SYNTHESES RELATED TO THE PREPARATION OF SUBSTITUTED GLYCOSYL DERIVATIVES OF PYRROLO[3,2-f]QUINOLINES : SPECTROSCOPIC STUDIES OF ACETYLATED GLYCOSYLAMINE DERIVATIVES.

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D O C T O R O F P H I L O S O P H Y

by

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S U M M A R Y.

The synthesis of 25 acetylated glycopyranosylamine derivatives (15 of which are newly reported here) from substituted sugar derivatives and amines is described. Eleven different methods were employed in these syntheses. Of the compounds prepared, 15 are substituted glycosylindoline derivatives. The stereospecific synthesis of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)indoline from 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate) and indoline is reported for the first time. The dehydrogenation of 10 substituted glycopyranosylindoline derivatives to the corresponding glycopyranosylindole derivatives (of which 7 are newly reported) by two methods, is described.

As 2-methylpyrrolo[3,2-f]quinoline and 2,7-dimethylpyrrolo[3,2-f]quinolinium iodide did not react with D-glucose or penta-*O*-acetyl-β-D-glucopyranose, attempts were made to prepare 2,3-dihydro-derivatives of substituted pyrrolo[3,2-f]quinolines by chemical reduction and by hydrogenation. When the desired products could not be obtained, the synthesis of 2,3-dihydro-5,6-dimethylpyrrolo[3,2-f]quinolines was attempted starting from 2,3-dimethyl-β-chlorovinylaldehyde and either 5-aminoindoline or *N*-acetyl-5-aminoindoline.

The acetylated glycopyranosylamine derivatives were studied by mass spectroscopy in order to obtain some further insight into the fragmentation patterns of acetylated sugar derivatives, and of structurally related nucleoside derivatives. Pathways for the fragmentation of the sugar moiety of acetylated hexo-, L-rhamno- and pentopyranosylamine derivatives, and those of the nitrogen-containing fragments of acetylated glycopyranosylamine derivatives, are suggested, although the limitations of such schemes are noted.

The substituted glycopyranosylamine derivatives that were prepared were studied by NMR spectroscopy to determine their

stereochemistry. First-order analyses of most of these spectra were obtained. Anisotropic chemical shifts of the acetoxy signals of acetylated glycosylindole derivatives arise from the shielding caused by the unsaturation of the indolyl moiety. Owing to the restricted rotation about the glycosidic bond, these shifts are large. These shifts are measured by comparing the chemical shifts of the individual acetoxy signals of acetylated glycosylindole derivatives and the corresponding glycosylindoline derivatives. From a consideration of these chemical shift differences, a new method has been developed for the determination of the anomeric configuration and the ring conformation of the glycosyl moiety of acetylated glycopyranosylindole derivatives. This method has been used to predict the anomeric configuration of 1-(2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl)indole, for which the configuration could not be determined unambiguously from the splitting observed in the NMR spectrum. The scope of this method is discussed.

C O N T E N T S.

A B B R E V I A T I O N S.

The following abbreviations are used in the course of this thesis:

E.I.	Electron-impact.
F.I.	Field ionisation.
NMR	Proton magnetic resonance spectroscopy.
MHz	Megahertz.
TLC	Thin layer chromatography.
P.C.	Paper chromatography.
EtOH	Ethanol.
MeOH	Methanol.
HOAc	Acetic acid.
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone.
1-BuOH	1-Butanol.
$CDCl_3$	Deuterochloroform.
TMS	Tetramethylsilane.
eV	Electron volts.
IR	Infra-red spectroscopy.
HCBD	Hexachlorobutadiene.
EtOAc	Ethyl acetate.
NaOMe	Sodium methoxide.
temp	Temperature.
hr	hour(s).
min	minutes.
psi	Pounds per square inch.
mmHg	millimetres of mercury.
conc	concentrated.
THF	tetrahydrofuran.
mmole	millimoles.
calc.	calculated.
b.p.	boiling point.
m.p.	melting point.
sec	seconds.

SECTION 1.

INTRODUCTION.

1. INTRODUCTION.

Cancer is the name given to the family of related disorders which can be defined as a mass of new tissue which grows independently, and invades surrounding structures, and which has no physical use. This definition refers to solid tumours. The leukaemias are diseases of the blood-forming organs, characterised by a marked increase in the number of white blood cells and their precursors in the blood stream, together with enlargement and proliferation of the lymphoid tissue of the spleen, lymphatic glands and bone marrow[1]. Experience has shown that certain types of chemotherapeutic agents are effective against cancers to a limited extent : alkylating agents such as Mustargen [methyl bis(2-chloroethyl)-amine], nitrogen mustards such as mannitol nitrogen mustard [1,6-bis(2-chloroethylamino)-1,6-dideoxy - D - mannitol] and antimetabolites such as 9-β-D-ribofuranosyl-6-mercaptopurine. Several natural products such as certain alkaloids and antibiotics have been shown to possess anticancer properties. Several of these antibiotics can be classed as antimetabolites, which can be loosely described as materials whose chemical structures closely resemble those of naturally occurring metabolites (in particular the nucleosides), and which enter into cellular metabolism because of their similarity to normal constituents, but interfere with the processes that depend on these normal constituents. Thus certain nucleoside analogues might be expected to be incorporated into the nucleic acid chain, but to prevent reproduction of this chain, thus reducing the rate at which the cancer might grow. A certain amount of success has been achieved in the treatment of cancer with synthetic drugs of the antimetabolite type, but unfortunately, resistance to these drugs usually occurs and use of any similar drug has no effect. Another limitation to the use of these compounds against cancer is that they are not specifically directed against

the rapidly proliferating tissue. A greater proportion of success might be expected if the cancerous cells could be attacked preferentially. Tumour cells apparently have a higher surface negative charge[2,3] than ordinary cells, and this suggests that basic compounds could be concentrated in these cells. If these basic compounds were themselves cytotoxic, they should exhibit selective toxicity towards cancerous cells, as was to some extent demonstrated by studies on the cytotoxic activity of a series of bisquaternary ammonium heterocycles[4,5].

Anti-tumour screening of compounds prepared in this department showed that 2,7-dimethylpyrrolo[3,2-f]quinolinium iodide and 2,6-dimethylpyrrolo[2,3-f]quinolinium iodide exhibited considerable activity towards those cancers employed in the test systems. These materials passed the second stage of the sequential testing at the United States Department of Health, Education and Welfare, Bethesda, Maryland. Modifying these materials so that they resemble nucleoside derivatives may be expected to increase their activity against the disease.

Purine nucleoside* analogues, such as 9-(β-D-ribofuranosyl)-6-mercaptopurine, psicofuranine and angustmycin A[6-amino-9-(6-deoxy-β-D-*erythro*-hex-5-enofuran-2-ulosyl)purine], have been known to exhibit antitumour activity. Certain 7-deazanucleoside analogues, such as tubercidin {4-amino-7-(β-D-ribofuranosyl)-pyrrolo[2,3-d]pyrimidine}[6-8] and toyocamycin {4-amino-5-cyano-7-(β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine}[8,9], possess the same property[10]. The facts that certain 1-(β-D-ribofuranosyl)-benzimidazoles exhibit antiviral activity[11], and that 5,6-dimethyl-1-(α-D-ribofuranosyl)benzimidazole is an integral part

*The term "purine nucleoside" refers to all glycosyl derivatives of purines, both synthetic and natural, and it has been proposed [6] that this terminology should cover the entire field of heterocyclic glycosides[7].

of the chemical structure of vitamin B_{12}[7], and the suggestion that 5,6-dichloro-1-(β-D-ribofuranosyl)benzimidazole prevents the synthesis of protein by interfering with a preliminary synthesis of RNA[13], has led to much work on the synthesis of similar benzimidazole nucleosides. Compounds containing the indole nucleus, tryptophan and serotonin, for example, are physiologically active. Thus it was felt that the preparation of a series of indole nucleosides would not only lead to compounds displaying considerable pharmacological activity, but would also serve as preliminary syntheses for glycosylpyrroloquinolines in an area where surprisingly little work has been done.

The problem, then, has been to prepare a series of substituted glycosylindole derivatives, to study their properties by NMR and mass spectra, and to apply the results obtained towards the synthesis of substituted glycosylpyrroloquinolines.

SECTION 2.

MASS SPECTROSCOPIC STUDIES ON SUBSTITUTED ACETYLATED GLYCOPYRANOSYLAMINES.

2.1. INTRODUCTION.

Since few natural products in general, and nucleosides in particular, are isolated in large amounts, mass spectroscopy has proved invaluable in assisting structural determinations. The usefulness of mass spectroscopic structural determinations of nucleosides has, however, been limited, owing to the low volatility of unsubstituted nucleosides, which generally give rise to low-intensity molecular ions and, indeed, only few peaks of high intensity.

Electron-impact (E.I.) mass spectroscopy of nucleosides has, in general, been confined to studies of unsubstituted and *O*-trimethylsilyl-substituted nucleoside derivatives[15-25]. Acetylation of the nucleoside derivatives leads to spectra showing several peaks of relatively high intensity, among which is the molecular ion peak[26]. The low-resolution E.I. mass spectra of acetylated glycopyranosylamine derivatives may be expected to be similar to those obtained for acetylated nucleoside derivatives, and a study of possible fragmentation pathways for the former compounds has therefore been undertaken with a view to their use in the elucidation of the structures of new nucleoside derivatives.

Since the publication of a short study of the low-resolution E.I. spectra of uridine, deoxyuridine, adenosine and deoxyadenosine[15,16], several papers on the fragmentation of nucleoside derivatives have appeared[17-26]. In the spectra of nucleosides, the most prominent ions have been found at M-89($M-C_3H_5O_3$), M',B+30($B+CH_2O$),B+2 and B+1*, and these have been established by accurate mass measurements. There are also many other peaks of very low intensity (including that due to the molecular ion) which can be of little use in structural determinations. Structures for the prominent ions have been postulated. These mass spectra permit elucidation of certain fundamental structural features of nucleosides, among which are the molecular

*M,M' and B have m/e corresponding respectively to the molecular ion, the sugar moiety resulting from cleavage of the glycosidic bond, and the nitrogen-containing base less one proton.

weight (and hence the exact elemental composition), and the extent to which the base is substituted. Identification of the position of substitution of the base, and the exact nature of the sugar moiety is seldom possible. It was felt that a more complete knowledge of the fragmentation of these compounds might facilitate identification of these features.

Two distinct disadvantages of E.I. mass spectra are the thermal decomposition of the sample in the ion source prior to ionisation, and the rapid fragmentation ($<\sim 10^{-15}$ sec) of the highly energetic molecular ions formed at 70eV. In successful attempts to minimise the thermal degradation prior to ionisation, and to reduce the formation of such highly energetic molecular ions, two groups of workers[21,22] have prepared *O*-trimethylsilyl derivatives of nucleosides and nucleotides. The acetoxy groups used in the present work would be expected to have the same effect as *O*-trimethylsilyl groups in reducing thermal decomposition[26,27].

An instrumental method that has recently been used to overcome the rapid fragmentation of energetic molecular ions is that of field ionisation (F.I.) mass spectrometry[28]. A heated probe is used to reduce thermal degradation as far as possible, and the spectrum is obtained at low ionisation voltage, which produces low-energy molecular ions, resistant to fragmentation. Spectra thus obtained are greatly simplified compared to the corresponding E.I. spectra. In addition, the steep gradient of the ionising electric field in the F.I. source causes ions to be accelerated before sufficient time (10^{-8}-10^{-6} sec) has elapsed for rearrangement processes to take place; only ions resulting from simple cleavages (10^{-14}-10^{-12} sec) are observed. These F.I. spectra give M+1, M, M', B+2 and B+1 ion peaks almost exclusively.

Eggers *et al*[26] have studied the E.I. mass spectra of acetylated and unacetylated puromycin nucleosides, and have reported significant peaks due to M, M', B+30 and B+1 ions, with

the parent ion is readily calculated.

It was felt that a mass spectrometric study of the several series of acetylated glycopyranosylamine derivatives would help to extend the knowledge of the fragmentation of both acetylated carbohydrate derivatives and of substituted nucleoside derivatives. Although it is unlikely that stereochemical effects would be apparent in the mass spectra of carbohydrate derivatives, a study was undertaken to find any differences between various sugar derivatives that might be attributed to stereochemical effects.

Possible fragmentation pathways are presented for the E.I. fragmentation of acetylated hexopyranosyl, L - rhamnopyranosyl and pentopyranosylamine derivatives. While it is realised that the postulation of structures for fragments is fraught with uncertainty, and that no proof of these structures is possible without large numbers of isotope-labelling experiments, such fragmentation schemes do nevertheless enable predictions of possible fragmentation pathways in related compounds to be made.

2.2. RESULTS.

The 70eV mass spectra of compounds I-XXXVI were recorded at probe temperatures varying from 100 to 220°. The spectra were normalised by choosing as the base peak, the peak (other than that at m/e 43) of highest intensity. The relative intensities of the ion peaks were tabulated, and compared with those of other compounds containing the same sugar moiety or the same aglycone. These tables were then divided to show the nitrogen-containing (Tables 2.2.1.1.1., 2.2.1.2.1., through 2.2.3.4.1., and 2.2.4.1.1., 2.2.4.2.1., through 2.2.4.6.1.) and sugar-containing ions (Tables 2.2.1.1.2., 2.2.1.2.2., through 2.2.4.6.2.). This was done by noting the variation of the m/e values of the more intense peaks with the change in molecular weight of the compound, and by comparing the intensities of peaks having the same m/e values in derivatives of a particular sugar. Further division of the

tables of nitrogen-containing ions is possible. Across a particular series of substituted glycopyranosylamine derivatives there are certain ions common to the whole series. The $^{m}/_{e}$ values of these ions, which vary from one series to another, correspond to fragments containing the nitrogen-containing moiety to which certain groups are attached. An example of a fragment of this type is the B+30 ion.

Spectra of compound XVI were obtained at both 165° and at 220°. Comparison of the relative intensities of the peaks due to the major ions in these two spectra showed no significant changes, and it was therefore assumed that thermal degradation prior to ionisation was minimal.

Fragmentation of the sugar moieties occurs by several mechanisms [loss of CHOAc(72), HOAc(60), CH_2CO(42), H_2O(18), CO(28), and by retro-Diels-Alder fission (RDA)]. Possible loss of the acetoxy radical (·OAc,59) has also been suggested.

The relative intensities of the peaks due to the ions resulting from the fragmentation of the sugar moiety of D-glucopyranosyl, D-galactopyranosyl and D-mannopyranosyl derivatives of *p*-nitroaniline(I,II,III), indoline(VIII,IX,X ; Fig. 2.1.),indole(XVI, XVII), 5-nitroindoline(XXIV, XXV,XXVI), 5-nitroindole(XXX), 2-methylindoline(XXXII), 2-methylindole(XXXIII), 1,2,3,4-tetrahydroquinoline(XXXIV) and 6-aminoquinoline(XXXVI) are given in Tables 2.2.1.1.2., 2.2.1.2.2. and 2.2.1.3.2. respectively.

Table 2.2.2.1.2. shows the relative intensities of the peaks due to ions resulting from the fragmentation of the L-rhamnopyranosyl moiety of compounds IV,XI,XIX,XXVII and XXXI (Fig. 2.2.).

The relative intensities of the peaks due to ions arising from the fragmentation of the sugar moieties of acetylated D-xylopyranosylamine(V,XII,XX,XXVIII,XXXV), D-lyxopyranosylamine(VII,XIII,XXI ; Fig. 2.3.), L-arabinopyranosylamine(VI,XIV,XXII,XXIX) and D-ribopyranosylamine(XV,XXIII)

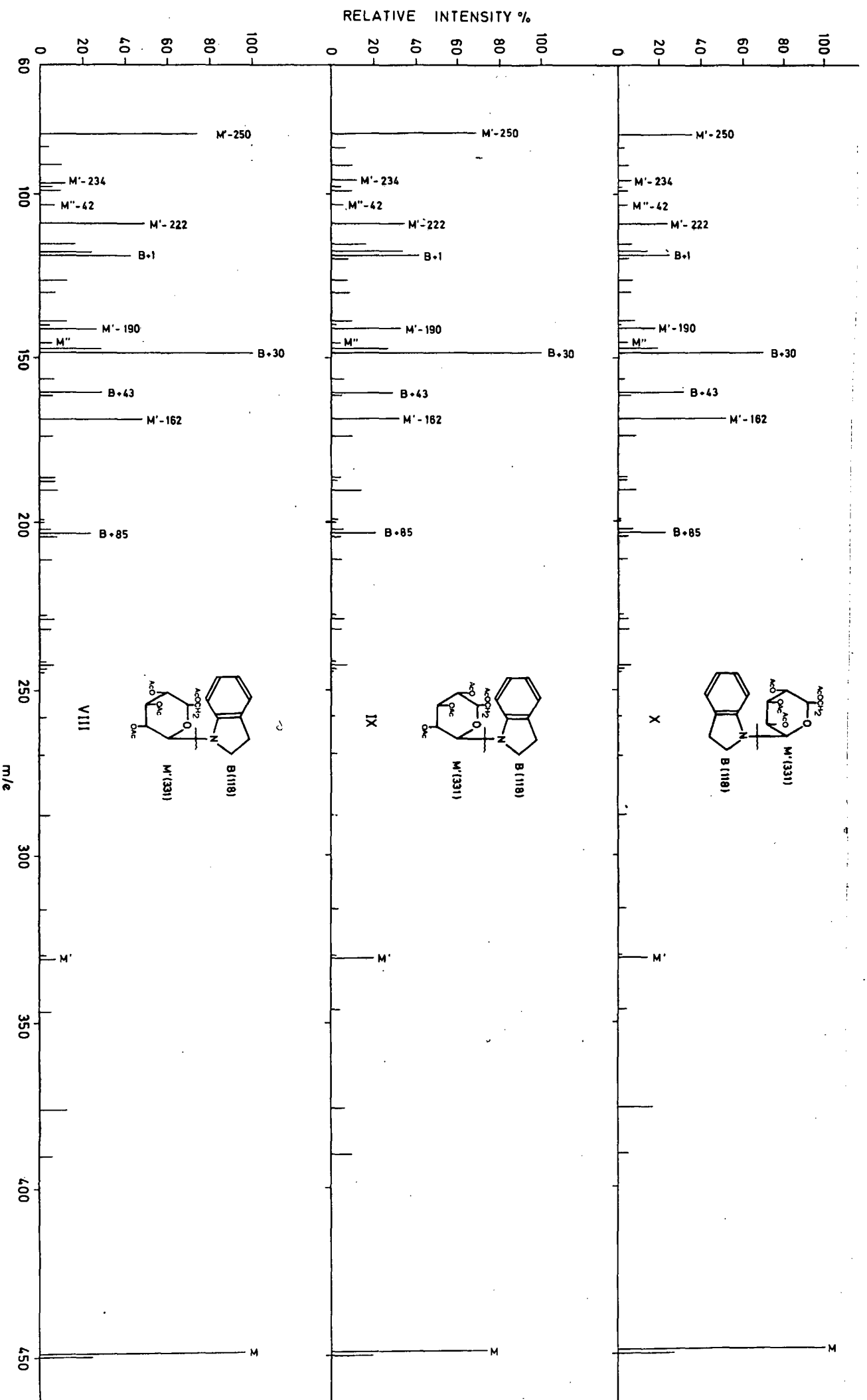


FIG. 2.1. E.I. MASS SPECTRA OF VIII, IX and X.

Designation	m/e	I 175°	m/e	VIII	m/e	XVI 165°	m/e	XXXI 130°	m/e	XXXII 130°	m/e	XXIV 215°	m/e	XXX 220°	m/e	XXXIV	m/e	XXXVI 220°
M+1	469	12	450	25	448	12	464	25	462	19	495	8	493	7	464	21	475	34
M	468	42	449	96	447	44	463	85	461	66	494	27	492	22	463	71	474	100
M-59	409	1	390	6	388	<<1	404	5	402	<1	435	<1	433	<1	404	7	415	1
M-60	408	1	389	<1	387	<<1	403	<<1	401	1	434	1	432	<<1	403	<1	414	2
M-73	395	2	376	13	374	<1	390	13	388	<1	421	4	419	<<1	390	12	401	3
M-102	366	1	347	6	345	<1	361	3	359	1	392	<1	390	<1	361	3	372	3
M-119	349	7	330	3	328	1	344	2	342	2	375	1	373	<1	344	2	355	5
M-120	348	5	329	<<1	327	<<1	343	3	341	<<1	374	<<1	372	<1	343	x	354	<<1
M-133	335	4	316	4	314	<<1	330	2	328	x	361	1	359	x	330	3	341	4
M-162	306	3	287	1	285	<<1	301	<1	299	<<1	332	4	330	<<1	301	2	312	2
M-179	289	5	270	2	268	2	284	<1	282	<1	315	1	313	1	284	1	295	6
M-180	288	3	269	x	267	<<1	283	<1	281	<<1	314	x	312	1	283	x	294	<1
M-192	276	3	257	<<1	255	<1	271	<1	269	x	302	<1	300	<1	271	1	282	<<1
M-193	275	14	256	<1	254	2	270	<1	268	<<1	301	<1	299	2	270	<1	281	3
B+170	307	2	288	5	286	<1	302	2	300	<1	333	2	331	30	302	2	313	3
B+169	306	3	287	1	285	<<1	301	4	299	1	332	4	330	<<1	301	1	312	2
B+128	265	1	246	1	244	<1	260	11	258	2	291	1	289	1	260	<1	271	2
B+127	264	2	245	2	243	<1	259	2	257	2	290	<1	288	1	259	3	270	3
B+114	251	6	232	6	230	2	246	3	244	1	277	2	275	2	246	4	257	3
M-217	251	6	232	6	230	2	246	3	244	1	277	2	275	2	246	4	257	3
M-221	247	8	228	3	226	3	242	<1	240	1	273	1	271	8	242	5	253	7
B+110	247	8	228	3	226	3	242	<1	240	1	273	1	271	8	242	5	253	7
M-222	246	6	227	<1	225	1	241	1	239	2	272	<1	270	2	241	<1	252	3
B+86	223	3	204	7	202	3	218	4	216	2	249	2	247	3	218	4	229	10
B+85	222	20	203	24	201	3	217	17	215	4	248	9	246	2	217	18	228	18
B+84	221	11	202	6	200	7	216	5	214	5	247	3	245	7	216	5	227	17
B+72	209	9	190	9	188	3	204	6	202	1	235	3	233	4	204	11	215	8
B+71	208	<1	189	<1	187	5	203	1	201	<1	234	x	232	<<1	203	<1	214	<1
B+68	205	9	186	8	184	1	200	3	198	2	231	2	229	7	200	6	211	15
B+56	193	10	174	7	172	6	188	9	186	9	219	6	217	6	188	7	199	15
B+44	181	7	162	6	160	4	176	4	174	6	207	4	205	3	176	5	187	14
B+43	180	38	161	29	159	12	175	22	173	14	206	26	204	10	175	27	186	35
B+30	167	27	148	100	146	7	162	100	160	10	193	52	191	3	162	100	173	80
B+29	166	4	147	29	145	14	161	28	159	16	192	11	190	5	161	26	172	24
B+2	139	18	120	8	118	12	134	7	132	14	165	3	163	3	134	7	145	31
B+1	138	9	119	42	117	44	133	20	131	56	164	11	162	8	133	39	144	63
B	137	2	118	24	116	6	132	8	130	30	163	3	161	2	132	17	143	10
	71	5	71	5	71	2	71	4	71	2	71	2	71	5	71	2	71	3
	85	10	85	4	85	7	85	7	85	4	85	6	85	10	85	5	85	6
B-45	92	10									118	9	116	19				
B-46	91	3									117	7	115	25				
B-47	90	2									116	4	114					

Temperatures are probe temps at which the spectra were obtained.

Table 2.2.1.1.1. Mass Spectra of Acetylated D-Glucopyranosylamine Derivatives; Nitrogen-containing Fragments.

Designation	m/e	I 175°	VIII	XVI 165°	XXXII 130°	XXXIII 130°	XXIV 215°	XXX 220°	XXXIV	XXXVI 220°	β-D-Glu-(OAc)$_5$
M'+1	332	5	2	5	2	2	4	5	2	2	<1
M'	331	35	7	29	7	12	22	30	9	12	2
M'-42	289	5	2	<1	<1	1	<1	1	<1	<<1	1
M'-60	271	4	1	7	<1	1	2	8	1	2	1
M'-72	259	<1	3	<1	3	<1	2	2	3	1	1
M'-87	244	2	3	<1	<1	1	<1	<1	2	<<1	1
M'-88	243	11	7	<1	3	<<1	3	1	11	3	7
M'-89	242	3	3	2	<1	<1	1	<1	5	2	55
M'-102	229	9	6	6	3	7	4	7	3	10	2
M'-120	211	10	6	8	3	4	5	6	6	15	5
M'-130	201	4	5	3	4	<1	4	2	6	2	4
M'-131	200	5	2	7	3	<1	2	<1	6	4	34
M'-132	199	2	2	<1	1	1	1	1	2	15	14
M'-144	187	3	8	5	4	7	4	5	4	14	3
M'-162	169	78	48	100	38	100	100	100	48	60	11
M'-172	159	3	3	12	2	16	3	4	1	<1	3
M'-174	157	14	7	2	3	2	7	4	8	23	52
M''	145	16	6	14	6	10	11	10	6	31	19
M'-190	141	36	27	3	24	4	27	7	35	21	5
M'-191	140	9	4	2	1	2	3	3	4	4	28
M'-192	139	18	12	13	12	12	13	23	11	18	9
M'-201	130	4	8	14	20	30	6	7	7	11	
M'-204	127	24	12	20	10	24	23	32	8	18	7
M'-216	115	38	17	12	15	17	24	25	22	21	100
M'-222	109	76	49	52	31	71	74	88	36	46	11
M''-42	103	27	7	7	5	9	11	11	8	9	34
M'-232	99	25	10	5	7	4	4	9	9	12	10
	98	36	6	3	9	2	7	6	8	9	70
M'-234	97	24	12	9	12	8	13	21	16	16	17
M'-246	85	10	4	4	7	4	6	10	5	6	14
M'-250	81	100	74	11	55	13	56	26	75	46	16
M'-262	69	18	7	3	9	4	6	10	6	9	13

Table 2.2.1.1.2. Mass Spectra of Acetylated D-Gluco-pyranosylamine Derivatives: Nitrogen-free Fragments.

Designation	m/e	II 175°	m/e	IX 100°	m/e	XVII	m/e	XXV 130°
M+1	469	18	450	20	448	18	495	15
M	468	64	449	74	447	69	494	57
M-59	409	11	390	10	388	<1	435	4
M-60	408	5	389	<1	387	1	434	<1
M-73	395	2	376	7	374	<<1	421	4
M-102	366	3	347	4	345	<1	392	2
M-119	349	11	330	2	328	1	375	1
M-120	348	2	329	<<1	327	<<1	374	<<1
M-133	335	2	316	3	314	x	361	1
M-162	306	2	287	1	285	<<1	332	9
M-179	289	3	270	4	268	1	315	1
M-180	288	2	269	<<1	267	<<1	314	<<1
M-192	276	1	257	5	255	<1	302	<<1
M-193	275	5	256	<1	254	<1	301	<<1
B+170	307	2	288	3	286	<1	333	3
B+169	306	2	287	<1	285	<<1	332	9
B+128	265	<1	246	<1	244	<1	291	1
B+127	264	1	245	1	243	<1	290	<1
B+114	251	6	232	5	230	2	277	2
M-217	251	6	232	5	230	2	277	2
M-221	247	6	228	2	226	2	273	2
B+110	247	6	228	2	226	2	273	2
M-222	246	4	227	2	225	<1	272	<<1
B+86	223	3	204	5	202	1	249	3
B+85	222	16	203	21	201	3	248	13
B+84	221	10	202	6	200	5	247	7
B+72	209	16	190	14	188	3	235	8
B+71	208	2	189	<1	187	5	234	<1
B+68	205	10	186	4	184	3	231	3
B+56	193	10	174	10	172	5	219	9
B+44	181	6	162	5	160	4	207	6
B+43	180	34	161	29	159	12	206	33
B+30	167	36	148	100	146	13	193	90
B+29	166	5	147	27	145	19	192	18
B+2	139	14	120	8	118	14	165	5
B+1	138	6	119	41	117	60	164	17
B	137	2	118	33	116	7	163	10
	71	3	71	11	71	3	71	6
	85	8	85	7	85	7	85	11
B-45	92	5					118	13
B-46	91	2					117	11
B-47	90	1					116	6

Table 2.2.1.2.1. Mass Spectra of Acetylated D-Galacto-pyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	II 175°	IX 100°	XVII	XXV 130°
M'+1	332	8	3	16	9
M'	331	45	20	93	52
M'-42	289	3	1	1	2
M'-60	271	1	1	1	1
M'-72	259	1	2	<<1	3
M'-87	244	2	3	<1	<1
M'-88	243	14	8	<1	6
M'-89	242	2	2	1	2
M'-102	229	13	6	7	9
M'-120	211	12	5	5	9
M'-130	201	9	5	3	7
M'-131	200	10	2	5	1
M'-132	199	4	3	<1	1
M'-144	187	3	4	5	5
M'-162	169	52	32	100	100
M'-172	159	5		5	6
M'-174	157	9	6	2	9
M''	145	14	4	19	9
M'-190	141	54	32	7	41
M'-191	140	10	2	1	1
M'-192	139	14	10	8	13
M'-201	130	3	9	13	8
M'-204	127	20	9	28	21
M'-216	115	23	17	12	23
M'-222	109	43	34	69	68
M''-42	103	20	6	10	11
M'-232	99	29	10	9	19
	98	25	5	3	8
M'-234	97	14	12	8	15
M'-246	85	8	7	7	11
M'-250	81	100	69	28	94
M'-262	69	11	11	5	13

Table 2.2.1.2.2. Mass Spectra of Acetylated D-Galactopyranosylamine Derivatives : Nitrogen-free Fragments.

Designation	m/e	III 150°	m/e	X 150°	m/e	XXVI 155°
M+1	469	9	450	28	495	11
M	468	30	449	100	494	44
M-59	409	1	390	5	435	2
M-60	408	2	389	2	434	<1
M-73	395	4	376	18	421	7
M-102	366	2	347	4	392	1
M-119	349	6	330	2	375	1
M-120	348	5	329	<<1	374	<<1
M-133	335	4	316	4	361	2
M-162	306	3	287	1	332	6
M-179	289	6	270	2	315	2
M-180	288	3	269	<<1	314	<1
M-192	276	1	257	<<1	302	<1
M-193	275	1	256	<1	301	1
B+170	307	2	288	4	333	3
B+169	306	3	287	1	332	6
B+128	265	1	246	<1	291	1
B+127	264	3	245	2	290	<1
B+114	251	8	232	6	277	4
M-217	251	8	232	6	277	4
M-221	247	8	228	2	273	2
B+110	247	8	228	2	273	2
M-222	246	7	227	1	272	1
B+86	223	5	204	5	249	3
B+85	222	25	203	23	248	13
B+84	221	13	202	7	247	6
B+72	209	12	190	9	235	4
B+71	208	<1	189	<1	234	<1
B+68	205	16	186	4	231	3
B+56	193	16	174	8	219	8
B+44	181	8	162	6	207	6
B+43	180	45	161	31	206	36
B+30	167	28	148	69	193	77
B+29	166	2	147	19	192	17
B+2	139	18	120	5	165	3
B+1	138	14	119	25	164	8
B	137	1	118	14	163	3
	71	4			71	4
	85	10	85	3	85	8
B-45	92	11			118	11
B-46	91	2			117	9
B-47	90	1			116	5

Table 2.2.1.3.1. Mass Spectra of Acetylated D-Mannopyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	III 150°	X 150°	XXVI 155°
M'+1	332	7	3	6
M'	331	38	14	41
M'-42	289	6	1	2
M'-60	271	5	1	4
M'-72	259	2	2	3
M'-87	244	<<1	3	1
M'-88	243	12	6	6
M'-89	242	1	<<1	2
M'-102	229	9	5	6
M'-120	211	10	4	8
M'-130	201	7	5	5
M'-131	200	7	1	2
M'-132	199	2	1	1
M'-144	187	4	4	4
M'-162	169	76	52	100
M'-172	159	3	1	4
M'-174	157	11	3	6
M''	145	16	4	10
M'-190	141	35	19	31
M'-191	140	9	1	7
M'-192	139	18	8	13
M'-201	130	2	6	8
M'-204	127	23	7	17
M'-216	115	30	7	21
M'-222	109	70	24	67
M''-42	103	25	4	11
M'-232	99	25	5	17
	98	38	2	7
M'-234	97	25	7	15
M'-246	85	10	3	8
M'-250	81	100	36	72
M'-262	69	20	4	9

Table 2.2.1.3.2. Mass Spectra of Acetylated D-Mannopyranosylamine Derivatives: Nitrogen-free Fragments.

Designation	m/e	IV 135°	m/e	XI 115°	m/e	XIX 130°	m/e	XXVII 125°	m/e	XXXI 120°
M+1	411	29	392	24	390	26	437	8	435	11
M	410	100	391	100	389	100	436	33	434	48
M-59	351	2	332	2	330	<<1	377	1	375	1
M-60	350	<1	331	<1	329	<<1	376	<<1	374	<<1
M-73	337	x	318	<<1	316	<<1	363	x	361	<<1
M-102	308	1	289	1	287	<1	334	<1	332	<<1
M-119	291	6	272	1	270	<1	317	<1	315	x
M-120	290	10	271	1	269	<1	316	x	314	x
M-133	277	x	258	x	256	<1	303	x	301	<<1
M-162	248	2	229	1	227	<1	274	9	272	<<1
M-179	231	6	212	2	210	4	257	2	255	1
M-180	230	2	211	3	209	<1	256	4	254	<<1
M-192	218	x	199	<1	197	<1	244	<1	242	1
M-193	217	<<1	198	<1	196	<1	243	x	241	<<1
B+170	307	2	288	5	286	<1	333	2	331	<1
B+169	306	2	287	<<1	285	<<1	332	<<1	330	<<1
B+128	265	1	246	<1	244	1	291	2	289	<<1
B+127	264	1	245	<1	243	<1	290	<<1	288	<1
B+114	251	2	232	1	230	1	277	<1	275	2
M-217	193	13	174	6	172	16	219	7	217	4
B+110	247	4	228	1	226	3	273	55	271	<1
M-221	189	<1	170	1	168	1	215	2	213	15
M-222	188	<1	169	1	167	1	214	4	212	<<1
B+86	223	8	204	8	202	5	249	6	247	2
B+85	222	38	203	33	201	8	248	25	246	2
B+84	221	12	202	6	200	13	247	6	245	4
B+72	209	15	190	9	188	5	235	4	233	1
B+71	208	<1	189	<1	187	<1	234	<<1	232	<<1
B+68	205	15	186	6	184	4	231	4	229	2
B+56	193	13	174	6	172	16	219	7	217	4
B+44	181	9	162	7	160	5	207	10	205	2
B+43	180	65	161	33	159	23	206	69	204	10
B+30	167	39	148	83	146	24	193	100	191	8
B+29	166	4	147	25	145	33	192	21	190	6
B+2	139	2	120	8	118	20	165	7	163	4
B+1	138	3	119	40	117	69	164	36	162	8
B	137	<1	118	23	116	9	163	8	161	1
	71	14	71	6	71	12	71	22	71	15
	85	3	85	3	85	5	85	2	85	6
B-45	92	4					118	30	116	11
B-46	91	4					117	25	115	10
B-47	90	1					116	11	114	2

Table 2.2.2.1.1. Mass Spectra of Acetylated L-Rhamnopyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	IV 135°	XI 115°	XIX 130°	XXVII 125°	XXXI 120°
M'+1	274	11	2	5	9	7
M'	273	72	14	31	55	51
M'-42	231	6	<1	1	4	2
M'-60	213	19	4	9	25	15
M'-72	201	2	2	8	4	1
M'-87	186	1	6	1	3	1
M'-88	185	15	13	4	15	1
M'-89	184	7	3	4	12	<1
M'-102	171	12	10	36	25	37
M'-120	153	36	28	95	75	88
M'-130	143	9	7	5	12	3
M'-131	142	13	2	3	11	2
M'-132	141	1	2	1	1	1
M'-144	129	8	8	20	17	14
M'-162	111	34	43	93	88	100
M'-172	101	9	4	8	10	6
M'-174	99	13	13	12	23	9
M''	145	6	2	33	7	5
M'-190	83	56	55	64	88	48
M'-191	82	7	2	3	8	4
M'-192	81	1	2	1	1	4
M'-201	72	1	<<1	1	1	1
M'-204	69	5	7	10	10	12
M'-216	57	5	6	8	12	12
M'-222	51		2	2		2
M''-42	103	12	7	8	16	7
	100	14	3	5	13	6

Table 2.2.2.1.2. Mass Spectra of Acetylated L-Rhamnopyranosylamine Derivatives : Nitrogen-free Fragments.

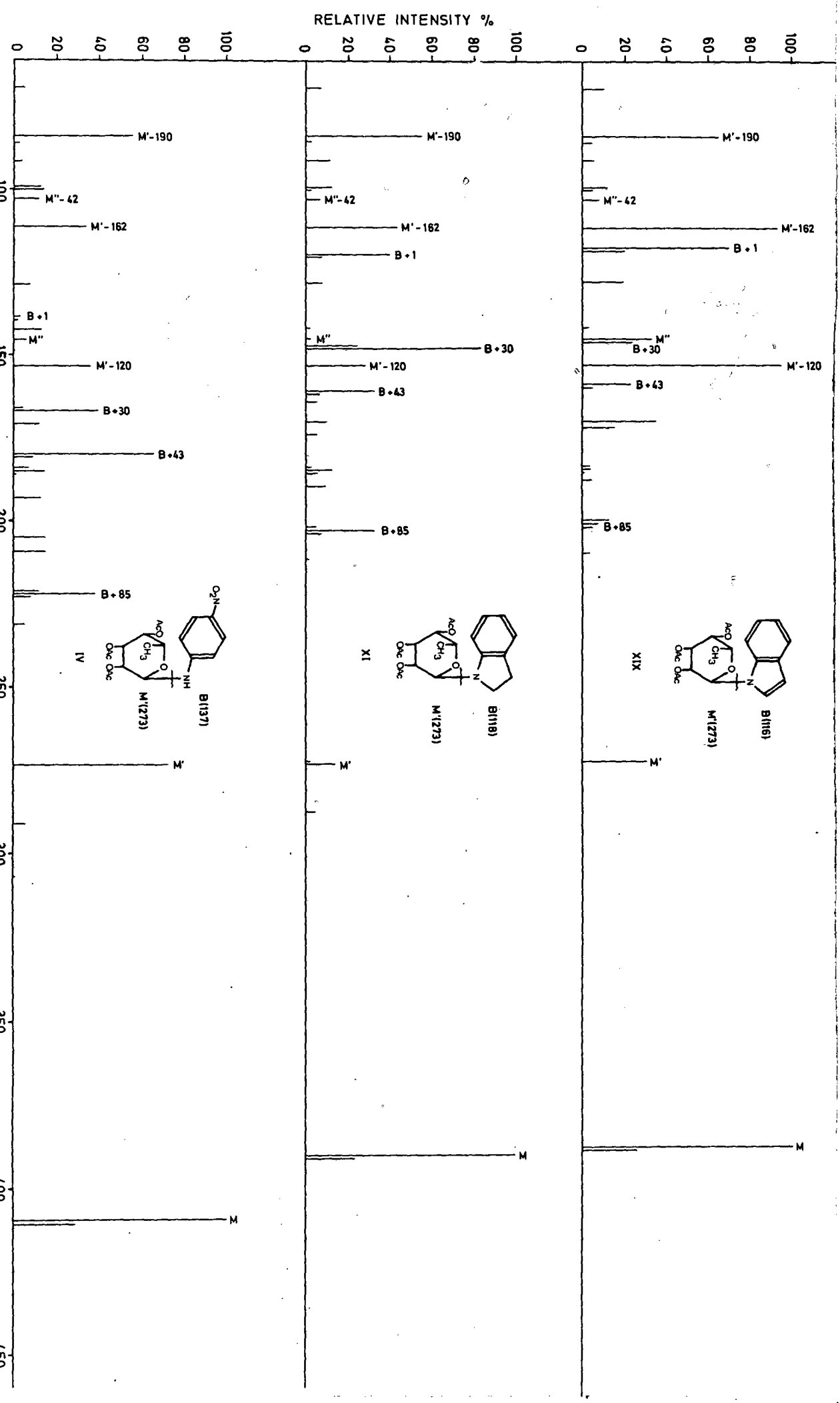


FIG. 2.2. E.I. MASS SPECTRA OF IV, XI and XIX.

