ADDIS ABABA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

Synthesis of Open Chain and Heterocyclic Compounds Starting from 3-Aminothioacryl Amides

Getachew Gebremarian

June , 1987

SYNTHESIS OF OPEN CHAIN AND HETEROCYCLIC COMPOUNDS STARTING FROM 3-AMINOTHIOACRYLAMIDES

A Thesis

presented to

The School of Graduate Studies

Addis Ababa University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science in Chemistry

By

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ACKNOWLEDGEMENTS

I would like to express my deepest gratitude to Dr. J. Liebscher and Dr. Berhanu Abegaz, my advisors, who gave of their time, energy and advice with no reservations. I also express my thanks to Dr. Ermias Dagne, Dr. Tarekegne Gebreyesus and Ato Tecle Habte for running the ^{1}H- and ^{13}C-NMR spectra of some of our samples.

I extend my thanks to Ato Naod Kebede who did an excellent drawings of the structures of the compounds in the manuscript; Ato Gizachew Alemayehu, W/t Genait Dagne, Ato Dawit Gizachew, Ato Abiy Yenesew and Ato Tenkir Asfaw for their collaboration during my work and Ato Yilma Tamiru for typing this thesis.

I extend my deepest gratitude to members of Humboldt University, Chemistry section (GDR) who kindly did the MS and elemental analyses of the compounds.

Financial support from the Swedish Agency for Research Cooperation with Developing Countries (SAREC) obtained through the Ethiopian Science and Technology Commission and the Addis Ababa University which was used to partially cover the expense incurred in the study undertaken and in the preparation of the manuscript is highly acknowledged.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF SCHEMES

LIST OF APPENDICES

ABBREVIATIONS

The following abbreviations are used in the text.

Ar	Aryl
DMF	Dimethylformamide
DMSO	Dimethylsulphoxide
Cpd	Compound
Fig.	Figure
M.p.	Melting point
IR	Infrared
NMR	Nuclear magnetic resonance
MS	Mass spectrum (spectra)
M.W	Molecular weight
Me	Methyl
Ph	Phenyl
Nu	Nucleophile
E	Electrophile
p-sub.Ar.	Para substituted aromatic
p-	Para
Sub.	Substituted
O-	Ortho
O-sub.Ar.	Ortho substituted aromatic

ABSTRACT

Synthesis of Open Chain and Heterocyclic Compounds Starting from 3-Aminothioacrylamides

by

Getachew Gebremariam

Advisors: Dr. J. Liebscher and Dr. Berhanu Abegaz

The 3-aminothioacrylamides used in this study were synthesized by iminoformylation reactions of thioacetamides. In the present work the thioacrylamides were used as starting materials to implement the synthesis of 3-(2-pyridylamine)thioacrylmorpholoides, 3-(2-thiazolylamine)thioacryl morpholides, 3-(2-benzthiazolylamine)thioacrylmorpholides, pyride (1,2-a) pyrimidin-5-ium compounds, thiazole (3,2-a) pyrimidin-4-ium compounds, pyrimide (2,1-b) benzthiazol-5-ium compounds and pyrazole (1,5-a) pyrimidines. The reaction did not produce the expected pyrido (1,2-a) pyrimidin-5-ium, thiazolo (3,2-a) pyrimidin-4-ium and pyrimido (2,1-b) benzthiazol-5-ium compounds. But gave the hydrolysis products. Possible mechanisms for the formation of these compounds have been suggested. In most cases reactions were smooth and yields were good.

I. INTRODUCTION

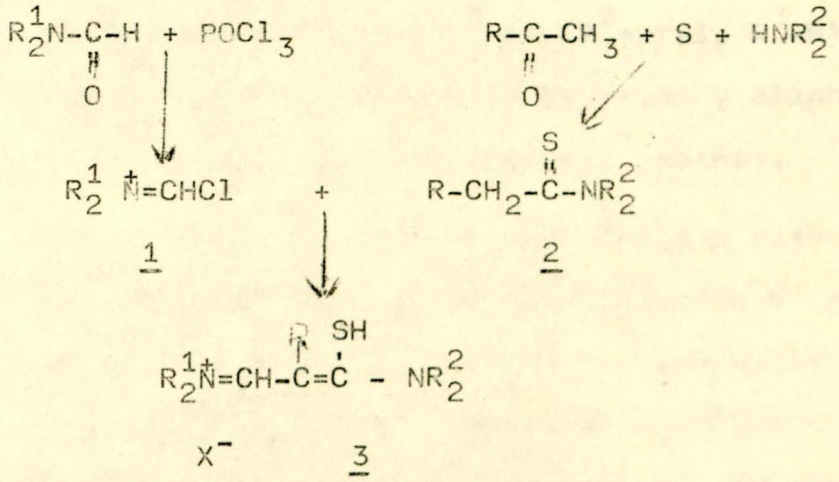
A heterocyclic compound is one which possesses a cyclic structure with at least two different kinds of atoms in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways.[1,2] Most of the sugars and their derivatives, including vitamin C, for instance, exist largely in the form of five-membered (furan) or six-membered (pyran) rings containing one oxygen atom. Most members of the vitamin B group possess heterocyclic rings containing nitrogen. Most of the alkaloids, which are nitrogenous bases occurring in plants, and many antibiotics, including penicillin, also contain heterocyclic ring systems. A large number of synthetic heterocyclic compounds have valuable properties as drugs, dyestuffs, chemotherapeutic agents and co-polymers. It is, therefore, not surprising that much effort has been expended in studying their chemistry.

Several researchers have designed different routes that lead to the synthesis of heterocyclic compounds. These synthetic approaches include cycloaddition, cyclocondensation or enamine condensation reactions, etc. One of the common features of all these synthetic procedures is that, they involve ring-closure reactions which may be effected either by a head to tail connection of a bifunctional compound or by cyclization reaction of two

precursors.

One of the fundamental requirements in the synthesis of heterocyclic compounds with one or more heteroatoms is the availability of suitably functionalized starting materials. Recently Liebscher et al[3] have synthesized 3-aminothioacrylamides 3 from the reactions of foramide chlorides 1 with thioacetamides 2 as shown in Scheme 1. The thioacrylamides 3 were crystallized best as colorless, crystalline perchlorates. The thioacetamides used in this study were easily synthesized from methyl ketones by Willgerodt - Kindler reaction. The mechanism leading to the formation of these compounds 2 is not yet understood.

Scheme 1: Iminoformylation reactions of thioacetamides (R_2^1N=Dimethylamino, NR_2^2=morpholino, R=aromatic and $X^- = ClO_4^-$).



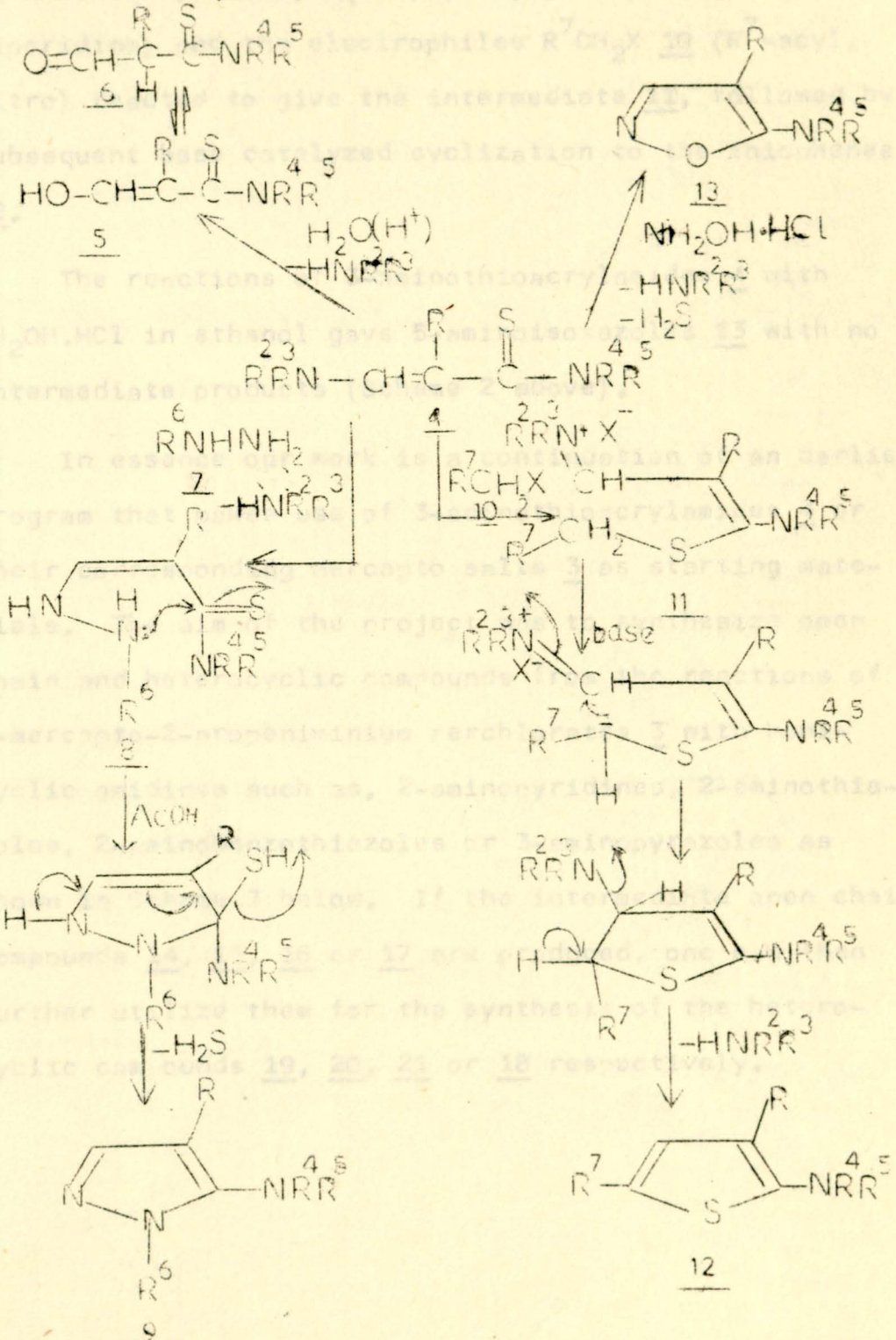
Relevant to the present work, a variety of open

chain and heterocyclic compounds have been synthesized from the reactions of 3-aminothioacrylamides with different types of nucleophiles (Scheme 2). In reactions with simple nucleophiles, one usually finds the substitution of the 3-amino group only. For example 3-hydroxythioacrylamides 5 or their tautomers 6 are formed by mild acidic hydrolysis regardless of the substituents R^2 and R^3.[3,4]

The interaction of hydrazines[5] 7 (R^6=H or aryl) with the thioacrylamides 4 (R=aryl, NR^4R^5=morpholino and R^2R^3N=dialkylamino) also gave the corresponding substitution products. The subsequent nucleophilic attack at position 1 of 8 resulted in the substitution of the thiocarbonyl-S-atom to give pyrazoles 9. In order to increase the leaving tendency of the thiocarbonyl-S-atom the intermediate 3-hydrazinothioacrylamides 8 were S-alkylated sometimes. The amino group attached to position 3 of the thioacrylamides 4 (R^2, R^3=alkyl)[5] or (R^2=aryl, R^3=H)[6] can also be selectively substituted by primary aliphatic and aromatic[5-7] or by secondary aromatic[5] amines.

The interaction of 3-aminothioacrylamides with alkylating reagents gives rise to an alkylation of the thiocarbonyl sulphur atom.[5,8] A subsequent, usually base catalyzed, cyclization of the resulting 1-methylmercaptotrimethinium salts by nucleophilic attack of the deprotonated methylene group at position 3 is possible as long as R^7 is electron withdrawing. 3-aminothioacrylamides 4

Scheme 2: Substitution and cyclization reactions of 3-aminothioacrylamides.

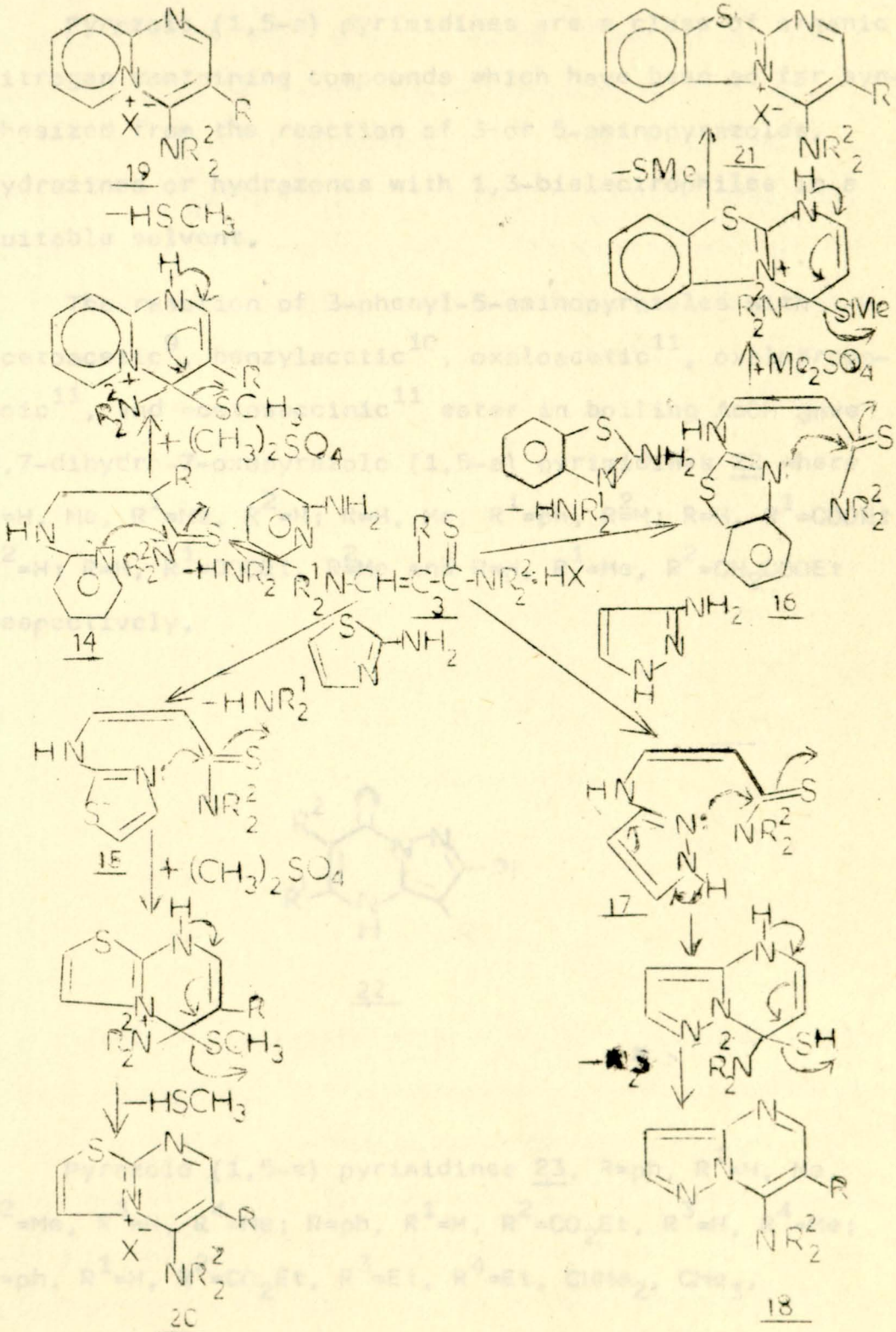


(NR^2R^3=dialkylamino, R=alkyl, aryl, NR^4R^5=morpholino or piperidino) and the electrophiles R^7CH_2X 10 (R^7=acyl, nitro) reacted to give the intermediate 11, followed by subsequent base catalyzed cyclization to the thiophenes 12.

The reactions of 3-aminothioacrylamides 4 with $NH_2OH.HCl$ in ethanol gave 5-aminoisoxazoles 13 with no intermediate products (Scheme 2 above).

In essence our work is a continuation of an earlier program that makes use of 3-aminothioacrylamides 4 or their corresponding mercapto salts 3 as starting materials. The aim of the project was to synthesize open chain and heterocyclic compounds from the reactions of 3-mercapto-2-propeniminium perchlorates 3 with hemicyclic amidines such as, 2-aminopyridines, 2-aminothiazoles, 2-aminobenzothiazoles or 3-aminopyrazoles as shown in Scheme 3 below. If the intermediate open chain compounds 14, 15, 16 or 17 are produced, one can then further utilize them for the synthesis of the heterocyclic compounds 19, 20, 21 or 18 respectively.

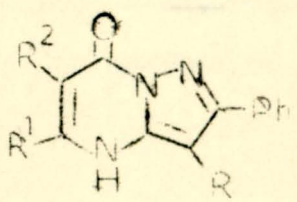
Scheme 3: Proposed reactions of 3-mercapto-2-propeniminium perchlorates 3 with hemicyclic amidines.



II. THEORETICAL BACK GROUND

Pyrazolo (1,5-a) pyrimidines are a class of organic nitrogen containing compounds which have been so far synthesized from the reaction of 3-or 5-aminopyrazoles, hydrazines or hydrazones with 1,3-bielectrophiles in a suitable solvent.

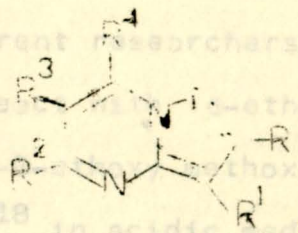
The reaction of 3-phenyl-5-aminopyrazoles with acetoacetic[9], benzylacetic[10], oxaloacetic[11], oxalopropanoic[11], and acetosuccinic[11] ester in boiling AcOH gave 4,7-dihydro-7-oxopyrazolo (1,5-a) pyrimidines 22 where R=H, Me, R^1=Me, R^2=H; R=H, Me, R^1=ph, R^2=H; R=H, R^1=COOEt, R^2=H; R=H, R^1=COOEt, R^2=Me and R=H, R^1=Me, R^2=CH_2COOEt respectively.



22

Pyrazolo (1,5-a) pyrimidines 23, R=ph, R^1=H, Me, R^2=Me, R^3=H, R^4=Me; R=ph, R^1=H, R^2=CO_2Et, R^3=H, R^4=Me; R=ph, R^1=H, R^2=CO_2Et, R^3=Et, R^4=Et, $CHMe_2$, CMe_3,

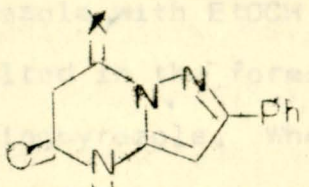
CH_2CHMe_2, ph; R=H, Me, R^1=H, NO_2, R^2=H, R^3=H, Me, Et, ph, $CHMe_2$, Bu, $Me(CH_2)_4$, R^4=H; R=ph, R^1=H, R^2=H, R^3=CO_2Et; R^4=CO_2Et; R=ph, R^1=H, R^2=H, R^3=COMe, R^4=Me; have also been prepared by treating 5-aminopyrazoles with AC_2CH_2,[10] $MeCOCH_2COCO_2Et$,[11] $R_4COCH_2COCO_2Et$[12], EtOCH: CR^3CHO,[13] EtOCH: $C(CO_2Et)COCO_2Et$[14], $(MeCO)_2C$: $CHOEt$[14] and EtOCH: $C(COMe)COCO_2Et$[14] respectively. The interaction of the latter one with 5-aminopyrazole afforded two compounds one having the substituents (R=ph, R^1=R^2=H, R^3=$COCO_2Et$, R^4=Me) and the other (R=ph, R^1=R^2=H, R^3=COMe, R^4=CO_2Et).



23

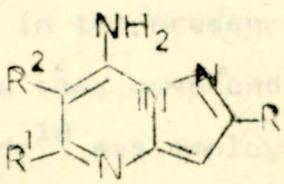
When 3-phenyl-5-aminopyrazole is treated with ethylmalonate and ethylcyanoacetate in the presence of sodium ethoxide, the 4,5,6,7-tetrahydro compounds 24 (X=O and NH)[15] were formed respectively. Furthermore, the interaction of 3-phenyl-5-aminopyrazole with benzylacetonitrile produced 7-imino-2,5-diphenyl-4,7-di-

hydropyrazolo(1,5-a) pyrimidine.[16]



24

7-aminopyrazolo (1,5-a) pyrimidine compounds 25 R=R^1=H, R^2=CN; R=R^2=Me, R^1=H and R=R^1=Me, R^2=H have been synthesized by different researchers when 5-aminopyrozoles are allowed to react with α-ethoxymethylenemalononitrile[17], α-methyl-ß-ethoxy methoxypropionitrile[18] and ß-iminobutyronitrile[18] in acidic media respectively. The latter compound was also prepared by the action of ß-iminobutyronitrile on hydrazine hydrate.[18]



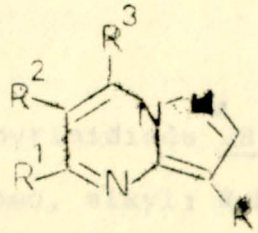
25

When 5-aminopyrazole is treated with compounds possessing bifunctional electrophilic sites two compounds at different proportion were formed. For example the reaction of 5-aminopyrazole with $EtOCH{=}C(CN)CO_2Et$[19] in alcoholic media resulted in the formation of ß-cyano-ß-carbothoxyvinyl-5-aminopyrazole. When this intermediate is further treated in the presence of an acid, 6-carbethoxy-7-amino and 6-cyano-7-oxo-4,7-dihydropyrazolo (1,5-a) pyrimidines were formed, the former was the major product. When sodium ethoxide is used as a condensation agent the 7-oxoanolog was found to be the major product. In the same way the reaction of $RC{\equiv}CCO_2Me$ with 5-aminopyrazole in dioxane afforded a mixture of 7-substituted 5-oxo-4,5-dihydro and 5-substituted 7-oxo-4,7-dihydropyrazolo (1,5-a) pyrimidines (R=Me, ph, CO_2Me, H).[20]

1-substituted 5-aminopyrazoles also condense to pyrazolopyrimidines when they are allowed to react with 1,3-bifunctional electrophiles. For example 3,4-dimethyl-5-aminopyrazole acetate reacts with α-methoxy propionitrile to give 2,3,5,6-tetramethyl-7-aminopyrazolo (1,5-a) pyrimidine[18] in the presence of alcoholic polyphosphoric acid. The same compound was obtained when hydrazinehydrochloride[18] was employed instead of the pyrazole. On the other hand the reaction of 5-amino-1-(o-toluensulfonyl)-pyrazole with $MeCOCH_2CO_2Et$[21] and $MeCOCH_2COR$ (R=Me, ph, OMe)[22] in amine salt gave 1-sul-

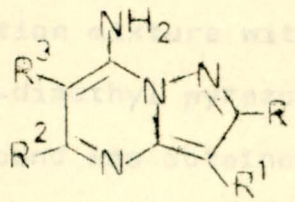
fonyl-N-(α-methyl-ß-carbethoxy vinyl)-5-aminopyrazole and 1-sulfonyl-N-(ß-sub. α-methyl vinyl) pyrazole as intermediate products respectively. When these intermediates are further treated with polyphosphoric acid 5-methyl-7-hydroxy and 7-sub. 5-methyl pyrazolo (1,5-a) pyrimidines are formed respectively.

Pyrazolo (1,5-a) pyrimidines have also been synthesized from 3-aminopyrazoles. The reaction of 3-aminopyrazoles with MeCOCH(NHAc)COMe[23], MeCOCH(NNph)COMe,[24] R_3COCH (R_2) COR_1[25], $(MeO)_2CHCH_2CH(MeO)_2$[26] and $R_1(OH)C$: $CHCOR_3$[27] in alcoholic media has provided pyrazolo (1,5-a) pyrimidines 26 (R=H, R^1=R^3=Me, R^2=NHAc), (R=H, R^1=R^3=Me, R^2=NNph), (R=halo, CN, $CONH_2$, NO_2, NH_2, R^1=H, alkyl, R^2=H, CO_2Et, OEt, R^3=alkyl, amino, OH, Cl, alkoxy), (R=R^1=R^2=R^3=H) and (R=ph, R^1=CF_3, C_2F_2, 4-FC_6H_4, R^2=H, R^3=Me, Et, CF_3, ph) respectively.



26

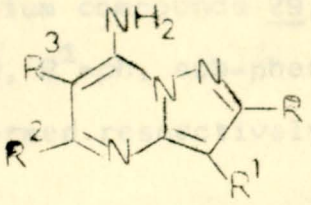
Different workers have synthesized 7-aminopyrazolopyrimidines 27, R=R^1=R^2=H, R^3=Me; R=R^2=Me, R^1=Br, R^3=H; R=H, R^1=Br, R^2=R^3=Me; R=H, R^1=CO_2Et, R^2=R^3=Me and R=R^2=H, R^1=Me, R^3=CO_2Et from the reaction of 3-aminopyrazoles with (MeO)(EtO)CHCH(Me)CN,[28] $Me(HN)CCH_2CN$[29], $CH_3(MeCO)$-CHCN,[30] Me(MeCO)CHCN[31] and $EtOCH:=C(CN)CO_2Et$[32] in alcoholic HCl respectively. In the latter case 4-methyl-(ß-cyano-ß-carbethoxy vinyl)-3-aminopyrazole was isolated as an intermediate product, but the cyclized product was also obtained. In a similar way the reaction of 1,4-dimethyl-3-aminopyrazole[33] with (MeO) (EtO)CHCH(Me)CN has given 1,3,6-trimethyl-7-aminopyrazolo (1,5-a) pyrimidine.



27

7-aminopyrazolopyrimidines 28 R=R^2=H, R^1=R^3=Me; R=R^2=R^3=alkyl, R^1=bromo, alkyl; R=R^2=Me, R^1=R^3=H and R=R^2=H, R^1=R^3=ph have been also prepared by the interaction of hydrazines with (EtO)(MeO)CHCH(Me)CN,[34] $RCOCHR^1CN$,[35] $Me(HN)CH_2CN$[36] and HCOCHphCN[37] in acidic

media respectively. However, in the latter case 4-phenyl-5-aminopyrazole was obtained as a mixture.



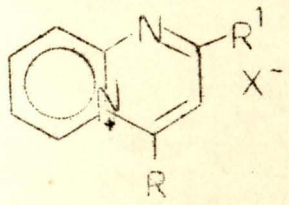
28

The treatment of the monoacetylhydrazones of the 1,3-dicarbonyl compounds ($NCCH_2CONHNC(Me)CH_2COMe$) with sodium hydroxide followed by subsequent neutralization of the resulting reaction mixture with HCl or AcOH yielded 2-hydroxy-5,7-dimethyl pyrazolo (1,5-a) pyrimidine.[38] The same compound was obtained when cyanoacetyl hydrazides ($NCCH_2CONHNH_2$) and pentane-2,4-dione were allowed to react in alcoholic HCl or AcOH and finally treating the resulting mixture with sodium hydroxide.

