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Synthesis and Characterization of Some New 4-Methyl-5-Imidazole Carbaldehyde Derivatives

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Abstract: Imidazole is a common and important heterocyclic fragment of many biologically important molecules. 5-imidazole-carbaldehydes containing mono- (N-1) methyl (or aryl) analogs are commonly used as building blocks in medical chemistry. In this study, starting from 4-methyl-1H-imidazole-5-carbaldehyde, the N-1 atom of the imidazole ring is derived with different alkyl groups. In addition, both N atoms of the starting imidazole-carbaldehyde were methylated to give 5-carbaldehyde-1,3,4-trimethyl-3-imidazolium salt. The salt which possess quite reactive carbaldehyde group could be used as a precursor for synthesis of other imidazolium derivatives. Furthermore, 4-methyl-5-imidazole carbaldehyde was converted into the benzoxazole, benzothiazole and benzoimidazole by a two-step reaction over the aldehyde group. These new compounds could display some biological activities.

Keywords: Imidazole, imidazolium derivatives, biologically active imidazole.

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INTRODUCTION

Imidazole ring is one of the most basic groups of biologically important compounds. Many biologically active compounds containing the imidazole ring have been synthesized. Imidazole derivatives are used for the development of antifungal, antibacterial, anticancer, and antimalarial drugs. Until now, many drug and drug candidate isomers, containing imidazole and mono-N-alkylated imidazole rings, have been synthesized. For example, ipronidazole is a drug developed as an anti-protozoal agent (1). Nimorazole, a heterocyclic N-alkyl substituted compound, is an effective antimicrobial drug in parasites of the genus trichomonas, synthesized in 1970 (2). The imidazole derivative known under the trade name of moxnidazole is an antimicrobial drug acting with trichomonas parasites.

Another imidazole derivative that is effective against the Trichomonas parasites is flunidazole (3-6). Imidazole derivatives also have been used in the development of drugs for the treatment of ulcers. For example, the imidazole derivative known as Cimetidine is a highly effective drug in the treatment of ulcers (7). Highly complex imidazole-based drugs containing the imidazole group have also been developed. For example, the imidazole derivative known as dazadrol, is used as an anti-depressant (8). The drug called cimicoxib, which exhibits anti-inflammatory properties, is also an imidazole derivative (9). The imidazole derivative, Cipralisant, synthesized in recent years, has been found to be effective in attention deficit syndrome on animal studies. This compound is probably thought to be good for Alzheimer's disease (10-12). Imidazolium derivatives have begun to work in recent years. James H. Davis, Jr. et al. synthesized the first biologically active ionic liquid crystalline imidazolium cation starting from miconazole which exhibit antifungal properties (13). Azami et al. have synthesized many 1,3-dialkyl imidazolium derivatives and some of these compounds have antibacterial properties (14). In another study, imidazolium derivatives containing long alkyl chains on the N atom were synthesized and these compounds were found to have quite good antimicrobial activity on gram-negative, gram-positive bacteria and fungi (15). Donald D. Ourth et al. isolated and elucidated its structure of 1,3-methylimidazolium derivatives which occurred naturally; this compound showed a broad-spectrum antiviral properties for insects. This compound also contemplated that can be used in HIV-1 and HSV viruses seen in humans (16-18). Jadwiga Zabielska-Matejuk et al. have synthesized several 1,3-dialkyimidazolium derivatives and studied their antifungal properties to protect wood materials. The synthesized imidazolium salts have been found to inhibit the growth of fungus, in particular *Sclerophoma pityophila* (19-27).

5-Imidazole-carbaldehyde and its mono- (N-1) alkyl or aryl analogs are often used in medicine as drug building blocks, but their dialkyl (N-1 and N-3) analogs are less visible in the literature. In this work, new imidazole derivatives were synthesized from 4-methyl-5-imidazole carbaldehyde by alkylation of N atom or condensation of carbonyl group with appropriate reagents.

EXPERIMENTAL

General

The starting chemicals were commercially purchased from Merck, Aldrich, Acros Organics, and ABCR.

