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SYNTHESIS OF 4-AMINO-5-SUBSTITUTEDDITHIOBIURETO-N-[2-(DIETHYL-AMINO) ETHYL]-O-ANISAMIDE

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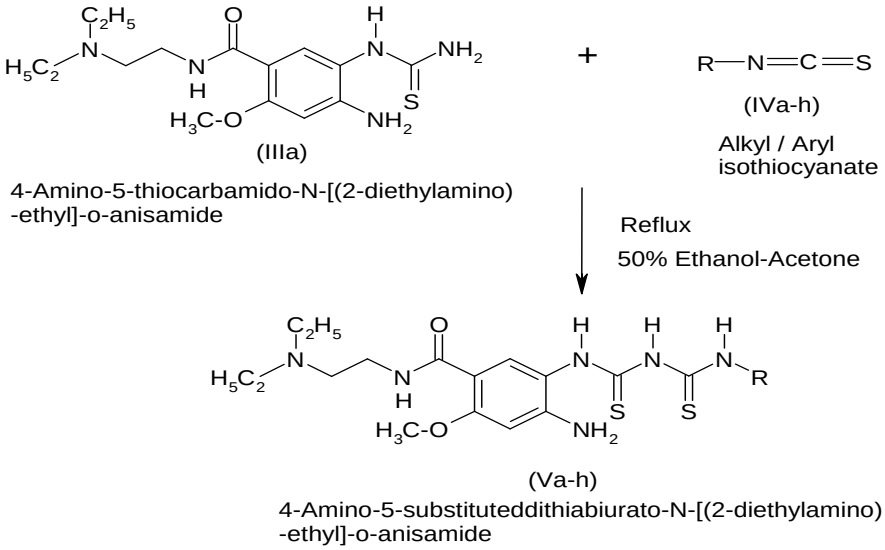
ABSTRACT

Recently in this laboratory suitable method for synthesis of 4-amino-5-substituteddithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamides **(Va-h)** was developed. The interactions of 4-amino-5-substituted thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide **(IIIa)** with various isothiocyanate **(IVa-h)** in 50% acetone-ethanol medium was carried out on water bath to synthesized . The structure of the synthesized compounds was justified on the basis of chemical characteristics, elemental analysis and spectral studies.

KEY WORDS:-Various isoyhiocyanate, 4-amino-5-substitutedthiocarbamido-N-[2-(diethylamino)- ethyl]-o-anisamide and acetone-ethanol.