Pyrido (1,2-a) pyrimidin-5-ium compounds are a class of organic nitrogen containing heterocycles that have been synthesized so far from the reaction of 2-aminopyridines or 2-aminopyridine salts with the suitable reagents mostly in alcoholic media.

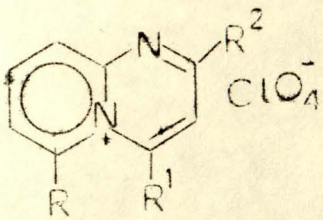
The reaction of 2-aminopyridine with ß-keto ace-

tals ($RCOCH_2CH(OMe)_2$)[39] and $R_1COCHCl$[40] resulted in the formation of 2-acylanils of 2-aminopyridine and 1-(ß-keto-vinyl)-2-aminopyridinium salts respectively. When these intermediates are further treated with acids pyrido (1,2-a) pyrimidin-5-ium compounds 29, R^1=H, R=Me, pr, ph, X^-=Br^-, ClO_4^- and R=H, R^1=ph, sub-phenyl, naphtyl, X^-=Cl^-, ClO_4^- were formed resnectively.



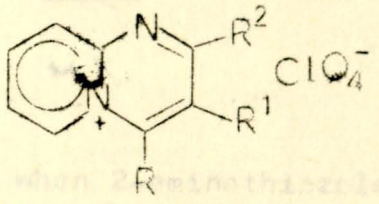
29

But when 2-aminopyridines were allowed to react with $MeCOCH_2CH(OMe)_2$[41] and ($Me_2N(Cl)C{=}CHC(Cl)NMe_2Cl$)[42] no intermediate products were found. Instead pyridopyrimidinium perchlorates 30 R=R^2=Me, R^1=H and R=H, R^1=R^2=NMe_2 respectively were obtained.



30

The reaction of 2-aminopyridine perchlorates with $(EtO)_2CHCH_2CH(OEt)_2$, $MeCOCH_2COMe$, $MeCOCH(Me)COMe$ and $MeCOCH(Et)COMe$ in alcoholic media afforded pyrido (1,2-a) pyrimidin-5-ium perchlorates 31[43] $R=R^1=R^2=H$; $R=R^2=Me$, $R^1=H$; $R=R^1=R^2=Me$ and $R=R^2=Me$, $R^1=Et$ respectively.

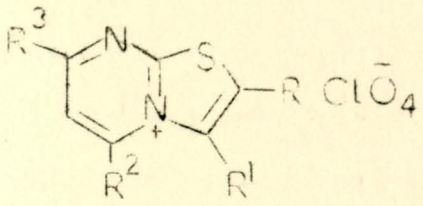


31

In the same media, when 2-aminopyridine hydrogen iodide was allowed to react with $MeCOCH_2COMe$,[44] 3,4-dimethyl pyrido (1.2-a) pyrimidin-5-ium iodide was obtained.

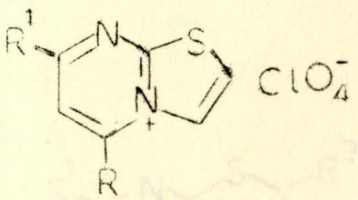
A number of thiazolo (3,2-a) pyrimidin-4-ium compounds have been synthesized from the reaction of substituted thioureas or 2-aminothiazoles with the proper reagents in a suitable solvent.

For example the reaction of 2-aminothiazoles with $MeCOCH_2COMe$[45] and $(EtO)_2CHCH_2CH(OEt)_2$[46] in alcoholic perchloric acid resulted in the formation of thiazolo (3,2-a) pyrimidin-4-ium perchlorates 32, $R=R^1=H$, $R^2=R^3=Me$ and $R^2=R^3=H$, $R=H$, $R^1=H$, Me, ph, $RR^1=(CH_2)_4$ respectively.



32

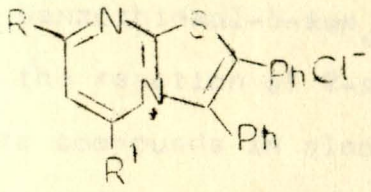
Unlike the above, when 2-aminothiazoles are treated with MeCOCHCHCl,[47] $phCOCH_2COMe$[48], $EtCOCH_2COMe$[48] or $EtOCH_2COCH_2COMe$[48] in alcoholic perchloric acid thiazolo (3,2-a) pyrimidin-4-ium perchlorate 33 R=H, R^1=Me; R=ph, R^1=Me; R=Et, R^1=Me and R=CH_2OEt, R^1=Me and their isomers were formed respectively.



33

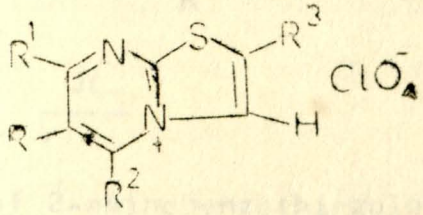
Thiazolo (3,2-a) pyrimidin-4-ium chlorides 34 R=R^1=Me; R=Me, R^1=H and R=R^1=H have also been synthesized from the reaction of 4,5-diphenyl-2-amino thiazole hydrogen chloride with $MeCOCH_2COMe$,

MeCOCHCHCl and $(EtO)_2CHCH_2CH(OEt)_2$ in alcoholic media respectively.[49]



34

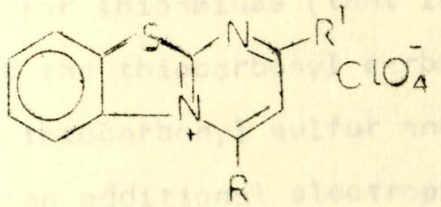
In a similar way, when 2-aminothiazoles are allowed to react with acroleins ($HCOCR=CR_1Cl$) in alcoholic $HClO_4$, thiazolo (3,2-a) pyrimidin-4-ium perchlorates 35 whose substituents R, R^1, R^2, R^3 given: Me, Me, H, H; Me, Me, ph, H; Me, Me, Me, Me; Me, Me, Me, H and $RR^1=(CH_2)_4$, ph, H were obtained.[50]



35

The reaction of substituted thiourea [$MeCOCH_2CMe_2$-$NHCS(NHCH_3)$][51] with $BrCH_2COMe$ in HBr produced iminium bromide as an intermediate. When this intermediate is further heated 3,5,5,7,8-penta methyl-5,8-dihydrothiazolo (3,2-a) pyrimidin-4-ium bromide was obtained.

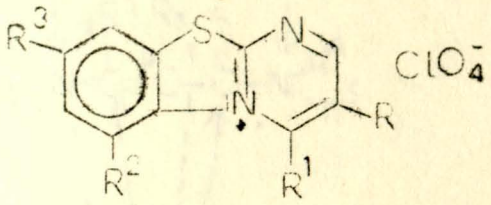
Pyrimido (2,1-b) benzothiozol-5-ium compounds have been synthesized from the reaction of 2-aminobenzothiazole with the appropriate compounds in alcoholic media. For example the reaction of 2-aminobenzothiazole with $MeCOCHClCl$,[47] $phCOCH_2COMe$,[48] $EtCOCH_2COMe$[48] or $EtOCH_2COCH_2$-$COMe$[48] in alcoholic $HClO_4$ afforded pyrimido (2,1-b) benzothiazol-5-ium perchlorates 36 R=Me, R^1=H; R=ph, R^1=Me; R=Et, R^1=Me; R=CH_2OEt, R^1=Me; and their corresponding isomers respectively.



36

But the reaction of 2-aminobenzothiazoles with $(EtO)_2CHCH_2CH(OEt)$[46] or $HCOCR=CR_1Cl$[50] in alcoholic $HClO_4$ gave pyrimido (2,1-b) benzothiazol-5-ium perchlorates 37 R=R^1=R^3=H, R^2=H, Me, MeO and R^2=H, R=R^1=Me,

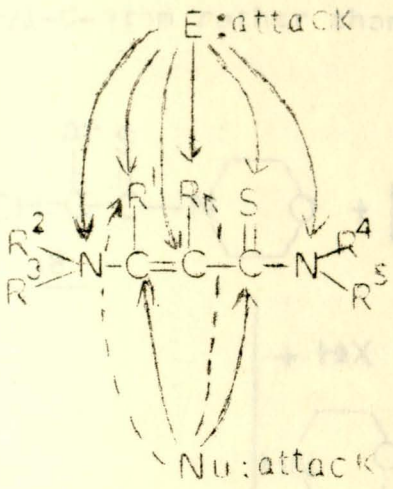
R_3=H, NO_2 respectively.



37

Recently a variety of heterocyclic compounds have been synthesized from 2-substituted dialkyl 3-amino thioacrylamides. 3-aminothioacrylamides with various substitution patterns exhibit polyfunctional reaction behavior and consequently can be used in the synthesis of a variety of heterocyclic compounds. Besides the reactive sites typical for thioamides (that is electrophilic properties at the thiocarbonyl carbon atom and nucleophilic at the thiocarbonyl sulfur and nitrogen atoms) they possess an additional electrophilic carbon atom at position 3, and further nucleophilic positions at the enamine carbon atom (position 2) and at the amino nitrogen atom connected to position 3 (see Scheme 4). Furthermore, it is possible that active sites may be found in the substituents R and R^1 as well as in the amino substituents. Due to this exceptionally polyfunctional reaction behavior, 3-aminothioacrylamides

possess a wide synthetic potential.

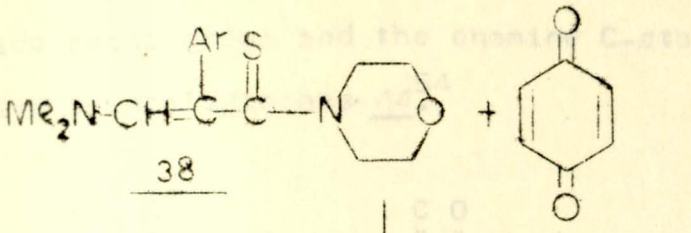


Scheme 4

Under this the application of 3-aminothioacrylamides as C-S-, N-C-S-, C-C-N, C_3-N-, N-C_3-N, C_3-N-C-, N-C_3-N-C-, C_3-N-C-S- and C_3N-C-N synthons with limited examples will be considered.

If a 3-aminothioacrylamide is to react as C-S-synthon in the synthesis of heterocycles the reactant must possess both, electrophilic and nucleophilic properties. There usually arises the problem that the electrophilic carbon atom at position 3 competes for the nucleophilic sites in the reactant. Hence 3-aminothioacrylamides are difficult to apply as C-S-synthon. The only heterocyclic synthesis so far is the reaction of 3-aminothioacrylamides 38 with benzoquinone rise to benzoxathiolium salts 39 and morpholine as the byproduct[52]. Probably the primary attack of the quinone

takes place at the thiocarbonyl-S-atom. The subsequent cyclization is then forced by the nucleophilic attack at the thiocarbonyl-C-atom rather than at position 3.



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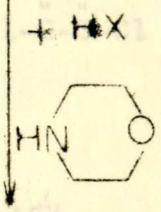
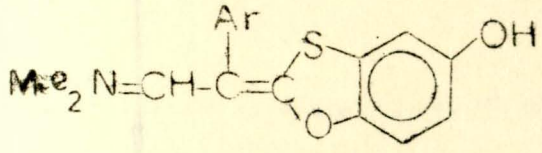
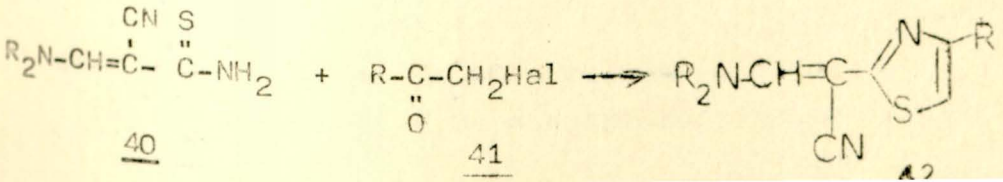




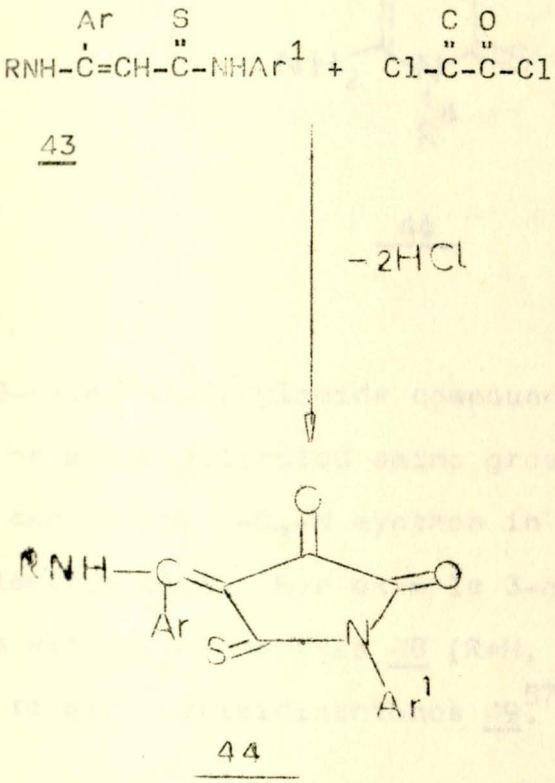
39

According to the reactivity pattern above (Scheme 4) 3-aminothioacrylamides can act as N-C-S-synthon if they are reacted with bifunctional electrophiles that attack both, the thioamide-S and the thioamide-N-atoms. As a precondition the amino group at position 1 has to bear at least one H-atom. The 3-aminothioacrylamides 40 react with α-haloketones 41 to give the aminovinylthiazole 42.[53] This is formed in the Hantzsch - like synthesis.

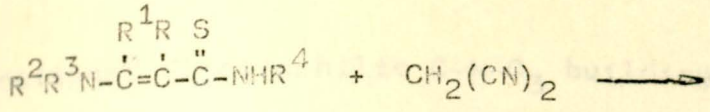


40 41 42

3-aminothioacrylamides have rarely been used as C-C-N-synthon. In the reactions of compounds 43 with oxalylchloride an electrophilic attack occurs at the thioamide amino group and the enamine C-atom at position 2 to give thiazolidinones 44.[54]



Pyridinthiones 46 (R=ph, H,, R^1=H, Et) or (RR^1=$(CH_2)_n$, R^4=aryl) have been synthesized directly starting from 3-aminothioacrylamides 45 as C_3-N-synthon.[55,56]



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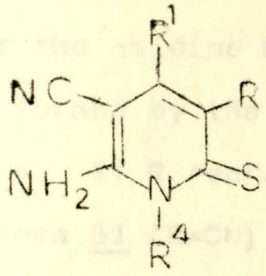
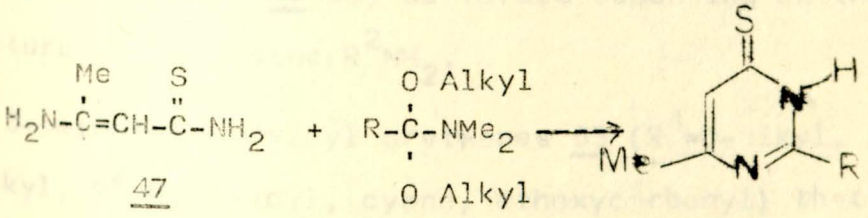


46

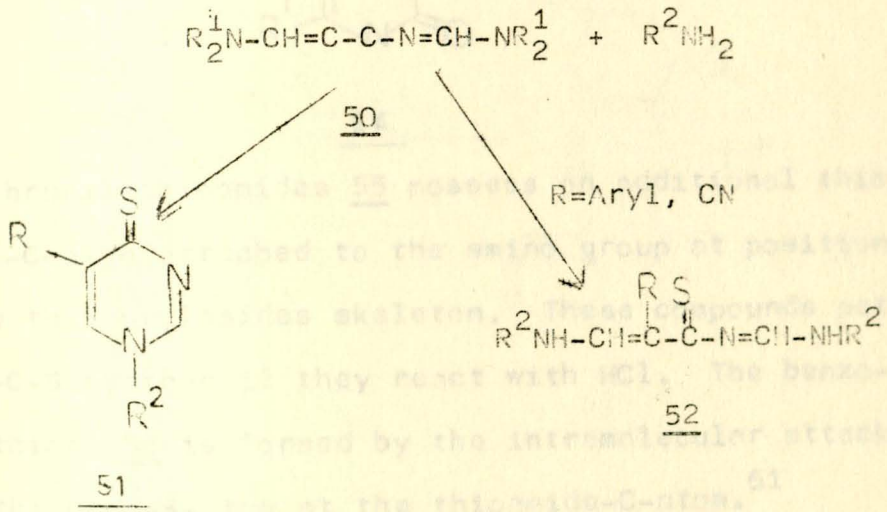
3-aminothioacrylamide compounds bearing unsubstituted or monosubstituted amino groups at both position 1 and 3 can act as $N-C_3-N$ synthon in reactions with suitable electrophiles. For example 3-aminothioacrylamide 47 reacts with amide acetals 48 (R=H, Me) as a C-building block to give pyrimidinthiones 49.[57]



47 48 49

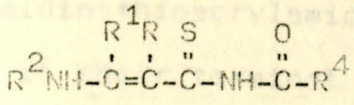
The application of 3-aminothioacrylamides system as

bifunctional electrophilic C-N-C_3 building blocks is only possible if the basic skeleton is extended by an additional electrophilic C-atom. This can be found in (3-aminothioacryl) formamidines 50 which are attached by primary amines (R^2=H, alkyl, aryl) or hydrazines R^2=NHR^1 at position 3 and at the amidine C-atom. Pyrimidin-4-thiones 51[58,59] are formed by the elimination of the terminal amino groups. If R represents a cyano group either pyrimidinthiones 51 (R=CN) or open chain disub-

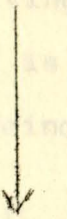


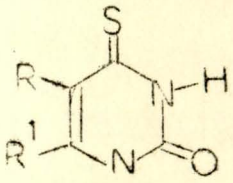
stitution products 52 may be formed depending on the structure of the amine, R^2NH_2.

3-aminothioacryloyl urethanes 53 (R^4=O-alkyl, R^1=alkyl, R^2=H, R=acyl, cyano, ethoxycarbonyl) that already possess a suitable primary amino group R^2NH undergo intramolecular cyclization to give monothiouracils 54.[60] In these cases the reactants 53 act as N-C_3-N-C synthon.



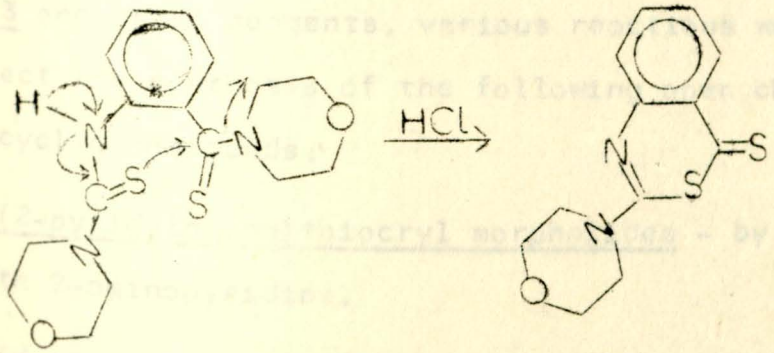
53





54

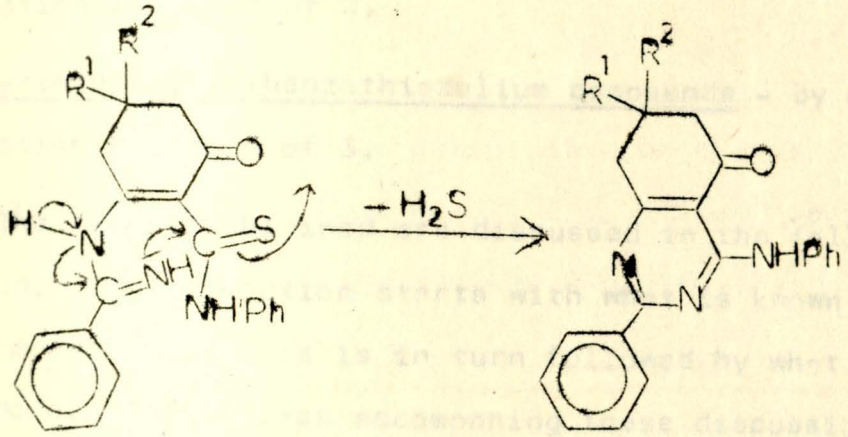
Anthranilothioamides 55 possess an additional thiocarbonyl-C-atom attached to the amino group at position 3 of the thioacrylamides skeleton. These compounds act as C_3-N-C-S synthon if they react with HCl. The benzothiazinthione 56 is formed by the intramolecular attack of the thiourea-S-atom at the thioamide-C-atom.[61]



55

56

The cyclic 3-amidinothioacrylamides 57 can be used as C_3-N-C-N synthon if their terminal amidin-N-atom bears H-atoms. On heating, this amino group attacks the thiocarbonyl C-atom giving rise to the formation of 4-aminopyrimidines 58.[62] It is noteworthy that H_2S is eliminated and not the 1-amino group.



57 58

In the present work by making use of the mercapto salts 3 and other reagents, various reactions were done to effect the synthesis of the following open chain and heterocyclic compounds:

1. 3-(2-pyridylamino)thiocryl morpholides - by reaction with 2-aminopyridine.
2. 3-(4-methyl-2-thiazolylamino)thioacryl morpholides - by reaction with 4-methyl-2-aminothiazole.
3. 3-(2-benzthiazolylamino)thioacryl morpholides - by

reaction with 2-aminobenzothiazole.

4. pyrazolo(1,5-a)pyrimidines - by reaction with 5-(4-chlorophenyl)-3-amino pyrazole.

5. Pyrido(1,2-a)pyrimidin-5-ium compounds - by cyclization reaction of 1.

6. Thiazolo(3,2-a)pyrimidin-4-ium compounds - by cyclization reaction of 2.

7. pyrimido(2,1-b)benzothiazolium compounds - by cyclization reaction of 3.

The results obtained are discussed in the following section. The subsection starts with what is known about the compounds and this is in turn followed by what we have done. The schemes accompaning these discussions summarize the synthetic approaches of the compounds under consideration. Melting points, yields, elemental analyses and spectroscopic data are also included in the following section. In addition to this some selected spectra are appended to the thesis.

III. RESULTS AND DISCUSSIONS

1. Synthesis of Starting Materials

The procedure towards the synthesis of the mercapto salts 3 was adopted from earlier reports.[3,5,8] The structures, melting points and yields of 3 used in this reasearch are given in Table 1 below.

Table 1: 3-Mercapto-2-propeniminium perchlorates 3 (R^3=Ph; R^4=p-tolyl; R^5=p-anisyl; R^6=p-chlorophenyl; R^1_2N=dimethylamino; NR^2_2=morpholino and HX=$HClO_4$)

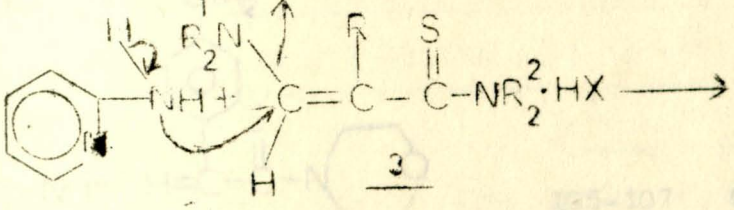
Cpd	Structure	M.p. °C+	Yield%
3a	$R^1_2N-CH=C(R^3)-C(=S)-NR^2_2.HX$	140-141	77
3b	$R^1_2N-CH=C(R^4)-C(=S)-NR^2_2.HX$	138-139	53
3c	$R^1_2N-CH=C(R^5)-C(=S)-NR^2_2.HX$	156-157	70
3d	$R^1_2N-CH=C(R^6)-C(=S)-NR^2_2.HX$	172-173	75

+ Recrystallized from acetic acid.

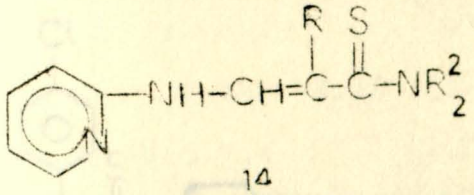
2. Synthesis of 3-(2-pyridylamino)thioacrylmorpholides 14

There are two sites for nucleophilic attack at positions 1 and 3 of the thioacrylamides 3. But in reactions with simple nucleophiles one usually finds the substitution of the 3-amino group only. A variety of open chain compounds have been synthesized by the action of different types of nucleophiles on 3-aminothioacrylamides.[5-7] It is worth mentioning that in all of these reports the 3-amino was substituted in place of the 1-amino group.

In the present work, the reactions of 2-aminopyridines with 3-mercapto-2-propeniminium perchlorates also resulted in the substitution of the 3-amino group. The most probable mechanism leading to the formation of these compounds is shown by equation 1 below.



3

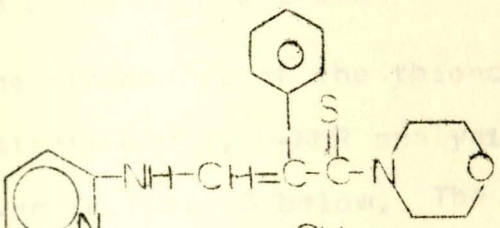
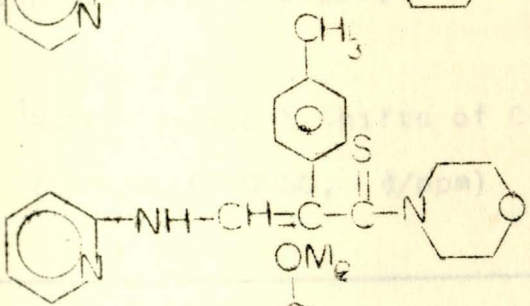
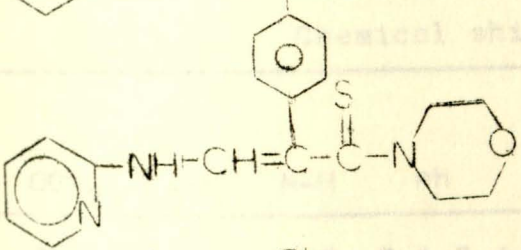
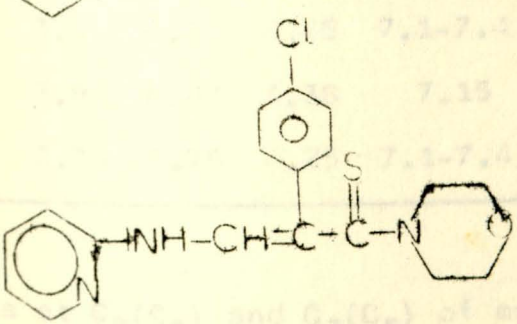


14 (1)

The synthesis of 14 was achieved by varying the substituent at position 2 of the thioacrylamide. The reactions were smooth and yields were

good. The structures of compounds 14a-d, melting points and yields are given in table 2 below. The yields of these compounds increased when the reactions were allowed to proceed for longer periods of time.