The ^{1}H NMR spectra were recorded on Bruker 400 MHz spectrometers for samples in DMSO and $CDCl_3$. The signals are expressed as parts per million down fields from $(CH_3)_4Si$, used as an internal standard. IR spectra were measured using a Jasco FT-IR-300E spectrometer. Electrospray ionization mass spectra were obtained in positive ion mode on a AB SCIEX LC - MS/MS spectrometer. Column chromatographic isolation was performed on Merck Kieselgel 60 (70-230 mesh) using ethyl acetate and n-hexane as the eluent. An analytical thin-layer chromatography was performed on Merck pre-coated silica gel 60 GF-254 with 0.25-mm thick TLC plates.

1,4-dimethyl-imidazole-5-carbaldehyde (1)

NaH (60%, 2.179 g, 0.0908 mol) in dry THF (120 mL) was added to 4-methyl-5-imidazole carbaldehyde (5 g, 0.0454 mol) at room temperature for 30 min. Methyl iodide (5.65 mL, 0.0908 mol) was then added and mixed at room temperature for 20 hours. As a result of the reaction, the mixture had solid and liquid phases. The THF phase was isolated, then the solid phase was washed several times with $CHCl_3$, then the organic phases were combined. The remaining precipitate was dissolved in water and extracted again with $CHCl_3$. Then all the organic phases were combined and the solvent was evaporated. The resulting brownish-yellow oily substance was purified by column chromatography using ethyl acetate over silica gel. Isomer **1** was obtained as a yellow oily solid (3.32 g, 59%). ^{1}H NMR (400 MHz, DMSO): d_H 2.46 (3H, s, CH_3), 3.60 (3H, s, CH_3), 7.73 (1H, s, imidazole C-H), 9.76 (1H, s, CHO).

1-Benzyl-4-methyl-imidazole-5-carbaldehyde (2)

4-Methyl-5-imidazole carbaldehyde (1 g, 9.08 mmol) was treated with NaH (60%, 720 mg, 18.16 mmol) in dry DMF (120 mL) at room temperature for 5 min. Benzyl chloride (1.36

mL, 11.8 mmol) was then added and mixed at room temperature for 20 h. After that saturated sodium carbonate solution (25 mL) was added to the mixture, extracted by addition of 30 mL of water and extraction with ethyl acetate (3 x 30 mL). The combined extracts were filtered after being dried over sodium sulfate. The solvent was removed on the rotary evaporator. The resulting brownish-yellow oily substance was purified by column chromatography using ethyl acetate over silica gel. Yellow oily solid (0.76 g, 42%). Mixture of isomers **2a** and **2b** ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.30 (3H, s, CH_3), 2.38 (3H, s, CH_3), 4.41 (2H, s, N-CH_2), 4.67 (2H, s, N-CH_2), 7.30-7.62 (10H, m, Ar-H), 9.79 (1H, s, CHO), 9.83 (1H, s, CHO).

1-(2-phenylethyl)-4-methyl-imidazole-5-carbaldehyde (3)

4-Methyl-5-imidazole carbaldehyde (0.5 g, 4.5 mmol) was treated with NaH (60%, 220 mg, 5.5 mmol) in dry DMF (120 mL) at room temperature for 5 min. It was allowed to mix. 2-Phenylethylbromide (0.7 mL, 5 mmol) was then added and mixed at room temperature for 20 h. Saturated sodium carbonate solution (25 mL) was then added to the mixture, extracted by addition of 25 mL of water and extraction with ethyl acetate (2 x V). The combined extracts were filtered after being dried over sodium sulfate. The solvent was removed on the rotary evaporator. The resulting brownish-yellow oily substance was purified by column chromatography eluting with ethyl acetate over silica gel. It was seen from the ^{1}H NMR spectrum that this compound was an isomeric mixture in approximately equal proportions. Yellow oily solid (0.48 g, 49%). Mixture of isomers **3a** and **3b** ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.27 (3H, s, CH_3), 2.41 (3H, s, CH_3), 2.93 (2x2H, t, 2xCH_2),4.05 (2H, t, N-CH_2), 4.40 (2H, t, N-CH_2), 6.94-7.25 (10H, m, Ar-H), 9.82 (1H, s, CHO), 9.85 (1H, s, CHO). IR (ATR, v/cm^{-1}): 3127, 2923-2852, 1662, 1610. ESI-MS: m/z = 215 (**M**)$^+$; Calcd. for $C_{13}H_{14}N_2O$:214.11.