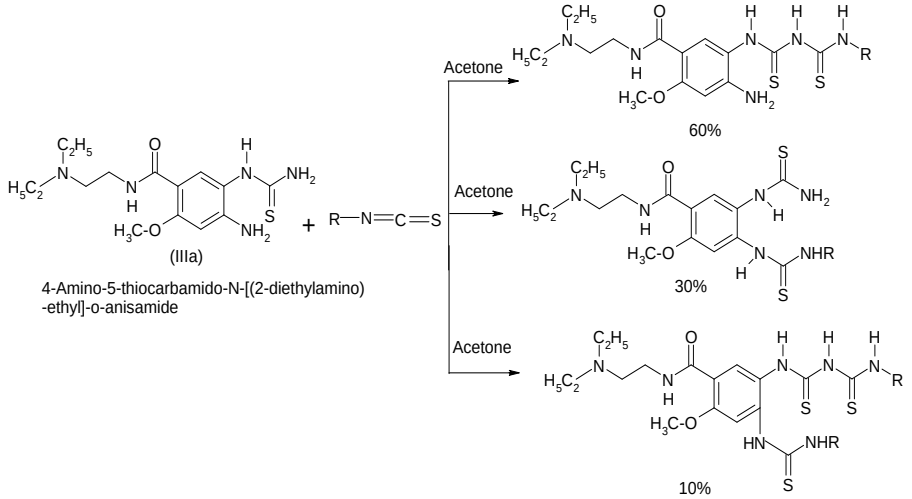
INTRODUCTION

The heteroacycles and heterocycles compounds contaningthiocarbamido, thiabiurato, dithiazine, dithiobiureto and thioamido nucleus have their own identity and significance, in pharmaceutical, agricultural, industrial and biochemical sciences.[1-4] These nucleus containing compounds enhance the potency and therapeutic value of that drug. Pund[5], Shelke[6], Bhagwatkar[7], Panpalia[8], Raghuvanshi[9] , Pandey[10], Pathe[11-13], Berad[14], Aprajit[15], Deohate[16], Kodape[17], Bhagwatkar[18] and Khobragade[19] synthesis several 5, 6 and 7 membered nitrogen, nitrogen and sulphurcontaining heterocycles with several references to 1,2,4-dithiazoles, 1,3,5-dithiazines, 1,3,5-thiadiazines. These compounds acts as drug and also possess properties that can be used in various medicinal, industrial, agricultural, biochemical applications. These types of compound possess most amazing properties like anti-tumor and anti-cancer.[20-22] Thiocarbamido nucleus containingheterocyclic compounds also showed antitubercular, antibacterial, antifungal, antiviral, and anti-inflammatory activities.[23-26] Considering this we designed present research work and developed new selective, suitable and direct method for the synthesis of the novel series of 4-amino-5-substituteddithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamides **(Va-h) Scheme-II.**



Scheme-II: Where R= -phenyl, -methyl, -ethyl, -t-butyl, -p-chlorophenyl, -o-tolyl, -m-tolyl, -p-tolyl

When this reaction is carried out in acetone medium then these types of products were isolated as shown below.



In ethanol this reaction is not possible so we carry out these reactions in various percentage compositions of acetone ethanol mixtures and we found that in 50% acetone ethanol mixture only one type of product is isolated **(Va-h)** as shown in (**scheme-II)**

MATERIALS AND METHOD

The melting point of the all synthesized compounds was recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29.IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400cm^{-1} in KBr pellets. PMR spectra were recorded on Brucker 400F spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as solvent. The purity of compound was checked on silica Gel-G Pellets by TLC with layer thickness of 0.3mm. All chemicals used were AR-grade.

Experiment No. 3

Synthesis of 4-amino-5-methyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Vc): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** methylisothiocyanate (0.1M) **(IVc)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4 hours on water bath, yellow crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 94 %, m.p.214˚C.

Experiment No. 4

Synthesis of 4-amino-5-t-butyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Vd): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** t-butylisothiocyanate (0.1M) **(IVd)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4 hours on water bath, faint yellow crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 88%, m.p. 218˚C.

Experiment No. 5

Synthesis of 4-amino-5-p-chlorophenyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Ve): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** p-chlorophenylisothio- cyanate (0.1M) **(IVe)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4 hours on water bath, lemon yellow crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 86%, m.p.226˚C.

Experiment No. 6

Synthesis of 4-amino-5-o-tolyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Vf): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** o-tolylisothiocyanate (0.1M) **(IVf)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4 hours on water bath, dark yellow crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 90%, m.p.222˚C.

Experiment No. 7

Synthesis of 4-amino-5-m-tolyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Vg): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** m-tolylisothiocyanate (0.1M) **(IVg)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4 hours on water bath, yellow crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 91%, m.p.220˚C.

Experiment No. 8

Synthesis of 4-amino-5-p-tolyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide (Vh): In 250 ml round bottom flask a mixture of 4-amino-5-thiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide (0.1M) **(IIIa),** p-tolylisothiocyanate (0.1M) **(IVh)** and 50% acetone-ethanol mixture (70 ml) was refluxed for 4

hours on water bath, ivory crystals were separated out, they were filtered and dried at room condition and recrystalised from ethanol. Yield 92%, m.p.230˚C.

RESULT AND DISCUSSION

a) Synthesis of 4-amino-5-phenyldithiobiureto-N-[2-(diethylamino)-ethyl] -o-anisamide (Va): 4-Amino-5-phenyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Va)** was synthesized by the refluxing 4-amino-5-substitutedthiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide **(IIIa)** with phenylisothiocyanate**(IVa)** in 1:1 molar proportion in 50% acetone-ethanol medium for 4 hours on water bath, ivory crystals were separated out, filtered and dried. Yield 94 %, m.p. 220˚C.

Properties:-It is pale yellow crystalline solid having m.p. 220 ˚C. It gave positive test for nitrogen and sulphur elements. It was desulphurized by alkaline plumbite solution. It was soluble in DMSO, dioxane, ethanol, acetone while insoluble in benzene. It formed picrate having m.p. 188˚C.**Elemental analysis:** C[(found 54.70%) calculated 55.69], H[found 06.60%)calculated06.32],N[(found17.20%)calculated17.72],S[(found12.56%)calculated13.50].

