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Selective Formation of 2-Amino-Iminoaldehyds: Synthesis of News Molecules of Benzimidazoles

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Abstract

The reaction of 1,2-phenylenediamines (o-PDA) 1 with aromatic aldehyds 2 allows simultaneous formation of two products 3 and 4. In this case, we adopted an operational process which enables us to direct our reaction towards the selective formation of only one product. From these results, we have prepared some news products of benzimidazole structure 5 by reaction of intramolecular heterocyclization of the molecules 3. An oxidation reaction of the nitrated compounds of 5 has allowed us to obtain their dehydrogenated homologues of structure 6.

Keywords: 1,2-Phenylenediamines, Schift bases, Benzimidazolines, Benzimidazoles.

Introduction

Benzimidazoles have interesting pharmacological properties [1,2]. They are widely used as antibacterial, antifugal, antiparasite and anti-viral agents [3-9]. Several methods have been developed for the preparation of benzimidazole derivatives. The usual procedure for the synthesis of these compounds is a condensation between ortho-phenylenediamines and carbonyl compounds in the presence of a catalyst, such as Lewis acids [10-15].

In the present study, a news benzimidazoline derivatives 5 and benzimidazole 6 were synthetized from substituted o-phenylenediamines 1. The condensation of aromatic aldehyds 2 with o-phenylenediamines 1 gave selectively in appropriate experimental conditions, the mono-imine compounds 3 or the diimine 4. The heterocyclization of the mono-imine derivatives 3 permit to yield a new benzimidazoline compounds 5. However, the benzimidazole derivatives 6 were prepared by oxidation reaction of benzimidazoline 5 in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ).

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Experimental

All chemicals were obtained from Aldrich. Melting points were taken on a Thomas Hoover apparatus and are uncorrected. Nuclear magnetic resonance spectra were obtained with a Bruker AC 300 at 300 MHz (^{1}H) or 75 MHz (^{13}C). The chemical shifts are reported in ppm (δ-scale) relative to internal TMS and coupling constants are reported in Hertz (Hz). The impact ionization mass spectra were recorded on a Nermag R10-10C at 70 eV.

General procedure for synthesis of 3

In 20 ml of ethanol containing 10^{-2} moles of o-PDA 1(a to c), we added drop by drop an equivalent of aldehyds 2 (a to d). The mixture was stirred at room temperature for 2 hours under magnetic agitation. We obtained, after filtration and dry vacuum the corresponding compound 3 (a to l).

N-(4-fluorobenzylidene) benzene-1,2-diamine 3a

Yield = 63%; M.P. = 165-167°C. RMN^{1}H à 300 MHz (CDCl3) δ (ppm): 6.29-7.18 (m, 8H, Harom); 7.37 (s, 2H, NH2); 8.21 (s,1H, N=C-H). RMN^{13}C à 75 MHz (CDCl3) δ (ppm): 108, 111, 114, 117, 119, 120, 123, 124(HCarom); 135, 137, 140, 156 (Cq); 159(-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$ = 214 (27%), 197(39%), 118 (21%).

N-(4-methoxybenzylidene) benzene-1,2-diamine 3b

This compound is obtained according to the same protocol as 3a, after 3 hours.

Yellow precipitate; yield = 69%; M.P. = 171-173°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.89 (s, 3H, O-CH3); 6.27- .15 (m, 8H, Harom); 7.85 (s, 2H, NH2); 8.45 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 46 (H3C-O); 108, 110, 115, 117, 118, 119, 122, 123 (HCarom); 134, 137, 140, 150 (Cq); 160(-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$ = 226 (35%), 209 (7%), 195 (13%), 118 (44%).

4-[(2-aminophenylimino) methyl]benzonitrile 3c

This compound is obtained according to the same protocol as 3a, after 4 hours.

Orange precipitate; Yield = 59%; M.P. = 175-177°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 4.21 (s, 2H, NH2); 6.33-7.31 (m, 8H, Harom); 8.59 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 105, 107, 111, 113, 122, 124, 125, 127 (HCarom); 121, 126, 135, 137, 139 (Cq); 159(-C=N). S.M. (70 eV), m/z : $M^{1+\cdot}$= 221 (59%), 194 (16%), 118 (23%).

