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# PHASE TRANSFER CATALYST: SYNTHESIS OF SOME NOVEL BIOLOGICAL ACTIVE SUBSTITUTED IMIDAZOLE DERIVATIVES

**Vijay V Dabholkar* and Bharat M Parmar**

*Organic Research Laboratory, Department of Chemistry,*
*K C College, Churchgate, Mumbai-400 020.*
E-mail: bparmar1976@rediffmail.com
vijaydabholkar@gmail.com

**Abstract:**

Effect of the phase transfer catalyst for improving yield of the compounds (E)1-substituted benzoyl-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1,3-imidazole **3 (a-e)** or (E)1-substituted benzoyl-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole **4 (a-e)** by reacting compound (E)1*H*-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1, 3-imidazole **1** or compound (E)1*H*-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole **2** with substituted benzoyl chloride in presence of Tetra butyl ammonium bromide (TBAB) were studied and compared with the yield obtained without using TBAB. Structure of synthesized compounds have been elucidated on the basis of the elemental analysis and spectral data.

**Introduction:**

Synthesis of substituted heterocyclic compounds from readily available reagent by simple and efficient methods are the major requirements of heterocyclic chemistry. A survey of the pertinent literature reveals that, substituted imidazoles possess diverse biological activities aprt from their synthetic interest[1-3]. They are reported to exhibit pharmacological activities such as antirheumatoid arthritis[4], anti tuberculosis[5], anti HIV[6], anti epileptic[7], anti cancer[8,9].

Substituted imidazole have attracted much attention due to their bactericidal[10] fungicidal[11], Plant growth regulating[12], antiviral[13], antibacterial[14], antihypertensive[15] fungicides[16], herbicides[17] and used as selective angiostenine II recepter antagonists[18]. Some of the best selling therapies today contain this versatile heterocycles in their core structures. Therefore it is difficult to underestimate the importance of imidazoles in the pharmaceutical industry. Structurally, imidazole shows all the typical properties of an aromatic ring system.

On the basis of the above observations, we have sought to synthesize novel substituted imidazoles by using phase transfer catalyst for the enhancement of the yield.

**Discussion:**

In the view of above facts we report here in the preparation of a new series of compounds bearing imidazole moiety. 2-butyl-5- chloro-4-formaldehyde-1,3 imidazole when stirred with triphenyl phosporonium salt of ethyl propionate at room temperature in presence of isopropyl acetate for 2 hrs give the product (E)1*H*-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1, 3-imidazole **1**. Compound **1** when refluxed with sodium methoxide in methanol for 3-4 hrs give compound (E)1*H*-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole **2.** Reaction of **1** with substituted benzoyl chloride in presence of triethyl amine as a base in toluene/ pyridine as solvent gives (E)1-substituted benzoyl-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1,3-

imidazole **3 (a-e).** Compounds **3 (a-e)** are also prepared by reacting (E)1*H*-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1,3-imidazole **1** with substituted benzoyl chloride in presence of sodium hydroxide as a base and Tetra butyl ammonium bromide as phase transfer catalyst in methylene chloride to give higher yields then previous method. The reaction of compound (E)1*H*-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole **2** with substituted benzoyl chloride in presence of triethyl amine as a base in toluene/ pyridine as solvent gives compounds (E)1-substituted benzoyl-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole **4 (a-e).** Compounds **4 (a-e)** are also prepared by reacting compound **2** with substituted benzoyl chloride in presence of sodium hydroxide as a base and Tetra butyl ammonium bromide as phase transfer catalyst in methylene chloride to give higher yields then previous method. Isolation of both compounds **3 (a-e)** and **4 (a-e)** were carried out by column chromatography using Ethyl acetate: n-Hexane (5:95) solvent mixture. The biological activities were studied on preliminary stage.

**Antibacterial activities**

The antibacterial activity was determined in vitro by filter paper disc diffusion method[19,20] by measuring inhibition zone in mm. All the tested compounds with standard drug were screened for antibacterial activity against bacterial strain at concentration of 250µg/ml. Nutrient agar was used as culture medium. Some of compounds exhibited antibacterial activity.

