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Diversified Synthesis of Novel Quinoline and Dibenzo Thiazepine Derivatives Using Known Active Intermediates

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The novel drug development to control resisting infections in conventional drug therapy is a need of today. Few antiulcer relative derivatives developed by approaching convergent synthesis. The derivatives synthesized successfully are dibenzo thiazepine-pyridine (SLN11-SLN15) and benzimidazole-hydroquinoline based derivatives (SLN16-SLN20). It involved the coupling through microwave, sonication and conventional techniques at final step. The efficient technology identified as sonication technique basically time and yield. The reported compounds were structural characterized by elemental analysis and spectral studies such as ^{1}H, ^{13}C NMR and MS.

Key Words: Sonication, Benzimidazole, Dibenzo thiazepine, Antiulcerative.

INTRODUCTION

For therapeutic purposes, a drug substance with well-known chemical structure is used for developing more efficient drugs. The basic idea to prepare more analogues compounds that related drug candidates with efficient technologies. Organic molecules owe their biological activity to a variety of structural features. Sometimes a set of activities is associated with the structural backbone of a molecule.

The antiulcer drugs, omeprazole (**a**), is a proton pump inhibitor (PPIs) and inhibits the action of hydrogen/potassium adenosine triphosphatase (H^+/K^+ATPase) in parietal cells[1-5]. Lansoprazole (**b**) is an antiulcer agent and proton pump inhibitor[4,5]. The structures of some antiulcer drugs available in market are given in Fig. 1.

Pantoprazole (**c**) suppresses the final step in gastric acid production by forming a covalent bond to two sites of the (H^+, K^+)-ATPase enzyme system at the secretary surface of the gastric parietal cell[6,7]. Rabeprazole (**d**) is also demonstrated efficacy in healing and symptom relief of gastric and duodenal ulcers[8-10]. Ilaprazole (**e**) is a proton pump inhibitor (PPI) used in the treatment of dyspepsia, peptic ulcer disease (PUD) and duodenal ulcer[11]. Tenatoprazole is an extended plasma half-life which makes it more effective in the treatment of nocturnal acid breakthrough than esomeprazole[12].

The art has endeavoured to synthesize a variety of piperzine derivatives. Among the piperzine derivatives available as antiulcer drugs, 1-[2-(*ortho*chloro-chlorobenzydryloxy) ethyl]-4-(*ortho*-methylbenzyl)piperzine well known[13,14]. The

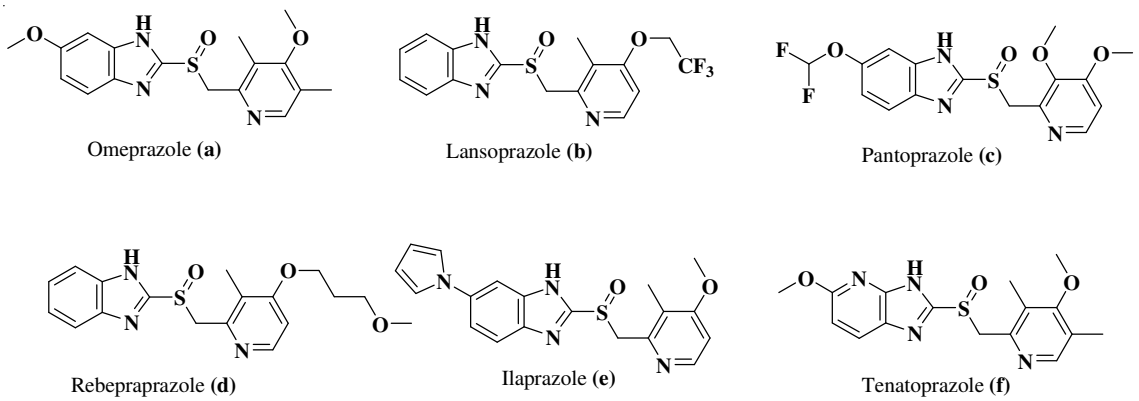


Fig. 1. Several antiulcer drugs in the market

selection of well-known skeleton, strategic synthetic approach, technologies applied for reactions. The maximum antiulcerative drugs are prazoles. The prazoles skeleton considered for development of novel moieties into literature. The idea to incorporate the piperzine with pyridine derivatives of prazoles considered to design new skeleton (a) and benzimidazoles of different prazoles with hydroquinoline derivative.