Designation	m/e	V 165°	m/e	XII 100°	m/e	XX 115°	m/e	XXVIII 125°	m/e	XXXV 110°
M+1	397	9	378	23	376	8	423	4	392	11
M	396	44	377	91	375	38	422	13	391	48
M-59	337	<1	318	3	316	<<1	363	1	332	2
M-60	336	<1	317	<1	315	<<1	362	3	331	<1
M-73	323	<<1	304	<<1	302	<1	349	<<1	318	<<1
M-102	294	2	275	1	273	<<1	320	<1	289	<1
M-119	277	5	258	2	256	<1	303	1	272	<1
M-120	276	5	257	<<1	255	<1	302	3	271	<<1
M-133	263	<1	244	<<1	242	2	289	<1	258	<<1
M-162	234	3	215	<1	213	<1	260	5	229	<<1
M-179	217	7	198	2	196	2	243	2	212	1
M-180	216	3	197	<<1	195	<<1	242	<1	211	<<1
M-192	204	2	185	<<1	183	<1	230	2	199	5
M-193	203	<1	184	<<1	182	<<1	229	<1	198	<<1
B+170	307	<<1	288	2	286	<<1	333	<1	302	1
B+169	306	<1	287	<<1	285	<<1	332	1	301	<<1
B+128	265	<1	246	<<1	244	<<1	291	<1	260	<1
B+127	264	<1	245	<<1	243	<<1	290	<1	259	4
B+114	251	1	232	2	230	1	277	<1	246	<1
M-217	179	2	160	4	158	7	205	2	174	3
M-221	175	2	156	3	154	2	201	3	170	5
B+110	247	<1	228	<1	226	<<1	273	<1	242	<<1
M-222	174	<1	155	<<1	153	<<1	200	3	169	<<1
B+86	223	2	204	4	202	1	249	1	218	2
B+85	222	14	203	19	201	2	248	6	217	8
B+84	221	4	202	3	200	5	247	2	216	1
B+72	209	11	190	22	188	3	235	5	204	12
B+71	208	1	189	<1	187	1	234	<1	203	<<1
B+68	205	7	186	3	184	2	231	2	200	2
B+56	193	7	174	7	172	4	219	3	188	2
B+44	181	4	162	4	160	2	207	3	176	3
B+43	180	37	161	22	159	7	206	16	175	15
B+30	167	44	148	100	146	8	193	36	162	100
B+29	166	5	147	17	145	8	192	9	161	14
B+2	139	32	120	7	118	10	165	2	134	4
B+1	138	5	119	43	117	52	164	4	133	17
B	137	3	118	25	116	5	163	25	132	10
	71	4	71	1	71	3	71	7	71	<1
	85	18	85	14	85	8	85	15	85	7
B-45	92	6					118	25		
B-46	91	2					117	24		
B-47	90	1					116	10		

Table 2.2.3.1.1. Mass Spectra of Acetylated D-Xylopyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	V 165°	XII 100°	XX 115°	XXVIII 125°	XXXV 110°
M' + 1	260	4	1	3	5	<1
M'	259	25	10	19	20	4
M'-42	217	7	1	<<1	1	8
M'-60	199	19	16	30	26	5
M'-72	187	3	5	<1	1	3
M'-87	172	2	1	<<1	1	1
M'-88	171	16	7	1	6	7
M'-89	170	14	2	1	3	5
M'-102	157	52	25	54	59	16
M'-120	139	32	28	51	57	10
M'-130	129	13	5	2	9	3
M'-131	128	36	5	2	8	4
M'-132	127	6	7	3	5	4
M'-144	115	27	9	12	17	6
M'-162	97	88	37	100	100	15
M'-172	87	8	1	2	4	<1
M'-174	85	18	14	8	15	8
M''	145	5	1	8	4	1
M'-190	69	100	33	19	35	19
M'-191	68	15	1	4	8	1
M'-192	67	2	<1	1	4	<1
M'-204	55		2	7	8	1
M''-42	103	19	7	4	10	4
	86	14	2	7	5	3

Table 2.2.3.1.2. Mass Spectra of Acetylated D-Xylopyranosylamine Derivatives : Nitrogen-free Fragments.

Designation	m/e	VII 160°	XIII 140°	XXI 100°
M'+1	260	3	<1	3
M'	259	17	5	23
M'-42	217	4	<1	2
M'-60	199	14	5	15
M'-72	187	2	3	2
M'-87	172	2	1	8
M'-88	171	20	4	1
M'-89	170	24	1	3
M'-102	157	57	17	64
M'-120	139	36	15	68
M'-130	129	12	5	4
M'-131	128	38	4	4
M'-132	127	6	3	4
M'-144	115	29	8	19
M'-162	97	62	26	100
M'-172	87	6	1	3
M'-174	85	30	12	15
M''	145	4	1	15
M'-190	69	100	27	26
M'-191	68	19	1	4
M'-192	67		<<1	1
M'-204	55		2	10
M''-42	103	20	5	7
	86	31	2	4

Table 2.2.3.2.2. Mass Spectra of Acetylated D-Lyxopyranosylamine Derivatives : Nitrogen-free Fragments.

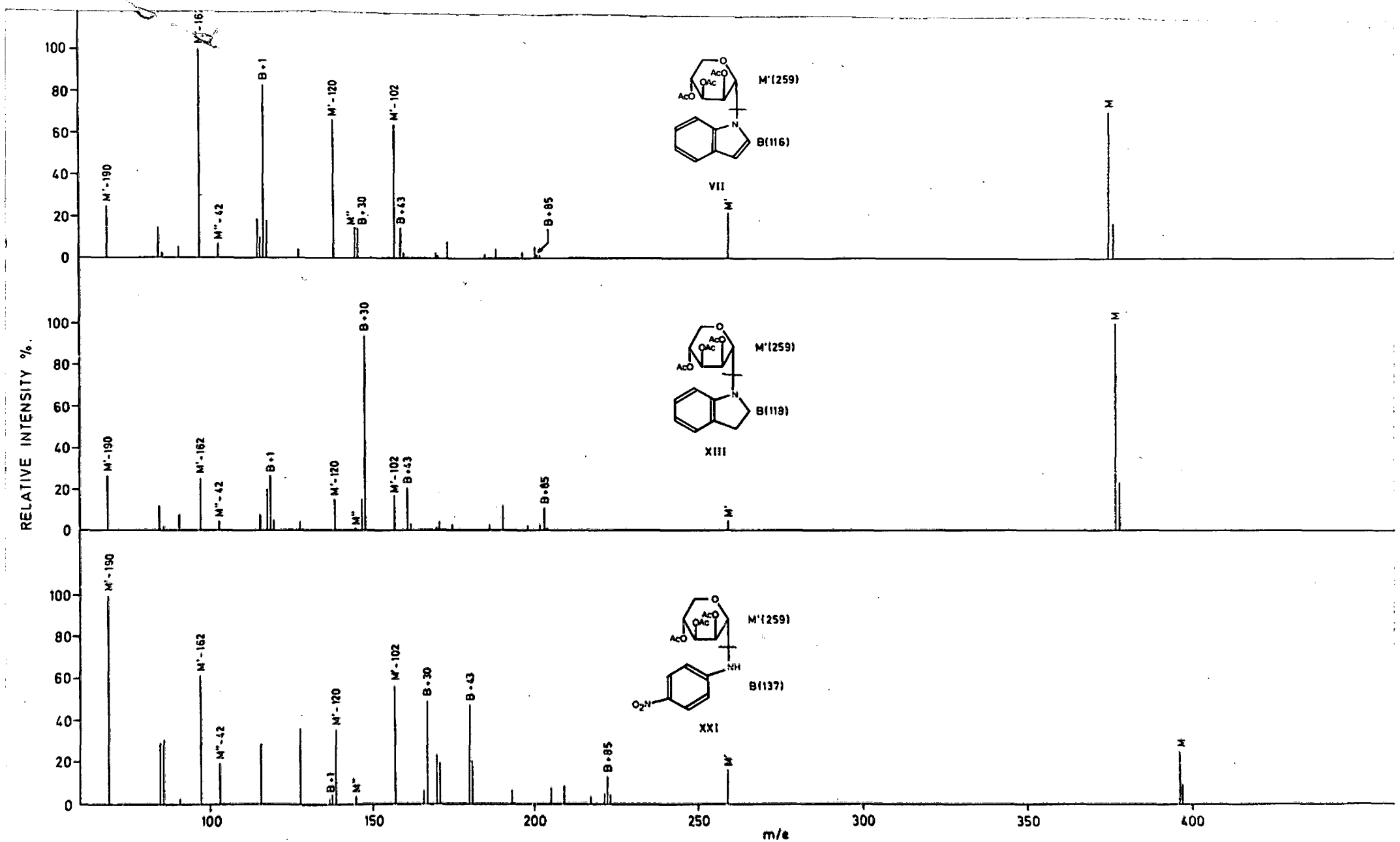


FIG. 2.3. E.I. MASS SPECTRA of VII, XIII and XXI.

Designation	m/e	VI 170°	m/e	XIV 90°	m/e	XXII 115°	m/e	XXIX 125°
M+1	397	14	378	12	376	7	423	10
M	396	52	377	48	375	30	422	42
M-59	337	4	318	2	316	<<1	363	1
M-60	336	4	317	1	315	<1	362	<1
M-73	323	<<1	304	<<1	302	x	349	1
M-102	294	4	275	1	273	<<1	320	<<1
M-119	277	21	258	1	256	1	303	3
M-120	276	5	257	<<1	255	<<1	302	<1
M-133	263	<<1	244	<<1	242	x	289	<<1
M-162	234	7	215	<1	213	<<1	260	9
M-179	217	19	198	2	196	4	243	3
M-180	216	4	197	<1	195	<1	242	<<1
M-192	204	3	185	<1	183	<1	230	3
M-193	203	1	184	<1	182	<<1	229	<1
B+170	307	<<1	288	3	286	<<1	333	<1
B+169	306	<1	287	<<1	285	<<1	332	<<1
B+128	265	<<1	246	<1	244	<1	291	<1
B+127	264	<1	245	<<1	243	<<1	290	<<1
B+114	251	4	232	<1	230	1	277	<1
M-217	179	5	160	5	158	7	205	3
M-221	175	3	156	3	154	1	201	2
B+110	247	1	228	<<1	226	<1	273	<<1
M-222	174	1	155	<1	153	<1	200	2
B+86	223	4	204	3	202	<1	249	2
B+85	222	24	203	11	201	1	248	7
B+84	221	9	202	2	200	3	247	4
B+72	209	34	190	18	188	4	235	11
B+71	208	5	189	1	187	1	234	<1
B+68	205	11	186	3	184	2	231	2
B+56	193	14	174	3	172	3	219	7
B+44	181	9	162	10	160	3	207	9
B+43	180	63	161	60	159	8	206	51
B+30	167	100	148	100	146	15	193	84
B+29	166	12	147	19	145	12	192	13
B+2	139	9	120	10	118	14	165	7
B+1	138	2	119	85	117	67	164	49
B	137	<1	118	73	116	8	163	7
	71	1	71	6	71	3	71	5
	85	13	85	14	85	10	85	24
B-45	92	5					118	32
B-46	91	2					117	27
B-47	90	1					116	9

Table 2.2.3.3.1. Mass Spectra of Acetylated L-Arabinopyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	VI 170°	XIV 90°	XXII 115°	XXIX 125°
M' + 1	260	9	2	4	9
M'	259	63	11	33	63
M'-42	217	19	2	<1	3
M'-60	199	32	4	9	13
M'-72	187	5	6	1	3
M'-87	172	6	2	3	2
M'-88	171	63	8	1	16
M'-89	170	39	7	1	9
M'-102	157	72	16	44	44
M'-120	139	9	23	79	79
M'-130	129	17	7	4	16
M'-131	128	39	9	3	15
M'-132	127	6	4	4	8
M'-144	115	24	14	15	31
M'-162	97	51	39	100	90
M'-172	87	4	2	3	6
M'-174	85	13	14	10	24
M''	145	6	3	12	4
M'-190	69	56	51	30	100
M'-191	68	10	4	3	9
M'-192	67	<1	2	<1	3
M'-204	55	2	8	8	8
M''-42	103	18	10	5	20
	86	10	5	3	9

Table 2.2.3.3.2. Mass Spectra of Acetylated L-Arabinopyranosylamine Derivatives : Nitrogen-free Fragments.

Designation	m/e	XV 100°	m/e	XXIII 120°
M+1	378	17	376	24
M	377	78	375	100
M-59	318	4	316	<<1
M-60	317	<1	315	<<1
M-73	304	<<1	302	<<1
M-102	275	1	273	<<1
M-119	258	1	256	<<1
M-120	257	<<1	255	<<1
M-133	244	<<1	242	<<1
M-162	215	<<1	213	<<1
M-179	198	1	196	2
M-180	197	x	195	<<1
M-192	185	<<1	183	<1
M-193	184	<<1	182	<<1
B+170	288	2	286	<<1
B+169	287	x	285	<<1
B+128	246	<<1	244	<<1
B+127	245	<<1	243	<<1
B+114	232		230	<<1
M-217	160	4	158	6
M-221	156	3	154	2
B+110	228	<<1	226	<<1
M-222	155	<<1	153	<1
B+86	204	3	202	1
B+85	203	15	201	2
B+84	202	3	200	2
B+72	190	15	188	4
B+71	189	<<1	187	<1
B+68	186	2	184	1
B+56	174	3	172	4
B+44	162	4	160	2
B+43	161	20	159	10
B+30	148	100	146	19
B+29	147	14	145	10
B+2	120	5	118	10
B+1	119	32	117	63
B	118	18	116	5
	71	<1	71	1
	85	10	85	6

Table 2.2.3.4.1. Mass Spectra of Acetylated D-Ribopyranosylamine Derivatives : Nitrogen-containing Fragments.

Designation	m/e	$\frac{XV}{100^{o}}$	$\frac{XXIII}{120^{o}}$
M'+1	260	2	8
M'	259	15	64
M'+42	217	1	<1
M'-60	199	4	4
M'-72	187	3	<1
M'-87	172	2	4
M'-88	171	7	<1
M'-89	170	7	1
M'-102	157	12	35
M'-120	139	20	64
M'-130	129	5	4
M'-131	128	8	3
M'-132	127	4	4
M'-144	115	11	9
M'-162	97	23	55
M'-172	87	2	1
M'-174	85	10	6
M''	145	2	10
M'-190	69	43	20
M'-191	68	2	1
M'-192	67	1	<1
M'-204	55	3	5
M''-42	103	10	4
	86	4	2

Table 2.2.3.4.2. Mass Spectra of Acetylated D-Ribopyranosylamine Derivatives : Nitrogen-free Fragments.

derivatives are given in Tables 2.2.3.1.2., 2.2.3.2.2., 2.2.3.3.2. and 2.2.3.4.2. respectively.

The relative intensities of the peaks due to the nitrogen-containing fragments of the following series of acetylated glycopyranosylamines: *N*-*p*-nitrophenyl, indoline, indole, 5-nitroindoline, 5-nitroindole and 1,2,3,4-tetrahydroquinoline are shown in Tables 2.2.4.1.1., 2.2.4.2.1., through 2.2.4.6.1. The intensities of the ion peaks arising from the fragmentation of the sugar moiety of these compounds are compared in Tables 2.2.4.1.2., through 2.2.4.6.2.

As all of these mass spectra are so similar, accurate mass measurements were obtained for only one compound (XVI). The formulae calculated from these accurate masses provided a means of checking some of the fragmentations suggested.

2.3. DISCUSSION.

2.3.1. Acetylated Hexopyranosylamine Derivatives.

From a study of the ions in Tables 2.2.1.1.2., 2.2.1.2.2. and 2.2.1.3.2., metastable scans for the ions at $^{m}/_{e}$ 169 and 109 in compound XVI, and from metastable ions, several possible fragmentation pathways have been drawn up.

Chart 2.3.1.1. shows one possible fragmentation pathway for the sugar moiety of XVI[34,35]. Although the relative intensities of several of the key fragments are low, there are metastable peaks corresponding to several of these transitions.

Metastable scanning on the ions $^{m}/_{e}$ 169 and 109 of compound XVI showed the following ions to be precursors: $^{m}/_{e}$ 211,229,271,M' and M and $^{m}/_{e}$ 127,169,187,211 and 229 respectively. These results, while they support the scheme suggested, indicate that a concerted loss of more than one fragment does occur, although to a limited extent.

Designation	m/e	I 175°	II 175°	III 150°	m/e	IV 135°	m/e	V 165°	VI 170°	VII 160°
M+1	469	12	18	9	411	29	397	9	14	10
M	468	42	64	30	410	100	396	44	52	26
M-16	452	2	3	2	394	5	380	1	3	2
M-29	439	1	1	<1	381	1	367	1	<1	2
M-30	438	3	3	2	380	3	366	1	2	4
M-59	409	1	11	1	351	2	337	<1	4	<1
M-60	408	1	5	2	350	<1	336	<1	4	<1
M-73	395	2	2	4	337	x	323	<<1	<<1	<<1
M-102	366	1	3	2	308	1	294	2	4	1
M-119	349	7	11	6	291	6	277	5	21	5
M-120	348	5	2	5	290	10	276	5	5	4
M-133	335	4	2	4	277	x	263	<1	<<1	<<1
M-162	306	3	2	3	248	2	234	3	7	2
M-179	289	5	3	6	231	6	217	7	19	4
M-180	288	3	2	3	230	2	216	3	4	2
M-192	276	3	1	1	218	x	204	2	3	2
M-193	275	14	5	1	217	<<1	203	<1	1	1
B+170	307	2	2	2	307	2	307	<<1	<<1	<<1
B+169	306	3	2	3	306	2	306	<1	<1	<<1
B+128	265	1	<1	1	265	1	265	<1	<<1	<1
B+127	264	2	1	3	264	1	264	<1	<1	<1
B+114	251	6	6	8	251	2	251	1	4	1
M-217	251	6	6	8	193	13	179	2	5	3
M-221	247	8	6	8	189	<1	175	2	3	2
B+110	247	8	6	8	247	4	247	<1	1	<1
M-222	246	6	4	7	188	<1	174	<1	1	<1
B+86	223	3	3	5	223	8	223	2	4	5
B+85	222	20	16	25	222	38	222	14	24	13
B+84	221	11	10	13	221	12	221	4	9	5
B+72	209	9	16	12	209	15	209	11	34	9
B+71	208	<1	2	<1	208	<1	208	1	5	1
B+68	205	9	10	16	205	15	205	7	11	7
B+56	193	10	10	16	193	13	193	7	14	7
B+44	181	7	6	8	181	9	181	4	9	21
B+43	180	38	34	45	180	65	180	37	63	48
B+30	167	27	36	28	167	39	167	44	100	50
B+29	166	4	5	2	166	4	166	5	12	7
B+2	139	18	14	18	139	2	139	32	9	36
B+1	138	9	6	14	138	3	138	5	2	5
B	137	2	2	1	137	<1	137	3	<1	3
	71	5	3	4	71	14	71	4	1	5
	85	10	8	10	85	3	85	18	13	30
B-45	92	10	5	11	92	4	92	6	5	6
B-46	91	3	2	2	91	4	91	2	2	3
B-47	90	2	1	1	90	1	90	1	1	2

Table 2.2.4.1.1: Mass Spectra of Acetylated *N*-*p*-nitrophenylglycopyranosylamine Derivatives: Nitrogen-containing Fragments.

Designation	m/e	$\overline{\text{I}}$ 175°	$\overline{\text{II}}$ 175°	$\overline{\text{III}}$ 150°	m/e	$\overline{\text{IV}}$ 135°	m/e	$\overline{\text{V}}$ 165°	$\overline{\text{VI}}$ 170°	$\overline{\text{VII}}$ 160°
M'+1	332	5	8	7	274	11	260	4	9	3
M'	331	35	45	38	273	72	259	25	63	17
M'-42	289	5	3	6	231	6	217	7	19	4
M'-60	271	4	1	5	213	19	199	19	32	14
M'-72	259	<1	1	2	201	2	187	3	5	2
M'-87	244	2	2	<<1	186	1	172	2	6	2
M'-88	243	11	14	12	185	15	171	16	63	20
M'-89	242	3	2	1	184	7	170	14	39	24
M'-102	229	9	13	9	171	12	157	52	72	57
M'-120	211	10	12	10	153	36	139	32	9	36
M'-130	201	4	9	7	143	9	129	13	17	12
M'-131	200	5	10	7	142	13	128	36	39	38
M'-132	199	2	4	2	141	1	127	6	6	6
M'-144	187	3	3	4	129	8	115	27	24	29
M'-162	169	78	52	76	111	34	97	88	51	62
M'-172	159	3	5	3	101	9	87	8	4	6
M'-174	157	14	9	11	99	13	85	18	13	30
M''	145	16	14	16	145	6	145	5	6	4
M'-190	141	36	54	35	83	56	69	100	56	100
M'-191	140	9	10	9	82	7	68	15	10	19
M'-192	139	18	14	18	81	1	67	2	<1	
M'-201	130	4	3	2	72	1				
M'-204	127	24	20	23	69	5	55		2	
M'-216	115	38	23	30	57	5				
M'-222	109	76	43	70	51					
M''-42	103	27	20	25	103	12	103	19	18	20
M'-232	99	25	29	25						
	98	36	25	38	100	14	86	14	10	31
M'-234	97	24	14	25						
M'-246	85	10	8	10						
M'-250	81	100	100	100						
M'-262	69	18	11	20						

Table 2.2.4.1.2. Mass Spectra of Acetylated *N*-*p*-nitrophenylglycopyranosylamine Derivatives: Nitrogen-free Fragments.

Desig-nation	m/e	VIII	IX 100°	X 150°	m/e	XI 115°	m/e	XII 100°	XIII 140°	XIV 90°	XV 100°
M+1	450	25	20	28	392	24	378	23	23	12	17
M	449	96	74	100	391	100	377	91	100	48	78
M-59	390	6	10	5	332	2	318	3	2	2	4
M-60	389	<1	<1	2	331	<1	317	<1	<1	1	<1
M-73	376	13	7	18	318	<<1	304	<<1	x	<<1	<<1
M-102	347	6	4	4	289	1	275	1	1	1	1
M-119	330	3	2	2	272	1	258	2	1	1	1
M-120	329	<<1	<<1	<<1	271	1	257	<<1	<<1	<<1	<<1
M-133	316	4	3	4	258	x	244	<<1	<<1	<<1	<<1
M-162	287	1	1	1	229	1	215	<1	<1	<1	<<1
M-179	270	2	4	2	212	2	198	2	2	2	1
M-180	269	x	<<1	<<1	211	3	197	<<1	<<1	<1	x
M-192	257	<<1	5	<<1	199	<1	185	<<1	<1	<1	<<1
M-193	256	<1	<1	<1	198	<1	184	<<1	<1	<1	<<1
B+170	288	5	3	4	288	5	288	2	<<1	3	2
B+169	287	1	<1	1	287	<<1	287	<<1	<<1	<<1	x
B+128	246	1	<1	<1	246	<1	246	<<1	<<1	<1	<<1
B+127	245	2	1	2	245	<1	245	<<1	<<1	<<1	<<1
B+114	232	6	5	6	232	1	232	2	1	<1	
M-217	232	6	5	6	174	6	160	4	4	5	4
M-221	228	3	2	2	170	1	156	3	3	3	3
B+110	228	3	2	2	228	1	228	<1	<<1	<<1	<<1
M-222	227	<1	2	1	169	1	155	<<1	<<1	<1	<<1
B+86	204	7	5	5	204	8	204	4	1	3	3
B+85	203	24	21	23	203	33	203	19	11	11	15
B+84	202	6	6	7	202	6	202	3	3	2	3
B+72	190	9	14	9	190	9	190	22	12	18	15
B+71	189	<1	<1	<1	189	<1	189	<1	<1	1	<<1
B+68	186	8	4	4	186	6	186	3	2	3	2
B+56	174	7	10	8	174	6	174	7	3	3	3
B+44	162	6	5	6	162	7	162	4	4	10	4
B+43	161	29	29	31	161	33	161	22	21	60	20
B+30	148	100	100	69	148	83	148	100	94	100	100
B+29	147	29	27	19	147	25	147	17	16	19	14
B+2	120	8	8	5	120	8	120	7	5	10	5
B+1	119	42	41	25	119	40	119	43	27	85	32
B	118	24	33	14	118	23	118	25	20	73	18
	71	5	11		71	6	71	1	1	6	<1
	85	4	7	3	85	3	85	14	12	14	10

Table 2.2.4.2.1. Mass Spectra of Acetylated Glycopyranosyl-indoline Derivatives : Nitrogen-containing Fragments.

Designation	m/e	VIII	IX 100°	X 150°	m/e	XI 115°	m/e	XII 100°	XIII 140°	XIV 90°	XV 100°
M'+1	332	2	3	3	274	2	260	1	<1	2	2
M'	331	7	20	14	273	14	259	10	5	11	15
M'-42	289	2	1	1	231	<1	217	1	<1	2	1
M'-60	271	1	1	1	213	4	199	16	5	4	4
M'-72	259	3	2	2	201	2	187	5	3	6	3
M'-87	244	3	3	3	186	6	172	1	1	2	2
M'-88	243	7	8	6	185	13	171	7	4	8	7
M'-89	242	3	2	<<1	184	3	170	2	1	7	7
M'-102	229	6	6	5	171	10	157	25	17	16	12
M'-120	211	6	5	4	153	28	139	28	15	23	20
M'-130	201	5	5	5	143	7	129	5	5	7	5
M'-131	200	2	2	1	142	2	128	5	4	9	8
M'-132	199	2	3	1	141	2	127	7	3	4	4
M'-144	187	8	4	4	129	8	115	9	8	14	11
M'-162	169	48	32	52	111	43	97	37	26	39	23
M'-172	159	3		1	101	4	87	1	1	2	2
M'-174	157	7	6	3	99	13	85	14	12	14	10
M''	145	6	4	4	145	2	145	1	1	3	2
M'-190	141	27	32	19	83	55	69	33	27	51	43
M'-191	140	4	2	1	82	2	68	1	1	4	2
M'-192	139	12	10	8	81	2	67	<1	<<1	2	1
M'-201	130	8	9	6	72	<<1					
M'-204	127	12	9	7	69	7	55	2	2	8	3
M'-216	115	17	17	7	57	6					
M'-222	109	49	34	24	51	2					
M''-42	103	7	6	4	103	7	103	7	5	10	10
M'-232	99	10	10	5							
	98	6	5	2	100	3	86	2	2	5	4
M'-234	97	12	12	7							
M'-246	85	4	7	3							
M'-250	81	74	69	36							
M'-262	69	7	11	4							

Table 2.2.4.2.2. Mass Spectra of Acetylated Glycosylindoline Derivatives : Nitrogen-free Fragments.

Designation	m/e	XVI 165°	XVII	m/e	XIX 130°	m/e	XX 115°	XXI 100°	XXII 115°	XXIII 120°
M+1	448	12	18	390	26	376	8	17	7	24
M	447	44	69	389	100	375	38	71	30	100
M-59	388	<<1	<1	330	<<1	316	<<1	<<1	<<1	<<1
M-60	387	<<1	1	329	<<1	315	<<1	<<1	<1	<<1
M-73	374	<1	<<1	316	<<1	302	<<1	x	x	<<1
M-102	345	<1	<1	287	<1	273	<<1	<<1	<<1	<<1
M-119	328	1	1	270	<1	256	<1	<1	1	<<1
M-120	327	<<1	<<1	269	<1	255	<1	<<1	<<1	<<1
M-133	314	<<1	x	256	<1	242	2	<<1	x	<<1
M-162	285	<<1	<<1	227	<1	213	<1	<1	<<1	<<1
M-179	268	2	1	210	4	196	2	3	4	2
M-180	267	<<1	<<1	209	<1	195	<<1	<<1	<1	<<1
M-192	255	<1	<1	197	<1	183	<1	<1	<1	<1
M-193	254	2	<1	196	<1	182	<<1	<<1	<<1	<<1
B+170	286	<1	<1	286	<1	286	<<1	<<1	<<1	<<1
B+169	285	<<1	<<1	285	<<1	285	<<1	<<1	<<1	<<1
B+128	244	<1	<1	244	1	244	<<1	<<1	<1	<<1
B+127	243	<1	<1	243	<1	243	<<1	<<1	<<1	<<1
B+114	230	2	2	230	1	230	1	1	1	<<1
M-217	230	2	2	172	16	158	7	9	7	6
M-221	226	3	2	168	1	154	2	3	1	2
B+110	226	3	2	226	3	226	<<1	<<1	<<1	<<1
M-222	225	1	<1	167	1	153	<<1	<1	<<1	<1
B+86	202	3	1	202	5	202	1	1	<<1	1
B+85	201	3	3	201	8	201	2	2	1	2
B+84	200	7	5	200	13	200	5	6	3	2
B+72	188	3	3	188	5	188	3	4	4	4
B+71	187	5	5	187	<1	187	1	2	1	<1
B+68	184	1	3	184	4	184	2	2	2	1
B+56	172	6	5	172	16	172	4	8	3	4
B+44	160	4	4	160	5	160	2	3	3	2
B+43	159	12	12	159	23	159	7	14	8	10
B+30	146	7	13	146	24	146	8	14	15	19
B+29	145	14	19	145	33	145	8	15	12	10
B+2	118	12	14	118	20	118	10	18	14	10
B+1	117	44	60	117	69	117	52	83	67	63
B	116	6	7	116	9	116	5	11	8	5
	71	2	3	71	12	71	3	4	3	1
	85	7	7	85	5	85	8	18	10	6

Table 2.2.4.3.1. Mass Spectra of Acetylated Glycopyranosyl-indole Derivatives : Nitrogen-containing Fragments.

Designation	m/e	XVI 165°	XVII	m/e	XIX 130°	m/e	XX 115°	XXI 100°	XXII 115°	XXIII 120°
M'+1	332	5	16	274	5	260	3	3	4	8
M'	331	29	93	273	31	259	19	23	33	64
M'-42	289	<1	1	231	1	217	<<1	2	<1	<1
M'-60	271	7	1	213	9	199	30	15	9	4
M'-72	259	<1	<<1	201	8	187	<1	2	1	<1
M'-87	244	<1	<1	186	1	172	<<1	8	3	4
M'-88	243	<1	<1	185	4	171	1	1	1	<1
M'-89	242	2	1	184	3	170	1	3	1	1
M'-102	229	6	7	171	36	157	54	64	44	35
M'-120	211	8	5	153	95	139	51	68	79	64
M'-130	201	3	3	143	5	129	2	4	4	4
M'-131	200	7	5	142	3	128	2	4	3	3
M'-132	199	<1	<1	141	1	127	3	4	4	4
M'-144	187	5	5	129	20	115	12	19	15	9
M'-162	169	100	100	111	93	97	100	100	100	55
M'-172	159	12	5	101	8	87	2	3	3	1
M'-174	157	2	2	99	12	85	8	15	10	6
M''	145	14	19	145	33	145	8	15	12	10
M'-190	141	3	7	83	64	69	19	26	30	20
M'-191	140	2	1	82	3	68	4	4	3	1
M'-192	139	13	8	81	1	67	1	1	<1	<1
M'-201	130	14	13	72	1					
M'-204	127	20	28	69	10	55	7	10	8	5
M'-216	115	12	12	57	8					
M'-222	109	52	69	51	2					
M''-42	103	7	10	103	8	103	4	7	5	4
M'-232	99	5	9							
	98	3	3	100	5	86	7	4	3	2
M'-234	97	9	8							
M'-246	85	4	7							
M'-250	81	11	28							
M'-262	69	3	5							

Table 2.2.4.3.2. Mass Spectra of Acetylated Glycopyranosylindole Derivatives : Nitrogen-free Fragments.

Designation	m/e	XXIV 215°	XXV 130°	XXVI 155°	m/e	XXVII 125°	m/e	XXVIII 125°	XXIX 125°
M+1	495	8	15	11	437	8	423	4	10
M	494	21	57	44	436	33	422	13	42
M-16	478	1	2	2	420	2	406	<1	2
M-29	465	<1	3	1	407	2	393	1	1
M-30	464	2	10	4	406	7	392	4	4
M-59	435	<1	4	2	377	1	363	1	1
M-60	434	1	<1	<1	376	<<1	362	3	<1
M-73	421	4	4	7	363	x	349	<<1	1
M-102	392	<1	2	1	334	<1	320	<1	<<1
M-119	375	1	1	1	317	<1	303	1	3
M-120	374	<<1	<<1	<<1	316	x	302	3	<1
M-133	361	1	1	2	303	x	289	<1	<<1
M-162	332	4	9	6	274	9	260	5	9
M-179	315	1	1	2	257	2	243	2	3
M-180	314	x	<<1	<1	256	4	242	<1	<<1
M-192	302	<1	<<1	<1	244	<1	230	2	3
M-193	301	<1	<<1	1	243	x	229	<1	<1
B+170	333	2	3	3	333	2	333	<1	<1
B+169	332	4	9	6	332	<<1	332	1	<<1
B+128	291	1	1	1	291	2	291	<1	<1
B+127	290	<1	<1	<1	290	<<1	290	<1	<<1
B+114	277	2	2	4	277	<1	277	<1	<1
M-217	277	2	2	4	219	7	205	2	3
M-221	273	1	2	2	215	2	201	3	2
B+110	273	1	2	2	273	55	273	<1	<<1
M-222	272	<1	<<1	1	214	4	200	3	2
B+86	249	2	3	3	249	6	249	1	2
B+85	248	9	13	13	248	25	248	6	7
B+84	247	3	7	6	247	6	247	2	4
B+72	235	3	8	4	235	4	235	5	11
B+71	234	x	<1	<1	234	<<1	234	<1	<1
B+68	231	2	3	3	231	4	231	2	2
B+56	219	6	9	8	219	7	219	3	7
B+44	207	4	6	6	207	10	207	3	9
B+43	206	26	33	36	206	69	206	16	51
B+30	193	52	90	77	193	100	193	36	84
B+29	192	11	18	17	192	21	192	9	13
B+2	165	3	5	3	165	7	165	2	7
B+1	164	11	17	8	164	36	164	4	49
B	163	3	10	3	163	8	163	25	7
	71	2	6	4	71	22	71	7	5
	85	6	11	8	85	2	85	15	24
B-45	118	9	13	11	118	30	118	25	32
B-46	117	7	11	9	117	25	117	24	27
B-47	116	4	6	5	116	11	116	10	9

Table 2.2.4.4.1. Mass Spectra of Acetylated Glycopyranosyl-5-nitroindoline Derivatives : Nitrogen-containing Fragments.

Designation	m/e	XXIV 215°	XXV 130°	XXVI 155°	m/e	XXVII 125°	m/e	XXVIII 125°	XXIX 125°
M'+1	332	4	9	6	274	9	260	5	9
M'	331	22	52	41	273	55	259	20	63
M'-42	289	<1	2	2	231	4	217	1	3
M'-60	271	2	1	4	213	25	199	26	13
M'-72	259	2	3	3	201	4	187	1	3
M'-87	244	<1	<1	1	186	3	172	1	2
M'-88	243	3	6	6	185	15	171	6	16
M'-89	242	1	2	2	184	12	170	3	9
M'-102	229	4	9	6	171	25	157	59	44
M'-120	211	5	9	8	153	75	139	57	79
M'-130	201	4	7	5	143	12	129	9	16
M'-131	200	2	1	2	142	11	128	8	15
M'-132	199	1	1	1	141	1	127	5	8
M'-144	187	4	5	4	129	17	115	17	31
M'-162	169	100	100	100	111	88	97	100	90
M'-172	159	3	6	4	101	10	87	4	6
M'-174	157	7	9	6	99	23	85	15	24
M''	145	11	9	10	145	7	145	4	4
M'-190	141	27	41	31	83	88	69	35	100
M'-191	140	3	1	7	82	8	68	8	9
M'-192	139	13	13	13	81	1	67	4	3
M'-201	130	6	8	8	72	1			
M'-204	127	23	21	17	69	10	55	8	8
M'-216	115	24	23	21	57	12			
M'-222	109	74	68	67					
M''-42	103	11	11	11	103	16	103	10	20
M'-232	99	4	19	17					
	98	7	8	7	100	13	86	5	9
M'-234	97	13	15	15					
M'-246	85	6	11	8					
M'-250	81	56	94	72					
M'-262	69	6	13	9					

Table 2.2.4.4.2. Mass Spectra of Acetylated Glycosyl-5-nitroindoline Derivatives : Nitrogen-free Fragments.

Designation	m/e	XXX 220°	m/e	XXXI 120°
M+1	493	7	435	11
M	492	22	434	48
M-16	476	1	418	2
M-29	463	<1	405	1
M-30	462	2	404	3
M-59	433	<1	375	?
M-60	432	<<1	374	<<1
M-73	419	<<1	361	<<1
M-102	390	<1	332	<<1
M-119	373	<1	315	x
M-120	372	<1	314	x
M-133	359	x	301	<<1
M-162	330	<<1	272	<<1
M-179	313	1	255	1
M-180	312	1	254	<<1
M-192	300	<1	242	1
M-193	299	2	241	<<1
B+170	331	30	331	<1
B+169	330	<<1	330	<<1
B+128	289	1	289	<<1
B+127	288	1	288	<1
B+114	275	2	275	2
M-217	275	2	217	4
M-221	271	8	213	15
B+110	271	8	271	<1
M-222	270	2	212	<<1
B+86	247	3	247	2
B+85	246	2	246	2
B+84	245	7	245	4
B+72	233	4	233	1
B+71	232	<<1	232	<<1
B+68	229	7	229	2
B+56	217	6	217	4
B+44	205	3	205	2
B+43	204	10	204	10
B+30	191	3	191	8
B+29	190	5	190	6
B+2	163	3	163	4
B+1	162	8	162	8
B	161	2	161	1
	71	5	71	15
	85	10	85	6
B-45	116	19	116	11
B-46	115	25	115	10
B-47	114		114	2

Table 2.2.4.5.1. Mass Spectra of Acetylated Glycopyranosyl-5-nitroindole Derivatives : Nitrogen-containing Fragments.

Designation	m/e	$\frac{\overline{XXX}}{220^{o}}$	m/e	$\frac{\overline{XXXI}}{120^{o}}$
M'+1	332	5	274	7
M'	331	30	273	51
M'-42	289	1	231	2
M'-60	271	8	213	15
M'-72	259	2	201	1
M'-87	244	<1	186	1
M'-88	243	1	185	1
M'-89	242	<1	184	<1
M'-102	229	7	171	37
M'-120	211	6	153	88
M'-130	201	2	143	3
M'-131	200	<1	142	2
M'-132	199	1	141	1
M'-144	187	5	129	14
M'-162	169	100	111	100
M'-172	159	4	101	6
M'-174	157	4	99	9
M''	145	10	145	5
M'-190	141	7	83	48
M'-191	140	3	82	4
M'-192	139	23	81	4
M'-201	130	7	72	1
M'-204	127	32	69	12
M'-216	115	25	57	12
M'-222	109	88	51	2
M''-42	103	11	103	7
M'-232	99	9		
	98	6	100	6
M'-234	97	21		
M'-246	85	10		
M'-250	81	26		
M'-262	69	10		

Table 2.2.4.5.2. Máss Spectra of Acetylated Glycosyl-5-nitroindole Derivatives : Nitrogen-free Fragments.

Designation	m/e	XXXIV	m/e	XXXV 110°
M+1	464	21	392	11
M	463	71	391	48
M-59	404	7	332	2
M-60	403	<1	331	<1
M-73	390	12	318	<<1
M-102	361	3	289	<1
M-119	344	2	272	<1
M-120	343	x	271	<<1
M-133	330	3	258	<<1
M-162	301	2	229	<<1
M-179	284	1	212	1
M-180	283	x	211	<<1
M-192	271	1	199	5
M-193	270	<1	198	<<1
B+170	302	2	302	1
B+169	301	1	301	<<1
B+128	260	<1	260	<1
B+127	259	3	259	4
B+114	246	4	246	<1
M-217	246	4	174	3
M-221	242	5	170	5
B+110	242	5	242	<<1
M-222	241	<1	169	<<1
B+86	218	4	218	2
B+85	217	18	217	8
B+84	216	5	216	1
B+72	204	11	204	12
B+71	203	<1	203	<<1
B+68	200	6	200	2
B+56	188	7	188	2
B+44	176	5	176	3
B+43	175	27	175	15
B+30	162	100	162	100
B+29	161	26	161	14
B+2	134	7	134	4
B+1	133	39	133	17
B	132	17	132	10
	71	2	71	<1
	85	5	85	7

Table 2.2.4.6.1. Mass Spectra of Acetylated Glycopyranosyl-1,2,3,4-tetrahydroquinoline Derivatives : Nitrogen-containing Fragments.

Designation	m/e	XXXIV	m/e	XXXV 110°
M'+1	332	2	260	<1
M'	331	9	259	4
M'-42	289	<1	217	8
M'-60	271	1	199	5
M'-72	259	3	187	3
M'-87	244	2	172	1
M'-88	243	11	171	7
M'-89	242	5	170	5
M'-102	229	3	157	16
M'-120	211	6	139	10
M'-130	201	6	129	3
M'-131	200	6	128	4
M'-132	199	2	127	4
M'-144	187	4	115	6
M'-162	169	48	97	15
M'-172	159	1	87	<1
M'-174	157	8	85	8
M''	145	6	145	1
M'-190	141	35	69	19
M'-191	140	4	68	1
M'-192	139	11	67	<1
M'-201	130	7		
M'-204	127	8	55	1
M'-216	115	22		
M'-222	109	36		
M''-42	103	8	103	4
M'-232	99	9		
	98	8	86	3
M'-234	97	16		
M'-246	85	5		
M'-250	81	75		
M'-262	69	1		

Table 2.2.4.6.2. Mass Spectra of Acetylated Glycosyl-1,2,3,4-tetrahydroquinoline Derivatives: Nitrogen-free Fragments.

