International Journal of Chemistry and Pharmaceutical Sciences

Journal Home Page: www.pharmaresearchlibrary.com/ijcps

Research Article **Open Access**

Synthesis and Characterization of 6-Phenylimidazo [1, 2-A] Pyridin-2-yl)-1H-Pyrazoamine Derivatives

Denish C. Karia[*1], Nilay Shah[2]

[1]*Assistant Professor Patel J. D. K. Science College Borsad-388540 Gujarat India*
[2]*Senior Executive, Cadila Health care Pvt. Ltd, Changodar-382219, Gujarat, India*

A B S T R A C T

2-amino-5-bromo pyridine was treated with ethyl bromopyruvate followed by Suzuki coupling, acetonitrile-n-Buli reaction and cyclized with hydrazine hydrate at 80°C to get 6-phenylimidazo[1,2-a]pyridin-2-yl)-1H-pyrazoamine (5). This key intermediate was treated with acid chloride, aldehyde and methane sulphonyl chloride to yield desired compounds 6a-c, 7a-c and 8 respectively.

Keywords: 6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazoamine

A R T I C L E I N F O

CONTENTS

Article History: Received 24 June 2015, **Accepted** 29 July 2015, **Available Online** 27 August 2015

***Corresponding Author**
Denish C. Karia
Assistant Professor,
Patel J. D. K. Science College
Borsad-388540 Gujarat, India
Manuscript ID: IJCPS2654

PAPER-QR CODE

Citation: Denish C. Karia. Synthesis and Characterization of 6-Phenylimidazo [1, 2-A] Pyridin-2-yl)-1H-Pyrazoamine Derivatives. *Int. J. Chem, Pharm, Sci*., 2015, 3(8): 1906-1910.

1. Introduction

Imidazole moiety fused with the pyridine ring called imidazopyridine, is significant biologically active nitrogen containing heterocyclic compound. [1] Amongst the various Imidazopyridine derivatives, the imidazole [1,2-a] pyridine scaffold is the most important in the part of natural products and pharmaceuticals. From the current literature survey, Imidazopyridine derivatives show a wide range of biological activities, e.g. antitumor, anti-apoptotic, antifungal, antibacterial, anti-inflammatory, antipyretic, antiviral, antiprotozoal, analgesic, hypnoselective [2–12]

They also used as GABA and benzodiazepine receptor agonists, cardiotonic agents and β-amyloid development inhibitors. [13–16] There are several drugs such as zolpidem [17], alpidem, olprinone [18], zolimidine [19], necopidem and saripidem [20] obtainable in the market which contains imidazo [1,2-a] pyridine moiety. The optically active GSK812397 is a drug for the treatment of HIV infection. [21] The antibiotic drug Rifaximin also contains this fused heterocyclic moiety [22]. In addition, some abnormal N-heterocyclic carbenes are also prepared based on imidazo[1,2-a] pyridines. [23,24] The imidazo [1,2-a] pyridine moiety used in the field of optoelectronics, which contain 2-hydroxyphenyl substituent at the 2-position exhibits excited state intramolecular proton transfer. [25] Encouraged by their promising medicinal properties of Imidazopyridine, we design new compound which contains Imidazopyridine derivative with pyrazole scaffold. So we have synthesized new 3-(6-phenylimidazo [1,2-a] pyridin-2-yl)-1H-pyrazol-5-amine derivative by three consecutive steps via conventional method.

2. Experimental

Melting points were measured in open capillaries and are uncorrected. ^{1}HNMR spectra were recorded on Brukur spectrophotometer (400MHz). Chemical shifts are expressed in units relative to TMS signal as internal reference. IR spectra were recorded on FT-IR Shimadzu-FT-IR 8400 spectrophotometer on KBr pallets. Mass spectra were recorded on LCMS chromatograph. Thin Layer Chromatography was performed on silica gel-G using Hexane: ethyl acetate and DCM: Methanol solvent system.