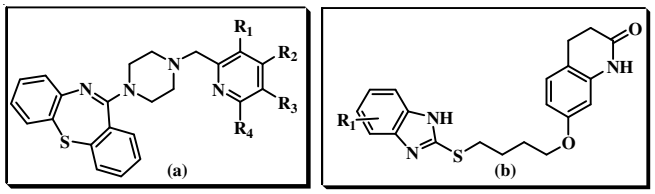


Fig. 2. Designed skeletons

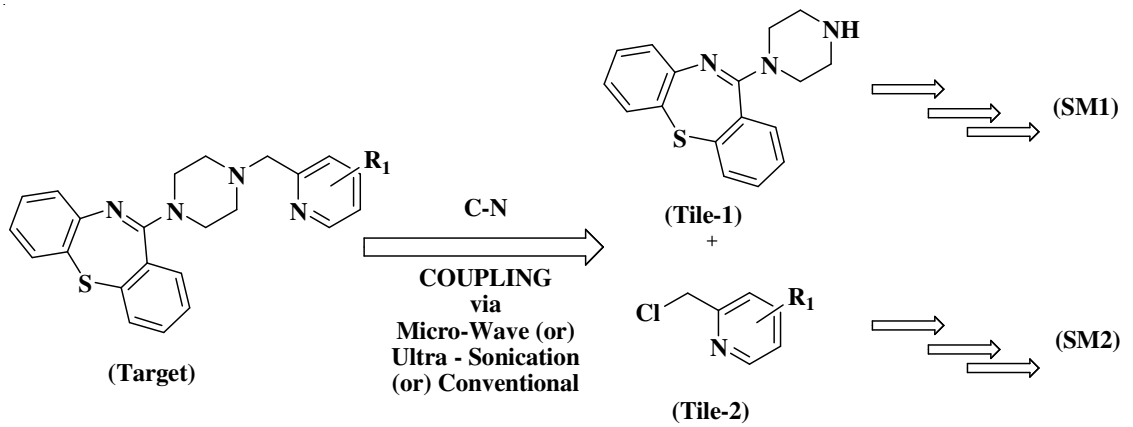
A strategy of convergent synthesis, that aims to improve the efficiency of multi-step chemical synthesis, most often in organic synthesis. In linear synthesis the overall yield quickly drops with each reaction step. Here in, the synthesis of two tile derivatives and coupled considered easy and found excellent literature for easy synthesis of both ends approached convergent than linear.

The reliable technology useful for reaching target is very important to reach target very simple and cost effective. The second technology is the way of reaction conditions are using, for getting lesser reaction timings and high yield. The N-alkylation step differentiated *via* microwave, sonication and conventional method.

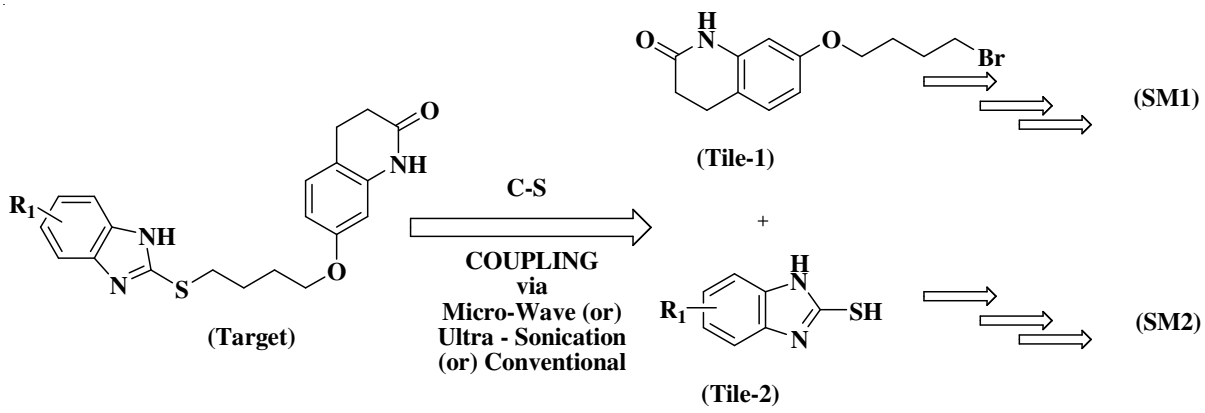
The microwave mediated organic reactions[15] take place more rapidly, safely and in an environmentally friendly manner, with high yields. Very little solvent and even the use of water as a solvent is a big advantage of microwave chemistry. Recently, microwave[16] and ultrasonication[17] assisted synthesis in organic chemistry is quickly growing. Many organic reactions proceed much faster with higher yields under microwave irradiation compared to conventional heating. It has long been known that molecules undergo excitation with electromagnetic radiation is a technique for microwave synthesis[18]. Simultaneously, sonication reactions enhances the reaction rates up to a million times, believed to be due small cavities (100 μ) which implode, creating tremendous heat and pressure, shock waves and particular accelerations.

EXPERIMENTAL

All the reactions routinely monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F_{254} coated aluminium plates using several solvent systems of different polarity. The following mobile phases were employed ethyl acetate/hexane, ethylacetate/dichloromethane, methanol/dichloromethane and methanol-ethyl acetate with different percentage combinations. The column chromatography by using all vensil columns are used for purification of compounds used (60-120 mesh) silica-gel. The melting points were determined in open capillaries on a Thermonick melting point apparatus and found uncorrected. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) recorded on $CDCl_3$ and DMSO-d_6 solution in a 5 mm tube on Varian 400 MHz Unity Inova using TMS



Scheme-I: Retro of the skeleton (a) based on convergent methodology



Scheme-II: Retro of the skeleton (b) based on convergent methodology

internal reference standard (chemical shifts in δ). Mass spectra were recorded on Agilent 6310 Ion Trap and Shimadzu LCMS (e/z and relative intensity). Microwave reactions are carried out in SEM Discovery (sixty). Ultra sonication reactions performed in Sonirex sonicator.

General procedure for preparation of diazathiazapine-pyridine derivatives (SLN11-SLN15) and benzimidazole-hydroquinoline derivatives (SLN16 - SLN20)

Conventional method (A): To a mixture of (Int-1 or Int-2), (Int-3 to Int-12) and potassium carbonate in anhydrous DMF at room temperature. The reaction mixture was stirred at 40 ºC for 5-6 h. The reaction mixture was diluted with water and extracted product into ethyl acetate. The resultant crude product purified through silica-gel (60-120 mesh) column chromatography to afford yield (calcd. 35-52 %) (SLN11-SLN20).

