MnO₂ Nanoparticles as Efficient Oxidant for Ultrasound-Assisted Synthesis of 2-substituted Benzimidazoles under Mild Conditions

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In this article, a novel method for synthesis of 2-substituted benzimidazoles using MnO₂ nanoparticles as a convenient oxidant agent in ethanol-water (1:1) as solvent under ultrasound irradiation was demonstrated. In this protocol the desired products were purely obtained in high yields. The main advantages of this research are: mild procedure, simplicity of method, easily work-up, high yields, and short reaction times. The MnO₂ nanoparticles were synthesized through a solid-state reaction route using simple starting materials. Furthermore, their structure was characterized by X-ray diffraction (XRD), scanning electron microscopy (SEM), and Fourier transform infrared spectroscopy (FT-IR).

Key Words: Aryl aldehyde, Benzimidazoles, MnO₂ nanoparticles, O-phenylenediamine, ultrasound irradiation

INTRODUCTION

The benzimidazole ring system is an important class of bioactive molecules in modern drug discovery and pharmaceutical. Benzimidazole and its derivatives have been applied as anti-parasitic, fungicide, anti-histaminic, anti-tumor,
anti-viral and immunosuppressant (1–5). Attentive to their widespread pharmacological activity, synthesis, and application, a number of procedures have been applied for the synthesis of benzimidazole and its derivatives. Generally, the synthesis of 2-substituted benzimidazoles involves the treatment of o-phenylenediamine either with carboxylic acids or various derivatives (6) and the condensation of o-phenylenediamine with aldehydes in the presence of various oxidant agents (7–18). On the other hand, these derivatives also generated from the condensation of o-phenylenediamine with ortho-esters in the presence of various Lewis acid catalysts, such as ZrCl4, SnCl4.5H2O, TiCl4, BF3.Et2O, ZrOCl2.8H2O, and HfCl4 (19). However, all of these procedures have some problems, including severe side-reactions, low yields, prolonged reaction, drastic reaction conditions.

Ultrasonic-assisted organic synthesis as an eco-friendly synthetic approach is a powerful technique that is being used more and more to accelerate organic reactions (20–24). The significant features of the ultrasound approach are increased formation of products in high yields, reaction rates, facile manipulation, and considered a processing aid in terms of energy conservation and waste minimization, which compared with traditional methods. In this context, we reported a one-pot, simple, and high-yield method of synthesis of benzimidazole derivatives using MnO2 nanoparticles as efficient and convenient oxidant agent under ultrasound irradiation.

EXPERIMENTAL

Materials and Apparatus

All commercially available reagents were used without further purification and purchased from the Merck Chemical Company in high purity. The used solvents were purified by standard procedure. IR spectra were recorded as KBr pellets on a Perkin-Elmer 781 spectrophotometer and an Impact 400 Nicolet FT-IR spectrophotometer. 1H NMR and 13C NMR were recorded in DMSO and CDCl3 solvents on a Bruker DRX-400 spectrometer with tetramethylsilane as internal reference. The BANDELIN ultrasonic HD 3200 with probe model KE 76, 6 mm diameter, was used to produce ultrasonic irradiation and homogenizing the reaction mixture. X-ray diffraction (XRD) analysis of the MnO2 nanoparticles was conducted on a Rigaku D/max-2000 X-ray powder diffractometer with a CuKa radiation (40 kV, 250 mA) scanned over the 2 h range of 10–90°. Melting points obtained with a Yanagimoto micro melting point apparatus are uncorrected. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company).
General Procedure for the Preparation of MnO₂ Nanoparticles

MnSO₄·H₂O and (NH₄)₂C₂O₄·H₂O with a mole ratio of 1:1.2 were mixed and well ground in a mortar at room temperature. In the grinding process, the solid-state reaction took place, accompanying with the hydrated water releasing gradually from the starting materials. Ground for 40 min, the wet mixture was transferred to a thermostatic water bath of 80°C for several hours, and then a dry mixture was obtained. The mixture was washed with distilled water to remove the dissoluble substances, and dried in an oven at 110°C for 10 h, and then a white MnC₂O₄ precursor was obtained. The precursor was calcined in atmosphere at 400°C in a muffle furnace at 10 h for oxidative decomposition. Afterwards, the calcined product (manganese oxide) was subjected to acid-treatment in 2 mol L⁻¹ H₂SO₄ solution at 80°C for 2 h under magnetic stirring, in order to increase its degree of oxidation. After that, the product was washed thoroughly with distilled water, filtered, and dried at 105°C, and then a final product (MnO₂ material) was obtained.