Typical synthetic procedure for 3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (4) Ethyl 6-bromoimidazo[1,2-a]pyridine-2-carboxylate (1)

2-amino-5-bromopyridine (5.0 g, 28.90 mmol) and ethyl bromopyruvate (6.76 g, 34.68 mmol) were added in ethanol (50 ml) and the reaction mixture was heated to 80°C for 8 hrs. Reaction progress was monitored by TLC (Ethyl acetate: n-Hexane 5:5). After completion of the reaction, the reaction mixture was poured into saturated aqueous $NaHCO_3$, and extracted with ethyl acetate. After conventional work-up, the resulting residue was washed with ethyl acetate to afford 5.0 g of the titled compound as a brown powder (yield: 64.35%). LCMS (ESI) m/z (M+H)+: 268.93, 1H-NMR (400MHz, $CDCl_3$); δ 1.44 (3H, t J=7.2Hz), 4.46 (2H, q, J=7.2Hz), 7.31 (1H, dd, J=1.8, 9.6Hz), 7.59 (1H, d, J=9.6Hz), 8.14 (1H, s), 8.29 (1H, d, J=1.8Hz)

Ethyl 6-phenylimidazo[1,2-a] pyridine-2-carboxylate (2)

Ethyl 6-bromoimidazo[1,2-a] pyridine-2-carboxylate **(1)** (5.0 g; 18.58 mmol), Phenyl boronic acid (2.72 g; 22.30 mmol) followed by K_2CO_3 aqueous solution (5.13g 37.17 mmol) were added in 1,4 dioxane (30 ml) and the reaction mixture was degassed with nitrogen. Finally Pd $(PPh_3)_4$ (1.07 g, 0.92 mmol; 5 mol percent) was added under a nitrogen atmosphere. The reaction mixture was heated to 100°C for 2h. (Reaction progress was monitored by TLC (Ethyl acetate: n-Hexane 5:5). After completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate. The organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Yield: 4.8 g (97.16%). LCMS (ESI) m/z (M+H)+: 267.11, 1H-NMR (DMSO-d_6) δ: 1.83 (3H, s), 3.41 (2H,t, J=5.7 Hz), 3.78 (1H, dd, J=8.7, 6.3 Hz), 4.17 (1H, t, J=8.7 Hz), 4.73-4.78 (1H, m), 7.39-7.45 (2H, m), 7.60-7.68 (3H,m), 7.99 (1H, s), 8.26 (1H, t, J=5.4 Hz), 8.79 (1H, s).

3-oxo-3-(6-phenylimidazo[1,2-a]pyridin-2-yl) propanenitrile (3)

Acetonitrile (0.88g g; 21.60 mmol) was added in tetrahydrofuran (48 ml) and the reaction mixture was cooled to -78°C with dry ice in acetone bath and n-Buli (1.6M in n-Hexane) (16.90 ml, 27.03 mmol) was added drop wise into reaction and reaction mixture was maintained for 45 minutes at -78°C. Then solution of Ethyl 6-phenylimidazo [1,2-a] pyridine-2-carboxylate **(2)** (4.80 g, 18.02 mmol; 5 mol percent) was added under a nitrogen atmosphere. The reaction mixture was stirred at -78 °C for 30 min. (Reaction progress was monitored by TLC (MeOH: MDC 1:9) after completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure.

Yield: 3.7g (74.46percent).

LCMS (ESI) m/z (M+H) +: 262.09,

3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (4): 3-Oxo-3-(6-phenylimidazo[1,2-a] pyridin-2-yl) propanenitrile (3) (3.7 g, 14.16 mmol) and Hydrazine hydrate (80%) (6.76 g, 34.68 mmol) were added in ethanol (50 ml) and the reaction mixture was heated to 80°C for 12 hrs. Reaction progress was monitored by TLC (MeOH: MDC 1:9). After completion of the reaction, the reaction mixture was distilled out under reduced pressure and finally triturate with diethyl ether (yield 3.42: 87.91%). LCMS (ESI) m/z (M+H) +: 268.93.