Micro-wave method (B): To a mixture of (Int-1 or Int-2), (Int-3 to Int-12) and potassium carbonate in anhydrous DMF at room temperature in a micro tube. The reaction mixture was stirred at 80 ºC for 0.5 h, 100-200 watts. The reaction mixture was diluted with water and extracted product into ethyl acetate. The resultant crude product purified through silica-gel (60-120 mesh) column chromatography to afford yield (calcd. 35-50 %) (SLN11-SLN20).

Sonication method (C): To a mixture of (Int-1 or Int-2), (Int-3 to Int-12) and potassium carbonate in anhydrous DMF at room temperature. The reaction mixture was sonicated at 40 ºC for 0.5 h. The reaction mixture was diluted with water and extracted product into ethyl acetate. The resultant crude product purified through silica-gel (60-120 mesh) column chromatography to afford yield (calcd. 45-70 %) (SLN11-SLN20).

SLN11: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.21 (s, 3H), 2.31(s, 3H), 2.49-2.55 (m, 4H), 3.44-3.65 (m, 4H), 3.65 (s, 2H), 3.72 (s, 3H), 6.69 (t, 1H), 7.01-7.18 (m, 3H), 7.34-7.38 (m, 2H), 7.39 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 2Hz, 1H), 8.20 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 11.04, 13.27, 59.84, 62.84, 122.66, 125.14, 125.31, 126.23, 127.97, 128.21, 129.04, 130.70, 132.06, 132.02, 132.12, 134.11, 139.81, 148.58, 148.98, 155.91, 160.84, 164.078; MS (e/z): 445 (M^+). Anal. calcd. (%) for $C_{26}H_{28}N_4OS$: C, 70.24; H, 6.35; N, 12.60; O, 3.60; S, 7.21. Found (%): C, 70.31; H, 6.42; N, 12.69; O, 3.69; S, 7.29.

SLN12: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.02-2.07 (m, 2H), 2.25 (s, 3H), 2.39-2.61 (m, 4H), 3.01-3.32 (m, 4H), 3.33 (s, 3H), 3.52 (t, 2H), 3.68 (s, 2H), 4.06 (t, 2H), 6.60 (d, *J* = 6Hz, 2H), 7.10 (d, *J* = 6.2Hz, 2H), 7.13 (t, 1H), 7.19-7.32 (m, 2H), 7.39 (d, *J* = 6.2Hz, 1H), 7.49 (d, *J* = 6.2Hz,1H), 8.26 (d, *J* = 6Hz, 1H)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 10.60, 29.39, 53.12, 58.72, 62.84, 64.86, 68.94, 105.49, 121.92, 122.63, 125.3127.96, 128.18, 129.02, 130.06, 132.05, 132.12, 134.16, 139.84, 147.40, 149.02, 156.49, 160.80, 163.27; MS (e/z): 489 (M^+). Anal. calcd. (%) for $C_{28}H_{32}N_4O_2S$: C, 68.82; H, 6.60; N, 11.47; O, 6.55; S, 6.56. Found (%): C, 68.89; H, 6.69; N, 11.54; O, 6.64; S, 6.64.

SLN13: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.40-2.80 (m, 4H), 3.20-3.49 (m, 4H), 4.35 (m, 2H) 6.60 (d, *J* = 6Hz, 2H), 6.84 (t, 1H), 7.12 (d, *J* = 6.2Hz, 1H), 7.14 (t, 1H), 7.21-7.32 (m, 4H), 7.39 (d, *J* = 6.2Hz, 1H), 7.49 (d, *J* = 6.2Hz, 1H), 8.31(d, *J* = 6Hz, 1H)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 10.61, 29.41, 53.13, 58.74, 62.85, 64.87, 68.96, 105.51, 121.94, 122.63, 122.71, 125.3127.96, 128.18, 129.02, 130.06, 132.05, 132.12, 134.16, 139.84, 147.40, 149.02, 156.49, 160.80, 163.27; MS (e/z): 499 (M^+). Anal. calcd. (%) for $C_{26}H_{25}F_3N_4OS$: C, 62.64; H, 5.05; F, 11.43; N, 11.24; O, 3.21; S, 6.43. Found (%): C, 62.64; H, 5.05; F, 11.43; N, 11.24; O, 3.21; S, 6.43.