N-(4-nitrobenzylidene) benzene-1,2-diamine 3d

This compound is obtained according to the same protocol as 3a, after 5 hours.

Red precipitate; Yield = 53% ; M.P. = 183-185°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 5.32 (s, 2H, NH2); 6.31-7.34 (m, 8H, Harom); 8.75 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 107, 109, 111, 113, 124, 126, 129, 131 (HCarom); 134, 139, 140, 148 (Cq); 158(-C=N). S.M. (70 eV), m/z : $M^{1+\cdot}$= 241 (59%), 195 (38%), 118 (19%).

N-(4-fluorobenzylidene)-4-methylbenzene-1,2-diamine 3e

This compound is obtained according to the same protocol as 3a, after 3 hours.

White precipitate; Yield = 64%; M.P. = 178-180°C.

RMN^{1}H à 300 MHz (CDCl3) δ (ppm): 3.12 (s, 3H, CH3); 6.11-7.13 (m, 7H, Harom); 6.87 (s, 2H, NH2); 8.14 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 27(CH3); 106, 109, 112, 123, 124, 126, 128 (HCarom); 132, 135, 137, 141, 154 (Cq); 158(-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$= 228 (67%), 211 (25%), 133 (19%), 117 (22%).

N-(4-methoxybenzylidene)-4-methylbenzene-1,2-diamine 3f

This compound is obtained according to the same protocol as 3a, after 2 hours 30 minutes.

Yellow precitate; Yield = 75%; M.P. = 185-187°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.19 (s, 3H, CH3); 3.81 (s, 3H, O-CH3); 6.22-7.11 (m, 7H, Harom); 7.22 (s, 2H, NH2); 8.39 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 26 (CH3); 41 (H3C-O); 105, 107, 110, 115, 117, 119, 120 (HCarom); 132, 136, 138, 141, 149 (Cq); 159 (-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$= 240 (53%), 208 (14%), 133 (8%).

N-(4-cyanobenzylidene)-4-methylbenzene-1,2-diamine 3g

This compound is obtained according to the same protocol as 3a, after 3 hours 15 minutes.

Green yellow precipitate; Yield = 65% ; M.P. = 188-190°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.17 (s, 3H, CH3); 4.76 (s, 2H, NH2); 6.32-7.36 (m, 7H, Harom); 8.41 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 27 (CH3); 105, 107, 109, 121, 122, 128, 129 (HCarom); 119, 123, 136, 133, 139, 140 (Cq); 158(-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$= 235 (42%), 208 (21%), 133 (11%), 117 (14%).

N-(4-nitrobenzylidene)-4-methylbenzene-1,2-diamine 3h

This compound is obtained according to the same protocol as 3a, after 4 hours 30 minutes.

Orange precipitate; Yield = 59%; M.P. = 193-195°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.15 (s, 3H, CH3); 6.07 (s, 2H, NH2); 6.35-7.42 (m, 7H, Harom); 8.89 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 29 (CH3); 106, 109, 111, 123, 124, 127, 129 (HCarom); 135, 137, 140, 141, 150 (Cq); 159 (-C=N). S.M. (70 eV), m/z : $M^{1+\cdot}$= 255 (66%), 209 (32%), 117 (24%).

N-(4-fluorobenzylidene)-5-nitrobenzene-1,2-diamine 3i

This compound is obtained according to the same protocol as 3a, after 4 hours.

Light yellow precipitate; Yield = 55%; M.P. = 191-193°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.38-7.85 (m, 7H, Harom); 8.37 (s, 2H, NH2); 9.06 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 115, 118, 120, 122, 124, 125, 127 (HCarom); 136, 138, 141, 146, 154 (Cq); 158(-C=N). S.M. (70 eV), m/z : $M^{1+\cdot}$= 259 (34%), 213 (27%), 118 (19%).