1-(2-Chlorobenzyl)-4-methyl-imidazole-5-carbaldehyde (4)

4-Methyl-5-imidazole carbaldehyde (1 g, 9 mmol) was treated with NaH (60%, 720 mg, 18 mmol) in dry DMF (120 mL) at room temperature for 5 min. It was allowed to mix. 2-chlorobenzyl bromide (1.53 mL, 10 mmol) was then added and mixed at room temperature for 1 day. Saturated sodium carbonate solution (25 mL) was then added to the mixture extracted by the addition of about 25-30 mL of water and extraction with ethyl acetate (3 x 40 mL). The combined extracts were filtered after being dried over sodium sulfate. The solvent was removed on the rotary evaporator. The resulting brown-yellow oily substance was purified by column chromatography eluting with ethyl acetate over silica gel. Yellow oily solid was observed as a mixture of products in ^{1}H NMR (0.82 g, 39%).
Main product **4a** (%85): ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.42 (3H, s, CH_3), 5.48 (2H, s, CH_2), 6.90-7.48 (5H, m, Ar-H), 9.73 (1H, s, CHO).
By-product **4b** (%15): ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.37 (3H, s, CH_3), 4.66 (2H, s, CH_2), 6.90-7.48 (5H, m, Ar-H), 9.85 (1H, s, CHO). IR (ATR, v/cm^{-1}): 3111, 2851, 1661, 1543. ESI-MS : m/z = 235(**M**)$^+$; Calc. for $C_{12}H_{11}ClN_2O$:234.05.

1-(3-Chlorobenzyl)-4-methyl-imidazole-5-carbaldehyde (5)

4-Methyl-5-imidazole carbaldehyde (1 g, 9 mmol) was treated with NaH (60%, 720 mg, 18 mmol) in dry DMF (120 mL) at room temperature for 5 min. It was allowed to mix. 3-Chlorobenzyl bromide (1.4 mL, 10 mmol) was then added and mixed at room temperature for 1 day. Saturated sodium carbonate solution (25 mL) was then added to the mixture extracted by addition of 25 mL of water and extraction with ethyl acetate (3 x 40 mL). The combined extracts were filtered after being dried over sodium sulfate. Solvent was removed on the rotary evaporator. The resulting oily substance was purified by column chromatography eluting with ethyl acetate over silica gel. Yellow oily solid (0.71 g, 33%). It was found from the ^{1}H NMR results that the material was isolated as an isomeric mixture.
Main product **5a** (%71): ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.43 (3H, s, CH_3), 5.36 (2H, s, CH_2), 6.98-7.54 (5H, m, Ar-H), 9.74 (1H, s, CHO).
By-product **5b** (%29): ^{1}H NMR (400 MHz, $CDCl_3$): d_H 2.34 (3H, s, CH_3), 4.95 (2H, s, CH_2), 6.98-7.54 (5H, m, Ar-H), 9.88 (1H, s, CHO). IR (ATR, v/cm^{-1}): 3088, 2936, 2841, 1659, 1598. ESI-MS : m/z = 235(**M**)$^+$; Calc. for $C_{12}H_{11}ClN_2O$:234.05.