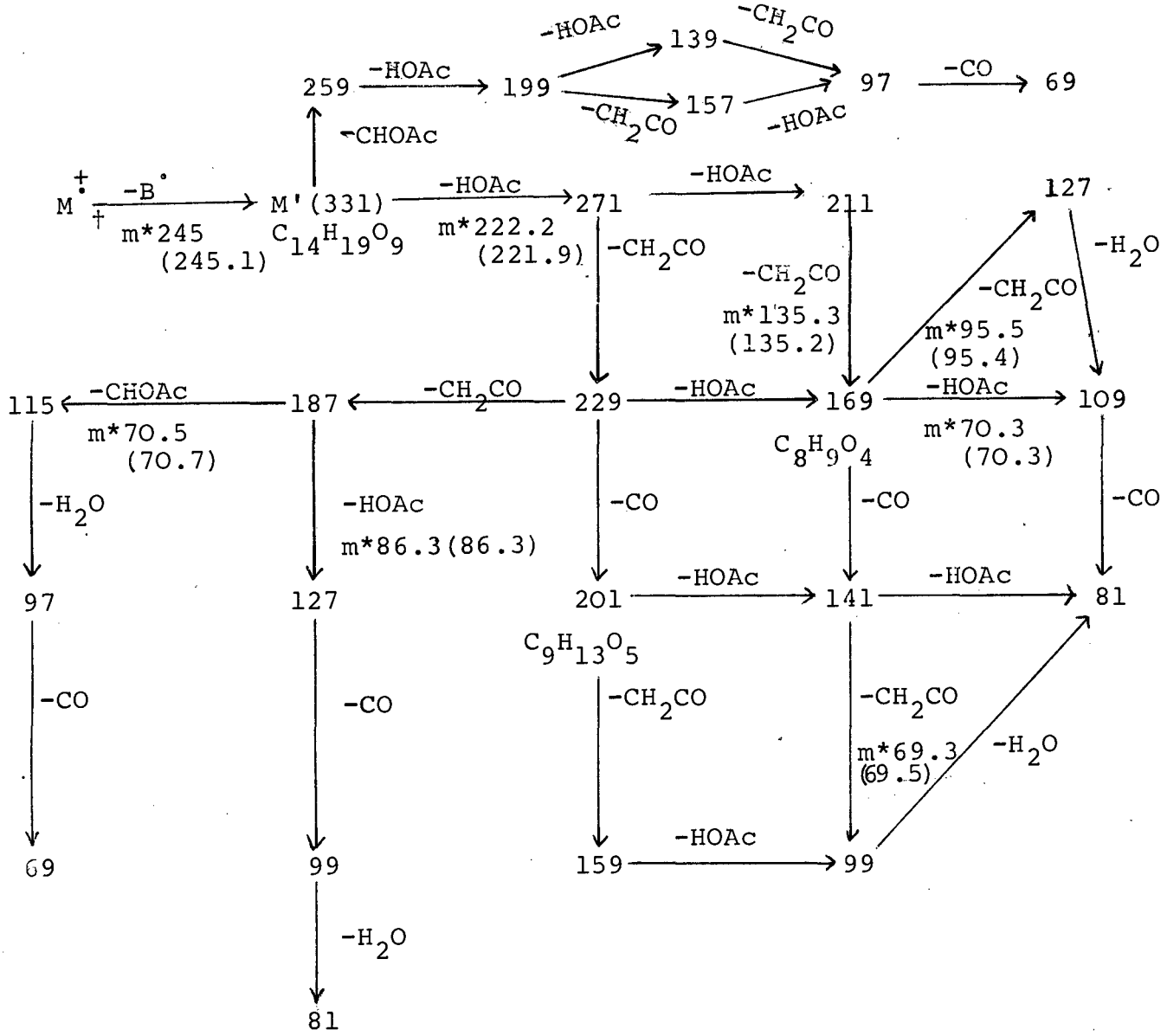


Chart 2.3.1.1.[35] (See Appendix 1)

†Metastable peaks in spectrum (calculated value in parenthesis).

With due regard for the uncertainty of structures postulated for fragments formed in the mass spectrometer, the scheme suggested in Chart 2.3.1.1. has been tentatively elaborated in Appendix 1. (In pocket in back cover). Although several of the ions postulated, in particular, that at $^{m}/_{e}$ 127, might be expected to rearrange to more stable structures, their further fragmentation depends on the structure drawn. Rosenthal[32] has suggested the pyronium ion structure for the ion $^{m}/_{e}$ 81, but it is felt that the furanoid ion suggested in Appendix 1 is more plausible. This ion may well rearrange to the pyronium ion, which is possibly more stable. There appears to be

no way of fitting pyronium ion structures for fragments $^{m}/_{e}$ 201,141,99, 81 and 69 to the remainder of the fragmentation pathway.

Chart 2.3.1.2. gives the structures of the ion radicals $^{m}/_{e}$ 242,200,140 and 98 suggested by Biemann *et al*[29,30] for penta-*O*-acetyl-β-D-glucopyranose* (Table 2.2.1.1.2.), where they constitute one of the major fragmentation pathways. It must be noted that the relative intensity of the $^{m}/_{e}$ 98 ion is distinctly greater in the case of tetra-*O*-acetyl-*N*-*p*-nitrophenyl-hexopyranosylamine derivatives than in other hexopyranosylamine derivatives. The ions $^{m}/_{e}$ 242,200 and 140 have similar, but low, intensities in all of the hexopyranosylamine derivatives studied.

Chart 2.3.1.3. shows the structures that have been suggested[29,31] for the M''($^{m}/_{e}$ 145) and M''-42($^{m}/_{e}$ 103) ions, which are found in the mass spectra of all acetylated sugar derivatives, while Chart 2.3.1.4. suggests an alternative source of M''. This fragmentation involves a retro-Diels-Alder(RDA) fission of the M' ion. It is pertinent to note that the relative intensity of M'' is less for acetylated pentopyranosylamine derivatives than for acetylated hexopyranosylamine derivatives.

2.3.2. Acetylated L-Rhamnopyranosylamine Derivatives.

Consideration of the ion peaks presented in Table 2.2.2.1.2. in the light of possible fragmentations that the compound can undergo, of metastable peaks found in the various spectra, and of the charts devised for the fragmentation of acetylated hexopyranosylamine derivatives, leads to the fragmentations suggested below.

*An alternate fragmentation pathway, suggested by Heyns and Muller[31], giving rise to the fragments $^{m}/_{e}$ 242,200,140 and 98 cannot operate here. This, together with the fact that the nitrogen atom has a greater ability to hold a positive charge than has the ring oxygen, explains the observed difference in intensity.

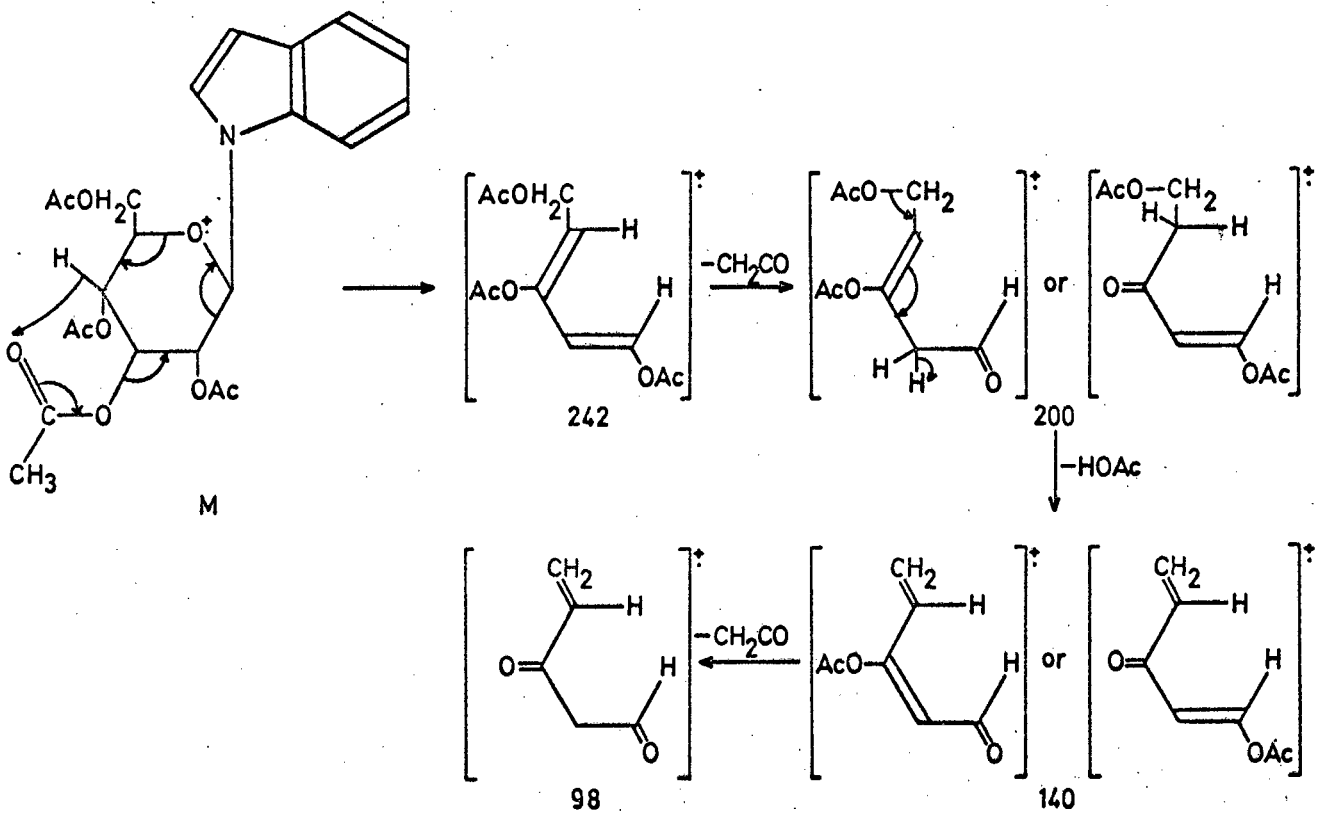


Chart 2.3.1.2

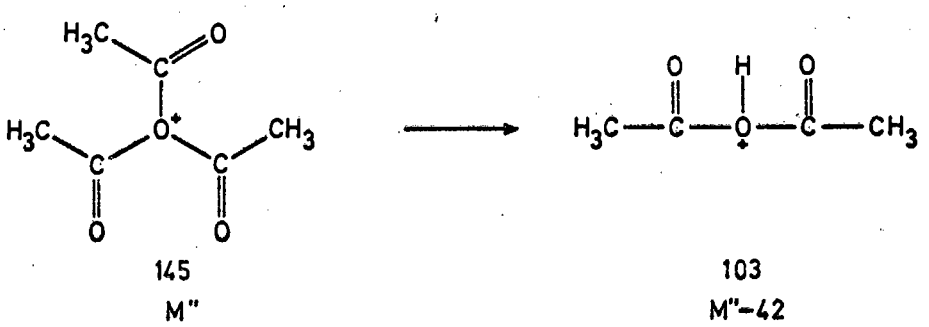


Chart 2.3.1.3

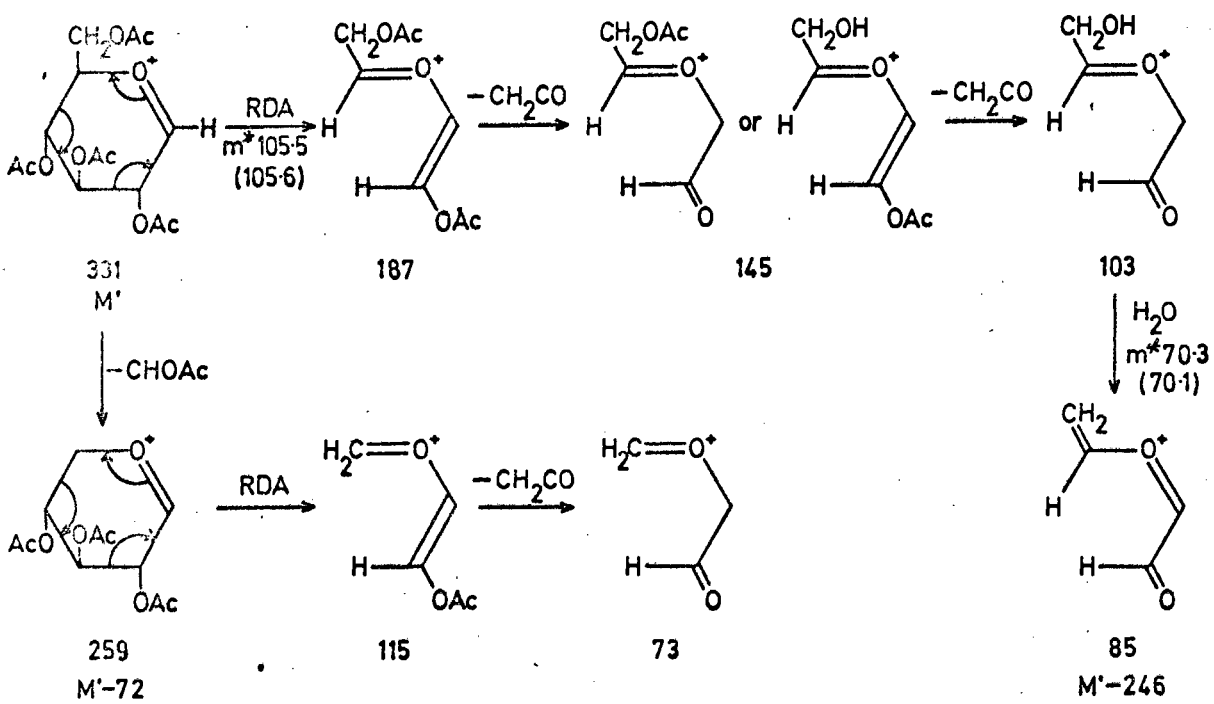


Chart 2.3.1.4

Chart 2.3.2.1., which accounts for most of the major ions due to fragmentation of the sugar moiety, shows a possible fragmentation pathway for the sugar moiety of 1-(2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl)indole(XIX). An elaboration of this chart is given in Appendix 2. Chart 2.3.2.2. shows several ions which cannot be fitted into the schemes suggested.

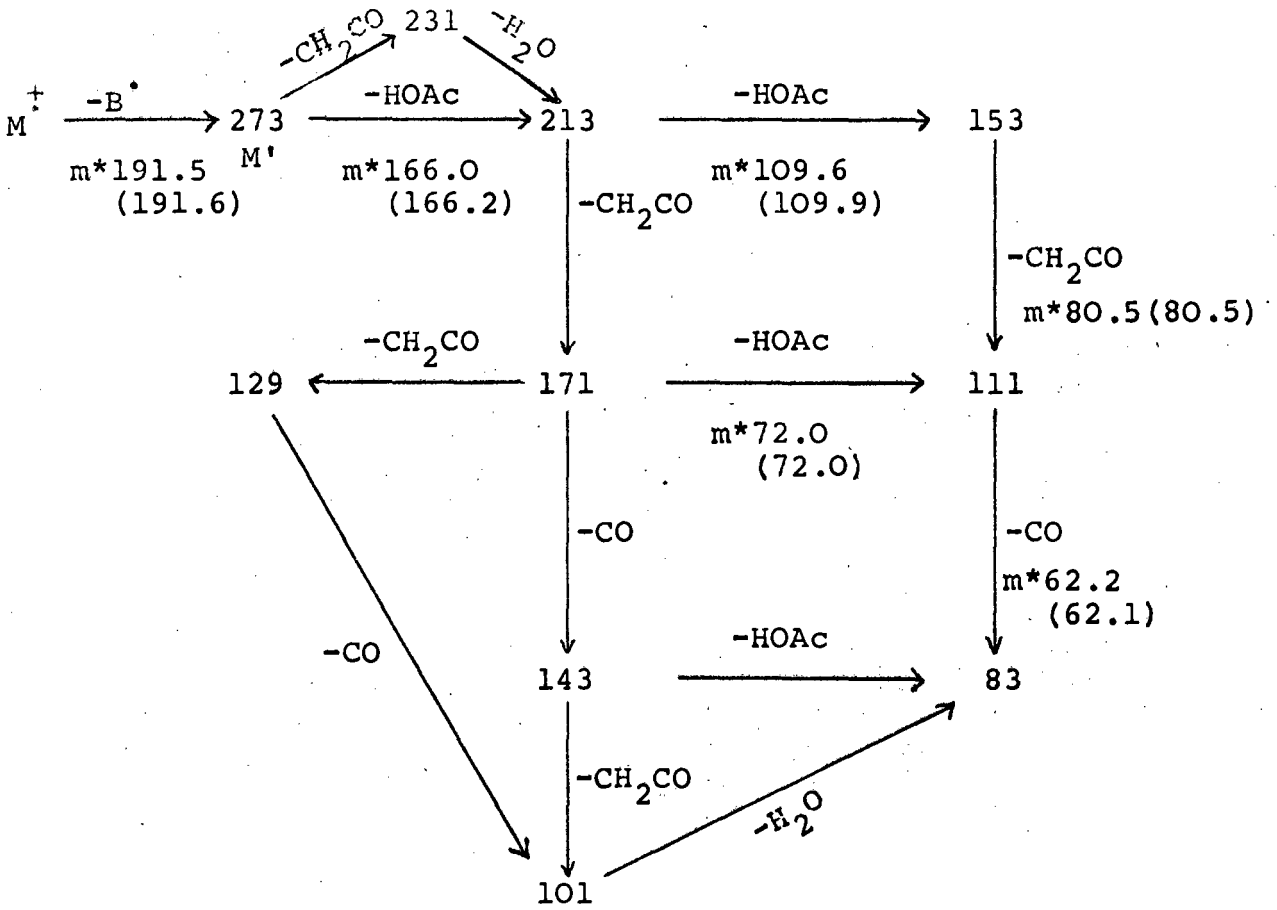


Chart 2.3.2.1. (See Appendix 2).

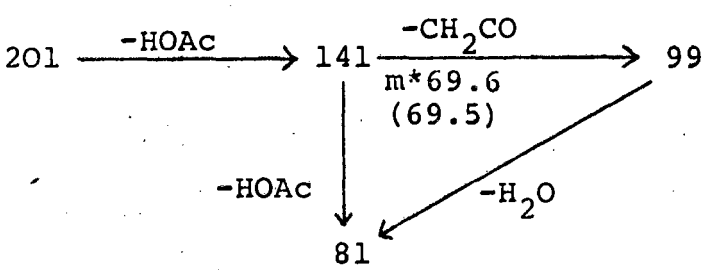


Chart 2.3.2.2.

Charts 2.3.2.3. (Appendix 3) and 2.3.2.4. (Appendix 4) show fragmentations corresponding to those given in Charts 2.3.1.2. and 2.3.1.4. respectively.

$$M^{+\cdot} \longrightarrow 184 \xrightarrow[m^{*}109.6\ (109.6)]{-CH_2CO} 142 \xrightarrow{-CH_2CO} 100$$

Chart 2.3.2.3. (See Appendix 3).

$$M' \xrightarrow{RDA} 129 \xrightarrow{-CH_2CO} 87$$

Chart 2.3.2.4. (See Appendix 4).

2.3.3. Acetylated Pentopyranosylamine Derivatives.

Possible pathways for the fragmentation of these compounds (Tables 2.2.3.1.2., 2.2.3.2.2., 2.2.3.3.2., and 2.2.3.4.2.) have been devised by consideration of the possible modes of fragmentation, by a study of the metastable peaks and by comparison with the fragmentation pathways suggested in 2.3.1.

Chart 2.3.3.1. (Appendix 5) gives a possible fragmentation pathway for the sugar moiety of 1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)indole(XX). This scheme accounts for most of the more prominent ions due to the sugar moiety, although several fragments cannot be connected to this scheme: M'-72($^{m}/_{e}$ 187), M'-87($^{m}/_{e}$ 172), M'-88($^{m}/_{e}$ 171), M'-132($^{m}/_{e}$ 127), M'-174($^{m}/_{e}$ 85), M'-191($^{m}/_{e}$ 68), M'-192($^{m}/_{e}$ 67) and M'-204($^{m}/_{e}$ 55). Chart 2.3.3.2. explains how most of these ions can arise from M'-72, but how this ion can be derived cannot be readily seen.

The fragmentations suggested in Charts 2.3.3.3. (Appendix 6) and 2.3.3.4. (Appendix 7) correspond to those suggested in Charts 2.3.1.2. and 2.3.1.4. respectively.

$$M^{+\cdot} \longrightarrow 170 \xrightarrow{-CH_2CO} 128 \xrightarrow{-CH_2CO} 86$$

Chart 2.3.3.3. (See Appendix 6)

$$M' \xrightarrow{RDA} 115 \xrightarrow{-CH_2CO} 73$$

Chart 2.3.3.4. (See Appendix 7).

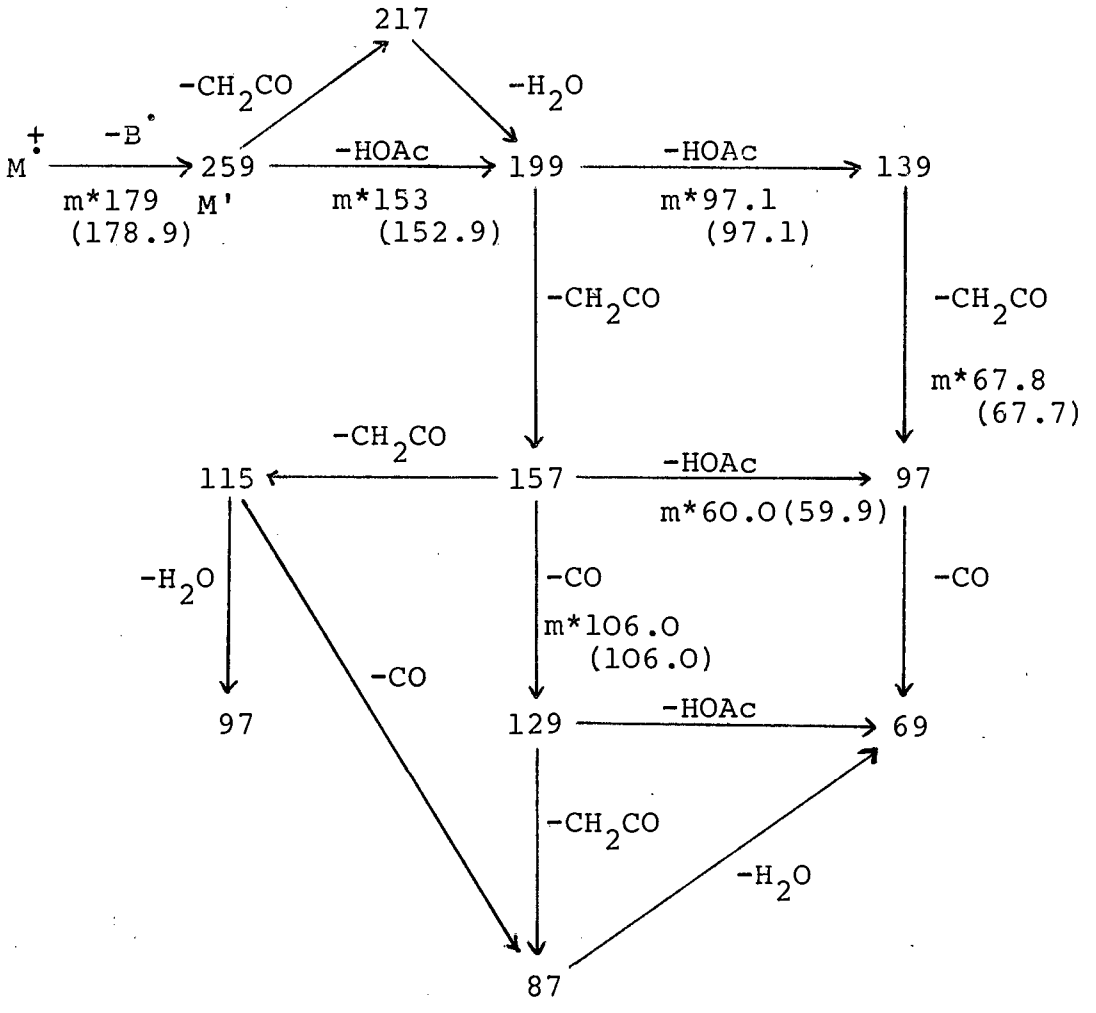


Chart 2.3.3.1. (See Appendix 5).

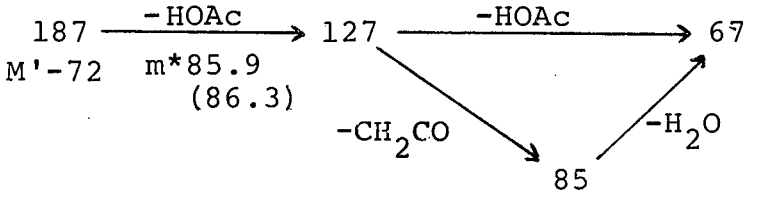


Chart 2.3.3.2.

2.3.4. Acetylated Glycopyranosylamine Derivatives.

From Tables 2.2.4.1.1., through 2.2.4.6.1. possible fragmentation pathways have been constructed for ions containing a nitrogen atom.

One possible fragmentation pathway that takes account of several of the odd-electron species of the type B+x for compound XVI is suggested in Chart 2.3.4.1., and elaborated in Appendix 8. The fragmentation scheme involves the loss of a molecule of HOAc from the molecular ion, followed by a RDA fission of the resultant ion. Depending on the position from

which HOAc is lost, there are four possible RDA fragmentations. Most of the more intense nitrogen-containing ions in the spectrum are accounted for by this scheme.

The major exceptions are the even-electron ions at B+72 B+68, B+56, B+30, B+2 and B. A metastable scan for the B+1 ion in XVI lends credence to part of this scheme in that it shows that the precursor ions are at M, B+43 and B+29 only. Even-electron species similar to those in Chart 2.2.4.1. and Appendix 8 can be obtained from M+1 by similar fragmentations. This would account for the lesser intensity of most of these ions relative to those arising from M.

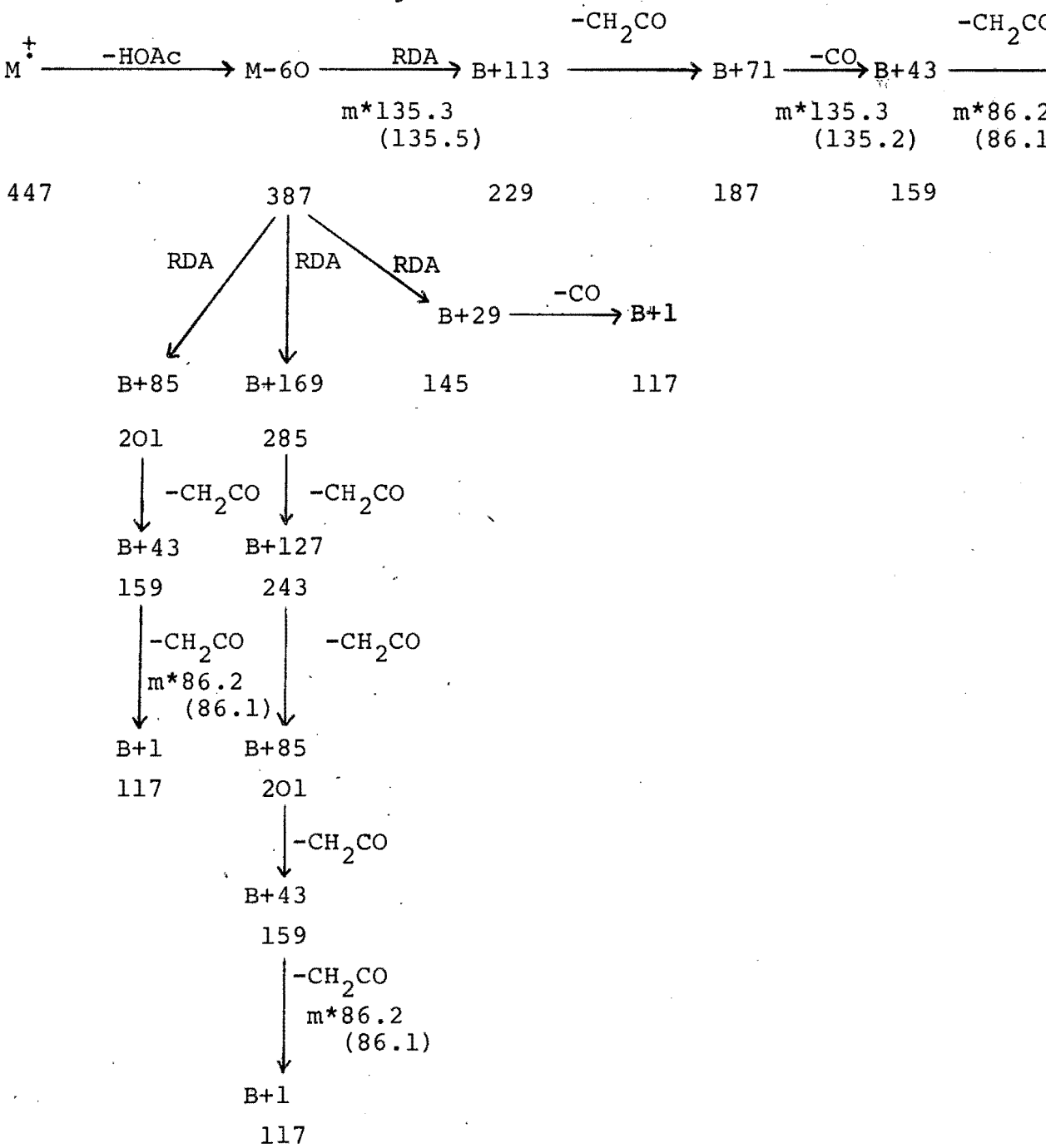


Chart 2.3.4.1. (See Appendix 8).

A possible source of the B+30 ion is suggested in Chart 2.3.4.2.[26] Homolytic fission of the C_1 - C_2 bond of the molecular ion, followed by a McLafferty rearrangement of the resultant radical-ion, leads directly to the B+30 ion, with the transfer of the hydrogen at C_4. The relative intensity of this ion is considerably greater for acetylated glycosylindolines than for the corresponding acetylated glycosylindoles. This can be explained by the use of the lone pair on nitrogen by the indole moiety to attain aromaticity; it is thus not readily available for forming the additional bond. In glycosylindoline derivatives these electrons are readily available, so that B+30 ions of high intensity are found.

Several ion peaks of fairly high intensity have not been accounted for in the schemes suggested. Chart 2.3.4.3. outlines fragmentations that an ion B+170 (which must contain C_5 of the sugar ring and its substituent) could undergo. Ions at B+170, B+128, B+110 and B+68 have intensities that are much greater for acetylated hexopyranosylamine derivatives than for the other compounds studied. This suggests that an acetoxymethyl group on C_5 is present in these fragments. The daughter ion at B+56 is of approximately equal intensity in all of the compounds studied, and thus must be unsubstituted at C_5.

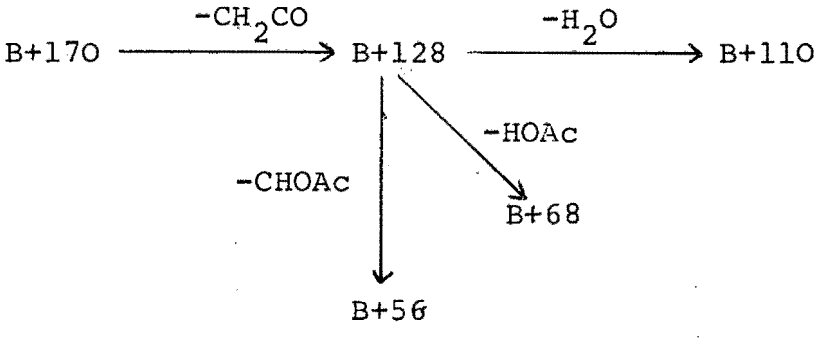


Chart 2.3.4.3.

Accurate mass measurements were obtained for the following ions of compound XVI: M($^m/e$ 447, $C_{22}H_{25}NO_9$), M-73($^m/e$

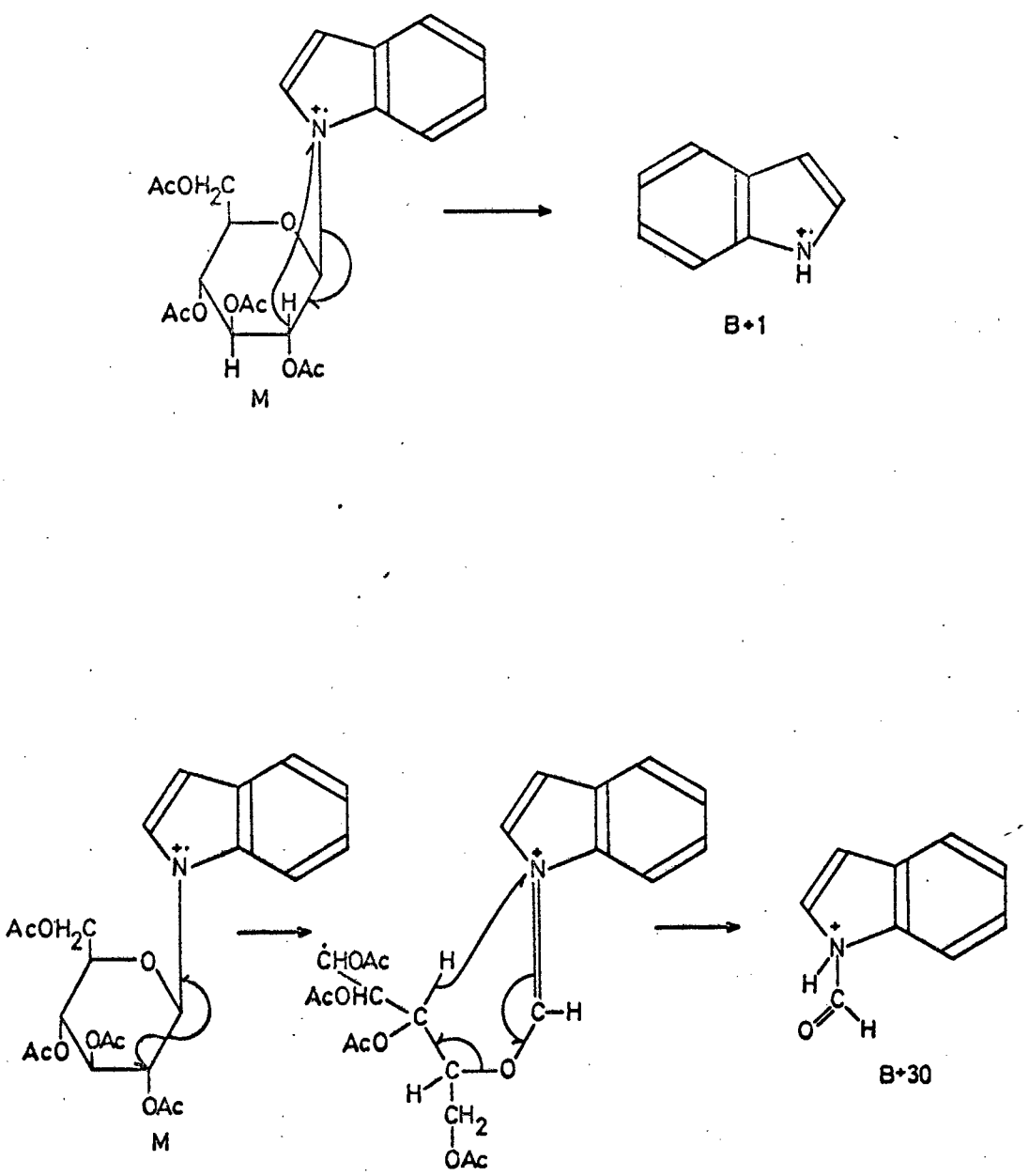


Chart 2.3.4.2

374, $C_{19}H_{20}NO_7$), B+85($^m/e$ 201, $C_{12}H_{11}NO_2$), B+72($^m/e$ 188, $C_{11}H_{10}NO_2$), B+68($^m/e$ 184, $C_{12}H_{10}NO$), B+43($^m/e$ 159, $C_{10}H_9NO$), B+30($^m/e$ 146, C_9H_8NO), B+1($^m/e$ 117, C_8H_7N) and $^m/e$ 91 (C_7H_7).

Table 2.3.1. shows the relative intensities of some of the major nitrogen-containing ions in the acetylated glycopyranosylamine derivatives studied. Table 2.3.2. shows the ratio of the more intense ions in the spectra relative to neighbouring ions.

From these tables it can be seen that, in general, the B+30, M, B+43 and B+85 ions are of greater intensity for glycosylindoline derivatives than the corresponding glycosylindole derivatives, whereas the reverse is true for the B+84 and B+2 ions. The ratios $^M/M'$ and $^{B+85}/B+84$ for each acetylated glycosylindole derivative is considerably larger than those for each acetylated glycosylindoline derivative. The reverse is true for the ratios $^{B+1}/B$ and $^{B+2}/B$, while the ratio $^{B+2}/B+1$ is fairly constant for indole and indoline derivatives. For acetylated *N*-*p*-nitrophenylglycosylamines, the ratios $^{B+2}/B+1$ and $^{B+2}/B$ are considerably larger than for acetylated glycosylindole and glycosylindoline derivatives. The author is unable to explain these differences.

The differences noted above may be of considerable importance in determining the degree of unsaturation of an unknown aglycone. If, in particular, the B+30 peak in the mass spectrum of an acetylated nucleoside derivative is of low intensity, the lone pair of electrons on the nitrogen atom is probably involved in an aromatic system, whereas if this peak is of high intensity, the aglycone is probably not aromatic.

Compound	M	B+170	B+169	B+128	B+110	B+86	B+85	B+84	B+72	B+68	B+56	B+44	B+43	B+30	B+29	B+2	B+1	B
I	42	2	3	1	8	3	20	11	9	9	10	7	38	27	4	18	9	2
II	64	2	2	<1	6	3	16	10	16	10	10	6	34	36	5	14	6	2
III	30	2	3	1	8	5	25	13	12	16	16	8	45	28	2	18	14	1
IV	100	2	2	1	4	8	38	12	15	15	13	9	65	39	4	2	3	<1
V	44	<<1	<1	<1	<1	2	14	4	11	7	7	4	37	44	5	32	5	3
VI	52	<<1	<1	<<1	1	4	24	9	34	11	14	9	63	100	12	9	2	<1
VII	26	<<1	<<1	<1	<1	5	13	5	9	7	7	21	48	50	7	36	5	3
VIII	96	5	1	1	3	7	24	6	9	8	7	6	29	100	29	8	42	24
IX	74	3	<1	<1	2	5	21	6	14	4	10	5	29	100	27	8	41	33
X	100	4	1	<1	2	5	23	7	9	4	8	6	31	69	19	5	25	14
XI	100	5	<<1	<1	1	8	33	6	9	6	6	7	33	83	25	8	40	23
XII	91	2	<<1	<<1	<1	4	19	3	22	3	7	4	22	100	17	7	43	25
XIII	100	<<1	<<1	<<1	<<1	1	11	3	12	2	3	4	21	94	16	5	27	20
XIV	48	3	<<1	<1	<<1	3	11	2	18	3	3	10	60	100	19	10	85	73
XV	78	2	x	<<1	<<1	3	15	3	15	2	3	4	20	100	14	5	32	18
XVI	44	<1	<<1	<1	3	3	3	7	3	1	6	4	12	7	14	12	44	6
XVII	69	<1	<<1	<1	2	1	3	5	3	3	5	4	12	13	19	14	60	7
XIX	100	<1	<<1	1	3	5	8	13	5	4	16	5	23	24	33	20	69	9
XX	38	<<1	<<1	<<1	<<1	1	2	5	3	2	4	2	7	8	8	10	52	5
XXI	71	<<1	<<1	<<1	<<1	1	2	6	4	2	8	3	14	14	15	18	83	11
XXII	30	<<1	<<1	<1	<<1	<<1	1	3	4	2	3	3	8	15	12	14	67	8
XXIII	100	<<1	<<1	<<1	<<1	1	2	2	4	1	4	2	10	19	10	10	63	5
XXIV	21	2	4	1	1	2	9	3	3	2	6	4	26	52	11	3	11	3
XXV	57	3	9	1	2	3	13	7	8	3	9	6	33	90	18	5	17	10
XXVI	44	3	6	1	2	3	13	6	4	3	8	6	36	77	17	3	8	3
XXVII	33	2	<<1	2	55	6	25	6	4	4	7	10	69	100	21	7	36	8
XXVIII	13	<1	1	<1	<1	1	6	2	5	2	3	3	16	36	9	2	4	25
XXIX	42	<1	<<1	<1	<<1	2	7	4	11	2	7	9	51	84	13	7	49	7
XXX	22	30	<<1	1	8	3	2	7	4	7	6	3	10	3	5	3	8	2
XXXI	48	<1	<<1	<<1	<1	2	2	4	1	2	4	2	10	8	6	4	8	1
XXXII	85	2	4	11	<1	4	17	5	6	3	9	4	22	100	28	7	20	8
XXXIII	66	<1	1	2	1	2	4	5	1	2	9	6	14	10	16	14	56	30
XXXIV	71	2	1	<1	5	4	18	5	11	6	7	5	27	100	26	7	39	17
XXXV	48	1	<<1	<1	<<1	2	8	1	12	2	2	3	15	100	14	4	17	10
XXXVI	100	3	2	2	7	10	18	17	8	15	15	14	35	80	24	31	63	10

Table 2.3.1. Relative Intensities of Major Nitrogen-containing Ions of Acetylated Glycopyranosylamine Derivatives.