N-(4-methoxybenzylidene)-5-nitrobenzene-1,2-diamine 3j

This compound is obtained according to the same protocol as 3a, after 3 hours 20 minutes.

Orange precipitate; Yield = 66% ; M.P. = 195-197°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.92 (s, 3H, O-CH3); 6.41-7.95 (m, 7H, Harom); 8.46 (s, 2H, NH2); 9.13 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 41 (H3C-O); 113, 115, 117, 119, 120, 123, 124 (HCarom); 135, 139, 140, 149, 151 (Cq); 159 (-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$= 271 (35%), 225 (20%), 164 (17%), 118 (8%).

N-(4-cyanobenzylidene)-5-nitrobenzene-1,2-diamine 3k

This compound is obtained according to the same protocol as 3a, after 5 hours.

Orange precipitate; Yield = 57%; M.P. = 199-201°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 5.02(s, 2H, NH2); 6.75-8.06 (m, 7H, Harom); 8.69(s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 113, 115, 118, 120, 122, 126, 128 (HCarom); 119, 122, 137, 138, 142, 146 (Cq); 160 (-C=N). S.M. (70 eV), m/z : $M^{1+\cdot}$= 266 (31%), 239 (44%), 220 (27%), 117 (29%).

N-(4-nitrobenzylidene)-5-nitrobenzene-1,2-diamine 3l

This compound is obtained according to the same protocol as 3a, after 6 hours 30 minutes.

Red precipitate; Yield = 53% ; M.P. = 203-205°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.79-8.08 (m, 7H, Harom); 6.93(s, 2H, NH2); 9.02 (s, 1H, N=C-H). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 114, 117, 119, 123, 124, 127, 130 (HCarom); 139, 140, 141, 148, 151 (Cq); 160 (-C=N). S.M. (70 eV), m/z: $M^{1+\cdot}$= 284 (49%), 238 (25%), 192 (33%), 117 (38%).

General procedure for synthesis of 4

In 20 ml ethanol containing 10^{-2} moles of aldehyds 2 (a to d), we added drop by drop two equivalents of o-PDA 1(a to c). The mixture was stirred at room temperature for 2 hours under magnetic agitation. We obtained, after filtration and dry vacuum the corresponding compound 4 (a to l).

N,N-bis(4-fluorobenzilidene)benzene-1,2-diamine 4a

Yield = 91%; Melting Point = 187-189°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 7.19-7.41 (m, 12H, Harom); 9.17 (s, 2H, N=C-H).

N,N-bis(4-methoxybenzylidene)benzene-1,2-diamine 4b

This compound is obtained according to the same protocol as 4a, after 20 minutes.

Light yellow precipitate; Yield = 87%; M.P. = 190-192°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.78 (s, 6H, O-CH3); 6.83-7.62 (m, 12H, Harom); 9.08 (s, 2H, N=C-H).

N,N-bis(4-cyanobenzylidene)benzene-1,2-diamine 4c

This compound is obtained according to the same protocol as 4a, after 40 minutes.

Orange precipitate; Yield = 78%; M.P. = 194-196°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.93-7.47 (m, 12H, Harom); 9.36 (s, 2H, N=C-H).

N,N-bis(4-nitrobenzylidene)benzene-1,2-diamine 4d

This compound is obtained according to the same protocol as 4a, after 1hour.

Red precipitate; Yield = 73%; M.P. = 197-199°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.95-7.56 (m, 12H, Harom); 9.47 (s, 2H, N=C-H).

N,N-bis(4-fluorobenzylidene)-4-methylbenzene-1,2-diamine 4e

This compound is obtained according to the same protocol as 4a, after 45 minutes.

White precipitate; Yield = 87%; M.P. = 199-201°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 2.76 (s, 3H, CH3); 6.91-7.37 (m, 11H, Harom); 9.14 (s, 2H, N=C-H).

N,N-bis(4-methoxybenzylidene)-4-methylbenzene-1,2-diamine 4f

This compound is obtained according to the same protocol as 4a, after 45 minutes.