5-formyl-1,3,4-trimethyl-imidazolium tetrafluoroborate (6)

1,4-dimethyl-1H-imidazole-5-carbaldehyde (1 g, 8.77 mmol) and trimethyloxonium tetrafluoroborate (1.55 g, 0.0105 mol) were stirred in dry ethyl acetate (15 mL) for 2 hours at room temperature. The solvent was removed on the rotary evaporator. Due to the fact that the product is highly polar, the organic phase could not be extracted and also could not be purified by chromatography. The mixture was further left to rinse in a mixture of ethanol and chloroform. ^{1}H NMR analysis was performed on pure white crystals and the expected product was observed to be formed. ^{1}H NMR (400 MHz, DMSO): d_H 2.59 (3H, s, CH_3), 3.79 (3H, s, N-CH_3), 4.00 (3H, s, N-CH_3), 9.14 (1H, s, imidazolium C-H), 9.94 (1H, s, CHO).

2-((4-methyl-1H-imidazole-5-yl)methyleneamino)phenol (8)

4-methyl-1H-imidazole-5-carbaldehyde (1 g, 9.082 mmol), 2-aminophenol (0.99 g, 9.082 mmol) was refluxed in 95% EtOH for 1 day. The reaction mixture was allowed to crystallize with EtOH. A light yellow solid 4.3.1 (0.81 g, 44%) was obtained. Compound **8** was found to have very little impurity from the ^{1}H NMR spectrum. ^{1}H NMR (400 MHz, DMSO): d_H 2.38 (3H, s, CH_3), 6.8-7.07 (4H, m, Ar-H), 7.45 (1H, s, N=C-H), 7.83 (1H, s, imidazole C-H), 8.73 (1H, s, Ar-OH), 12.61 (1H, broad s, N-H).

2-((4-methyl-1H-imidazole-5-yl)methyleneamino)benzenethiol (9)

4-Methyl-5-imidazole carbaldehyde (1 g, 9.082 mmol) and 2-aminothiophenol (1.137 g, 9.082 mmol) were refluxed in EtOH (20 mL) for 1 hour. The reaction was followed by TLC (50% EtOAc / n-Hexane) .The reaction was continued until the starting material was finished in the TLC. When the reaction mixture was allowed to cool, it was immediately observed that light cream crystals began to form. A quantity of the obtained solid light cream matter (1.494 g) was observed to be **12** by 1 H NMR analysis **9** as well as part of the material being converted to ring closure reaction. It was detected from the ^{1}H NMR spectrum that the ratio of **9** to **12** was 79:21.

Main product **9** (%79): ^{1}H NMR (400 MHz, DMSO): d_H 2.16 (3H, s, CH_3), 3.38 (1H, s, SH), 6.48-6.59 (3H, m, Ar-H), 6.61-6.97 (2H, m, Ar-H), 7.45 (1H, s, imidazole C-H), 8.02 (1H, s, N=C-H), 11.93 (1H, broad s, N-H).

By-product **12** (%21): ^{1}H NMR (400 MHz, DMSO): d_H 2.66 (3H,s, CH_3), 7.34-7.48 (2H, d.t., 2xAr-H), 7.70 (1H, s, imidazole C-H), 7.90- 8.04 (2H, d.d., 2xAr-H), 12.56 (1H, broad s, N-H).

2-((4-methyl-1H-imidazole-5-yl)methyleneamino)aniline (10)

1-2-diaminobenzene (1.178 g, 10.9 mmol) with 4-methyl-5-imidazolecarbaldehyde (1 g, 9.082 mmol) was refluxed in 20 mL EtOH for 1 day. The reaction was extracted by TLC (20% EtOH, EtOAc), the product was observed to be lower in TLC as it was more polar than imidazole. The solvent was removed and the remaining mixture was purified by flash column chromatography on silica gel using n-hexane, ethyl acetate and EtOH. (The solvent polarity for the separation was 20% acetate-n-hexane and the temperature was increased to 50% EtOH / EtOAc mixture). The fractions of the product were collected and the solvent was removed to give the target compound **10** as a light brown solid (1.66 g, 90%).