N-(3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-yl)isobutyramide (5a)

To a solution of 3-(6-phenylimidazo [1,2-a] pyridin-2-yl) -1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in THF (10 ml) was added Triethyl amine (0.366g 3.63 mmol) and the reaction mixture was stirred for 10 minutes, then after solution of Isobutyryl chloride (0.21g 1.99 mmol) In THF was added and the reaction mixture was stirred at 35°C for 45 minutes Reaction progress was monitored by TLC (MeOH: MDC 1:9). After completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate; the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.5% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 56mg: 8.91%); mp 212-219°C, LCMS (ESI) m/z (M+H**)** : 346.39, IR (cm-1): 3150 (N-H stretching of amide) 3058 (C-H stretching of aromatic ring), 1670 (C=O stretching of amide), 1544, 1500 and 1452 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6**)** δ: 1.09 (d, *J*=8.7 Hz, 6H) 2.61-2.67 (m, 1H), 6.93 (s, 1H), 7.40-7.44 (m, 1H), 7.50-7.58 (m, 2H), 7.63-7.68 (m, 2H), 7.34-7.58 (m, 2H), 8.28 (s, 1H), 8.96 (s, 1H), 10.14 (s, 1H), 12.91 (s, 1H). Anal. Calcd. For $C_{20}H_{19}N_5O$: C, 69.55;

H, 5.54; N, 20.28; O, 4.63; Found: C, 69.53; H, 5.55; N, 20.30; O, 4.62%

N-(3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-yl)pivalamide (5b)

To a solution of 3-(6-phenylimidazo [1,2-a] pyridin-2-yl) -1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in THF (10 ml) was added Triethyl amine (0.366g 3.63 mmol) and the reaction mixture was stirred for 10 minutes, then after solution of pivaloyl chloride (0.24g 1.99 mmol) in THF was added and the reaction mixture was stirred at 35°C for 45 minutes. Reaction progress was monitored by TLC (MeOH: MDC 1:9) after completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.5% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 92mg: 14.11%), LCMS (ESI) m/z (M+H**)** : 360.35, mp 222-230°C IR (cm-1): 3160 (N-H stretching of amide) 3060 (C-H stretching of aromatic ring), 1671 (C=O stretching of amide), 1543, 1500 and 1451 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6**)** δ: 1.21 (s, 9H), 6.91 (d, *J*=2.0 Hz 1H), 7.38-7.64 (m, 5H), 7.26-7.55 (m, 2H), 8.26 (s, 1H), 8.96 (s, 1H), 9.86 (s, 1H), 12.94 (s, 1H). Anal. Calcd. For $C_{21}H_{21}N_5O$: C, 70.17; H, 5.89; N, 19.48; O, 4.45; Found: C, 70.51; H, 5.56; N, 19.50; O, 4.43%

N-(3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-yl)acryl amide (5c)

To a solution of 3-(6-phenylimidazo [1,2-a] pyridin-2-yl) -1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in THF (10 ml) was added Triethyl amine (0.366g 3.63 mmol) and the reaction mixture was stirred for 10 minutes, then after solution of Acryloyl chloride (0.18g 1.99 mmol) In THF was added and the reaction mixture was stirred at 35°C for 45 minutes Reaction progress was monitored by TLC (MeOH: MDC 1:9) after completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.6% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 55mg: 9.19%); mp 205-209°C ESI MS (ESI) m/z (M+H**)** : 330.4, IR (cm-1): 3152 (N-H stretching of amide) 3060 (C-H stretching of aromatic ring), 1672 (C=O stretching of amide), 1543, 1500 and 1451 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6) δ: 5.50 (dd, J=1.6, 9.6 Hz 1H), 6.01-6.20. (m, 2H), 6.85 (d, J=2.0 Hz 1H), 7.35-7.67 (m, 5H), 7.29-7.59 (m, 2H), 8.27 (s, 1H), 8.91 (s, 1H), 9.88 (s, 1H), 12.66 (s, 1H). Anal. Calcd. For $C_{19}H_{15}N_5O$: C, 69.29; H, 4.59; N, 21.26; O, 4.46; Found: C, 69.31; H, 4.58; N, 21.26; O, 4.46%