**Experimental:**

IR spectra (KBr in $cm^{-1}$) were recorded on Perkin-Elmer spectrum One FTIR spectrophotometer in the range of 4000-400 $cm^{-1}$. Melting points of all the compounds were determined in soft glass open capillaries on an electrothermal apparatus and are uncorrected. $^1H$ NMR spectra as well as $^{13}C$ NMR were recorded on JEOL AL 400 FT NMR spectrophotometer using DMSO-$d_6$ as solvent and TMS as an internal standard (chemical shifts in δ ppm). Mass spectra were recorded on 1100 series LC/MSD trap, Agilent. The substiuted benzoyl chlorides were prepared according to the literature procedure[21,22]. Ammonium acetate, Wittig reagent i.e. triphenyl phosporonium salt of ethyl-2-propionate were used of Aldrich make**.** 2-butyl-5- chloro-4-formaldehyde-1,3 imidazole were used as per literature procedure[23]**.**

**(E) 1*H*-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1, 3-imidazole 1**

Compound 2-butyl-5- chloro-4-formaldehyde-1,3 imidazole (2.0 gms, 0.0107 mole) and tri phenyl phosphoronium salt of ethyl 2- propionate (4.1 gms, 0.0107 mole) in 25 ml iso propyl acetate stirred for 2 hrs. Reaction was monitored on TLC using mobile phase ethyl acetate: n-Hexane (3:7). After the completion of reaction, the reaction mass concentrated under vacuum at 60-70°C and purified by column chromatography using ethylacetate: n-Hexane (10:90). Main fraction collected was concentrated under vacuum at 50-60°C to yield 1.3 gms. (90 %, m.p.: 79-82°C).

1) This compound was obtained as light cream coloured powder in yield 90 %, m.p. 79-82°C. Anal.Calcd for $C_{13}H_{19}N_2O_2Cl$: C, 57.67; H, 7.02; N, 10.35. found : C, 57.68; H, 7.00; N, 10.34. IR ($cm^1$) 1707 (C=O), 3068 (CH), 3124 (NH), $^1$HNMR $CDCl_3$ (ppm) 0.87 (t, 3H, $CH_3$, J= 7.3Hz), 1.30 (t, 3H, $CH_3$), 1.35 (m, 2H, $CH_2$), 1.63-1.71 (m, 2H, $CH_2$), 2.10 (s, 3H, $CH_3$), 2.67 (t, 2H, $CH_2$, J=7.8Hz), 4.22 (q, 2H, $CH_2$, J=7.2Hz), 7.46 (s, 1H, CH), 9.81 (s, 1H, NH), $^{13}C$ NMR

(ppm) 13.6 ($CH_3$), 14.1 ($CH_3$), 14.3 ($CH_3$), 22.3 ($CH_2$), 28.6 ($CH_2$), 30.1 ($CH_2$), 61.1 ($CH_2$), 123.6 (CH), 122.9-150.4 (Ar-C), 168.1 (C=O), MS (m/z): 271.2

**(E) 1*H*-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole 2**

Charged compound **1** (2.0 gms, 0.0074 mole) and sodium methoxide (0.40 gms, 0.0074 mole) in 20 ml methanol and refluxed the reaction mass at 65-67°C for 6-8 hrs. Reaction monitored on TLC using mobile phase ethyl acetate: n-Hexane (2.5:7.5). after the reaction completion, concentrated the reaction mass under vacuum at 50-55°C. Charged 25 ml water to the concentrated reaction mass and extracted the product with 25 ml of methylene chloride. Methylene chloride layer dried over anhydrous sodium sulphate and concentrated under vacuum to yield 1.8 gms .