It was determined that there is an isomeric mixture of **10** from ^{1}H NMR spectrum. The isomeric mixture may possibly be an E/Z mixture around -N=CH-. The isomeric ratios were found to be 63% for the main isomer and 37% for the other isomer. ^{1}H NMR (400 MHz, DMSO): d_H 2.56 (3H, s, CH_3), 2.65 (3H, s, CH_3), 7.10-7.59 (8H, m, Ar-H), 7.48 (1H, s, imidazole C-H), 7.71 (1H, s, imidazole C-H), 7.82 (2H, s, N=C-H), 12.25 (2H, broad s, N-H).

2-(4-methyl-1H-imidazole-5-yl)benzo[d]oxazole (11)

2-((4-methyl-1H-imidazol-5-yl)methyleneamino)phenol **(8)** (0.6 g, 2.28 mmol) and lead tetraacetate (1.32 g, 2.98 mmol) were dissolved in acetic acid (12 mL) at 45-50 ^{0}C for 24 hours. The reaction was monitored by TLC (25% EtOH / EtOAc); TLC was observed to walk faster because it is less polar than the starting material of the product. The reaction mixture was basified in ice bath with about 20 mL of 10% NaOH. The organic extracts were extracted with chloroform and the organic phase was dried over sodium sulfate. The mixture was separated by column chromatography on silica gel using n-hexane,

ethyl acetate, and EtOH. (The solvent polarity for the separation was 5% ethyl acetate-n-hexane and eluted to 25% EtOH / EtOAc mixture). Compound **11** was isolated as a pale yellow solid (0.41 g, 69%). ^{1}H NMR (400 MHz, DMSO): d_H 2.63 (3H,s, CH_3), 7.35 (2H, m, 2xAr-H), 7.72 (2H, m, 2xAr-H), 7.83 (1H, s, imidazole C-H). IR (ATR, v/cm^{-1}): 3379, 1642. ESI-MS : m/z = 200(**M**)$^+$; Calcd. for $C_{11}H_9N_3O$:199.07.

2-(4-methyl-1H-imidazole-5-yl)benzo[d]thiazole (12)

Compound **9** (0.6 g, 2.764 mmol) and lead tetraacetate (1.2 g, 2.764 mmol) were stirred in acetic acid (10 mL) at 45-50 °C for 1 day. After termination of the reaction, the mixture was basified in ice bath with about 20 mL of NaOH. The organic material was extracted with chloroform and the organic phase was dried over sodium sulfate. The solvent was removed and the residue was chromatographed on silica gel in a mixture of ethyl acetate-n-hexane (1: 1). Compound **12** was obtained as a yellow solid (0.348 g, 30%). ^{1}H NMR (400 MHz, DMSO): d_H 2.66 (3H,s, CH_3), 7.33-7.48 (2H, d.t., 2xAr-H), 7.71 (1H, s, imidazole C-H), 7.91- 8.05 (2H, d.d., 2xAr-H), 12.58 (1H, broad s, N-H). IR (ATR, v/cm^{-1}): 3054, 3015, 2937-2838-2711, 1603. ESI-MS : m/z = 216(**M**)$^+$; Calc. for $C_{11}H_9N_3S$:215.05.

2-(4-methyl-1H-imidazole-5-yl)-1H-benzimidazole (13)

2-((4-methyl-1H-imidazole-5-yl)methyleneamino)aniline **(10)** (1.1281 g, 5.63 mmol) and lead acetate (2.49 g, 5.63 mol) in glacial acetic acid (20 mL) was added for 24 hours at 35-40 ^{0}C. It was basified with 10% NaOH. Extraction with chloroform was performed. (3xV) and the organic phase was dried over sodium sulfate. Crystallization yielded **13** as a light yellow solid (0.66 g, 59%). ^{1}H NMR (400 MHz, DMSO): d_H 2.55 (3H,s, CH_3), 7.14 (2H, m, 2xAr-H), 7.39 (1H, s), 7.58 (2H, m, 2xAr-H), 7.80 (1H, s, imidazole C-H), 12.45 (1H, broad s, N-H).
IR (ATR, v/cm^{-1}): 3127, 2922, 2852, 1606. ESI-MS : 293.1(**M**)$^+$; Calc. for $C_{11}H_{10}N_4$:198.09.