Table 2: 3-(2-pyridylamino)thioacrylmorpholides

Cpd	Structure	M.p.$^{o}C^{+}$	Yield%
14a		149.5	66
14b		150	60
14c		105-107	69.1
14d		136-137	50

The compounds 14a-d were characterized by elemental analyses and spectroscopic methods. The IR spectra showed the stretching frequencies of the (N-H), (C=N), (C-N), (C=S) and (C-O) groups from (3300-3350), (1640-1650), (1295-1300), (1220-1245) and (1100-1120) cm^{-1} respectively. In addition bands between 805 and 820 cm^{-1} that show the substitution pattern in aromatic compounds (p-substituted aromatic) were also observed in the IR spectra of compounds 14b-d

The structures of the thioacrylamides (14a-d) were also established by ^{1}H-NMR analysis. The ^{1}H-NMR results are given in Table 3 below. The signals of the methylene

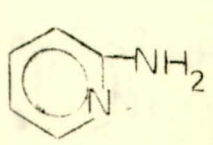
Table 3: ^{1}H-NMR Chemical Shifts of Compounds 14a-d
(Ext. ref. DMSO, δ/ppm)

Cpd	Chemical shifts (δ) in ppm									
							2-pyridyl			
	NCH_2	OCH_2	C_3-H	N-H	Ph	CH_3	C_3-H	C_4-H	C_5-H	C_6-H
14a	3.7	3.9	6.9	4.45	7.1-7.4		7.8	8.25	7.6	8.75
14b	3.63	3.83	6.83	4.38	7.15	2.32	7.73	8.18	7.68	8.63
14d	3.5	3.75	6.75	4.25	7.1-7.4		7.7	8.1	7.5	8.7

protons at $C_2(C_6)$ and $C_3(C_5)$ of morpholino appeared as multiplet due to mesomeric interaction of the thiocarbo-

nyl to the amide nitrogen.[63,64] In NMR, the methine protons of the substituents at positions 2 and 3 of the thioacrylamides (14a-d) absorp in the same region. These effects caused overlapping of signals in this region and consequently the singals that correspond to the methine protons of these substituents also appeared as multiplet in the NMR spectra of these series of compounds. In addition the C_3-H (enamine) signal was observed at 6.8 ppm as multiplet in the NMR spectra. Although the stereochemistry of these compounds is not studied, comparison of the δ(NH) value (4.38 ppm) of 14a-d with reported δ(NH) values (12.62 ppm) of related compounds[64] indicates the absence of hydrogen bonding in these thioacrylamides and suggests that these compounds might exist in the E-configuration. The results obtained from the ^{1}H-NMR study were in agreement with the structures proposed (see Table 3).

The ^{13}C-NMR chemical shifts of the compounds also supported the structures suggested. The ^{13}C-NMR chemical shifts of compounds (14a-d) were assigned by co-rrelation with structurally similar compounds (see below).



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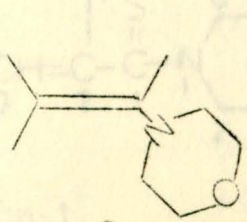

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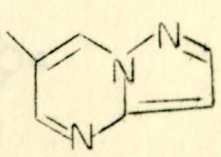


61

The chemical shifts of the 2-pyridylamino and morpholino carbon atoms were assigned by comparison with the ^{13}C-NMR chemical shifts of compounds 59 and 60 respectively.[65] For the carbon atoms C_2 and C_3 of the thioacrylamides the corresponding values were alloted by considering the chemical shifts of compounds (61) possessing an enamine group in their structures[13]. The remaining signals were assigned to the carbon atoms of the aromatic group at position 2 of the thioacrylamides by considering peak intensity and substituent incremental parameters for this particular system. The ^{13}C-NMR chemical shifts of compounds 14a-d are given in Table 4 below. In the ^{13}C-NMR spectra the carbon atoms C_2 and C_6, C_3 and C_5 of the aromatic group at position 2 of the thioacrylamides as well as C_3 and C_5 of morpholino were found to be identical. On the other hand the carbon atoms C_2 and C_6 of morpholino were found to be magnetically non-equivalent due to the anisotropic effects of the thiocarbonyl group (see Table 4). The numbering of the carbon atoms in these compounds is shown in figure 1 below.

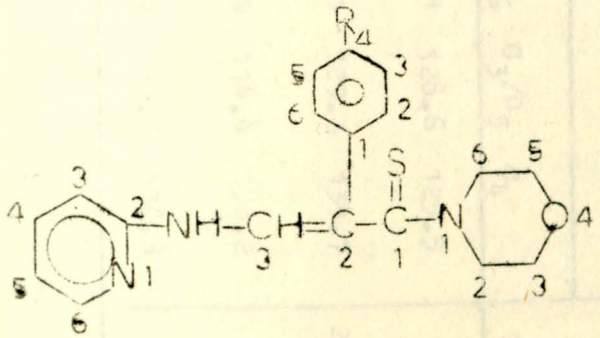


Fig-1

Table 4: ^{13}C-NMR Chemical Shifts of Compounds 14-d (Ext. ref. DMSO, δ/ppm)

Chemical shifts (δ) in ppm																
			Morpholino			2-pyridyl					Ph					
	C_2	C_3	C_2	C_6	C_3/C_5	C_2	C_3	C_4	C_5	C_6	C_1	C_2/C_6	C_3/C_5	C_4	Me	C
.5	116.8	131.4	48.4	51.1	65.8	153.5	110.2	137.7	115.6	147.6	120.1	124.1	128.6	125.5		
.6	116.8	134	48.2	50.9	65.7	153.5	110.2	137.7	115.7	147.6	120.2	124.1	129.3	134.7	20.6	
.1	116	130.1	48.2	51.9	66.4	153.1	109.6	137.8	115.0	148.1	117.8	125.9	114.4	158.2		5
.1	116	130	48.4	51.2	65.8	153.5	110.5	138	115.6	147.7	121.4	125.9	128.7	136.8		

Elemental analyees for compounds 14a and 14c has been done and the results obtained are in satisfactory agreement with the calculated values (see Table 5 below).

The structures of compounds 14b and 14c were further confirmed by mass spectral analysis. The mass spectra gave the molecular ion peaks and showed fragment ions that comply with the structures proposed (see data under experimental part).

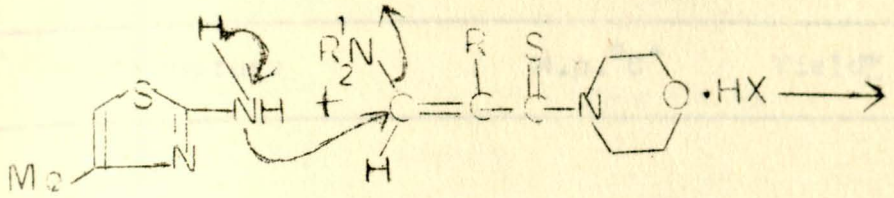
Table 5: Elemental Analyses for Compounds 14a and 14c

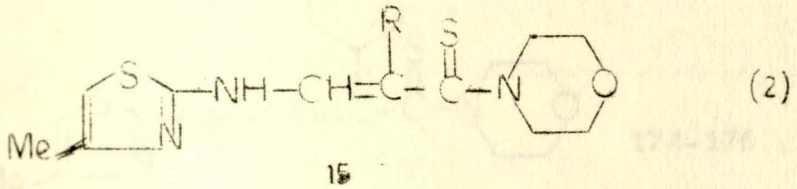
Cpd	Formula (M.W)		C%	H%	N%	S%
14a	$C_{18}H_{19}N_3OS$	Calc.	66.43	5.88	12.91	9.85
	(325)	Found	66.87	6.18	13.01	10.07
14c	$C_{19}H_{21}N_3O_2S$	Calc.	64.2	5.99	11.89	9.02
	(355)	Found	65.08	6.26	12.26	9.28

3. Synthesis of 3-(4-methyl-2-thiazolylamino)thioacrylmorpholides 15

These compounds were obtained by the reaction of 4-methyl-2-aminothiazole with 3-mercapto-2-propeniminium perchlorates according to equation (2). The synthesis of these com ounds for

NR_2=dimethylamino; R=ph, p-tolyl, p-anisyl or p-chlorophenyl was achieved under basic conditions.





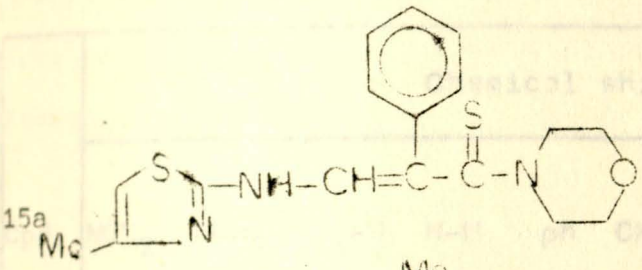
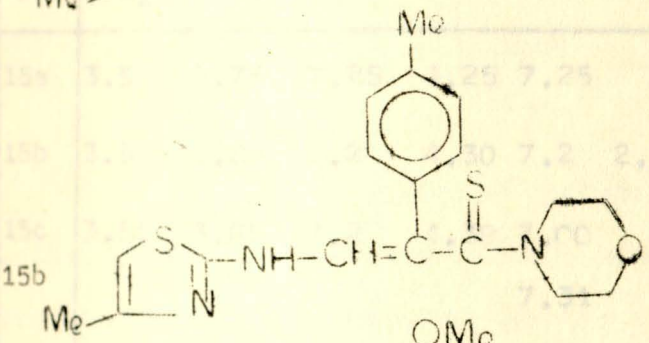
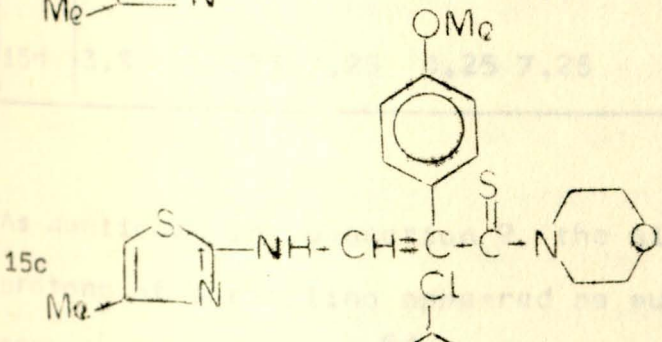
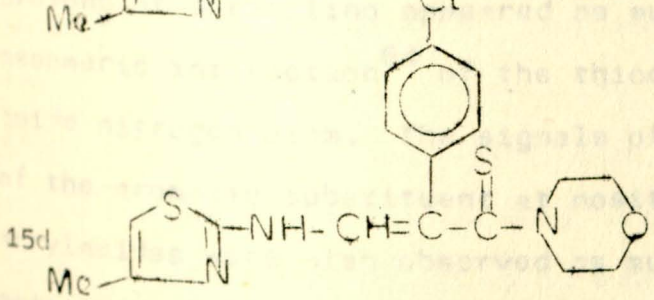
(2)

15

In all cases the reactions resulted in the substitution of the 3-amino group (see eq. 2 above). The products were isolated as yellow solids. The yields vary from 58 to 76.5% and increased when the reactions were allowed to proceed for longer periods of time. The structures of the compounds, melting points and yields are given in Table 6 below.

Identification of these compounds was based on elemental and spectroscopic analysis. For compounds 15a-d, the IR spectra gave the stretching frequencies of the functional groups as follows: N-H(3130-3440), C=N(1630-1640), C-N(1280), C=S(1220-1225) and C-O(1100-1110) cm^{-1}. Furthermore, bands between 801 and 820 cm^{-1} which are characteristic of p-substituted aromatic compounds were also observed in the IR spectra (see data in the experimental section).

Table 6: 3-(4-methyl-2-thiazolylamino)thioacrylmorpholides (15a-d)

Cpd	Structure	M.p.°C+	Yield%
15a		174-176	60
15b		190-192	58
15c		180-182	64
15d		215-217	76.5

The ^{1}H-NMR spectra of compounds 15a-d gave the chemical shifts of the protons as shown in Table 7 below.

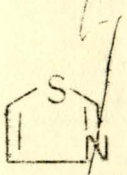
Table 7: ^{1}H-NMR Chemical Shifts of Compounds 15a-d (Ext. ref. DMSO, δ/ppm)

Cpd	Chemical shifts (δ) in ppm								
								2-thiazolyl	
	NCH_2	OCH_2	C_3-H	N-H	ph	CH_3	OCH_3	C_5-H	CH_3
15a	3.5	3.75	7.25	4.25	7.25			6.35	2.15
15b	3.5	3.80	7.2	4.30	7.2	2.25		6.43	2.15
15c	3.55	3.85	7.2	4.39	7.00 7.31		3.85	6.5	2.25
15d	3.5	3.75	7.25	4.25	7.25			6.40	2.15

As mentioned in subsection 2, the signals of the methylene protons of morpholino appeared as multiplet due to the mesomeric interaction[64] of the thiocarbonyl to the amide nitrogen atom. The signals of the methine protons of the aromatic substituent at position 2 of the thioacrylamides were also observed as multiplet due to the anisotropic effects of the thiocarbonyl group[6]. On the other hand the signal of the methine proton of 2-thiazolyl appeared as singlet in the NMR spectra of these

compounds. Comparison of the δ(NH) values (4.25 - 4.39 ppm) of (15a-d) with reported values (12.62 ppm)[64] of related compounds indicates the absence of hydrogen bonding in these compounds and suggests that these compounds might exist in the E-configuration.

The ^{13}C-NMR chemical shifts of the compounds were assigned by co-rrelation with structurally similar compounds (see below).



62

For the carbon atoms of morpholino and 2-thiazolylamino the corresponding values were alloted by comparison with the chemical shifts of compounds 60 and 62 respectively. The ^{13}C-NMR chemical shifts of C_1 and C_2 of the thioacrylamides were assigned by co-rrelation with the chemical shifts of compound 61. The remaining signals were assigned to the carbon atoms of the aromatic group at position 2 of the thioacrylamides by taking into account peak intensity and substituent incremental shift for this particular system. The chemical shifts of C_2 and C_6 as well as C_3 and C_5 of the aromatic group were found to be identical in the ^{13}C-NMR spectra of compound 15. The mesomeric interaction of the thiocarbonyl to the amide nitrogen was felt in these series of compounds and as a result the

chemical shifts of C_2 and C_6 as well as C_3 and C_5 of morpholino were found to be magnetically non-equivalent. This might be due to the steric effect of the phenyl group that forces the $C(S)-NR_2^2$ moiety (NR_2^2=morpholino) to be twisted from the common plane, where the whole mesomeric interaction is now limited to the amide side. The ^{13}C-NMR results are given in Table 8 below. The numbering of the carbon atoms in these compounds is shown in figure 2 below.

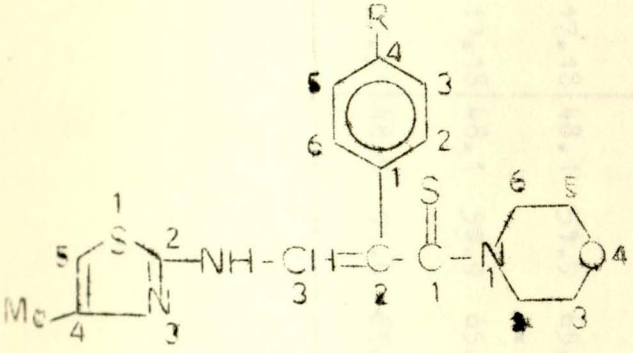


Fig.2

Elemental analyses for compounds 15b and 15d has been done and the results obtained were in satisfactory agreement with the calculated values. (See Table 9 below).

Beside these, the structures of compounds 15b and 15c were further confirmed by mass spectral analysis. The mass spectra gave the molecular ion peaks and showed fragment ions that comply with the structures proposed (see data under experimental part). On

Table 8: ^{13}C-NMR Chemical Shifts of Compounds 15a-d (Ext. ref. DMSo, δ/ppm)

	Chemical shifts (δ) in ppm														
				2-thiazolyl				Morpholino				Ph				
	C_1	C_2	C_3	C_2	C_4	C_5	Me	C_2	C_6	C_3	C_5	C_1	C_2/C_6	C_3/C_5	C_4	Me
	194.6	117.2	132.6	162.8	147.4	103.8	17.08	48.1	50.8	65.4	66	120.6	124.4	128.4	125.9	
	194.8	118.1	133.8	162.7	147.7	103.6	17.18	48.1	50.9	65.5	65.9	120.5	124.2	129.3	132.2	20.6
	194.8	118.1	129.3	162.8	147.6	103.4	17.18	48.1	50.9	65.5	65.9	120	126.3	114.2	157.8	
	194.5	117.1	130.6	162.9	148.1	104.4	17.51	48.5	51.4	65.7	66.3	122.1	126.3	128.9	136.1	

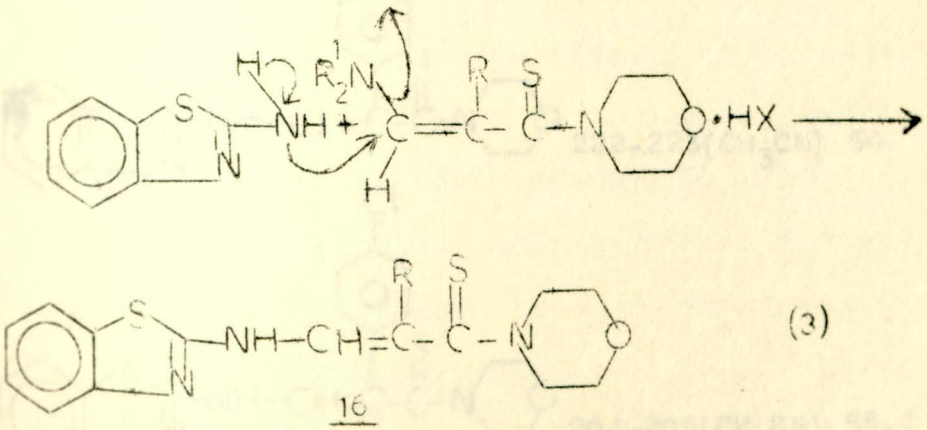
these grounds the structures of the compounds were established as 15a-d

Table 9: Elemental Analyses for Compounds 15b and 15d

Cpd	Formula (M.W)		C%	H%	N%	S%	Cl%
15b	$C_{18}H_{21}N_3OS_2$	Calc.	60.13	5.89	11.69	17.83	
	(359)	Found	59.83	6.11	12.04	18.21	
15d	$C_{17}H_{18}N_2OS_2Cl$	Calc.	53.74	4.77	11.06	16.88	9.33
	(379)	Found	53.34	4.88	11.14	17.4	9.02

4. Synthesis of 3-(2-benzthiazolylamino)thioacrylmorpholides 16

These compounds were synthesized by the reaction of 2-aminobenzthiazole with 3-mercapto-2-propeniminium perchlorates (3) under basic conditions (eq.3). The synthesis of these compounds was achieved by varying the substituent at position 2 of the thioacrylamides.

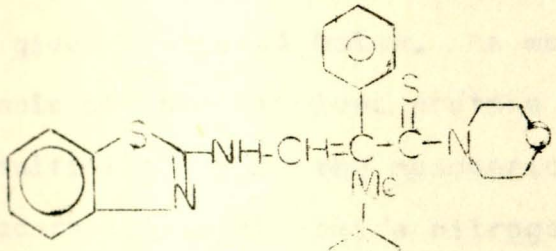
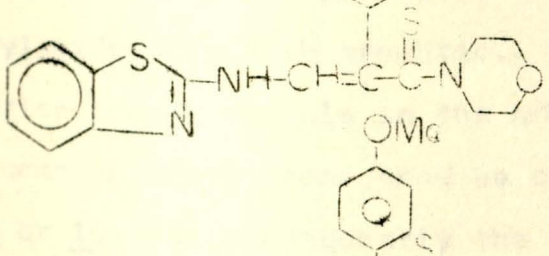
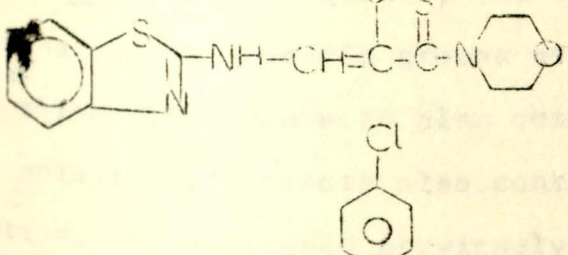
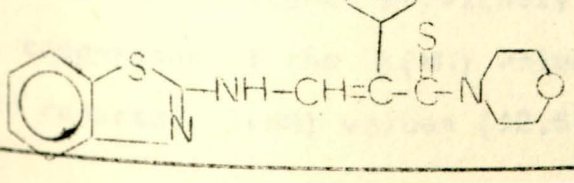


(3)

16

The reactions resulted in the substitution of the 3-amino group as shown in equation 3 above. The reactions were smooth and products were isolated as yellow solids. The structures of the compounds, melting points and yields are given in Table 10 below. The yields vary from 54 to 71% and increased upon prolonged heating.

Table 10: 3-(2-benzthiazolylamino)thioacrylmorpholides 16a-d

Cpd	Structure	M.p.°C	Yields%
16a		143-145(EtOH)	71
16b		196-198(EtOH)	56
16c		222-223(CH_3CN)	54
16d		204-205(CH_3CN)	55.4

The compounds were characterized by elemental analyses and spectroscopic methods. The IR spectra showed the stretching frequencies of the functional groups as follows: N-H(3150-3270); C=N(1625-1660); C-N(1260-1280); C=S(1210-1230) and C-O(1100-1120 cm^{-1}. In addition bands between 801 and 820 cm^{-1} which are characteristic of p-substituted aromatic compounds were also observed in the IR spectra. The results obtained from the IR spectra were compatible with the structures proposed (see under the experimental part).

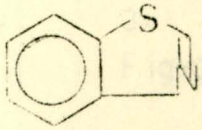
The structures of compounds 16a-d were also established by ^{1}H-NMR analysis. The ^{1}H-NMR chemical shifts are given in Table 11 below. As mentioned earlier the signals of the methylene protons of morpholino appeared as multiplet due to the mesomeric interaction of the thiocarbonyl to the amide nitrogen atom. Furthermore, the substituents at positions 2 and 3 of these thioacrylamides are both aromatic. Due to this effect overlapping of signals in the NMR spectra of this class of compounds was pronounced as compared to the others (14 or 15) and consequently the signals of the methine protons of the aromatic groups at positions 2 and 3 of the thioacrylamides were also observed as multiplet. The anisotropic effects also contributed to this situation. As mentioned previously (sub-sections 2 and 3), comparison of the δ(NH) values (4.35-4.4 ppm) with reported δ(NH) values (12.62 ppm) of related

compounds also indicated the absence of hydrogen bonding in these series of compounds and suggested that these thioacrylamides might exist in the 'E'-configuration. The results obtained from the ^{1}H-NMR spectra are in agreement with the structures proposed (see Table 11).

Table 11: ^{1}H-NMR Chemical Shifts of Compounds 16a-d (Ext.ref. DMSO, δ/ppm)

Cpd	Chemical shifts (δ) in ppm					
	NCH_2	OCH_2	N-H	C_3-H/C-H(Ar)	Me	OMe
16a	3.64	3.85	4.35	6.69-7.08		
16b	3.6	3.8	4.35	7.2-7.9	2.3	
16c	3.7	3.85	4.4	7-7.9		3.85
16d	3.6	3.8	4.4	7.6		

The structures of compounds 16a-d were further established by ^{13}C-NMR analysis. The ^{13}C-NMR chemical shifts were assigned by comparison with structurally similar compounds (see below). The results obtained are given in Table 12 below.



The chemical shifts of the morphilino and 2-benzthiazolylamino carbon atoms were assigned by considering the ^{13}C-NMR chemical shifts of compounds 60 and 63 respectively. For the carbon atoms C_2 and C_3 of the thioacrylamides the corresponding values were alloted by comparison with the ^{13}C-NMR chemical shifts of compound 61. The remaining signals were assigned to the carbon atoms of the aromatic group at position 2 of the thioacrylamides by considering peak intensity and substituent incremental parameters. The mesomeric interaction of the thiocarbonyl to the amide nitrogen was also felt in these series of compounds and as a result the chemical shifts of C_2 and C_6 as well as C_3 and C_5 of morpholino were found to be magnetically nonequivalent. On the other hand the chemical shifts of C_2 and C_6 as well as C_3 and C_5 of the aromatic group at position 2 of the thioacrylamides were found identical. In addition the chemical shifts of C_5 and C_6 of the 2-benzthiazolylamino group were also found to be identical in the ^{13}C-NMR spectra of compounds 16b-d. (See Table 12). The numbering of the carbon atoms in compounds 16a-d is shown in figure 3 below.

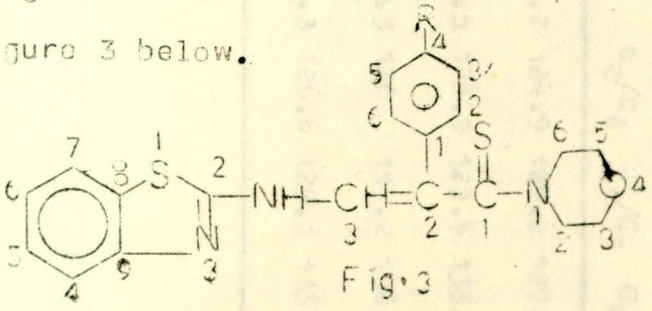


Fig. 3

Table 12: ^{13}C-NMR Chemical Shifts of Compounds 16a-d (Ext. ref. DMSO, δ/ppm)

	Chemical shifts (δ) in ppm																	
				Morpholino				2-benzthiazolyl						Ph				
	C_1	C_2	C_3	C_2	C_6	C_3	C_5	C_2	C_4	C_5/C_6	C_7	C_8	C_9	C_1	C_2/C_6	C_3/C_5	C_4	Me
	195.4	120.2	131	48.3	51.45	66.4	66.4	161.7	122	125/126	123	136.2	151.6	121.2	124.9	129.2	127.3	
	194.4	119.1	131	48.1	51.1	65.5	65.9	161.8	121	126	122	133.5	151.1	120.5	124.5	129.4	135.7	20.
	194.4	119.1	129	48.1	51.1	65.5	65.9	161.8	121	126	122	131.1	151.1	120.3	126	114.2	158.1	55.
	194.1	119.4	131	48.5	51.5	65.8	66.3	162.1	122	126.3	123	131.1	151.2	121.3	126.6	129.1	135.7	

Elemental analyses has been done for compounds 16a and 16b and the results obtained were in satisfactory agreement with the calculated values (see Table 13 below).