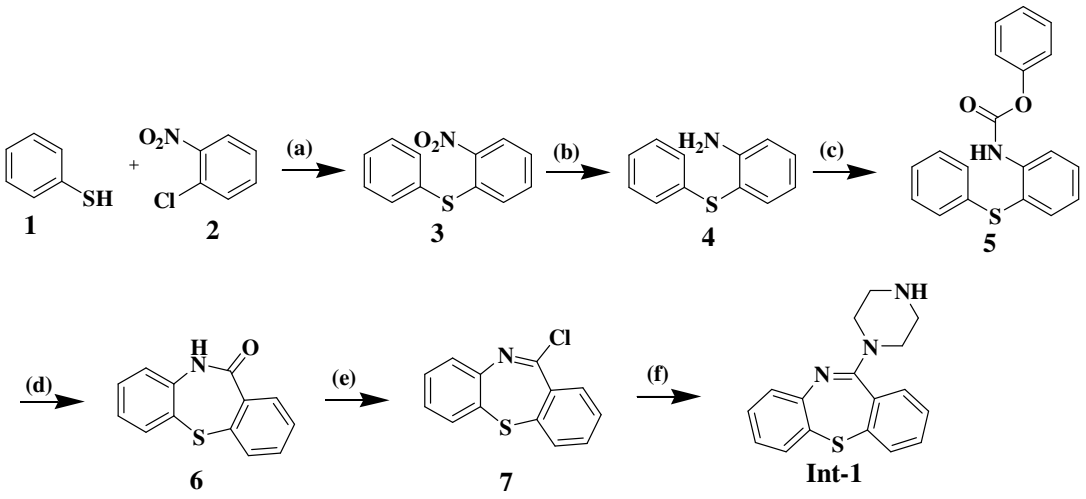
SLN14: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.42-2.81 (m, 4H), 3.21-3.49 (m, 4H), 3.65 (s, 2H), 3.72 (s, 3H), 6.76 (d, *J* = 6Hz, 2H), 7.14 (t, 1H), 7.21-7.32 (m, 4H), 7.39 (d, *J* = 6.2Hz, 1H), 7.49 (d, *J* = 6.2Hz,1H), 8.23(d, *J* = 6Hz, 1H)). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 59.84, 53.13, 58.74, 62.84, 62.85, 64.87, 68.96, 105.53, 121.95, 122.64, 122.72, 125.82, 127.96, 128.18, 129.12, 130.08, 132.07, 132.15, 134.19, 139.88, 147.48, 149.08, 156.51, 160.83, 163.31; MS (e/z): 431 (M^+). Anal. calcd. (%) for $C_{25}H_{26}N_4OS$: C, 69.74; H, 6.09; N, 13.01; O, 3.72; S, 7.45. Found (%): C, 69.83; H, 6.17; N, 13.05; O, 3.83; S, 7.53.

SLN15: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.50-2.57 (m, 4H), 3.46-3.68 (m, 4H), 3.85 (s, 2H), 3.87 (s, 3H), 388 (s, 3H), 6.67 (d, *J* = 5.6 Hz, 1H), 6.84-6.88 (m, 2H), 7.04-7.07 (m, 2H), 7.34-7.38 (m, 2H), 7.38 (d, *J* = 1.6 Hz, 1H), 7.49 (d, *J* = 2Hz, 1H), 8.29 (d, *J* = 6Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 10.55, 53.13, 55.33, 62.80, 104.74, 121.94, 122.66, 125.34, 127.99, 128.18, 129.05, 130.66, 132.08, 132.14, 134.19, 139.90, 147.47, 149.02, 156.48, 160.83, 163.98; MS (e/z): 447 (M^+). Anal. calcd. (%) for $C_{25}H_{26}N_4O_2S$: C, 67.24; H, 5.87; N, 12.55; O, 7.17; S, 7.18. Found (%): C, 67.28; H, 5.94; N, 12.62; O, 7.25; S, 7.243.

SLN16: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.62-1.84 (m, 4H), 2.53 (t, 2H), 2.75 (t, 2H), 3.22 (t, 2H), 3.64 (t, 2H), 6.25 (t, 1H), 6.35 (t, 1H), 6.75 (m, 2H), 6.89 (d, *J* = 8.4Hz,1H), 7.00 (s, 1H), 7.42 (d, *J* = 8.8Hz, 1H), 8.29 (s, 1H), 9.61(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 24.38, 26.35, 28.05, 30.94, 31.00, 32.57, 67.24, 102.19, 109.14, 111.45, 115.66, 128.59, 138.07, 149.63, 156.12, 158.37, 172.94; MS (e/z): 368 (M^+). Anal. calcd. (%) for $C_{20}H_{21}N_3O_2S$: C, 65.37; H, 5.76; N, 11.44; O, 8.71; S, 8.73. Found (%): C, 65.42; H, 5.81; N, 11.47; O, 8.75; S, 8.75.

SLN17: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84-1.85 (m, 4H), 2.61 (brs, 2H), 2.82 (brs, 2H), 2.83 (brs, 2H), 3.31 (brs, 2H), 6.25-6.27 (brm, 2H), 6.41 (brs, 2H), 6.95 (brs, 2H), 7.32 (brs, 2H), 9.77(brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 24.31, 26.31, 28.05, 30.97, 32.28, 67.28, 102.33, 109.14, 113.97, 115.04, 115.78, 116.55, 119.12, 128.64, 137.99, 146.69, 152.33, 158.37, 173.18; MS (e/z): 434 (M^+). Anal. calcd. (%) for $C_{21}H_{21}F_2N_3O_3S$: C, 58.19; H, 4.88; F, 8.77; N, 9.69; O, 11.07; S, 7.40. Found (%): C, 58.23; H, 4.93; F, 8.82; N, 9.73; O, 11.13; S, 7.52.