Light yellow precipitate; Yield = 89%; M.P. = 105-207°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 2.81 (s, 3H, CH3); 3.85 (s, 3H, O-CH3); 6.74-7.28 (m, 11H, Harom); 9.26 (s, 2H, N=C-H).

N,N-bis(4-cyanobenzylidene)-4-methylbenzene-1,2-diamine 4g

This compound is obtained according to the same protocol as 4a, after 1hour.

Green yellow precipitate; Yield = 73%; M.P. = 209-211°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 2.79 (s, 3H, CH3); 6.72-7.39 (m, 11H, Harom); 9.34 (s, 1H, N=C-H).

N,N-bis(4-nitrobenzylidene)-4-methylbenzene-1,2-diamine 4h

This compound is obtained according to the same protocol as 4a, after 1 heure 15 minutes.

Light red precipitate; Yield = 63%; M.P. = 214-216°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 2.73 (s, 3H, CH3); 6.76-7.42 (m, 11H, Harom); 9.37 (s, 1H, N=C-H).

N,N-bis(4-fluorobenzylidene)-4-nitrobenzene-1,2-diamine 4i

This compound is obtained according to the same protocol as 4a, after 1 hour 25 minutes.

Yellow precipitate; Yield = 65%; M.P. = 209-211°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.59-7.45 (m, 11H, Harom); 9.34 (s, 2H, N=C-H).

N,N-bis(4-methoxybenzylidene)-4-nitrobenzene-1,2-diamine 4j

This compound is obtained according to the same protocol as 4a, after 1 hour 10 minutes.

Orange precipitate; Yield = 69% ; M.P. = 217-219°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.84 (s, 3H, O-CH3); 6.47-7.85 (m, 11H, Harom); 9.37 (s, 2H, N=C-H).

N,N-bis(4-cyanobenzylidene)-4-nitrobenzene-1,2-diamine 4k

This compound is obtained according to the same protocol as 4a, after 1 hour 50 minutes.

Orange precipitate; Yield = 59%; M.P = 221-223°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.81-7.93 (m, 7H, Harom); 9.41(s, 2H, N=C-H).

N,N-bis(4-nitrobenzylidene)-4-nitrobenzene-1,2-diamine 4l

This compound is obtained according to the same protocol as 4a, after 2 hours 30 minutes.

Red precipitate; Yield = 57%; M.P. = 225-227°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.83-7.97 (m, 11H, Harom); 9.46 (s, 2H, N=C-H).

General procedure for synthesis of 5

Compound 3 (10^{-2} mol) in 20 ml of ethanol in the presence of two drops of concentrated sulphuric acid, was refluxed for 6h under magnetic stirring. After filtration and dry vacuum, we obtained the corresponding compounds 5 (a to l).

2-(4-fluorophenyl)-2,3-dihydro-1H- benzo[d]imidazole 5a. Yield =58%; M.P. = 217-219°C. RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 4.57 (s, 2H, 2NH); 5.10 (s, 1H, CH); 6.33-7.21 (m, 8H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 74(CH); 112, 113, 115, 117, 119, 122, 123, 124 (HCarom); 136, 138, 156 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$ = 214 (36%), 118 (28%).

2-(4-methoxyphenyl)-2,3-dihydro-1H- benzo[d]imidazole 5b

This compound is obtained, according to the same protocol as 5a, after a refluxing of 5 hours.

Yellow precipitate; Yield = 63%; m.p. = 222-224°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.91 (s, 3H, H3C-O); 4.61 (s, 2H, 2NH); 5.07 (s, 1H, CH); 6.34-6.91 (m, 8H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 39 (CH3-O), 73 (CH); 110, 112, 114, 117, 119, 121, 123, 124 (HCarom); 134, 135, 153 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 226 (27%), 195 (49%), 118 (31%).