RESULTS AND DISCUSSION

The alkylation reaction of 4-methyl-5-imidazole carbaldehyde is shown in Figure 1. The acidic N-H hydrogen in the imidazole ring was first ionized with strong base NaH and then converted to the corresponding primary alkyl halides (N-alkylation) by reaction with the S_N2 type reaction.

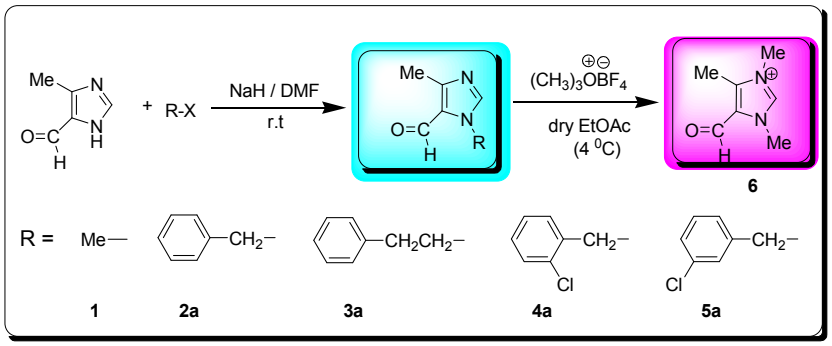

Figure 1. The alkylation reaction of 4-methyl-5-imidazole carbaldehyde.

An isomeric mixture or polyalkylation can be expected because of the presence of two N atoms on the imidazole ring. As a result of the reaction with Me-I, very pure N-methylated imidazole derivative was obtained. ^{1}H-NMR analyses showed that there was only one isomer **1** for this compound. In the Me-I reaction, although more than two equivalents of Me-I was taken, multiple alkylation has not been detected.

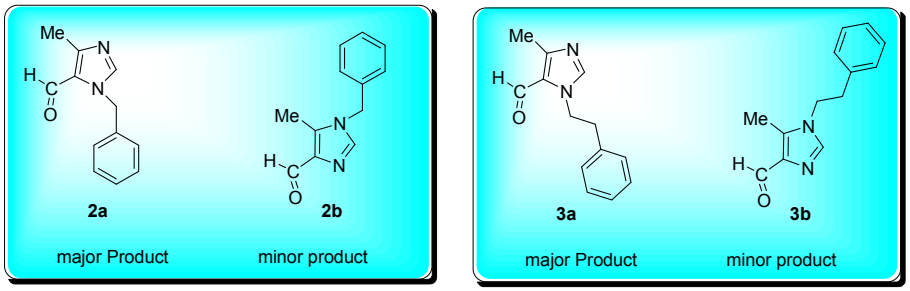

Figure 2. Isomeric mixtures of **2a**, **2b** and **3a**,**3b**.

The second reaction of this section is the reaction with benzyl chloride ($PhCH_2Cl$). Among the alkyl halides used, only benzyl chloride is less reactive than the others (other alkyl halides are alkyl bromides and iodides). From the benzyl chloride reaction, the product was impure and is also an isomeric mixture. However, when the alkylation reaction was carried out with sterically more hindered alkyl group, such as 2-phenylethyl bromide, isomeric mixture (**3a** and **3b)** were obtained (Figure 2). The ^{1}H-NMR analysis showed that the isomeric mixture almost in the vicinity of 50:50. When alkylation reactions was carried out with 2-chlorobenzyl bromide or 3-chlorobenzyl bromide, which are structurally very similar with benzyl chloride, the reaction proceeded smoothly and expected products (**4a** and **5a**) were obtained. In all alkylation reactions, except Me-I, the product was obtained both as a low yield and as an isomeric mixture; for instance, the alkylation reaction of 4-methyl-5-imidazole carbaldehyde with 2-chlorobenzyl bromide or 3-chlorobenzyl bromide gave about 30% yield and the products were isomeric mixture (**4a** / **4b** and **5a** / **5b**). But from the similar reaction with Me-I, only one isomer with higher yield (60%) was obtained.