General Procedure for the Synthesis of Benzimidazoles from o-Phenylenediamine

To a mixture of an aromatic aldehydes (1 mmol), o-phenylenediamine (1 mmol) and 0.017 g (20 mol%) of MnO₂ nanoparticles were added to EtOH/H₂O (1:1) as solvent, then ultrasonic probe was directly immersed in the reactor. The progress of the reactions was monitored by TLC. After completion of the reaction, the reaction mixture was cooled and MnO₂ nanoparticles were collected by filtration. Then, the reaction mixture was added drop wise into a mixture of water and ice, so the crude solid were filtered off and washed with water. The product was purified by recrystallization from methanol/H₂O (1:1). They were characterized by comparison of their physical and spectral data with those of authentic samples.

2-Phenyl-benzimidazole (2a): Pale yellow solid, mp 286–288°C, (mp 288–290°C) (25), IR(KBr)/ ν(cm⁻¹): 3446, 1622, 1590, 1445; ¹H NMR (DMSO, 400 MHz)/ δ ppm: 7.19 (m, 2H, Ar), 7.48–7.64 (m, 5H, Ar), 8.17 (m, 2H, Ar); ¹³C NMR (DMSO, 100 MHz)/ δ ppm: 111.1, 118.6, 121.9, 126.2, 128.6, 129.5, 130.0, 134.8, 143.5, 151.0.

2-(4-Methylphenyl)-benzimidazole (2b): White solid, mp 258–260°C, (mp 261–263°C) (26), IR (KBr)/ ν(cm⁻¹): 3429, 1620, 1587, 1433; ¹H NMR (DMSO, 400 MHz)/ δ ppm: 2.36 (s, 3H, CH₃) 7.18 (m, 2H, J = 3.2, Ar), 7.34 (d, 2H, J = 8, Ar), 7.57 (m, 2H, J = 3.2, Ar), 8.06 (d, 2H, J = 8, Ar), 12.8 (s, 1H, NH); ¹³C NMR (DMSO, 100 MHz)/ δ ppm: 21.41, 115.50, 122.43, 125.89, 127.93, 129.97, 139, 140.03, 151.90.
2-(3-Methoxyphenyl)-benzimidazole (2c): Yellow solid, mp 203–205°C (mp 205–206°C) (27), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3437, 1596, 1541, 1464; \(^1\)H NMR (400 MHz, DMSO)/ \( \delta \) ppm: 3.9 (s, 3H, CH\(_3\)), 7.05 (m, 1H, Ar), 7.19 (m, 2H, Ar), 7.45 (s, 1H, Ar), 7.59 (m, 2H, J = 8, Ar), 7.74 (m, 2H, J = 8, Ar), 12.9 (s, 1H, NH); \(^{13}\)C NMR (DMSO, 100 MHz)/ \( \delta \) ppm: 56.01, 114.03, 115.25, 116.50, 117.80, 124.49, 130.47, 132.63, 138.99, 152.23, 159.10.

2-(4-Methoxyphenyl)-benzimidazole (2d): Yellow solid, mp 226–228°C, (mp 229.2–231.1°C) (28), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3344, 1608, 1506, 1461; \(^1\)H NMR (DMSO, 400 MHz)/ \( \delta \) ppm: 3.89 (s, 3H, CH\(_3\)), 7.2 (d, 2H, J = 8, Ar), 7.52 (m, 2H, J = 4, Ar), 7.79 (m, 2H, J = 8, Ar), 8.38 (d, 2H, J = 8, Ar), 15.3 (s, 1H, NH); \(^{13}\)C NMR (DMSO, 100 MHz)/ \( \delta \) ppm: 56.24, 114.06, 115.34, 115.53, 126.03, 130.62, 132, 148.91, 163.61.

2-(3,4-Dimethoxyphenyl)-benzimidazole (2e): Yellow solid, mp 232–234°C, (mp 235.5–236.7°C) (25), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3434, 1606, 1504, 1439; \(^1\)H NMR (CDCl\(_3\), 400 MHz)/ \( \delta \) ppm: 3.83 (s, 3H, CH\(_3\)), 3.93 (s, 3H, CH\(_3\)), 6.93 (d, 1H, J = 8.4, Ar), 7.27 (m, 3H, Ar), 7.56 (d, 1H, J = 8.4, Ar), 7.63 (s, 1H, Ar), 7.74 (s, 1H, Ar), 10.4 (br. s, 1H, NH).; \(^{13}\)C NMR (CDCl\(_3\), 100 MHz)/ \( \delta \) ppm: 55.73, 55.98, 109.74, 111.17, 119.26, 120.08, 122.62, 122.86, 135.07, 149.45, 150.82, 152.13.