Compound	M/M'	$\frac{B+85}{B+84}$	$\frac{B+30}{B+29}$	$\frac{B+2}{B+1}$	$\frac{B+1}{B}$	$\frac{B+2}{B}$	Compound	M/M'	$\frac{B+85}{B+84}$	$\frac{B+30}{B+29}$	$\frac{B+2}{B+1}$	$\frac{B+1}{B}$	$\frac{B+2}{B}$
Glu-IH_2	13.7	4.0	3.5	0.2	1.7	0.3	Man-5-NO_2IH_2	1.1	2.2	4.5	0.4	2.7	1.0
Glu-I	1.5	0.4	0.5	0.3	7.3	2.0	Rha-5-NO_2IH_2	0.6	4.2	4.8	0.2	4.5	0.9
Gal-IH_2	3.7	3.4	3.7	0.2	1.3	0.2	Rha-5-NO_2I	0.9	0.5	1.3	0.5	8.0	4.0
Gal-I	0.7	0.6	0.7	0.2	8.6	2.0	Xyl-5-NO_2IH_2	0.6	3.0	4.0	0.5	0.2	0.1
Man-IH_2	7.2	3.3	3.6	0.2	1.8	0.4	Arab-5-NO_2IH_2	0.7	1.8	6.5	0.1	7.0	1.0
Rha-IH_2	6.7	5.5	3.3	0.2	1.7	0.3	Glu-2-MeIH_2	12.1	3.4	3.6	0.4	2.5	0.9
Rha-I	3.2	0.6	0.7	0.3	7.7	2.2	Glu-2-MeI	3.8	0.8	0.6	0.3	1.9	0.4
Xyl-IH_2	9.1	6.3	5.9	0.2	1.7	0.3	Glu-THQ	8.3	3.6	3.8	0.2	2.3	0.4
Xyl-I	1.7	0.4	1.0	0.2	10.4	2.0	Xyl-THQ	12.0	8.0	7.1	0.2	1.7	0.4
Lyx-IH_2	20.0	3.7	5.9	0.2	1.4	0.3	Glu-6-NH_2Q	7.9	1.1	3.3	0.5	6.3	3.1
Lyx-I	3.1	0.3	0.9	0.2	7.5	1.6	Glu-*p*-NO_2Ph	1.2	1.8	6.8	2.0	4.5	9.0
Arab-IH_2	4.4	5.5	5.3	0.1	1.2	0.1	Gal-*p*-NO_2Ph	1.4	1.6	7.2	2.3	3.0	7.0
Arab-I	0.9	0.3	1.3	0.2	8.4	1.7	Man-*p*-NO_2Ph	0.8	1.9	14.0	1.3	14.0	18.0
Rib-IH_2	5.2	5.0	7.2	0.2	1.8	0.3	Rha-*p*-NO_2Ph	1.4	3.2	9.8	0.7		
Rib-I	1.6	1.0	1.9	0.2	12.6	2.0	Xyl-*p*-NO_2Ph	1.8	3.5	8.8	6.4	1.7	10.1
Glu-5-NO_2IH_2	1.1	3.0	4.7	0.3	3.7	1.0	Lyx-*p*-NO_2Ph	1.5	2.7	7.1	7.2	1.7	12.0
Glu-5-NO_2I	0.7	0.3	0.6	0.4	4.0	1.5	Arab-*p*-NO_2Ph	0.7	2.7	8.3	4.5		
Gal-5-NO_2IH_2	1.1	1.9	5.0	0.3	1.7	0.5							

IH_2	indoline	2-MeIH_2	2-methylindoline
I	indole	2-MeI	2-methylindole
5-NO_2IH_2	5-Nitroindoline	THQ	1,2,3,4-tetrahydroquinoline
5-NO_2I	5-Nitroindole	*p*-NO_2Ph	*p*-nitroaniline
		6-NH_2Q	6-aminoquincline

Table 2.3.2. Ion-peak Intensity Ratios for Acetylated Glycopyranosylamine Derivatives.

SECTION 3.

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPIC STUDIES ON SUBSTITUTED ACETYLATED GLYCOPYRANOSYLAMINES.

3.1. INTRODUCTION.

Before the advent of NMR spectroscopy, the determination of the anomeric configuration of molecules containing a sugar moiety was based on Hudson's rules of isorotation[36], and on reactions giving compounds of known configuration. Configurational assignments on the basis of optical rotations becomes more difficult when only one anomer is available, and it has been noted that a reversal of the normal rotatory relationships between anomers occurs with certain substituent groups on C_2 of the sugar ring[37]. In general, purine nucleosides do, and pyrimidine nucleosides do not obey Hudson's rules of isorotation[38,39]. Both the anomeric configuration and the conformation of sugar-containing molecules in solution can be determined by NMR. This is of particular importance in dealing with biological systems, such as nucleosides, where steric considerations are of such great importance.

Even the use of this more rigorous spectroscopic method does not always give rise to unambiguous results. The reasons for this are twofold: 1) the interacting protons in carbohydrate molecules are located in similar electron-density environments[40] and 2) rapid interconversion of conformers can take place in solution, giving rise to a weighted mean of the coupling constants of the interconverting forms[41]. The first factor can be overcome by operating the spectrometer at higher magnetic field, or by converting the carbohydrate to a derivative, so that the desired resonance peaks are shifted away from the complex region. One method of achieving the latter object is to link the anomeric carbon atom to some atom more electronegative than carbon. This forces downfield the signal due to the anomeric proton, and an estimate of the splittings of the anomeric proton can be made. The interconversion of the two energetically non-equivalent chairlike conformations occurs to a far greater extent than their interconversion to the energetically unfavourable boat forms, but one conformer usually

predominates; the time-averaged spectrum that is observed corresponds more closely to that expected for the more predominant conformer. Running the spectrum at a lower temperature redùces the rate at which interconversion occurs; under these conditions the conformations and the percentage of each can be determined from the two superimposed spectra.

In one of the earliest papers on the NMR spectra of carbohydrate derivatives, Lemieux *et al*[42] concluded that an equatorially orientated proton comes into resonance at a lower field than that of a chemically similar but axially orientated proton, and that, as a rule, the same holds for acetoxy groups. They also noted that the splitting between protons on adjacent carbon atoms is two to three times greater (*ca.* 9 Hz) when their projected bond angle (dihedral angle) is *ca.* 180° (*trans*-diaxial or *anti*-periplanar) than when the angle is *ca.*60° (*gauche* or *syn*-clinal). This angular dependence of the coupling constant was rationalised by Karplus[43], by means of equation (1):

$$J = J_o \mathrm{Cos}^2\phi + K \quad \mathrm{Hz} \qquad (1).$$

where J is the coupling constant between protons on adjacent carbons which are separated by a projected valency angle of ϕ. J_o and K are parameters whose values were evaluated as K= -0.28 and J_o = 8.5 for $0^o \leqslant \phi \leqslant 90^o$ and J_o = 9.5 for $90^o \leqslant \phi \leqslant 180^o$. Equation (1) was modified by the introduction of a scaling factor F (equation (2))[44] for which the value F=1.09 ± 0.05 was assigned, and again by Karplus[45] to give equation (3).

$$J = F(J_o \mathrm{Cos}^2\phi + K) \quad \mathrm{Hz} \qquad (2).$$

$$J = A + B\mathrm{Cos}\phi + C\mathrm{Cos}2\phi \quad \mathrm{Hz} \qquad (3).$$

For a C-C bond length of 1.543Å, sp^3 hybridization and an average energy equal to 9eV, the constants are A = 4.22, B = -0.5 and C = 4.5 Hz. In this paper[45] Karplus warned of the risk of attempting to calculate dihedral angles accurately. He suggests that these equations should be used as rough guides

only.

Application of these equations to the pyranose sugar rings leads to the finding that, whereas *trans*-diaxial protons are split to the extent of *ca.* 9 Hz, equatorial-axial proton interaction leads to splittings of *ca.* 3.5 Hz, and equatorial-equatorial proton interaction to splittings of *ca.* 1 Hz. Thus from the splittings of ring-protons an estimate of the conformation of particular sugars can be made.

The explicit analysis of a spectrum due to interacting protons usually requires sophisticated mathematics, relying on computerisation. The simplest approach, and one that is most commonly used among organic chemists, is the first-order analysis, where splittings and chemical shifts are measured directly from the spectrum. It is only reasonable to use the first-order approximation in cases where $J/\Delta\nu$ is small (say <0.1) for all protons involved in the spin system. The use of this approximation outside these limits may lead to values of coupling constants and chemical shifts which are seriously in error. In some cases a second-order spectrum may show more lines than the corresponding first-order spectrum, and in most cases the spacing between the lines does not correspond to the coupling constant, nor do the chemical shift and the centre of a multiplet correspond.

Long-range coupling (over more than four σ bonds) is seldom significant in the spectra of carbohydrates, and has been ignored.

Although it was claimed that equatorial groups come into resonance at higher field than axial groups in a similar chemical environment[42,47], recent work has shown that a number of exceptions exist, particularly for acetoxy-substituents in 3-amino-3-deoxy nucleosides[48]. This casts doubt upon configurational assignments made on the basis of chemical shift data. It is certainly better to base conformational assignments

on splittings rather than chemical shifts. A number of workers[48-54] have used coupling constants to obtain both the configuration and conformation of pyranose rings. If the splittings of the anomeric proton and of one other proton in this ring are known, both the configuration and the conformation can be fixed, in most cases unequivocally. The use of splittings to define stereochemistry in furanose sugar derivatives is far more uncertain, and has been the subject of much research, particularly with D-ribofuranose and 2-deoxy-D-ribofuranose derivatives[54,55].

Unsaturation in an organic molecule can result in a shift of the resonances of protons several bonds away from the unsaturation. This effect, caused by the diamagnetic anisotropy of the double bond, is dependent on the actual position of the proton in space with respect to the double bond. It has been found that the anistropic effect is maximal at the symmetry axes of hypothetical truncated cones drawn through the double bond perpendicular to the plane of the double bond (Fig. 3.1.), and decreases by the reciprocal of the third power of the distance between any axis and the group in question[48,56]. Any proton falling in the region of positive shielding will be shifted to higher field. Any proton falling in the region of negative shielding will be shifted to lower field. The region of negative shielding is that area outside the truncated cones. It is maximal in the plane of the double bond, and decreases by the reciprocal of the third power of the distance, as in the case of positive shielding.

Thus in nucleosides where there is restricted rotation about the glycosidic bond[48,57-60], the aglycone will adopt a substantial population of a preferred conformation, and anisotropic shifts will occur. The anisotropic shifts of acetoxy resonances of several acetylated nucleoside derivatives have been studied[48], and the suggestion was made that this property might be used for the determination of the anomeric configuration

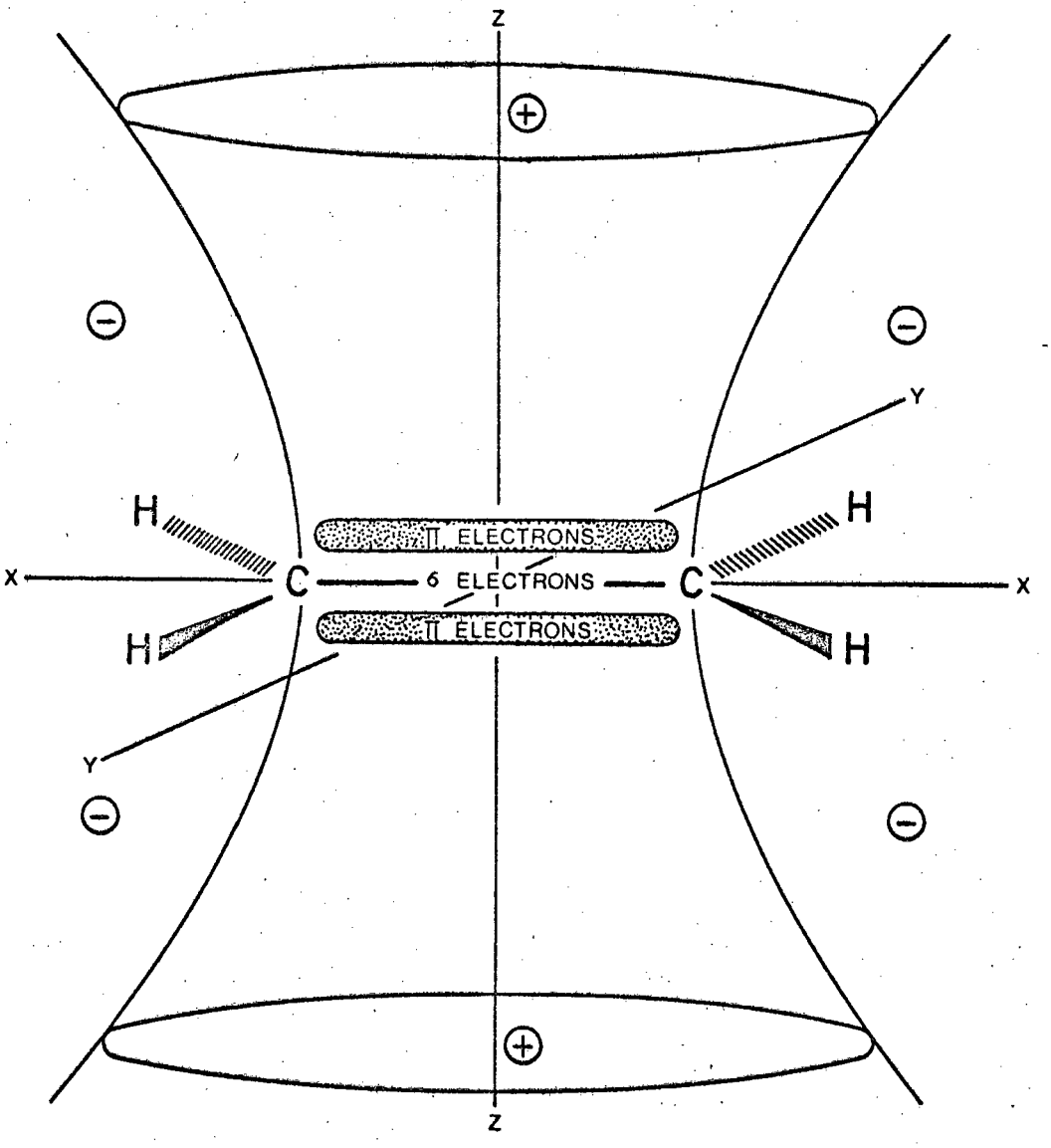
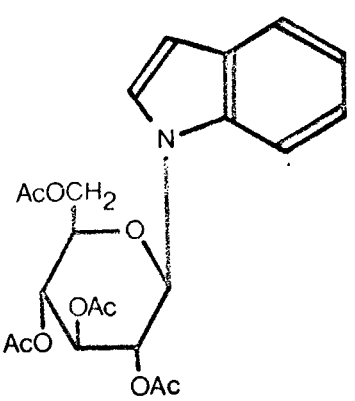


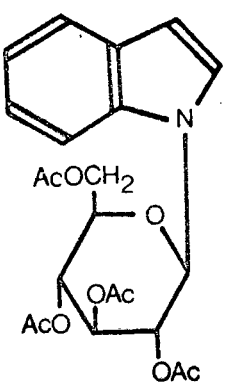
Fig. 3.1. The Long Range Shielding Effect of the Carbon-Carbon Double Bond. Protons situated near the z-axis of the cones are more strongly shielded (+) than protons away from the axis. Protons near the plane of the C=C bond(xyplane) are more strongly deshielded (-) than protons farther removed from the plane.

of nucleosides. This work has recently been extended to acetylated indole nucleosides, where similar restricted rotation takes place.

Donohue and Trueblood[58] defined the torsion angle ϕ by referring to rotation about the glycosidic bond between C_1 of ribose and N_9 of a purine, or N_1 of a pyrimidine (Fig.3.2.). The same definition applies to pyranosyl nucleoside derivatives, and ϕ is defined as the dihedral angle between the plane of the nitrogen-containing base and the plane formed by the C_1-O bond of the pyranose ring and the C_1-N bond. The molecule is viewed along the C_1-N bond, and ϕ is zero when O lies directly in front of C_2 of the base. Positive angles are measured when C_1-O is rotated in a clockwise direction when viewing from C_1 to N. Haschemeyer and Rich[59] calculated the distances of closest approach of various groups by considering the van der Waal's radii on altering ϕ by increments of 10°. They found that there are two preferred configurations of the aglycone, and that these occur at $\phi = -35 \pm 30^{\circ}$ (*anti*-form) and at $\phi = +138^{\circ}$ (*syn*-form; only one example was found[59]). Cushley *et al*[61] found that indole nucleosides exist in the *anti*-form.



XVI (*anti*-form)



XVI (*syn*-form)

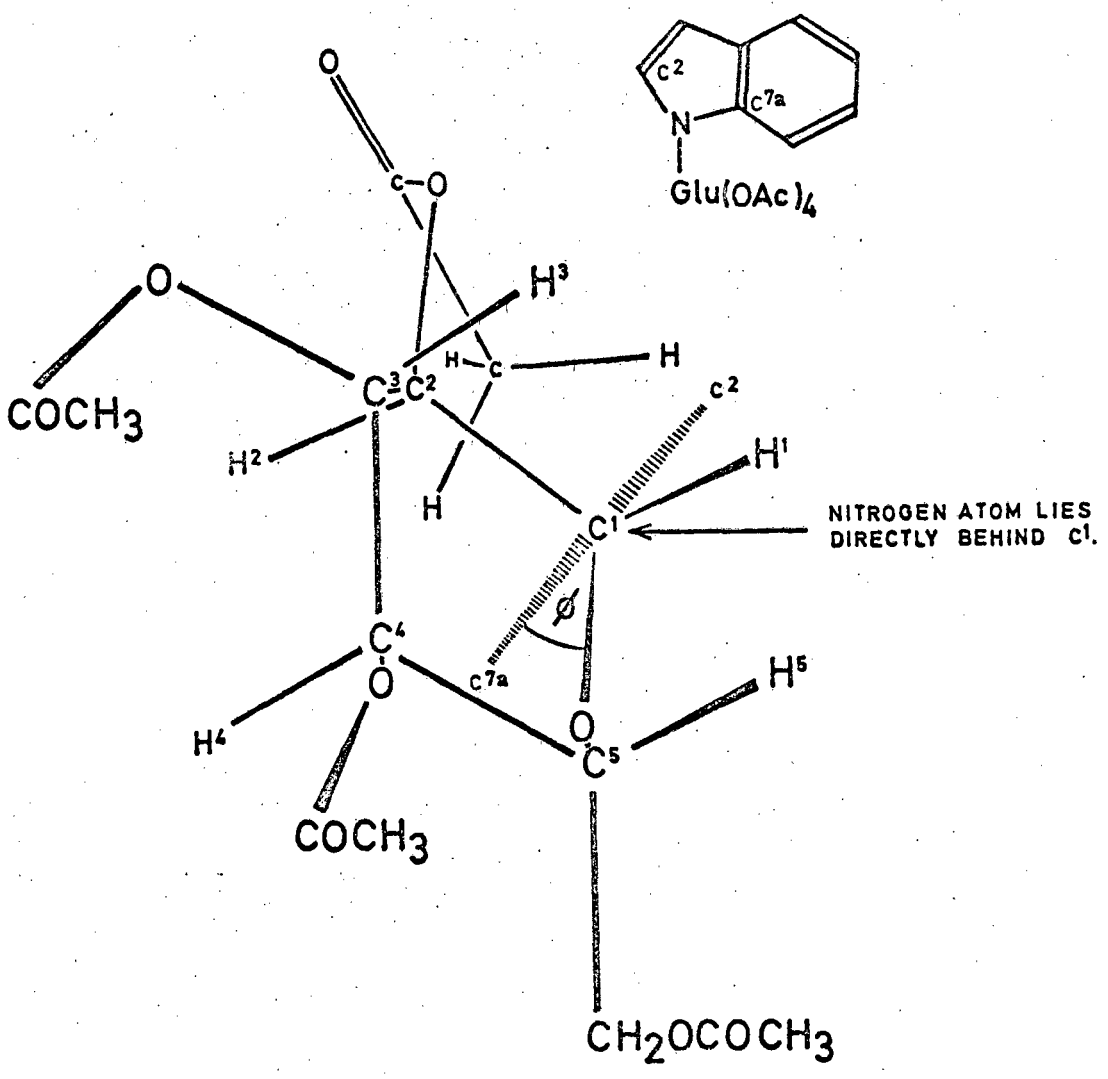


Fig. 3.2. Schematic Illustration of the Torsion Angle (ϕ) in 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-gluco-pyranosyl)indole(XVI). The nitrogen atom lies directly behind the anomeric carbon atom. ϕ has the value *ca.*-30° in this illustration.

If, then, the anisotropic effects of the aglycone in a series of acetylated indole nucleosides could be studied by removal of the anisotropy, the shifts of the various acetoxy proton signals could be determined. For a particular configuration of the aglycone, the anisotropic shifts of the acetoxy signals could be predicted for each conformation and anomeric configuration. From the experimentally found shifts it should be possible to determine both the anomeric configuration and the conformation. A problem that arises in these studies is the uncertainty in the specification of the various acetoxy groups.

In addition to the shift of the sugar-ring protons due to the anisotropic effect, the chemical shifts of these protons, and that of the anomeric proton in particular, will depend on the inductive effect of the aglycone. Evidence of the importance of this effect should readily be obtained by a consideration of the differences in chemical shift of the anomeric proton when the aglycone is altered.

3.2. RESULTS.

The NMR parameters obtained by first-order analyses of the 100 MHz spectra of acetylated D-glucopyranosyl, D-galactopyranosyl, D-mannopyranosyl, L-rhamnopyranosyl, D-xylopyranosyl, D-lyxopyranosyl, L-arabinopyranosyl and D-ribopyranosyl derivatives are shown in Tables 3.2.1.1. through 3.2.1.8. respectively. The first-order parameters obtained for acetylated glycopyranosyl derivatives of *p*-nitroaniline, indoline, indole, 5-nitroindoline, 5-nitroindole and 1,2,3,4-tetrahydroquinoline are shown in Tables 3.2.2.1. through 3.2.2.6. Spectra which did not show complete first-order characteristics are marked †.

The parameters were obtained by direct measurement of the single-scan spectrum. The spectra of I, VIII, XVI

Compound *	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	τ_{acetyl}				τ_{N-H}	$\tau_{aromatic}$	$\tau_{indolic}$	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{aromatic}$ J_{N-1}	J_{46}	J_{67}	$J_{indolic}$ J_{23}
I	$CDCl_3$	5.14	4.94	4.60	4.93	6.10	5.69	5.91	7.94	7.94	7.94	7.94	4.36	H_3, H_5 H_2, H_6 1.90(m) 3.34(m)		8.9	9.0	9.1	9.7	5.6	2.3	-12.3	7.6			
VIII	C_6H_6	5.13	4.52	4.63	4.80	6.62	5.76	6.14	8.33	8.33	8.24	8.22		obscured by solvent	obscured by solvent	9.0	9.6	9.0	9.8	5.2	2.2	-12.3				
† VIII	$CDCl_3$	4.6 - 5.1(m)				6.25	5.75	5.96	8.05	8.03	8.00	7.99		H_4 3.46 H_6 3.29 H_5 2.95 H_7 2.92	H_2, $H_{2'}$ H_3, $H_{3'}$ ~6.39(m) ~7.05(m)				9.7	4.3	2.8	-12.3				
† XVI	C_6H_6	4.4 - 4.8(m)				6.52	5.77	6.06	8.62	8.33	8.28	8.27		obscured by solvent	obscured by solvent				9.7	5.0	2.5	-12.4				
† XVI	$CDCl_3$	4.3 - 4.8(m)				6.02	5.71	5.86	8.36	8.00	7.96	7.95		2.37-2.96(m)	H_2 2.82 H_3 3.46				9.6	5.2	2.2	-12.2				3.5
† XXIV	$CDCl_3$	4.6 - 5.0(m)				6.12	5.74	5.89	8.06	7.98	7.98	7.96		H_4 H_6 H_7 2.06 1.92 3.46	H_2, $H_{2'}$ H_3, $H_{3'}$ ~6.20(m) ~6.94(m)				9.8	5.0	2.2	-12.4		2.0	9.4	
† XXX	$CDCl_3$	4.2 - 4.8(m)				~5.95	5.63	5.82	8.33	7.97	7.93	7.93		H_4 H_6 H_7 1.46 1.86 2.46	H_2 2.59 H_3 3.27					4.8	2.0	-12.2		2.0	9.4	3.6
XXXII	$CDCl_3$	5.06	4.52	4.61	4.88	6.24	5.77	5.88	8.16	8.00	8.00	7.98		2.88-3.53(m)	H_2 ~6.0 H_3 ~6.85 $H_{3'}$ ~7.52	8.9	8.0	8.5	9.7	4.6	2.4	-11.8				
† XXXIII	$CDCl_3$	4.2 - 4.8 (m)				6.09	5.70	5.83	8.39	8.03	7.98	7.97		2.50-3.06(m)	H_3 3.79				9.6	4.4	2.6	-12.2				
XXXIV	$CDCl_3$	4.94	4.86	~4.6	4.92	6.26	5.75	5.92	8.07	7.99	7.96	7.96		2.84-3.36(m)		9.0	9.5	9.7	9.8	4.8	2.8	-12.0				
XXXVI	$CDCl_3$	5.12	4.87	4.75	4.89	6.07	5.68	5.91	7.98	7.96	7.96	7.96	4.79	2.00-2.16(m), 2.66-3.16(m)		9.0	8.9	9.0	9.6	5.7	2.4	-12.2	8.8			

m multiplet

TABLE 3.2.1.1. Parameters Obtained from 100 MHz Spectra of Acetylated D-Glucopyranosylamine Derivatives .

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	$\tau_5, \tau_6, \tau_{6'}$	τ_{acetyl}				τ_{N-H}	$\tau_{aromatic}$		$\tau_{indolic}$		J_{12}	J_{23}	J_{34}	J_{45}	J_{N-1}	$J_{aromatic}$ J_{46}	J_{67}	$J_{indolic}$ J_{23}
† II	$CDCl_3$	5.15	4.6 - 4.9(m)			5.87	7.99	7.97	7.84	7.93	4.35	H_3, H_5 1.90(m)	H_2, H_6 3.32(m)			8.9				8.8			
† IX	$CDCl_3$	5.02	4.52	4.81	4.58	5.97	8.00	8.00	7.82	7.97		2.84 - 3.48(m)		$H_2, H_{2'}$ ~6.33(m)	$H_3, H_{3'}$ ~7.05(m)	9.0	10.2	3.5	3.9				
† XVII	$CDCl_3$	4.43	4.25	4.73	4.46	5.82	8.36	8.02	7.78	8.00		2.36 - 2.98(m)		H_2 2.75	H_3 3.46	8.6	9.9	3.4	3.6				3.6
† XXV	$CDCl_3$	4.97	4.52	4.81	4.53	5.89	8.06	8.00	7.93	8.00		H_4 2.08	H_6 1.96	H_7 3.44	$H_2, H_{2'}$ ~6.16(m)	$H_3, H_{3'}$ ~6.94(m)	8.8	10.0	3.4			2.2	8.8	

TABLE 3.2.1.2. Parameters Obtained from 100 MHz Spectra of Acetylated D-Galactopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	τ_{acetyl}				τ_{N-H}	$\tau_{aromatic}$		$\tau_{indolic}$		J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	J_{N-1}	$J_{aromatic}$ J_{46}	J_{67}
III	$CDCl_3$	4.95	4.46	4.85	4.78	6.15	5.67	5.89	7.73	8.00	7.95	7.95	4.66	H_3, H_5 1.89(m)	H_2, H_6 3.30(m)			~1	~3	10.0	9.2	6.0	2.6	-12.2	8.6		
† X*	$CDCl_3$	5.27	4.4 - 5.0(m)			~5.8			7.78	7.99	7.99	7.97		2.9-3.5(m)													
XXVI	$CDCl_3$	4.99	4.36	4.87	4.69	~6.15	5.72	5.86	7.86	8.03	7.97	7.97		H_4 2.10	H_6 1.99	H_7 3.44	$H_2, H_{2'}$ ~6.2(m)	$H_3, H_{3'}$ ~6.96(m)	~1	~3	10.0	9.2	5.8	3.2	-16.4		- 1.6	8.8

*60 MHz Spectrum

TABLE 3.2.1.3. Parameters Obtained from 100 MHz Spectra of Acetylated D-Mannopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_{Me}		τ_{acetyl}	τ_{N-H}	$\tau_{aromatic}$	$\tau_{indolic}$	J_{12}	J_{23}	J_{34}	J_{45}	J_{5-Me}	J_{N-1}	$J_{aromatic}$ J_{46}	J_{67}	$J_{indolic}$ J_{23}
†IV	$CDCl_3$	4.97	4.49	~4.9	~4.9	6.29	8.72	7.76	8.01	7.94	4.67	H_3, H_5 1.92(m)	H_2, H_6 3.31(m)	~1	~3		9.0	6.0	8.6		
†XI β	$CDCl_3$	5.27	4.45	4.67	4.86	5.90	8.73	7.82	8.02	7.97		2.80-3.47(m)	H_2, H_2' ~6.30(m)	H_3, H_3' ~6.97(m)	2.5	3.1	9.1	8.8	6.4			
†XI α	$CDCl_3$	5.10	4.37	~4.9	~4.9	6.27	8.75	7.85	8.02	7.98		2.80-3.47(m)	H_2, H_2' ~6.30(m)	H_3, H_3' ~6.97(m)	0.6	2.9		9.0	6.0			
†XIX	$CDCl_3$	4.21	4.46	~4.76	~4.76	6.24	8.67	8.03	8.01	7.93		2.35-3.00(m)	H_2 2.74	H_3 3.51	1.3	2.7		9.0	6.0			3.8
†XXVII	$CDCl_3$	4.93	4.64	~4.86	~4.86	6.28	8.68	7.84	8.00	7.92		H_4 2.12	H_6 1.98	H_7 3.42	H_2, H_2' ~6.16(m)	H_3, H_3' ~6.94(m)	1.2	~2.2	9.0	6.0		2.0	9.6	
†XXXI	$CDCl_3$	4.13	4.43	~4.54	~4.54	6.25	8.61	8.02	8.01	7.90		H_4 1.61	H_6 1.93	H_7 2.53	H_2 2.60	H_3 3.35	~1	~2	9.0	6.0		2.0	9.6	3.6

TABLE 3.2.1.4. Parameters Obtained from 100 MHz Spectra of Acetylated L-Rhamnopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ_{acetyl}			τ_{N-H}	$\tau_{aromatic}$		$\tau_{indolic}$		J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{N-1}	$J_{aromatic}$ J_{46}	J_{67}	$J_{indolic}$ J_{23}
												H_3, H_5	H_2, H_6												
V	$CDCl_3$	5.24	4.99	4.62	4.97	5.87	6.56	7.94	7.94	7.94	4.42	1.91(m)	3.32(m)			8.9	8.9	9.0	5.6	10.4-11.8		8.0			
														$H_2, H_{2'}$	$H_3, H_{3'}$										
XII	$CDCl_3$	5.08	4.65	4.78	5.00	5.92	6.66	8.02	7.97	7.96		2.84-3.50(m)		~6.42(m)	~7.05(m)	8.9	8.9	9.0	5.7	10.5-11.6					
														H_2	H_3										
† XX	$CDCl_3$	4.4-4.6(m)			~4.8	5.73	6.45	8.37	7.98	7.95		2.37-3.00(m)		2.80	3.47			~7	5.6	10.4-11.6					3.6
												H_4	H_6 H_7	$H_{2'}, H_{2'}$	$H_{3'}, H_{3'}$										
XXVIII	$CDCl_3$	5.02	4.62	4.78	4.98	5.87	6.56	8.08	7.97	7.97		2.10	1.99 3.47	~6.24(m)	~6.97(m)	9.0	9.0	8.8	5.5	10.5-11.4			2.2	8.8	
† XXXV	$CDCl_3$	4.6 - 5.1(m)				5.91	6.65	8.07	7.97	7.97		2.84 - 3.37(m)							5.6	10.5-11.4					

TABLE 3.2.1.5. Parameters Obtained from 100MHz Spectra of Acetylated D-Xylopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ acetyl			$\tau_{aromatic}$		$\tau_{indolic}$		J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	$J_{indolic}$ J_{23}
												$H_2, H_{2'}$	$H_3, H_{3'}$							
† XIII	$CDCl_3$	4.85	4.59	4.54	5.13	6.04	6.04	8.00	7.88	7.84	2.84-3.42(m)	~6.46(m)	~7.03(m)	9.0	3.4	2.0	2.0				
† XIII *	$CDCl_3$							8.00	7.86	7.82											
												H_2	H_3								
† XXI *	$CDCl_3$	4.2 - 4.6(m)			~5.1	~6.0	~6.0	8.34	7.87	7.87	~2.3-3.0(m)	~2.7	~3.6							~3.6	

*60 MHz Spectrum.

TABLE 3.2.1.6. Parameters Obtained from 100MHz Spectra of Acetylated D-Lyxopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ acetyl	τ_{N-H}	τ aromatic	τ indolic	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{N-1}	J_{46} aromatic	J_{67} aromatic	J_{23} indolic
										H_3, H_5 H_2, H_6										
†VI	$CDCl_3$	5.23	~4.7	~4.7	~4.62	5.94	6.19	7.95 7.94 7.85	4.81	1.93(m) 3.31(m)	$H_2, H_{2'}$ $H_3, H_{3'}$	8.6			2.0	1.2	-13.4	8.4			
XIV	$CDCl_3$	5.14	4.50	4.86	4.71	6.01	6.34	8.03 8.00 7.86		2.92-3.47(m)	~6.33(m) ~7.05(m)	9.0	9.9	3.5	2.0	1.0	-13.4				
XXII	$CDCl_3$	4.56	4.24	4.76	4.59	5.88	6.19	8.37 8.01 7.80		2.36-3.00(m)	H_2 2.75 H_3 3.55	9.0	10.0	3.5	2.0	1.1	-13.3				3.6
										H_4 H_6 H_7	$H_2, H_{2'}$ $H_3, H_{3'}$										
XXIX	$CDCl_3$	5.10	4.50	4.84	4.66	5.91	6.28	8.06 7.99 7.83		~2.08 1.94 3.45	~6.17(m) ~6.95(m)	9.0	9.9	3.6	2.0	1.2	-13.6		2.2	8.6	

TABLE 3.2.1.7. Parameters Obtained from 100 MHz Spectra of Acetylated L - Arabinopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	$\tau_{5'}$	τ acetyl	τ aromatic	τ indolic	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{23} indolic
†XV*	$CDCl_3$	4.80	4.80	4.30	4.99	6.17		8.00 7.77 7.97	2.84-3.46(m)	$H_2, H_{2'}$ ~6.5(m) $H_3, H_{3'}$ ~7.06(m)							
XXIII	$CDCl_3$	4.19	4.55	4.20	4.81	~6.0	~6.0	8.34 7.78 8.00	2.38-3.00(m)	H_2 2.85 H_3 3.28	9.6	2.9	2.9	6.8	9.9		3.8

*Ring Parameters Quoted by Preobrazhenskaya *et al*[62].

TABLE 3.2.1.8. Parameters Obtained from 100 MHz Spectra of Acetylated D-Ribopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	$\tau_{5'}$	τ_{Me}	τ_{acetyl}	τ_{N-H}	$\tau_{aromatic}$ H_3, H_5	H_2, H_6	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{45'}$	$J_{55'}$	$J_{5\text{-Me}}$	J_{N-1}
I	$CDCl_3$	5.14	4.94	4.60	4.93	6.10	5.69	5.91			7.94 7.94 7.94 7.94	4.36	1.90(m)	3.34(m)	8.9	9.0	9.1	9.7	5.6	2.3	-12.3				7.6
† II	$CDCl_3$	5.15	4.6	- 4.9(m)			5.87				7.99 7.97 7.84 7.93	4.35	1.90(m)	3.32(m)	8.9										8.8
III	$CDCl_3$	4.95	4.46	4.85	4.78	6.15	5.67	5.89			7.73 8.00 7.95 7.95	4.66	1.89(m)	3.30(m)	~1	~3	10.0	9.2	6.0	2.6	-12.2				8.6
† IV	$CDCl_3$	4.97	4.49	~4.9	~4.9	6.29				8.72	7.76 8.01 7.94	4.67	1.92(m)	3.31(m)	~1	~3		9.0						6.0	8.6
V	$CDCl_3$	5.24	4.99	4.62	4.97	5.87			6.56		7.94 7.94 7.94	4.42	1.91(m)	3.32(m)	8.9	8.9	9.0	5.6				10.4	-11.8		8.0
† VI	$CDCl_3$	5.23	~4.7	~4.7	~4.62	5.94			6.19		7.95 7.94 7.85	4.81	1.93(m)	3.31(m)	8.6			2.0				1.2	-13.4		8.4

TABLE 3.2.2.1. Parameters Obtained from 100 MHz Spectra of Acetylated N-p-nitrophenylglycopyranosylamine Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	$\tau_{5'}$	τ_{Me}	τ_{acetyl}	$\tau_{aromatic}$	$\tau_{indolinic}$ H_2, H_2'	H_3, H_3'	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{45'}$	$J_{55'}$	$J_{5\text{-Me}}$
VIII	C_6H_6	5.13	4.52	4.63	4.80	6.62	5.76	6.14			8.33 8.33 8.24 8.22	obscured by solvent	obscured by solvent		9.0	9.6	9.0	9.8	5.2	2.2	-12.3			
† VIII	$CDCl_3$	4.6	~5.1(m)			6.25	5.75	5.96			8.05 8.03 8.00 7.99	H_4 3.46 H_6 3.29 H_5 2.95 H_7 2.92	~6.39(m)	~7.05(m)				9.7	4.3	2.8	-12.3			
† IX	$CDCl_3$	5.02	4.52	4.81	4.58		5.97				8.00 8.00 7.82 7.97	2.84-3.48(m)	~6.33(m)	~7.05(m)	9.0	10.2	3.5	3.9						
† X *	$CDCl_3$	5.27	4.4 - 5.0(m)				~5.8				7.78 7.99 7.99 7.97	2.9-3.5(m)												
XI β	$CDCl_3$	5.27	4.45	4.67	4.86	5.90				8.73	7.82 8.02 7.97	2.80-3.47(m)	~6.30(m)	~6.97(m)	2.5	3.1	9.1	8.8						6.4
† α	$CDCl_3$	5.10	4.37	~4.9	~4.9	6.27				8.75	7.85 8.02 7.98	2.80-3.47(m)	~6.30(m)	~6.97(m)	0.6	2.9		9.0						6.0
XII	$CDCl_3$	5.08	4.65	4.78	5.00	5.92			6.66		8.02 7.97 7.96	2.84-3.50(m)	~6.42(m)	~7.05(m)	8.9	8.9	9.0	5.7				10.5	-11.6	
† XIII	$CDCl_3$	4.85	4.59	4.54	5.13	6.04			6.04		8.00 7.88 7.84	2.84-3.42(m)	~6.46(m)	~7.03(m)	9.0	3.4	2.0	2.0						
XIV	$CDCl_3$	5.14	4.50	4.86	4.71	6.01			6.34		8.03 8.00 7.86	2.92-3.47(m)	~6.33(m)	~7.05(m)	9.0	9.9	3.5	2.0				1.0	-13.4	
† XV **	$CDCl_3$	4.80	4.80	4.30	4.99	6.17					8.00 7.77 7.97	2.84-3.46(m)	~6.5(m)	~7.06(m)										

* 60 MHz Spectrum

** Ring parameters quoted by Preobrazhenskaya *et al*[62].

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	$\tau_{5'}$	τ_{Me}	τ_{acetyl}	$\tau_{aromatic}$	$\tau_{indolic}$		J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{45'}$	$J_{55'}$	$J_{5\text{-Me}}$	$J_{indolic}$ J_{23}
† XVI	C_6H_6	4.4 - 4.8(m)				6.52	5.77	6.06			8.62 8.33 8.28 8.27	obscured by solvent	H_2 obscured by solvent	H_3				9.7	5.0	2.5	-12.4				
† XVI	$CDCl_3$	4.3 - 4.8(m)				6.02	5.71	5.86			8.36 8.00 7.96 7.95	2.37-2.96(m)	2.82	3.46				9.6	5.2	2.2	-12.2				3.5
† XVII	$CDCl_3$	4.43	4.25	4.73	4.46		5.82				8.36 8.02 7.78 8.00	2.36-2.98(m)	2.75	3.46	8.6	9.9	3.4	3.6							3.6
† XIX	$CDCl_3$	4.21	4.46	~4.76	~4.76	6.24				8.67	8.03 8.01 7.93	2.35-3.00(m)	2.74	3.51	1.3	2.7		9.0						6.0	3.8
† XX	$CDCl_3$	4.4 - 4.6(m)			~4.8	5.73			6.45		8.37 7.98 7.95	2.37-3.00(m)	2.80	3.47			~ 7	5.6				10.4	-11.6		3.6
† XXI *	$CDCl_3$	4.2 - 4.6(m)			~5.1	~6.0			~6.0		8.34 7.87 7.87	~ 2.3-3.0(m)	~ 2.7	~3.6											~3.6
XXII	$CDCl_3$	4.56	4.24	4.76	4.59	5.88			6.19		8.37 8.01 7.80	2.36-3.00(m)	2.75	3.55	9.0	10.0	3.5	2.0				1.1	-13.3		3.6
XXIII	$CDCl_3$	4.19	4.55	4.20	4.81	~6.0			~6.0		8.34 7.78 8.00	2.38-3.00(m)	2.85	3.28	9.6	2.9	2.9	6.8				9.9			3.8

* 60 MHz Spectrum.