This compound was obtained as cream coloured powder in yield 91%, m.p. 96-100°C. Anal.Calcd for $C_{12}H_{17}N_2O_2Cl$: C, 56.14; H, 6.62; N, 10.92. found : C, 56.15; H, 6.60; N, 10.93. $^1$HNMR $CDCl_3$ (ppm) 0.92 (t, 3H, $CH_3$, J=7.3Hz), 1.37 (m, 2H, $CH_2$, J=14.9, 7.3Hz), 1.67-1.75 (m, 2H, $CH_2$), 2.13 (s, 3H, $CH_3$), 2.70 (t, 2H, $CH_2$, J= 7.8 Hz), 3.79 (s, 3H, $CH_3$), 7.48 (s, 1H, CH), 9.13 (s, 1H, NH), $^{13}$C NMR (ppm) 13.7 ($CH_3$), 14.1 ($CH_3$), 22.3 ($CH_2$), 28.6 ($CH_2$), 30.0 ($CH_2$), 52.3 ($CH_3$), 123.6 (CH), 121.8-150.4 (Ar-C), 168.1 (C=O), MS (m/z): 257.2

**Method A: Without using phase transfer catalyst**

**(E)1-para anisoyl-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1,3-imidazole 3a**

Compound **1** (2.4 gms, 0.0088 mole) in toluene (36 ml)/ pyridine (24 ml) was stirred for 10 mins till dissolves. Triethyl amine (3.56 gms, 0.0352 mole) and para-anisoyl chloride (3.0 gms, 0.0176 mole) was added and strirred further at room temperature for 2 hrs. Reaction monitored on TLC using mobile phase ethyl acetate: n-Hexane (1.5:8.5). After the completion of reaction, the mass washed with 25 ml of water followed by 10 % sodium bicarbonate solution (25 ml × 2) and dried over anhydrous sodium sulphate. The clear organic layer then concentrated under vacuum at 60-65°C, purified by column chromatography using ethylacetate: n-Hexane (5:95). Main fraction collected and concentrated under vacuum at 50-60°C to yield yellow coloured oil 2.5 gms. Yield 70%, b.p. above 300°C. Anal.Calcd for $C_{21}H_{25}N_2O_4Cl$: C, 62.30; H, 6.18; N, 6.92. found : C, 62.29; H, 6.19; N, 6.93. IR ($cm^{-1}$) 1703 ($COOC_2H_5$), 1600 (C=O), $^1$HNMR $CDCl_3$ (ppm) 0.83 (t, 3H, $CH_3$, J= 7.3 Hz), 1.27-1.32 (m, 2H, $CH_2$), 1.63 (m, 2H, $CH_2$ J= 7.6 Hz), 2.68 (t, 2H, $CH_2$, J= 7.7 Hz), 2.42 (s, 3H, $CH_3$), 1.27-1.32 (t, 3H, $CH_3$), 3.88 (s, 3H, $CH_3$), 4.22 (q, 2H, $CH_2$), 6.95-7.68 (m, 5H, Ar-H and CH), $^{13}$C NMR (ppm) 13.6 ($CH_3$), 13.9 ($CH_3$), 14.3 ($CH_3$), 55.7 ($CH_3$), 22.2 ($CH_2$), 28.3 ($CH_2$), 29.7 ($CH_2$), 60.7 ($CH_2$), 114.5-165.4 (Ar-C and C=C), 166.3 and 168.8 (C=O), MS (m/z): 405

The compounds **3b-3e** were prepared in a similar manner and their analytical data are reported in **table-I.**

