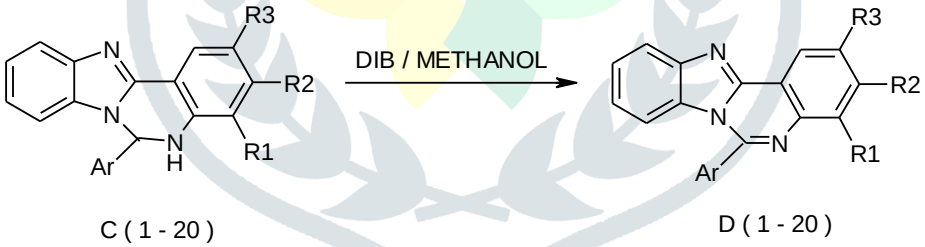
For B

a) Benzaldehyde b) 2-hydroxy benzadehyde

c) 4-methoxy benzaldehyde d) 4-nitro benzaldehyde

c) Synthesis of substituted 6-aryl benzimidazo[1,2-c] quinazolines:

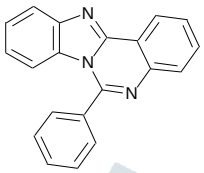
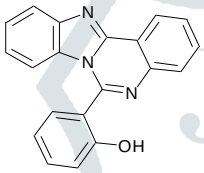
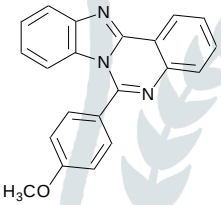
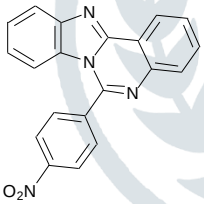
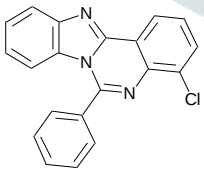
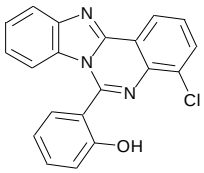
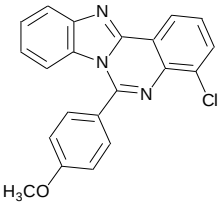
6-aryl 5,6-dihydro benzimidazo [1,2-c] quinazolines (0.05 m) dissolved in 100 ml methyl alcohol. To this 0.01 m of Diacetoxy Iodo Benzene is added and refluxed for 2 hrs. The resulted solution is concentrated under vacuum to obtain 6-aryl benzimidazo[1,2-c] quinazolines (Scheme-03). The product was filtered and recrystalised from alcohol.

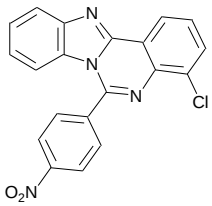
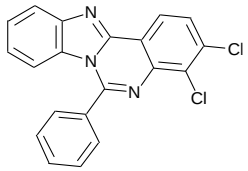
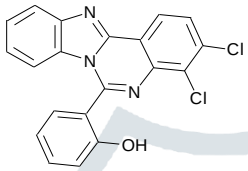
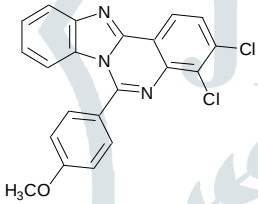
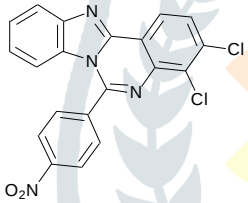
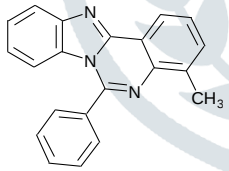
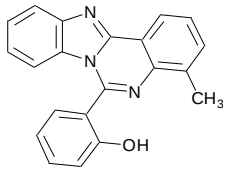
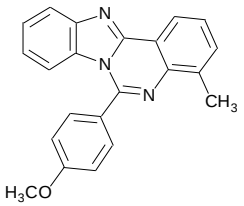
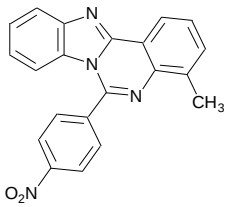


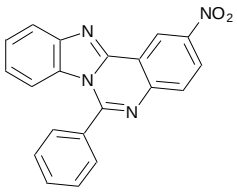
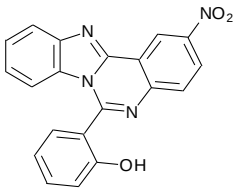
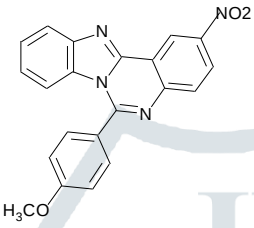
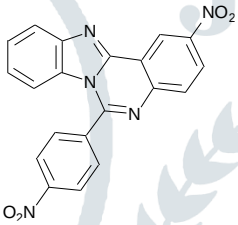
The M.P. yield and elemental analysis are listed in experimental section. The purity of the compound was checked by TLC.