TABLE 3.2.2.3. Parameters obtained from 100MHz Spectra of Acetylated Glycopyranosylindole Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	$\tau_{5'}$	τ_{Me}	τ_{acetyl}	$\tau_{aromatic}$ H_4	H_6	H_7	$\tau_{indolinic}$ H_2, $H_{2'}$	H_3, $H_{3'}$	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{45'}$	$J_{55'}$	$J_{5\text{-Me}}$	$J_{aromatic}$ J_{46}	J_{67}
†XXIV	$CDCl_3$		4.6 - 5.0(m)			6.12	5.74	5.89			8.06 7.98 7.98 7.96	2.06	1.92	3.46	≈6.20(m)	≈6.94(m)				9.8	5.0	2.2	-12.4				2.0	9.4
†XXV	$CDCl_3$	4.97	4.52	4.81	4.53		5.89				8.06 8.00 7.93 8.00	2.08	1.96	3.44	≈6.16(m)	≈6.94(m)	8.8	10.0	3.4								2.2	8.8
XXVI	$CDCl_3$	4.99	4.36	4.87	4.69	~6.15	5.72	5.86			7.86 8.03 7.97 7.97	2.10	1.99	3.44	≈6.2(m)	≈6.96(m)	~1	~3	10.0	9.2	5.8	3.2	-16.4				~1.6	8.8
†XXVII	$CDCl_3$	4.93	4.64	~4.86	~4.86	6.28				8.68	7.84 8.00 7.92	2.12	1.98	3.42	~6.16(m)	~6.94(m)	1.2	~2.2		9.0						6.0	2.0	9.6
XXVIII	$CDCl_3$	5.02	4.62	4.78	4.98	5.87			6.56		8.08 7.97 7.97	2.10	1.99	3.47	≈6.24(m)	≈6.97(m)	9.0	9.0	8.8	5.5				10.5	-11.4		2.2	8.8
XXIX	$CDCl_3$	5.10	4.50	4.84	4.66	5.91			6.28		8.06 7.99 7.83	~2.08	1.94	3.45	≈6.17(m)	≈6.95(m)	9.0	9.9	3.6	2.0				1.2	-13.6		2.2	8.6

TABLE 3.2.2.4. Parameters Obtained from 100 MHz Spectra of Acetylated Glycopyranosyl-5-nitroindoline Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	τ_{Me}	τ_{acetyl}	$\tau_{aromatic}$ H_4	H_6	H_7	τ_{indole} H_2	H_3	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{5\text{-Me}}$	$J_{aromatic}$ J_{46}	J_{67}	J_{indole} J_{23}
†XXX	$CDCl_3$	4.2	- 4.8(m)			~5.95	5.63	5.82		8.33 7.97 7.93 7.93	1.46	1.86	2.46	2.59	3.27					4.8	2.0	-12.2		2.0	9.4	3.6
†XXXI	$CDCl_3$	4.13	4.43	~4.54	~4.54	6.25			8.61	8.02 8.01 7.90	1.61	1.93	2.53	2.60	3.35	~1	~2		9.0				6.0	2.0	9.6	3.6

TABLE 3.2.2.5. Parameters Obtained from 100 MHz Spectra of Acetylated Glycopyranosyl-5-nitroindole Derivatives.

Compound	Solvent	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6	$\tau_{6'}$	$\tau_{5'}$	τ_{acetyl}	$\tau_{aromatic}$	$\tau_{methylene}$	J_{12}	J_{23}	J_{34}	J_{45}	J_{56}	$J_{56'}$	$J_{66'}$	$J_{45'}$	$J_{55'}$
XXXIV	$CDCl_3$	4.94	4.86	~4.6	4.92	6.26	5.75	5.92		8.07 7.99 7.96 7.96	2.84-3.36(m)	7.30(m), 6.73(m), ≈8.17(m)	9.0	9.5	9.7	9.8	4.8	2.8	-12.0		
†XXXV	$CDCl_3$		4.6 - 5.1(m)			5.91			6.65	8.07 7.97 7.97	2.84-3.37(m)	≈7.29(m), 6.70(m), ≈8.18(m)				5.6				10.5	-11.4

TABLE 3.2.2.6. Parameters Obtained from 100 MHz Spectra of Acetylated Glycopyranosyl-1,2,3,4-Tetrahydroquinoline Derivatives.

and XXX in $CDCl_3$ were run several times, and the line positions averaged. In these spectra the signals due to protons on C_5 and C_6 were analysed as ABX patterns by standard procedures[65]. The spectrum of VIII in benzene (Fig.3.3c.) allowed first-order parameters to be obtained for the sugar moiety protons. These parameters were varied until agreement between a computed spectrum (Fig.3.3b.) and the observed spectrum was reached.

Table 3.2.3. shows assignments that have been made for the various acetoxy signals in several acetylated nucleoside derivatives. Table 3.2.4. gives the assignment of acetoxy signals of the acetylated glycopyranosylindoline and glycopyranosylindole derivatives prepared, and the chemical shift differences (Δ) found between corresponding derivatives. Table 3.2.5. shows the anisotropic shifts predicted for the various chair-like conformations and configurations of the acetylated glycopyranosylindoles prepared. A strong chemical shift difference is one of the order of 0.3 τ, a medium shift 0.05 - 0.1 τ and a weak shift $\lesssim$0.02 τ. Table 3.2.6. shows the conformation and configuration of glycosylindolines and glycosylindoles found by a consideration of the splittings and of the Reeve's instability factors[63], and by measurement of the chemical shift differences for the various acetoxy signals on removal of the anisotropic group.

3.3. DISCUSSION.

3.3.1. Acetylated D-Glucopyranosylamine Derivatives.

The parameters measured for this series of compounds are presented in Table 3.2.1.1. The splittings, with the exception of J_{56}, $J_{56'}$ and $J_{66'}$, are all of the order of 9 Hz. Thus all the hydrogens in the sugar ring must bear a *trans*-diaxial relationship to each other, and the conformation and

Compound	B	Solvent	C_2-OAc	C_3-OAc	C_4-OAc	C_6-OAc	Ref.
β-D-Glu$_p$(OAc)$_4$B	U	DMSO-d_6	8.08	8.04	7.98	7.98	64
	G	"	8.11	8.02	7.96	7.96	64
	A	"	8.12	8.04	7.99	7.99	64
	I	"	8.37	8.03	8.02	7.96	61
	IH_2	"	8.08	8.04	8.03	8.00	61
3-NHAc-β-D-Glu$_p$(OAc)$_3$B	UH_2	"	8.07	-	8.04	8.00	64
	UH_2	"	8.06	-	8.00	8.02	48
	U	"	8.11	-	8.02	7.99	64
	U	"	8.11	-	7.97	8.02	48
	Z	"	8.29	-	8.02	8.00	64
	Y	"	8.30	-	8.04	7.99	64
	X	"	8.30	-	8.04	8.01	64
	W	"	8.31	-	8.04	8.01	64
	V	"	8.28	-	8.02	8.00	64
β-D-Gal$_p$(OAc)$_4$B	U	"	8.05	8.05	7.83	8.00	64
	C	"	8.10	8.06	7.82	8.00	64
	G	"	8.10	8.06	7.82	8.01	64
	A	"	8.10	8.06	7.82	8.02	64
	I	$CDCl_3$	8.33	8.00	7.76	7.97	62
	IH_2	"	8.02	8.02	7.83	7.99	62
3-NHAc-β-D-Gal$_p$(OAc)$_3$B	U	DMSO-d_6	8.07	-	7.84	8.02	64
	U	"	8.10	-	8.03	8.03	48
	UH_2	"	8.05	-	8.11	8.05	48
	A	"	8.12	-	7.82	8.02	64
	Z	"	8.31	-	7.83	8.05	64
	X	"	8.30	-	7.75	8.02	64
	W	"	8.30	-	7.80	8.05	64
	V	"	8.24	-	7.83	8.05	64
3-NHAc-β-D-Man$_p$(OAc)$_3$B	U	"	7.92	-	7.97	7.97	48
	UH_2	"	8.13	-	7.97	8.03	48
	Z	"	7.95	-	7.95	7.95	64
	X	"	7.92	-	8.00	7.95	64
	W	"	7.96	-	7.96	7.96	64
	V	"	7.99	-	8.05	7.99	64
β-D-Rib$_p$(OAc)$_3$B	I	"	8.33	7.76	7.99		61
	I	$CDCl_3$	8.29	7.75	7.95		62
	IH_2	"	8.01	7.79	7.99		62
	IH_2	DMSO-d_6	8.05	7.80	8.03		61
	$6\text{-}NO_2I$	$CDCl_3$	8.26	7.68	7.93		62
	$6\text{-}NO_2IH_2$	"	7.99	7.72	7.96		62

Continued overleaf..

B	BH
U	uracil
UH_2	5,6-dihydrouracil
A	4-ethoxy-2-oxo-1,2-dihydropyrimidine
C	cytosine
G	*N*-acetylcytosine
I	indole
IH_2	indoline
$6\text{-}NO_2I$	6-nitroindole
$6\text{-}NO_2IH_2$	6-nitroindoline
Z	6-hydroxypurine
Y	6-methylmercaptopurine
X	6-aminopurine
W	6-dimethylaminopurine
V	theophilline.

Table 3.2.3. Acetoxy Resonances of Acetylated Glycopyranosyl-nucleoside Derivatives.

Compound	B	C_2-OAc	C_3-OAc	C_4-OAc	C_6-OAc	Δ 2	Δ 3	Δ 4	Δ 6
β-D-Glu$_p$(OAc)$_4$B	I	8.36	8.00	7.96	7.95				
	IH_2	8.05	8.03	8.00	7.99	0.31	-0.03	-0.04	-0.04
	5-NO_2I	8.33	7.97	7.93	7.93				
	5-NO_2IH_2	8.06	7.98	7.98	7.96	0.27	-0.01	-0.05	-0.03
	2-MeI	8.39	8.00	7.98	7.97				
	2-MeIH_2	8.16	8.00	8.00	7.98	0.23	0.00	-0.02	-0.01
β-D-Gal$_p$(OAc)$_4$B	I	8.36	8.02	7.78	8.00				
	IH_2	8.00	8.00	7.88	7.97	0.36	0.02	-0.10	0.03
D-Man$_p$(OAc)$_4$B	I								
	*IH_2	7.88	7.99	7.99	7.98				
β-L-Rha$_p$(OAc)$_3$B	I	8.03	8.01	7.93					
	IH_2	7.85	8.02	7.98		0.18	-0.01	-0.05	
	5-NO_2I	8.02	8.01	7.90					
	5-NO_2IH_2	7.84	8.00	7.92		0.18	0.01	-0.02	
β-D-Xyl$_p$(OAc)$_3$B	I	8.37	7.98	7.95					
	IH_2	8.02	7.97	7.96		0.35	0.01	-0.01	
α-D-Lyx$_p$(OAc)$_3$B	*I	8.34	7.87	7.87					
	*IH_2	8.00	7.82	7.86		0.34	0.05	0.01	
α-L-Arab$_p$(OAc)$_3$B	I	8.37	8.01	7.80					
	IH_2	8.03	8.00	7.86		0.34	0.01	-0.06	
β-D-Rib$_p$(OAc)$_3$B	I	8.24	7.78	8.00					
	IH_2	8.00	7.77	7.97		0.24	0.01	-0.03	

* 60 MHz spectrum.

B	BH
I	indole
IH_2	indoline
5-NO_2I	5-nitroindole
5-NO_2IH_2	5-nitroindoline
2-MeI	2-methylindole
2-MeIH_2	2-methylindoline

Table 3.2.4. Acetoxy Resonances of Acetylated Glycopyranosylindoles and Glycopyranosylindolines in $CDCl_3$.

Compound	Config. & Conform.	C_2-OAc		C_3-OAc		C_4-OAc		C_6-OAc	
		upfield	downfield	upfield	downfield	upfield	downfield	upfield	downfield
XVI	Clα		w			w			w
	Clβ	s			w		w		w
	1Cβ		w	s			w		s
	1Cα	s			w	-	-		m
	Found	0.31			0.03		0.04		0.04
XXX	Found	0.27			0.01		0.05		0.03
XXXII	Found	0.23			0.00		0.02		0.01
XVII	Clα	s		-	-		w		w
	Clβ	s			w		m		w
	1Cβ		w	s			w	w	
	1Cα	s			w	-	-		w
	Found	0.36		0.02			0.10	0.03	
XVIII	Clα		m		w-m	m			w
	Clβ	s			w		w		w-m
	1Cβ	s		s			w	m	
	1Cα	s			w	-	-		w
	Found								
XIX	Clα	s			w		w		
	Clβ	m		s			w		
	1Cβ	m-s			w		w		
	1Cα		m	w		m			
	Found	0.18			0.01		0.05		
XXXI	Found	0.18		0.01			0.02		
XX	Clα		w	w		w			
	Clβ	s		-	-		w		
	1Cβ		w	s			w		
	1Cα	s			w	-	-		
	Found	0.35		0.01			0.01		
XXI	Clα		m		m	w			
	Clβ	s			w		w		
	1Cβ		m		w		w		
	1Cα	s		w-m		-	-		
	Found*	0.34		0.05		0.01			
XXII	Clα	s			w		m		
	Clβ	s			w	-	-		
	1Cβ	s			w		w		
	1Cα		w-m	s			m		
	Found	0.34		0.01			0.06		
XXIII	Clα	s		s		m			
	Clβ	s			w	-	-		
	1Cβ		w	w			w		
	1Cα	s			w		w		
	Found	0.24		0.01			0.03		

*60 MHz spectrum

Table 3.2.5. Prediction of Anisotropic Shifts of Acetoxy Groups in Glycopyranosylindole Derivatives.

Compound	From NMR Parameters	From Anisotropic Effect	From Instability Factors
I	C1β		C1β
VIII	C1β		C1β
XVI	C1β	C1β	C1β
XXIV	C1β		C1β
XXX	C1β	C1β	C1β
XXXII	C1β		C1β
XXXIII	C1β	C1β	C1β
XXXIV	C1β		C1β
XXXVI	C1β		C1β
II	C1β		C1β
IX	C1β		C1β
XVII	C1β	C1β	C1β
XXV	C1β		C1β
III	C1α		C1α
X			C1α
XXVI	C1α		C1α
IV	1Cα		1Cα
XI	1Cβ + α		1Cα
XIX	1Cα or β	1Cβ	1Cα
XXVII	1Cα or β		1Cα
XXXI	1Cα or β	1Cβ	1Cα
V	C1β		C1β
XII	C1β		C1β
XX	C1β	C1β	C1β
XXVIII	C1β		C1β
XXXV	C1β		C1β
XIII	1Cα		1Cα
XXI	1Cα	1Cα	1Cα
VI	C1α		C1α
XIV	C1α		C1α
XXII	C1α	C1α	C1α
XXIX	C1α		C1α
XV	C1β		C1β
XXIII	C1β	C1β	C1β

Table 3.2.6. Conformation and Configuration of Glycopyranosyl-indoles.

configuration of the D-glucosyl moiety must then be fixed as Clβ. Because the splittings are all close to 9 Hz, this chair conformation must predominate greatly, and only very small amounts of the 1C form can be present. (See Fig.3.4a.).

As a spectrum can show first-order characteristics only when the chemical shifts between adjacent protons is large, *i.e.* $^{J}/\Delta\nu$ is small, the triplet at lowest field must be due to H_3 in compound I (Fig. 3.5.). This gives the largest possible values of $\Delta\nu$ between H_2 and H_3, and between H_3 and H_4. The assignment of the remaining signals due to the D-glucosyl moiety can be made on the basis of the magnitude of their splittings. H_5, H_6 and H_6, are found as an ABX pattern, having an additional splitting (J_{45}) due to the H_4-H_5 interaction. The spectrum of compound VIII gave a first-order spectrum (Fig. 3.3c.). The computed spectrum obtained by varying these parameters is shown in Fig. 3.3b. The two spectra were very nearly identical, proving the assignments made.

Although most of the remaining D-glucopyranosyl derivatives gave spectra that were not of first-order character, ABX analyses of the multiplets due to H_5, H_6 and H_6, enabled estimation of J_{45}, J_{56}, $J_{56'}$ and $J_{66'}$ to be made. As J_{45} in each case was approximately 9.7 Hz, the C1 conformation must be present. The β-configuration was assigned in each case by a consideration of the Reeve's instability factors[63], and by noting that the optical rotation for each of the derivatives studied was of the same order. (See Section 4.2.).

The parameters found from the spectrum of XXXII in $CDCl_3$ differ slightly from those found from I and VIII. This could be due to buckling of the ring caused by interaction of the 2-methyl group of the aglycone with the C_2-acetoxy group, as evinced by the abnormally high chemical shift (8.16 τ) of the latter. Another possible explanation of this abnormal chemical shift is that in this molecule there is a significant

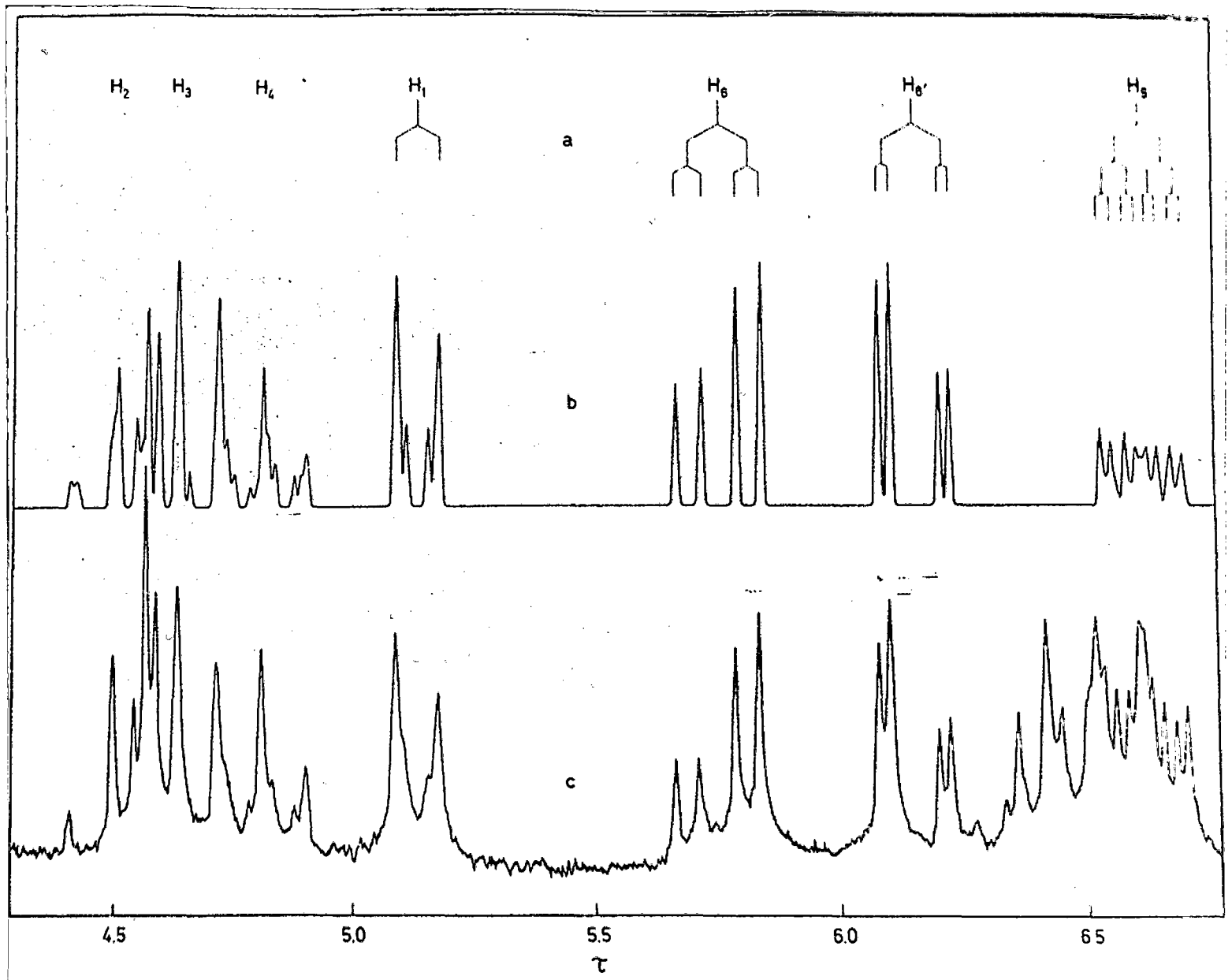
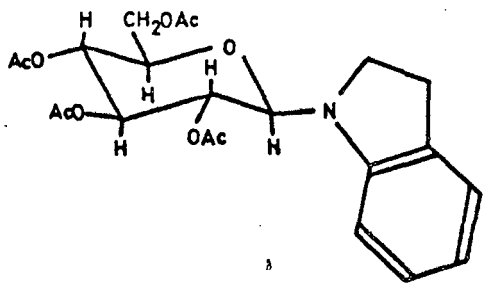


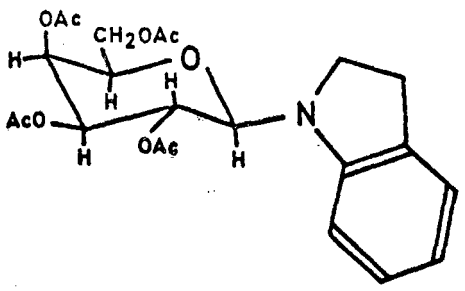
FIG. 3.3. 100 MHz SPECTRUM OF VIII IN C_6H_6. a) First-order analysis. b) Computed spectrum. c) Experimental spectrum.

a)



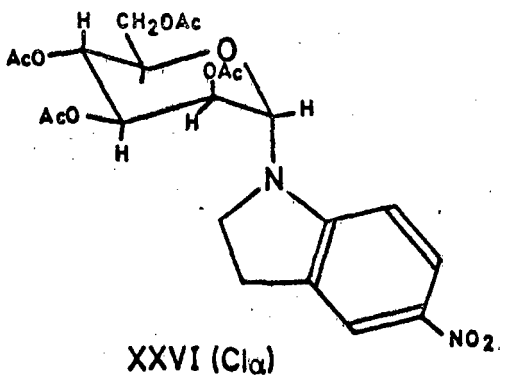
VIII (Clβ)

b)



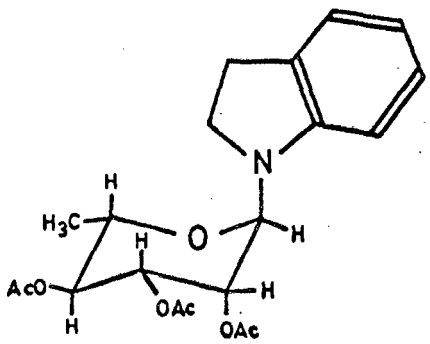
IX (Clβ)

c)

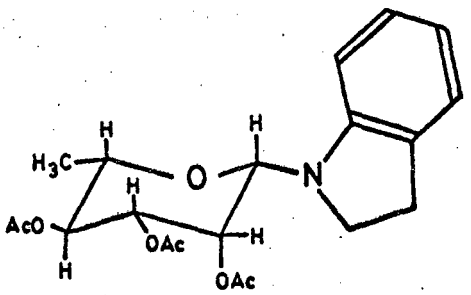


XXVI (Clα)

d)

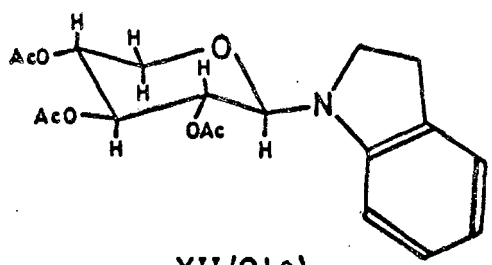


XI (IC α)



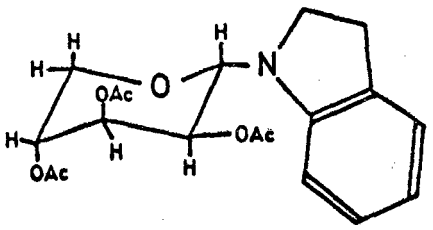
XI (IC β)

e)



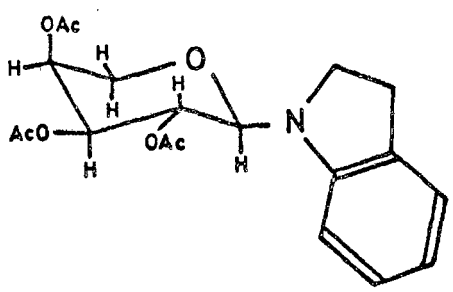
XII (Cl β)

f)



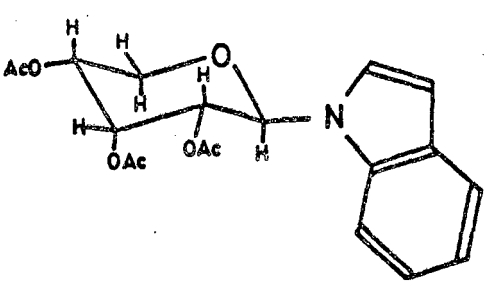
XIII (IC α)

g)



XIV (Cl α)

h)



XV (Cl β)

FIG. 3.4. CONFORMATIONS AND ANOMERIC CONFIGURATIONS OF ACETYLATED GLYCOPYRANOSYLAMINE DERIVATIVES IN SOLUTION

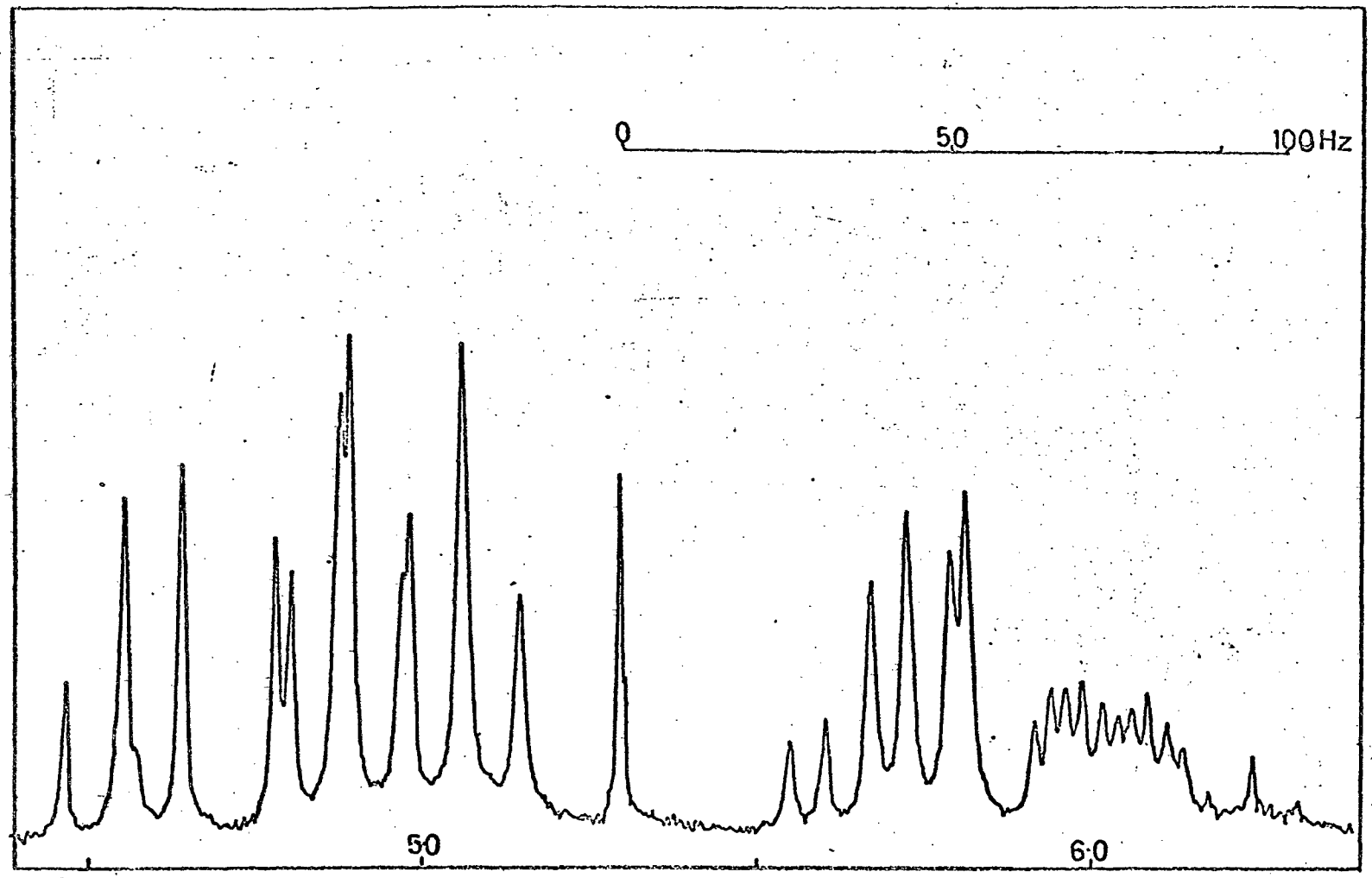


Fig. 3.5. 100 MHz Spectrum of I in $CDCl_3$.

population of the *syn*-form, causing the C_2-acetoxy group to be shielded by the benzene ring of 2-methylindoline. The chemical shift of this acetoxy signal in compound XXXIII is 8.39 τ, which is approximately the value expected on the basis of studies on other acetylated glycosylindoles.

3.3.2. Acetylated D-Galactopyranosylamine Derivatives.

Table 3.2.1.2. shows the parameters obtained from the first-order analysis of the 100 MHz spectra of compounds II, IX, XVII and XXV. None of these spectra was completely of first-order character, and the H_5, H_6 and $H_{6'}$ signals appear as a single peak. In the spectrum of II in $CDCl_3$, only the parameters for the anomeric proton can be found. The first-order analyses show that the anomeric proton is split to the extent of *ca.* 9Hz, and that J_{23} is *ca.* 10Hz in each case. J_{34} and J_{45} are found to be 3.5 - 4.0 Hz, indicating axial-equatorial interaction. Thus the C1 conformation and β-configuration must predominate (See Fig. 3.4b.).

3.3.3. Acetylated D-Mannopyranosylamine Derivatives.

The parameters for this series of compounds are presented in Table 3.2.1.3. The splitting due to the anomeric proton (*ca.* 1Hz) can be caused by interaction of two protons having diequatorial arrangements in space. The splittings J_{34} and J_{45} are found to be *ca.* 10 Hz and 9 Hz respectively. These molecules thus exist almost entirely in the C1 conformation with α-configuration, as predicted by a consideration of the instability factors. (See Fig. 3.4c.). No parameters could be measured from the spectrum of X, but the optical rotation of this compound is of the opposite sign to that for the remaining compounds in the series (See section 4.2.). For this reason no structure for X is suggested.

3.3.4. Acetylated L-Rhamnopyranosylamine Derivatives.

Table 3.2.1.4. shows the parameters found for compounds IV, XI (Fig. 3.6.), XIX, XXVII and XXXI. The anomeric splitting for all of these compounds, with the exception of compound XI, is found to be *ca.* 1 Hz, which may result from diequatorial or axial-equatorial interactions. The splitting due to the H_4, H_5 interaction is 9 Hz, and this can occur only in the 1C conformation.

Consideration of the Reeve's instability factors suggest that L-rhamnopyranosylamine derivatives exist predominatly in the 1C conformation with α-configuration.

The spectrum of compound XI in $CDCl_3$ is complicated. Analysis shows that there is a mixture of both α and β anomers in the 1C conformation in solution, with the β isomer in excess (Fig. 3.4d.). The latter anomer is the only L-rhamnopyranosylamine compound studied whose NMR spectrum showed first-order characteristics. For the remaining compounds, the signals due to H_3 and H_4 could not be separated, and J_{45} was obtained by a first-order analysis of the multiplet due to H_5.

3.3.5. Acetylated D-Xylopyranosylamine Derivatives.

The 100 MHz NMR parameters of compounds V, XII, XX, XXVIII and XXXIV are given in Table 3.2.1.5. The spectra of V, XII and XXVIII can be analysed by first-order methods, but the remaining two spectra are too complex. The splittings, with the exception of J_{45} and $J_{45'}$, are of the order of 9 Hz, and these D-xylopyranosylamine derivatives therefore exist in the C1 conformation with β configuration, as predicted by consideration of the Reeve's instability factors (Fig. 3.4e).

The splittings J_{45} and $J_{45'}$ show that the dihedral angle between H_4 and H_5 and H_4 and H_5, will be *ca.* 30° and *ca.* 160°, by application of the Karplus equation[43]. This indicates only a slight deviation from the perfect chair geometry.

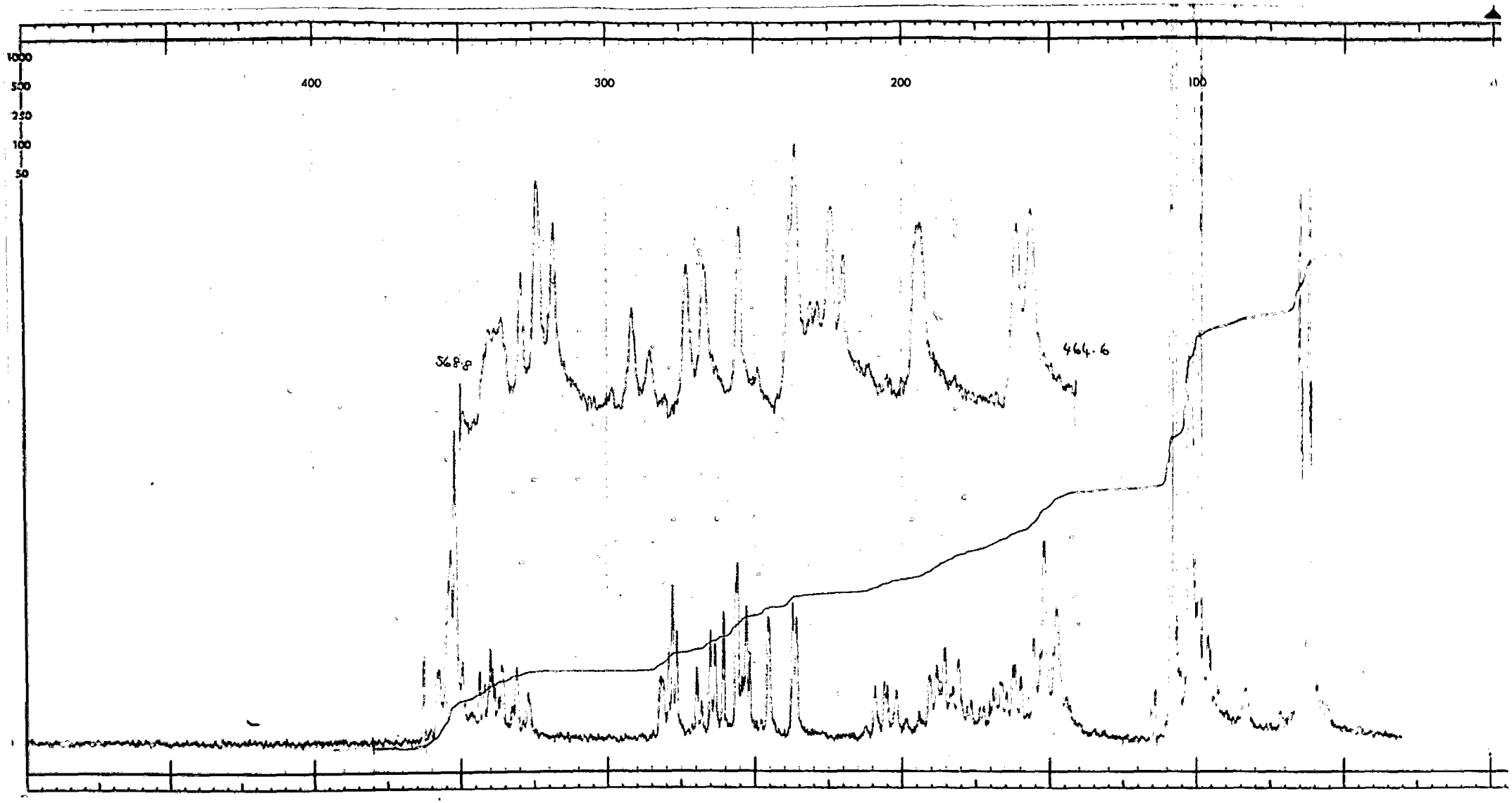


Fig. 3.6 100 MHz NMR Spectrum in $CDCl_3$ of XI

3.3.6. Acetylated D-Lyxopyranosylamine Derivatives.

These derivatives (Table 3.2.1.6., compounds XIII, XXI) exist in the 1C conformation with α-configuration when in solution. Although the parameters for XIII only could be obtained from the 100 MHz spectra, comparison of the 60 MHz spectra of the two compounds is possible. XIII and XXI have been assumed to exist having the same geometry. That J_{12} is found to be 9.0 Hz and J_{45} to be 2.0 Hz fixes these compounds in the conformation and configuration given above (Fig. 3.4f.). Reeve's instability factors support these assignments.

3.3.7. Acetylated L-Arabinopyranosylamine Derivatives.

The parameters found by a first-order analysis of the spectra of compounds VI, XIV, XXII and XXIX (Fig. 3.7.) are presented in Table 3.2.1.7. The splittings indicate that in $CDCl_3$ solution these L-arabinopyranosylamine derivatives exist predominantly in the C1 chair form with α-configuration (Fig. 3.4g). Application of the Karplus equation[43] to the splittings found for the H_4, H_5 and H_4, H_5, interactions suggests that the dihedral angles present are *ca.* 60° and *ca.* 65°. These angles indicate that there is little distortion in the ring.

3.3.8. Acetylated D-Ribopyranosylamine Derivatives.

A study of the instability factors of compounds XV and XXIII (Table 3.2.1.8., see Fig. 3.8.) suggests that they exist predominately in the C1 conformation with β-configuration. The spectrum of XXIII in $CDCl_3$ supports this prediction. The splitting of the anomeric proton is 9.6 Hz, and this can only be due to a *trans*-diaxial interaction. Investigation of the multiplets due H_5 and H_5, show J_{45} and J_{45}, to be 6.8 and 9.9 Hz respectively. Application of the Karplus relationship[43] shows the dihedral angles to be *ca.* 20° and *ca.* 180°, which correspond to those expected for the C1 chair form (Fig. 3.4h.).