**3b)** This compound was obtained as yellowish brown coloured oil. MS (m/z): 375

**3c)** This compound was obtained as yellow coloured oil. Anal.Calcd for $C_{21}H_{25}N_2O_3Cl$: C, 64.86; H, 6.43; N, 7.21. found : C, 64.85; H, 6.42; N, 7.22. $^1$HNMR $CDCl_3$ (ppm) 0.80 (t, 3H, $CH_3$, J=7.3 Hz), 1.24-1.29 (q, 2H, $CH_2$), 1.24 (t, 3H, $CH_3$), 1.56-1.64 (m, 2H, $CH_2$), 2.40 (2xs, 6H, $CH_3$x2, J= 7.1Hz), 2.66 (t, 2H, $CH_2$, J=7.8 Hz), 4.19 (q, 2H, $CH_2$), 7.26-7.57 (m, 5H, Ar-H and CH), $^{13}$C NMR (ppm) 13.6 ($CH_3$), 14.0 ($CH_3$), 14.3 ($CH_3$), 22.0 ($CH_3$), 22.2 ($CH_2$), 28.4 ($CH_2$), 29.7 ($CH_2$), 60.7 ($CH_2$), 117.6-149.8 (Ar-C and C=C), 167.1 and 168.9 (C=O), MS (m/z): 389.0

**3d)** This compound was obtained as light yellow coloured oil. MS (m/z): 405
**3e)** This compound was obtained as yellow coloured oil. Anal.Calcd for $C_{18}H_{21}N_2O_4Cl$: C, 59.26; H, 5.76; N, 7.68. found : C, 59.25; H, 5.77; N, 7.67. $^1$HNMR $CDCl_3$ (ppm) 0.79 (t, 3H, $CH_3$, J= 7.4 Hz), 1.25 (m, 2H, $CH_2$, J=7.2Hz), 1.57-1.64 (m, 2H, $CH_2$), 2.65 (t, 2H, $CH_2$, J=7.7 Hz), 2.35 (s, 3H, $CH_3$), 1.25 (t, 3H, $CH_3$), 4.17 (q, 2H, $CH_2$ ,J= 7.1Hz), 6.61-7.69 (m, 4H, Ar-H and CH), MS (m/z): 365.1

**(E) 1-*para* anisoyl-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole 4a**

Compound **2** (2.4 gms, 0.0093 mole) in toluene (36 ml) / pyridine (24 ml) was stirred for 10 mins till dissolves. Triethyl amine (3.75 gms, 0.0372 mole) and para-anisoyl chloride (3.17 gms, 0.0186 mole) was added and stirred further at room temperature for 2 hrs. Reaction monitored on TLC using mobile phase ethyl acetate: n-Hexane (1.5:8.5). After the completion of reaction, the mass washed with 25 ml of water followed by 10 % sodium bicarbonate solution (25 ml × 2) and dried over anhydrous sodium sulphate. The clear organic layer then concentrated under vacuum at 60-65°C, purified by column chromatography using ethylacetate: n-Hexane (5:95). Main fraction collected and concentrated under vacuum at 50-60°C to yield light cream coloured powder 2.5 gms. Yield 69 %, m.p.80-84°C. Anal.Calcd for $C_{20}H_{23}N_2O_4Cl$: C, 61.46; H, 5.89; N, 7.17. found : C, 61.45; H, 5.88; N, 7.18. IR ($cm^{-1}$) 1714 (C=O), 1697 ($COOCH_3$), 1595 (C=O), $^1$HNMR $CDCl_3$ (ppm) 0.83 (t, 3H, $CH_3$, J= 7.3 Hz), 1.30 (m, 2H, $CH_2$ J= 14.9,7.5 Hz), 1.60-1.67 (m, 2H, $CH_2$), 2.43 (s, 3H, $CH_3$), 2.67 (t, 2H, $CH_2$, J= 7.7 Hz), 3.77 (s, 3H, $CH_3$), 3.88 (s, 3H, $CH_3$), 6.95-7.68 (m, 5H, Ar-H and CH), $^{13}$C NMR (ppm) 13.6 ($CH_3$), 13.9 ($CH_3$), 51.9 ($CH_3$), 55.7 ($CH_3$), 22.2 ($CH_2$), 28.3 ($CH_2$), 29.7 ($CH_2$), 114.5-165.4 (Ar-C), 166.2 and 169.3 (C=O), MS (m/z): 391.2