Table No. 3

Analytical and Physical data of 6-aryl benzimidazo [1,2c] quinazoline

Sr. No.	Product	M.F.	M.P. (^{0}C)	Yield
1.		$C_{20}H_{13}N_3$	220	70%
2.		$C_{20}H_{13}N_3O$	268	65%
3.		$C_{21}H_{15}N_3O$	187	70%
4.		$C_{20}H_2N_4O_2$	252	65%
5.		$C_{20}H_{12}ClN_3$	240	60%
6.		$C_{20}H_{12}ClN_3O$	235	67%
7.		$C_{21}H_{14}N_3OCl$	244	62%

8.		$C_{20}H_{11}N_4O_2Cl$	238	68%
9.		$C_{20}H_{11}N_3Cl_2$	249	60%
10.		$C_{20}H_{11}N_3Cl_2$	198	74%
11.		$C_{21}H_{13}Cl_2N_3O$	220	60%
12.		$C_{20}H_{10}Cl_2N_4O_2$	212	64%
13.		$C_{21}H_{15}N_3$	265	70%
14.		$C_{21}H_{15}N_3O$	252	68%
15.		$C_{21}H_{14}ClN_3O$	175	62%
16.		$C_{20}H_{11}ClN_4O_2$	205	60%

17.		$C_{20}H_{12}N_4O_2$	234	58%
18.		$C_{20}H_{12}N_4O_3$	225	60%
19.		$C_{21}H_{14}N_4O_3$	242	62%
20.		$C_{20}H_{11}N_5O_4$	254	60%

3.5 EXPETIMENTAL:

All the chemicals used were of S.D. Fine chemicals. All the solvent used were distilled previously. DIB was purchased from Aldrich chemicals.

Melting points were measured in open glass capillaries on a Perfit Electrothermal melting-point apparatus and are uncorrected. The reactions were monitored by TLC using precoated plates (Merck). The products were also characterized by comparison of their melting point with literature values.

A) SYNTHESIS OF SUBSTITUTED 2-(2-AMINOPHENYL) BENZIMIDAZOLE :

To a solution of isatoic anhydride (1mmol) in acetic acid (2ml) is added the o-phenylene diamine(1mmol) ,the reaction mixture heated on a steam bath for 2hr. and left aside overnight. The raction mixture isolated was separated into substituted 2-(2-aminophenyl) benzimidazole (Scheme-01) and substituted benzimidazo(1,1c) quinazolin-6(5H)-one by preparative TLC using benzene-methanol mixture.

B) SYNTHESIS OF SUBSTITUTED 6-ARYL 5,6-DIHYDRO BENZIMIDAZO [1,2-C]QUINAZOLINES :

2-(2-aminophenyl) benzimidazole (0.05 m) dissolved in 200 ml alcohol. To this 0.05 m of aldehyde is added and refluxed for 5 hrs. The resulted solution is concentrated under vacuum to obtain 6-aryl 5,6-dihydro benzimidazo [1,2-c]quinazolines (Scheme - 02). It was filtered and recrystalised from alcohol.

C) SYNTHESIS OF SUBSTITUTED 6-ARYL BENZIMIDAZO[1,2-C]QUINAZOLINES:

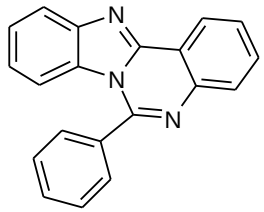
6-aryl 5,6-dihydro benzimidazo [1,2-c] quinazolines (0.05 m) dissolved in 100 ml methyl alcohol. To this 0.01 m of Diacetoxy Iodo Benzene was added. The reaction mixture immediately turns to yellowish

colour. The reaction mixture was further refluxed for 2 hrs. The progress of reaction was monitored by TLC. The resulted solution was concentrated under vacuum to obtain 6-aryl benzimidazo[1,2-c] quinazolines (Scheme-03). The residue obtained was purified by silica gel column chromatography (10% EtOAc–hexane) as eluent to afford the pure products.

The M.P. yield and elemental analysis are listed in experimental section.

SPECTRAL ANALYSIS :

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



6-Phenyl-benzimidazo[1,2- *c*]quinazoline

Mol. Formula: $C_{20}H_{13}N_3$

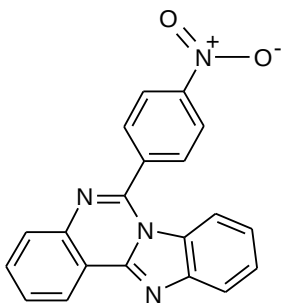
Melting point : 220 °C,

I.R. **:** 1621, 1586, 1529, 1457, 1380, 773, 753, 732

^{1}H NMR **:** δ 6.84 (t, 1H); 6.88 (d, 1H, 3J=7.7 Hz); 7.09 (d, 1H, 3J=1.3 Hz); 7.10 (t, 1H); 7.15 (d, 1H, 3J=6.7 Hz); 7.18 (t, 1H); 7.26 (t, 1H); 7.32 (m, 5H, H-*o*, *m*, *p*); 7.62 (d, 1H, NH, 3J=1.3 Hz); 7.67 (d, 1H, 3J=7.9 Hz); 7.98 (dd, 1H, 3J=7.7 Hz, 4J=1.3 Hz).

