SYNTHESIS OF BENZOTHIAZOLE DERIVATIVES

Dissertation submitted to GOA UNIVERSITY in partial fulfilment of the requirement for the degree of

Master of Science in Chemistry

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STATEMENT

I hereby declare that the matter presented in this dissertation entitled, “Synthesis of Benzothiazole Derivatives” is based on the result of investigation carried out by me in the School Of Chemical Science, Goa University under the supervision of Ms Siddhali. V. Girkar and the same has not been submitted elsewhere for the award of a degree or diploma.

Utkarsha .U. Mayekar

CH-18-045

CERTIFICATE

This is to certify that the dissertation entitled, “Synthesis of Benzothiazole Derivatives” is bonafide work carried out by ‘Utkarsha U. Mayekar’ under my supervision in partial fulfilment of the requirements for the award of the degree of Master of Science in Chemistry at the School Of Chemical Science, Goa University.

Ms.Siddhali V. Girkar

Guiding Teacher

School Of Chemical Sciences

Goa University

ACKNOWLEDGEMENT

It gives us an immense pleasure to present this project report entitled ‘Synthesis of Benzothiazole Derivatives’.

The success and final outcome of this project required a lot of guidance and assistance from many people and I am extremely privileged to have got this all along the completion of my project. All that I have done is only due to such supervision and assistance and I would not forget to thank them.

I take this opportunity to express my deep gratitude and indebtness to my project guide Ms.Siddhali V. Girkar, Assistant Professor, School of Chemical Science, Goa University for her valuable guidance, encouragement and thoughtful discussion during the course of work. I am very grateful to her to give us the opportunity and appreciate ideas and allowing us the freedom take on the tasks independently, helping us to explore the things and enriching us with the knowledge.

My sincere thanks to Prof. V.S.Nadkarni, Dean of the School of Chemical Sciences, Goa University for permitting me to carry out this project work in our laboratory by providing all the necessary facilities during the project work.

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My deep sense of gratitude goes to all my friends and classmates for helping me and sharing ideas throughout my dissertation.

GENERAL REMARKS

IR spectra were recorded on Shimadzu FT-IR spectrophotometer (solid- KBr pellet/liquid-neat).

All melting points were measured by Thiel's tube method and are uncorrected.

Distilled solvents are used in all cases.

Commercial reagents were used without any further purification.

Ethyl acetate and pet ether for recording TLC refers to petroleum fraction boiling between 60 and 80^0C

All solvents and reagents were purified and dried by standard techniques.

All the reactions were monitored by thin layer chromatography (TLC) on silica gel.

Room temperature: 25-27^0C.

ABREVIATIONS

GENERAL ABREVATIONS:

MEASUREMENTS:

Aq. - Aqueous

Equiv - equivalent

Fig - Figure

G - Grams

Min - minutes

Mmol - milimol

m.p - melting point

r.t - room temperature

^{0}C - degree Celsius

TECHNIQUES:

TLC - Thin layer chromatography

IR - Infra Red

cm^{-1} - frequency in wavenumber

Δ - Delta (chemical shifts in ppm)

-

EXPERIMENTAL WORK:

1. Procedures for the synthesis of derivatives of Benzothiazole
   Chemicals required:
   p-substituted anilines :(0.1mole)
   Ammonium thiocynate: (0.2mole)
   Glacial acetic acid
   Bromine: (0.2mole)

A mixture of p-substituted anilines (0.1 mole) and ammonium thiocynate (0.2 mole) in 15 ml of glacial acetic acid were cooled in an ice bath and and stirred mechanically to the solution, bromine (0.2 mole) in 2.5 ml glacial acetic acid was added drop wise at such a rate to keep the temperature below 10^0C throughout the addition stirring was continued for another thirty minutes after the bromine addition. The precipitated of the Benzothiazole hydro bromide was collected, dissolved in hot water and basified with a sodium hydroxide solution. The product was filtered under vacuum washed with water, dried and recrystallized from the water.