IR Spectrum[27-31]: The IR spectrum was carried out in KBr- pellets The important absorptions are correlated as (cm) 3391.14 C–H (Ar) Stretching,1644.21C = O stretching, 1428.20N-H stretching,1239.23C-N stretching,1018.12C=S stretching. **NMR Spectrum:** The NMR Spectrum[30] was carried out in DMSO-d_6 and $CDCl_3$This spectrum distinctly displayed the signals due to Ph-NH protons at δ 9.8829 ppm, and AR-H proton at δ 8.5041-6.4832 ppm, NH_2 protons at δ 5.9345-5.1091 ppm, NH protons at δ 4.6014-4.2602, -OCH_3 protons at δ 3.3998 ppm, CH_2 protons at δ2.5175-2.0898ppm, -CH_3 protons at δ 1.2371-0.9604 ppm.

b)Synthesis of 4-amino-5-ethyldithiobiureto-N-[2-(diethylamino) ethyl]-o-anisamide (Vb): 4-Amino-5-ethyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Vb)** was synthesized by refluxing the mixture of 4-amino-5-substitutedthiocarbamido-N-[2-(diethylamino)ethyl]-o-anisamide **(IIIa)** with ethylthiourea **(IVb)** in 50% acetone-ethanol medium for 4 hours in water bath, in 1:1 molar proportion, pale yellow crystals were separated out, they were filtered and dried. Yield 88%, m.p. 216˚C**.**

Properties:-It is pale yellow crystalline solid, m.p. 216˚C. It gave positive test gave for nitrogen and sulphur. It was desulpurized by alkaline plumbited solutions. It was soluble in DMSO, dioxane, ethanol, acetone, while insoluble in benzene. It formed picrate having m.p. 190˚C. **Elemental Analysis:** C[(found 50.00%) calculated 50.70], H[found06.50%) calculated07.04], N[(found18.70%) calculated19.71], S[(found14.71%)calculated15.02]. **IR Spectrum[27-31]:** The IR spectrum was carried out in KBr-pellets . The important absorptions are correlated as (cm):- 3435.2 C – H (Ar) Streching, 1644.00 C = O stretching, 1633.5 N-H stretching, 1248.6 C-N stretching, 1020.2 C=S stretching. **NMR Spectrum:** The NMR Spectrum[30] was carried out in DMSO-d_6 and $CDCl_3$. This spectrum distinctly displayed the signals due to Ar-H protons at δ 8.2978 ppm, NH proton at 3.3523 ppm, NH_2 protons δ 2.5151-2.5063 ppm, -OCH_3 protons at δ2.5018-2.4974 ppm, CH_2 protons at δ 2.0884 ppm, CH_3 protons at δ 1.25 ppm.

Similarly,4-Amino-5-methyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Vc),** 4-amino-5-t-butyldithiobiureto-N-[2-(diethyl amino) ethyl]-o-anisamide **(Vd),** 4-amino-5-p-chlorophenyldithiobiureto-N-[2-(diethyl amino)-ethyl]-o-anisamide **(Ve),** 4-amino-5-o-tolyldithiobiureto-N-[2-(diethyl amino)ethyl]-o-anisamide **(Vf),** 4-amino-5-m-tolyldithiobiureto-N-[2-(diethyl amino-ethyl]-o-anisamide **(Vg)** and 4-amino-5-p-tolyldithiobiureto-N-[2-(diethyl- amino)ethyl]-o-anisamide **(Vh)** were synthesis by the interactions of methyl- isothiocyanate**(IVc),** t-butylisothiocyanate **(IVd),** p-chlorophenylisothiocyanate **(IVe),** o-tolyl-isothiocyanate **(IVf),** m-tolylisothiocyanate **(IVg)** and p-tolylisothiocyanate **(IVh)** with 4-amino-5-thiocarbamido-N-[2-(diethyl-amino)ethyl]-o-anisamide **(IIIa)** in 50% acetone-ethanol medium respectively by above mentioned method. **(Table No. 1)**

Table No. 1

Sr. No	Expt. No.	4-Amino-5-**substituted**dithiobiureto -N-[2-(diethylamino)ethyl--anisamide	Yield (%)	M.P. (^{0}C)
1.	3.	4-Amino-5-**methyl**dithiobiureto-N-[2(diethylamino)ethyl]-o-anisamide	214	94
2.	4.	4-Amino-5-**t-butyl**dithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide	218	88
3.	5.	4-Amino-5-**p-chlorophenyl**dithio-biureto-N-[2-(diethylamino)ethyl]-o-anisamide	226	86
4.	6.	4-Amino-5-**o-tolyl**dithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide	222	90
5.	7.	4-Amino-5-**m-tolyl**dithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide	220	91
6.	8.	4-Amino-5-**p-tolyl**dithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide	230	92

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