2-(4-cyanophenyl)-2,3-dihydro-1H- benzo[d]imidazole 5c

This compound is obtained, according to the same protocol as 5a, after a refluxing of 7 hours

Orange precipitate; Yield = 49%; m.p. = 229-231°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 5.02 (s, 2H, 2NH); 5.27 (s, 1H, CH); 6.38-8.11 (m, 8H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 73 (CH); 116, 117, 119, 120, 121, 122, 124, 126 (HCarom); 123, 125, 137, 141 (Cq). S.M. (70 eV), m/z : $M^{1+\cdot}$= 221 (24%), 183 (29%), 118 (67%).

2-(4-nitrophenyl)-2,3-dihydro-1H- benzo[d]imidazole 5d

This compound is obtained, according to the same protocol as 5a, after a refluxing of 9 hours.

Brick red precipitate; Yield = 41%; m.p. = 232-234 °C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 5.01 (s, 2H, 2NH); 5.34 (s, 1H, CH); 6.39-8.17 (m, 8H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 74 (CH); 117, 118, 120, 121, 123, 124, 126, 127 (HCarom); 137, 143, 147 (Cq). S.M. (70 eV), m/z : $M^{1+\cdot}$= 241 (47%), 197 (15%), 118 (26%).

2-(4-fluorophenyl)-5-methyl-2,3-dihydro-1H-benzo[d]imidazole 5e

This compound is obtained, according to the same protocol as 5a, after a refluxing of 6 hours.

White precipitate; Yield = 69%; m.p. = 224-226°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.16 (s, 3H, CH3); 4.38 (s, 2H, 2NH); 5.11 (s, 1H, CH), 6.18-7.01 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 28 (CH3); 73 (CH); 109, 111, 113, 117, 118, 120, 121 (HCarom); 132, 134, 137, 138, 155 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 228 (32%), 133 (57%), 117 (9%).

2-(4-methoxyphenyl)-5-methyl-2,3-dihydro-1H- benzo[d]imidazole 5f

This compound is obtained, according to the same protocol as 5a, after a refluxing of 5 hours.

Yellowish white precipitate; Yield = 81%; m.p. = 225-227°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.17 (s, 3H, CH3); 3.84 (s, 3H, H3C-O); 4.53 (s, 2H, 2NH); 5.04 (s, 1H, CH); 6.17-6.77 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 27 (CH3); 41 (CH3-O); 72 (CH); 108, 109, 111, 113, 115, 117, 119 (HCarom); 131, 133, 135, 137, 148 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 240 (69%), 207 (13%), 133 (41%), 117 (13%).

2-(4-cyanophenyl)-5-methyl-2,3-dihydro-1H- benzo[d]imidazole 5g

This compound is obtained, according to the same protocol as 5a, after a refluxing of 7 hours.

Yellow precipitate; Yield = 72% ; m.p. = 227-229°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.16 (s, 3H, CH3); 4.09 (s, 2H, 2NH); 5.59 (s, 1H, CH); 6.36-7.85 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 27 (CH3); 71 (CH); 109, 110, 112, 120, 121, 123, 125 (HCarom); 121, 125, 130, 134, 137, 142 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 235 (38%), 220 (15%), 133 (68%), 117 (19%).

2-(4-nitrophenyl)-5-methyl-2,3-dihydro-1H- benzo[d]imidazole 5h

This compound is obtained, according to the same protocol as 5a, after a refluxing of 8 hours.

Orange precipitate; Yield = 65%; m.p. = 231-233°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.18 (s, 3H, CH3); 4.81 (s, 2H, 2NH); 5.61 (s, 1H, CH); 6.39-7.91 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 28 (CH3); 72 (CH); 110, 111, 113, 123, 124, 127, 129 (HCarom); 131, 133, 136, 137, 146 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 255 (59%), 133 (15%), 117 (31%).

2-(4-fluorophenyl)-5-nitro-2,3-dihydro-1H-benzo[d]imidazole 5i

This compound is obtained, according to the same protocol as 5a, after a refluxing of 8 hours.

Yellow precipitate; Yield = 53% ; m.p. = 231-233°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 4.61 (s, 2H, 2NH); 5.39 (s, 1H, CH); 6.28-7.57 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 75 (CH); 115, 117, 119, 123, 125, 127, 128 (HCarom); 132, 138, 139, 141, 154 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 259 (63%), 213 (22%), 164 (27%), 117 (35%).