The compounds **4b-4e** were prepared in a similar manner and their analytical data are reported in **table-I.**
**4b)** This compound was obtained as yellow coloured oil. Anal.Calcd for $C_{19}H_{21}N_2O_3Cl$: C, 63.24; H, 5.82; N, 7.77. found : C, 63.22; H, 5.83; N, 7.78. $^1$HNMR $CDCl_3$ (ppm) 0.84 (t, 3H, $CH_3$, J=7.3Hz), 1.32 (m, 2H, $CH_2$, J= 14.7,7.3 Hz), 1.62-1.70 (m, 2H, $CH_2$), 2.45 (s, 3H, $CH_3$), 2.72 (t, 2H, $CH_2$ J= 7.8Hz), 3.78 (s, 3H, $CH_3$), 7.37-8.14 (m, 6H, Ar-H and CH), $^{13}$C NMR (ppm) 13.6 ($CH_3$), 13.9 ($CH_3$), 22.1 ($CH_2$), 28.3 ($CH_2$), 29.7 ($CH_2$), 52.0 ($CH_3$), 117.0-150.0 (Ar-C), 167.3 and 169.2 (C=O), MS (m/z): 361.3
**4c)** This compound was obtained as off white coloured solid. Anal.Calcd for $C_{20}H_{23}N_2O_3Cl$: C, 64.08; H, 6.14; N, 7.48. found : C, 64.09; H, 6.13; N, 7.47. IR ($cm^{-1}$) 1606(C=O), 1712-1703 ($COOCH_3$), $^1$HNMR $CDCl_3$ (ppm) 0.79 (t, 3H, $CH_3$, J= 7.3Hz), 1.26 (m, 2H, $CH_2$, J= 14.6,7.2Hz) , 1.56-1.64 (m, 2H, $CH_2$), 2.66 (t, 2H, $CH_2$ ,J= 7.7 Hz), 2.39 ( 2xs, 6H, $CH_3$x2), 3.73 (s, 3H, $CH_3$), 7.25-7.97 (m, 5H, Ar-H and CH), MS (m/z): 375.2
**4d)** This compound was obtained as light yellow coloured oil. Anal.Calcd for $C_{20}H_{23}N_2O_4Cl$: C, 61.46; H, 5.89; N, 7.17. found : C, 61.47; H, 5.90; N, 7.16. $^1$HNMR DMSO (ppm) 0.88 (t, 3H, $CH_3$, J= 7.3 Hz), 1.35 (m, 2H, $CH_2$ J= 14.8,7.3 Hz), 1.65-1.73 (m, 2H, $CH_2$), 2.47 (s, 3H, $CH_3$), 2.74 (t, 2H, $CH_2$, J= 7.7 Hz), 3.81(s, 3H, $CH_3$), 3.88 (s,3H,$CH_3$), 7.22-7.42 (m,5H,Ar-H and CH), $^{13}$C NMR (ppm) 13.6 ($CH_3$), 14.0 ($CH_3$), 52.0 ($CH_3$), 55.6 ($CH_3$), 22.2 ($CH_2$), 28.4 ($CH_2$), 29.7 ($CH_2$), 114.7-160.0 (Ar-C and C=C), 167.3 and 169.3 (C=O), MS (m/z): 391.2
**4e)** This compound was obtained as cream coloured solid. Anal.Calcd for $C_{17}H_{19}N_2O_4Cl$: C, 58.20; H, 5.42; N, 7.99. found : C, 58.21; H, 5.43; N, 7.97. IR ($cm^{-1}$) 1650 (C=O), 1712

($COOCH_3$), $^1$HNMR $CDCl_3$ (ppm) 0.86 (t, 3H, $CH_3$, J= 7.2 Hz), 1.33 (m, 2H, $CH_2$, J= 7.2 Hz), 1.64-1.71 (m, 2H, $CH_2$), 2.42 (s, 3H, $CH_3$), 2.72 (t, 2H, $CH_2$, J= 7.3 Hz), 3.78 (s, 3H, $CH_3$), 6.67-7.75 (m, 4H, Ar-H and CH), MS (m/z): 351.3