N-benzyl-3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (6a)

To a solution of 3-(6-phenylimidazo[1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in methanol (15 ml) was added benzaldehyde (0.578g 5.45 mmol) and reaction mixture was stirred for 5h at 35°C, then after $NaBH_4$ (0.345g 9.09 mmol) was added and reaction mixture was stirred at 35°C for 5 hrs Reaction progress was monitor by TLC (MeOH: MDC 1:9) after completion of reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.3% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 75mg: 11.31%).LCMS (ESI) m/z (M+H**)** +: 366.45; mp 192-199°C IR (cm-1): 3550 (N-H stretching of secondary amine), 3058 (C-H stretching of aromatic ring), 1544, 1500 and 1452 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6**)** δ: 4.27 (s, 2H), 5.86 (br, 1H), 7.20-7.23 (m, 1H), 7.30-7.33 (m, 2H), 7.39-7.43 (m, 4H), 7.49-7.61 (m, 4H), 7.72 (d, *J*=7.2 Hz, 2H), 8.16 (s, 1H), 8.92 (s, 1H), 12.07 (s, 1H). Anal. Calcd. For $C_{23}H_{19}N_5$: C, 75.59; H, 5.24; N, 19.16; Found: C, 75.58; H, 5.25; N, 19.16%

N-(4-methoxybenzyl)-3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (6b)

To a solution of 3-(6-phenylimidazo[1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (0.500g 1.81 mmol) in methanol (15 ml) was added 4-methoxy benzaldehyde (0.741g 5.45 mmol) and reaction mixture was stirred for 5h at 35°C, then after $NaBH_4$ (0.345g 9.09 mmol) was added and reaction mixture was stirred at 35°C for 5 hrs Reaction progress was monitor by TLC (MeOH: MDC 1:9) after completion of reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.3% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 72mg: 10.28%), LCMS (ESI) m/z (M+H**):** 396.60, ; mp 199-205°C IR (cm-1): 3552 (N-H stretching of secondary amine),3059 (C-H stretching of aromatic ring), 1542, 1501 and 1453 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6**)** δ: 3.72 (s, 3H), 4.19 (s, 2H), 5.84 (br, 1H), 6.88 (d, *J*=8.4 Hz, 2H), 7.31 (d, *J*=8.4 Hz, 2H), 7.39-7.41 (m, 1H), 7.49-7.61 (m, 5H), 7.72 (d, *J*=7.6 Hz, 2H), 8.15 (s, 1H), 8.92 (s, 1H), 12.08 (s, 1H). Anal. Calcd. For $C_{24}H_{21}N_5O$: C, 72.89; H, 5.35; N, 17.71, O, 4.05; Found: C, 72.90; H, 5.36; N, 17.73, O, 4.05%