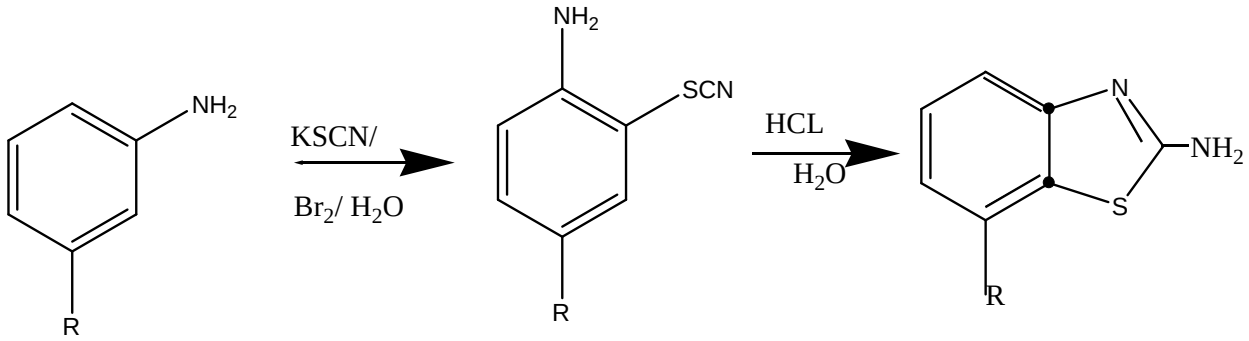
Literature review

Benzothiazole is a privileged bicyclic ring system with multiple applications. In the 1950s, a number of 2-aminobenzothiazoles were intensively studied as central muscle relaxants. Being a heterocyclic compound, Benzothiazole finds use in research as a starting material for the synthesis of larger, usually bioactive structures. Its aromaticity makes it relatively stable; although, as a heterocycle, it has reactive sites, which allow for functionalization. Benzothiazole is a colourless, slightly viscous liquid with a melting point of 2°C and a boiling point of 227-228°C. The density of Benzothiazole is 1.24 g/mL, and its molecular mass is 135.19 $gmol^{-1}$. Benzothiazole has no household use. It is used in industry and research.

Scheme 1:

Equimolar quantity of substituted aniline (0.02mol) & NH_4SCN (1.5g of 0.02mol) which dissolved in ethanol containing conc HCl (2mL) to this add Br_2 in glacial acetic acid then the reaction is refluxed for 1 hour after that cool the compound in ice water & obtain precipitate was filtered and wash using cold water & dried the precipitate. Then crude product is recrystallized with rectified spirit (95% ethanol) precipitate filtered using cold ethanol.

(Using KSCN)
Synthesis of 6-Cyno-2-aminobenzothiazole



Scheme 2

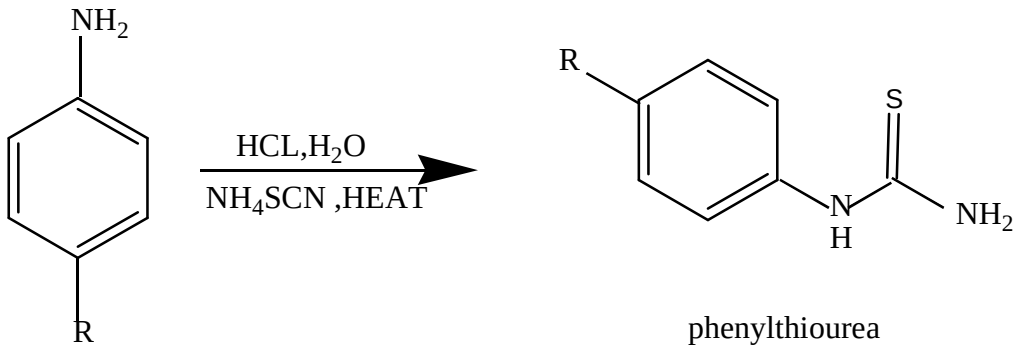
SYNTHESIS OF PHENYL THIOUREA

To substituted aniline 0.1mol in water, conc HCl was added and the solution was warmed. A saturated solution of potassium thiocynate 0.8 mole in water was added slowly with stirring in above HCl salt solution. Then the solution was heated for 4-5 hours until the solution became turbid. The turbid solution was poured in cold water. The separated precipitate was filtered, washed with water and recrystallized from ethanol, so as to obtain pure compound phenylthiourea.

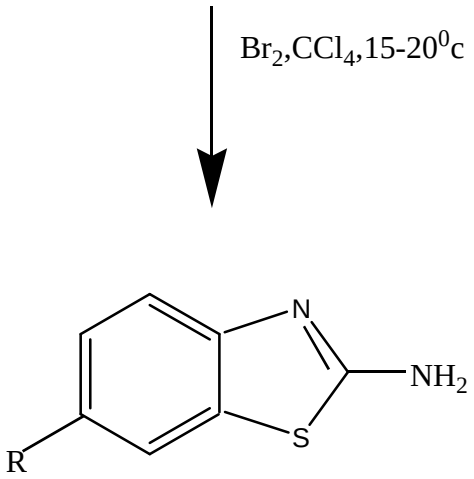
SYNTHESIS OF 2-AMINOBENZOTHIAZOLE

A solution of Br_2 (0.12 mol) in carbon tetrachloride was added drop wise to a solution of phenylthiourea (0.1 mol) in carbon tetrachloride. The reaction mixture was stirred for 2.5 hours at 15-20^{0}C. Then solvent was evaporated and the residue was dissolved in hot water, filtered and neutralized by aqueous ammonia to obtain white precipitate, which was recrystallized from ethanol, so as to obtain pure 2-aminobenzothiazole.