This assignment agrees with that made by Preobrazhenskaya *et al*[62] for these two compounds (their studies on XV, for which

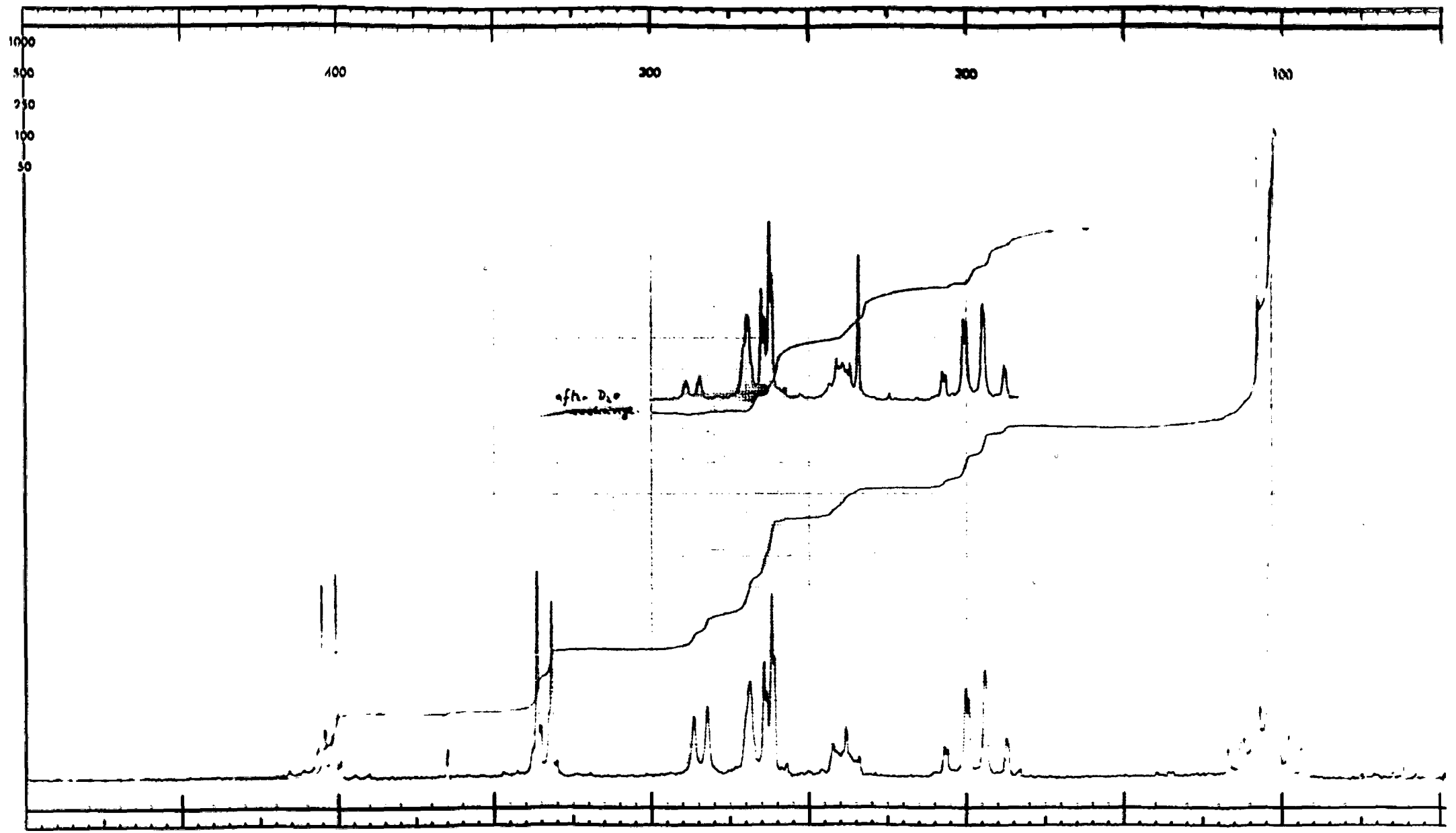


Fig 3.7 100 MHz NMR Spectrum in $CDCl_3$ of XXIX

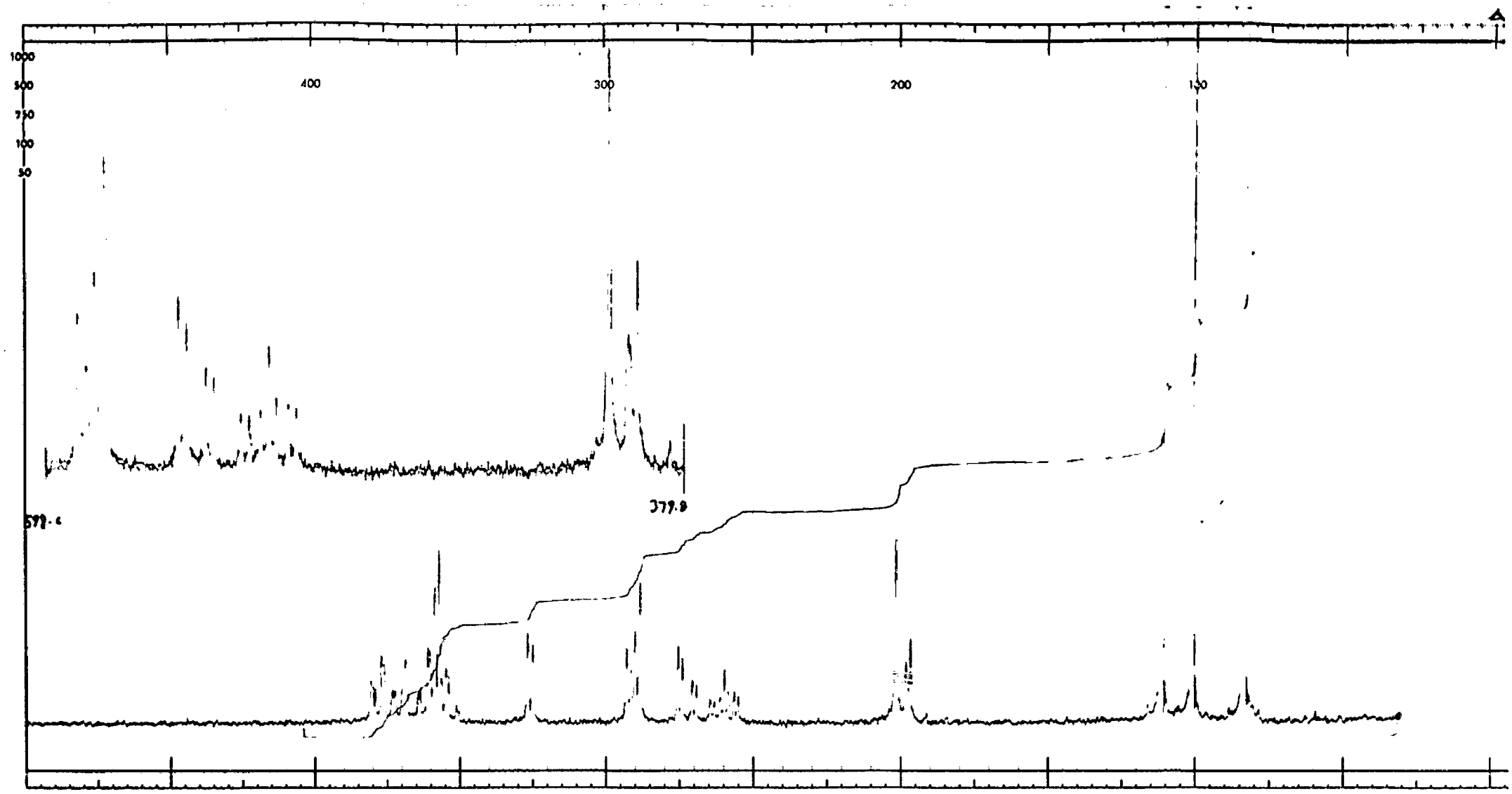


Fig 3.8 100 MHz NMR spectrum in $CDCl_3$ of XXIII

the spectrum was very complex, were made by means of double resonance experiments). The coupling constants differ quite considerably from those quoted by Durette, Horton and Bhacca[41] for tetra-*O*-acetyl-β-D-ribopyranose in acetone-d_6; these authors found an equilibrium mixture of C1 and 1C conformers in the ratio 11:9.

Although NMR often enables a ready evaluation of both conformation and configuration to be made, spectra are frequently too complex to permit any evaluation without double resonance experiments. It would be very useful to have such an alternative means of determining configuration and conformation.

3.3.9. Determination of Configuration and Conformation by Consideration of the Chemical Shifts of Acetoxy Signals.

It has been reported that an acetoxy group in an equatorial orientation comes into resonance at higher field than does an axial group in a similar electron environment[42,47]. Several exceptions to this rule have been pointed out[48], but, in many cases, this generalisation does hold[64]. If the signals due to various acetoxy groups can be assigned as axial or equatorial, the ring conformation will be fixed, and the anomeric configuration determined. An example of the application of this method is given by compound XIII where two acetoxy groups fall into the range quoted for axial groups (τ 7.84, 7.88) and one in the range for equatorial acetoxy groups (τ 8.00). Thus, the conformation is probably mainly 1C.

Table 3.2.3. lists the acetoxy chemical shifts for several acetylated glycopyranosylnucleoside derivatives. The discrepancies between the assignments for the C_4 and C_6 acetoxy groups are noted in the cases of *N*-acetyl-1-(2,4,6-tri-*O*-acetyl-3-amino-3-deoxy-β-D-glucopyranosyl)uracil, the corresponding 1,2-dihydrouracil derivative and *N*-acetyl-1-(2,4,6-tri-*O*-acetyl-3-amino-3-deoxy-β-D-galactopyranosyl)uracil. From these published figures[48,64], several of which have been proved by the

preparation of acetoxy-d_3-substituted derivatives, it appears that the acetoxy signal appearing at highest field in the absence of any anisotropic effect is due to the group attached to C_2 when in an equatorial orientation. Lichtenthaler *et al*[64] suggest that the acetoxy signal at lowest field is that due to the C_6-acetoxy group, while Cushley *et al*[48] suggest that it is due to the C_4-acetoxy group. Both schools agree that the acetoxy signal at next-to-highest is due to the C_3-acetoxy group. On the basis of these figures (but with their limitations in mind) Table 3.2.4. has been constructed for the acetylated glycosylindoline and glycosylindole compounds studied.

The acetoxy signals in compounds $\overline{\text{I}}$, $\overline{\text{VIII}}$ and penta-*O*-acetyl-β-D-glucopyranose occur at very nearly the same chemical shifts. This fact indicates that in compound $\overline{\text{VIII}}$ there is no anisotropic shift of any acetoxy signal. This is possible only in the *anti*-form; in the *syn*-form, one would expect a downfield shift of the C_6-acetoxy group. Conversion of an acetylated glycosylindoline to the corresponding glycosylindole derivative will result in anisotropic shifts of the signals in the spectrum. The signals due to the ring hydrogens and some of the acetoxy groups will be shifted downfield, while other acetoxy signals will be shifted upfield. In acetylated glycosylindoles any group that is orientated preferentially in the cones of positive shielding due to the pyrrole portion of the indole ring will be shielded, while groups in the plane of the aromatic rings will be strongly deshielded. Table 3.2.5. shows the anisotropic shifts expected for the various conformations and configurations of acetylated glycopyranosylindoles. The shifts of the acetoxy signals that are found are given in the same table (s indicates a strong shift, *ca.* 0.3 τ; m, a medium shift, *ca.* 0.1 τ; and w a weak shift, *ca.* 0.01 τ). From a consideration of these figures, the conformation and configuration of each acetylated glycopyranosylindole derivative can be found. Table 3.2.6., which shows the conformation and configuration predicted on the basis

of NMR splittings, by a consideration of the anisotropic shifts of the acetoxy signals and by a consideration of instability factors, enables the applicability of this method to be gauged. The anomeric configuration of compound XIX is fixed by this method to be β. This shows the usefulness of this method in indicating anomeric configuration where an assignment cannot be made from the splittings. To establish this method as general, much more work is necessary, but its uses can be seen immediately. In the most complicated spectrum the acetoxy signals can usually be found, even in very dilute solutions, where most signals are hidden by the electronic noise background pattern. Removal of the anisotropy of the aromatic aglycone by hydrogenation (room temp, atmospheric pressure, 5% rhodium on alumina[66]) and rerunning the spectrum will then give the shifts of the acetoxy signals, from which conformation and configuration can be found. The uncertainty of assigning individual acetoxy resonances does, at the moment, prevent full use of this method.

From a study of the chemical shifts of the various ring protons, no conclusion regarding the inductive effect of the aglycone could be reached.

SECTION 4.

PREPARATIVE WORK.

4.1. DISCUSSION.

4.1.1. Substituted Glycosylamine Derivatives.

The literature on glycosylamine derivatives has been reviewed recently [67,68]. Surprisingly little work has been reported on the synthesis of glycosylamines from amines other than purines, pyrimidines and related compounds, such as benzimidazoles. Reviews on the chemistry of nucleoside derivatives are numerous[69-75], and recently a review on benzimidazole, benztriazole, indazole and indole nucleosides[7] has appeared.

The synthesis of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)indole(XVI)[76,77] by proceeding through the intermediate 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-indoline (VIII) provides a relatively simple method whereby a series of glycosylindole derivatives can be prepared. The determination of the conformation and configuration of any antimetabolite must lead towards an understanding of its mode of action, and,for this reason, the geometry of these glycosylamine derivatives was determined in solution by NMR. The intermediate glycosylindoline derivatives provide a larger number of compounds on which spectral correlations can be carried out, so that any generalisations made can be tested more fully.

Initially the object of the present work was the synthesis, and NMR and mass spectral investigation of the acetylated glycopyranosyl derivatives of indoline, indole, 2-methylindoline, 2-methylindole, 5-nitroindoline, 5-nitroindole, 2-methyl-2,3-dihydropyrrolo[3,2-f]- and-[2,3-f]quinolines and 2-methylpyrrolo[3,2-f]- and-[2,3-f]quinolines. The sugars to be used in this investigation were D-glucose, D-galactose, D-mannose, L-rhamnose, D-xylose, D-lyxose, L-arabinose and D-ribose. To facilitate the spectroscopic correlations, a series of acetylated *N*-*p*-nitrophenylglycopyranosylamines was prepared as model compounds.

Several new syntheses of nucleosides have been published during the past few years[75,78-89]. Two of these methods were attempted for the synthesis of 2,3,4,6-tetra-*O*-acetyl-*N*-*p*-nitrophenyl-β-D-glucopyranosylamine (I), 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzimidazole and 1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)benzimidazole (fusion synthesis[78,79]), and 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-2-methylindoline (XXXII; condensation of an acetobromosugar and base in the presence of a proton acceptor such as mercuric cyanide[89]). In no case could any trace of product be found on TLC.

Two of the syntheses described for the preparation of *O*-glycosides[90-92] were adapted to the synthesis of acetylated glycosylamine derivatives. The first, which is itself an adaptation of the Koenigs-Knorr synthesis[93] but using mercuric salts as proton acceptors[90], was used in an abortive attempt to prepare compound I. The second, which involves the stereospecific reaction of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate) with the required aglycone[91,92], was used to prepare compound VIII in 7% yield. Obviously optimum reaction conditions for this reaction must be found before it can be generally used.

The series of acetylated glycopyranosylindolines and glycopyranosyl-5-nitroindolines were prepared either by published methods or by adaptation of these methods[76,77,94]. The synthesis of acetylated glycosyl-2-methylindolines failed, except in the case of compound XXXII, where the yield was low. Dehydrogenation of most of the acetylated glycopyranosylindolines to the corresponding glycopyranosylindoles with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) occurred readily, but conversion of the acetylated glycopyranosyl-5-nitroindolines to the corresponding glycosyl-5-nitroindoles proceeded with difficulty; only the acetylated D-glucosyl and L-rhamnosyl derivatives could be separated from the reaction mixtures. The yields were very

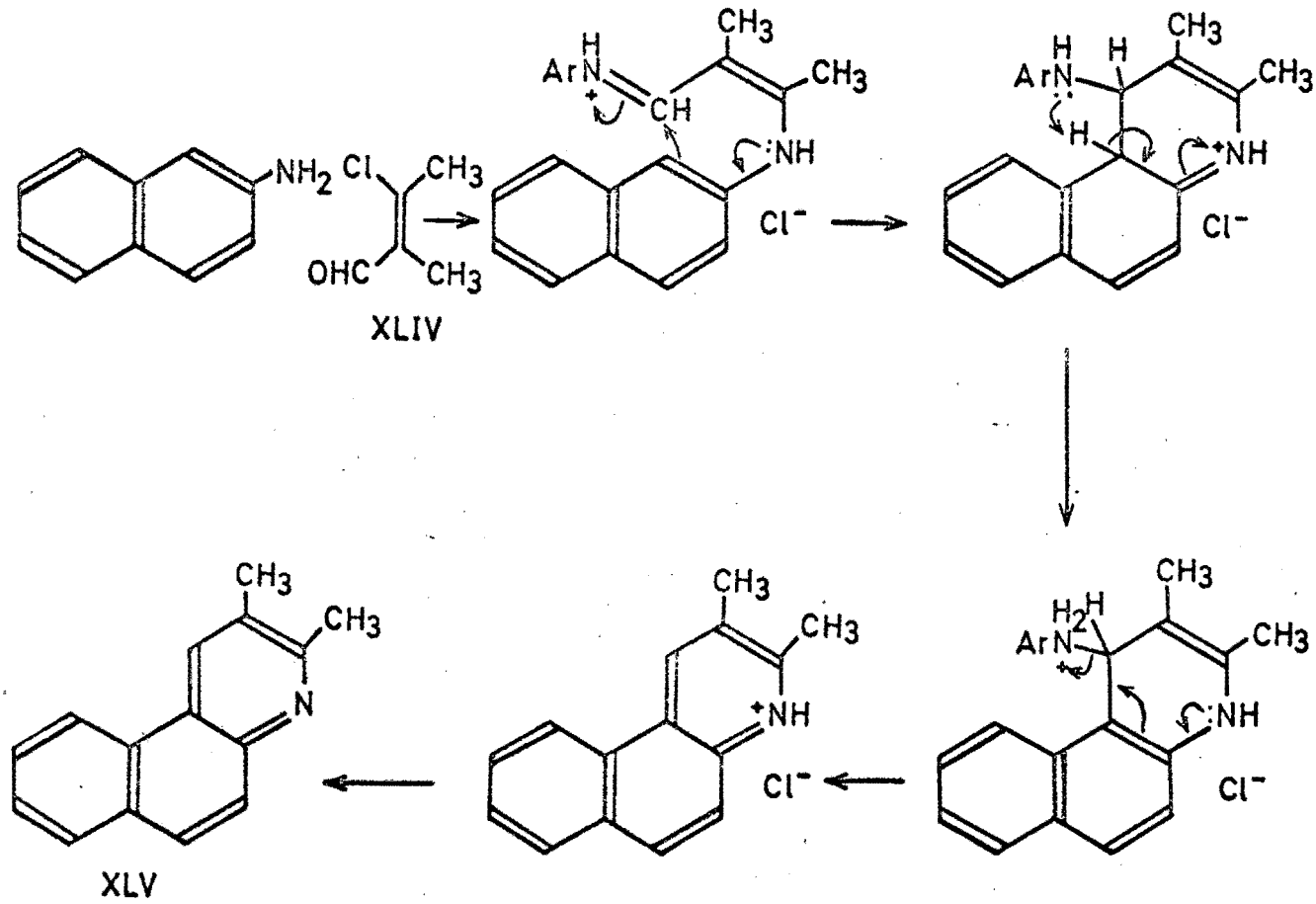
low. The synthesis of acetylated glycosyl-1,2,3,4-tetrahydroquinolines and -aminoquinolines was attempted; 1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3,4-tetrahydroquinoline, 1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,3,4-tetrahydroquinoline and 1-(2,3,4,6- tetra-*O*-acetyl-β-D-glucopyranosyl)-6-aminoquinoline were the only products obtained. The synthesis of D-glucosyl derivatives of 5-methylindoline and 2,5-dimethylindoline could not be achieved; attempts to synthesise 1-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl) benzimidazole from benzimidazole and 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl chloride also failed.

4.1.2. Attempted Syntheses of 2,3-Dihydropyrrolo[3,2-f]- and -[2,3-f]quinolines.

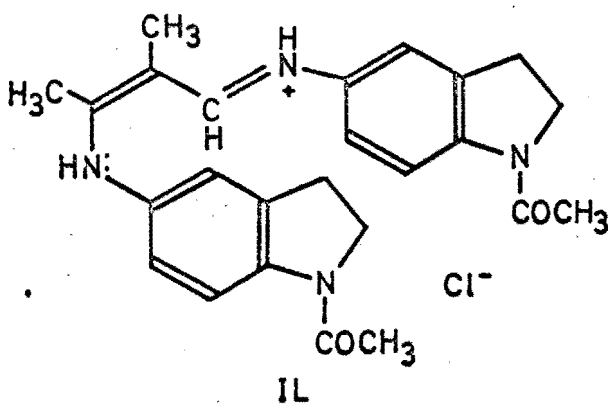
2-Methylpyrrolo[3,2-f]quinoline (XL), prepared from 6-nitroquinoline by the method described by Antonis[95], did not react with D-glucose. An attempt was made to reduce compound XL with diborane in tetrahydrofuran (THF)[96]. The resultant yellow solid was shown by TLC to contain four components. It is possible to hydrogenate both indole[97] and *N*-methylquinolinium iodide[98] over Raney nickel catalyst to indoline and *N*-methyl-1,2,3,4-tetrahydroquinoline respectively. Hydrogenation of 2,7-dimethylpyrrolo[3,2-f]quinolinium iodide to give 2,7-dimethyl-2,3,4,5,6,7-hexahydropyrrolo[3,2-f]-quinoline was attempted under the same conditions. Characterisation as the picrate and as the *N*-acetyl derivative of the colourless unstable liquid product obtained could not be achieved, and an unsuccessful attempt was made to react the hydrogenation product with penta-*O*-acetyl-β-D-glucopyranose. The product from a Skraup synthesis starting from *N*-acetyl-5-diacetylaminoindoline was a small quantity of a yellow solid which could not be identified.

2,3-Dimethyl-β-chlorovinylaldehyde (XLIV) is reported

to react with aromatic amines to give high yields of 2,3-dimethylquinolines[99,100]. 2,3-Dimethylbenzo[f]quinoline(XLV) was prepared from 2-naphthylamine in 59% yield using this method. The mechanism suggested[99] for this reaction is given below:



Reaction of 5-aminoindoline and XLIV resulted in a deep red solution, and the reaction mixture was discarded. Addition of *N*-acetyl-5-aminoindoline[101] (prepared by hydrogenation of *N*-acetyl-5-nitroindoline) to a solution of XLIV resulted in a yellow product for which structure IL is suggested. Attempts to cyclise this product to 2,3-dihydro-5,6-dimethylpyrrolo[3,2-f]quinoline by heating in benzene - EtOH(1:1, v/v), 1-BuOH or dimethylformamide were unavailing.



IL

The cyclisation of *N*-allylaniline to give a mixture of 2-methylindoline and 2-methylindole was described by Hyre and Bader[102] and by Bader *et al*[103]. Similar cyclisation of *N*-allyl-5-aminoquinoline would be expected to result in a mixture of 2-methylpyrrolo[2,3-f]quinoline and 2-methyl-2,3-dihydropyrrolo-[2,3-f]quinoline. The synthesis of *N*-allyl -5-aminoquinoline by the methods described for the preparation of *N*-allyl-8-amino-quinoline[104] and *N*-allylaniline[102,105] was attempted, but without success.

4.2. EXPERIMENTAL.

All melting points, which are uncorrected, were determined on a Fisher-Johns melting-point apparatus. NMR spectra were obtained from dilute solutions in benzene and $CDCl_3$ on a Varian HA-100 spectrometer in the National Chemical Research Laboratory (N.C.R.L.) of the C.S.I.R., Pretoria, and on a Varian A60 spectrometer in this department. TMS was used as internal standard. Mass spectra were determined using the direct insertion technique at 70eV on an A.E.I. MS9 spectrometer at the N.C.R.L., C.S.I.R., Pretoria. The metastable scanning experiments and some of the accurate mass determinations were performed by G.E.C.-A.E.I.(Electronics) Ltd. on an A.E.I. MS 902 spectrometer. IR spectra were recorded on a Perkin-Elmer 237 spectrometer as hexachlorobutadiene (HCBD) mulls on sodium chloride plates or as potassium chloride discs. X-ray diffraction spectra were determined on a Philips X-ray diffractometer using Cu radiation, Ni filter and proportional counter with discrimination. The scanning speed was 2^{o}/min.

TLC was carried out on silica-gel plates with the following solvent systems (all $^{v}/_{v}$):

A. $CHCl_3$ - EtOAc (5:2),

B. MeOH - Water (6:4),

C. Benzene - EtOAc (19:1),

D. Benzene - EtOAc (4:1),

E. Benzene - $CHCl_3$ (1:3),

F. Benzene-Dioxan(2:1).

Components were made visible by spraying with *p*-dimethylamino-benzaldehyde in HCl solution (Ehrlich reagent) or 2*N*-H_2SO_4, or by subliming iodine onto the plate. P.C. was performed on Whatman No. 1 paper, eluted with 1-BuOH - EtOH - water(4:1:5, $^{v}/_{v}$) and sprayed with Ehrlich reagent or *p*-anisidine hydrochloride in 1-BuOH.

Compound	Method of Prep.	% Yield	m.p.	$[\alpha]_D$ ($CHCl_3$)	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula	Mass Spec. Tables	NMR Tables
I	A B	55 47	156-157°	- 94°(c2.2)*	pale yellow needles	51.2	5.1	5.8	51.3	5.3	6.0	$C_{20}H_{24}N_2O_{11}$	2.2.1.1.1,2. 2.2.4.1.1,2.	3.2.1.1. 3.2.2.1.
	(lit)[106,107,108]		182-183° 180° 155°	-101° -101°										
II	A B	46 39	98-100°	-68°(c1.1)*	yellow amorphous powder	51.1	5.1	5.8	51.3	5.3	6.0	$C_{20}H_{24}N_2O_{11}$	2.2.1.2.1,2. 2.2.4.1.1,2.	3.2.1.2. 3.2.2.1.
	(lit)[106,108]		98°	- 72° - 73°										
III	A B	38 42	189-190°	-131°(c2.1)*	pale yellow needles	51.1	5.1	5.9	51.3	5.3	6.0	$C_{20}H_{24}N_2O_{11}$	2.2.1.3.1,2. 2.2.4.1.1,2.	3.2.1.3. 3.2.2.1.
	(lit)[106,108]		210-211° 184°	-150° -153°										
IV	B	32	211-212°	+149°(c1.1)*	bright yellow needles	52.4	5.3	6.8	52.7	5.4	6.8	$C_{18}H_{22}N_2O_9$	2.2.2.1.1,2. 2.2.4.1.1,2.	3.2.1.4. 3.2.2.1.
	(lit)[108]		209°	+123°										
V	A. B E	46 36 41	214-215°	- 31°(c 2.0)*	pale yellow needles	51.3	5.1	7.1	51.5	5.1	7.1	$C_{17}H_{20}N_2O_9$	2.2.3.1.1,2. 2.2.4.1.1,2.	3.2.1.5. 3.2.2.1.
	(lit)[106]		212-213°	- 40°										
VI	A B	23 34	178-179°	+ 6°(c 1.9)*	yellow platelets	51.8	5.1	7.2	51.5	5.1	7.1	$C_{17}H_{20}N_2O_9$	2.2.3.3.1,2. 2.2.4.1.1,2.	3.2.1.7. 3.2.2.1.
	(lit)[106]		177-178°	+ 5°										
VII	B	12	209-210°	-126°(c 1.5)*	yellow amorphous powder								2.2.3.2.1,2. 2.2.4.1.1,2.	

*Measured after 3 min.

TLC: solvent system A.

Table 4.2.1.1. Physical Properties of Acetylated *N*-*p*-nitrophenylglycopyranosylamines.

Microanalyses were performed by Dr. K.G. Fuhr in this department.

4.2.1. Acetylated *N* - *p* - nitrophenylglycopyranosylamines.

Table 4.2.1.1. describes the seven compounds that were prepared in this series (see Fig. 4.1.).

4.2.1.1. 2,3,4,6-Tetra-*O*-acetyl-*N*-*p*-nitrophenyl-β-D-glucopyranosylamine(I).

I was prepared using the following methods:

Method A. D - Glucose (1g, 5.56 mmole) and *p*-nitroaniline (1g, 7.25 mmole) were heated under reflux in a solvent mixture of MeOH-water (8:1 $^{v}/_{v}$, 2.1 ml) and glacial HOAc (1 ml)[106]. The mixture was heated for three minutes after an homogeneous solution had been obtained. After cooling the mixture, the solid product was filtered, washed with cold EtOH and ether, and dried *in vacuo* over P_2O_5. The crude *N*-*p*-nitrophenyl-glucosylamine was acetylated by dissolving it in a mixture of pyridine and acetic anhydride (1:1, 20 ml), and storing at 0^{o} for 12 hr. When this solution was poured into ice-water, the acetylated *N*-*p*-nitrophenylglucosylamine was obtained. Re-crystallisation from EtOH gave I.

Method B. D - Glucose (1g, 5.56 mmole) and *p*-nitroaniline (1g, 7.25 mmole) were suspended in MeOH containing a trace of HCl(0.14 ml conc HCl per 200 ml MeOH, 22 ml) and the mixture was heated under reflux on a steam bath for 15 min[107]. After the clear solution had been cooled, crystals were deposited. These crystals were removed by filtration, dried over P_2O_5 *in vacuo*, and acetylated as in Method A. Also, the mother liquors were evaporated *in vacuo* to give a yellow froth which was acetylated in the same manner. When the pyridine solution was poured into ice-water, crystals were deposited, which were recrystallised from EtOH to give I.

The following two methods were used in further attempts to prepare I.

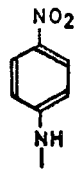
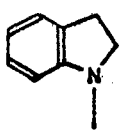
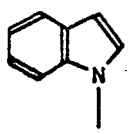
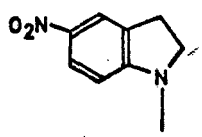
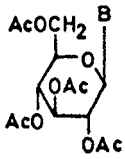
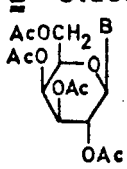
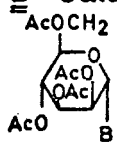
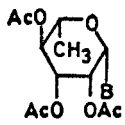
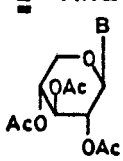
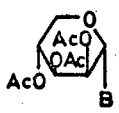
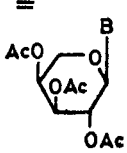
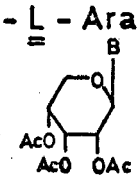
ACETYLATED SUGAR CONFIGURATION	B: 			
	I	VIII	XVI	XXIV
β - D - Gluco - 	II	IX	XVII	XXV
β - D - Galacto - 	III	X	XVIII	XXVI
α - D - Manno - 	IV	XI	XIX	XXVII
β - L - Rhamno - 	V	XII	XX	XXVIII
β - D - Xylo - 	VII	XIII	XXI	
α - D - Lyxo - 	VI	XIV	XXII	XXIX
α - L - Arabino - 		XV	XXIII	
β - D - Ribo -				

FIG. 4.1. Structures of Acetylated Glycopyranosyl Derivatives (I - XXIX) of the Base BH

Method C. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl bromide (1g, 2.5 mmole) and *p*-nitroaniline (0.33g, 2.4 mmole) were mixed with yellow mercuric oxide (0.52g, 2.4 mmole), anhydrous calcium sulphate (drierite, 1g, No. 8 mesh) and mercuric bromi (0.1g) in benzene (20 ml)[89]. The mixture was stirred at room temperature for 17 days, during which time the colour changed from yellow to red. The mixture was filtered through a bed o Celite 521 (Johns Manville) and concentrated *in vacuo*, leaving a syrup. TLC (solvent system A) showed the presence of both acetobromoglucose and *p* - nitroaniline, as well as two further products, neither of which corresponded to I. No more work on this reaction was carried out.

Method D. Penta-*O*-acetyl-β-D-glucopyranose (4.5g, 11.5 mmole) and *p*-nitroaniline (1.43g, 10.4 mmole) were thoroughly mixed and fused at 200° on an oil bath[78,79]. When fusion was compl chloroacetic acid (0.02g) was added and the mixture was heated *in vacuo* (*ca.* 10 mmHg) for 15 min at a bath temp of 150°. After cooling, benzene was added, and the syrupy product was dissolved. Filtration, followed by concentration of the solution *in vacuo*, gave a dark red syrup which on TLC (solvent system A) was shown to contain penta-*O*-acetyl-D-glucose and *p*-nitroaniline, as well as small amounts of two other compound No more work was done on this reaction.

As the m.p. of I did not agree with that reported[106] a sample of I was obtained from Dr. R.D. Guthrie. This sample had m.p. 156-157°, and a mixed m.p. of I with this material was not depressed. The specific rotation of the two materials was found to be the same (-94° in $CHCl_3$) after three min. TLC showed the two materials to be homogeneous and identical; they had identical IR spectra : ν_{max}^{HCBD} cm^{-1} 1760-173(1225-1205(acetyl); 3110-2840 (C-H stretching, for penta-*O*-acet β-D-glucopyranose 2960-2895); N-H stretching at 3400. The X-ray diffraction spectra of I (*ex* Magnin) and I (*ex* Guthr

(Table 4.2.1.2.) showed that, although there are a great many peaks in common, those peaks occurring at larger θ have intensities differing by several orders of magnitude in the two spectra. These differences are probably due to the fact that the crystallinity of the sample prepared here is more clearly defined than that prepared overseas.

Ī (ex Magnin)		Ī (ex Guthrie)		Ī (ex Magnin)		Ī (ex Guthrie)	
d	intensity	d	intensity	d	intensity	d	intensity
14.73	m	14.73	m	4.25	w	4.27	vw
12.68	vw			4.19	vw		
10.28	vs	10.28	vs	4.15	vw	4.16	vw
8.07	m	8.10	m	4.02	vw(sh)	4.03	vw
7.38	vw	7.38	vw	3.97	m	3.97	vw
6.87	vw			3.69	s	3.70	s
6.54	m	6.57	m	3.62	s	3.62	vw
5.38	vw	5.40	vw	3.53	s	3.55	vw
5.11	vw	5.14	vw	3.52	s	3.52	vw
4.92	vw	4.92	vw	3.33	vs	3.34	vw
4.65	vs	4.67	m	3.27	w	3.28	vw
		4.54	vw	3.19	m	3.20	vw
4.49	m	4.49	vw	3.04	vw		
4.40	vw	4.40	vw	2.96	m	2.96	m

s(strong), m(medium), w(weak), sh(shoulder)

Table 4.2.1.2. X-ray Diffraction Spectra of Ī.

4.2.1.1.1. *N* - *p* -Nitrophenyl - β-D-glucopyranosylamine.

NaOMe in MeOH [Na(800mg) in MeOH(100 ml), 2 ml] was added to a solution of Ī(250mg, 0.54 mmole) in MeOH(2 ml) at 0°. The mixture was kept at 0° overnight. The resulting solution was acidified with dilute HOAc and the precipitate was filtered and washed with MeOH and $CHCl_3$ to give *N*-*p*-nitrophenyl-β-D-glucopyranosylamine (120 mg, 75%). TLC(solvent system B) showed, after charring with 2*N*-H_2SO_4, that the product was homogeneous. P.C. showed a single component having R_f 0.58

(*cf.* *N*-*p*-nitrophenyl-β-D-galactopyranosylamine, R_f 0.54; *p*-nitroaniline, R_f 0.88).

4.2.1.2. 2,3,4,6-Tetra-*O*-acetyl-*N*-*p*-nitrophenyl-β-D-galactopyranosylamine (II).

II was prepared from D-galactose (1g, 5.56 mmole) and *p*-nitroaniline (1g, 7.25 mmole) by methods A and B. The IR spectrum of the product, recrystallised from EtOH, showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1715, 1220-1200 (acetyl); 3110-2830 (C-H stretching, for penta-*O*-acetyl-β-D-galactopyranose 3020-2880); N-H stretching at 3350.

4.2.1.3. 2,3,4,6-Tetra-*O*-acetyl-*N*-*p*-nitrophenyl-α-D-mannopyranosylamine (III).

III was prepared by methods A and B from D-mannose (1g, 5.56 mmole) and *p*-nitroaniline (1g, 7.25 mmole). The product, which was recrystallised from EtOH, showed the following bands in its IR spectrum: ν_{max}^{HCBD} cm^{-1} 1755-1730, 1225-1210 (acetyl); 2990-2840 (C-H stretching); 1525, 1370 (NO_2); N-H stretching at 3380.

A sample obtained from Dr. Guthrie had m.p.189-190°, which was not depressed on admixture with III.

The X-ray diffraction spectra (Table 4.2.1.3) of the two materials have few features in common. This suggests that the two materials have different crystalline forms.

III (ex Magnin)		III (ex Guthrie)		III (ex Magnin)		III (ex Guthrie)	
d	intensity	d	intensity	d	intensity	d	intensity
11.42	w	11.33	vw	3.80	vw		
10.58	w(sh)	10.70	s	3.74	vw		
10.50	w(sh)			3.70	vw		
10.38	s					3.64	vw
		8.41	w	3.59	s		
8.34	m			3.49	vs	3.53	vw
6.81	w			3.44	m	3.46	vw
		6.51	w	3.42	m	3.40	vw
6.36	m(sh)			3.28	vw		
6.27	vs	6.26	s	3.21	vw		
6.19	vs			3.12	w		
		5.79	vw	3.06	w		
5.70	vw			2.96	w	2.96	m
5.28	vs	5.29	vs	2.88	vw		
5.02	vw			2.74	w		
4.93	vs	4.93	m			2.61	vw
4.87	m(sh)	4.90	m(sh)			2.59	vw(d)
4.67	vw			2.49	vs	2.47	vw
		4.21	vw(d)	2.42	vw		
		4.18				2.22	vw
4.17	vs					2.15	vw
4.02	vw					2.01	vw
3.95	vw						

d (doublet)

Table 4.2.1.3. X-ray Diffraction Spectra of III.

4.2.1.4. 2,3,4-Tri-*O*-acetyl-*N*-*p*-nitrophenyl-β-L-rhamnopyranosylamine (IV).

IV was prepared from L-rhamnose (1g, 6.1 mmole) and *p*-nitroaniline (1g, 7.25 mmole) by method B. The IR spectrum gave the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1740, 1225-1200 (acetyl); 2980-2860 (C-H stretching); 1500, 1355(NO_2); N-H stretching at 3380. The X-ray diffraction spectrum is presented in Table 4.2.1.4.

IV				VI			
d	intensity	d	intensity	d	intensity	d	intensity
11.05	vs	4.17	w	11.63	vw	4.01	w
7.60	w	4.11	w	9.74	s	3.85	s
7.39	vs	4.01	s	9.25	m	3.75	m
7.03	vs	3.88	w	8.28	m	3.60	w
6.74	m	3.75	w	7.92	w	3.58	m
6.52	vs	3.72	w	7.04	s	3.56	vs
6.10	w	3.38	s	5.02	m	3.43	w
5.61	w	3.26	s	4.72	vs	3.39	w
5.43	m	3.01	m	4.53	w	3.35	m
4.62	w	2.84	w	4.42	vs	3.29	w
4.53	s	2.32	m	4.14	vs	2.38	m
4.48	w	2.28	w	4.04	m		

Table 4.2.1.4. X-ray Diffraction Spectra of IV and VI.

4.2.1.5. 2,3,4-Tri-*O*-acetyl-*N*-*p*-nitrophenyl-β-D-xylopyranosylamine (V).

V was prepared by methods A and B from D-xylose (1g, 6.66 mmole) and *p*-nitroaniline (1g, 7.25 mmole). Method E (below) was also used.