2-(4-Hydroxyphenyl)-benzimidazole (2f): White solid, mp 253–255°C, (mp 254.1–256.6°C) (28), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3383, 3202, 1668, 1600, 1457; \(^1\)H NMR (DMSO, 400 MHz)/ \( \delta \) ppm: 6.91–7.50 (m, 4H, Ar), 7.73–8.21 (m, 4H, Ar), 9.7 (s, 1H, OH), 15.2 (s, 1H, NH); \(^{13}\)C NMR (DMSO, 100 MHz)/ \( \delta \) ppm: 113.06, 114.04, 116.83, 126.03, 131.62, 132, 149.93, 160.71.

2-(2,3-Dihydroxyphenyl)-benzimidazole (2g): Yellow solid, mp 144–146°C (Decomposition : 225°C) (29), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3393, 3315, 1612, 1571, 1458; \(^1\)H NMR (CDCl\(_3\), 400 MHz)/ \( \delta \) ppm: 5.85 (br. s, 1H, OH), 6.81–6.85 (m, 2H, Ar), 6.88 (d, 1H, J = 8, Ar), 7.00 (d, 1H, J = 1.2, Ar), 7.06–7.08 (m, 2H, Ar), 7.13 (t, 1H, J = 7.6, Ar), 8.62 (s, 1H, NH), 13.6 (br. s, 1H, OH); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz)/ \( \delta \) ppm: 109.64, 117.82, 118.54, 119.08, 119.33, 122.99, 128.35, 134.86, 140.57, 144.99, 148.51, 162.09.

2-(2-Hydroxy1-naphtyl)-benzimidazole (2h): Brown solid, mp 258–260°C (mp 260–262°C) (30), IR (KBr)/ \( \nu (\text{cm}^{-1}) \): 3471, 3373, 1610, 1559, 1489; \(^1\)H NMR (CDCl\(_3\), 400 MHz)/ \( \delta \) ppm: 6.83–6.86 (m, 2H, Ar), 6.88 (d, 1H, J = 8, Ar), 7.00 (d, 1H, J = 1.2, Ar), 7.06–7.08 (m, 2H, Ar), 7.13 (t, 1H, J = 7.6, Ar), 8.62 (s, 1H, NH), 13.6 (br. s, 1H, OH); \(^{13}\)C NMR (CDCl\(_3\), 100 MHz)/ \( \delta \) ppm: 109.64, 116.12, 118.83, 119.13, 119.9, 120.59, 123.62, 127.64, 127.97, 128.04, 129.34, 132.88, 135.64, 140.37, 156.99, 165.67.
2-(2-Chlorophenyl)-benzimidazole (2i): Yellow solid, mp 230–232°C, (mp 232–234°C) (31) IR (KBr)/ν(cm⁻¹): 3444, 1591, 1575, 1440; ¹H NMR (DMSO, 400 MHz)/δ ppm: 7.2 (2H, m, Ar), 7.50–7.89 (6H, m, Ar), 12.9 (1H, s, NH); ¹³C NMR (DMSO, 100 MHz)/δ ppm: 116.02, 122.72, 127.87, 130.40, 130.80, 131.64, 132.16, 132.54, 139.50, 149.64.

2-(4-Chlorophenyl)-benzimidazole (2j): Yellow solid, mp 290–292°C, (mp 291–293°C) (32), IR (KBr)/ν(cm⁻¹): 3442, 1598, 1580, 1429; ¹H NMR (DMSO, 400 MHz)/δ ppm: 7.2 (m, 2H, Ar), 7.50–7.89 (m, 6H, Ar), 13 (s, 1H, NH); ¹³C NMR (DMSO, 100 MHz)/δ ppm: 113.5, 123.7, 127.6, 128.3, 129.4, 133.4, 138.9, 151.8.

2-(2,4-Dichlorophenyl)-benzimidazole (2k): Yellow solid, mp 224–226°C, (mp 227°C) (41), IR (KBr)/ν(cm⁻¹): 3437, 1592, 1555, 1423; ¹H NMR (CDCl₃, 400 MHz)/δ ppm: 7.33- 7.70 (m, 6H, Ar), 8.37 (s, 1H, Ar), 10.37 (br. s, 1H, NH); ¹³C NMR (DMSO, 100 MHz)/δ ppm: 122.9, 128.19, 129.28, 130.35, 133.05, 133.72, 135.48, 148.56.