**Method B: Using phase transfer catalyst**

**(E) 1-para anisoyl-2-butyl-4-chloro-5-(2-carbethoxy-1-propylen)-1,3-imidazole 3a**

Compound **1** (2.4 gms, 0.0088 mole), methylene chloride (36 ml) stirred for 10 mins till it dissolves. Sodium hydroxide (0.37 gms, 0.0093 mole), water (18 ml) and phase transfer catalyst i.e. tetra butyl ammonium bromide (0.24 gms) were added. Para-anisoyl chloride (1.58 gms, 0.0093 mole) was then added dropwise at room temperature for 10 mins. The reaction mixture was strirred further at room temperature for 1 hrs. After the completion of reaction completion ( monitored by TLC using mobile phase ethyl acetate: n-Hexane (1.5:8.5), organic layer was washed with 25 ml of water followed by 10 % sodium bicarbonate solution (25 ml × 2) and dried over anhydrous sodium sulphate. The clear organic layer concentrated under vacuum at 60-65°C and purified the product by column chromatography with ethylacetate: n-Hexane (5:95). Main fraction collected was concentrated under vacuum at 50-60°C to yield light yellow coloured oil 3.2 gms. Yield 90%, b.p. above 300°C.

The compounds **3b-3e** were prepared in a similar manner and their analytical data found to be similar to method A.

**(E)1-*para* anisoyl-2-butyl-4-chloro-5-(2-carbmethoxy-1-propylen)-1, 3-imidazole 4a**

Compound **2** (2.4 gms, 0.0093 mole), methylene chloride (36 ml) and stirred for 10 mins till dissolves. Sodium hydroxide (0.392 gms, 0.0098 mole), water (18 ml) and phase transfer catalyst i.e. tetra butyl ammonium bromide (0.24 gms) were added. Para- anisoyl chloride (1.67 gms, 0.0098 mole) was them added drop wise at room temperature for 10 mins. The reaction mixture was stirred further at room temperature for 1 hrs. After the completion of reaction completion ( monitored by TLC using mobile phase ethyl acetate: n-Hexane (1.5:8.5)), organic layer was washed with 25 ml of water followed by 10 % sodium bicarbonate solution (25 ml × 2) and dried over anhydrous sodium sulphate. The clear organic layer concentrated under vacuum at 60-65°C and purified the product by column chromatography with ethylacetate: n-Hexane (5:95). Main fraction collected was concentrated under vacuum at 50-60°C to yield light cream coloured powder 3.2 gms. Yield 91 %, m.p.80-84°C.

The compounds **4b-4e** were prepared in a similar manner which were found to be similar to the compound obtain by method A.

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**Table –I characterization of synthesized compounds 3a-e and 4a-e**

| Comps **3** | Ar | Molecular Formula | Molecular Weight | B.P. | Yield (%) A | B |
|---|---|---|---|---|---|---|
| 3a | *p*-$C_6H_4OCH_3$ | $C_{21}H_{25}N_2O_4Cl$ | 404.5 | >300°C | 70 | 90 |
| 3b | -$C_6H_5$ | $C_{20}H_{23}N_2O_3Cl$ | 374.5 | 272-276°C | 75 | 82 |
| 3c | *p*-$C_6H_4CH_3$ | $C_{21}H_{25}N_2O_3Cl$ | 388.5 | >300°C | 78 | 89 |
| 3d | *m*-$C_6H_4OCH_3$ | $C_{21}H_{25}N_2O_4Cl$ | 404.5 | >300°C | 71 | 80 |
| 3e | -$C_4H_3O$ | $C_{18}H_{21}N_2O_4Cl$ | 364.5 | >300°C | 68 | 81 |