Method E. Tetra-*O*-acetyl-β-D-xylopyranose (0.40g, 1.26 mmole) and *p*-nitroaniline (0.63g, 4.2 mmole) were dissolved in a mixture of absolute EtOH (40 ml) and acetic acid (1 ml) with slight warming. Overnight, yellow prisms were deposited. Recrystallisation from EtOH yielded V. The IR spectrum of V showed the following bands: ν_{max}^{HCBD} cm^{-1} 1740-1720, 1240-1215 (acetyl); 2980-2850 (C-H stretching, for tetra-*O*-acetyl-β-D-xylopyranose 3130-2830); 1480, 1330(NO_2); N-H stretching at 3360. The X-ray diffraction spectra of V and a sample of tri-*O*-acetyl-*N*-*p*-nitrophenyl-β-D-xylopyranosylamine obtained from Dr. Guthrie (a mixed m.p. of the two materials was not depressed) are given in Table 4.2.1.5. From this table it can be seen that the two materials have many peaks in common, but that those occurring at larger θ have intensities that

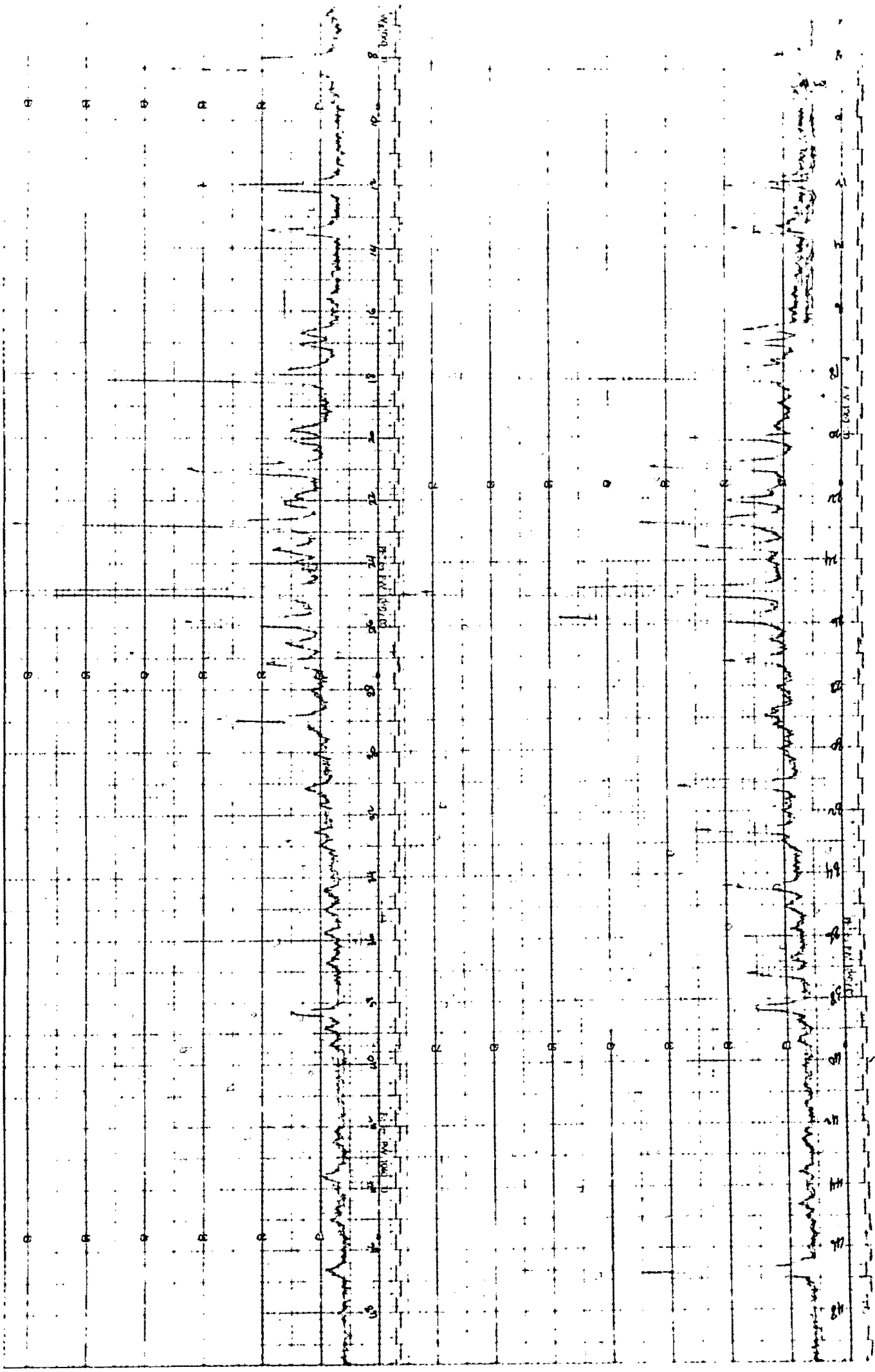


Fig. 4.2 X-ray Diffraction Spectra of V. Lower trace ex Magnin, Upper trace ex Guthrie.

Compound	Method of Prep.	% Yield	m.p.	$[\alpha]_D$($CHCl_3$)	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula	Mass Spec. Tables	NMR Tables	TLC Solvent Systems
VIII	F G H	74 27 7	119-120°	+8°(c2.1)	white needles	58.8	6.2	3.2	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.1.1,2. 2.2.4.2.1,2.	3.2.1.1. 3.2.2.2.	A C
	(lit)[77]		117.8-118.5°	+11°(c6)											
IX	I J	58 11	109°-110°	+27°(c7.6)	white needles	57.3	6.2	2.9	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.2.1,2. 2.2.4.2.1,2.	3.2.1.2. 3.2.2.2.	A D
	(lit)[113]		108.5-109.5°	+20°(c5)											
X	I	26	130-131°	+58°(c2.4)	white needles	58.4	5.9	3.2	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.3.1,2. 2.2.4.2.1,2.	3.2.1.3. 3.2.2.2.	A D
XI*	I	33	164-165°	+34°(c8.0)	white needles	61.1	6.4	3.6	61.4	6.4	3.6	$C_{20}H_{25}NO_7$	2.2.2.1.1,2. 2.2.4.2.1,2.	3.2.1.4. 3.2.2.2.	A D
XII	K L	25 38	108-109°	+47°(c4.2)	white needles	60.4	6.0	3.9	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.1.1,2. 2.2.4.2.1,2.	3.2.1.5. 3.2.2.2.	A C
XIII	K	41	147-148°	-104°(c4.0)	white needles	60.4	5.9	3.9	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.2.1,2. 2.2.4.2.1,2.	3.2.1.6. 3.2.2.2.	A C
XIV	I	42	121-122°	+102°(c4.5)	white needles	60.5	6.1	3.5	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.3.1,2. 2.2.4.2.1,2.	3.2.1.7. 3.2.2.2.	A D
XV	I	59	150-151°	+ 76°(c4.5)	white needles	60.2	6.3	3.5	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.4.1,2. 2.2.4.2.1,2.	3.2.1.8. 3.2.2.2.	A C
	(lit)[94] [121]		151-153° 147-148°	+ 76°(c1) + 69°(c5)											

*obtained as a mixture of anomers.

Table 4.2.2.1. Physical Properties of Acetylated Glycopyranosylindolines.

Com-pound	Method of Prep.	% Yield	m.p.	$[\alpha]_D$(CHCl$_3$)	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula	Mass Spec. Tables	NMR Tables	TLC Solvent Systems
VIII	F G H	74 27 7	119-120°	+8°(c2.1)	white needles	58.8	6.2	3.2	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.1.1,2. 2.2.4.2.1,2.	3.2.1.1. 3.2.2.2.	A C
	(lit)[77]		117.8-118.5°	+11°(c6)											
IX	I J	58 11	109°-110°	+27°(c7.6)	white needles	57.3	6.2	2.9	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.2.1,2. 2.2.4.2.1,2.	3.2.1.2. 3.2.2.2.	A D
	(lit)[113]		108.5-109.5°	+20°(c5)											
X	I	26	130-131°	+58°(c2.4)	white needles	58.4	5.9	3.2	58.8	6.1	3.1	$C_{22}H_{27}NO_9$	2.2.1.3.1,2. 2.2.4.2.1,2.	3.2.1.3. 3.2.2.2.	A D
XI*	I	33	164-165°	+34°(c8.0)	white needles	61.1	6.4	3.6	61.4	6.4	3.6	$C_{20}H_{25}NO_7$	2.2.2.1.1,2. 2.2.4.2.1,2.	3.2.1.4. 3.2.2.2.	A D
XII	K L	25 38	108-109°	+47°(c4.2)	white needles	60.4	6.0	3.9	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.1.1,2. 2.2.4.2.1,2.	3.2.1.5. 3.2.2.2.	A C
XIII	K	41	147-148°	-104°(c4.0)	white needles	60.4	5.9	3.9	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.2.1,2. 2.2.4.2.1,2.	3.2.1.6. 3.2.2.2.	A C
XIV	I	42	121-122°	+102°(c4.5)	white needles	60.5	6.1	3.5	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.3.1,2. 2.2.4.2.1,2.	3.2.1.7. 3.2.2.2.	A D
XV	I	59	150-151°	+ 76°(c4.5)	white needles	60.2	6.3	3.5	60.5	6.2	3.8	$C_{19}H_{23}NO_7$	2.2.3.4.1,2. 2.2.4.2.1,2.	3.2.1.8. 3.2.2.2.	A C
	(lit)[94] [121]		151-153° 147-148°	+ 76°(c1) + 69°(c5)											

*obtained as a mixture of anomers.

Table 4.2.2.1. Physical Properties of Acetylated Glycopyranosylindolines.

The small quantity of product obtained precluded the acquisition of NMR and X-ray diffraction spectra and an analysis. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1710, 1235-1210(acetyl); 3100-2840(C-H stretching, for tetra-*O*-acetyl-α-D-lyxose 3040-2820); N-H stretching at 3400.

4.2.2. Acetylated Glycopyranosylindolines.

Table 4.2.2.1. describes the eight compounds prepared in this series.

4.2.2.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)indoline (VIII).

VIII was prepared by the following methods:

Method F. Penta-*O*-acetyl-β-D-glucopyranose (the α-anomer can also be used; 1g, 2.56 mmole), indoline (1g, 8.40 mmole) and HOAc (1 ml) were dissolved in absolute EtOH(20 ml), and kept at room temp overnight[76,77]. The crystals that were deposited were recrystallised from EtOH. Addition of water to the mother liquors afforded *N*-acetylindoline as white needles, m.p. 104-105° (lit[109]106°).

Method G. D-Glucose (9g,50.0 mmole), indoline (6g, 50.5 mmole) and water (1 ml) were stirred on a boiling water bath for 30 min after solution had occurred[76,77]. The solution was diluted with MeOH(20 ml), and filtered. The mother liquors were evaporated *in vacuo*, and the residue was washed with ether and dried *in vacuo* over P_2O_5 to give a pale yellow froth. This froth was dissolved in pyridine (80 ml), cooled to 0°, and acetic anhydride (35 ml) was added. After remaining at 0° overnight, the solution was poured, with stirring, on to chipped ice. The crystals that deposited were collected and recrystallised several times from EtOH to yield VIII.

Method H. A modification of the stereospecific glycoside synthesis developed by Kochetkov *et al*[91,92] was used to prepare VIII. A mixture of 3,4,6-tri-*O*-acetyl-α-D-glucopyranose 1,2-(ethyl orthoacetate)[110,111] (150mg, 0.40 mmole), indoline (47mg, 0.40

mmole) and anhydrous EtOH(2 ml) was stirred with gentle warming (50°) until solution was complete[112]. After two hr at room temp, the solvent was removed *in vacuo*, and the syrup was crystallised from ether-light petroleum (40-60°). TLC (solvent system A) showed VIII to be the major product. The minor product, which afforded VIII on acetylation, is possibly 1-(3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl)indoline. Recrystallisation of the product from EtOH afforded VIII.

When indoline and the orthoacetate were boiled with mercuric bromide[92], in nitromethane, the minor product above was formed preferentially. This was acetylated to obtain VIII, but otherwise this experiment was not continued.

The IR spectrum of VIII showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1750, 1260-1180(acetyl); 3090-2840(C-H stretching, for penta-*O*-acetyl-β-D-glucopyranose 2960-2895, for indoline 3010-2840); N-H stretching at 3360 absent.

4.2.2.1.1. 1-(β-D-Glucopyranosyl)indoline.

NaOMe in MeOH [Na(800mg) in MeOH(100ml),2ml] was added to a solution of VIII (100mg, 0.22 mmole) in MeOH (1 ml) at 0°. The mixture was kept at this temp overnight. CO_2 gas was passed into the solution to destroy NaOMe and the solvent was removed *in vacuo*. The product, which is unstable, was kept for several weeks at 0° in a vacuum desiccator. P.C. of the product showed R_f 0.69.

4.2.2.2. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-indoline(IX).

IX was prepared by the following methods:

METHOD I. Penta-*O*-acetyl-β-D-galactopyranose (1g, 2.56 mmole) was dissolved in hot EtOH (18 ml). On cooling to 40°, indoline (0.61g, 5.12 mmole) and acetic acid (0.9 ml) were added. The solution was stirred at room temp[94] until no further reaction took place (4 days); the reaction was monitored by TLC (solvent system D). The solvent volume was reduced *in vacuo* to 6 ml

and the solution was cooled to 0^{o} overnight. The crystals that deposited were filtered, washed with light petroleum ($40-60^{o}$) and recrystallised from EtOH.

METHOD J. D-Galactose (2.2g, 12.2 mmole) and indoline (1.46g, 12.2 mmole) were dissolved in MeOH (20 ml) containing a trace of HCl (see 4.2.1.1.), by heating under reflux for 30 min. Filtration of the hot solution to remove any undissolved material afforded a yellow solution which, after evaporation *in vacuo*, and drying over P_2O_5, gave a yellow froth. The froth was acetylated as in method A above to give white crystals which, on recrystallisation from EtOH gave IX.

The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1740, 1235-1210(acetyl); 3080-2860(C-H stretching, for penta-*O*-acetyl-β-D-galactopyranose 3020-2880, for indoline 3010-2840); N-H stretching at 3360 absent.

4.2.2.3. 1-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-indoline (X).

X was prepared by method I from penta-*O*-acetyl-α-D-mannopyranose[114] (2g, 5.12 mmole) and indoline (1.22g, 10.24 mmole). Recrystallisation from EtOH gave X, which showed the following bands in its IR spectrum: ν_{max}^{HCBD} cm^{-1} 1760-1730, 1230-1210(acetyl); 3090-2830(C-H stretching, for indoline 3010-2840); N-H stretching at 3360 absent.

4.2.2.4. 1-(2,3,4-Tri-*O*-acetyl-α(+β)-L-rhamnopyranosyl)-indoline (XI).

XI was prepared by method I from tetra-*O*-acetyl-α-L-rhamnopyranose[115] * (3.3g, 9.94 mmole) and indoline (2.16g, 18.12 mmole) to give dark red needles, which on recrystallisation from EtOH afforded XI. This compound was

*Prepared by treating methyl-α-L-rhamnopyranoside[116] with acetic anhydride and conc H_2SO_4 as in reference[114].

found by NMR to be a mixture of α- and β- anomers. No attempt was made to separate the two anomers. The IR spectrum of XI showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1725, 1240-1210 (acetyl); 3100-2850(C-H stretching); N-H stretching at 3360 absent.

4.2.2.5. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)indoline(XII).

XII was prepared by the following methods:

Method K. Tetra-*O*-acetyl-β-D-xylopyranose[117] (0.40g, 1.27 mmole) and indoline (0.50g, 4.2 mmole) were dissolved in a mixture of absolute EtOH(10 ml) and acetic acid (1 ml) with slight warming. Storage at room temp overnight, followed by removal of the solvent *in vacuo*, gave a syrup which was induced to crystallise by trituration with EtOH. Recrystallisation from EtOH afforded XII.

Method L. Tetra-*O*-acetyl-β-D-xylopyranose (5.03g, 15.7 mmole) was dissolved in EtOH (88 ml) and treated with freshly distilled indoline (3.52g, 29.6 mmole) and acetic acid (4.5 ml). The solution was stirred at room temp for two days and then was concentrated *in vacuo* to 10 ml. A seed crystal of XII was added and the crystals that deposited were washed with cold EtOH and recrystallised from EtOH.

The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1730, 1240-1210(acetyl); 3080-2860(C-H stretching, for tetra-*O*-acetyl-β-D-xylopyranose 3130-2830, for indoline 3010-2840); N-H stretching at 3360 absent.

4.2.2.6. 1-(2,3,4-Tri-*O*-acetyl-α-D-lyxopyranosyl)indoline(XIII).

XIII was prepared from tetra-*O*-acetyl-α-D-lyxopyranose[118] (0.20g, 0.63 mmole) and indoline (0.25g, 2.1 mmole) by method K. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1720, 1225-1200(acetyl); 3080-2860(C-H stretching, for tetra-*O*-acetyl-α-D-lyxopyranose 3040-2820, for indoline 3010-2840); N-H

stretching at 3360 absent.

4.2.2.7. 1-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)indoline(XIV).

XIV was prepared by method I from tetra-*O*-acetyl -α-L-arabinopyranose* (3.03g, 9.52 mmole) and indoline (2.26g, 19.04 mmole). The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1730, 1240-1210(acetyl); 3060-2860(C-H stretching, for indoline 3010-2840); N-H stretching at 3360 absent.

4.2.2.8. 1-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)indoline(XV).

XV was prepared by method I[94] from indoline (0.7g, 5.9 mmole) and tetra-*O*-acetyl-β-D-ribopyranose[119,120] (1g, 3.14 mmole). The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1730, 1240-1210(acetyl); 3080-2790(C-H stretching, for tetra-*O*-acetyl-β-D-ribopyranose 3090-2880, for indoline 3010-2840); N-H stretching band at 3360 absent.

4.2.3. Acetylated Glycopyranosylindole Derivatives.

Table 4.2.3.1. describes the properties of the seven compounds prepared in this series.

4.2.3.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-indole[76,77,112] (XVI).

XVI was prepared by the following methods:

Method M. VIII(0.45g, 1.0 mmole) and chloranil(0.23g, 1.0 mmole) in dry *m*-xylene(15 ml) were heated under reflux, and a portion (4 ml) of the xylene was removed by distillation[77]. The solution that remained was heated under reflux for 6 hr, water being excluded by means of a $CaCl_2$ tube. A further 7 ml xylene was distilled, the solution was filtered hot and the filtrate was

*Prepared by treating methyl-β-L-arabinopyranoside with acetic anhydride and conc H_2SO_4 as in reference[114].

Compound	Method of Prep.	% Yield	m.p.	$[\alpha]_D$ ($CHCl_3$)	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula	Mass Spec. Tables	NMR Tables
XVI	M	25	134-135°	+2° (c2.2)	White needles	58.8	5.7	3.2	59.1	5.6	3.1	$C_{22}H_{25}NO_9$	2.2.1.1.1,2.	3.2.1.1.
	N	78											2.2.4.3.1,2.	3.2.2.3.
	(lit)[77,94]		148.5-149° 149.5-152°	+1.5° (c5.5)										
XVII	N	48	128-129°	+9° (c3.9)	white needles	59.2	5.7	3.1	59.1	5.6	3.1	$C_{22}H_{25}NO_9$	2.2.1.2.1,2. 2.2.4.3.1,2.	3.2.1.2. 3.2.2.3.
	(lit)[113]		123-125°	+12° (c4)										
XIX	N	32	117-118°	+20° (c3.0)	white plates	61.8	6.0	3.5	61.7	6.0	3.6	$C_{20}H_{23}NO_7$	2.2.2.1.1,2. 2.2.4.3.1,2.	3.2.1.4. 3.2.2.3.
XX	N	70	152.0-152.5°	+15° (c3.9)	white needles	60.7	5.8	3.7	60.8	5.6	3.7	$C_{19}H_{21}NO_7$	2.2.3.1.1,2. 2.2.4.3.1,2.	3.2.1.5. 3.2.2.3.
XXI	N		syrup										2.2.3.2.1,2. 2.2.4.3.1,2.	
XXII	N	40	136.5-137.0°	+54° (c3.9)	white platelets	60.6	5.7	3.8	60.8	5.6	3.7	$C_{19}H_{21}NO_7$	2.2.3.3.1,2. 2.2.4.3.1,2.	3.2.1.7. 3.2.2.3.
XXIII	N	42	173-174°	+41° (c4.6)	white plates	59.8	5.5	3.6	60.8	5.6	3.7	$C_{19}H_{21}NO_7$	2.2.3.4.1,2. 2.2.4.3.1,2.	3.2.1.8. 3.2.2.3.
	(lit)[94,121]		169-171° 165-166°	+40° +37.28°										

Solvent systems A and D used throughout.

Table 4.2.3.1. Physical Properties of Acetylated Glycopyranosylindoles.

cooled to 0° overnight. The precipitated crystals were collected, washed with cold EtOH, and recrystallised from EtOH. The mother liquors were passed through a short column (containing *ca.*4g basic alumina), and the fractions containing XVI were combined to give a further crop of crystals.

Method N.

VIII (3.0g, 6.7 mmole) in dry *m*-xylene (80 ml) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ,1.51g, 6.7 mmole) and the solution was heated under reflux for 3 hr. The solution was filtered while hot, and half of the solvent was removed *in vacuo*[94]. On cooling this solution overnight, crystals were deposited. These were recrystallised from EtOH.

A sample of XVI recovered from the benzene solution used in the NMR study of this compound (Section 3) had m.p. 159.5°. Seeding a benzene solution of the material of lower m.p. with a crystal of that of higher m.p. resulted in crystals having m.p. 157.5°. Suvorov and Preobrazhenskaya [77] report two crystalline forms of XVI melting at 149° and 158°. The results above suggest that there may be three crystalline modifications of this compound.

The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1742, 1255-1200(acetyl); 3140-2890(C-H stretching, for penta-*O*-acetyl-β-D-glucopyranose 2960-2895, for indole 3110-2880); N-H stretching at 3360 absent.

4.2.3.2. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-indole(XVII).

IX (1g, 2.23 mmole) and DDQ (0.51g, 2.24 mmole) in *m*-xylene (10 ml) were treated as in method N for 4 hr. Recrystallisation from EtOH gave the required product. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1730, 1235-1210(acetyl); 3150-2900(C-H stretching, for penta-*O*-acetyl-β-D-galactopyranose 3020-2880, for indole 3110-2880); N-H stretching at 3360 absent.

4.2.3.3. 1-(2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl)-indole(XVIII).

An attempt to prepare XVIII from X (1g, 2.23 mmole) and DDQ (0.51g, 2.24 mmole) by method N resulted in a dark red syrup which could not be purified.

4.2.3.4. 1-(2,3,4-Tri-*O*-acetyl-β-L-rhamnopyranosyl)indole(XIX).

XIX was prepared from XI (0.50g, 1.27 mmole) and DDQ (0.29g, 1.28 mmole) by method N. The product was recrystallised from EtOH. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1730, 1225-1210(acetyl); 3180-2890(C-H stretching, for indole 3110-2880); N-H stretching at 3360 absent.

4.2.3.5. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)indole(XX).

XX was prepared by method N from XII (0.66g, 1.75 mmole) and DDQ(0.40g, 1.76 mmole). The product was recrystallised from EtOH. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1720, 1240-1210(acetyl); 3105-2890(C-H stretching, for tetra-*O*-acetyl-β-D-xylopyranose 3130-2830, for indole 3110-2880); N-H stretching at 3360 absent.

4.2.3.6. 1-(2,3,4-Tri-*O*-acetyl-α-D-lyxopyranosyl)indole(XXI).

XIII (0.70g, 1.86 mmole) was treated with DDQ(0.44g, 1.94 mmole) according to method N to give a red syrup. Treatment with charcoal in EtOH gave a pale pink syrup.

4.2.3.7. 1-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)indole(XXII).

Method N was employed to prepare XXII from XIV (0.50g, 1.33 mmole) and DDQ(0.30g,1.32 mmole). After recrystallisation from EtOH, the product showed the following bands in its IR spectrum: ν_{max}^{HCBD} cm^{-1} 1750-1730, 1225-1205(acetyl); 3110-2890(C-H stretching, for indole 3110-2880); N-H stretching at 3360 absent.

4.2.3.8. 1-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)indole(XXIII).

XV(0.50g, 1.33 mmole) and DDQ(0.30g, 1.32 mmole) were treated under the conditions of method N to form XXIII, which was recrystallised from EtOH. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1725, 1240-1215(acetyl); 3140-2900(C-H stretching, for tetra-*O*-acetyl-β-D-ribopyranose 3090-2880, for indole 3110-2880); N-H stretching band at 3360 absent.

4.2.4. Acetylated Glycopyranosyl-5-nitroindolines.

Table 4.2.4.1. describes the six compounds prepared in this series.

4.2.4.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-5-nitroindoline(XXIV)[112].

XXIV was prepared by the following methods:

Method O. 5-Nitroindoline(2.75g,16.7 mmole), D-glucose(3.0g, 16.7 mmole) and water (1 ml) were stirred on a boiling water bath for 1 hr after a clear solution had been obtained. On cooling, the reaction mixture solidified. The solid was dissolved in MeOH(20 ml), filtered and evaporated *in vacuo* to give a yellow froth. After drying over P_2O_5 *in vacuo*, the froth was acetylated as in method A. Recrystallisation from EtOH gave the expected product.

Method P. 5-Nitroindoline(1.2g, 7.3 mmole) and D-glucose(1.0g, 5.5 mmole) in MeOH (20 ml) containing a trace of HCl were heated under reflux on a water bath until solution was complete. The solution was filtered and the solvent removed *in vacuo* to give a yellow froth. The froth was acetylated as described in method A, and the product was recrystallised from EtOH. Concentration of the mother liquor from this recrystallisation resulted in the deposition of a second compound, *N*-acetyl-5-nitroindoline, as yellow needles, m.p. 175-176°(lit 173.5-175.5°[122]). (Found: C, 58.1; H, 4.8; N, 13.7. Calc. for $C_{10}H_{10}N_2O_3$: C, 58.2; H, 4.9; N, 13.6%).

Com-pound	Method of Prep.	% Yield	m.p.	$[\alpha]_D$($CHCl_3$)	Crystals	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Formula	Mass Spec. Tables	NMR Tables
XIV	O	38	162-163° (d)	+30°(c0.4)	yellow needles	52.6	5.2	4.9	53.4	5.3	5.7	$C_{22}H_{26}N_2O_{11}$	2.2.1.1.1,2. 2.2.4.4.1,2.	3.2.1.1. 3.2.2.4.
	P	43												
XV	P	78	162.5-163.5°	+67°(c4.3)	yellow plates	53.3	5.3	5.6	53.4	5.3	5.7	$C_{22}H_{26}N_2O_{11}$	2.2.1.2.1,2. 2.2.4.4.1,2.	3.2.1.2. 3.2.2.4.
XVI	P	23	219-220°	-56°(c2.3)	yellow needles	53.5	5.4	5.8	53.4	5.3	5.7	$C_{22}H_{26}N_2O_{11}$	2.2.1.3.1,2. 2.2.4.4.1,2.	3.2.1.3. 3.2.2.4.
XVII	O	34	145-147°	+29°(c4.3)	yellow plates	54.5	5.3	6.8	55.0	5.5	6.4	$C_{20}H_{24}N_2O_9$	2.2.2.1.1,2. 2.2.4.4.1,2.	3.2.1.4. 3.2.2.4.
XVIII	P	39	188-189°	+126°(c2.0)	yellow rods	54.0	5.1	6.4	54.0	5.3	6.6	$C_{19}H_{22}N_2O_9$	2.2.3.1.1,2. 2.2.4.4.1,2.	3.2.1.5. 3.2.2.4.
XIX	P	50	152-154°	-107°(c2.3)	yellow needles	53.9	5.2	6.5	54.0	5.3	6.6	$C_{19}H_{22}N_2O_9$	2.2.3.3.1,2. 2.2.4.4.1,2.	3.2.1.7. 3.2.2.4.

d decomposition point. TLC solvent systems A and C used throughout.

Table 4.2.4.1. Physical Properties of Acetylated Glycopyranosyl-5-nitroindolines.

was recrystallised from EtOH. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1730, 1230-1215(acetyl); 3100-2850(C-H stretching); 1510, 1360(NO_2); N-H stretching at 3360 absent.

4.2.4.6. 1-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-5-nitroindoline(XXIX).

L-Arabinose(1.0g, 6.7 mmole) and 5-nitroindoline (1.2g, 7.3 mmole) were reacted under the conditions of method P to give XXIX, which was recrystallised from EtOH. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1750-1715, 1240-1200(acetyl); 3100-2890(C-H stretching); 1510, 1370(NO_2); N-H stretching at 3360 absent.

4.2.4.7. 1-(2,3,4-Tri-*O*-acetyl-β-D-ribopyranosyl)-5-nitroindoline.

Attempts to prepare this compound by methods P and I failed to yield sufficient product for isolation. Only a trace of product was noted on TLC (solvent system A) even after heating the solution under reflux for 14 days.

4.2.5. Acetylated Glycopyranosyl-5-nitroindoles.

4.2.5.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-5-nitroindole[35](XXX).

The following two methods were used in attempts to prepare XXX.

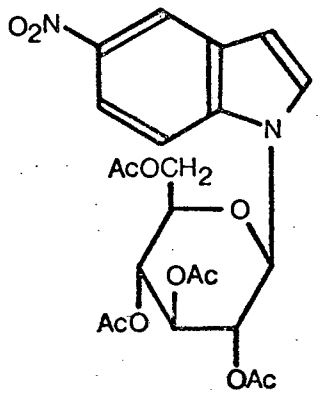
Method Q. XXIV(4.94g, 10.0 mmole) in dry *m*-xylene(120 ml) was heated under reflux for 3 hr with DDQ(2.27g, 10.0 mmole). The hot solution was filtered, and the volume was reduced to 60 ml *in vacuo*. The crystals that were deposited were recrystallised twice from EtOH, with the aid of charcoal as decolorising agent, to give pale yellow needles, which were shown by NMR to be predominantly unchanged XXIV. Further reduction of the volume of the mother liquor resulted in a further crop of yellow needles, shown by NMR to be a mixture

of XXIV and XXX (no separation on TLC could be effected). After two days a further crop of crystals was collected from the mother liquor; this product was shown by NMR (Tables 3.2.1.1. and 3.2.2.5) and mass spectroscopy (Tables 2.2.1.1.1,2 and 2.2.4.5.1,2) to be the expected product. Recrystallisation from EtOH afforded 0.4g(8%) of fine yellow needles, m.p. 195-197°, $[\alpha]_D$+7°(c 2 in $CHCl_3$).(Found:C,53.9; H,4.9; N,5.5. $C_{22}H_{24}N_2O_{11}$ requires:C,53.7; H,4.9; N,5.7%). TLC (solvent systems A and C) showed the presence of the sugar moiety in the yellow spot obtained. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1740, 1245-1205(acetyl); 3120-2860(C-H stretching); 1525, 1355(NO_2); N-H stretching at 3300 absent.

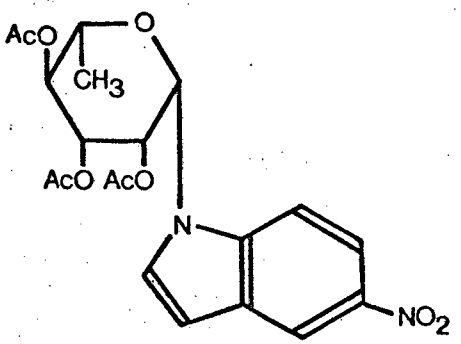
Method R. XXIV(150 mg, 0.30 mmole), *N*-bromosuccinimide(125 mg, 0.70 mmole) and benzoyl peroxide (*ca*.1 mg) were warmed in CCl_4 for 30 min.[123] A mixture of Br_2 and CCl_4 was distilled while the volume was kept constant by addition of CCl_4 containing a trace of benzoyl peroxide. When the reaction was essentially complete (1 hr; monitoring by u.v. spectroscopy), the solution was cooled, and the yellow crystals (140 mg) were collected, m.p. 226-232°. TLC (solvent system A) indicated the crystals to be a mixture of succinimide and a 5-nitroindole-containing compound which could not be isolated. Evaporation of the mother liquor *in vacuo* gave a yellow syrup, which was crystallised by triturating in EtOH to a yellow solid. TLC(solvent system A) showed this solid to consist of two sugar-containing components, neither of which corresponded to XXX. No further work on this method was done.

4.2.5.2. 1-(2,3,4-Tri-*O*-acetyl-β-L-rhamnopyranosyl)-5-nitroindole(XXXI).

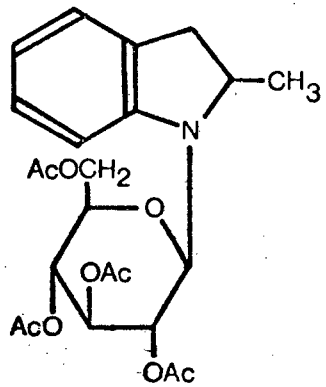
XXXI was prepared by method Q from XXVII (0.50g, 1.15 mmole) and DDQ(0.27g, 1.19 mmole) to give yellow plates on recrystallisation from EtOH, m.p. 194-195°, $[\alpha]_D$-13°(c 2.8 in $CHCl_3$).



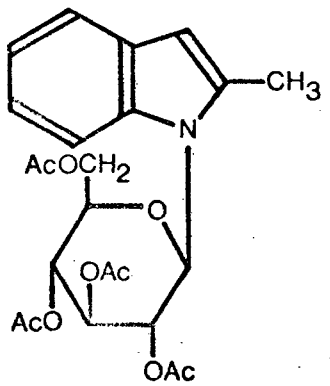
XXX



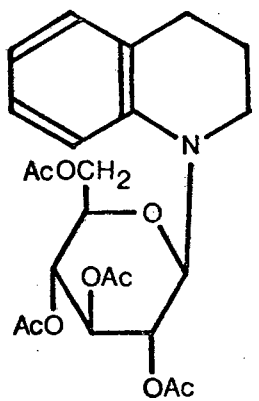
XXXI



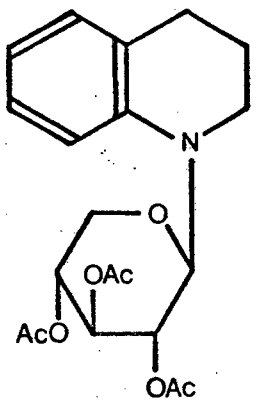
XXXII



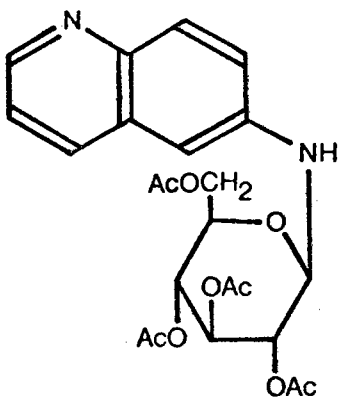
XXXIII



XXXIV



XXXV



XXXVI

(Found: C, 55.3; H, 5.2; N, 6.6. $C_{20}H_{22}N_2O_9$ requires: C, 55.3; H, 5.1; N, 6.5%). Yield 120 mg(24%). TLC(solvent systems A and C) showed the presence of the sugar moiety in the yellow spot found. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1725, 1230-1210(acetyl); 3105-2840(C-H stretching); 1510, 1370 (NO_2); N-H stretching at 3300 absent. The mass spectra are presented in Tables 2.2.2.1.1,2 and 2.2.4.5.1, 2 and the NMR spectra in Tables 3.2.1.4 and 3.2.2.5.

4.2.5.3. Attempts to prepare 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-5-nitroindole, 1-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-5-nitroindole, 1-(2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl)-5-nitroindole and 1-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl)-5-nitroindole resulted in products having m.p. 149-152°, 201-202°, 229-230° and 165-166° respectively. NMR in each case showed the product to be a mixture of the starting material and the expected product. Attempts at separation by fractional crystallisation failed in each case.

4.2.6. Acetylated Glycopyranosyl-2-methylindolines.

4.2.6.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-2-methylindoline[112] (XXXII).

XXXII was prepared by the following methods:

Method S. 2-Methylindoline(2.0g, 15.0 mmole), penta-*O*-acetyl-β-D-glucopyranose(3g, 7.69 mmole) and acetic acid (2 ml) were dissolved in EtOH (40 ml) with gentle warming and the solution was kept at room temp for 1 week. TLC(solvent system E) showed the presence of both *N*-acetyl-2-methylindoline and XXXII in this solution. After removal of one-half of the solvent *in vacuo*, and cooling overnight, crystals were deposited. These were washed with cold EtOH, and recrystallised from EtOH to give white needles, m.p. 135-136°, $[\alpha]_D$ -5°(c 0.84 in $CHCl_3$).(Found: C,59.2; H,6.3; N, 3.1. $C_{23}H_{29}NO_2$ requires: C, 59.6; H, 6.3; N, 3.0%). Concentration of the mother liquor gave a further crop of crystals;

total yield 0.3g(8.5%). The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1760-1740, 1270-1215(acetyl); 3020-2840(C-H stretching, for penta-*O*-acetyl-β-D-glucopyranose 2960-2895, for 2-methylindoline 3070-2840); N-H stretching at 3360 absent. The NMR and mass spectral data are presented in Tables 3.2.1.1. and 2.2.1.1.1,2 respectively.

2-Methylindoline(2.9g, 21.8 mmole) and D-glucose(3.05g, 17.0 mmole) were reacted under the conditions of Method B. After neutralisation of the HCl with NH_4OH solution, the solvent was removed *in vacuo*, and the resultant syrup was dried over P_2O_5. Acetylation and recrystallisation of the solid product from EtOH afforded 1.2g(15%) XXXII.

Synthesis of XXXII by the following methods was attempted:

a) Method T. 2-Methylindoline(2.0g, 15.0 mmole), 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide[124](6.15g, 15.0 mmole), mercuric cyanide(3.73g, 14.8 mmole), drierite(7.5g, No. 8 mesh) and nitromethane[89](149 ml, dried by azeotropic distillation) were heated under reflux for 3 hr. The hot solution was filtered, the filter-cake was washed with hot nitromethane (15 ml) and the washings were added to the dark green filtrate. The solvent was removed *in vacuo*, leaving a dark syrup which could neither be crystallised nor separated.

b) Method U. 2-Methylindoline(3.7g, 27.8 mmole) and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide(3.7g, 9.04 mmole) were dissolved in dry benzene (20 ml) and heated under reflux for 30 min. After storage at room temp overnight, the colour of the solution changed from green to brown. The solvent was removed *in vacuo*, leaving a dark syrup. TLC(solvent systems A and F) showed a complex mixture of products, and the syrup was discarded.

c) Penta-*O*-acetyl-β-D-glucopyranose(1.0g, 2.56 mmole) was reacted with 2-methylindoline(0.68g, 5.12 mmole) under the conditions

of Method I. TLC(solvent systems A and C) showed that only a very small quantity of product had formed after 5 weeks, and the mixture was discarded.

4.2.6.2. An attempt to prepare 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-methylindoline from penta-*O*-acetyl-β-D-galactopyranose by method I showed no product after 3 weeks, and the solution was discarded.

4.2.7. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-2-methylindole[35] (XXXIII).

XXXII (0.71g, 1.53 mmole) and DDQ (0.35g, 1.54 mmole) were heated under reflux in dry *m*-xylene (25 ml) for 3 hr. The hot reaction mixture was filtered, the volume of the filtrate reduced to 10 ml *in vacuo*, and the concentrated solution allowed to cool. After separation of the brown precipitated crystals (100mg), the xylene volume was further reduced; the solution was cooled to 0° and a second crop of the solid collected. TLC(solvent systems A and E) showed that the product (400 mg, 57%), which was homogeneous, contained both indole and sugar moieties (R_f slightly less than that of XXXII.)

A solution of XXXIII in hot benzene was treated twice with charcoal, and the filtrate was concentrated to give light brown crystals. Recrystallisation from EtOH yielded pale yellow needles, m.p. 160-161°, $[\alpha]_D$ -3°(c 6.7 in $CHCl_3$). (Found: C, 59.9; H, 6.0; N, 2.8. $C_{23}H_{27}NO_9$ requires: C, 59.9; H, 5.9; N, 3.0%). The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1735, 1255-1210(acetyl); 3080-2840(C-H stretching; for penta-*O*-acetyl-β-D-glucopyranose 2960-2895, for 2-methylindole 3080-2840); N-H stretching at 3390 absent. The NMR and mass spectral data are presented in Tables 3.2.1.1. and 2.2.1.1.1,2 respectively.

4.2.8. Acetylated Glycopyranosyl-1,2,3,4-tetrahydroquinolines.

4.2.8.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-1,2,3,4-tetrahydroquinoline[35] (XXXIV).

1,2,3,4-Tetrahydroquinoline(10.0g, 75.3 mmole) and D-glucose(13.5g, 75.0 mmole) were reacted under the conditions of method B. Removal of one-half of the solvent *in vacuo*, and cooling to 0° overnight afforded white crystals. These were dried *in vacuo* over P_2O_5, and acetylated as in method A to give 3.5g XXXIV as white needles on recrystallisation from EtOH. Evaporation of the mother liquor, and acetylation of the yellow syrupy residue as before gave the same product (12.0g, total yield 43%), m.p. 133-135°, $[\alpha]_D$ + 70° (c 4.4 in $CHCl_3$). (Found: C, 59.7; H, 6.5; N, 3.0. $C_{23}H_{29}NO_9$ requires: C,59.7; H, 6.3; N, 3.0%). TLC(solvent systems C and E) showed the presence of the sugar moeity in the single spot obtained. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1755-1720, 1250-1215(acetyl); 3040-2900(C-H stretching, for penta-*O*-acetyl-β-D-glucopyranose 2960-2895, for 1,2,3,4-tetrahydroquinoline 3040-2780); N-H stretching at 3410 absent. The NMR and mass spectral data are presented in Tables 3.2.1.1. and 3.2.1.5. and 2.2.1.1.1,2 and 2.2.4.6.1,2 respectively.

4.2.8.2. 1-(2,3,4-Tri-*O*-acetyl-β-D-xylopyranosyl)-1,2,3,4-tetrahydroquinoline(XXXV).

XXXV was prepared by method B from D-xylose(1.13g, 7.5 mmole) and 1,2,3,4-tetrahydroquinoline(1.0g, 7.5 mmole) as white needles on recrystallisation from EtOH(1.2g, 41%), m.p. 121-122°, $[\alpha]_D$ + 102°(c 3.2 in $CHCl_3$).(Found: C,60.6; H, 6.4; N, 3.5. $C_{20}H_{25}NO_7$ requires: C,61.4; H, 6.4; N, 3.6%). TLC (solvent systems C and E) showed the presence of the sugar moiety in the single spot. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1765-1750, 1230-1210(acetyl); 3080-2760(C-H stretching, for tetra-*O*-acetyl-β-D-xylopyranose 3130-2830, for 1,2,3,4-tetrahydroquinoline 3040-2780); N-H stretching at 3410 absent.

The NMR and mass spectral data are presented in Tables 3.2.1.5. and 3.2.2.6. and 2.2.3.1.1,2 and 2.2.4.6.1,2 respectively.

