International Journal for Pharmaceutical Research Scholars (IJPRS)

V-5, I-4, 2016 ISSN No: 2277 - 7873

RESEARCH ARTICLE

Efficient Synthesis and Characterization of Novel 2-Aminobenzothiazole Derivatives

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Manuscript No: IJPRS/V5/I4/00160, Received On: 08/12/2016, Accepted On: 16/12/2016

ABSTRACT

Benzothiazole, a multifaceted nucleus, has been under research for the last two decades. Being a heterocyclic compound, benzothiazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. As a part of systematic investigations several new derivatives of 2-aminobenzothiazols 5a-e have been prepared. The structure elucidation of these compounds was completed by means of chemical tests, elemental (C, H, N and S) and spectral (IR, ^{1}H NMR and mass) analysis.

KEYWORDS

2-aminobenzothiazole, benzamides, benzoyl isothiocyanate

INTRODUCTION

The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide because heterocyclic compounds are widely occurring in nature and are significantly essential to life[1]. A number of heterocyclic derivatives containing nitrogen and sulphur atom serve as a unique and versatile scaffolds for experimental drug design and form the core structure of many biologically active[2,3]. Benzothiazoles have been found to possess a broad spectrum of pharmacological activities such as antibacterial[4], anticancer[5,6], antidiabetic[7], antifungal[8], anti-Inflammatory[9,10], antimicrobial[11,12], anti-proliferative[13], antimalarial[14], antitumor[15,16], antiviral[17], anthelmintics[18,19] and anticonvulsant[20] activities.

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In view of the applications of 2-aminobenzothiazoles and benzoyliso-thiocyanates, several new compounds containing these moieties have been synthesized. The structures of compounds are confirmed by elemental (C, H, N and S) and spectral (IR, ^{1}H NMR and mass) analysis.

MATERIALS AND METHODS

All reactions were performed in oven-dried glassware's with magnetic stirring. All the chemicals and solvents are obtained from E-Merck, India (AR grade) and were used without further purification. Melting points of compounds were taken in an open capillary tubes by Toshniwal melting point apparatus in Celsius scale and uncorrected. The purity of the compound was verified by performing thin layer chromatography (TLC) on silica gel G (Merck) coated glass plates and spots were visualized by exposure to iodine vapors using Toluene : ethyl acetate (1:1) as a solvent system. IR spectra were recorded using KBr pellets on FTIR spectrophotometer (Perkin Elmer - Spectrum RX-IFTIR). ^{1}H-NMR spectra were recorded on

sophisticated multinuclear FT NMR Spectrometer model Advance-II (Bruker) (CIL, Chandigarh, India); ^{1}H frequency is 400 MHz Chemical shift (δ) are expressed in ppm relative to tetra methyl silane (TMS) as an internal standard. Mass spectra (FAB-MS) were recorded on Waters Micromass Q-T of Microspectrophotometer (SAIF, Chandigarh, India) and elemental analysis were carried out using Elementar Vario EL III CHN analyzer (STIC India, Cochin).

General Procedure for the Synthesis of 2-Aminobenzothiazoles [2]

A saturated solution of ammonium thiocyanate (0.12 mole) 30g in 60 mL water was added slowly on to the warm mixture of aniline (0.25 mole) and conc. HCl (0.25 mole) with shaking. The solid obtained (phenyl thiourea) was filtered, washed with water, dried and crystallized from distilled water so as to get pure compound.

To the Phenylthiourea (0.5 mole) sufficient amount of chloroform was added to get slurry and brominated using 5% bromine solution in chloroform till orange red colour appeared. The slurry was kept overnight. The solid hydrobromide obtained was filtered and washed several times with chloroform till the disappearance of orange red color. It was dissolved in alcohol and basified with 10% NH_4OH. The solid 2-aminobenzothiazole was filtered, washed with water, dried and recrystallized from ethanol.[21]