2-(2-Nitrophenyl)-benzimidazole (2l): Yellow solid, mp 260–262°C, (mp 262–264°C) (33), IR (KBr)/ν(cm⁻¹): 3428, 1622, 1530, 1458; ¹H NMR (CDCl₃, 400 MHz)/δ ppm: 7.54–7.57 (m, 2H, Ar), 7.85-7.87 (m, 2H, Ar), 7.99 (t, 1H, Ar), 8.05 (m, 1H, Ar), 8.12 (d, 1H, Ar), 8.37 (d, 1H, Ar).

2-(4-Nitrophenyl)-benzimidazole (2m): Yellow solid, mp 302-304°C, (mp 312–314°C) (33), IR (KBr)/ν(cm⁻¹): 3421, 1606, 1524, 1451; ¹H NMR (DMSO, 400 MHz)/δ ppm: 7.51-7.54 (m, 2H, Ar), 7.83 (m, 2H, Ar), 8.47 (d, 2H, Ar), 8.48–8.64 (d, 2H, Ar).

2-(4-Chloro-3-nitrophenyl)-benzimidazole (2n): Pale yellow solid, mp 193–194°C; IR (KBr)/ν(cm⁻¹): 3429, 1621, 1527, 1431; ¹H NMR (DMSO, 400 MHz)/δ ppm: 7.22–7.27 (m, 2H, Ar), 7.57 (d, 1H, J = 7.2, Ar), 7.70 (d, 1H, J = 7.2, Ar), 7.97 (d, 1H, J = 8.4, Ar), 8.43 (d, 1H, J = 6.8, Ar), 8.81 (s, 1H, ArH), 13.27 (s, 1H, NH); ¹³C NMR (DMSO, 100 MHz)/δ ppm: 112.22, 119.75, 122.75, 123.74, 123.91, 126.55, 130.93, 131.62, 133.07, 135.55, 144.03, 148.25, 148.65.

RESULTS AND DISCUSSION

In this article, a convenient method and efficient oxidant agent for the synthesis of 2-substituted benzimidazoles are described. We studied the model reaction involving o-phenylenediamine and aryl aldehyde derivatives 1a-n in a 1:1 mole ratio to afford the 2-substituted benzimidazole derivatives 2a-n (Scheme 1).

Initially, we prepared MnO₂ nanoparticles according to the procedure reported by Yuan et al. (34) and it was successfully used as oxidizing agent in the
The synthesis of benzimidazole derivatives. The FT-IR spectra of MnO$_2$ nanoparticles are shown in Figure 1.

The oxides and hydroxides of metal nanoparticles generally give absorption peak in the fingerprint region, i.e., below wavelength of 1000 nm arising from inter-atomic vibrations. Herein, the band at 527 cm$^{-1}$ could be attributed to Mn–O stretching vibrations mode in MnO$_6$ octahedral (35). From the above results it was concluded that the synthesized nanomaterial was manganese oxide. The band at the 3428 cm$^{-1}$ should be attributed to the –OH stretching vibration in KBr pellet, and the band at the 1630 cm$^{-1}$ is usually related to the interaction of –OH with Mn atoms.

X-ray diffraction (XRD) pattern of the mechanochemically synthesized MnO$_2$ is shown in Figure 2. The diffraction angle and intensity of the characteristic peaks of the samples is consistent with that of the standard JCPDS card no. 14-0644. Also the XRD spectrum consists with the characteristics peaks of MnO$_2$ nanoparticles at 22.153 (1 0 1), 37.014 (2 1 0), 42.424 (2 1 1), and 55.982 (4 0 2), which are similar to the γ-MnO$_2$ reported in the literature (36). The value of 17 nm was calculated from XRD data for average particle size of this crystalline MnO$_2$ using Scherrer’s equation (37).

Figure 1: FT-IR spectra of MnO$_2$ nanoparticles.
As well as, scanning electron microscopy (SEM) micrograph of the MnO$_2$ nanoparticles is shown in Figure 3. It can be observed that the particles are almost 35.5–46.3 nm.

In order to the optimization of this procedure, the reaction was carried out for synthesis of 4-chlorobenzimidazole by using different solvents and various
Table 1: The synthesis of compound 4-chloro-1H-benzimidazole by using a constant amount of MnO$_2$ nanoparticles under ultrasonic irradiation at power 55 W

| Entry | Solvent    | MnO$_2$ NPs (mol%) | Time (min) | Yield$^a$ (%) |
|-------|------------|--------------------|------------|---------------|
| 1     | DMF        | 0.2                | 7          | 45            |
| 2     | EtOH       | 0.2                | 6          | 55            |
| 3     | CH$_3$CN   | 0.2                | 7          | 50            |
| 4     | H$_2$O/EtOH(1:1) | 0.2                | 4          | 85            |
| 5     | H$_2$O/EtOH(3:2) | 0.2                | 5          | 75            |