SLN18: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84-1.89 (m, 4H), 2.62 (t, 2H), 2.84 (t, 2H), 3.32 (t, 2H), 3.82 (t, 2H), 3.91(s, 3H), 6.27 (s, 1H), 6.37 (s, 1H), 6.44 (m, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.75 (d, *J* = 8.4 Hz,1H), 6.96 (d, *J* = 8.4Hz,1H), 7.72 (d, *J* = 8.8Hz, 1H), 9.35 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 24.43, 26.24, 28.05, 30.94, 31.00, 32.12, 53.96, 67.37, 102.40, 105.04, 109.08, 115.759, 128.577, 138.07, 158.42, 160.94, 172.76; MS (e/z): 398 (M^+). Anal. calcd. (%) for



Reaction & Conditions: (a) NaOH, DMSO, 80°C **(b)** Ra Ni, MeOH, H_2, 80PSI **(c)** Phenyl chloroformate, Na_2CO_3, THF, H_2O **(d)** PPA, 100°C **(e)** POCl3, N,N'-dimethyl aniline, DCM **(f)** Piperzine, Toluene/THF, triehtylamine.

Scheme-III: Synthesis of 11-pyrazolyldibenzo[b,f][1,4]thiazepine (Int-1)

$C_{20}H_{22}N_4O_3S$ $C_{21}H_{23}N_3O_3S$: C, 63.45; H, 5.83; N, 10.57; O, 12.08; S, 8.07. Found (%): C, 63.51; H, 5.92; N, 10.63; O, 12.15; S, 8.15.

SLN19: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.60-1.85 (m, 4H), 2.57 (t, 2H), 2.79 (t, 2H), 3.24 (t, 2H), 3.66 (t, 2H), 3.71(s, 3H), 6.29 (s, 1H), 6.37 (d, 1H), 6.77 (d, *J* = 8.4Hz,1H), 6.91 (d, *J* = 8.4Hz,1H), 7.01 (s, 1H), 7.43 (d, *J* = 8.8Hz, 1H), 9.61(s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 24.38, 26.35, 28.05, 30.94, 31.00, 32.57, 55.82, 67.24, 102.19, 109.14, 111.45, 115.66, 128.59, 138.07, 149.63, 156.12, 158.37, 172.94; MS (e/z): 399 (M^+). Anal. calcd. (%) for $C_{20}H_{22}N_4O_3S$: C, 60.28; H, 5.56; N, 14.06; O, 12.05; S, 8.05. Found (%): C, 60.35; H, 5.65; N, 14.12; O, 12.14; S, 8.11.

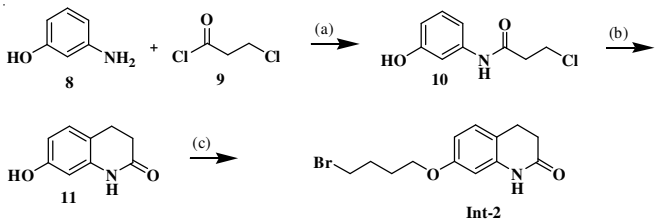
SLN20: ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84-1.88 (m, 4H), 2.60 (brs, 2H), 2.83 (brs, 2H), 2.85 (brs, 2H), 3.33 (brs, 2H), 6.02 (brs, 2H), 6.25-6.27 (brm, 2H), 6.41 (brs, 2H), 6.71 (brs, 2H) 6.95 (brs, 2H), 7.32 (brs, 1H), 9.77(brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 24.28, 26.29, 28.00, 30.92, 32.23, 67.24, 102.31, 208.19, 109.10, 113.90, 115.02, 115.71, 116.51, 117. 21, 119.10, 128.58, 137.96, 146.67, 152.36, 158.39, 173.19; MS (e/z): 433 (M^+). Anal. calcd. (%) for $C_{24}H_{24}N_4O_2S$: C, 66.64; H, 5.59; N, 12.95; O, 7.40; S, 7.41. Found (%): C, 66.64; H, 5.59; N, 12.95; O, 7.40; S, 7.41.

RESULTS AND DISCUSSION

In continuation of our research interest was to synthesize a series of novel (SLN11-SLN20) relevant to antiulcer related drug skeleton candidates prepared. The main focus in this paper described the synthesis and rest of the activity studies is under progress.

In the synthesis of Int-1, was followed the some earlier reported work[18]. The coupling of **1** and **2** using NaOH in DMSO at 80 ºC. The reduction of compound **3** with Ra Ni, H_2 in methanol into **4**. The carbamate **5** was prepared by protection of amine **4** using phenyl chloroformate and Na_2CO_3. The cyclisation of carbamate **5** into compound **6** was carried out in presence of PPA at 80-90 ºC. The imino chloride was prepared by treating **6** with $POCl_3$ and N,N'-dimethyl aniline at 105 ºC. The final coupling was carried out in presence of triethylamine in toluene/THF to afford Int-1 according to **Scheme-III**.

The reported procedure incorporated during the synthesis of 7-(4-bromobutoxy)-3,4-dihydroquinolin-2(1*H*)-one (Int-2)[19]. Simple acylation carried out on 3-amino phenol using $NaHCO_3$ in acetonitrile at 0 ºC to afford **10**. The cyclisation of **10** done with $AlCl_3$ in dichloromethane to afford **11**. Finally, **11** were coupled with 1,4-dibromo butane using K_2CO_3 in DMF at 60 ºC for 12 h to afford Int-2 according to **Scheme-IV**.