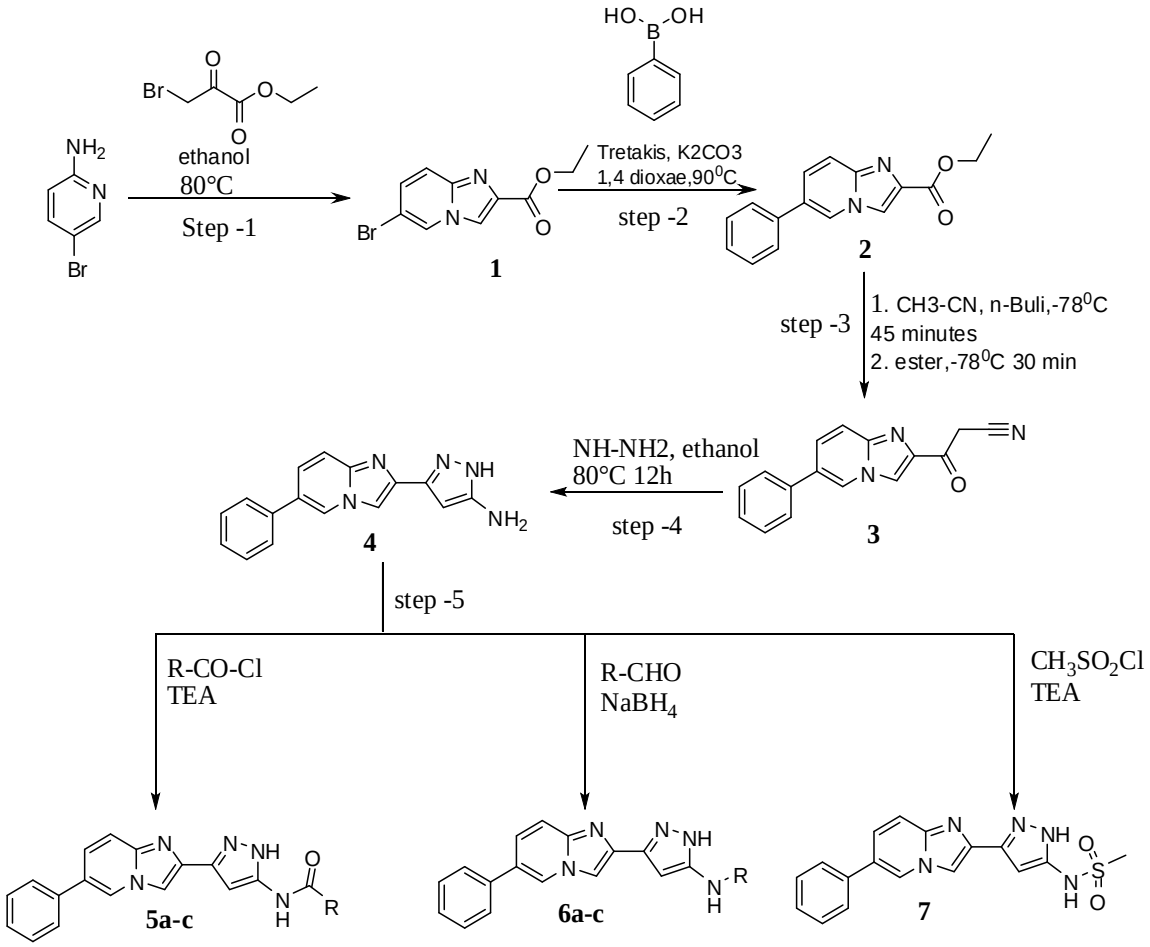
N-(4-fluorobenzyl)-3-(6-phenylimidazo [1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine (6c)

To a solution of 3-(6-phenylimidazo[1,2-a]pyridin-2-yl)-1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in methanol (15 ml) was added 4-fluoro benzaldehyde (0.675g 5.45 mmol) and reaction mixture was stirred for 5h at 35°C, then after $NaBH_4$ (0.345g 9.09 mmol) was added and reaction mixture was stirred at 35°C for 5 hrs Reaction progress was monitor by TLC (MeOH: MDC 1:9) after completion of reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.3% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 50mg: 7.18%).LCMS (ESI) m/z (M+H**):** 384.45; mp 202-210°C, IR (cm-1): 3555 (N-H stretching of secondary amine), 3059 (C-H stretching of aromatic ring), 1542, 1501 and 1453 (C=C stretching of aromatic ring),

1H-NMR (DMSO-d_6) δ: 4.26 (d, *J*=5.86 Hz, 2H) 5.86 (br, 1H), 7.14 (t, *J*=8.8 Hz, 2H), 7.31 (d, *J*=8.4 Hz, 2H), 7.41 (t, *J*=7.6 Hz, 1H), 7.55 (t, *J*=7.6 Hz, 2H), 7.61 (s, 2H), 7.72 (d, *J*=7.2 Hz, 2H), 8.16 (s, 1H), 8.92 (s, 1H), 12.08 (s, 1H). Anal. Calcd. For $C_{23}H_{18}FN_5$: C, 72.05; H, 4.73; F, 4.95; N, 18.27; Found: C, 72.06; H, 4.72; F, 4.93; N, 18.29%