SYNTHESIS OF 2-aminobenzothiazole



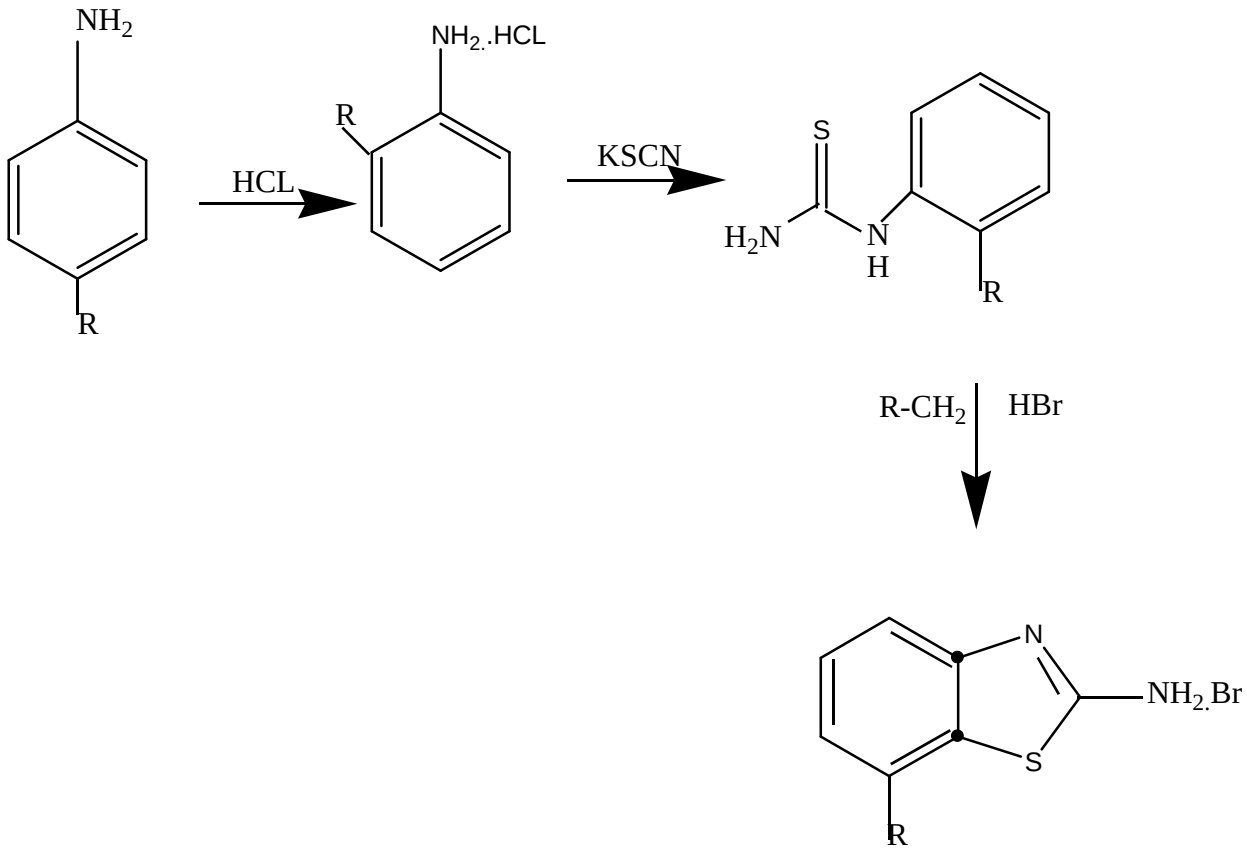
phenylthiourea



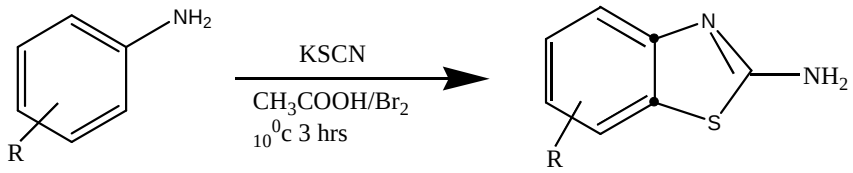
2-aminobenzothiazole

R= Cl, NO_2, CH_3

Scheme 3



Scheme 4