The structures of compounds 16a and 16b were further confirmed by mass spectral analysis. The mass spectra gave the molecular ion peaks. In addition the fragment ions observed were in accord with the structures proposed (see data in the experimental section).

Table 13: Elemental Analyses for Compounds 16a and 16b

Cpd	Formula (M.W.)		C%	H%	N%	S%
16a	$C_{20}H_{19}N_3OS_2$	Calc.	62.96	5.02	11.01	16.81
	(381)	Found	62.85	5.22	10.40	17.26
16b	$C_{21}H_{21}N_3OS_2$	Calc.	63.77	5.35	10.62	16.21
	(395)	Found	63.67	5.56	10.41	16.47

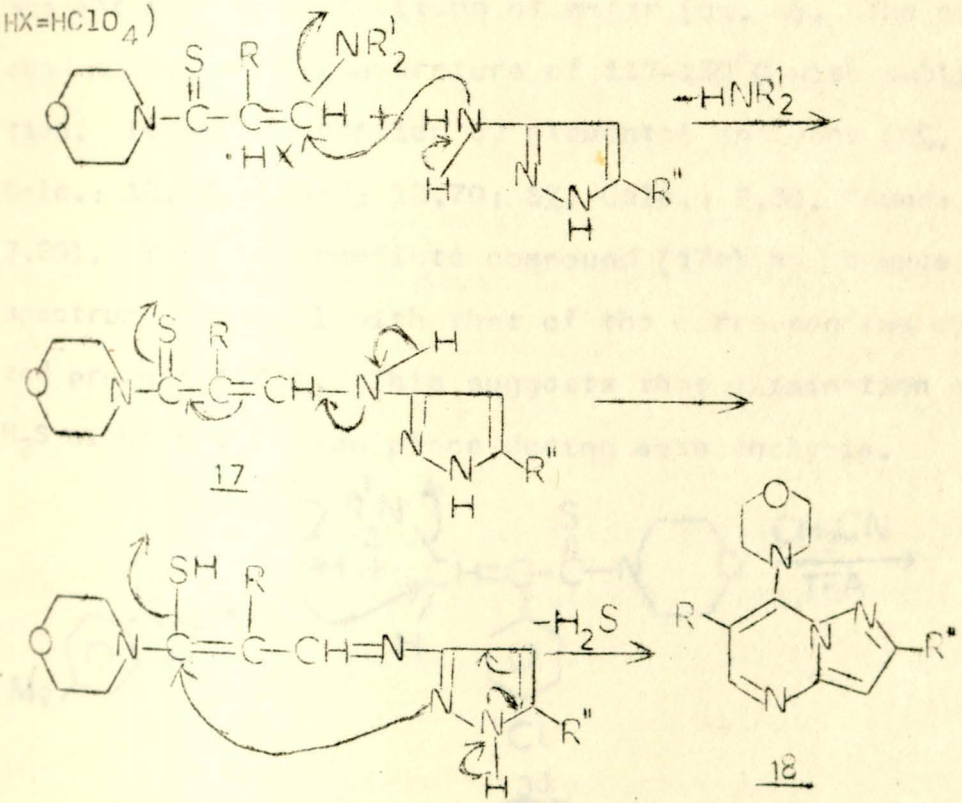
5. Synthesis of Pyrazolo(1,5-a)pyrimidines 18

This class of compounds have hitherto been synthesized by the reaction of 3- or 5-amino-pyrazoles with 1,3-dicarbonyl or related compounds. In most reports the reactions gave the heterocyclic compounds as end products. However, there are a few cases where intermediate pro-

ducts have been isolated and characterized.

In the present work pyrazolo(1,5-a)pyrimidines were achieved by the reaction of 3-aminopyrazoles with 3-mercapto-2-propeniminium perchlorate 3 under basic conditions. The possible mechanisms leading to the formation of these compounds are depicted in Scheme 5.

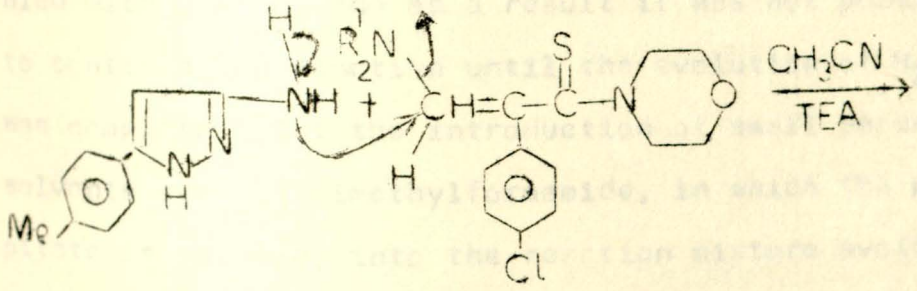
Scheme 5: Possible mechanisms for the formation of pyrazolo(1,5-a)pyrimidines 18 (R^1_2N=dimethylamino, HX=$HClO_4$)



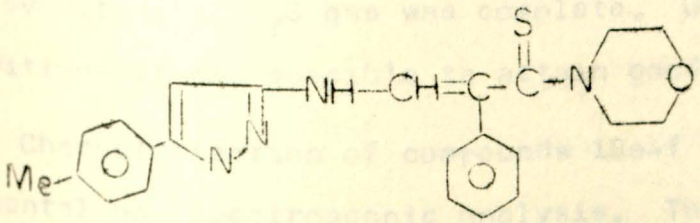
According to Scheme 5 the nucleophilic attack at position 3 of the thioacrylamides results in the formation of 3-(3-pyrazolylamino)thioacrylmorpholides as intermediate products. The intermediate 17 would then undergo further intramolecular cyclization by elimination of H_2S to give pyrazolo(1,5-a)pyrimidines 18.

The synthesis of 18 was achieved by varying the

at position 5 of the pyridine. The reactions exclusively gave the heterocyclic compounds with no intermediate products under the employed conditions. However, intermediate products have been also isolated under different conditions. For example, when a solution of 5-(4-methylphenyl)-3-aminopyrazole in acetonitrile was treated with 3-mercapto-2-(4-chlorophenyl)-2-propeniminium perchlorate 3d in the presence of triethylamine at room temperature, a yellow precipitate was obtained upon addition of water (eq. 4). The compound melted at a temperature of 110-130°C with sublimation. It was identified by elemental analyses (N%, Calc.: 12.77, found: 12.79; S%, Calc.: 7.30, found: 7.26). This intermediate compound (17e) had a mass spectrum identical with that of the corresponding cyclized product (10e). This suggests that elimination of H_2S might have taken place during mass analysis.



3d



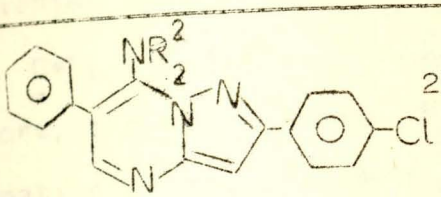
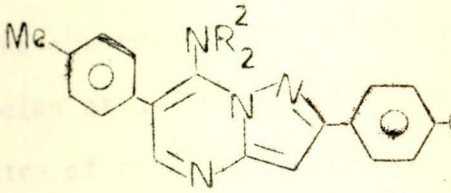
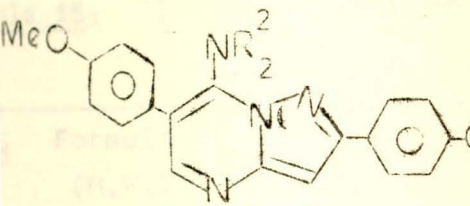
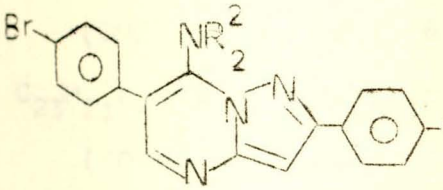
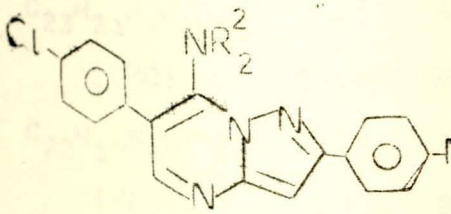
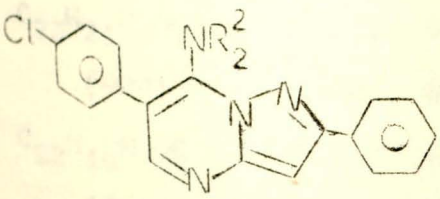
17e (4)

In contrast to 3-aminopyrazoles, the action of the former amidines (subsections 2-4) on the thioacrylamides produced only the open chain compounds under the same conditions. This effect might be attributed to differences in basicity within the amidines. In the latter case the basicity is increased by an additional nitrogen atom as compared to the former and consequently the intermediate is forced to undergo intramolecular cyclization by nucleophilic attack at position 1 of the thioacrylamide to give pyrazolo(1,5-a)pyrimidines as end products.

The compounds synthesized including their melting points and yields are given in Table 14 below. The yields of these compounds were intially poor because the reactions immediately formed a precipitate accompanied with bumping and as a result it was not possible to continue the reaction until the evolution of H_2S gas was complete. But the introduction of small amount of solvents such as dimethylformamide, in which the precipitate is soluble, into the reaction mixture avoided the bumping and allowed the reaction to proceed until the evolution of H_2S gas was complete. Under these conditions it was possible to attain good yields.

Characterization of compounds 18a-f was based on elemental and spectroscopic analysis. The micro analysis were in satisfactory agreement with the calculated

e 14: Pyrazolo(1,5-a)pyrimidines 18 (NR^2_2=morpholino)

Structure	M.p. °C	Yield%
	229-230(DMF)	51.3
	213-215(CH_3CN)	57
	202-203(CH_3CN)	59.5
	253-255(DMF)	64
	276-278(DMF)	94
	263-265(DMF)	67

values (see Table 15 below). In addition the structures of compounds 18a-c were further established on the basis of their IR spectra. The IR spectra showed the stretching frequencies of the following groups as follows: C=N(1610-1665), C-N(1270) and C-O at 1100 cm^{-1}. Furthermore, the elimination of H_2S and the corresponding formation of the cyclized products were supported by the absence of the (C=S) and (N-H) stretching frequencies at 1220 and 3300 cm^{-1} respectively in the IR spectra of compounds 18a-c.

Table 15: Elemental analyses for compounds 18a-f

Cpd	Formula (M.W.)		C%	H%	N%	Cl%
18a	$C_{22}H_{19}N_4OCl$	Calc.	67.4	4.8	14.3	9.06
	(390)	found	67.11	4.3	15.1	9.02
18b	$C_{23}H_{21}N_4OCl$	Calc.	68.2	5.2	13.8	8.8
	(404)	found	67.9	5.7	13.6	9.0
18c	$C_{23}H_{21}N_4O_2Cl$	Calc.	65.7	5.02	13.3	8.7
	(420)	found	65.04	5.3	12.7	8.8
18d	$C_{22}H_{18}N_4OBrCl$	Calc.	56.3	3.84	11.96	
	(468)	found	56.9	4.0	12.35	
18e	$C_{23}H_{21}N_4OCl$	Calc.	68.3	5.2	13.9	
	(404)	found	67.95	5.27	14.12	
18f	$C_{22}H_{19}N_4OCl$	Calc.	67.7	4.9	14.4	
	(390)	found	67.9	5.1	14.68	

The identification of compounds 18a, 18e and 18f was also achieved by ^{1}H-NMR spectroscopy. The signals of methylene protons of morpholino as well as methine protons of the aromatic substituent at position 6 of these compounds appeared as multiplet. On the other hand the signals of the methine protons at positions 3 and 5 of these compounds were observed as singlets. The results obtained from the proton NMR chemical shifts were in agreement with the structures suggested. The ^{1}H-NMR chemical shifts of compounds 18a, 18e and 18f are given in Table 16 below.

Table 16: ^{1}H-NMR (CF_3COOH) Chemical Shifts of Compounds 18a, 18e and 18d

	Chemical shifts (δ) in ppm						
					Substituent		
					Position 2		Position 6
Cpd	NCH_2	OCH_2	C_3-H	C_5-H	Ph	CH_3	Ph
18a	3.96	4.17	7.02	9.17	7.9		7.49
					7.99		7.59
18e	3.79	4.04	6.80	7.92	7.16	2.25	7.69
					7.42		
18f	3.79	4.00	6.80	7.90	7.29		7.73

The structures of compounds 18a-f were further confirmed by mass spectral analyses. The mass spectra gave the molecular ion peaks and showed fragment ions that comply with the strustures proposed. In addition sulphur test has been done for this class of compounds and all

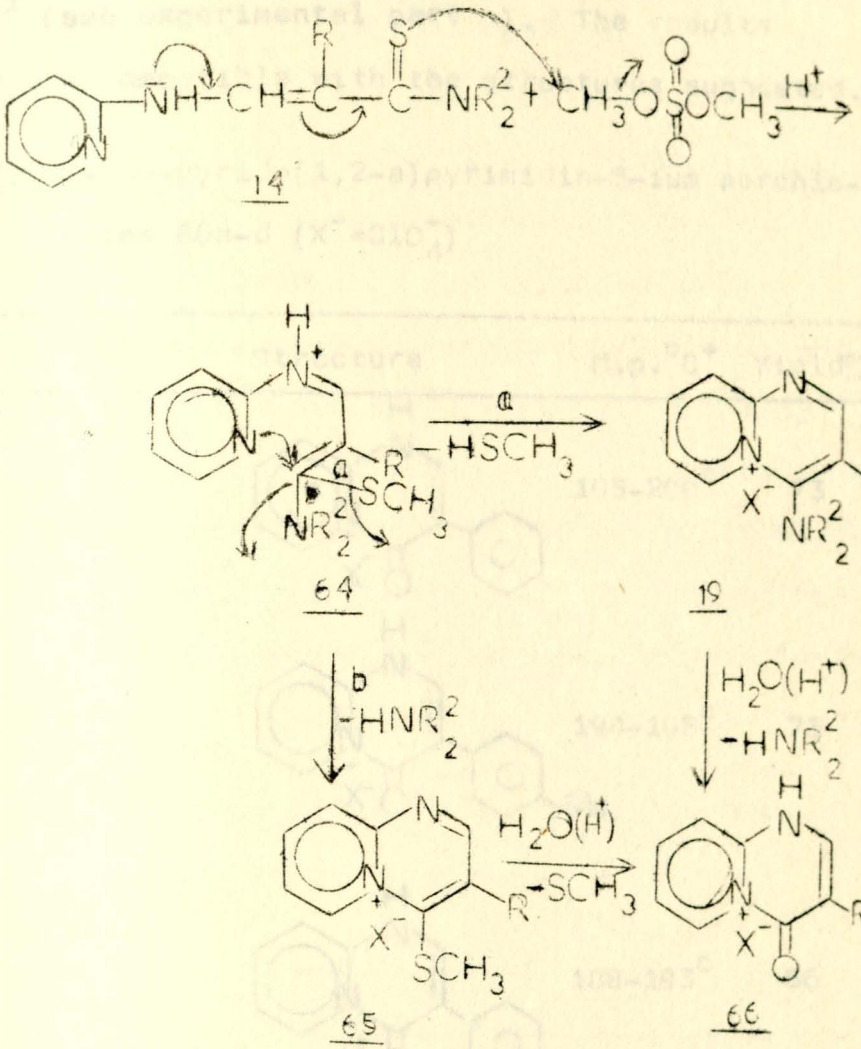
6. Synthesis of Pyrido(1,2-a)pyrimidin-5-ium Compounds 66

The synthesis of this class of compounds from the reaction of 2-aminopyridines with 1,3-bifunctional electrophiles such as 1,3-dicarbonyl or structurally related compounds has been reported since 1950.

In the present work pyrido(1,2-a)pyrimidin-5-ium compounds were achieved by the intramolecular cyclization reaction of 3-(2-pyridylamino)thioacrylmorpholides 14 in the presence of dimethylshlphate under acidic conditions. It was initially assumed that the nucleophilic attack at position 1 of the thioacrylamide 14 will eliminate either methylmercaptan or morpholino to give 4-morpholino or 4-methylmercapto-pyrido(1,2-a)pyrimidin-5-ium compounds 19 or 65 respectively (see Scheme 6). But unfortunately neither of these compounds was found. Instead the hydrolysis products, pyrido(1,2-a)pyrimidin-4-one-5-ium compounds (66) were obtained. Possible mechanisms leading to the formation of compounds 66 are depicted in Scheme 6.

According to Scheme 6 the interactions of compound 14 with dimethylsulphate gives rise to the methylation of the thiocarbonyl sulphur atom.

Scheme 6: possible mechanisms for the formation of compounds 66 (R=aryl, NR_2^2=morpholino)

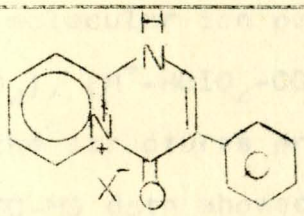
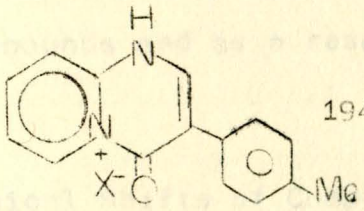
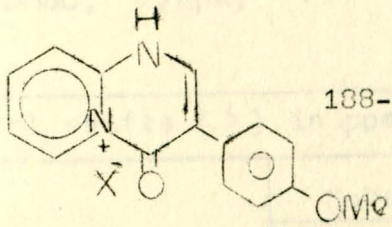
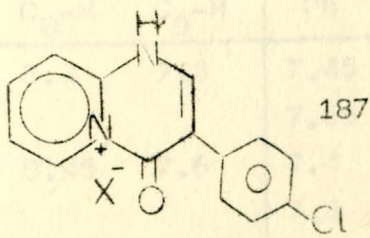


The subsequent nucleophilic attack at position 1 of the isothioamide 64 will result either in the formation of compound 19 or 65 by the elimination of methylmercaptan or morpholino respectively. Then the hydrolysis of these intermediates (19 or 65) gives compound 66.

The structures of the compounds, melting points and yields are given in Table 17 below. The identification of compounds 66a-d was achieved by spectro-

scopic methods. The IR spectra gave the stretching frequencies of the following groups as follows: C=O(1700-1720), C=N(1610-1638) and perchlorate at 1100 cm^{-1} (see experimental part). The results obtained are compatible with the structures suggested.

Table 17: 4-oxo-pyrido(1,2-a)pyrimidin-5-ium perchlorates 66a-d ($X^- = ClO_4^-$)

Cpd	Structure	M.p.°C[+]	Yield%
66a		195-200[c]	73
66b		194-198[c]	75
66c		188-193[c]	66
66d		187-193[c]	83

[+] Recrystallized from acetic acid.

[c] Melt with decomposition.

The structures of compounds 66a-d were also established by ^{1}H-NMR analyses. The signals of the methylene protons of morpholino at 3.65 and 3.95 ppm as well as the thiomethyl protons at 2.1 ppm were absent in the NMR spectra of these compounds. These evidences support the structures of the compounds as 66a-d. The ^{1}H-NMR chemical shifts are given in Table 18 below and are in agreement with the structures suggested. The mass spectra did not give the molecular ion peaks. But fragment ions for (M^+-$HClO_4$), (M^+-$HClO_4$-CO), etc. were observed and comply with the structures proposed (see experimental part). The GC-MS data showed trace impurities in these series of compounds and as a result need further purification.

Table 18: ^{1}H-NMR Chemical Shifts of Compounds 66a-d (Ext. ref. DMSO, δ/ppm)

Cpd	Chemical shifts (δ) in ppm						
						Substituent	
	C_2-H	C_6-H	C_7-H	C_8-H	C_9-H	Ph	CH_3
66a	8.75	9.25	7.9	8.4	7.8	7.45 7.65	
66b	8.85	9.35	8.05	8.45	7.6	7.4	2.45
66d	8.8	9.3	8.00	8.4	7.9	7.8 7.5 7.8	

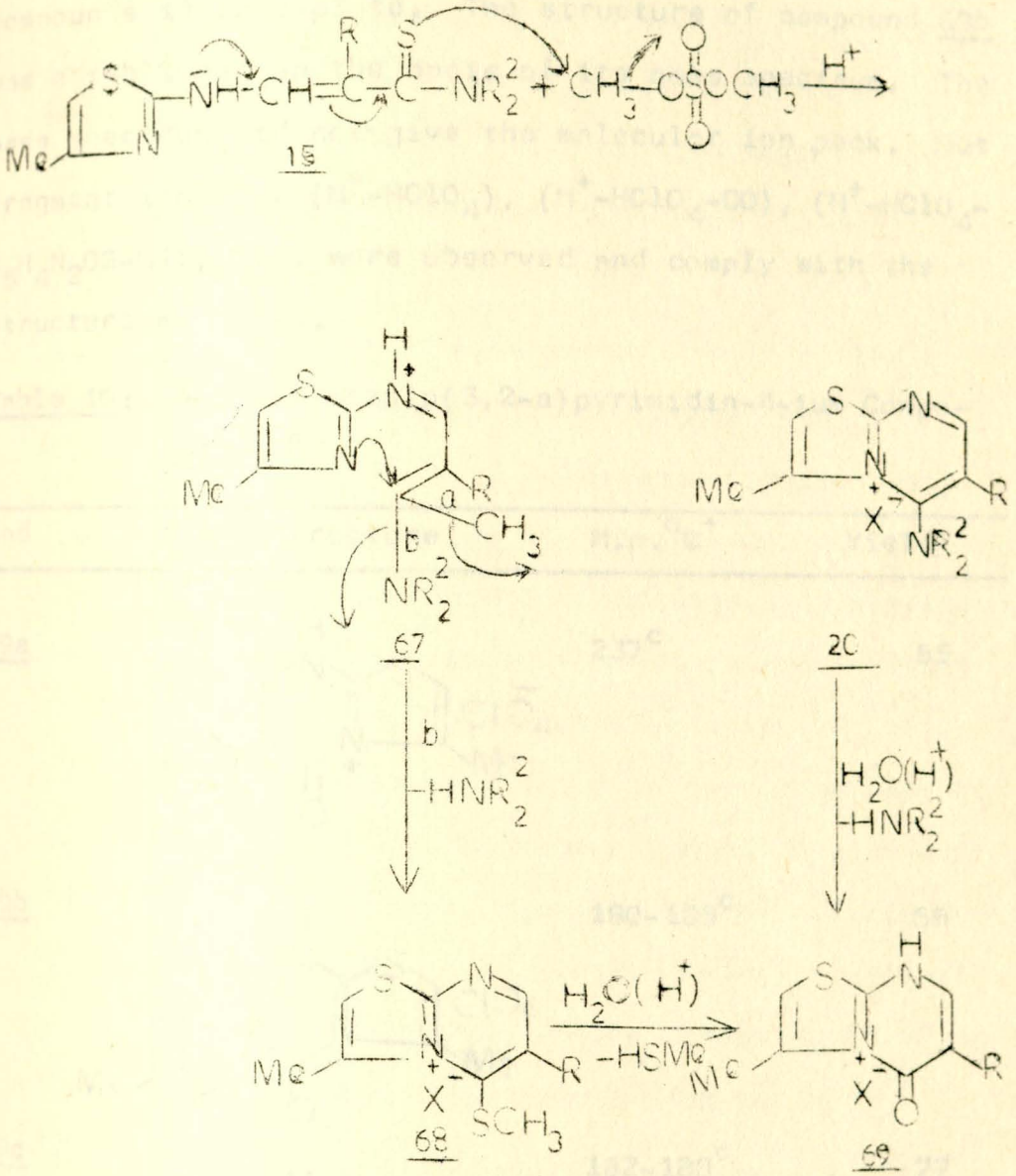
7. Synthesis of Thiazolo(3,2-a)pyrimidin-4-ium Compounds 69

The title compounds have been synthesized previously from the reactions of substituted thioureas or 2-aminothiazoles with 1,3-dicarbonyl or related compounds under acidic conditions.

In the present work the synthesis of these compounds was achieved by the intramolecular cyclization of 3-(2-thiazolylamino)thioacrylmorpholides 15 in the presence of dimethylsulphate under acidic conditions. As mentioned previously the nucleophilic attack at position 1 of the thioacrylamide 15 would result either in the substitution of methylmercaptan or morpholino to give compound 20 or 68 respectively. But these compounds were also not found as end products. Instead the hydrolysis products, thiazolo(3,2-a)pyrimidin-5-one-4-ium compounds 69 were obtained. Possible mechanisms for the formation of compound 69 are given in Scheme 7 below.

According to Scheme 7 the reaction of 15 with dimethylsulphate gives rise to the methylation of the thiocarbonyl sulphur atom. The resulting isothioamide 67 will then eliminate either methylmercaptan or morpholino to give compound 20 or 68

Scheme 7: Possible mechanism for the formation of compound 69 (R=aryl, NR_2^2=morpholino)

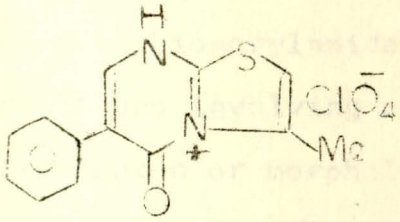
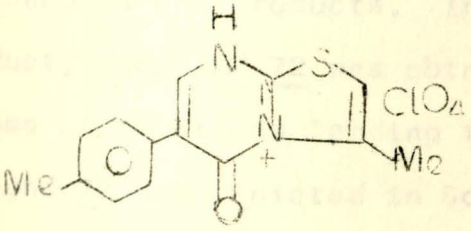
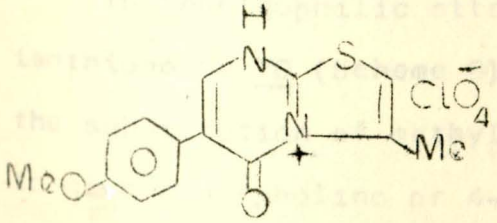
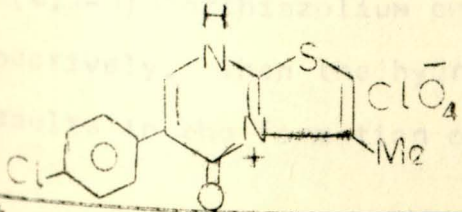


respectively. The subsequent hydrolysis of compound 20 or 68 will result in the formation of compound 69.