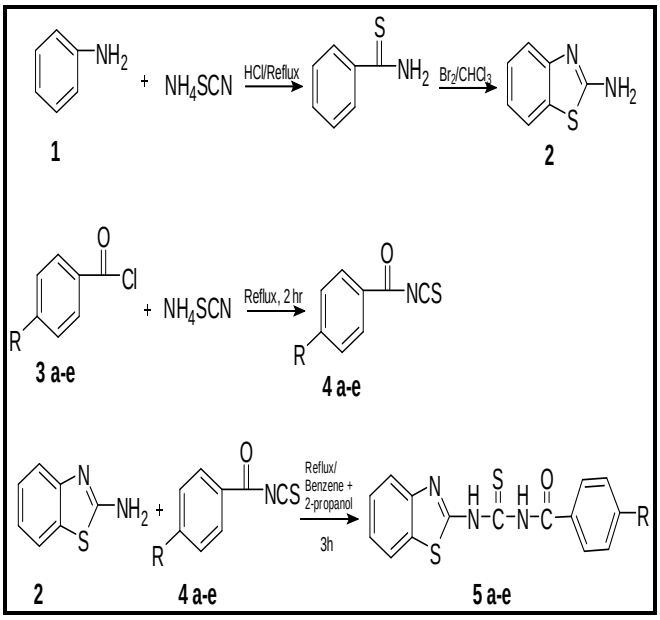
Synthesis of 4-substituted benzoyl isothiocyanate (4a-4e)

Substituted benzoyl chloride (0.1 mole) was added dropwise on to a solution of ammonium thiocyanate (0.1 mole) in dry benzene (25ml) with vigorous stirring. The mixture was boiled for two hours. cooled and filtered. The filtrate contains benzoyl isothiocyanate.[22]

Synthesis of Novel 2-Aminobenzothiazole Derivatives (5a-5e)

The mixture of 2-aminobenzothiazole (0.01mole) **(2)** and benzoyl isothiocynate (0.01mole) **(4a-e)** in dry benzene (25mL) and 2-propanol (5mL) was refluxed for 3 hours, The solid obtained solid was filtered, washed with benzene, dried and recrystallized from benzene.

Scheme I. Synthesis of novel 2-Aminobenzothiazole derivatives (5a-5e)



The spectral data of (5a-5e) are given below.

(5a).m.p.: 189; IR (KBr, ν_{max}, cm^{-1}): 1072.53 (C=S, stretching), 1547.25 (Ar C=C, stretching), 1612 (C=N, stretching), 1670.38 (C=O, stretching), 3056 (Ar C-H, stretching), 3378, 3169 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm), 7.52-8.07 (m, 9H, Ar-H), 8.18 (s, 1H, NHC=O, D_2O exchangeable), 12.28 (bs, 1H, NHC=S, D_2O exchangeable). Mass spectra, (EI) m/z: 313(M^+ peak).

(5b).m.p.: 254^{0}C; IR (KBr, ν_{max}, cm^{-1}): 801.12 (C-Cl, stretching), 1052.13 (C=S, stretching), 1544.15 (Ar C=C, stretching), 1642.71 (C=N, stretching), 1652.31 (C=O, stretching), 3106.24 (Ar C-H, stretching), 3368.34, 3143.54 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.58-8.28 (m, 8H, Ar-H), 8.84 (s, 1H, NHC=O, D_2O exchangeable), 13.05 (bs, 1H, NHC=S, D_2O exchangeable); Mass spectra, (EI) m/z: 347(M^+ peak).

(5c).m.p.: 199^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1091.13 (C=S, stretching), 1461 (CH_3, bend), 1591.18 (Ar C=C, stretching), 1598.73 (C=N, stretching), 1677.34 (C=O, stretching), 2923 (C–H, stretching), 3082.19 (Ar C-H, stretching),

Table 1: Physico-chemical properties of Novel 2-Aminobenzothiazole Derivatives

Product Code	R	R_1	Mol. formula	Mol. weight	Yield (%)	M.P ^0C	Found (calculated) %			
							C	H	N	S
5a	H	H	$C_{15}H_{11}N_3OS_2$	313.40	83	189	56.39 (57.49)	3.49 (3.54)	13.52 (13.41)	20.49 (20.46)
5b	H	4-Cl	$C_{15}H_{10}ClN_3OS_2$	347.84	80	254	51.82 (51.79)	2.88 (2.90)	11.93 (12.08)	18.56 (18.44)
5c	H	4-CH_3	$C_{16}H_{13}N_3OS_2$	327.42	78	199	58.81 (58.69)	3.96 (4.00)	12.68 (12.83)	19.48 (19.59)
5d	H	4-OCH_3	$C_{16}H_{13}N_3O_2S_2$	343.42	79	172	56.12 (55.96)	3.78 (3.82)	12.46 (12.24)	17.98 (18.67)
5e	H	4-NO_2	$C_{15}H_{10}N_4O_3S_2$	358.39	88	268	51.05 (50.27)	3.07 (2.81)	15.23 (15.63)	16.71 (17.89)