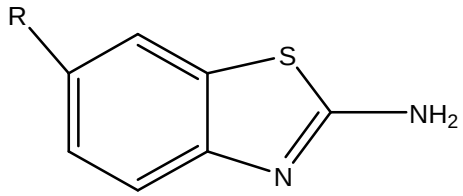


54% -64%

R- H,Cl, OH, NO_2, NH_2,CH_3,OMe

Present work

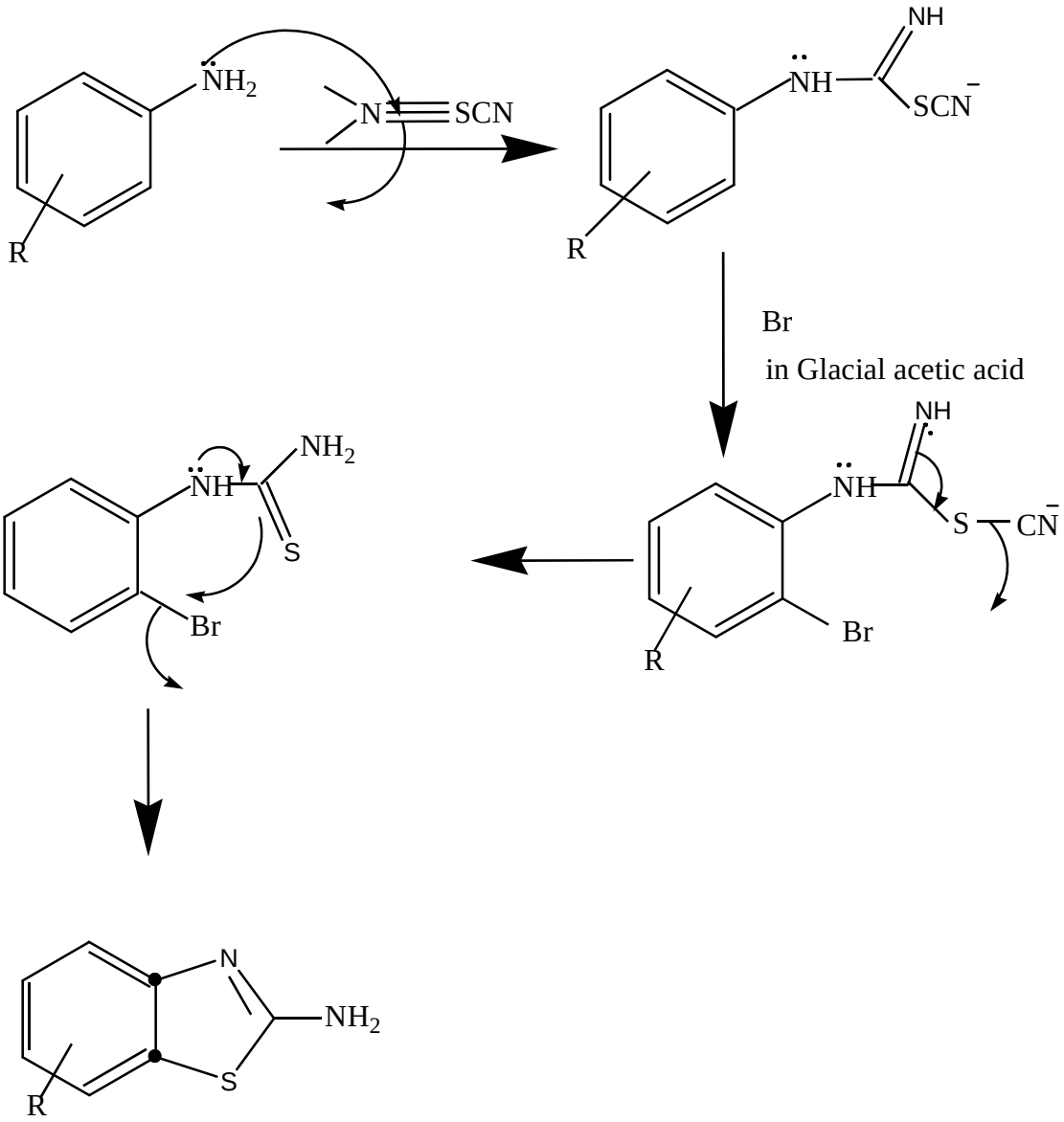
We have synthesized derivatives of Benzothiazole