The structures of the compounds, melting points and yields are given in Table 19 below. The IR spectra showed the stretching frequencies of (C=O), (C=N) and perchlorate from (1715-1720), (1610-1620) and at 1100 cm^{-1} respectively. The ^{1}H-NMR spectra of these

compounds were not taken due to insolubility. Other data for compounds 69a, 69c and 69d are also not available. Due to this reason the characterization of these compounds is incomplete. The structure of compound 69b was established on the basis of its mass spectrum. The mass spectrum did not give the molecular ion peak. But fragment ions for (M^+-$HClO_4$), (M^+-$HClO_4$-CO), (M^+-$HClO_4$-$C_5H_4N_2OS$-H$^\bullet$), etc. were observed and comply with the structure proposed.

Table 19: 5-oxo.thiazolo(3,2-a)pyrimidin-4-ium Compounds 69

Cnd	Structure	M.p. °C	Yield%
69a		237[c]	55
69b		180-185[c]	66
69c		182-188[c]	77
69d		187-192[c]	79

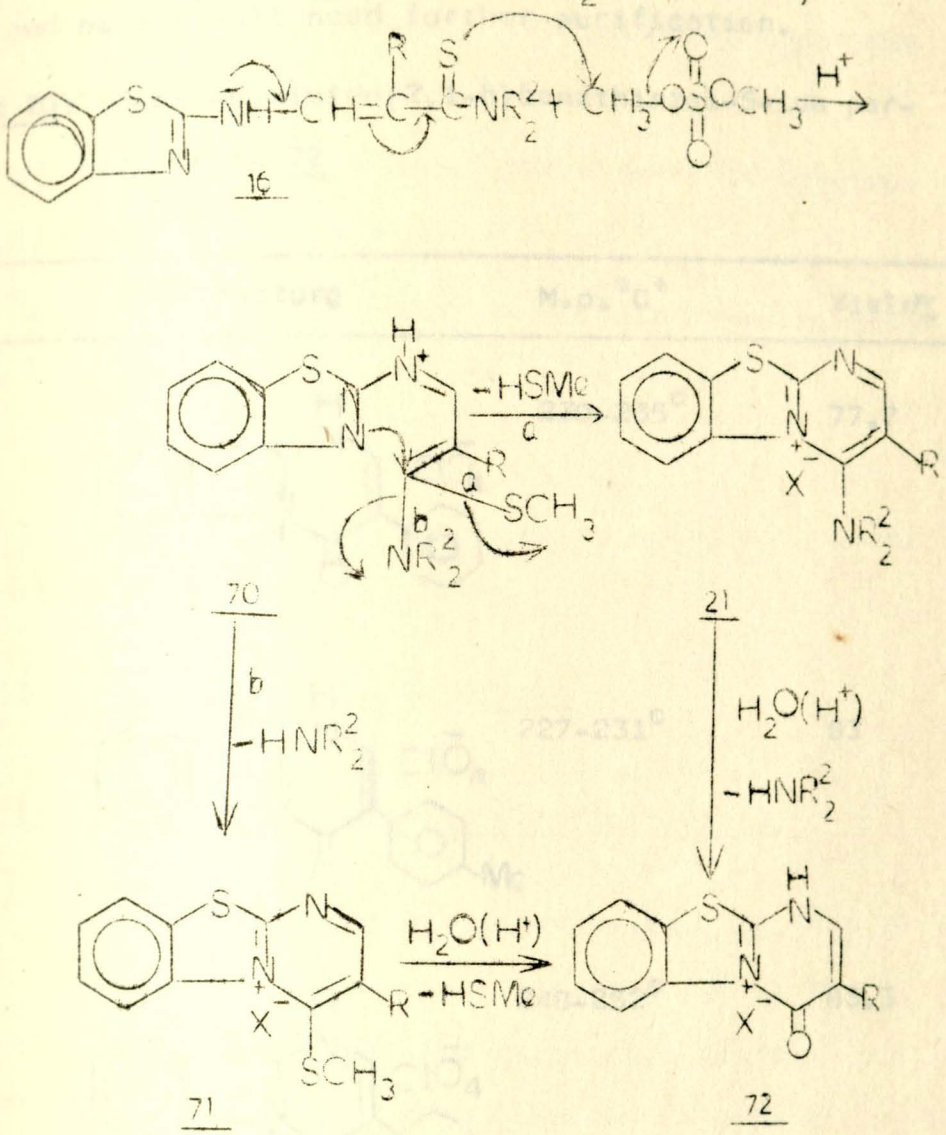
8. Synthesis of Pyrimido(2,1-b)benzthiazol-5-ium Compounds 72

The title compounds have been synthesized to date from the reactions of 2-aminobenzothiazole with 1,3-bifunctional electrophiles such as 1,3-dicarbonyl or related compounds under acidic conditions.

In the present work the synthesis of these compounds was effected by the intramolecular cyclization reaction of 3-(2-benzthiazolylamino)-thioacrylmorpholides 16 in the presence of dimethylsulphate under acidic conditions. As mentioned earlier the thioacrylamides would undergo cyclization reactions involving either elimination of methylmercaptan or morpholino to give conpounds 21 or 71 respectively. But these compounds were not found as end products. Instead the hydrolysis product, compound 72 was obtained. Possible mechanisms of reactions leading to the formation of compound 72 are depicted in Scheme 8 below.

The nucleophilic attack at position 1 of the isothioamide 70 (Scheme 8) will result either in the substitution of methylmercaptan or morpholino to give 4-morpholino or 4-methylmercapto-pyrimido(2,1-b)benzthiazolium compounds 21 or 71 respectively. Then the hydrolysis of these compounds results in the formation of compound 72.

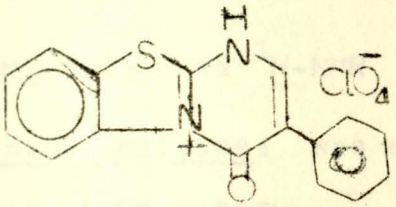
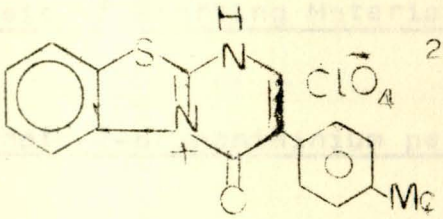
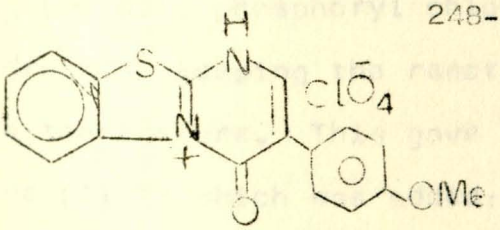
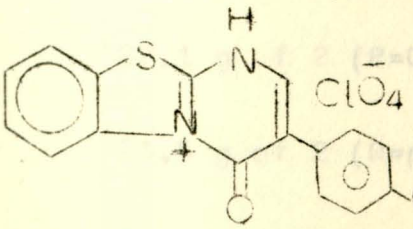
Scheme 8: Possible Mechanisms for the Formation of Compound 72 (R=aryl, NR^2_2=morpholino)



The structures of the compounds, melting points and yields are given in Table 20 below. The ^{1}H-NMR spectra of these compounds were not taken due to insolubility. The compounds were identified on the basis of their IR and mass spectra. The IR spectra gave the stretching frequencies of (C=O), (C=N) and perchlorate from (1705-1720), (1610-1640) and at 1100 cm^{-1} respectively

The mass spectra did not show the molecular ion peaks. But fragment ions for (M^+-$HClO_4$), (M^+-$HClO_4$-CO), etc. were observed and comply with the structures proposed. The GC-MS data showed trace impurities in these compounds and as a result need further purification.

Table 20: 4-oxo-pyrimido(2,1-b)benzthiazol-5-ium perchlorate 72

Cpd	Structure	M.p.°C[+]	Yield%
72a		230-235[c]	77.7
72b		227-231[c]	83
72c		248-252[c]	83.3
72d		258-263[c]	84

[+]Recrystallized from acetic acid.

[c]

IV. EXPERIMENTAL

Melting point: melting points were determined by unimelt Thomas Hover Capillary melting point apparatus and are uncorrected.

IR: by perkin-Elmer Model 727 B Infrared Spectrophotometer and values are given in cm^{-1}.

^{1}H-NMR: by Jeol FX 90 Q FT Nuclear Magnetic Resonance Spectrometer. Values are given in ppm.

^{13}C-NMR: Same as ^{1}H-NMR

Elemental Analyses: was done at Humboldt University section of Chemistry.

1. Synthesis of Starting Materials

3-Mercapto-2-propeniminium perchlorates (3)

To a solution of dimethylformamide (7.5 g) in CCl_4 (50 ml), phosphoryl chloride (16 g) was added dropwise keeping the reaction mixture at room temperature. This gave the formamide chloride (1) to which was added:

22.1 g of 2 ($R=C_6H_5$) or

23.5 g of 2 ($R=p\text{-}CH_3C_6H_4$) or

25.1 g of 2 ($R=p\text{-}CH_3OC_6H_4$) or

25.5 g of 2 (R=p-ClC_6H_4)

and the mixture was then refluxed for 45 minutes. The warm mixture was mixed with an equal amount of glacial acetic acid and about 10 ml of 70% $HClO_4$ added to it. The resulting mixture was stirred well, diluted with sufficient amount of diethylether and left aside for sometime till crystallization was complete. The product was suction filtered, washed with glacial acetic acid and diethyl ether, air dried and finally kept in a fridge.

2. Synthesis of 3-(2-pyridylamino)thioacrylmorpholides 14

To a solution of 0.94 g of 2-aminopyridine in 10 ml of ethanol was added;

3.75 g of (3a) or

3.9 g of (3b) or

4.06 g of (3c) or

4.1 g of (3d)

and the mixture was refluxed for one hour. It

was then allowed to cool to room temperature. The product was suction filtered, washed with ethanol, air dired and kept in a container.

14a

IR/KBr: 3350 (N-H); 3100, 3060, 3005 (Ar., C-H); 2950, 2900 (alkane, C-H); 1650 (C=N); 1300 (C-N); 1230 (C=S); 1120 (C-O); 740 - 780 (Mono sub. Ar.).

14b

IR/KBr: 3310 (N-H); 3090, 3050 (Ar. C-H), 2950, 2860 (alkane, C-H); 1645 (C=N); 1300 (C-N); 1220 (C=S); 1105 (C-O); 805 (p-sub- Ar).

MS: m/e (rel. int.); 18 (14.5), 28 (26.29), 78 (88.56), 79 (29.56), 95 (100), 96 (6.68), 227 (1.16), 245 (43.8), 246 (20.71), 306 (4.29), 307 (1.02), 339 (M^+, 36.92).

14c

IR/KBr: 3350 (N-H); 3100, 3050, 3005 (Ar. C-H); 2960, 2900 (alkane, C-H); 1650 (C=N); 1295 (C-N); 1245

(C=S); 1105, 1025 (C-O); 825 (p-sub. Ar.).

MS: m/e (rel. int.); 28 (34.6), 78 (94.3), 79 (35.1), 95 (97.9), 225 (40.5), 229 (45.4), 237 (29.5), 261 (100), 262 (39.8), 355 (M^+, 85.4).

14d

IR/KBr: 3300 (N-H); 3070, 3005 (Ar. C-H); 2947, 2860 (alkane, C-H); 1640 (C=N); 1300 (C-N); 1200 (C=S); 1100 (C-O); 810 (p-sub. Ar.).

3. Synthesis of 3-(4-methyl-2-thiazolylamino)thioacryl-morpholides (15)

1.14 g of 4-methyl-2-aminothiazole was dissolved in 10 ml of ethanol. To this was added:

3.76 g of (3a) or
3.9 g of (3b) or
4.06 of (3c) or
4.1 g of (3d)

and the mixture was refluxed for one hour. This

was allowed to cool. The product obtained was suction filtered, washed with ethanol and air dried.

15a

IR/KBr: 3130 (N-H); 3050, 3005 (Ar. C-H); 2950, 2860 (alkane, C-H); 1630 (C=N); 1280 (C-N); 1220 (C=S); 1105 (C-O).

15b

IR/KBr: 3190 (N-H); 3090, 3060, 3005 (Ar, C-H); 2945, 2870 (alkane, C-H); 1638 (C=N); 1280 (C-N); 1220 (C=S); 1110 (C-O); 801 (p-sub. Ar).

MS: m/e (rel. int.); 18 (13.20), 28 (35.94), 45 (50.17), 86 (26.30), 115 (59.38), 116 (15.81), 213 (67.29), 214 (17.29), 246 (100), 247 (17.80), 359 (M^+, 62.71).

15c

IR/KBr: 3200 (N-H); 3125, 3100, 3005 (Ar.CH), 2950, 2860 (alkane, CH); 1640 (C=N); 1280 (C-N); 1258, 1101, 1020 (C-O); 1225 (C=S); 820 (p-sub. Ar.).

MS: m/e (rel. int.); 28 (37.61), 45 (53.98), 86 (32.61), 114 (30.68), 115 (23.98), 130 (23.07), 229 (100), 230 (22.61), 257 (30.91), 261 (42.84), 262 (90), 263 (16.7), 287 (32.95), 375 (M^+, 92.05).

15d

IR/KBr: 3440 (N-H); 3100, 3005 (Ar. C-H); 2925, 2875 (alkane, C-H); 1630 (C=N); 1280 (C-N); 1220 (C=S); 1100 (C-O); 820 (p-sub. Ar).

4. Synthesis of 3-(2-benzothiazolylamino)thioacryl morpholides 16

To a solution prepared by dissolving 1.5 g of 2-aminobenzothiazole in 10 ml of ethanol;

3.76 g of (3a) or
3.9 g of (3b) or
4.6 g of (3c) or
4.1 g of (3d)

was added and the mixture was refluxed for one hour.

The resulting reaction mixture was cooled to room temperature, then suction filtered, washed with ethanol, and air dried.

16a

IR/KBr: 3270 (N-H); 3100, 3005 (Ar. C-H), 2960, 2900 (alkane, C-H); 1660 (C=N); 1280 (C-N); 1230 (C=S); 1120 (C-O).

MS: m/e (rel. int.); 28 (23.3), 45 (22.1), 134 (39.0), 150 (23.8), 151 (21.0), 199 (45.3) (46.9), 232 (100), 263 (33.1), 381 (M^+, 56.4).

16b

IR/KBr: 3250 (N-H); 3050, 3005 (Ar. C-H); 2945, 2855 (alkane, CH); 1630 (C=N); 1260 (C-N); 1220 (C=S); 1100 (C-O); 801 (p. sub. Ar.).

MS: M/e (rel. int.); 18 (18.22), 28 (29.96), 45 (29.25), 91(20.4) 115 (37.65), 130 (23.58), 134 (45.85), 135 (27.73), 150 (24.39), 151 (23.89) 161 (31.58), 213 (61), 245 (55.87), 246 (100), 247 (19.13),

277 (30.47), 395 (M^+, 65.99).

16c

IR/KBr: 3150 (NH); 3045, 3005 (Ar. CH); 2900, 2850 (alkane, CH); 1625 (C=N); 1280 (C-N); 1210 (C=S); 1105, 1010 (C-O); 820 (p-sub. Ar.).

16d

IR/KBr: 3200 (NH); 3060, 3005 (Ar. CH); 2925, 2880, (alkane, CH): 1625 (C=N); 1260 (C-N); 1220 (C=S); 1100 (C-O); 820 (p. sub. Ar.).

5. Synthesis of Pyrazolo(1,5-a)pyrimidines 18

To a solution prepared by dissolving 0.01 mole of 5-substituted 3-aminopyrazoles in 10 mls of 0.01 mole of ;

3a (R=ph) or

3b (R=p-tolyl) or

3c (R=p-anisyl) or

3d (R=p-chlorophenyl) or

3e (R=p-bromophenyl)

was added and the mixture was refluxed until the evolution of H_2S gas was diminished. Then it was allowed to cool to room temperature. The precipitate was filtered by suction, washed with ethanol and air dried.

18a

IR/KBr: 3150, 3080, 3005 (Ar. CH); 2950, 2900 (alkane, CH); 1665 (C=N); 1270 (C-N); 1100 (C-O); 820 - 860 (p. sub. Ar.).

MS: m/e (rel. int.); 18 (100), 28 (55.7), 102 (74.2), 138 (52.1), 140 (73.4), 305 (56.5), 345 (65.6), 346 (50.2), 347 (51.1), 390 (M^+, 91.1).

18b

IR/KBr: 3100, 3050, 3005 (Ar. CH); 2950, 2900 (alkane, CH); 1610 (C=N); 1270 (C-N); 1100 (C-O); 835 (p-sub. Ar).

MS: m/e (rel. mt.); 18 (27.5), 27 (27.7), 28 (49.3),

111 (45.3), 113 (23.2), 115 (100), 116 (69.8), 138 (43.5), 359 (54.5), 360 (39.8), 373 (32.8), 386 (36.9), 387 (22.2), 404 (M^+, 92.82).

18c

IR/KBr: 3100, 3050, 3005 (Ar. CH); 2950, 2900 (alkane, CH); 1610 (C=N); 1100, 1030 (C-O); 835 (p-sub. Ar.).

MS: m/e (rel. int.); 18 (70.2), 28 (48.7), 132 (44.4), 138 (36.4), 350 (35.5), 375 (44.1), 377 (37.4), 402 (40.9), 420 (M^+, 100).

18d

MS: m/e (rel. int.); 55 (24), 56 (10), 57 (19), 58 (10), 69 (15), 71 (11), 73 (100), 85 (9), 95 (9), 127 (20), 138 (11), 140 (25), 167 (10), 331 (14), 385 (13, 398 (11), 400 (10), 411 (9), 423 (11), 424 (11), 425 (14), 426 (12), 451 (10), 452 (11), 469 (M^+, 12), 470 (20),

MS: m/e (rel. int.); 27 (25.2), 28 (37.2), 91 (74.8); 118 (82.9), 319 (68.4), 334 (53.3), 359 (73.2), 360 (55.84), 361 (54.2), 373 (43.2), 386 (37.8), 387 (21.8), 404 (M^+, 100).

18f

MS: m/e (rel. int.); 77 (100), 104 (86.3), 136 (46.7), 140 (52.1) 305 (63), 320 (46.7), 345 (68.2), 346 (50), 347 (46), 390 (M^+, 89.3).

6. Synthesis of Pyrido(1,2-a)pyrimidin-5-ium compounds 66

To 0.01 mole of dimethylsulphate in 15 ml of acetic acid 0.01 mole of ;

14a or

14b or

14c or

14d

was added and the mixture refluxed until the evolution of methylmercaptan was diminished. The resulting reaction mixture was allowed to cool and about 0.5 ml of perchloric acid added to it. The product was filtered by suction, washed with acetic acid and diethylether then air dried.

66a

IR/KBr: 3100, 3060 (Ar. CH); 2950, 2860 (alkene, CH); 1700 (C=O); 1638 (C=N); 1100 (perchlorate).

66b

IR/KBr: 3100, 3050 (Ar. CH); 2950 (alkene, CH); 1720 (C=O); 1610 (C=N); 1100 (perchlorate).

MS: m/e (rel. int.): 27 (10.5), 39 (12), 51 (39), 52 (14), 77 (16), 78 (68), 79 (10), 103 (19), 115 (13) 117 (16), 130 (19), 207 (35), 208 (100), 209 (15), 236 (89), 237 (16).

66c

IR/KBr: 3100 (Ar. CH); 2940, 2860 (alkene, CH); 1720 (C=O)

MS: m/e (rel. int.); 15 (32), 18 (19), 51 (58), 52 (19), 78(100), 146 (20), 209 (61), 224 (21), 237 (20), 252 (68).

66d

IR/KBr: 3150, 3100 (Ar. CH); 1710 (C=O); 1620 (C=N) 1100 (perchlorate); 820 (p-sub. Ar.).

MS: m/e (rel. int.); 51 (19), 78 (94), 192 (17), 193 (9), 228 (100), 229 (17), 230 (33), 256 (78), 257 (12), 258 (22), 271 (4).

7. Synthesis of Thiazolo(3,2-a)pyrimidin-4-ium Compounds 69

To 0.01 mole of dimethylsulphate in 15 ml of acetic acid 0.01 mole of;

15a or

15b or

15c or

15d

was added and the mixture refluxed until the evolution of methylmercaptan was diminished. The resulting reaction mixture was allowed to cool and about 0.5 ml of perchloric acid added to it. The product was filtered by suction, washed with acetic acid and diethylether then air dried.

69a

IR/KBr: 3140 (Ar, CH); 2950, 2875 (alkane, CH); 1715 (C=O); 1620 (C=N); 1100 (perchlorate).

69b

1720 (C=O); 1610 (C=N); 1100 (perchlorate); 810 (p-sub. Ar.).

MS: m/e (rel. int.); 39 (21), 45 (20), 103 (17), 115 (49), 116 (16), 130 (33), 227 (20), 228 (52), 256 (100), 257 (18).

69c

IR/KBr: 3150 (Ar., CH); 2980, 2880 (alkane, CH); 2980, 2880 (alkane, CH); 1715 (C=O); 1620 (C=N); 1100 (perchlorate); 820 (p-sub. Ar.).

69d

IR/KBr: 3140 (Ar, CH); 2900, 2870 (alkane CH); 1710 (C=O); 1615 (C=N); 1100 (perchlorate); 810 (p-sub. Ar.).

8. Synthesis of Pyrimido(2,1-b)benzthiazol-5-ium Compound 72

To 0.01 mole of dimethylsulphate in 15 ml of acetic acid 0.01 mole of;

16a or

16b or

16c or

16d

was added and the mixture refluxed until the evolution of methylmercaptan was diminished. The resulting reaction mixture was allowed to cool and about 0.5 ml of perchloric acid added to it. The product was filtered by suction, washed with acetic acid and

72a

IR/KBr: 3140, 3090, 3020 (Ar, CH); 2930, 2860 (alkane, CH); 1705 (C=O); 1625 (C=N); 1100 (perchlorate); 750 (O-sub. Ar.).

MS: 39 (16), 44 (25.5) 63 (15.5), 89 (29.7), 90 (20.8), 116 (51.3), 249 (16.8), 250 (52.9), 278 (100), 279 (18.2).

72b

IR/KBr: 3150, 3100, 3025 (Ar. CH); 2940, 2860 (alkane, CH); 1710 (C=O); 1630 (C=N), 1100 (perchlorate); 810 (p-sub. Ar.).

MS: m/e (rel. int.); 77 (18.8), 103 (24.2), 115 (14.6), 130 (24), 145 (13.9), 263 (15), 292 (100), 293 (19).

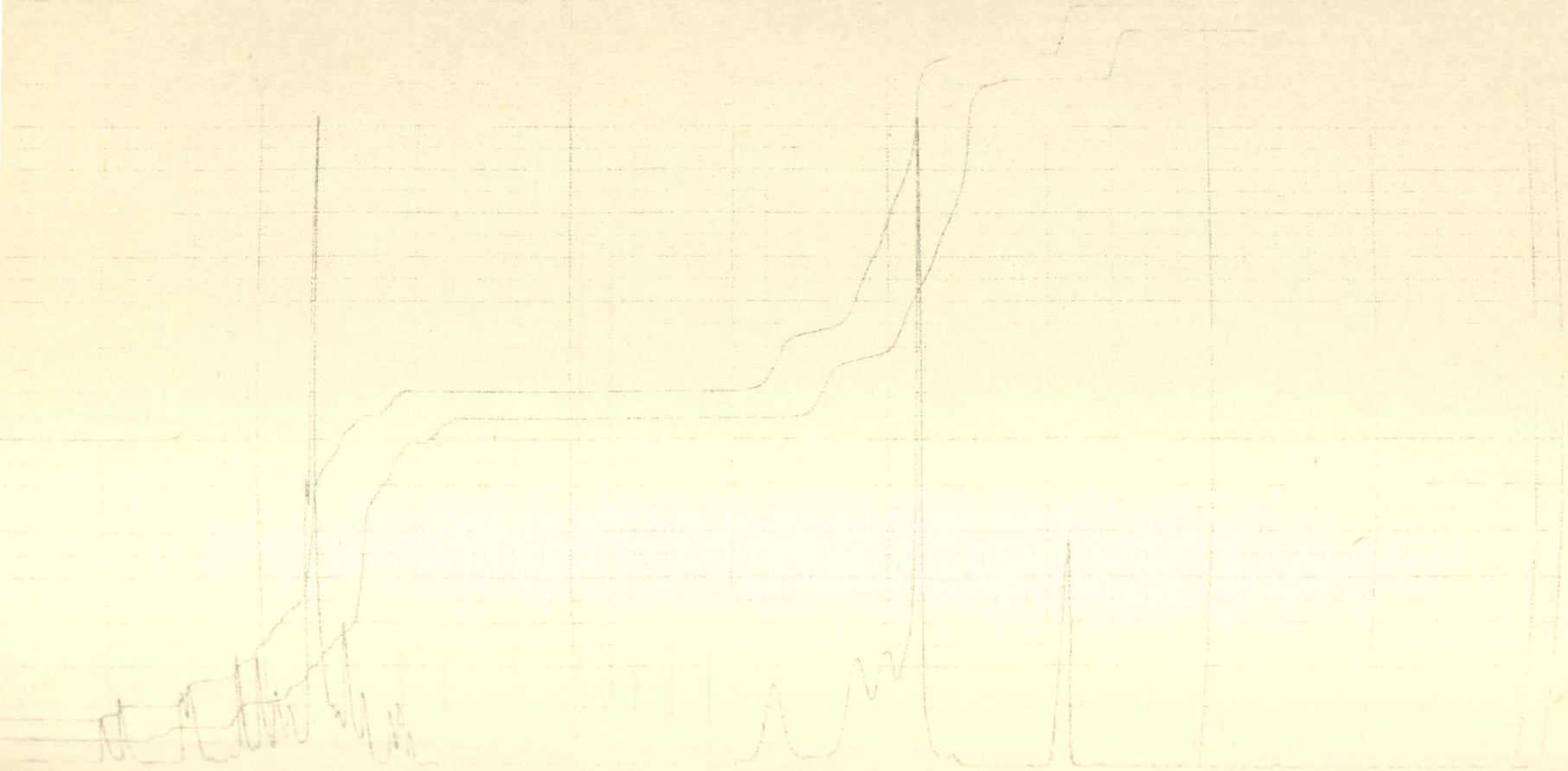
72c

IR/KBr: 3090 (Ar, CH); 2925, 2850 (alkane, CH); 1720 (C=O); 1610 (C=N); 1100 (perchlorate); 830 (p-sub. Ar.).