$a$) Isolated yield

Table 2: The synthesis of compound 4-chloro-1H-benzimidazole by using various amounts of MnO$_2$ nanoparticles under ultrasonic irradiation at power 55 W

| Entry | MnO$_2$ NPs (mol) | Time (min) | Yield$^a$ (%) |
|-------|-------------------|------------|---------------|
| 1     | —                 | 60         | -             |
| 2     | 0.1               | 6          | 40            |
| 3     | 0.15              | 5          | 65            |
| 4     | 0.2               | 4          | 85            |
| 5     | 0.25              | 4          | 85            |

$a$) Isolated yield

Table 3: Check the effect of ultrasonic irradiation on the formation of 4-chlorobenzimidazole using MnO$_2$ nanoparticles

| Entry | Power (W) | Time (min) | Yield$^a$ (%) |
|-------|-----------|------------|---------------|
| 1     | 40        | 5          | 38            |
| 2     | 45        | 6          | 45            |
| 3     | 50        | 5          | 68            |
| 4     | 55        | 4          | 85            |
| 5     | 60        | 4          | 85            |

$a$) Isolated yield

amount of oxidant agent under ultrasonic irradiation at power 55 W. The corresponding results are represented in Table 1 and Table 2, respectively. As can be seen in Table 1, the best solvent in the reaction was obtained H$_2$O/EtOH (1:1) in optimum amount of 20 mol% MnO$_2$ nanoparticles as oxidative agent. The reaction was initially accomplished without oxidative agent, and it was obtained any product (Table 2, entry 1). However, the sonochemical synthesis of benzimidazole derivatives using MnO$_2$ nanoparticles as an oxidant agent (20 mol%) were obtained the best result (Table 2, entry 4). Using lower amount
of oxidant agent resulted in lower yields, while higher amounts did not affect on the reaction times and yields.

In continuation of this research, the effect of various powers of ultrasonic irradiation has been investigated. First, it was synthesized 4-chlorobenzimidazole as model reaction in order to optimize the best suited reaction conditions. It was observed that the reaction in the presence of MnO$_2$ as oxidant agent and ultrasonic irradiation with power 55 W were afforded the best result as obtained product with 85% isolated yield during 4 min (Table 3, entry 4).

The effects of ultrasonic irradiation observed during organic reactions are due to cavitations. In the case of volatile molecules cavities are believed to act as a microreactor as the volatile molecules enter the microbubbles and the high temperature and the pressure produced during cavitations break their chemical bonds thus reacting with other species (38–40).

At last, the reaction of o-phenylenediamine with various aryl aldehydes was carried out according to the general experimental procedure. In all the cases, the corresponding benzimidazoles were obtained in good to high yields and short reaction times. The similar products are summarized in Table 4.

It was generally observed that the presence of electron withdrawing groups in the aromatic ring of benzaldehyde enhances the reaction yield with reduced reaction time. This result can be attributed to higher electrophilicity of the carbonyl carbon in the presence of electron withdrawing substituent which is an essential condition for first step of condensation. On the other hand, the aromatic aldehydes with electron donating groups in this reaction were relatively

\[ \text{Scheme 2: The proposed mechanism for preparation of benzimidazoles using MnO}_2 \text{ nanoparticles.} \]
Table 4: The results related to the reaction of o-phenylenediamine with aryl aldehydes using MnO₂ nanoparticles under ultrasonic irradiation at power 55 W

| Entry | Substrate (1) | Product a (2) | M.p (°C) | Time (min) | Yield b (%) |
|-------|---------------|---------------|----------|------------|-------------|
| 1     | OHC-苯-CH₃    |               | 286-288  | 3.4        | 84          |
| 2     | OHC-苯-OCH₃   |               | 258-260  | 4.3        | 85          |
| 3     | OHC-苯      |               | 203-205  | 4.3        | 84          |
| 4     | 2H-苯-OCH₃   |               | 226-228  | 4.1        | 83          |
| 5     | OHC-苯-OCH₃  |               | 232-234  | 5          | 82          |