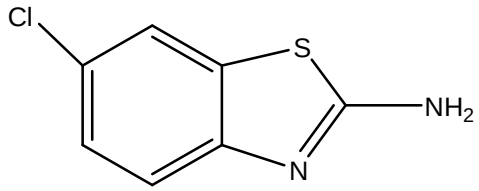
Compound	R	M.P (^{0}C)	Yield	Molecular formula	Molecular weight	Solvent for recrystallization
1	Cl	198-201	85%	$C_7H_5ClN_2S$	184	Distilled water
2	NO_2	243-247	80%	$C_7H_5NO_2N_2S$	195	Distilled water
3	CH_3	134-137	80%	$C_8H_8N_2S$	164	Distilled water
4	Br	213-217	70%	$C_7H_5BrN_2S$	245	Distilled water

Synthesised using above compounds and ammonium thiocynate and bromine in glacial acetic acid stirring for ½ hr in 10^0C. After that dissolved in min amount hot water and then basified using sodium hydroxide. Recrystallized using distilled water.

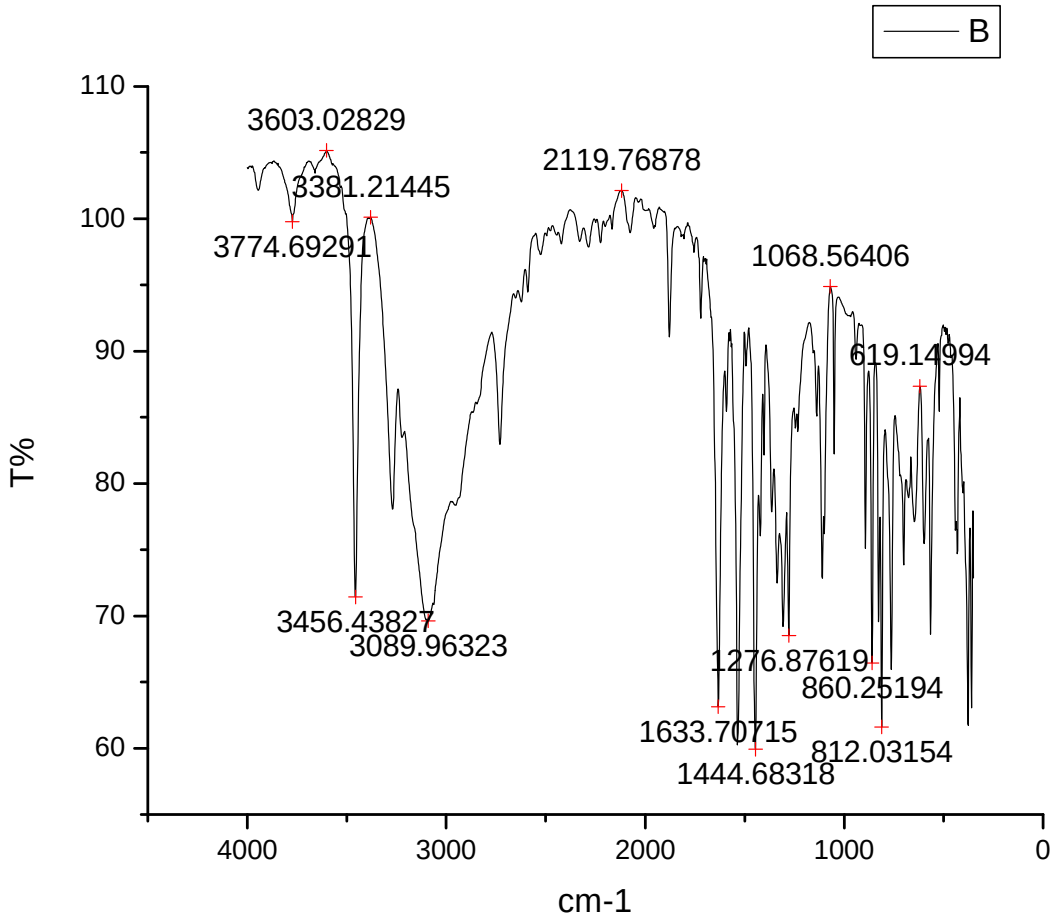
MECHANISM

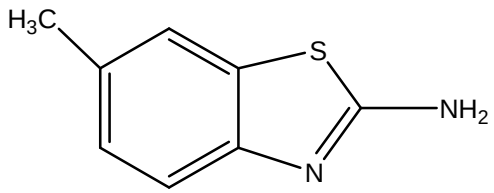


Spectral data

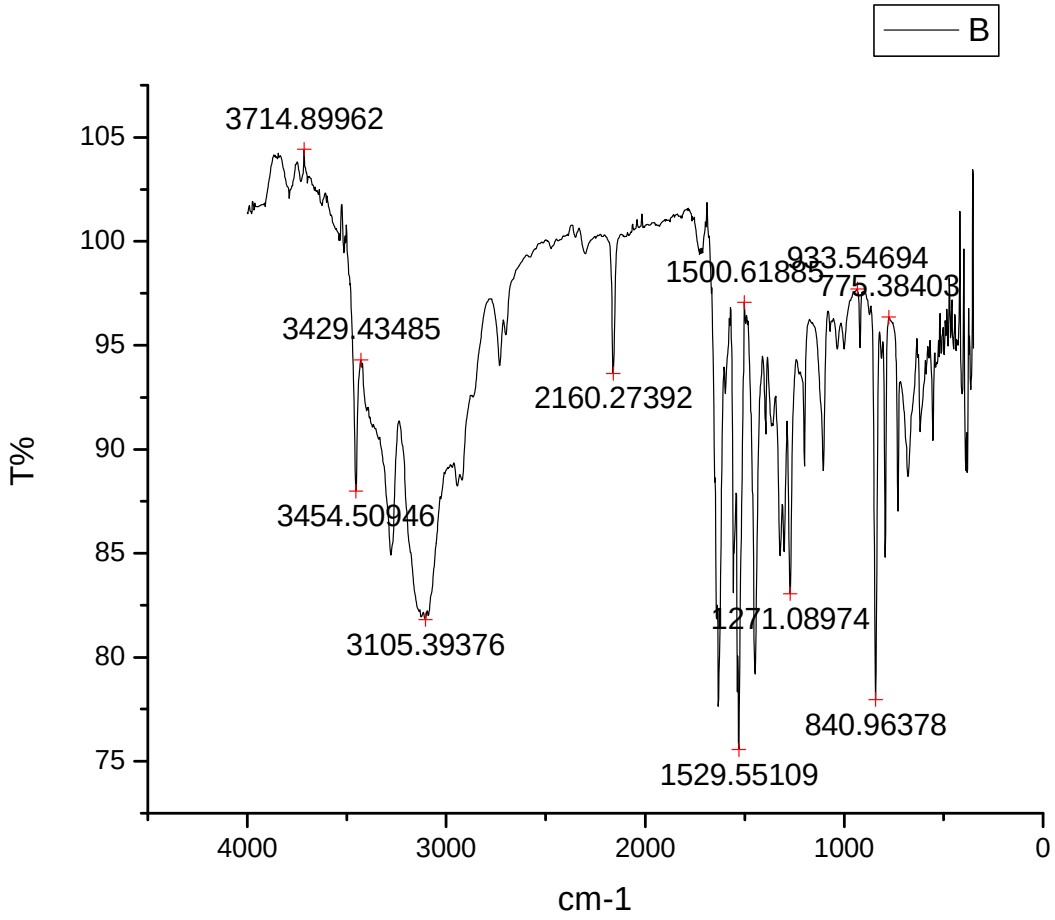


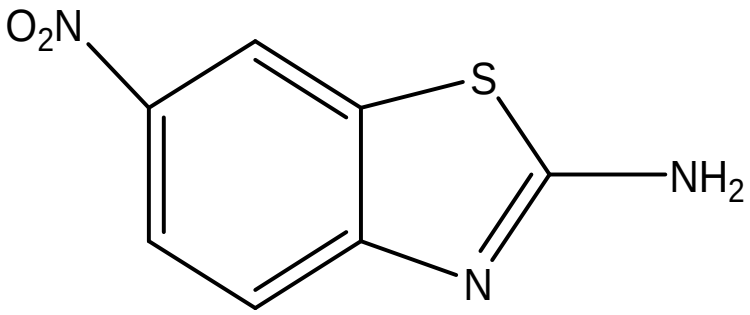
IR (KBr pellets): 3456.43(NH Stretch),3089.96(aromatic C-H Stretch), 1633.70(C=N Stretch), 1444.68(C-N Stretch), 1276.87(C-S Stretch), 812.03- 860.25(aromatic H bending), 619.14(C-Cl Stretching) cm^{-1}.