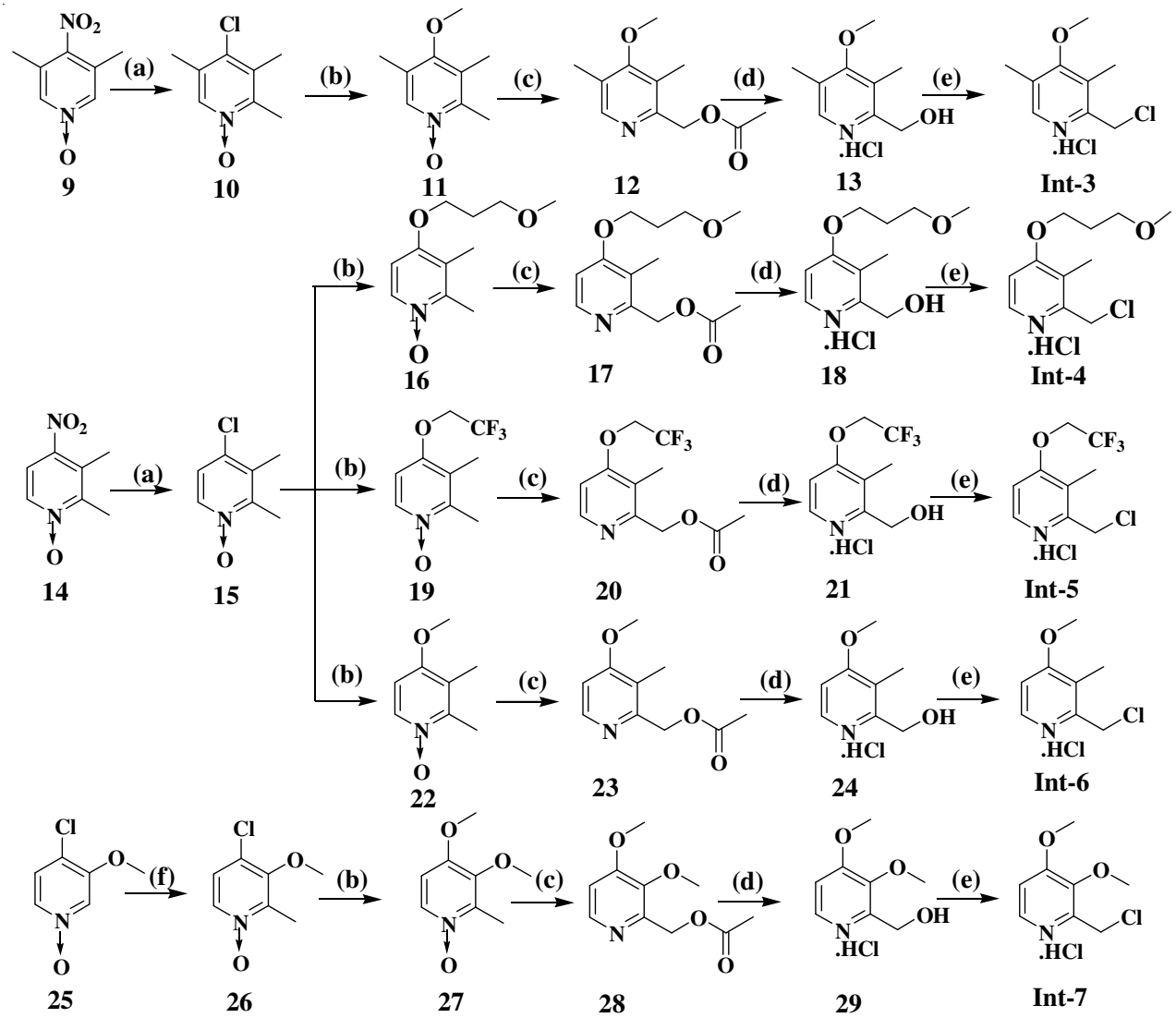


Reagents & Conditions: (a) $NaHCO_3$ **(b)** $AlCl_3$ **(c)** 1,4-dibromo butane

Scheme-IV: Synthesis of 7-(4-bromobutoxy)-3,4-dihydroquinolin-2(1*H*)-one (Int-2)

The traditional approach for the synthesis of Int-3 - Int-7 as shown in **Scheme-V**[20]. The conversion of nitro compounds **9** and **14** to corresponding chloro **10** and **15** using $POCl_3$ as a chlorinating reagent. The further conversation of choro compounds **10** and **15** into **11**, **16**, **17**, **22** and **27** using appropriate alcohols, the methylation of compound **25** using DMS to afford methylated compound **26**. The further conversion of compounds, **11**, **16**, **17**, **22** and **27** to acetate using acetic anhydride to afford compounds, **12**, **17**, **20**, **23** and **28**. All these compounds hydrolyzed using NaOH to afford **13**, **18**, **21**, **24** and **29**. Finally, alcohol of **13**, **18**, **21**, **24** and **29** converted to chloro using $SOCl_2$ to afford Int-3 to Int-7 according to **Scheme-V**[21,22].

The earlier reported paper used for the synthesis of Int-8[23]. Herein, the required 2-mercapto benzimidazole (Int-8) was prepared by refluxing *o*-phenylenediamine (**33**), CS_2 and



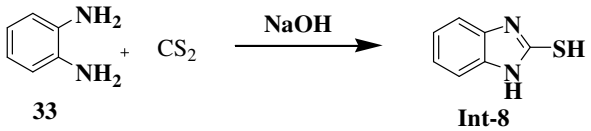
Reagents & Conditions: (a) $POCl_3$, reflux for 3-4h (b) appropriate alchohols and NaOH (c)acetic anhydride, acetic acid, MeOH, Toluene (d) NaOH, MeOH, MDC (e) $SOCl_2$ (f) DMS

Scheme-V: Synthesis of 2-chloromethyl-4-methoxy-3,5,-dimethyl-pyridine. HCl (Int-3), 2-chloromethyl-3-methyl-4-(3-methyoxypropoxy) pyridine. HCl (Int-4), 2-chloromethyl-3-methyl-4-(2,2,2-trifluoromethoxy)pyridine. HCl (Int-5), 2-Chloromethyl-3-methyl-4-methoxy pyridine. HCl (Int-6) and 2-chloromethyl-3,4-dimethoxypyridine.HCl (Int-7)

NaOH and further salt freed by using acetic acid according **Scheme-VI**.