13C NMR **:** d = 68.2 (C-6); 110.9 (C-8); 112.3 (C-12b); 115.2 (C-4); 118.6 (C-2); 119.0 (C-11); 122.4 (C-9); 122.6 (C-10); 125.0 (C-1); 126.4 (2C, C-*m*); 129.1 (2C, C- *o*); 129.3 (C-*p*); 132.0 (C-3); 133.2 (C-7a); 140.8 (C-*i*); 143.5 (C-4a); 144.2 (C-11a); 147.3

Mass **:** *m/z* (%) = 299 (M^++2)



6-(4-Nitrophenyl)-benzimidazo[1,2- *c*]quinazoline

Mol. Formula: $C_{20}H_{12}N_4O_2$

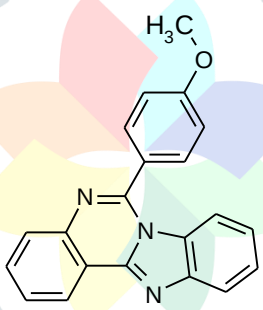
Melting point: 252 °C,

I.R. : 1450 (-NO_2) 3423, 1621, 1585, 1529, 1450, 1380, 773, 741, 732

^{1}H NMR : 6.86 (t, 1H); 6.87 (d, 1H, ^{3}J=7.5Hz); 7.16 (t, 1H); 7.22 (t, 1H,); 7.27 (t, 1H,); 7.34 (s, 1H,); 7.35 (d, 1H, ^{3}J=7.6 Hz); 7.44 (d, 2H, H-*o*, ^{3}J=8.4 Hz); 7.69 (d, 1H, ^{3}J=7.8 Hz); 7.81 (s, 1H, NH); 7.98 (d, 1H, ^{3}J=7.8 Hz); 8.19 (d, 2H, H-*m*, ^{3}J=7.8 Hz)

^{13}C NMR : 66.3, 110.2, 111.8, 114.9, 118.5, 118.8, 122.4, 122.4, 124.1 124.7, 126.9, 131.8, 132.6, 142.3, 143.7, 146.5, 147.2, 147.6

Mass : *m/z* (%) = 340 (M^+, 50), 220, 194.



6-(4-Methoxyphenyl-benzimidazo[1,2 -*c*]quinazoline

Mol. Formula: $C_{21}H_{15}N_3O$

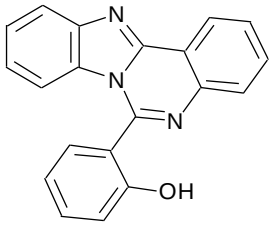
Melting point : 187 °C,

I.R. : 1256-1040(Symmetric strech of Aromatic ether, 1621, 1585, 1529, 1457, 1380, 773, 741, 732

^{1}H NMR : 3.7 (s, 3H, OCH_3); 6.83 (t, 1H); 6.87 (d, 1H, ^{3}J=8.3 Hz); 6.90 (d, 2H, H-*m*, ^{3}J=8.7 Hz). 6.98 (d, 1H, H-6, ^{3}J=1.7 Hz); 7.06 (t, 1H,); 7.07 (d, 1H, ^{3}J=7.6 Hz); 7.15 (m, 1H,); 7.25 (d, 2H, H-*o*, ^{3}J=8.7 Hz); 7.28 (t, 1H); 7.50 (d, 1H, NH, ^{3}J=1.7 Hz); 7.65 (d, 1H, ^{3}J=7.9 Hz); 7.95 (d, 1H, ^{3}J=7.7 Hz, ^{4}J=1.2 Hz).

^{13}C NMR : 55.5, 68.1, 111.0, 112.3, 114.5, 115.2, 118.5, 119.0, 122.3, 122.5, 125.0, 127.9, 132.0, 132.4, 133.2, 143.7, 144.3, 147.4, 160.1.

Mass : *m/z* (%) = 329 (M^++2).



6-(-2-hydroxy phenyl) benzimidazoquinazoline

Mol. Formula: $C_{20}H_{13}N_3O$

Melting point: 268^0C

I.R. **:** 3425, 1621, 1585, 1529, 1457, 1380, 773, 741, 732

^{1}H NMR **:** 6.65 (d, 1H, Ar, *J* 8.2Hz), 6.81 (d, 1H, Ar, *J* 8.4 Hz), 6.83 (t, 1H, Ar, *J* 7.4 Hz), 7.15-7.85 (m, 8H, Ar), 8.75 (dd, 1H, *J* 6.9, 2.5 Hz), 10.29 (s, 1H, -OH);

13C NMR **:** 112.4, 116.7, 120.3, 121.5, 122.4,125.8, 129.3, 131.5, 132.7, 139.2, 143.6, 152.5, 159.2, 161.4 (20 C, Ar-C);

Mass **:** *m/z* (%) = 311.

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