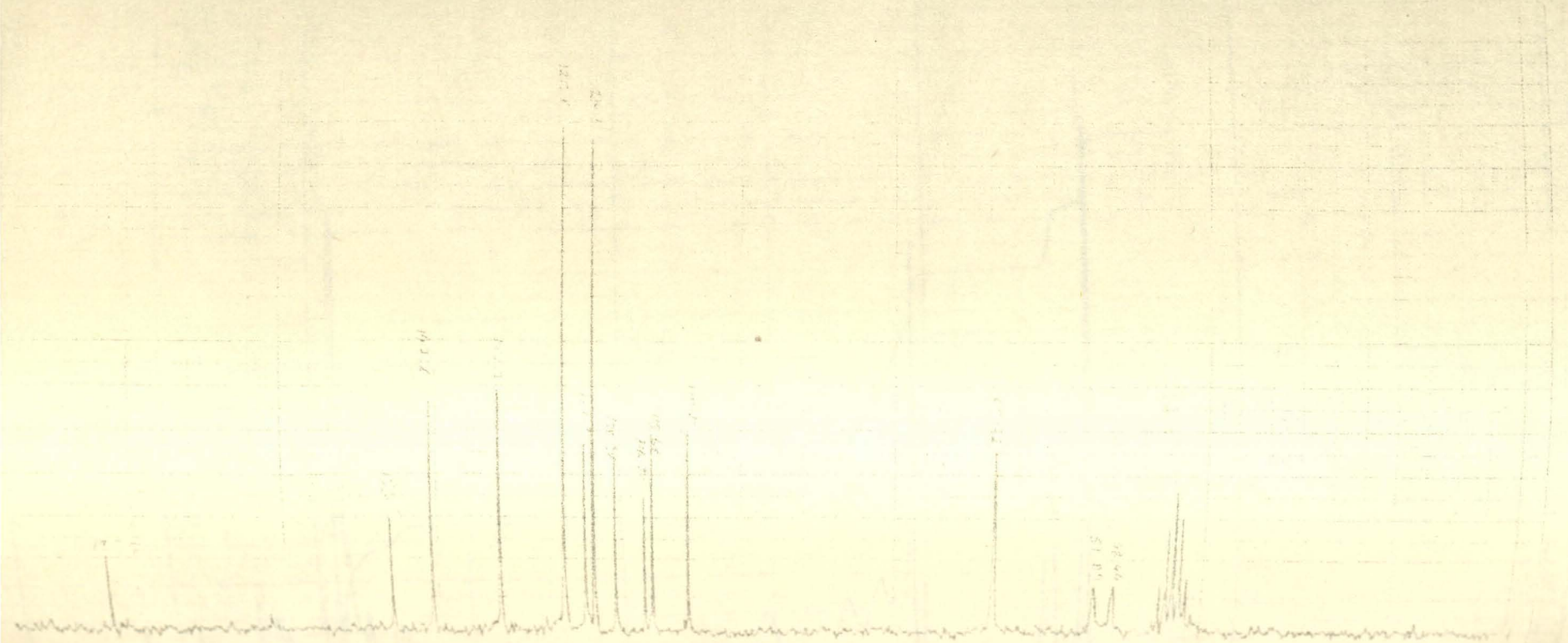
72d

IR/KBr: 3148, 3095, 3010 (Ar, CH); 2950, 2880 (alkane, CH; 1715 (C=O); 1640 (C=N); 1100 (perchlorate; (p-sub. Ar.).

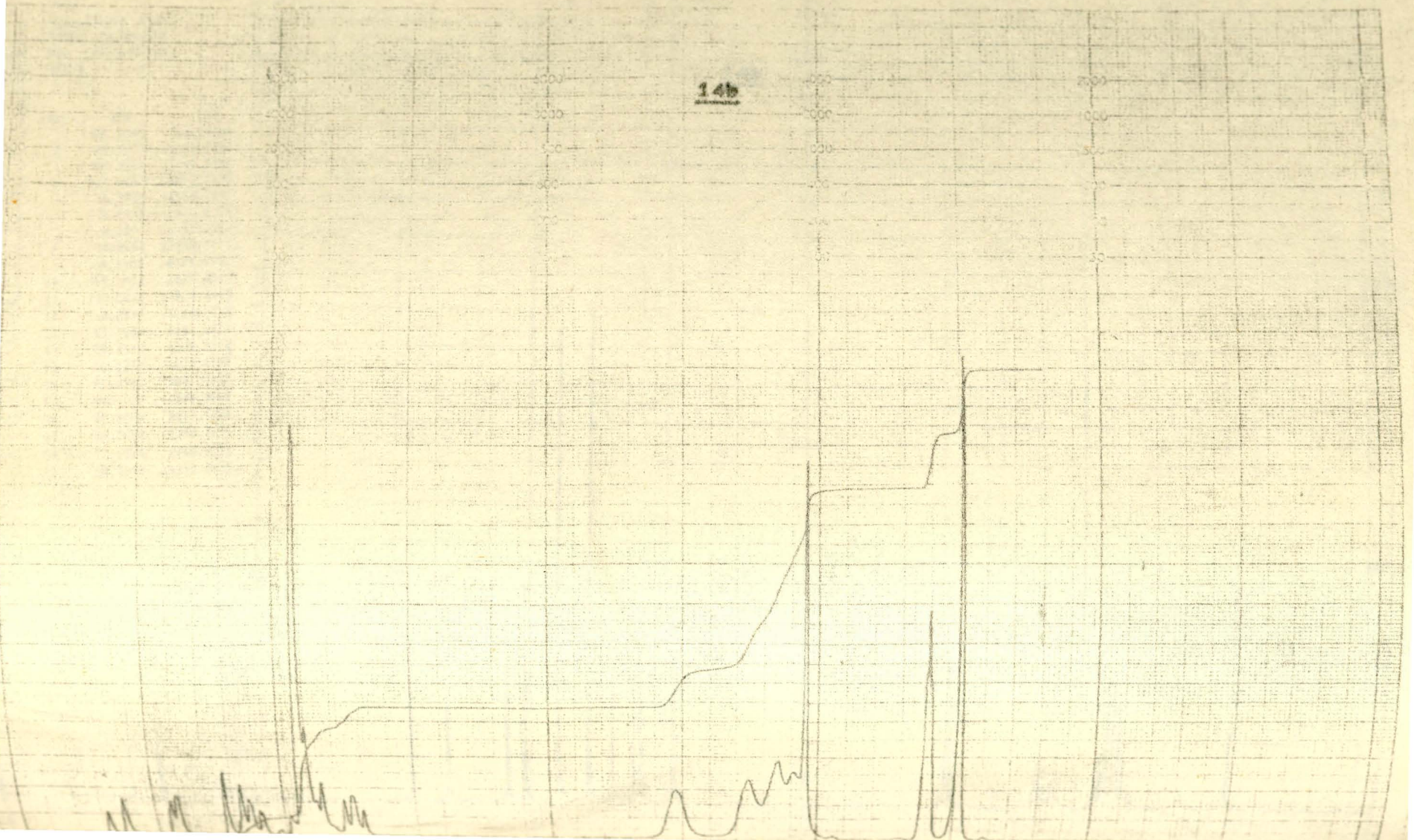
14a



14a



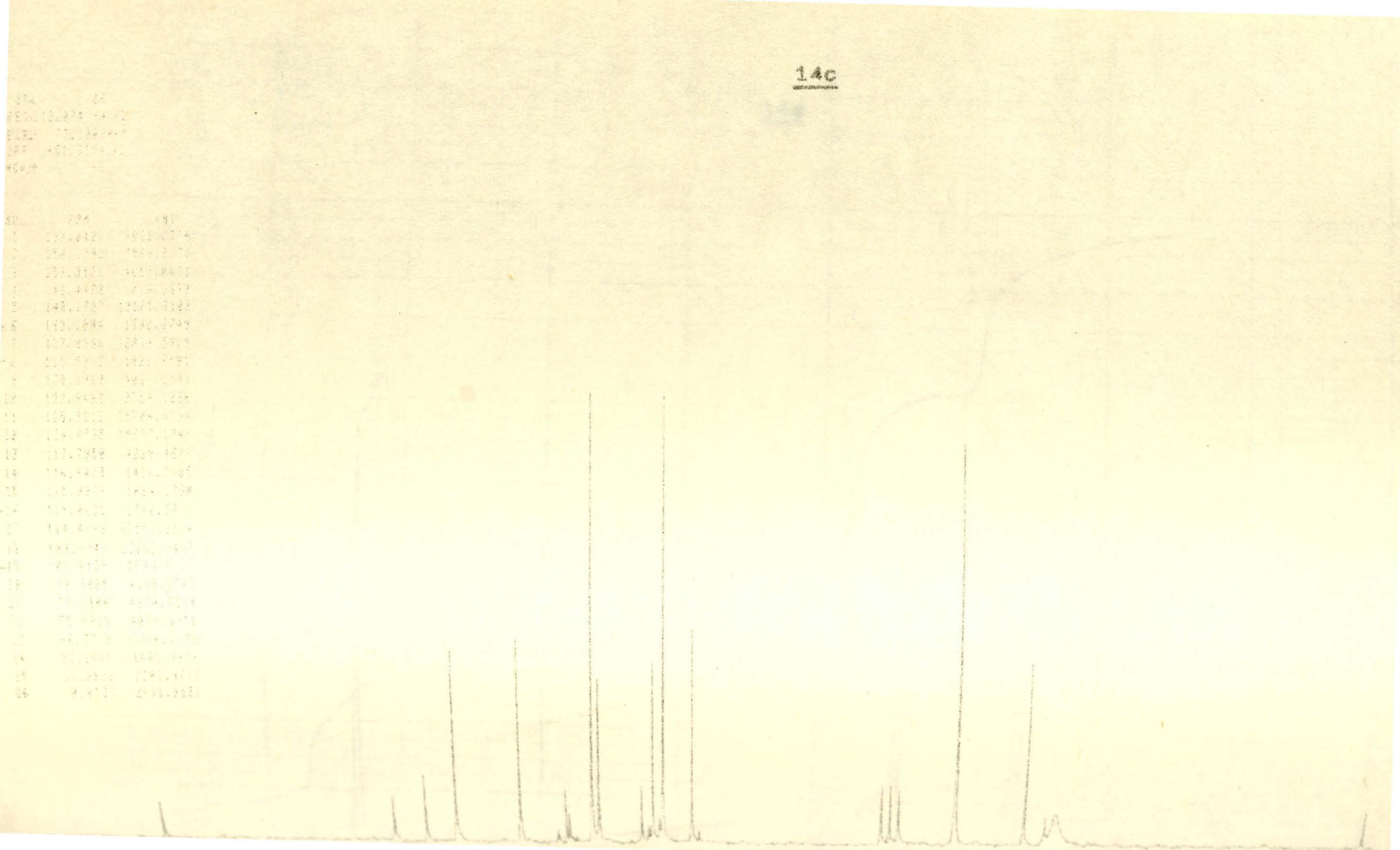
14b



TOTAL 21
RESOLUTION -4 HZ
EXPSF 39.5488PPM
OBS 1381.8359 HZ
NOISE -2

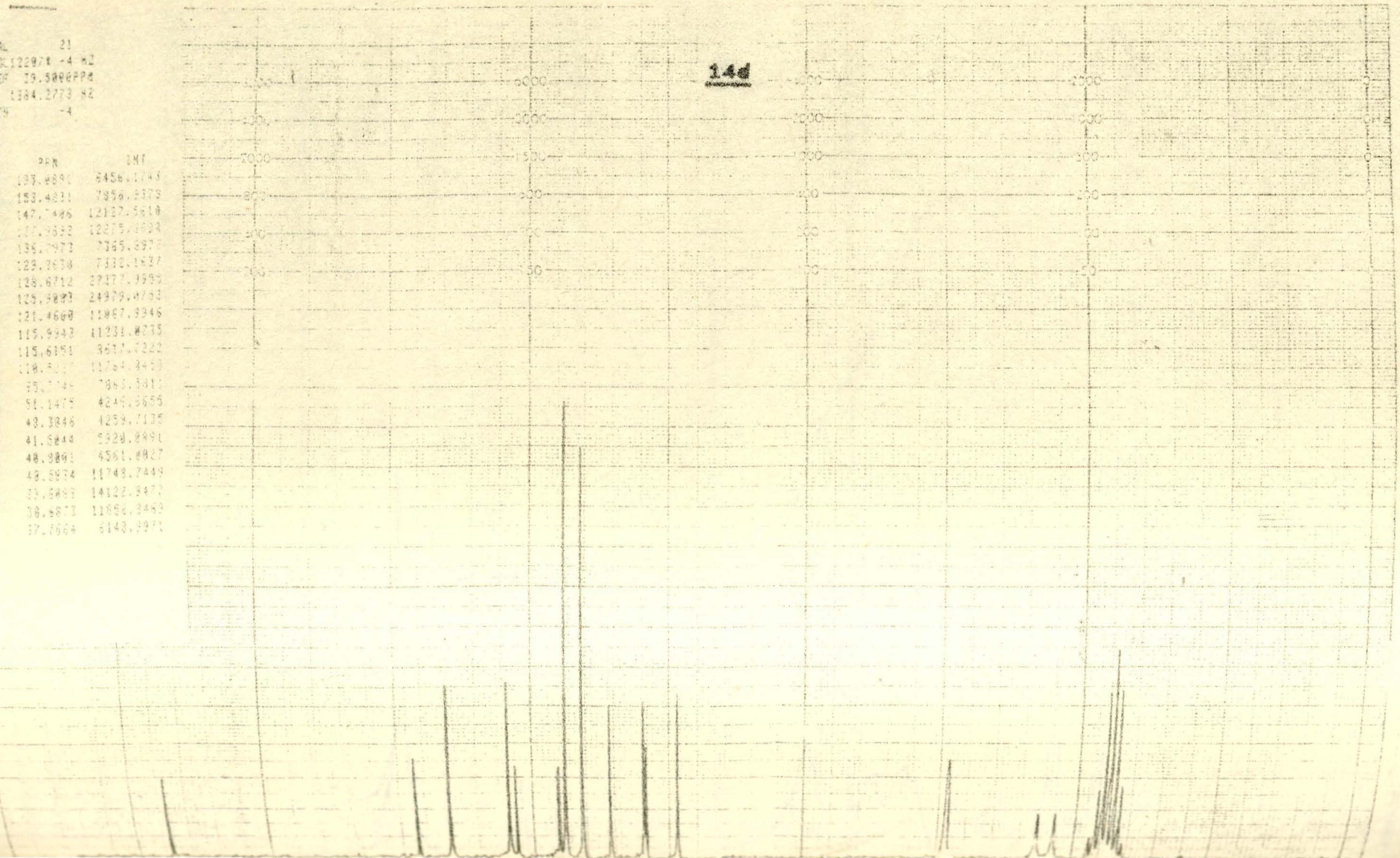
NO	PPM	INT
1	190.6305	7845.8780
2	151.9377	10292.7384
3	147.5781	17266.5151
4	137.7183	12015.2138
5	134.7935	10589.6957
6	134.4845	10922.8174
7	129.2671	16492.2891
8	124.8467	22950.5113
9	124.1658	10924.8311
10	115.8078	3871.8525
11	115.5868	12878.8463
12	110.2519	13110.2313
13	65.7294	9381.2832
14	59.9949	4372.5976
15	49.2229	4628.4859
16	41.3361	3881.9688
17	40.4751	7940.9688
18	39.5808	9687.5374
19	38.5796	8593.3828
20	37.6508	4368.4232
21	20.5948	14355.9815