3288.31, 3174.49 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.42-8.18 (m, 8H, Ar-H), 9.73 (s, 1H, NHC=O, D_2O exchangeable), 12.82 (bs, 1H, NHC=S, D_2O exchangeable), 2.37 (s, 3H, CH_3); Mass spectra, (EI) m/z: 327(M^+ peak).

(5d).m.p.: 172^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1123.83 (C=S, stretching), 1568.53 (C=N, stretching), 1681.14 (C=O, stretching), 1635.18 (Ar C=C, stretching), 2768 (O- CH_3, stretching), 2936.74 (C–H Aliph, stretching), 3071.13 (Ar C-H, stretching), 3381.39, 3167.37 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.22-8.12 (m, 8H, Ar-H), 8.20 (s, 1H, NHC=O, D_2O exchangeable), 12.59 (bs, 1H, NHC=S, D_2O exchangeable), 3.82 (s, 3H, OCH_3); Mass spectra, (EI) m/z: 343 (M^+ peak).

(5e).m.p.: 268^{0}C; IR (KBr, ν_{max}, cm^{-1}): 1113.16 (C=S, stretching), 1326 (C-NO_2, stretching), 1498.03 (Ar C=C, stretching), 1623.91 (C=N, stretching), 1661.80 (C=O, stretching), 3086.47 (Ar C-H, stretching), 3396.41, 3184.76 (NH, stretching); ^{1}H NMR (DMSO, δ, ppm): 7.25-8.26 (m, 8H, Ar-H), 9.86 (s, 1H, NHC=O, D_2O exchangeable), 13.02 (bs, 1H, NHC=S, D_2O exchangeable). Mass spectra (EI) m/z: 358 (M^+ peak).

RESULTS AND DISCUSSION

With the aim of obtaining more precise information about the course of reaction and some interesting pharmaceutical compounds, we have reported here the action of 2-aminobenzothiazole [2] on different benzoyl isothiocyanates [4a-e] to obtain new heterocyclic compounds with expected biological activity.

Synthesis of 2-aminobenzothizoles was carried out according to the synthetic root sketched in the scheme I. Anilines were converted into phenyl thiourea by reaction with HCl and ammonium thiocyanate which on cyclization with bromine produced corresponding hydrobromide which was converted into 2-aminobenzothiazoles upon basification. The yields of the respective 2-aminobenzothiazoles were found to be excellent. The 2-aminobenzothiazole showed characteristic peaks at 1257-1294 cm^{-1} for (C-S) , 1310-1434 cm^{-1} for (C-N), 1567-1625 cm^{-1} for (C=N), 3341 - 3410 cm^{-1} for (NH) in FTIR spectral data. The ^{1}H NMR Spectra shows a broad singlet at 5.21 - 6.28 ppm due to (–NH_2) protons (D_2O exchangeable) besides those for aromatic protons in the region 6.93 - 8.24ppm. Benzoylation of

ammonium thiocyanates gave corresponding products [4a-e]. The FTIR bands showed band for (C=O) at 1682-1728 cm^{-1} and (N-C-S) at 2125-2245 cm^{-1}. The ^{1}H-NMR spectrum showed multiplet at δ 7.19-8.39 for aromatic protons. The target compounds were synthesized by a slight modification of previously (less time and high yield) procedure[23], the reaction was carried out in benzene – 2-propanol (5:1) mixture. Thus, interaction of 2-aminobenzothiazoles [2] with benzoyl isothiocyanates [4a-e] gave [5a-e] with excellent yield (scheme I).

CONCLUSION

We have synthesized several novel derivatives of 2-aminobenzothiazole 5a-e in good to excellent yields and characterize by elemental and spectral analysis.

ACKNOWLEDGMENTS

We greatly acknowledge to The Principal and the Head of Department of Applied Chemistry, Shri Ramdeobaba College of Engineering and Management, Nagpur for their support for laboratory facilities.

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