The isomeric mixtures of **4a** and **4b** or **5a** and **5b**, could not be separated completely by column chromatography (Figure 3). ^{1}H NMR analysis indicated that the major isomer was **4a** and the minor isomer was **4b** and the ratio of the two isomers was 85:15. Similar way, the H NMR spectroscopy showed that the **5a** is major and the **5b** is minor and isomer ratio is 71/29. It is not surprising that, although the isomeric mixture is not observed in the reaction with MeI, the alkyl halides with a large R group causes isomerization. This can be attributed to the steric effect of the carbaldehyde group adjacent to the N-H group.

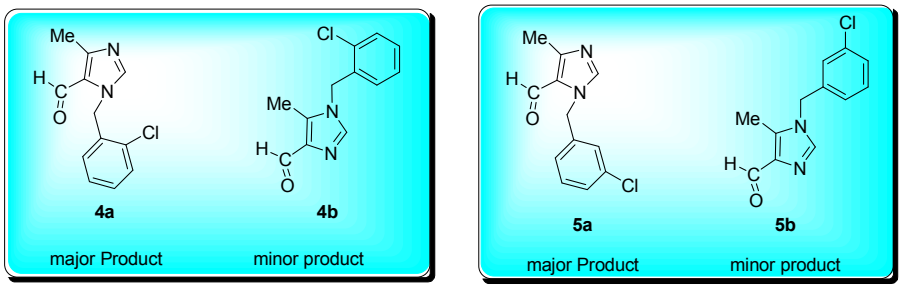

Figure 3. Isomeric mixtures of **4a**, **4b** and **5a**,**5b**.

4-Methyl-5-imidazole carbaldehydes (N-R) were tried to convert to their imidazolium salts using $(CH_3)_3O^+BF_4^-$, from this reaction only N-Me isomer **1** gave desired imidazolium salt **6**, but other isomers (N-R) for example **5a** could not converted to **7**(figure 4).

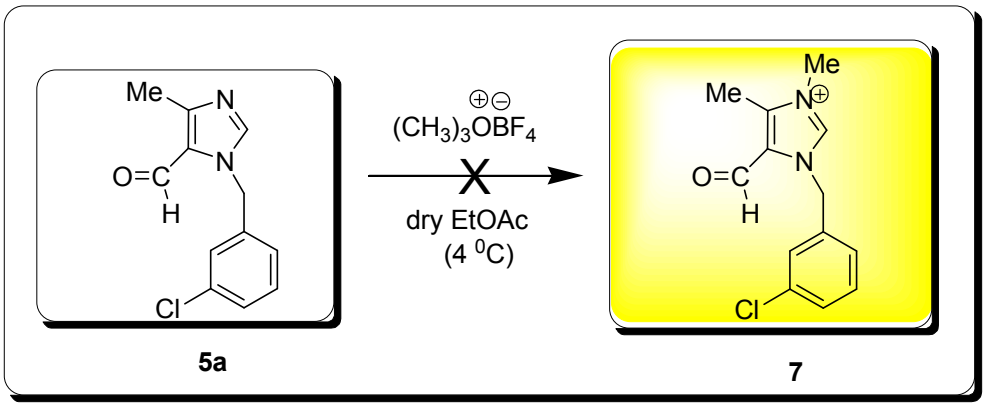

Figure 4. Unsuccessful synthesis of compound **7**.