14b

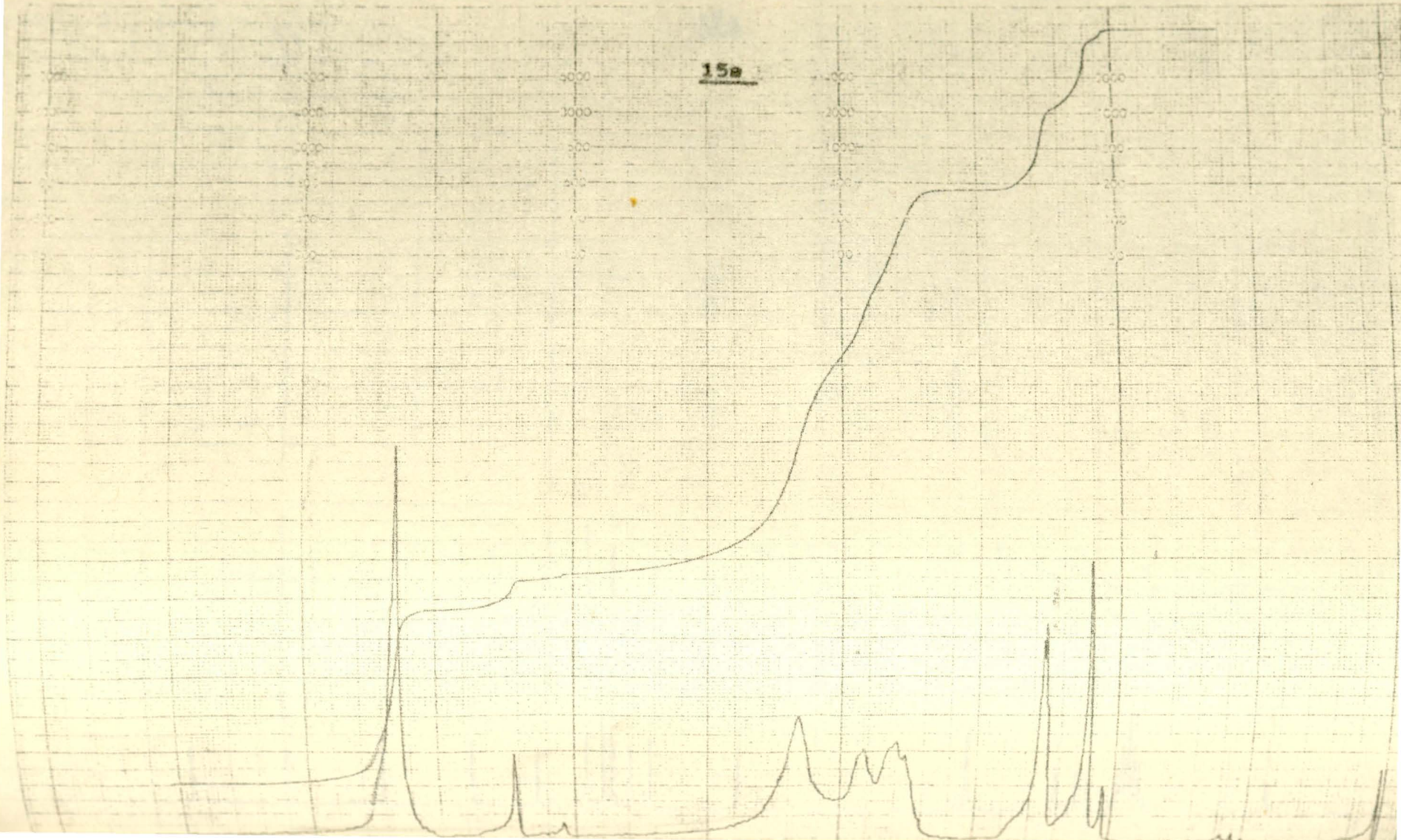



14d

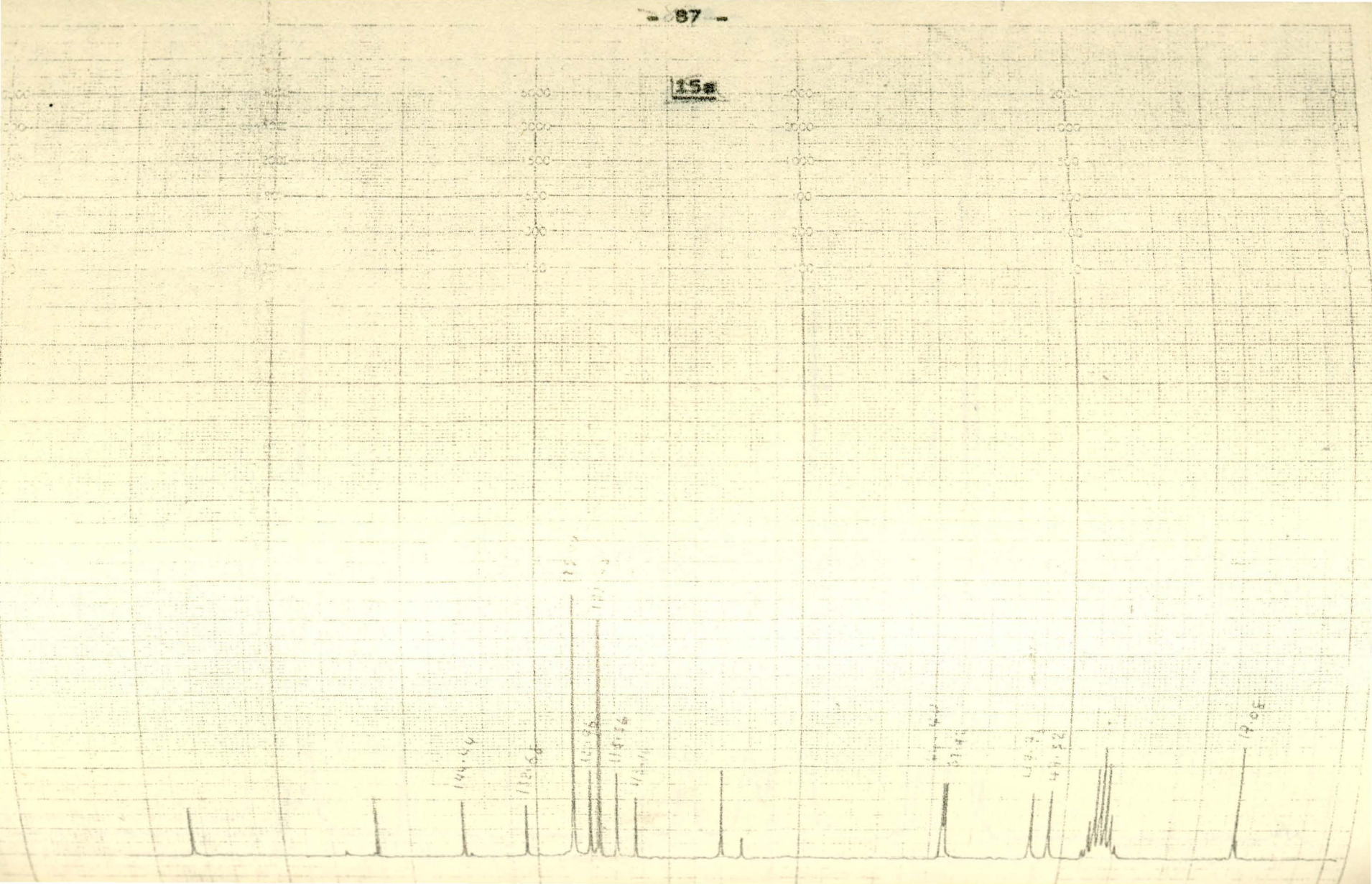
14d



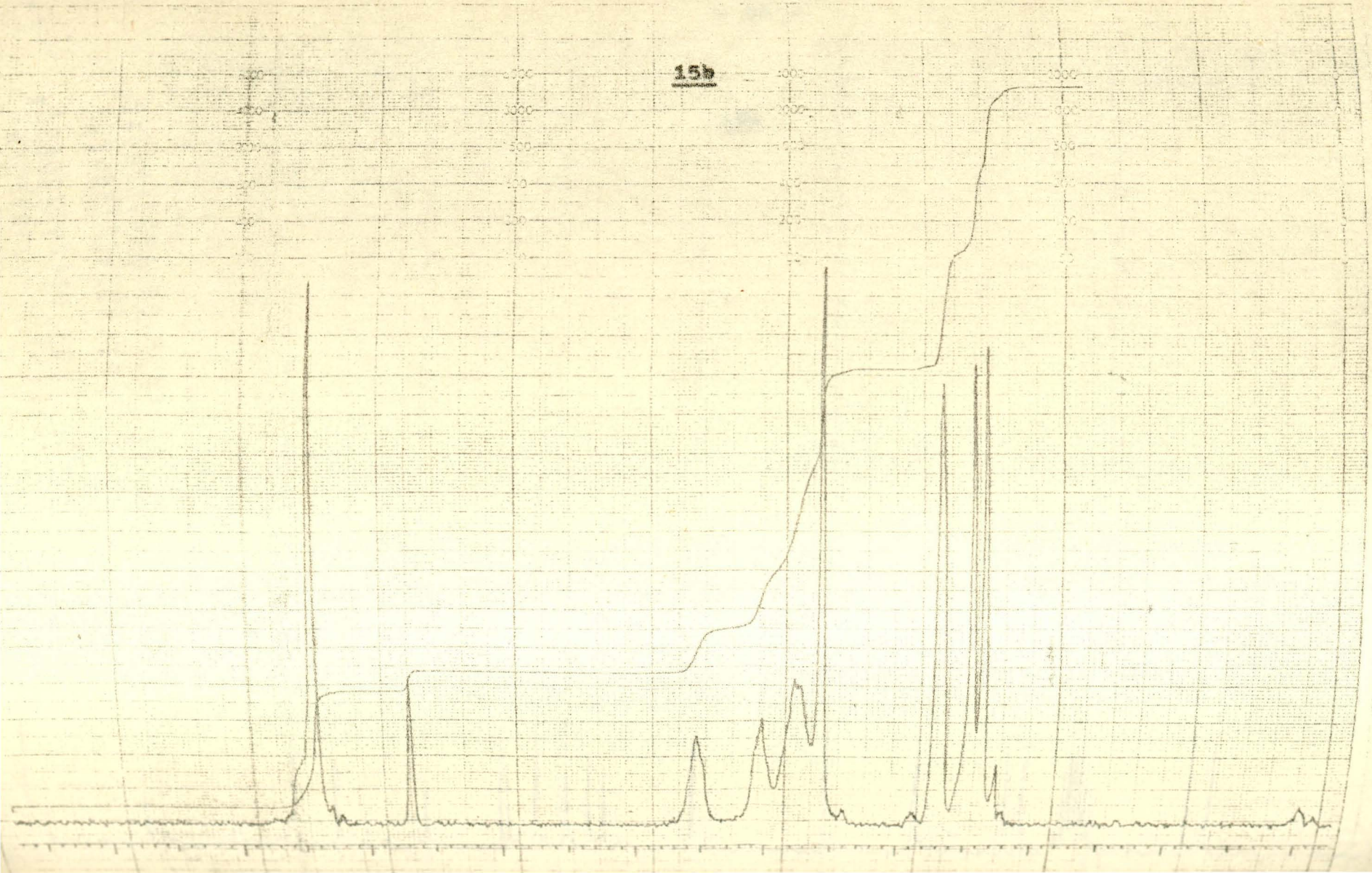
15a

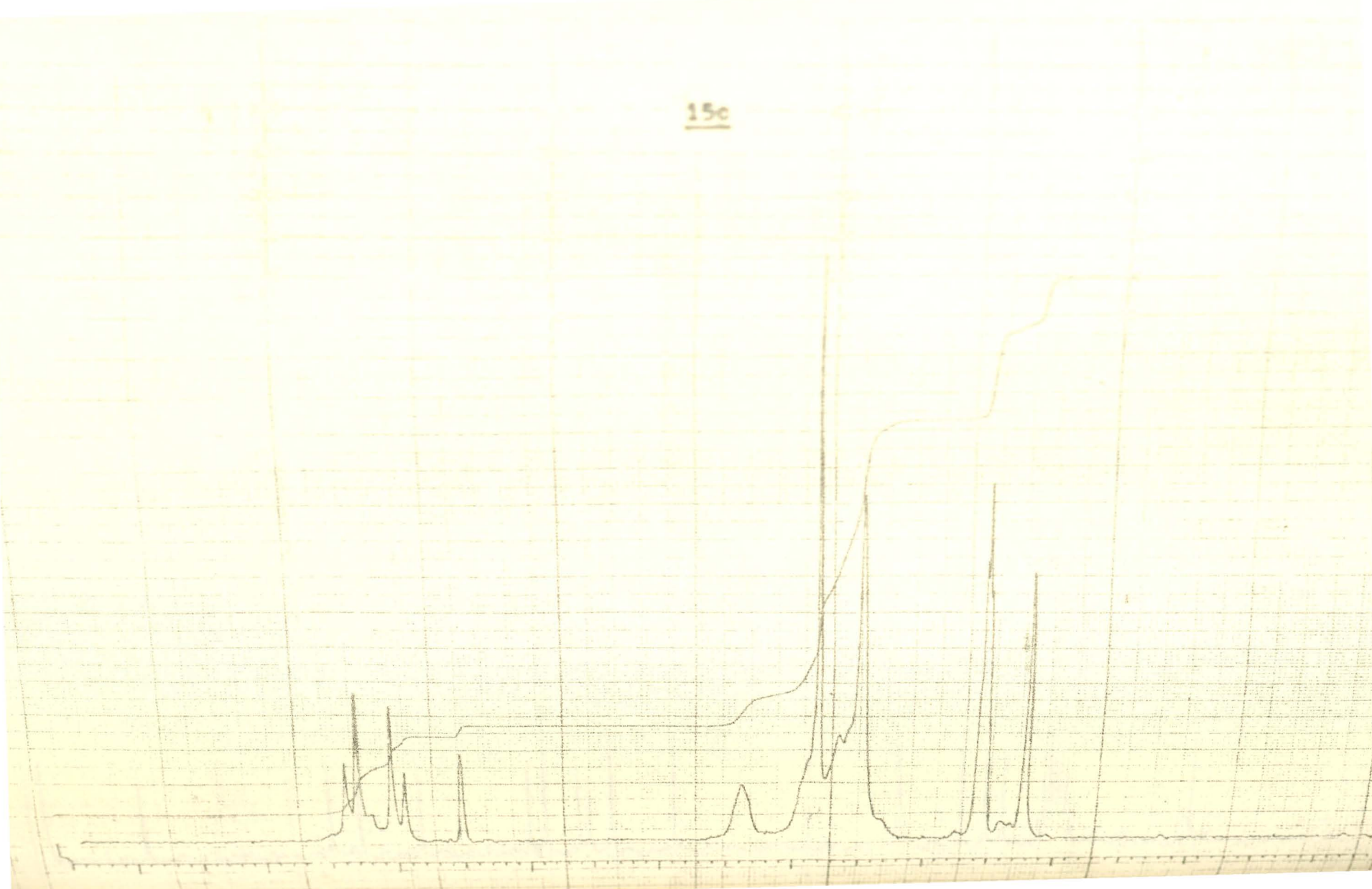


15a

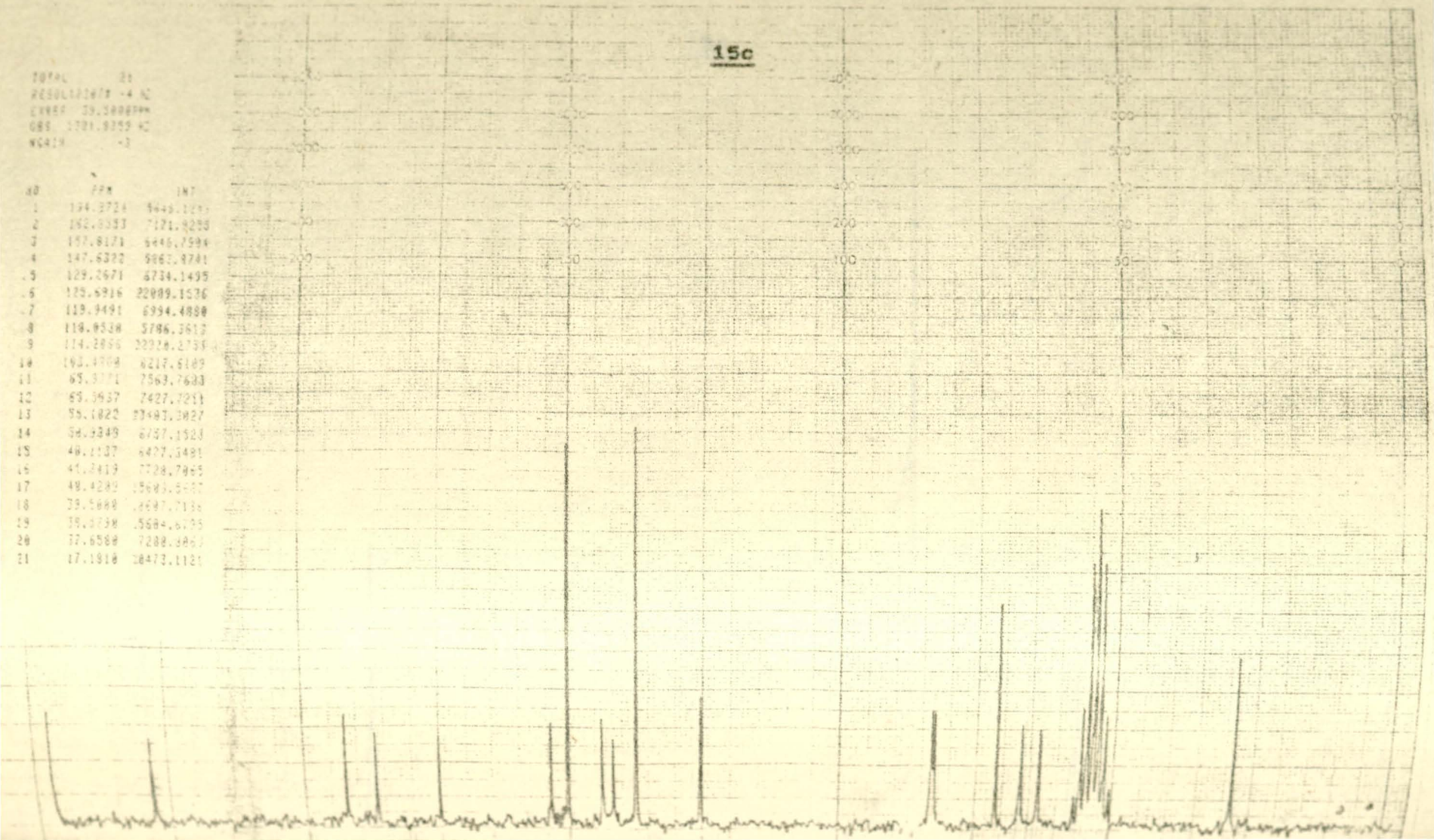


15b

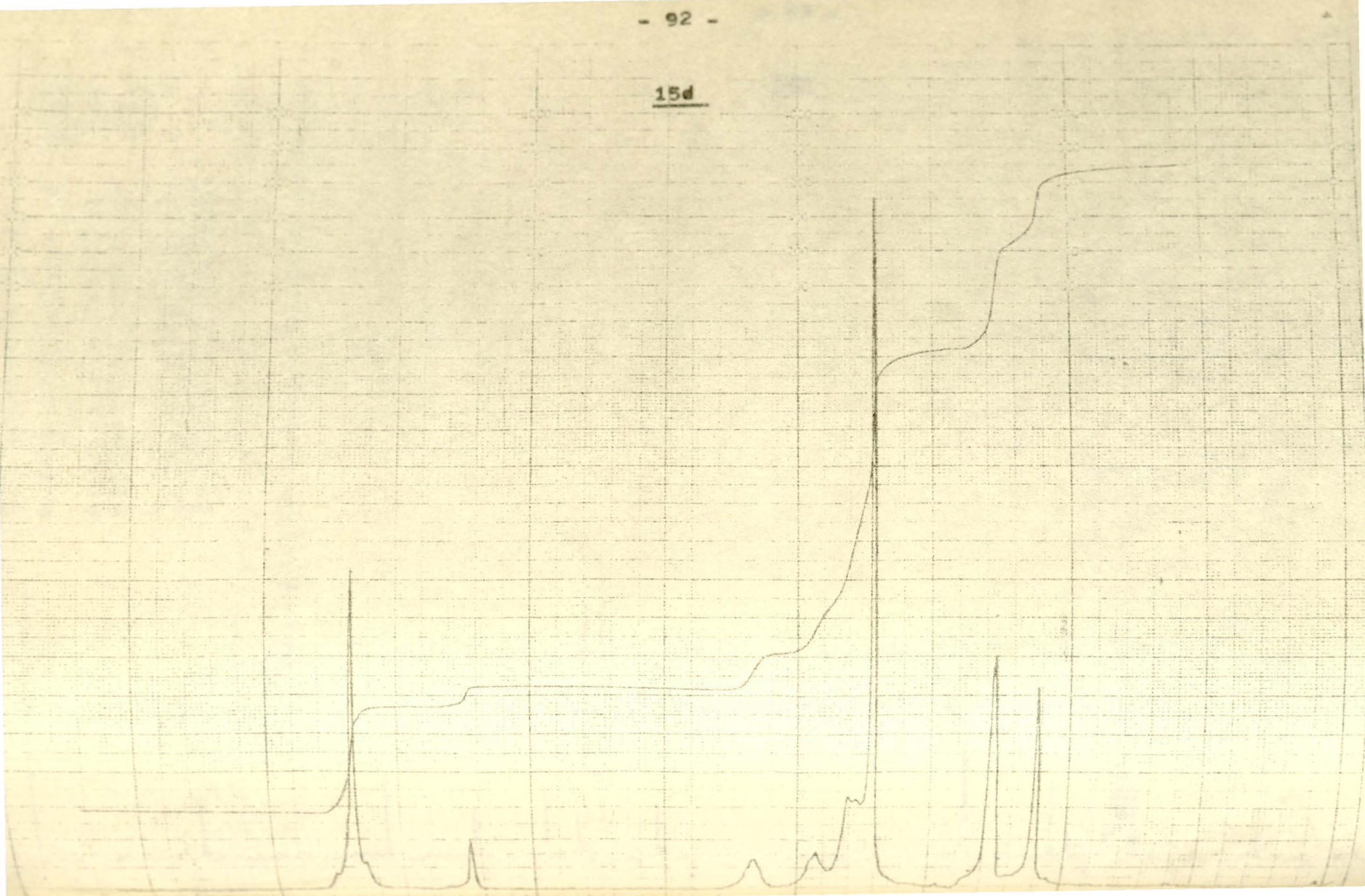




15c


TOTAL 21
RESOLUTION -4 HZ
CURSOR 39.5000PPM
OBS 1701.9259 HZ
NEGATIVE -3
NO PPM INT
1 194.3724 9449.1171
2 162.0353 7171.9299
3 157.8171 6446.7594
4 147.6322 5861.8741
5 129.2671 6734.1495
6 125.6916 22889.1576
7 119.9491 6994.4888
8 118.9538 5786.3613
9 114.2856 22938.2739
10 103.4704 6217.6189
11 65.3771 7563.7683
12 59.3637 7427.7251
13 55.1822 23491.3027
14 50.9349 6757.1523
15 48.2137 6427.3481
16 41.8413 7728.7965
17 40.4283 15803.5537
18 39.5000 8697.7136
19 38.3738 15584.6735
20 37.6588 7288.6863
21 37.1918 28473.1121

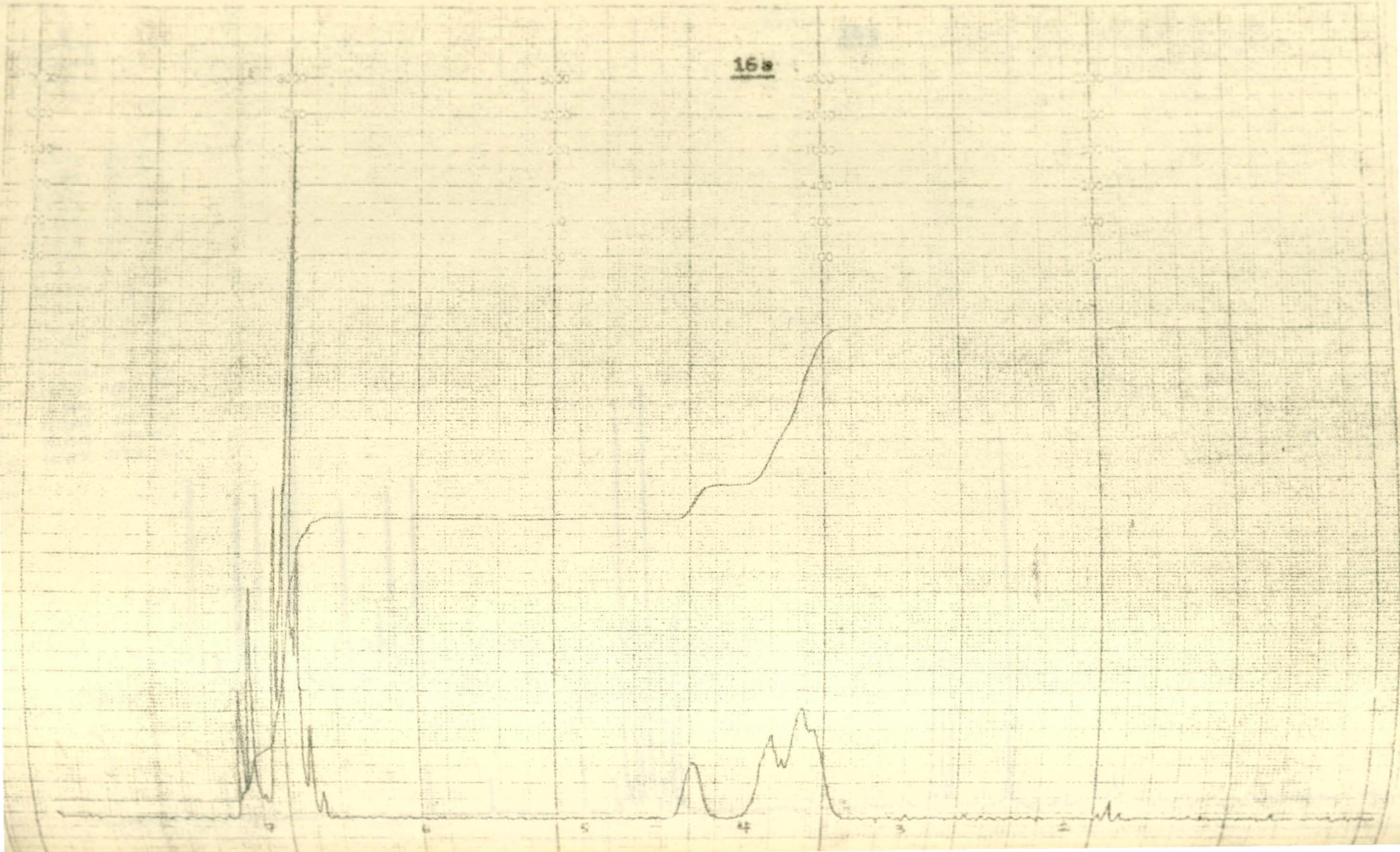
15d



15d

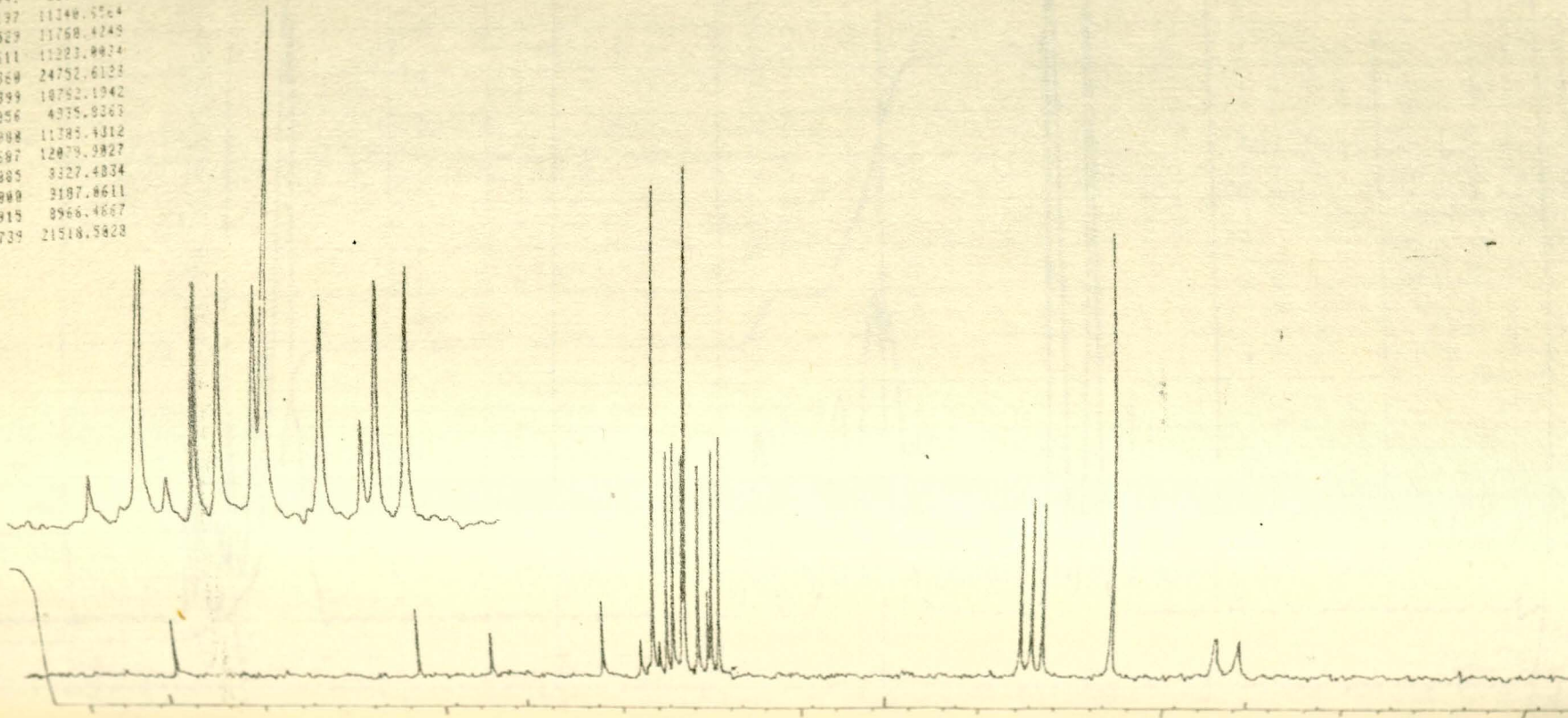
NO	PPM	INT
1	194.4032	4767.2814
2	162.3895	5108.8699
3	148.8956	4189.2958
4	136.8431	5666.2130
5	128.6215	19887.9269
6	125.9428	20839.4715
7	124.2417	19119.5039
8	12[illegible].4618	5882.2222
9	[illegible].1328	4857.3465
10	19[illegible].4152	7848.7279
11	69.2622	7332.9484
12	65.2746	7056.9891
13	52.7642	6587.0023
14	48.4929	6416.8719
15	40.6669	6736.9582
16	28.7488	13000.7156
17	25.8259	15263.9715
18	24.9641	12260.5736
19	23.8283	5824.9135
20	17.5868	10128.1899

16a

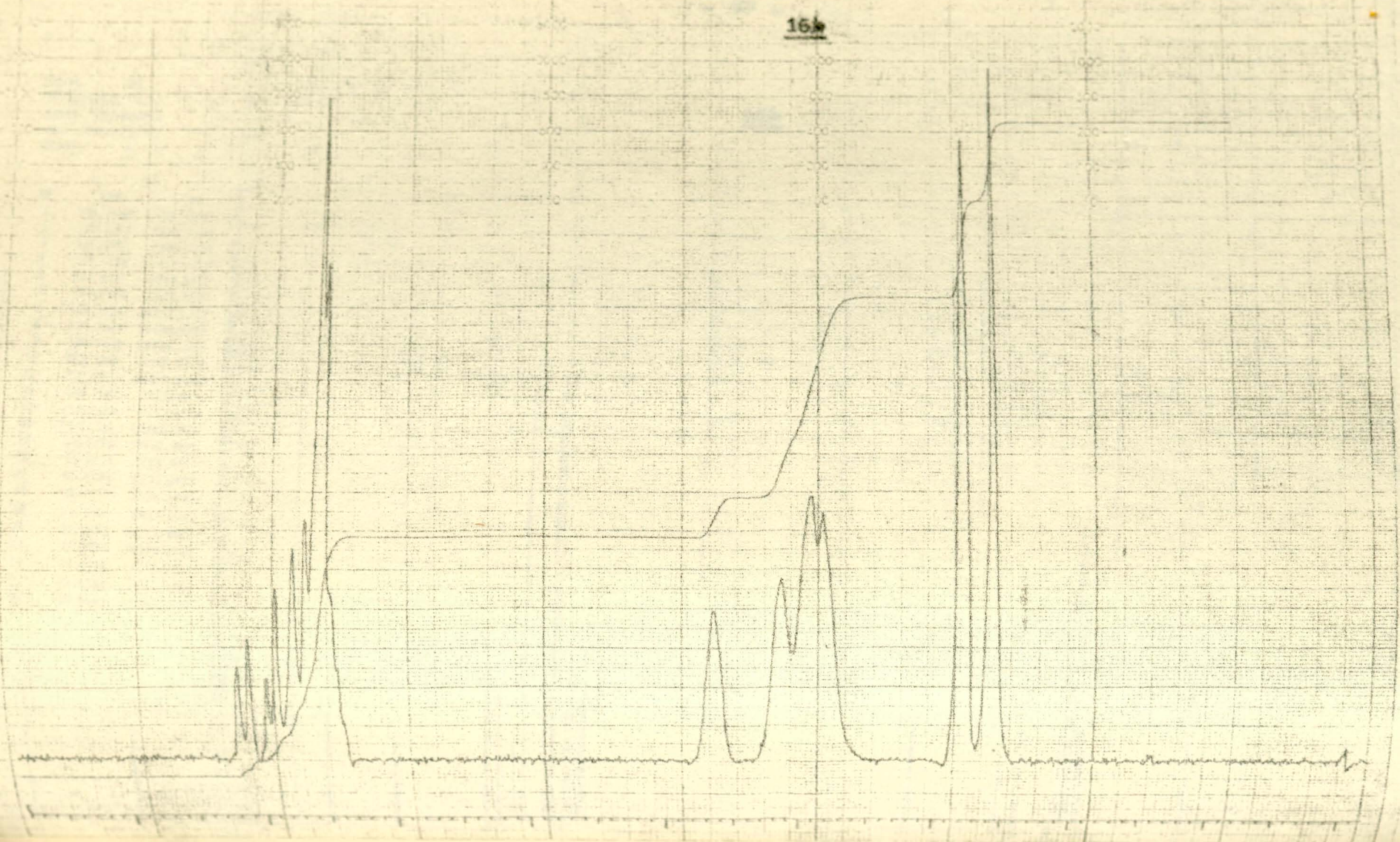


16a

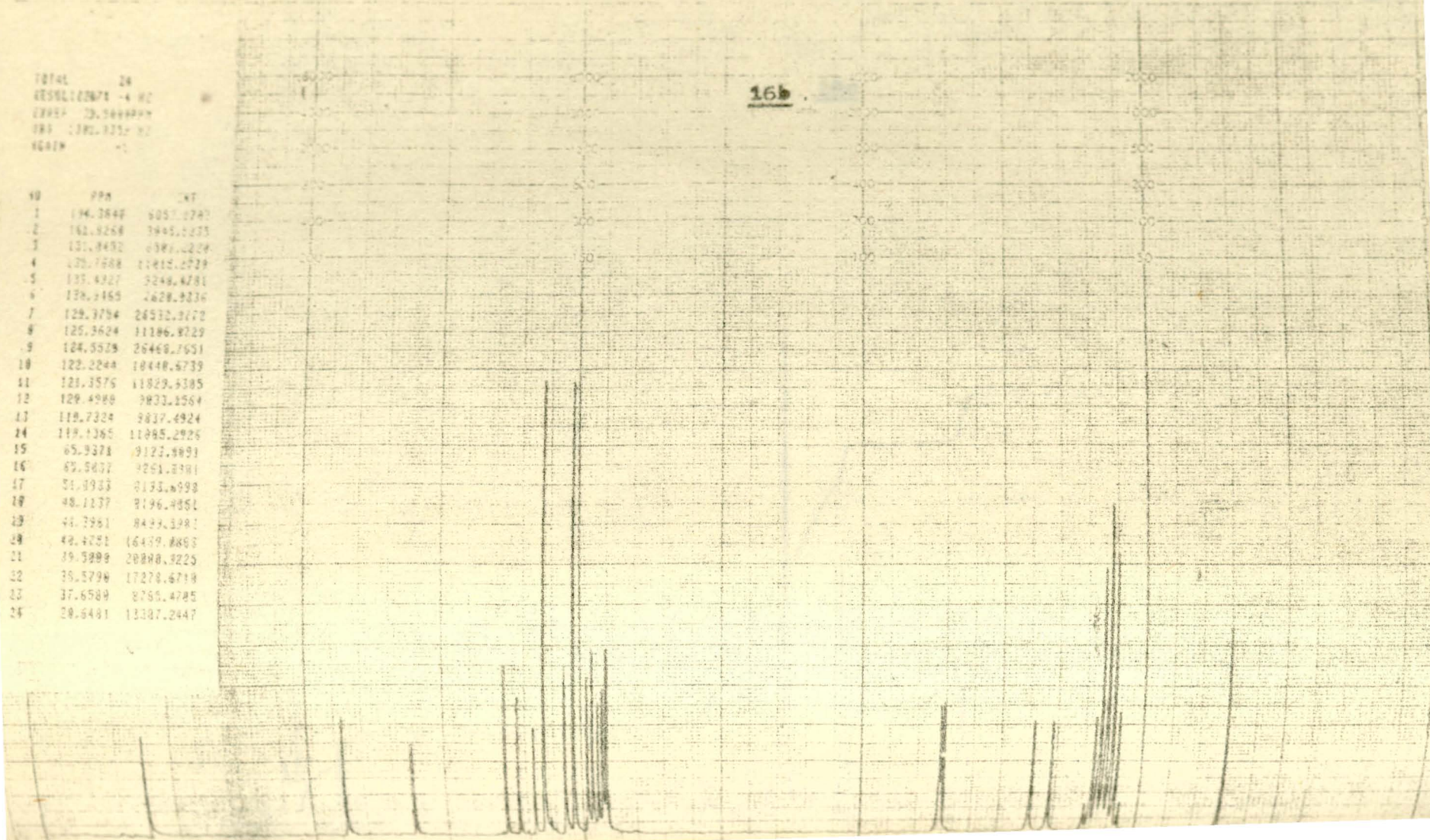
PPM	INT
65.4171	3467.4651
61.7285	4861.6516
51.5899	2697.3844
36.3443	4312.6854
30.8952	2387.3854
29.2158	23795.7247
28.2949	2261.4764
27.3197	11240.5564
126.4529	11768.4245
125.2611	11223.9824
124.9369	24752.6123
123.4399	10782.1942
121.6856	4935.8263
121.1988	11385.4312
120.1687	12079.9827
78.5685	3327.4834
77.1899	3187.8611
75.6915	8966.4667
66.3739	21518.5823