In this process, fluorination of 4-hydroxyacetanilide (**34**) yielded the intermediate N-[4-(difluoromethoxy)phenyl]-acetamide **35**. Subsequent reactions like nitration followed by hydrolysis, reduction and cyclization of intermediate **35** gave the title compound, 2-mercapto-5-difluoromethoxy-1*H*-benzimidazole Int-9 according **Scheme-VII**[24].

The important intermediate for omeprazole, 2-mercapto-5-methoxy benzimidazole (Int 10)[23] was prepared from anisidine (**39**), acetyl protection leads **40**. The Int 40, converted into



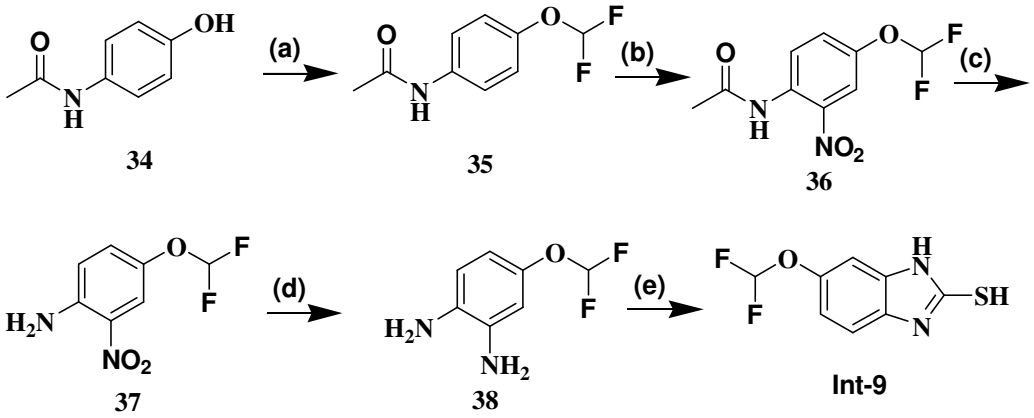
Scheme-VI: Synthesis of 2-mercapto benzimidazole

nitro compound **41** using HNO_3, H_2SO_4. Then deprotected **41** into **42** using NaOH, MeOH. The nitro group reduced using tin, HCl and further cyclized using KOH, CS_2 to afford Int 10 according to **Scheme-VIII**.

The coupling of **44** with sodium methoxide in methanol and further reduction and cyclisation leads Int-11 according to **Scheme-IX**[25].

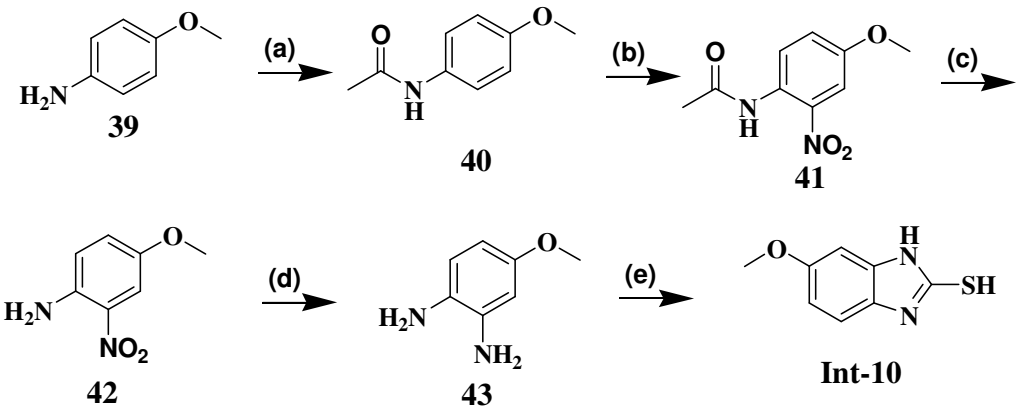
The reaction of 2-mercapto-5-nitrobenzimidazole **47** with iron and concentrated HCl in refluxing ethanol and water gives monoamine **48**, which on condensation with 2,5-dimethoxy-tetrahydrofuran **49** in acetic acid yields 2-mercapto-5-(1-pyrrolyl)benzimidazole Int-12 according to **Scheme-X**[26].

The novel targets (SLN11-SLN20) were synthesized by simple coupling using different technologies (microwave, ultra-sonication and normal conventional method). Basically, we observed ultra-sonication condition looking better comparatively with other techniques used based on yield according to Table-1.