2-(4-methoxyphenyl)-5-nitro-2,3-dihydro-1H- benzo[d]imidazole 5j

This compound is obtained, according to the same protocol as 5a, after a refluxing of 7 hours.

Yellow precipitate; Yield = 57% m.p. = 236-238°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.76 (s, 3H, H3C-O); 4.67 (s, 2H, 2NH); 5.23 (s, 1H, CH); 6.21-7.85 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 42 (CH3-O); 76 (CH); 113, 114, 117, 118, 122, 124, 126 (HCarom); 133, 135, 143, 145, 151 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 271 (29%), 164 (33%), 117 (44%).

2-(4-cyanophenyl)-5-nitro-2,3-dihydro-1H- benzo[d]imidazole 5k

This compound is obtained, according to the same protocol as 5a, after a refluxing of 7 hours.

Orange precipitate; Yield = 52%; m.p. = 240-242°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 4.70 (s, 2H, 2NH); 5.63 (s, 1H, CH); 7.01-7.87 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 78 (CH); 115, 117, 119, 121, 123, 126, 127 (HCarom); 122, 125, 135, 138, 141, 146 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 266 (51%), 239 (23%), 164 (17%), 117 (35%).

2-(4-nitrophenyl)-5-nitro-2,3-dihydro-1H- benzo[d]imidazole 5l

This compound is obtained, according to the same protocol as 5a, after a refluxing of 14 hours.

Red brick precipitate; Yield = 41%; m.p. = 246-248°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 4.71 (s, 2H, 2NH); 5.87 (s, 1H, CH); 7.01-8.08 (m, 7H, Harom). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 79 (CH); 119, 121, 123, 124, 125, 127, 128 (HCarom); 138, 139, 141, 143, 147 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$.= 286 (29%), 240 (17%), 164 (5%), 117 (14%).

General procedure for synthesis of 6

To the mixture of compounds 5 (10^{-2} moles), 20ml of chloroform and 10 ml of acetone placed at 0°C, was slowly added 1.12 10^{-2} moles (1.1 equiv.) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) dissolved in 10 ml of acetone. The solution is left under magnetic agitation at 0°C during one hour. After filtration of the formed hydroquinone and evaporation of the filtrate under vacuum we get back a powder.

2-(4-nitrophenyl)-1H- benzo[d]imidazole 6a

Yellow precipitate; Yield = 54%; M.p. = 218-220 °C. RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 7.18-8.25 (m, 8H, Harom); 9.29 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 114, 123, 125, 129 (HCarom); 136, 138, 149, 153 (Cq). S.M. (70 eV), m/z : $M^{1+\cdot}$= 239 (100%), 194 (31%), 117 (27%).

2-(4-nitrophenyl)-5-methyl-1H- benzo[d]imidazole 6b

Orange precipitate; Yield = 65%; M.p. = 221-223°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.02 (s, 3H, CH3); 7.06-8.17 (m, 7H, Harom); 9.07 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 26 (CH3); 114, 116, 121, 126, 128 (HCarom); 131, 134, 136, 139, 147, 153 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 253 (100%), 131 (52%), 117 (37%).

2-(4-fluorophenyl)-5-nitro-1H-benzo[d]imidazole 6c

Yellow precipitate; Yield = 64%; M.p. = 216-218°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 6.39-7.71 (m, 7H, Harom); 9.61 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 109, 112, 119, 123, 128 (HCarom); 133, 136, 141, 149, 153, 156 (Cq). S.M. (70 eV), m/z : $M^{1+\cdot}$= 257 (57%), 211 (35%), 117 (41%).

2-(4-methoxyphenyl)-5-nitro-1H- benzo[d]imidazole 6d

Grey precipitate; Yield = 67%; M.p. = 222-224°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 3.81 (s, 3H, H3C-O); 6.23-7.68 (m, 7H, Harom); 9.57 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 44 (CH3-O); 107, 114, 119, 123, 129 (HCarom); 133, 137, 141, 148, 152, 157 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 269 (35%), 162 (41%), 117 (27%).