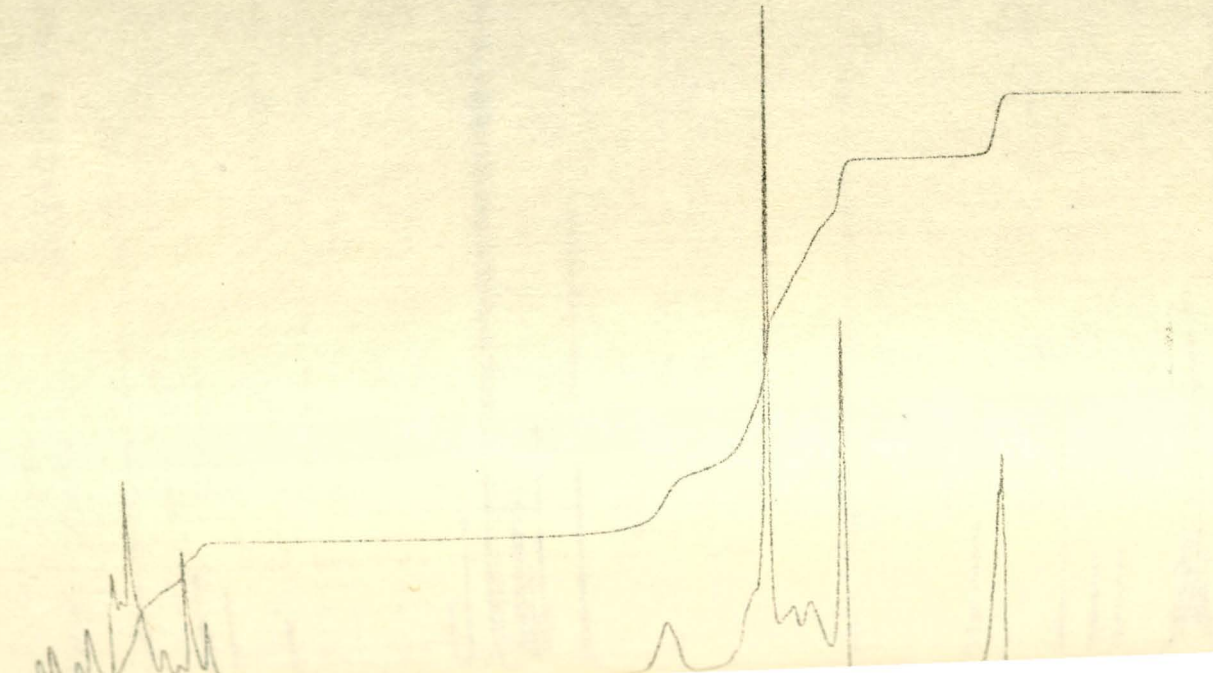
16b



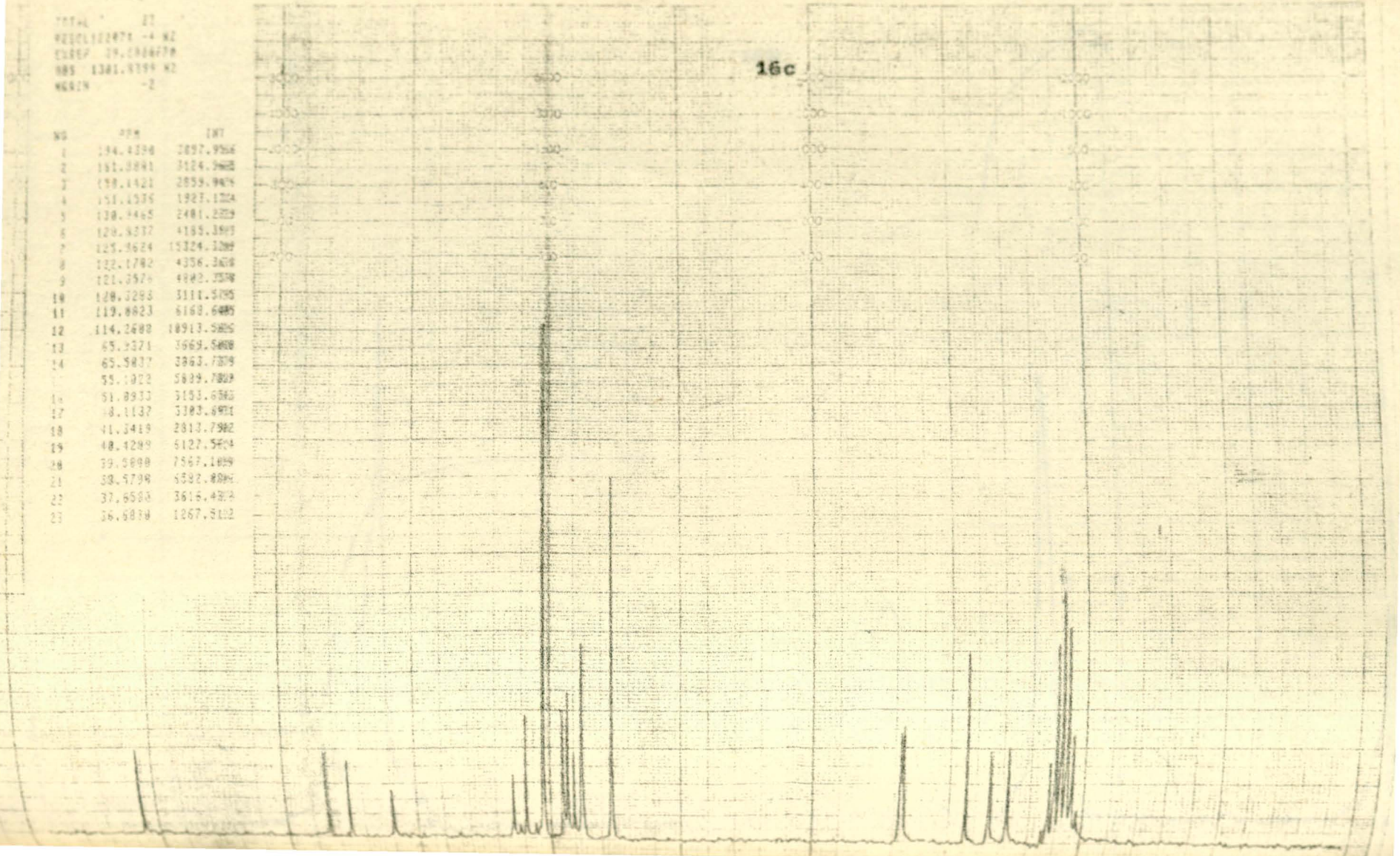
16b


TOTAL 24
RESOLUTION -4 HZ
EXPO? 29.5999999
DEL 1382.925+ HZ
AGAIN -1
NO PPM HZ
1 194.3848 6057.0747
2 182.9268 5945.5223
3 181.8452 6381.2229
4 175.7648 21815.2529
5 135.4927 9248.4781
6 138.2465 2628.9236
7 129.3754 26532.3772
8 125.3624 31386.8729
9 124.5529 26468.7651
10 122.2244 10448.6739
11 121.3576 11829.6385
12 120.4989 9832.2564
13 119.7324 9837.4924
14 119.1365 11085.2926
15 65.9371 9123.9891
16 62.5837 9261.8381
17 51.8935 8133.4998
18 48.1237 9196.9851
19 44.2961 8439.3981
20 42.4251 16439.8893
21 39.5899 20888.9225
22 38.5796 17278.6718
23 37.6589 8765.4785
24 28.6481 13387.2447

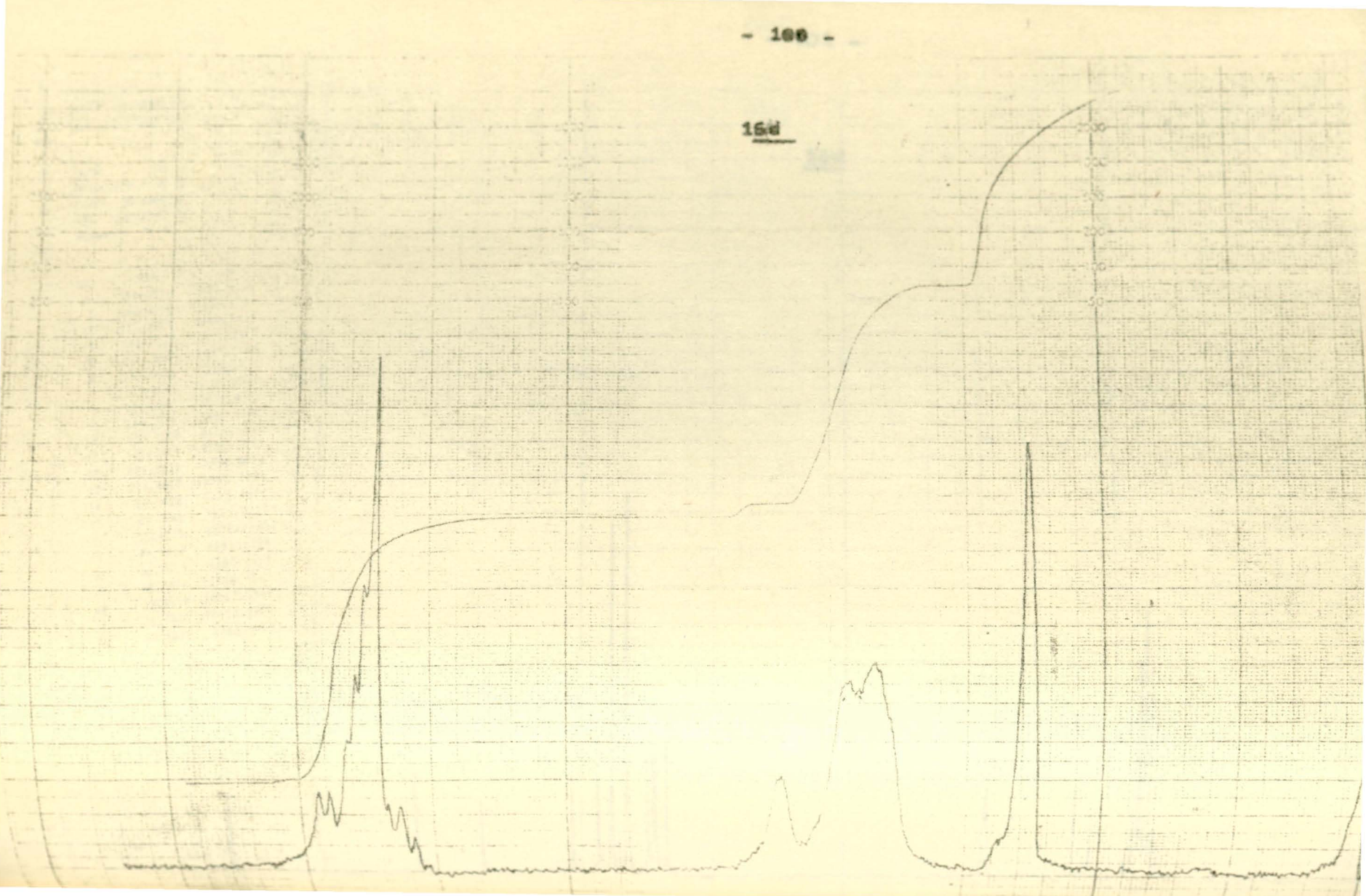
16c



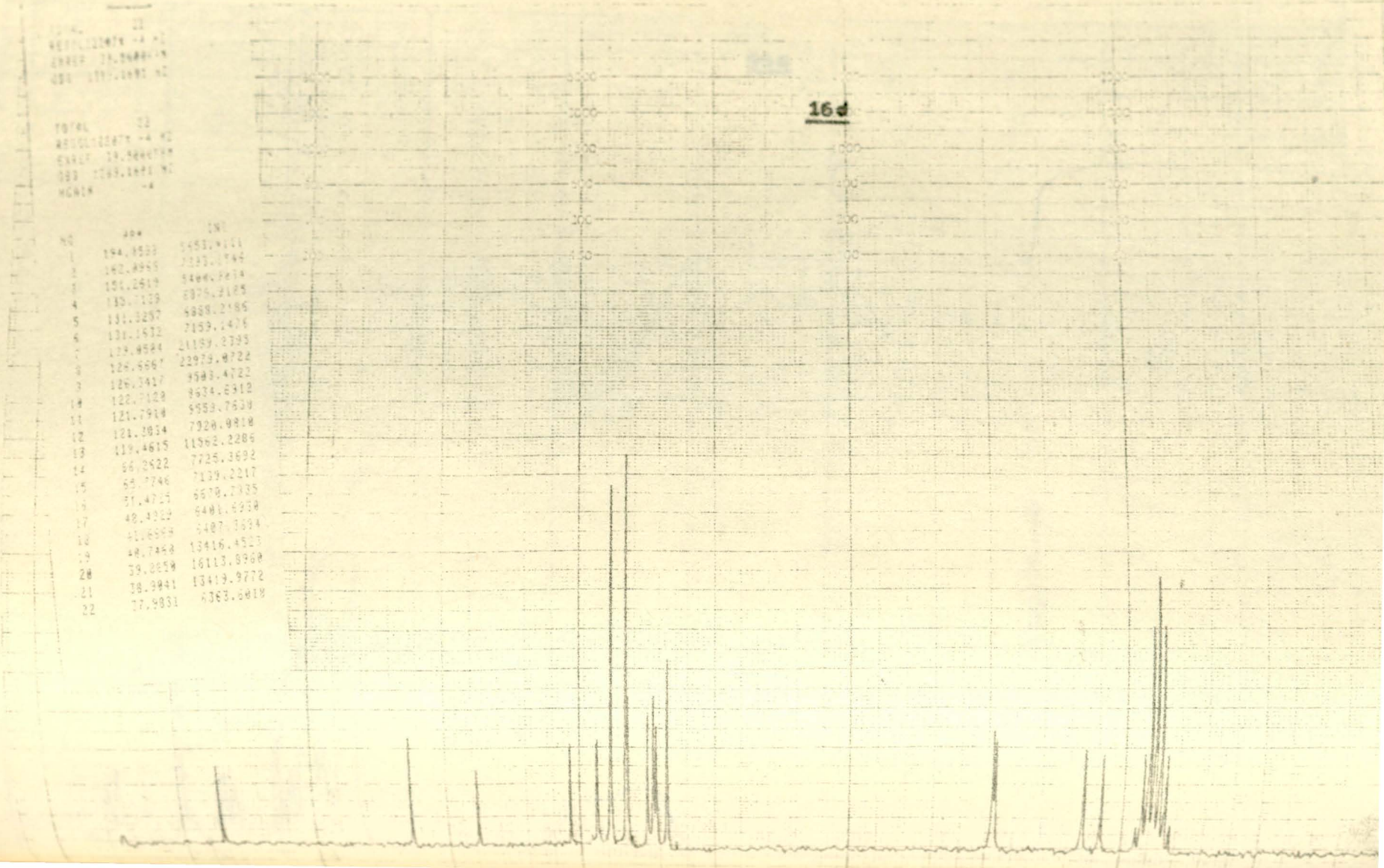
16c


TOTAL ZT
REGCL122071 -4 HZ
CURSF 19.0306770
SRS 1301.9799 HZ
WSRCH -2
NO PPM INT
1 194.4396 2897.9566
2 161.8841 3124.3668
3 150.1421 2859.9479
4 151.4375 1927.1224
5 130.9465 2481.2229
6 120.8237 4185.3593
7 125.3624 15324.3289
8 122.1782 4356.3658
9 121.3576 4882.3578
10 120.3293 3111.5795
11 119.8823 6163.6485
12 114.2688 10913.5805
13 65.3271 3669.5468
14 65.5837 3863.7379
55.1022 5829.7809
16 51.8933 3153.6565
17 48.1132 3383.6971
18 41.3419 2813.7582
19 40.1289 6127.5404
20 39.5898 7567.1859
21 38.5798 6582.8894
22 37.6588 3616.4824
23 36.5838 1267.5102

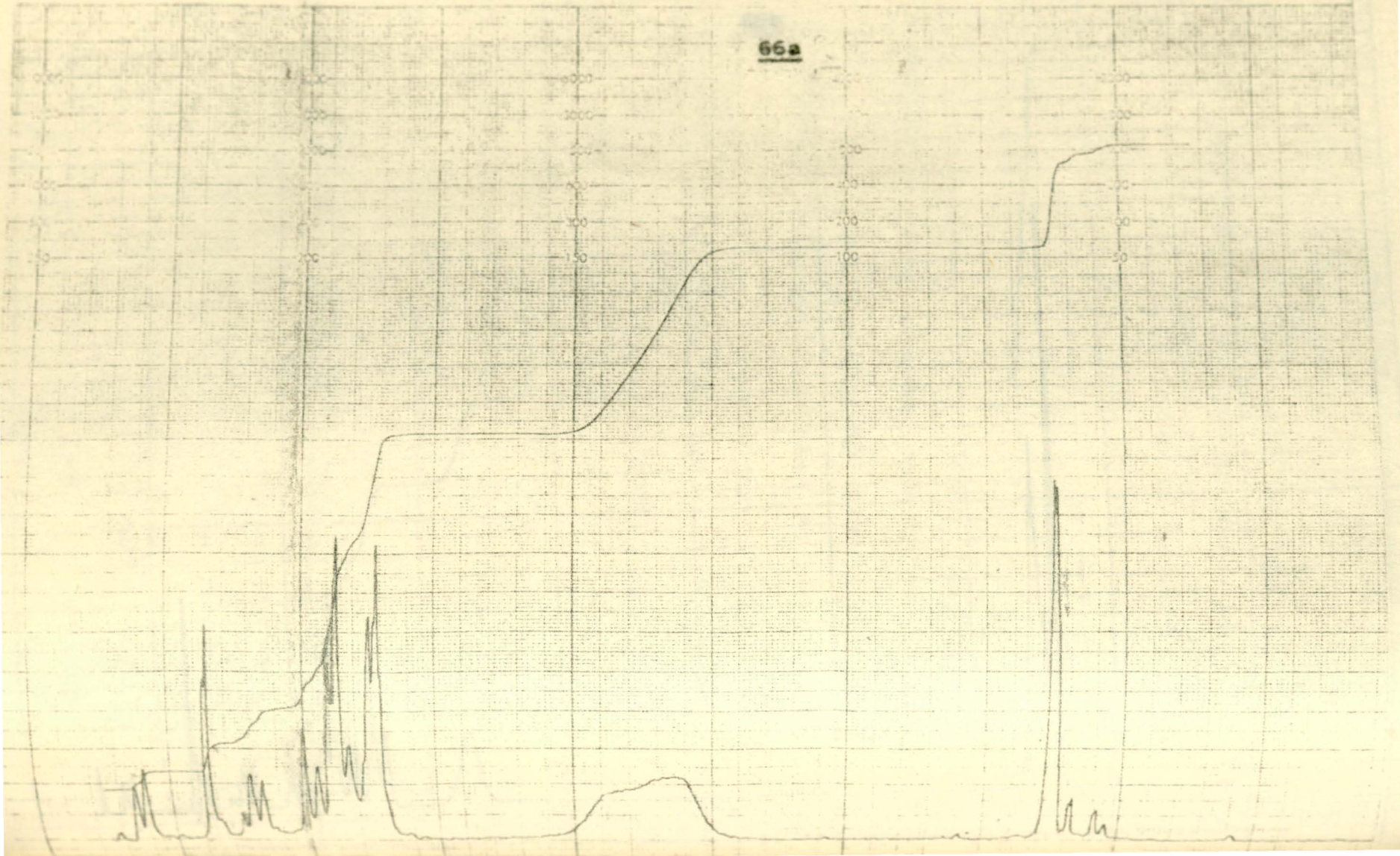
16d



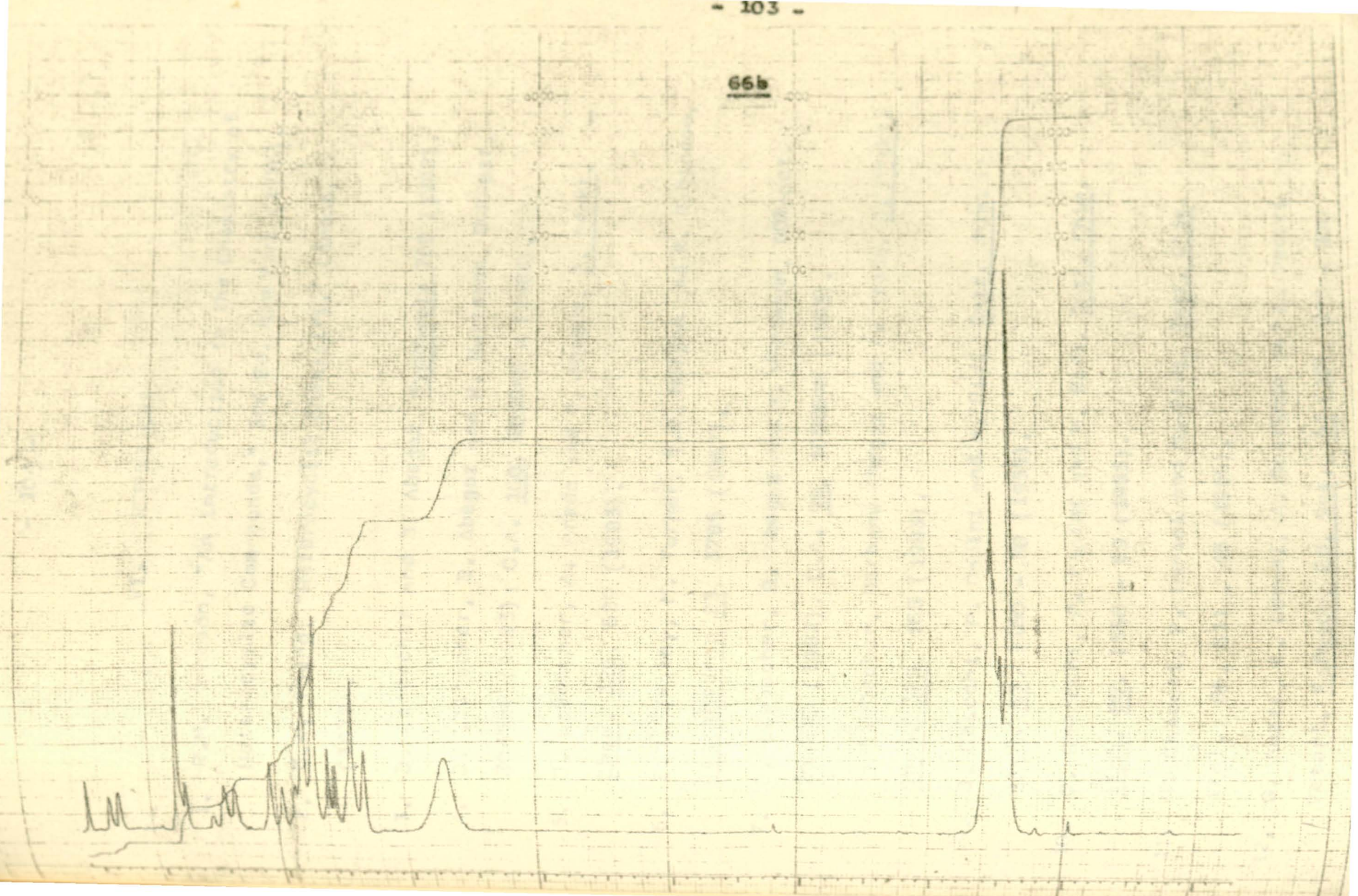
16d



66a



66b



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DECLARATION

I, the undersigned, declare that this thesis is my work and that all sources of material used for the thesis have been duly acknowleged.

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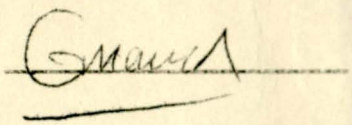
Signature: 

Place and date of submission, Chemistry Department, Addis Ababa University, June 1987.