Synthesis of benzoxazole, benzothiazole and benzimidazole derivatives from 4-methyl-5-imidazole carbaldehyde

In the literature, benzoxazole, benzothiazole and benzimidazole derivatives were synthesized from less reactive carbonyl compounds with 2-aminophenol, 2-aminobenzenethiol and 1,2-diaminobenzene etc via two step Schiff base reaction and their antimicrobial effects were investigated (28-32). Therefore, it was thought that the basic starting material used in this study, 4-methyl-5-imidazole carbaldehyde, could react with 2-aminophenol, 2-aminobenzenethiol, and 1,2-diaminobenzene. Thus, synthesis of benzoxazole, benzothiazole and benzimidazole derivatives containing imidazole rings has been tried to synthesize by a two-step reaction as shown in Figure 5. The intermediate products (**8**, **9** and **10**), obtained as a result of the first step shown in Figure 5, were isolated as an isomeric mixture or with some impurities (analyzed by ^{1}H NMR spectroscopy). The isomerization (cis / trans isomers) may be derived from the -N=CH- double bond. Further reaction of the intermediates gave new benzoxazole, benzothiazole and benzimidazoles (**11**, **12** and **13**) as pure compounds.

In addition, compounds 1, 2, 12 and 13 were synthesized by different methods from the literature (33-35).

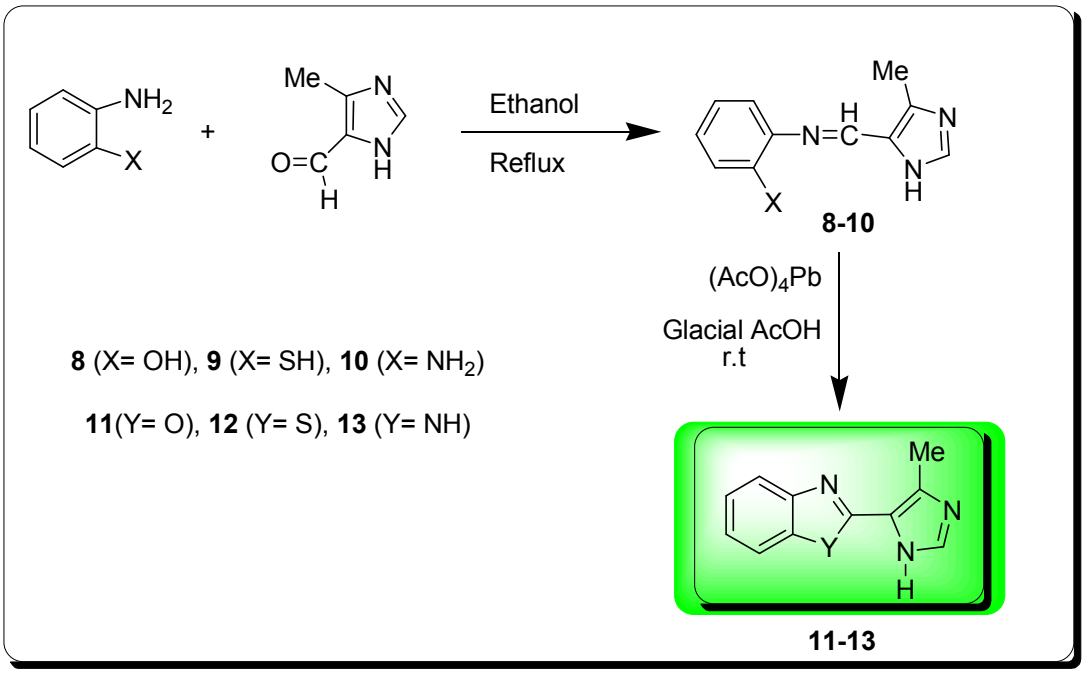

Figure 5. Synthesis of benzoxazole, benzothiazole and benzimidazole derivativescontaining imidazole ring.

CONCLUSIONS

In this work, the N-1 atom on the imidazole ring of the starting 4-methyl-1H-imidazole-5-carbaldehyde were derivatized with different alkyl groups. In addition, both N atoms of the starting imidazole-carbaldehyde were methylated to give 5-carbaldehyde-1,3,4-trimethyl-3-imidazolium salt. The salt which possess quite reactive carbaldehyde group could be used for synthesis of other imidazolium derivatives. Furthermore, 4-methyl-5-imidazole carbaldehyde was converted into the benzoxazole, benzothiazole and benzimidazoles by a two-step reaction over the aldehyde group. These new compounds could display some biological activities.

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