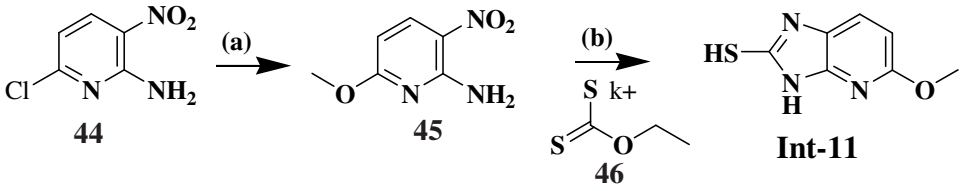
Reagents & conditions:
(a) PEG-600, difluoromethylenchloride, 50-55^{0}C, 70-74h (b)HNO_3, H_2SO_4, 20-25^{0}C, 2h.(c)CH3OH, Reflux, 3h. (d) Raney-Nickel, hydrazine hydrate, reflux, 4h. (e)CS_2, reflux, 4h.

Scheme-VII: Synthesis of 6-(difluromethoxy)-1*H*-benzo[d]imidazole-2-thiol (Int-9)



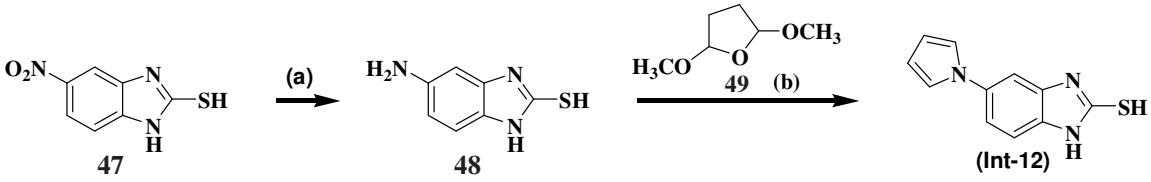
Reagents & Conditions: (a) acetic anhydride, acetic acid (b) HNO_3, H_2SO_4 (c) NaOH, MeOH (d) Sn, HCl (e) CS_2, KOH, EtOH

Scheme-VIII: Synthesis of 6-methoxy-1H-benzo[d]imidazole-2-thiol (Int-10)



Reagents & Conditions: (a) NaOMe, MeOH (b) Ra-Ni, H_2, EtOH

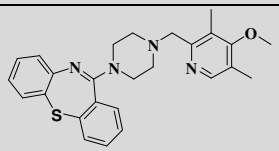
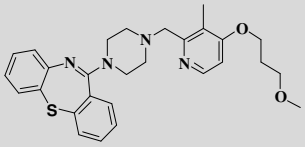
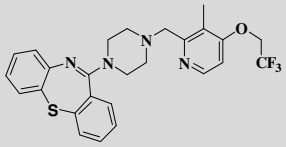
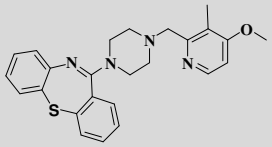
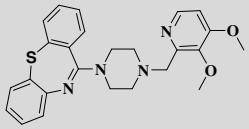
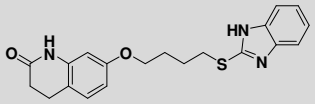
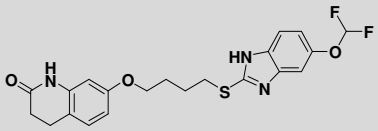
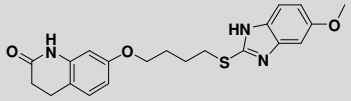
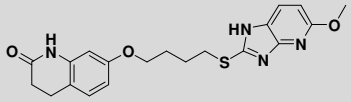
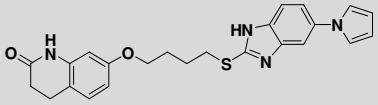
Scheme-IX: Synthesis of 5-methoxy-3*H*-imidazo[4,5-b]pyridine-2-thiol (Int-11)of 5-methoxy-3*H*-imidazo[4,5-b]pyridine-2-thiol (Int-11)



Reagents & Conditions: (a) Fe, Con.HCl, EtOH, H_2O **(b)** AcOH

Scheme-X: Synthesis of 5-(1*H*-pyrrol-l-yl)-1*H*-benzo[d]imidazole-2-thiol (Int-12)

TABLE-1
RESULTS OF TARGETS (SLN11-SLN20)

Entry-1	Entry-2	Product	Conventional method yield (%)	Microwave method yield (%)	Sonication method yield (%)
Int-1	Int-3	 SLN-11	52	50	70
Int-1	Int-4	 SLN-12	50	49	65
Int-1	Int-5	 SLN-13	49	49	55
Int-1	Int-6	 SLN-14	42	39	49
Int-1	Int-7	 SLN-15	50	49	55
Int-2	Int-8	 SLN-16	49	45	55
Int-2	Int-9	 SLN-17	39	41	47
Int-2	Int-10	 SLN-18	46	43	52
Int-2	Int-11	 SLN-19	35	35	45
Int-2	Int-12	 SLN-20	41	39	48

Conclusion

The quinoline and dibenzo thiazepine derivatives were (SLN11-SLN20) successfully synthesized by using literature procedure. The derivatives developed based on drug candidates, prepared skeleton. Simple convergent methodology worked for getting good yields overall. The final, C-N and C-S coupling approached three techniques, In this regard, sonication technique is good for getting good yield and time. In almost all reactions happened more spots in microwave reaction may be due to microwave other bonds also dislocated and afford low yield. The same conventional reaction yield shown less and taking long time. The explosive reactions, like azide and Mitsunobu reactions, *etc*. are not useful for bulk scale.

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