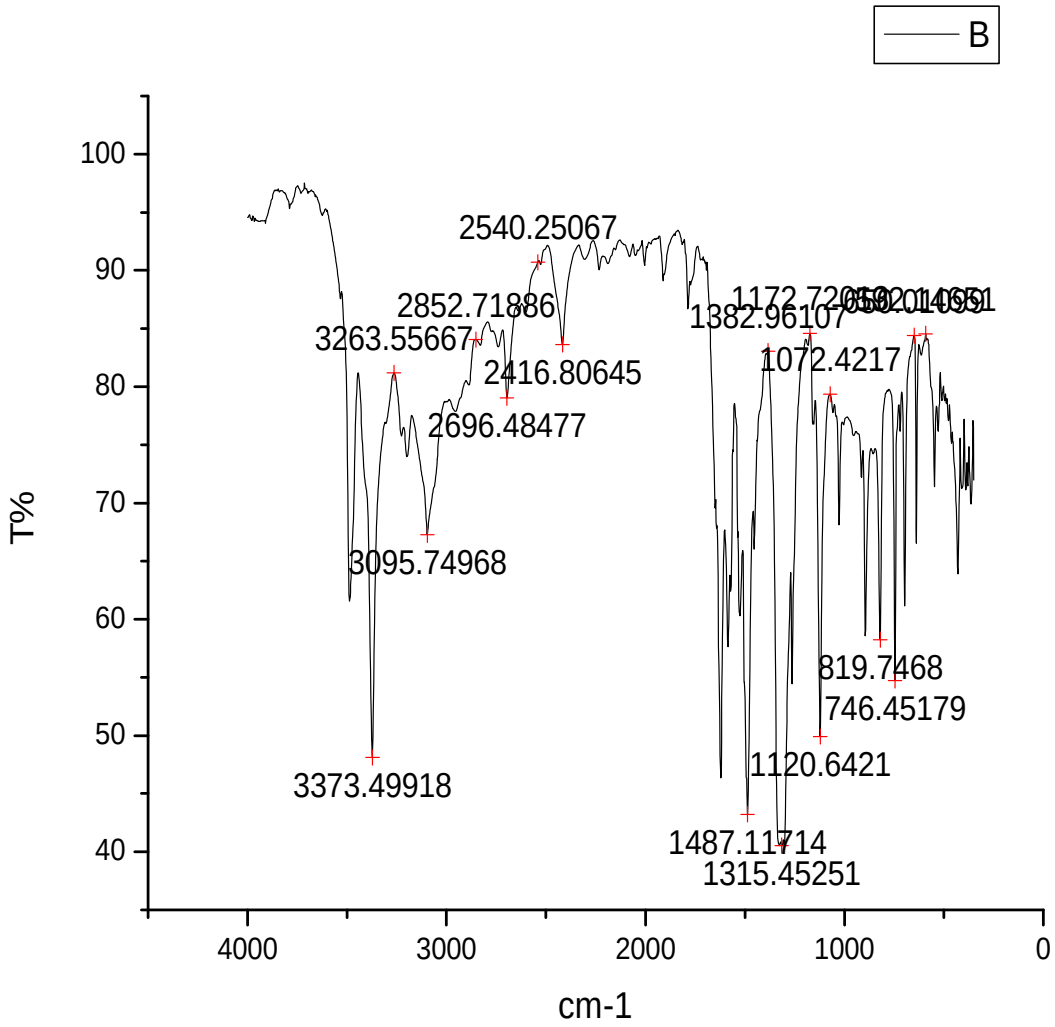


IR (KBr pellets): 3454.50(NH Stretch), 3105.39(aromatic C-H Stretch), 1529.55(C=N Stretch), 1500.61(C-N Stretch), 1271.08(C-S Stretch), 840.96-933.54(aromatic H Bending).





IR (KBr pellets): 3373.49(NH Stretch), 3095.74(aromatic C-H Stretch), 1622.13(C=N Stretch), 1487.11(C-N Stretch), 1120.64(C-S Stretch), 819.74-1072.42(aromatic H bending).



