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Synthesis of 3-[4-Amino-N-substituted-o-anisamido-5-yl]amino-5-substituted-1,2,4-dithiazole

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Abstract : A novel series of 3-{4-Amino-N-[2-(dithethylamino)ethyl]-o-anisamido-5-yl}amino-5-substitutedimino-1,2,4-dithiazole was synthesized by the oxidative cyclization of 4-amino-5-substituteddithiobiureto-N-[2-(dithethylamino)ethyl]-o-anisamide in chloroform medium by making the use of liquid bromine as oxidizing agent. The products were characterized and justified on the basis of elemental analysis, chemical characteristics and spectral studies.

Keywords : 3-{4-Amino-N-[2-(dithethylamino)ethyl]-o-anisamido-5-yl}amino-5-substitutedimino-1,2,4-dithiazole, 4-amino-5-substituteddithiobiureto-N-[2-(dithethylamino)ethyl]-o-anisamide, Bromine in Chloroform.

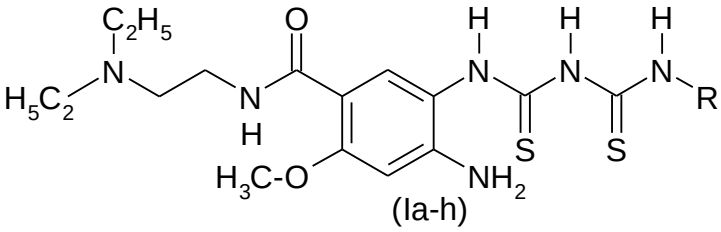
Introduction:

The literature survey shows that the dithiazolo, dithiazino and thiadiazino nucleus containing compounds are widely used in medicinal, industrial, agricultureal, biochemical sciences[1,7]. It was considered that these nucleus containing drugs possesses, antibacterial[8], antidiabetic[9], amoebicidal[10] herbicidal[11] properties. Iminosubstituted thiadiazolo nucleus also possesses noticeable pharmaceutical activities.

The heterocyclic compounds containing nitrogen, nitrogen and sulphur have gained huge important in our life. It was shows that thiadiazoles are also effective against copper corrosion[12] and additive in lubricating oil[13].

In recent years several 1,2,4-dithiazole and their derivatives were found to have prominent pharmacological activities such as anticonvulsant, analgesic anti-inflammatory activity.Dobolkar and Ansari[14] had successfully investigated oxidative cyclisation of cyanoamidino substituted thiocarbamide and N-substitutedformidinothiocarbamides.Various researchers[15-19] studied oxidative cyclisation of 1,3,4-thiadiazoles, 1,3,4-thiadiazolines and 1,2,4-triazoles.

As a part of research work presently undertaken in this laboratory in the synthesis of heteroacycles and heterocycles, it was thought interesting to investigate the cyclisation of 4-amino-5-substituteddithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamideswith liquid bromine in chloroform medium to obtain a novel series of 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-substitutedimino-1,2,4-dithiazoles which are heither to unknown. The present work describes suitable, convenient and somewhat direct method for this synthesis and depicted below

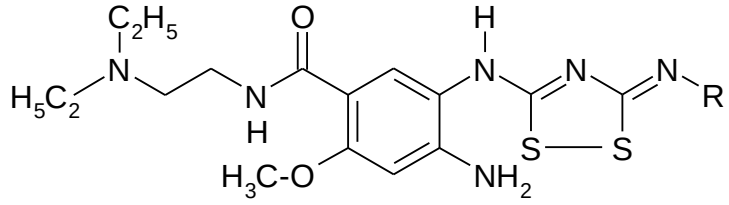


(Ia-h)

4-Amino-5-substituteddithiabiurato-N-[(2-diethylamino) -ethyl]-o-anisamide

Oxidative cyclisation

Br_2 $CHCl_3$



(IIa-h)

3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-substitutedimino-1,2,4-dithiazole.

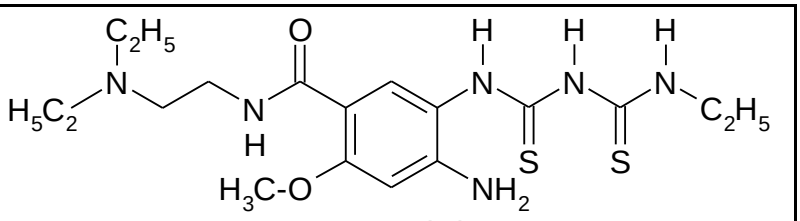
R= , methyl, t-butyl, phenyl, p-chlorophenyl, ethyl, o-tolyl, m-tolyl, p-tolyl.

Experimental:

The melting point of the all synthesized compounds was recorded using hot paraffin bath. The carbon and hydrogen analysis were carried out on Carlo-Ebra 1106 analyzer. Nitrogen estimation was carried out on Colman-N-analyzer-29. IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400 cm^{-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 0.3 mm. All chemicals used were AR-grade.