(Continued on next page)
Table 4: The results related to the reaction of o-phenylenediamine with aryl aldehydes using MnO$_2$ nanoparticles under ultrasonic irradiation at power 55 W (Continued)

| Entry | Substrate (1) | Product $^a$ (2) | M.p (°C) | Time (min) | Yield$^b$ (%) |
|-------|---------------|-------------------|----------|------------|---------------|
| 6     | ![Image](image1) | ![Image](image2) | 253-255  | 4          | 85            |
| 7     | ![Image](image3) | ![Image](image4) | 144-146  | 3          | 87            |
| 8     | ![Image](image5) | ![Image](image6) | 258-260  | 3.1        | 87            |
| 9     | ![Image](image7) | ![Image](image8) | 230-232  | 4.3        | 82            |
| 10    | ![Image](image9) | ![Image](image10) | 290-292  | 3.2        | 85            |
| No. | Structure | Yields (°C) | Yields (°C) | Yields (°C) |
|-----|-----------|-------------|-------------|-------------|
| 11  | ![Structure](image1) | 224-226     | 3           | 87          |
| 12  | ![Structure](image2) | 260-262     | 4           | 83          |
| 13  | ![Structure](image3) | 302-304     | 3           | 87          |
| 14  | ![Structure](image4) | 193-194     | 4           | 85          |

a) All compounds are known and their physical and spectroscopic data were in good agreement with those of authentic samples.

b) Yields refer to pure isolated products.
produced the benzimidazoles in high yield and short reaction times due to the stabilization of intermediate benzimidazoline by these substituents.

The proposed mechanism for preparation of benzimidazole using MnO₂ nanoparticles. First, the condensation of o-phenylenediamine and aryl aldehydes leads to the formation of unstable intermediate benzimidazoline with removal of a H₂O molecule. Then, the reaction proceeds in the presence of MnO₂ nanoparticles using a radical mechanism, in accordance to the a, b, c, and d steps and removal of Mn(OH)₂, the benzimidazole can be prepared (Scheme 2).

CONCLUSIONS

We described preparation and application of MnO₂ nanoparticles as a readily available, inexpensive, and efficient oxidant agent for the one-pot synthesis of benzimidazole derivatives. They were prepared by using o-phenylenediamine with various aromatic aldehydes in water/ethanol as solvent at 50 W under sonication. The advantages of this procedure are operational simplicity, high product yields, short reaction time, availability of catalyst and cost effective.

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SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher’s website.

REFERENCES

1. Zarrinmayeh, H., A. M. Nunes, P. L. Ornstein, D. M. Zimmerman, M. B. Arnold, D. A. Schober, R. F. Bruns, P. A. Hipskind, T. C. Britton, B. E. Cantrell, and D. R. Gehlert. “Synthesis and Evaluation of a Series of Novel 2-[(4-Chlorophenoxy)methyl]- benzimidazoles as Selective Neuropeptide Y Y1 Receptor Antagonists.” Journal of Medicinal Chemistry 41 (1998): 2709–19.

2. Nakano, H., T. Inoue, N. Kawasaki, H. Miyataka, H. Matsumoto, T. Taguchi, N. Inagaki, H. Nagai, and T. Satoh. “Synthesis and biological Activities of Novel Antiallergic Agents with 5-lipoxygenase Inhibiting Action.” Bioorganic & Medicinal Chemistry 8 (2000): 373–80.

3. Zhao, Z., D. O. Arnaiz, B. Griedel, S. Sakata, J. L. Dallas, M. Whitlow, L. Trinh, J. Post, A. Liang, M. M. Morrissey, and K. J. Shaw. “Design, Synthesis, and in vitro Biological Activity of Benzimidazole based Factor Xa Inhibitors” Journal of Bioorganic & Medicinal Chemistry Letters 10 (2000): 963–6.

4. White, A. W., R. Almassy, A. H. Calvert, N. J. Curtin, R. J. Griffin, Z. Hostomsky, K. Maegley, D. R. Newell, S. Srinivasan, and B. T. Golding. “Resistance-Modifying Agents.
9.1 Synthesis and Biological Properties of Benzimidazole Inhibitors of the DNA Repair Enzyme Poly(ADP-ribose) Polymerase." Journal of Medicinal Chemistry 43 (2000): 4084–97.

5. Zhu, Z. J., B. Lippa, J. C. Drach, and L. B. Townsend. “Design, Synthesis, and Biological Evaluation of Tricyclic Nucleosides (Dimensional Probes) as Analogues of Certain Antiviral Polyhalogenated Benzimidazole Ribonucleosides.” Journal of Medicinal Chemistry 43 (2000): 2430–7.

6. Huang, W., and R. M. Scarborough. “A New “Traceless” Solid-Phase Synthesis Strategy: Synthesis of Benzimidazole Library” Tetrahedron Letters 40 (1999): 2665–8.

7. Ravi, V., E. Ramu, K. Vijay, and A. Srinivas Rao. “Zn-Proline Catalyzed Selective Synthesis of 1,2-Disubstituted Benzimidazoles in Water.” Chemical and Pharmaceutical Bulletin 55 (2007): 1254–7.