N-(3-(6-phenylimidazo[1,2-a]pyridin-2-yl)-1H-pyrazol-5-yl)methanesulfonamide (7):

To a solution of 3-(6-phenylimidazo [1,2-a] pyridin-2-yl) -1H-pyrazol-5-amine**(4)** (0.500g 1.81 mmol) in THF (10 ml) was added Triethyl amine (0.366g 3.63 mmol) and the reaction mixture was stirred for 10 minutes, then after solution of methanesulfonyl chloride (0.230g 1.99 mmol) In THF was added and the reaction mixture was stirred at 35°C for 45 minutes Reaction progress was monitored by TLC (MeOH: MDC 1:9) after completion of the reaction, the reaction mixture was poured into water, and extracted with ethyl acetate, the organic layer was dried with Na_2SO_4 and distilled out under reduced pressure. Crude material was purified by column chromatography eluting 0.5% MDC in methanol. Pure fractions were combined and distilled out under reduced pressure. (Yield 56mg: 8.91%), LCMS (ESI) m/z (M+H):354.30; mp 232-239°C; IR (cm-1): IR (cm-1): 3366 (N-H stretching of secondary amine), 1338 and 1145 (SO2 str), 3058 (C-H stretching of aromatic ring), 1544, 1500 and 1452 (C=C stretching of aromatic ring), 1H-NMR (DMSO-d_6) δ: 3.11 (s, 3H), 6.72 (s, 1H), 7.47-7.59 (m, 3H), 7.79 (t, *J*=7.2 Hz, 2H), 7.89 (t, *J*=8.8 Hz, 1H), 8.10 (s, 1H), 8.52 (s, 1H), 9.23 (s, 1H), 10.19 (s, 1H), 13.87 (s, 1H). Anal. Calcd. For $C_{17}H_{15}N_5O_2S$: C, 57.78; H, 4.28; N, 19.82; O, 9.05; S, 9.07; Found: C, 57.78; H, 4.29; N, 19.83; O, 9.04; S, 9.06%



(i) Ethyl bromopyruvate, ethanol. 80°C, (ii) Phenyl boronic acid, Aq K_2CO_3 sol, Tetrakis, 2h ,(iii) (a) CH_3CN, n-Buli,-78°C 45min, (b) Ester,-78°C 30 min, (iv) NH2-NH2,ethanol 80°C, 12h, (v), (a) Acid chloride, TEA, THF, (b) Aldehyde, $NaBH_4$ (c)CH_3SO_2Cl, TEA,THF

3. Conclusion

Here, in this article we have incorporated an efficient method for the synthesis of Imidazole pyridine pyrazole derivatives. As per the literature survey these molecules of are showing excellent biological activity. At present we have not shown any biological screening of the newly synthesized compounds but the work is under progress. So, we will publish with their other computational studies like molecular docking and QSAR study.

4. Acknowledgement

The authors are thankful to Cadila Health care Pvt. Ltd for providing research facilities.