2-(4-cyanophenyl)-5-nitro-1H- benzo[d]imidazole 6e

Brown precipitate; Yield = 57% ; M.p. = 234-236°C.

MN ^{1}H à 300 MHz (CDCl3) δ (ppm): 7.09-7.94 (m, 7H, Harom); 9.67 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 116, 119, 121, 122, 127, 129 (HCarom); 107, 115, 136, 138, 144,150, 154 (Cq). S.M. (70 eV), m/z : $M^{1+\cdot}$= 264 (49%), 237 (31%), 117 (37%).

2-(4-nitrophenyl)-5-nitro-2,3-1H- benzo[d]imidazole 6f

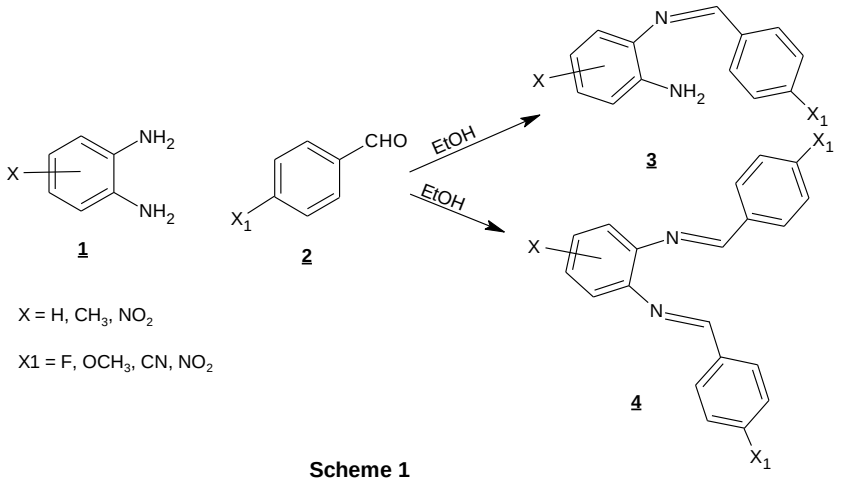
Red precipitate; Yield = 49%; M.p. = 241-243°C.

RMN ^{1}H à 300 MHz (CDCl3) δ (ppm): 7.15-8.03 (m, 7H, Harom); 9.73 (s, H, NH). RMN ^{13}C à 75 MHz (CDCl3) δ (ppm): 110, 116, 119, 123, 128 (HCarom); 137, 140, 143, 144, 148, 153 (Cq). S.M. (70 eV), m/z: $M^{1+\cdot}$= 284 (58%), 238 (27%), 162 (19%), 117 (36%)

Results and Discussion

In a previous work [16-18], we have described the synthesis of benzimidazole structure from the reaction of lactones (2-pyrone, tetronic acid and 2-acetylbutyrolactone) with substituted o-phenylenediamines in presence of masked (dimethylformamide-dimethylacetal, DMF-DMA) aldehyds. In continous of this work, we have extended the reaction of o-phenylenediamines to aldehyds in simple conditions.

We noticed the reaction of o-PDA 1 with aromatic aldehyds in an equimolar ratio gave a products mixture of 3 and 4 (Scheme 1).