RESULTS AND DISCUSSION

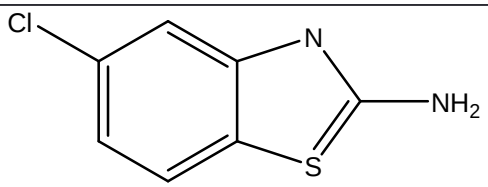
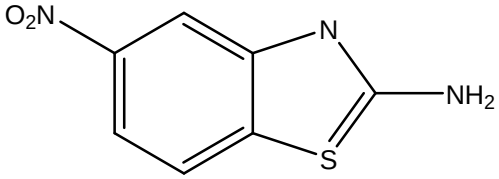
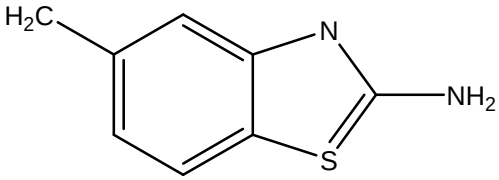
Entry	Structure	Name	colour	Yield	Time	Melting point
1		2-amino-6-chlorobenzathiazole	grey	70%	1 hr	100^0C
2		2-amino-6-nitrobenzathiazole	yellow	75%	1 hr	190^0C
3		2-amino-6-methylbenzatizole	white	70%	1 hr	120^0C

Table no 1:

Synthesis of 2-amino-6-chlorobenzothiazole by using KSCN synthesized compounds failed as they were sticky and spectral data also not matching i.e. m.p, IR, TLC.

Table No: 2

Synthesis of derivatives of phenylthiourea.

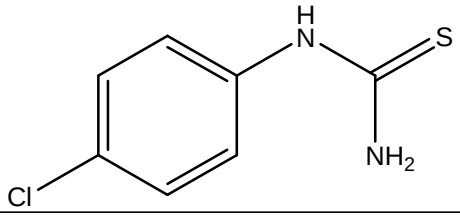
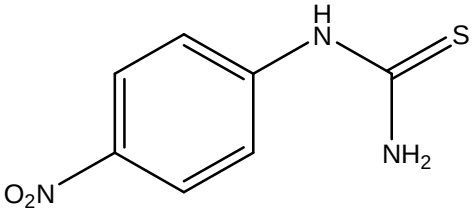
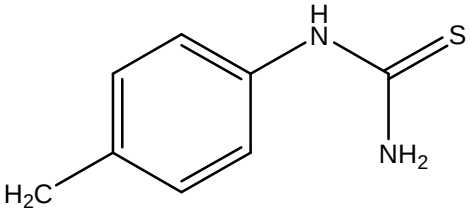
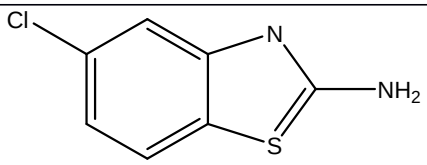
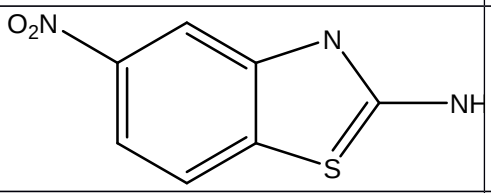
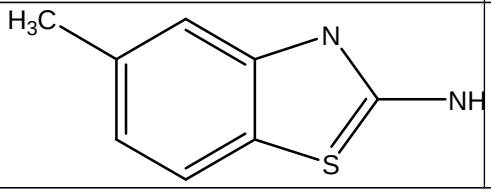
Entry	**Structure**	**Name**	**colour**	**Yield**	**Time**	**Melting point**
1		4-chlorophenylthiourea	grey	70%	4-5 hrs	–
2		4-nitrophenylthiourea	Yellow	75%	4-5 hrs	~243^{0}C
3		4-methylphenylthiourea/p-Tolylthiourea	white	70%	4-5 hrs	–

Table No:3

Synthesis of derivatives 2-amino-6-sub-benzothiazole

Entry	Structure	Name	Colour	Yield	Time	Melting point
1		2-amino-6-chlorobenzothiazole	grey	20%	2.5 hrs	110^0C
2		2-amino-6-nitrobenzothiazole	Yellow	40%	2.5 hrs	200^0C
3		2-amino-6-methylbenzotiazole	white	35%	2-5 hrs	150^0C

From TABLE NO 2 we had synthesized phenylthiourea and from this TABLE NO 3 we were to prepare 2-aminobenzathiazole but we synthesized phenylthiourea successfully but we failed to prepare 2-aminobenzathiourea as it was sticky and their spectral data was also not matching i.e TLC and melting point.

CONCLUSION:

Our aim was to synthesize Benzothiazole compounds from different derivatives.

So first we prepared four types of derivatives i.e. p-chloroaniline, p-toluidine , p-nitro aniline and p- bromoaniline.

But from some techniques that is melting point, TLC, and IR came to know that only two Benzothiazole derivatives was prepared and that is from p-chloroaniline and p-toluidine.

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