Synthesis of 3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-ethylimino-1,2,4-dithiazole

3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-ethylimino-1,2,4-dithiazoles was synthesized by the oxidative cyclization of 4-amino-5-ethyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide with liquid bromine in presence of chloroform. A paste of 4-amino-5-ethyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide was prepared in chloroform to it 10% liquid bromine in chloroform was added with constant stirring. Initially the colors of bromine disappear in the reaction mixture. The reaction mixture was allowed to stand for 8 hours, it afforded brown colored product. It was recrystalised from ethanol, yield 90%, m.p. 251˚C.

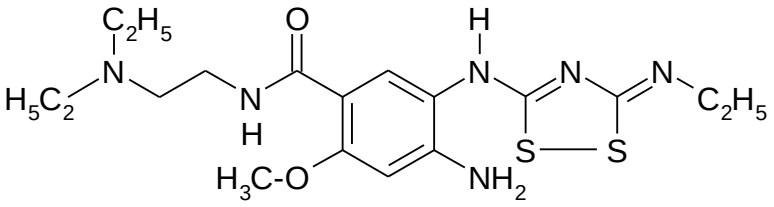


(Ia)

4-Amino-5-ethyldithiabiurato-N-[(2-diethylamino) -ethyl]-o-anisamide

Oxidative cyclisation

Br_2 $CHCl_3$



(IIa)

3-{4-Amino-N-[2-(diethylamino)-ethyl]-o-anisamido-5-yl}-amino-5-ethylimino-1,2,4-dithiazole.

Propertise :

It is brown colour crystalline solid having melting point 251˚C. It gave positive test gave for nitrogen and sulphur. It was desulpurized by alkaline plumbite solution. It formed picrate having melting point 179˚C.**Elemental Analysis :**C[(found 50.03%) calculated 50.94], H[(found 06.20%) calculated 06.60], N[(found 19.00%) calculated 19.81], S[(found 14.50%) calculated 15.09].**IR Spectrum**: The IR spectrum was carrid out in KBr pellets : 3429.00 (N-H stretching), 2923.24 (Ar-C=C stretching), 1639.05 (N-C=O stretching), 1506.08 (C=N stretching), 1092.21 (C-N stretching), 774.31 (C-S stretching). **NMR Spectrum**: The NMR spectrum of compound was carried out in $CDCl_3$ and DMSO-d_6. This spectrum distinctly displayed the signals due to Ar-H protons at δ 7.3000-7.152 ppm, –NH proton at δ 4.9072-4.2568 ppm, NH_2 protons at δ 3.9058-3.2062 ppm,-OCH_3 protons at δ 3.2009-3.0183 ppm, CH_2 protons at δ 2.9955-2.0929 ppm and N-CH_3 protons at δ 1.2269-1.1268 ppm.

From the above properties and spectral analysis of the compound **(IIa)**was assigned the structure as 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-ethylimino-1,2,4-dithiazoles **(IIa)**

Similarly, 4-amino-5-methyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Ib),** 4-amino-5-t-butyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide**(Ic),**4-amino-5-p-chloro-phenyldithiobiureto-N-[2(diethylamino)ethyl]-o-anisamide **(Id),** 4-amino-5-o-tolyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Ie),** 4-amino-5-m-tolyldithiobiureto-N-[2-(diethyl-amino)ethyl]-o-anisamide **(If),**4-amino-5-p-tolyldithiobiureto-N-[2-(diethylamino)ethyl]-o-anisamide **(Ig),** were successfully oxidative cyclised with bromine in chloroform medium to isolate 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-methylimino-1,2,4-dithiazole **(IIb),** 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-t-butyl-imino-1,2,4-dithiazole **(IIc),** 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-o-chlorophenylimino-1,2,4-dithiazole **(IId),** 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-o-tolylimino-1,2,4-dithiazole **(IIe)**, 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-m-tolylimino-1,2,4-dithiazole **(IIf),** 3-{4-amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-p-tolylimino-1,2,4-dithiazole **(IIg)**respectively by the above mention method in **Table No. 1**

Table No. 1

Sr. No.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**substituted**imino-1,2,4-dithiazoles	**Yield (%)**	**m.pt. (˚C)**
1.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5yl}-amino-5-**methyl**imino-1,2,4-dithiazole	88	245
2.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**t-buthyl**imino-1,2,4-dithiazole	81	249
3.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**p-chlorophenyl** imino-1,2,4-dithiazole	85	265
4.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**o-tolyl**imino-1,2,4 –dithiazole	90	261
5.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**m-tolyl**imino-1,2,4-dithiazole	80	255
6.	3-{4-Amino-N-[2-(diethylamino)ethyl]-o-anisamido-5-yl}-amino-5-**p-tolyl**imino-1,2,4 –dithiazole	90	270

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