8. Pätzold, F., F. Zeuner, T. Heyer, and H-J. Niclas. “Dehydrogenations Using Benzo-furoxan as Oxidant.” Synth. Communications 22 (1992): 281–8.

9. Bahrami, K., M. M. Khodaei, and I. Kavianinia “A Simple and Efficient One-Pot Synthesis of 2-Substituted Benzimidazoles.” Synthesis 4 (2007): 547–50.

10. Beaulieu, P. L., B. Hache, and E. Von Moos. “A Practical Ozone®-Mediated, High-Throughput, Solution-Phase Synthesis of Benzimidazoles from 1,2-Phenylenediamines and Aldehydes and its Application to Preparative Scale Synthesis.” Synthesis (2003): 1683–92.

11. Weidner-Wells, M. A., K. A. Ohemeng, V. N. Nguyen, S. Fraga-Spano, M. J. Macielag, H. M. Werblood, B. D. Foleno, G. C. Webb, J. F. Barrett, and D. J. Hlasta. “Amidino Benzimidazole Inhibitors of Bacterial Two-Component Systems.” Journal of Bioorganic Medicinal Chemistry Letters 11 (2001): 1545–1548.

12. Trivedi, R., S. K. De, and R. A. Gibbs. “A Convenient One-Pot Synthesis of 2-Substituted benzimidazoles.” Journal of Molecular Catalysis A: Chemistry 245 (2005): 8–11.

13. Ma, H. Q., Y. L. Wang, J. P. Li, and J. Y. Wang. “Selective Synthesis of 2-Aryl-1-aryl methyl-1H-1,3-benzimidazoles Promoted by Ionic Liquid.” Heterocycles 71 (2007): 135–40.

14. Chakrabarty, M., S. Karmakar, A. Mukherji, S. Arima, and Y. Harigaya. “Application of Sulfamic Acid as an Eco-friendly Catalyst in an Expedient Synthesis of Benzimidazoles.” Heterocycles 68 (2006): 967–74.

15. Massimo, C., E. Francesco, and M. Francesca. “Ytterbium Triflate Promoted Synthesis of Benzimidazole Derivatives.” Synletters 10 (2004): 1832–5.

16. Liu, X. W., X. S. Wang, X. W. Guo, G. Li, and H. S. Yan. “Regeneration of Lamina TS-1 Catalyst in the Epoxidation of Propylene with Hydrogen Peroxide” Catalysis Letters 97 (2004): 223–9.

17. Sharghi, H., M. Hosseini-Sarvari, and F. Moeini. “Copper-Catalyzed One-Pot Synthesis of Benzimidazole Derivatives” Canadian Journal of Chemistry 86 (2008): 1044–50.

18. Nagawade, R. R. and D. B. Shinde. “Zirconyl(IV) Chloride-Promoted Synthesis of Benzimidazole Derivatives” Russian Journal of Organic Chemistry 42 (2006): 453–4.

19. Chang, L., H. N. Sasirekha, and Y. W. Chen. “Au/MnO 2–TiO 2 Catalyst for Preferential oxidation of Carbon Monoxide in Hydrogen Stream.” Catalysis Communications 8 (2007): 1702–10.
20. Li, J. T., Y. W. Li, Y. L. Song, and G. F. Chen. “Improved Synthesis of 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) Derivatives Catalyzed by Urea under Ultrasound.” Ultrasonic Sonochemistry 19 (2012): 1–4.

21. Kowsari, E., M. Mallakmohammadi. “Ultrasound Promoted Synthesis of Quinolines using Basic Ionic Liquids in Aqueous Media as a Green Procedure” Ultrasonic Sonochemistry 18 (2011): 447–54.

22. Ghahereanzadeh, R., F. Fereshtehnejad, P. Mirzaei, and A. Bazgir. “Ultrasound-assisted Synthesis of 2,2’-(2-oxindoline-3,3-diyl)bis(1H-indene-1,3(2H)-dione) Derivatives.” Ultrasonic Sonochemistry 18 (2011): 415–8.

23. He, J. Y., H. X. Xin, H. Yan, X. Q. Song, and R. G. Zhong. “Convenient Ultrasound-Mediated Synthesis of 1,4-diazabutadienes under Solvent-Free Conditions.” Ultrasonic Sonochemistry 18 (2011): 466–9.

24. Li, J. T., Y. Yin, and M. X. Sun. “An Efficient One-Pot Synthesis of 2,3-epoxy-1,3-diaryl-1-Propanone Directly from Acetophenones and Aromatic Aldehydes under Ultrasound irradiation.” Ultrasonic Sonochemistry 17 (2010): 363–6.