| Comps **4** | Ar | Molecular Formula | Molecular Weight | M.P./B.P. | Yield (%) A | B |
|---|---|---|---|---|---|---|
| 4a | *p*-$C_6H_4OCH_3$ | $C_{20}H_{23}N_2O_4Cl$ | 390.5 | 80-84°C (M.P.) | 69 | 91 |
| 4b | -$C_6H_5$ | $C_{19}H_{21}N_2O_3Cl$ | 360.5 | 268-272°C (B.P.) | 74 | 88 |
| 4c | *p*-$C_6H_4CH_3$ | $C_{20}H_{23}N_2O_3Cl$ | 374.5 | 61-66°C (M.P.) | 78 | 90 |
| 4d | *m*-$C_6H_4OCH_3$ | $C_{20}H_{23}N_2O_4Cl$ | 390.5 | >300°C (B.P.) | 65 | 81 |
| 4e | -$C_4H_3O$ | $C_{17}H_{19}N_2O_4Cl$ | 350.5 | 62-66°C (M.P.) | 72 | 82 |

**Scheme 1**

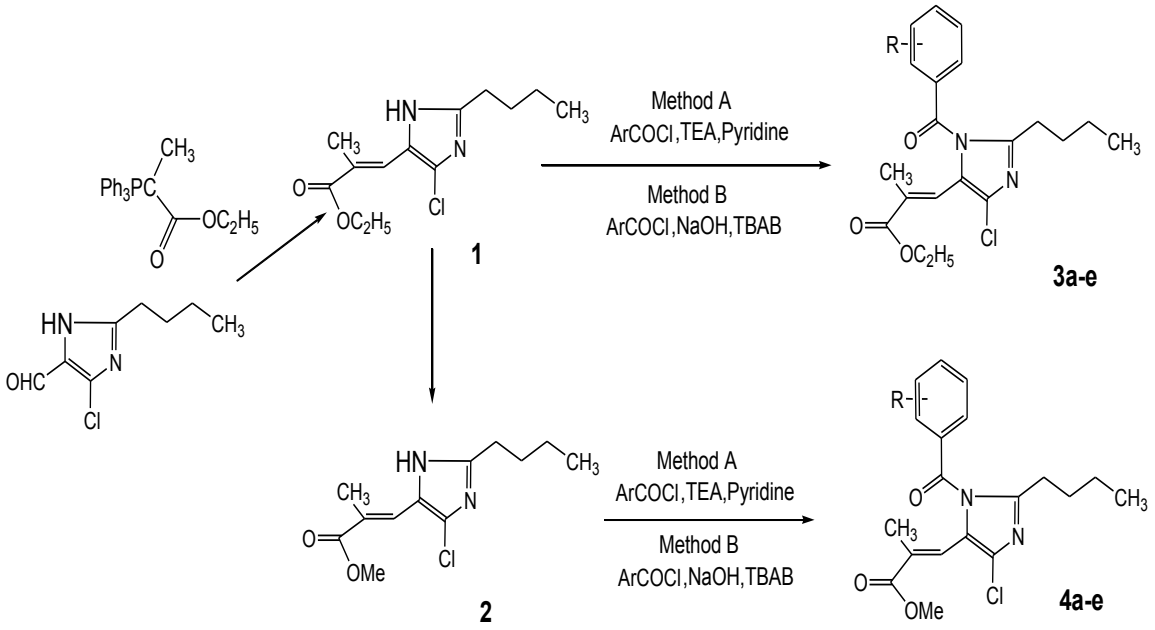


**Table III Antibacterial activity of compound 3a, 3b & 4c, 4e**

| Compound | Zone of Inhibition (in mm) | | | |
|---|---|---|---|---|
| | Gram Positive | | Gram Negative | |
| | *S. aureus* | *S.typhi* | *E.coli* | *B.Substilus* |
| **3a** | +++ | --- | --- | +++ |
| **3b** | +++ | --- | --- | +++ |
| **4c** | ++ | --- | --- | ++ |
| **4e** | ++ | --- | --- | ++ |
| **Ampicillin** | ++++ | ++++ | ++++ | ++++ |

*** Diameter of the hole was 6mm**

*** Zone of inhibition: (-) 6mm, (+) 6-10mm, (++) 10-15mm, (+++) 15-20, (++++) 20-25.**