5. References

1. F. Couty and G. Evano, in Comprehensive Heterocyclic Chemistry III, ed. A. R. Katritzky, C. A. Ramsden, E. F. V. Scriven and R. J. K. Taylor, Elsevier, Oxford, 2008, vol. 11, p. 409; (b) J. Liu and Q. Chen, Huaxue Jinzhan, 2010, 22, 631; (c) J. Zhou, J. Liu and Q. Chen, Youji Huaxue, 2009, 29, 1708; (d) C. Enguehard-Gueiffier and A. Gueiffier, Mini-Rev. Med. Chem., 2007, 7, 888; (e) G. Bartholini, L.E.R.S. Monogr. Ser., 1993, 8, 1; (f) E. Abignente, Actual. Chim. Ther., 1991, 18, 193.
2. Y. Rival, G. Grassy and G. Michel, Chem. Pharm. Bull., 1992, 40, 1170.
3. M. H. Fisher and A. Lusi, J. Med. Chem., 1972, 15, 982.
4. Y. Rival, G. Grassy, A. Taudou and R. Ecalle, Eur. J. Med. Chem., 1991, 26, 13.
5. C. Hamdouchi, J. de Blas, M. del Prado, J. Gruber, B. A. Heinz and L. Vance, J. Med. Chem., 1999, 42, 50.
6. J. J. Kaminsky and A. M. Doweyko, J. Med. Chem., 1999, 40, 427.
7. K. C. Rupert, J. R. Henry, J. H. Dodd, S. A. Wadsworth, D. E. Cavender, G. C. Olini, B. Fahmy and J. Siekierka, Bioorg. Med. Chem. Lett., 2003, 13, 347.
8. M. Hammad, A. Mequid, M. E. Ananni and N. Shafik, Egypt. J. Chem., 1987, 29, 5401.
9. E. Badaway and T. Kappe, Eur. J. Med. Chem., 1995, 30, 327.
10. M. Hranjec, M. Kralj, I. Piantanida, M. Sedi, L. Suman, K. Pavel and G. Karminski-Zamola, J. Med. Chem., 2007, 50, 5696.
11. S. K. Kotovskaya, Z.M. Baskakova, V. N. Charushin, O. N. Chupakhin, E. F. Belanov, N. I. Bormotov, S. M. Balakhnin and O. A. Serova, Pharm. Chem. J., 2005, 39, 574.
12. M. Lhassani, O. Chavignon, J. M. Chezal, J. C. Teulade, J. P. Chapat, R. Snoeck, G. Andrei, J. Balzarini, E. D. Clerc and A. Gueiffier, Eur. J. Med. Chem., 1999, 34, 271.
13. C. Humphries, E. Gancia, M. T. Gilligan, S. Goodacre, D. Hallett, K. J. Marchant and S. R. Thomas, Bioorg. Med. Chem. Lett., 2006, 16, 1518.
14. K. Fuchs, M. Romig, K. Mendla, H. Briem and K. Fechteler, WO2002014313, 2002 (Chem. Abstr., 2002, 136, 183824r).
15. D. Dvey, P. W. Erhardt, W. C. Lumma Jr., J. Wiggins, M. Sullivan, D. Pang and E. Cantor, J. Med. Chem., 1987, 30, 1337.
16. C. J. R. Fookes, T. Q. Pham, F. Mattner, I. Greguric, C. Loch, X. Liu,P. Berghofer, R. Shepherd, M.-C. Gregoire and A. Katsifis, J. Med. Chem., 2008, 51, 3700.
17. S. Z. Langer, S. Arbilla, J. Benavides and B. Scatton, Adv. Biochem. Psychopharmacol., 1990, 46, 61.
18. K. Mizushige, T. Ueda, K. Yukiiri and H. Suzuki, Cardiovasc. Drug Rev., 2002, 20, 163.
19. L. Almirante, L. Polo, A.Mugnaini, E. Provinciali, P. Rugarli, A. Biancotti, A. Gamba and W. Murmann, J. Med. Chem., 1965, 8, 305.
20. R. J. Boerner and H. J. Moller, Psychopharmakother, 1997, 4, 145.
21. K. Gudmundsson and S. D. Boggs, PCT Int. Appl., WO 2006026703, 2006.
22. H. L. Koo and H. L. Dupont, Curr. Opin. Gastroenterol., 2010, 26, 17.
23. John, M. M. Shaikh and P. Ghosh, Dalton Trans., 2009, 10581.
24. G. Song, Y. Zhang and X. Li, Organometallics, 2008, 27, 1936.
25. A. Douhal, F. Amat-Guerri and A. U. Acuna, J. Phys. Chem., 1995, 99, 76; (b) A. Douhal, F. Amat-Guerri and A. U. Acuna, Angew. Chem., Int. Ed. Engl., 1997, 36, 1514; (c) A. Douhal, Ber. Bunsen-Ges., 1998, 102, 448.