25. Nagawade, R. R. and D. B. Shinde. “BF$_3$.OEt$_2$ Promoted Solvent Free Synthesis of Benzimidazole Derivatives” Chinese Chemical Letters 17 (2006): 453–6.

26. Xiangming, H., M. Huiqiang, and W. Yulu. “p-TsOH Catalyzed Synthesis of 2-arylsubstituted Benzimidazoles.” Arkivoc 13 (2007): 150–4.

27. Montanari, F. and R. Passerini. “Richerche Sugli Eterociclici: Spettri di Assorbimento UV e Proprietà Cromoforiche - Nota 1: Imidazoli, Benzimidazoli e Fenil-Benzimidazoli.” Bulletin Science Chimiques Industrial Bologna, 11 (1953): 42–9.

28. Navarrete-Vazquez, G., H. Moreno-Diaz, F. Aguirre-Crespo, I. Leon-Rivera, R. Villalobs-Molina, O. Munoz-Munizd, and S. Estrada-Sotoa. “Design, Microwave-Assisted Synthesis, and Spasmolytic Activity of 2-(alkyloxyaryl)-1H-Benzimidazole Derivatives as Constrained Stilbene Bioisosteres.” Bioorganic & Medicinal Chemistry Letters. 16 (2006): 4169–73.

29. Adharvana Chari, M., D. Shobha, and T. Sasaki, T. “Room Temperature Synthesis of Benzimidazole Derivatives Using Reusable Cobalt Hydroxide (II) and Cobalt Oxide (II) as Efficient Solid Catalysts.” Tetrahedron Letters 52 (2011): 5575–80.

30. Tavman, A., A. Birteksoz, and F. Oksuzomer. “Spectral and Thermal Characterization and Antimicrobial Effect of 3-(5-H/Me/Cl/NO2-1H-benzimidazol-2-yl)-benzene-1,2-diols and Some Transition Metal Complexes.” African Journal of Chemistry 65 (2012): 150–5.

31. Behbahani, F. K. and P. Ziaei. “One-Pot Synthesis of 2-substituted Benzimidazoles Catalyzed by Anhydrous FePO$_4$.” Chemical Heterocyclic Compounds 48 (2012): 1011–7.

32. Nagawade, R. and D. B. Shinde. “TiCl$_4$ Promoted Synthesis of Benzimidazole Derivatives.” Indian Journal of Chemistry 46 (2007): 349–51.

33. Ramana, D. V., E. Kantharaj “Synthesis of 2-substituted Benzoaxes and Benzimidazoles based on Mass Spectral Ortho Interactions” Journal of the Chemical Society, Perkin Transaction 2 (1995): 1497–501.

34. Yuan, A., X. Wang, Y. Wang, and J. Hu. “Comparison of Nano-MnO$_2$ Derived from Different Manganese Sources and Influence of Active Material Weight Ratio on Performance of Nano-MnO2/Activated Carbon Supercapacitor.” Energy Conservation Management 51 (2010): 2588–94.

35. Ananth, M. V., S. Pethkar, and K. Dakshinamurthi. “Distortion of MnO$_6$ Octahedra and Electrochemical Activity of Nstutite-based MnO$_2$ Polymorphs for Alkaline Electrolytes—An FTIR Study.” Journal of Power Sources 75 (1998): 278–82.
36. Walanda, D. K., G. A. Lawrance, and S. W. Donne “Hydrothermal MnO2: Synthesis, Structure, Morphology and Discharge Performance.” Journal of Power Sources 139 (2005): 325–41.

37. Cullity, B. D. Elements of X-Ray Diffraction. vol. 1. (New York: Addison-Wesley, 1978).

38. Suslick, K. S. “Sonochemistry.” Science, 247 (1990): 1439–45.

39. Mason, T. J. “Ultrasound in Synthetic Organic Chemistry.” Chemical Society Reviews, 26 (1997): 443–51.

40. Cravotto, G. and P. Cintas. “Power Ultrasound in Organic Synthesis: Moving Cavitational Chemistry from Academia to Innovative and Large-Scale Applications.” Chemical Society Reviews, 35 (2006): 180–96.

41. Das Sharma S. and D Konwar. “Practical, Ecofriendly, and Chemoselective Method for the Synthesis of 2-Aryl-1-arylmethyl-1H-benzimidazoles Using Amberlite IR-120 as a Reusable Heterogeneous Catalyst in Aqueous Media” Synth. Commun. 39 (2009): 980–991.