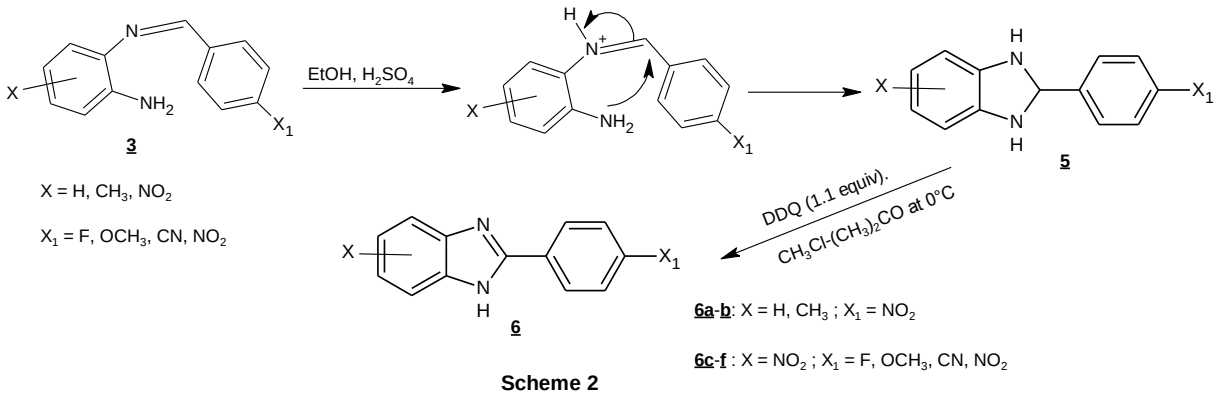
Scheme 1

Scheme 1

In order to get a better selectivity reaction, we have optimized the synthetic conditions by changing the introducing order of reagents and stoechiometry [19]. The addition of drip by drip of one equivalent of aldehyd 2 into ethanolic solution containing one equivalent of o-PDA 1 at room temperature formed a solid precipitate corresponding to mono-imine structure 3. All compounds were characterized on the basis of their spectroscopic data as such as H^{1} NMR, C^{13} NMR and mass spectrometry. Particularly, the appearance of two singlets at 4.21- 8.46 ppm and 8.60 ppm attributed to protons of NH_2 and imine (N=C-H), confirmed the structure 3.

Conversely, the addition of drip by drip of one equivalent of o-PDA 1 into ethanolic solution containing two equivalents of aldehyd 2 favorised formation of diimine 4. All isolated derivatives were caracterised by H^1 NMR; we observed one singlet at 9.20 ppm corresponding to two protons of diimine 4.

In a second step, the mono-imine derivatives 3 undergoes cyclization under acidic catalysis and leads to benzimidazoline structure 5 after a protonation of the imino group, on the one hand, and interaction between the amino group borne by the phenyl ring of 3 and the formed of iminium group, on the other hand (Scheme 2).



Scheme 2

Scheme 2

This intramolecular cyclization shows a clear tendency between the obtained yields and the nature of the substituent electronic effect. The structure 5 has been established on the basis of H^1 and C^{13} NMR. In particular, the appearence of a singlet at around 5.35 ppm attributable to the proton of C-H at position 2 of imidazoline ring. In addition, the C^{13} NMR shows a new signal at around 70 ppm attributed to the tertiary carbon in the position 2.

On other hand, we have used the nitrated derivatives of 2,3-dihydro-1H-benzo[d]imidazole 5 (benzimidazoline) to prepared the 1H-benzo[d]imidazole (benzimidazole) 6 by oxidative reaction in the presence of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) [20]. In mixture of chloroforme/acetone at 0°C, we obtained the benzimidazole 6 by dehydrogenation of the nitrated compounds of 5.

All derivatives of 6 were characterized by H^1 NMR, C^{13} NMR and mass spectrometry. In particular, on the specters of the RMN ^1H, we notice the absence of the signal of the hydrogen in position 2 of the cycle benzimidazoline, usually observed at around of 5.35 ppm in the structure 5. In RMN C^{13}, the appearance of a new signal at 138 ppm, explain the conversion of the tertiary carbon in position 2 of the cycle benzimidazoline 5 in quaternary carbon and confirmed the obtaining of the structure 6.

Conclusion

We isolated selectively news molecules of structures amino-2-iminoaldehydes 3 and 1,2-diiminoaldéhydes 4 in simple operating conditions. We made a success of the heterocyclisa-tion of the products 3 by easily obtaining of the new benzimidazole molecules 5. The reaction of oxidation of the nitrated derivatives of 5, allowed us to widen the series to their dehydrogenated benzimidazoles 6. A later study of the intramolecular cyclisation of 4 is envisaged, by the use of catalysts of bismuth [21].

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