4.2.8.3. Synthesis of 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1,2,3,4-tetrahydroquinoline, 1-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-1,2,3,4-tetrahydroquinoline, 1-(2,3,4-tri-*O*-acetyl-β-L-rhamnopyranosyl)-1,2,3,4-tetrahydroquinoline and 1-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl)-1,2,3,4-tetrahydroquinoline from 1,2,3,4-tetrahydroquinoline(1.0g, 7.5 mmole) and aldose (7.5 mmole) by method B, followed by acetylation in each case resulted in a dark syrup, which could not be purified.

Method I was also used in an attempt to prepare 1-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1,2,3,4-tetrahydroquinoline, but after two weeks only minute amounts of the expected product could be discerned by TLC.

4.2.9. Acetylated Glucopyranosylaminoquinolines.

4.2.9.1. 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-6-aminoquinoline[35] (XXXVI).

6-Aminoquinoline(0.52g, 3.6 mmole) and D-glucose (0.5g, 2.8 mmole) were reacted under the conditions of method B to give 0.64g(48%) of XXXVI as white needles on recrystallisation from EtOH, m.p. 217-218°, $[\alpha]_D$ -6°(c 21.9 in $CHCl_3$; equilibrium value). (Found: C, 58.1; H, 5.7; N, 5.7. $C_{23}H_{26}N_2O_9$ requires: C, 58.2; H, 5.5; N, 5.9%). TLC(solvent systems A and E) showed the presence of the sugar moiety in the single spot obtained. The IR spectrum showed the following bands: ν_{max}^{HCBD} cm^{-1} 1765-1740, 1255-1210(acetyl); 3080-2900(C-H stretching); N-H stretching at 3250 (for 6-aminoquinoline 3300, 3390). The NMR and mass spectral data are presented in Tables 3.2.1.1. and 2.2.1.1.1,2 respectively.

4.2.9.2. The synthesis of the 5-and 7-amino-analogues of XXXVI by method B failed to yield a product that could be isolated.

4.2.10. Studies Towards the Synthesis of Glycosylpyrrolo-[3,2-f]quinolines.

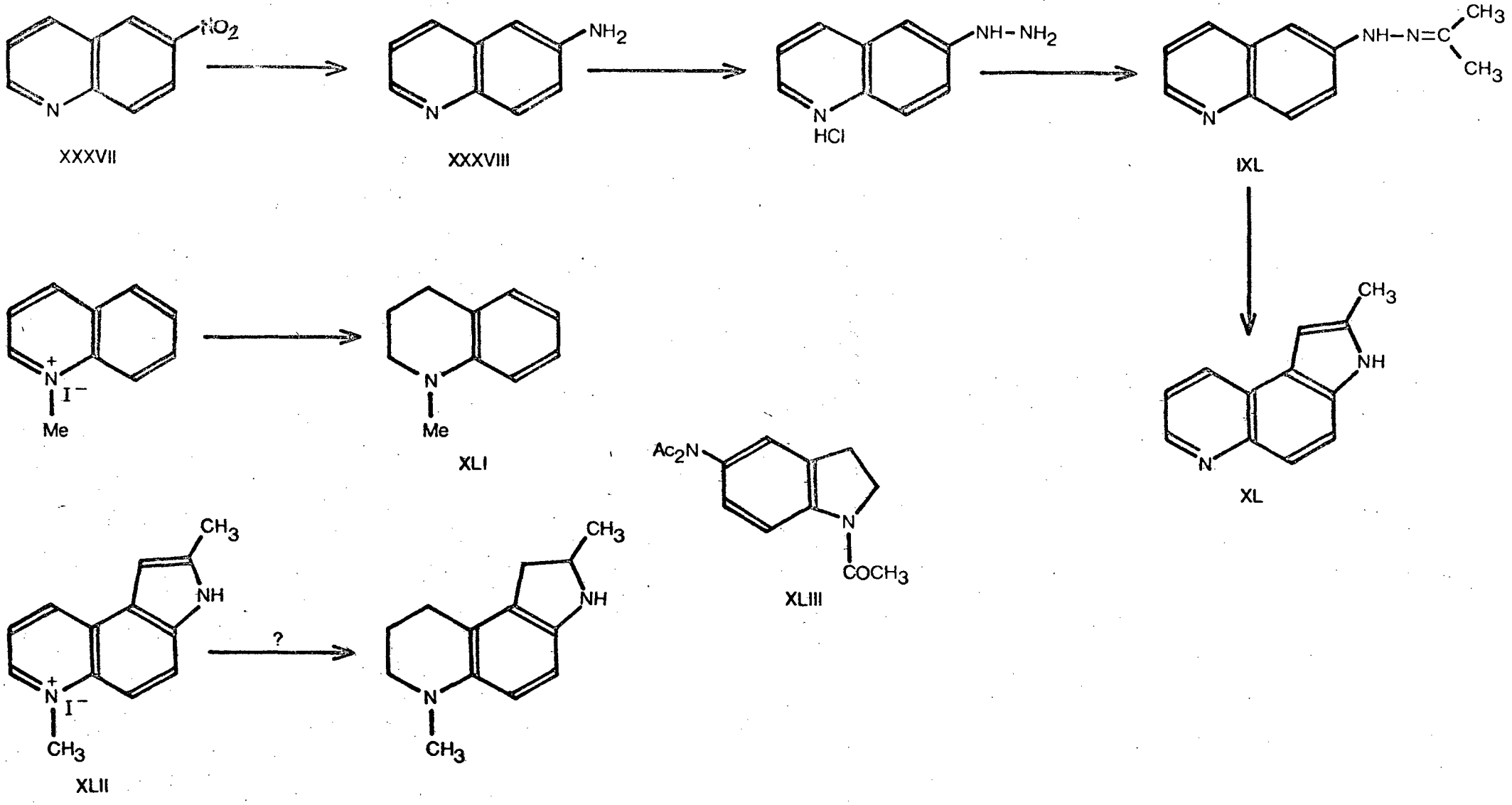
4.2.10.1. 2-Methylpyrrolo[3,2-f]quinoline[95,125].

4.2.10.1.1. 6-Nitroquinoline(XXXVII) was prepared from *p*-nitroaniline according to the method described by Antonis[95] in 65% yield. Pale yellow needles, m.p. 148-149°(lit[95]150°) were obtained. (Found: C,62.1; H,3.7; N,15.3. Calc. for $C_9H_{10}N_2O_2$: C,62.0; H,3.5; N, 16.1%).

4.2.10.1.2. 6-Aminoquinoline(XXXVIII). XXXVII(50g, 0.28 mole) was dissolved in a mixture of conc HCl(375 ml) and acetic acid (250 ml). Stannous chloride (250g,1.32 mole) was slowly added while the solution was stirred. After remaining at 60° for 1 hr, the solution was diluted and cooled[126]. Cold NaOH (40% $^{w}/_{v}$) was added until pH11 was reached, and the solution was kept at 0° overnight. The crystals that were deposited were recrystallised from EtOH-light petroleum (40-60°). Removal of all solvent by sublimation gave 36.8g (90%) of pale yellow rods, m.p. 113-114°(lit[95]114°). (Found: C,75.0; H,5.3; N,18.9. Calc. for $C_9H_8N_2$: C,75.0; H,5.6; N,19.4%).

4.2.10.1.3. 6-Hydrazinoquinoline hydrochloride was prepared from XXXVIII by the method described by Antonis[95] to yield the yellow product used in 4.2.10.1.4.

The removal of excess tin was also effected by elution with water from a column of Amberlite IR-120(H^+) ion exchange resin. After removal of the tin, the hydrazinoquinoline hydrochloride was eluted with dilute HCl. Evaporation of the solvent *in vacuo* afforded the yellow 6-hydrazinoquinoline hydrochloride.


NO2
NH2
NH–NH2
HCl
NH–N=C
CH3
CH3
XXXVII
XXXVIII
IXL
XL
Me
I−
XLI
Ac2N
COCH3
XLIII
CH3
NH
?
CH3
XLII

4.2.10.1.4. Acetone-6-quinolyl hydrazone(IXL). The product obtained above was used in this preparation[95]. The orange-brown solid, m.p. 160-162°(lit[95]163-164°) was prepared in 65% yield. (Found: C,72.0; H,7.1; N,20.4. Calc. for $C_{12}H_{13}N_3$: C,72.4; H,6.5; N,21.2%).

4.2.10.1.5. 2-Methylpyrrolo[3,2-f]quinoline(XL). IXL(3.6g, 18.1 mmole), powdered zinc chloride (4.4g, 32.7 mmole, fused) and *p*-cymene (16 ml, dried by azeotropic distillation) were heated under reflux for 3 hr at a bath temp of 180-185°[126]. The *p*-cymene was removed by filtration and the solid product was washed with light petroleum (40-60°). After drying, the solid was powdered and dissolved in hot HCl(1*N*, 200 ml), and the red solution obtained was poured with stirring into NaOH (25% $^{w}/_{v}$, 300 ml). After cooling, the brown crystals were collected, recrystallised from $CHCl_3$-light petroleum (40-60°) and freed from solvent by sublimation at 200° and 0.5 mmHg to give 1.5g (45%) of a pale yellow solid, m.p. 200°(lit[95]198°). (Found: C,78.8; H,5.5; N,15.5. Calc. for $C_{12}H_{10}N_2$: C,79.1; H,5.5; N,15.4%). The 60 MHz NMR spectrum of XL showed the following parameters:- H_1 at τ 0.47 (signal disappears on addition of D_2O); H_3 at τ 3.23; H_4 at τ 1.49(J_{45}=8.6, J_{46}=1.8); H_5 at τ 2.58(J_{56}=4.4); H_6 at τ 1.19; H_8 and H_9 at τ 2.18 and 2.35(J_{89}=8.8); CH_3 at τ 7.43. (Chemical shifts are measured relative to τ$CHCl_3$=2.73).

4.2.10.2. Attempted Synthesis of 1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)pyrrolo[3,2-f]quinoline.

XL(180 mg, 10.0 mmole) and D-glucose (140 mg, 7.8 mmole) were heated under reflux in MeOH(3 ml) containing a trace of HCl, for 15 min after a clear solution had been obtained.[107] Evaporation of the solvent *in vacuo*, followed by acetylation of the product, resulted in penta-*O*-acetyl-β-D-glucopyranose as the only product isolated.

4.2.10.3. Attempted Synthesis of 2-Methyl-2,3-dihydropyrrolo-[3,2-f]quinolines.

4.2.10.3.1. To indole (7.0g, 60.0 mmole) in tetrahydrofuran (10ml, THF) at 0°, a solution of diborane in THF (0.72 mmole/ml, 78 mmole) was added, according to the method of Plieninger *et al*[96]. 2.0g(28%) of a chromatographically pure product, b.p. 82-83° at 3 mmHg, was isolated. The IR spectrum of this product (indoline) showed the following bands: ν_{max} cm^{-1} 3360(N-H stretching); 3010-2840(C-H stretching); 1610,1485,1460 (C=C vibrations); 1240 (C-N stretching); 735(C-H deformation).

4.2.10.3.2. 5-Methylindoline. 5-Methylindole (2.0g, 15.3 mmole) in THF (5ml) was treated with a solution of diborane in THF (0.79 mmole/ml, 19.8 mmole). The solution was kept at 0° for 20 hr. The method of Plieninger *et al*[96] was used to recover 0.62g (31%) of a colourless liquid, b.p. 240-241°.

4.2.10.3.3. 2-Methylpyrrolo[3,2-f]quinoline (1.0g, 5.5 mmole) in dry THF (2 ml) was treated with a solution of diborane in THF (6.9 mmole) at 0°, the reaction mixture being kept at this temp for four days. Water was then added to decompose excess diborane. Removal of the solvents *in vacuo* gave yellow crystals. The product was dissolved in dilute HCl, to break up boron complexes, and this was followed by the addition of NaOH(40% $^{w}/_{v}$) until the solution was alkaline. Extraction of the basic solution with $CHCl_3$ afforded a yellow solution which was shown by TLC (solvent system F) to consist of four components. Separation of these fractions was not achieved.

4.2.10.3.4. Hydrogenation of Indole. Indole (1.0g, 8.55 mmole) in EtOH (5 ml) was mixed with Raney nickel W2[127] (*ca.*400 mg) and hydrogenated for 7 hr at 1500 psi and 90-100°[97]. The cooled solution was filtered and conc HCl (8.55 mmole) was added. After the solution had cooled, ether (10 ml) was added and the resultant precipitate collected, dissolved in NaOH (50% $^{w}/_{v}$) and

extracted into ether. Distillation of the product, b.p. 232-234°(lit[109] 228-230°), followed by TLC (solvent system C), showed that only a trace of indole remained in solution.

4.2.10.3.5. Hydrogenation of Quinoline Methiodide.

4.2.10.3.5.1. Quinoline methiodide[128,129] (3.85g, 14.4 mmole) in EtOH (52 ml) was treated with diethylamine (3.2 ml) and Raney nickel W2 (*ca.* 100 mg) and hydrogenated at 900 psi and 140° for 2 hr[98]. After the colourless solution had been filtered, Ag_2CO_3 (4.00g, 14.4 mmole) was added, and after shaking, the solution was again filtered. After removal of the solvent *in vacuo*, the product was dissolved in benzene; TLC (solvent system A) showed one major component. Distillation of the product gave 0.9g (43%) *N*-methyl-1,2,3,4-tetrahydroquinoline(XLI), b.p. 84-85° at 2 mmHg (lit[109] 112° at 8 mmHg).

4.2.10.3.5.2. 1,2,3,4-Tetrahydroquinoline(2.0g, 15.0 mmole) and methyl iodide (2.24g, 15.5 mmole) in acetone (10 ml) were treated with potassium carbonate (5.1g) and heated under reflux for 3 hr[98]. After the solution was filtered, the solvent was evaporated *in vacuo* to give 1.0g (41%) XLI as a pale yellow liquid, b.p. 94-96° at 3.6 mmHg (lit[109] 112°at 8 mmHg).

4.2.10.3.5.3. Quinoline methiodide (0.5g, 1.8 mmole) in EtOH (7 ml) was treated with diethylamine (0.4 ml) and hydrogenated for 7 hr over Raney nickel W2 at 1500 psi and 100°. TLC of the product (solvent system C) showed XLI to be the major component. It was decided to use these conditions for the hydrogenation of 2,7-dimethylpyrrolo[3,2-f]quinolinium iodide.

4.2.10.3.6. 2,7-Dimethylpyrrolo[3,2-f]quinolinium iodide[130] (XLII ; 550mg, 17.0 mmole) was hydrogenated under the conditions described in 4.2.10.3.5.3. above. After the solution had been filtered to remove the catalyst, $NaHCO_3$ was added to destroy HI (with Ag_2CO_3 a dark complex was formed). After shaking the solution, it was filtered in an atmosphere of nitrogen, and the

solvent was removed *in vacuo* at 20° to give a pale yellow syrup. Redissolving the syrup in benzene, followed by filtration of the solution and evaporation of the solvent *in vacuo*, gave 340mg (99%) of a very pale yellow syrup, which was kept under nitrogen. (When open to the atmosphere the syrup rapidly decomposed and became dark brown). Attempts to distil the product resulted in viscous red oils showing several components on TLC. Treatment of the product with acetic anhydride in pyridine gave an immediate blue coloration. After this solution had been stored at 0° for 12 hr, poured into ice-water, and extracted into chloroform, a brown solution was obtained. After removal of the solvent *in vacuo*, the NMR spectrum showed *N*-methyl and *N*-acetyl singlets, but only a broad singlet at τ *ca.* 8.5 for the *C*-methyl group, for which a doublet had been expected. Acetylation of the yellow syrup in a boiling solution of acetic anhydride and pyridine gave a red syrup. In neither case was purification possible. An ethanolic solution of the syrup was treated with picric acid, but no crystalline derivative could be obtained.

4.2.10.3.7. The syrupy product formed as described in 4.2.10.3.6. above (160mg) was stirred with penta-*O*-acetyl-β-D-glucopyranose (101mg, 0.4 mmole) at room temp for 10 days under the conditions used in method I. TLC (solvent systems A and E) showed that only a very small quantity of a sugar-containing product had been formed, but this could not be isolated.

4.2.10.4. Attempted Synthesis of 2,3-Dihydropyrrolo[3,2-f]-quinolines.

4.2.10.4.1. Hydrogenation of 5-Nitroindoline. 5-Nitroindoline (1.64g, 10.0 mmole) was hydrogenated in acetone (50 ml) over PtO_2 (0.2g) at room temp and 50 psi for 12 hr. The solution formed was initially colourless, but on contact with air it became violet. After removal of the solvent *in vacuo*, the product was heated under reflux in excess acetic anhydride (10 ml) for 1 hr.

Removal of the solvent *in vacuo*, followed by recrystallisation of the product from EtOH, gave 0.4g (15%) *N*-acetyl-5-diacetylaminoindoline(XLIII), m.p. 193-195° with softening at 175°. (Found: C,64.2; H,6.1; N,10.4. $C_{14}H_{16}N_2O_3$ requires: C,64.6; H,6.2; N,10.8%). The 60 MHz NMR spectrum of this compound in $CDCl_3$ showed three *N*-acetyl groups and no exchangeable hydrogens.

4.2.10.4.2. Skraup Reaction on XLIII. XLIII(0.26g, 1.08 mmole), syrupy arsenic acid (75% $^{w}/w$, 0.61g), H_2SO_4 (70% $^{v}/v$, 1 ml) and anhydrous glycerol (0.23g, 2.5 mmole) were heated at 210° for 2 hr. After cooling the solution, it was diluted to 15 ml with water and made alkaline with NaOH (50% $^{w}/v$). The solid product was filtered and extracted with boiling $CHCl_3$ to give a dark red solution, which on evaporation afforded a yellow solid. This solid was dissolved in EtOH and treated with light petroleum (40-60°) to give a small quantity (*ca.* 20 mg) of a dark brown material. Evaporation of the mother liquors and recrystallisation of the product from ether-light petroleum (40-60°) gave a yellow, amorphous product (*ca.* 10mg). Neither product could be identified.

4.2.10.4.3. Attempted Synthesis of 2,3-Dihydro-5,6- dimethyl-pyrrolo[3,2-f]quinoline.

4.2.10.4.3.1. Preparation of 2,3-Dimethyl-β-chlorovinylaldehyde (XLIV) [99,100,131]. Phosphorus oxychloride (20.0 ml, 21.8 mmole) was mechanically stirred at room temp while dimethylformamide (22 ml, 28.4 mmole) was added. After the mixture had been kept at 0° for 30 min, methyl ethyl ketone (10 ml, 13.9 mmole) was slowly added with stirring over a period of 1 hr. The mixture was stirred overnight as it warmed to room temp. Hydrolysis of the complex formed was effected by pouring the solution on to chipped ice. The product was extracted into ether, washed with aqueous $NaHCO_3$, and dried over Na_2SO_4. After evaporation of

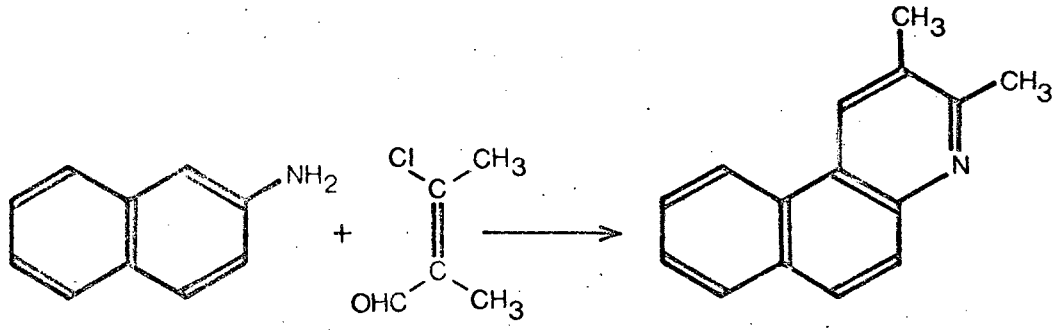
the solvent *in vacuo* XLIV was distilled *in vacuo* to yield 7.35g (45%) of a colourless liquid, b.p. 50-51° at 18 mmHg, 57-59° at 21 mmHg, 60-62° at 26 mmHg (lit[99] 57-59° at 21 mmHg).

The product was stored for several months at -10° as a white solid; at 0° it decomposes after two weeks.

4.2.10.4.3.2. Preparation of 2,3-Dimethylbenzo[f]quinoline(XLV).

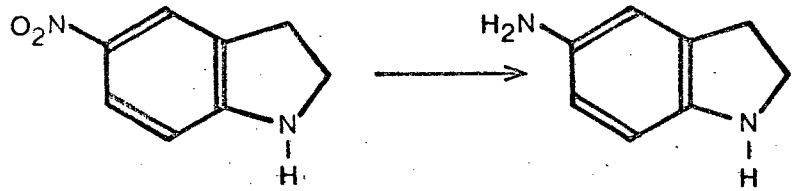
To XLIV (3.3g, 28.0 mmole) in 1-BuOH(10 ml) was added a warmed solution of 2-naphthylamine (3.98g, 28.0 mmole) in 1-BuOH(20 ml)[99]. The solution was heated under reflux for 2 hr. Soon after boiling began, yellow crystals were deposited. Filtration of the hot solution gave yellow needles which were recrystallised from MeOH. An ethanolic solution of these crystals showed the presence of halide ions on treatment with an ethanolic solution of $AgNO_3$. An aqueous solution of the crystals was made alkaline by the addition of NaOH, and the solvent was removed *in vacuo*. The product was distributed between $CHCl_3$ and water and the two layers were separated. Evaporation of the $CHCl_3$ *in vacuo* gave a pale yellow solid which, upon recrystallisation from light petroleum (40-60°), gave 3.4g (59%) of very pale yellow rods, m.p. 125.0-125.5° (lit[132] 124-125°). (Found: C,87.3; H,6.5; N,6.7. Calc. for $C_{15}H_{13}N$: C,86.9; H,6.3; N,6.8%). The picrate had m.p. *ca.* 260°. (Found: C,57.8; H,3.9; N,12.5. Calc. for $C_{21}H_{16}N_4O_7$: C,57.8; H,3.7; N,12.8%.)

4.2.10.4.3.3. Reduction of 1-Nitronaphthalene as a Model Experiment. 1-Nitronaphthalene (1.77g, 1.12 mmole) in MeOH (10 ml) was mixed with Raney nickel W2 (*ca.* 500 mg) and hydrazine hydrate (10 ml, excess) was added in small portions over 2 hr at 50-60°[133]. The solution was kept at this temp for 8 hr, and then cooled. Filtration of the solution followed by evaporation of the solvent *in vacuo* gave a brown solid, which on distillation *in vacuo* gave a white solid, *i.e.*, 1-naphthylamine, m.p. 50-51° (lit[109] 51°).

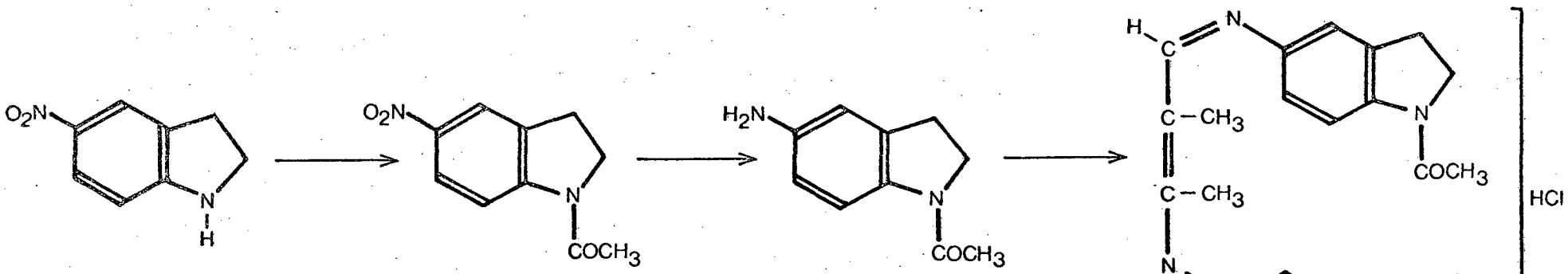


XLIV

XLV



XLVI



XLVIII

IL

4.2.10.4.3.4. 5-Aminoindoline(XLVI) was prepared by the reduction of 5-nitroindoline (1.64g, 10.0 mmole) by the method described in 4.2.10.4.3.3. above. The yellow product that resulted was recrystallised from *n*-heptane to give XLVI (700mg, 52%) as white needles, m.p. 65-68° (lit[133] 67-68.5°). These needles could be kept indefinitely *in vacuo*, but decomposed rapidly in air.

4.2.10.4.3.5. Attempted Synthesis of 2,3-Dihydro-5,6-dimethylpyrrolo[3,2-f]quinoline.

The following methods were used:

a) XLVI (700mg, 5.2 mmole) in 1-BuOH (10 ml) and XLIV (620mg, 7.3 mmole) in 1-BuOH (10 ml) were mixed at room temp and the resulting dark solution was heated under reflux for 6 hr. Soon after boiling commenced, a solid was precipitated. TLC (solvent system F) showed the solid to contain one major and three minor components, but isolation of these could not be achieved.

b) XLVI (155mg, 1.15 mmole) and XLIV (138mg, 1.15 mmole) in benzene-EtOH (1:1 $^{v}/_{v}$, 10 ml each) were slowly mixed at 0°. After addition of the first drop of XLIV the solution became blood-red. Further addition only deepened the colour. TLC (solvent system F) indicated that polymerisation had occurred.

c) XLVI (140mg, 1.04 mmole) and XLIV (125mg, 1.04 mmole) in 1-BuOH (5 ml each) were slowly mixed at -10°. A deep red colour was immediately produced. TLC (solvent system F) showed that polymerisation had occurred.

4.2.10.4.3.6. *N*-Acetyl-5-nitroindoline(XLVII) was prepared by heating 5-nitroindoline (1.0g, 6.1 mmole) under reflux for 30 min in acetic anhydride (10 ml). Removal of the solvent *in vacuo*, and recrystallisation of the product from EtOH afforded 1.05g (84%) yellow needles, m.p. 175-176° (lit[122] 173.5-175.5°).

(Found: C,58.1; H,4.8; N,13.7. Calc. for $C_{10}H_{10}N_2O_3$: C,58.3; H,4.9; N,13.6%).

4.2.10.4.3.7. Preparation of *N*-Acetyl-5-aminoindoline (XLVIII)

Two methods were used to prepare XLVIII:

a) XLVII (1.1g, 5.34 mmole) in EtOH (35 ml) was hydrogenated at 50 psi at room temp over 10% palladium on charcoal catalyst[134] (0.5g). After 18 hr the solution was filtered and the solvent removed *in vacuo*[101]. The solid product was recrystallised from benzene as white needles (400mg, 44%), m.p. 183-185° (lit[134] 184-185°, 185-186°[135]). (Found: C, H,6.9; N,15.7. Calc. for $C_{10}H_{12}N_2O$: C,68.2; H,6.9; N,15.9%

b) XLVII (0.50g, 2.43 mmole) was dissolved in conc HCl (3.5 ml) on a boiling water bath. Stannous chloride (3.95g, 20.9 mmole) was added and the mixture heated for 45 min. The clear solution was poured into water, and the resultant solution made alkaline. On cooling, white crystals (*ca.* 40mg, 9%) separated. TLC (solvent system A) showed the product to be XLVIII.

4.2.10.4.3.8. Reaction of 2,3-Dimethyl-β-chlorovinylaldehyde and *N*-Acetyl-5-aminoindoline.

Several sets of conditions were employed in this reaction:

a) XLVIII (170mg, 0.97 mmole) in benzene - EtOH (1:1 $^{v}/_{v}$, 10 m at 0° and XLIV (117 mg, 1.07 mmole) in the same solvent mixture (5 ml) were slowly mixed, and the solution was stirred at 0°. When the addition was complete, a pale orange precipitate was deposited from the yellow solution. After warming to room temp, the reaction mixture was stirred for 36 hr. The precipitate was collected by filtration and recrystallised from EtOH. The product (IL, 180mg, 86%) was found to be an amorphous orange solid m.p. 218.5-219.5°. (Found: C,65.4; H,6.5; N,12.1; Cl,8.0. $C_{25}H_{29}N_4O_2Cl$ requires : C,66.3; H,6.5; N,12.4; Cl,7.8%).

The IR spectrum showed the following bands: ν_{max}^{KCl} cm^{-1} 1635-1625(acetyl); 1595(C=N); 1320(C-N); 1020, 820(C-H, aromatic). The mass spectrum showed the ion of highest mass to be that at $^{m}/_{e}$ 416. Ion peaks at $^{m}/_{e}$ 36 and 38 were present, indicating a molecular weight of 452. The ion peak at $^{m}/e$ 240 might arise by a loss of $^{m}/_{e}$ 176 from $^{m}/e$ 416 (*i.e.* a loss of *N*-acetyl-5-aminoindoline), while that at $^{m}/_{e}$ 198 (the base peak) would probably be formed by a loss of ketene from the fragment $^{m}/_{e}$ 240. Other major ions are found at $^{m}/_{e}$ 176 (*N*-acetyl-5-aminoindoline), 134(5-aminoindoline) and 133 [(5-aminoindoline-1)]. Thus the structure IL has been suggested for this compound.

b) XLVIII (30mg, 0.17 mmole) in benzene - EtOH (1:1 $^{v}/_{v}$, 2.5 ml) and XLIV (20mg, 0.17 mmole) in the same solvent mixture (1 ml) were mixed at room temp and also at 60°. Precipitation began immediately at 60°, but only after 30 min at room temp. The solutions were stirred at these temps for 1 hr and then for a further 2 hr at 0°. The yellow precipitates were collected and recrystallised from EtOH to yield 35mg (91%) and 25mg (65%) of IL respectively.

c) XLVIII (160mg, 0.91 mmole) in 1-BuOH(10 ml) at 40° was slowly added to a solution of XLIV (100mg, 0.91 mmole) in 1-BuOH(5 ml) at 0°. The yellow precipitate which formed after 1 hr was recrystallised from EtOH to yield 120mg (58%) IL. The mother liquors were concentrated *in vacuo* to yield a further 30 mg IL, m.p. 217-219°.

SECTION 5.

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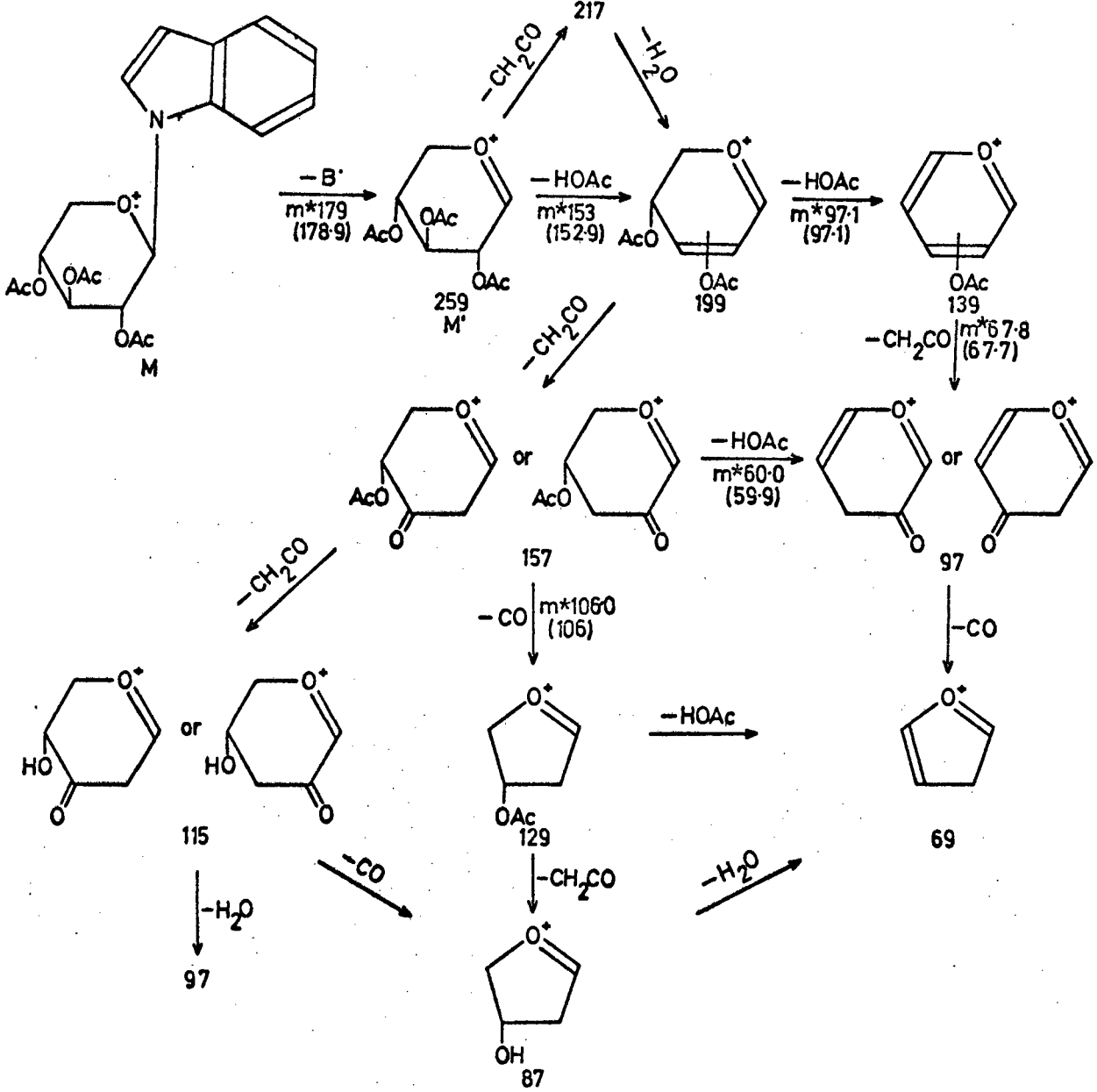

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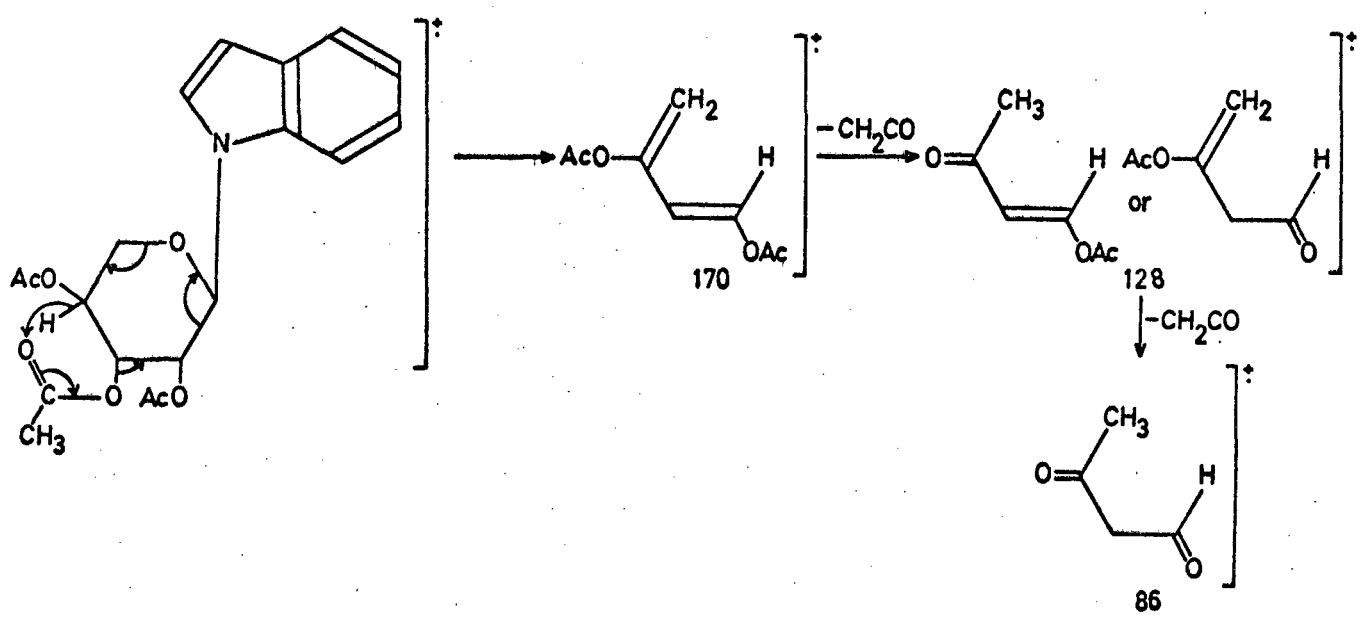

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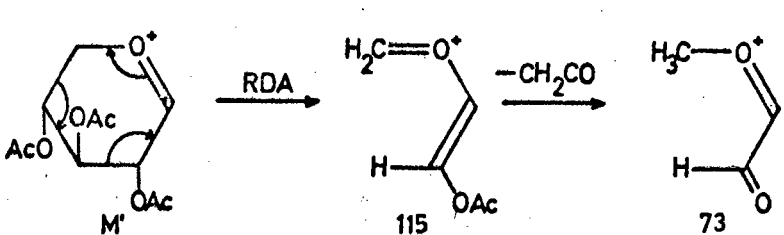

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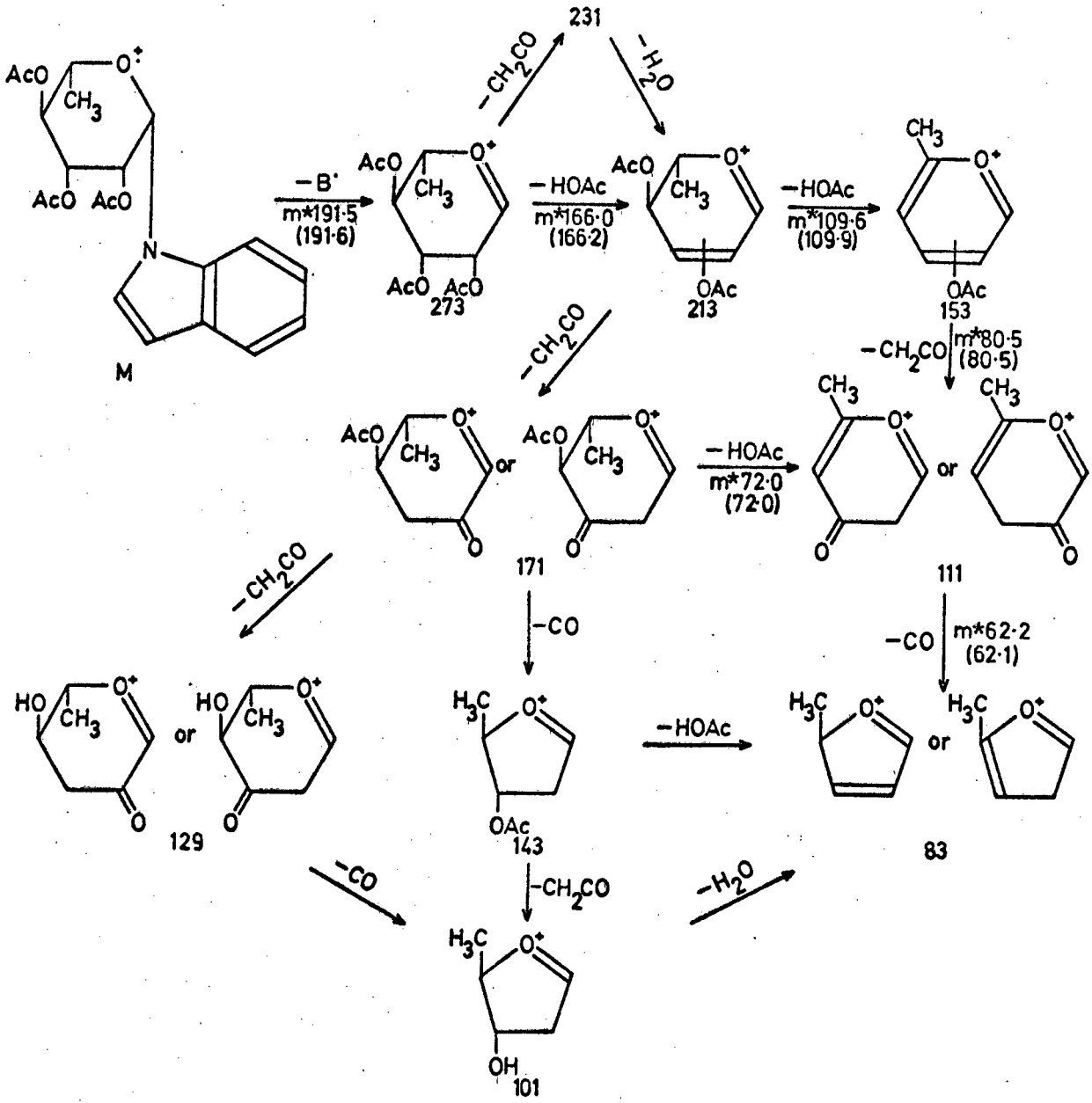

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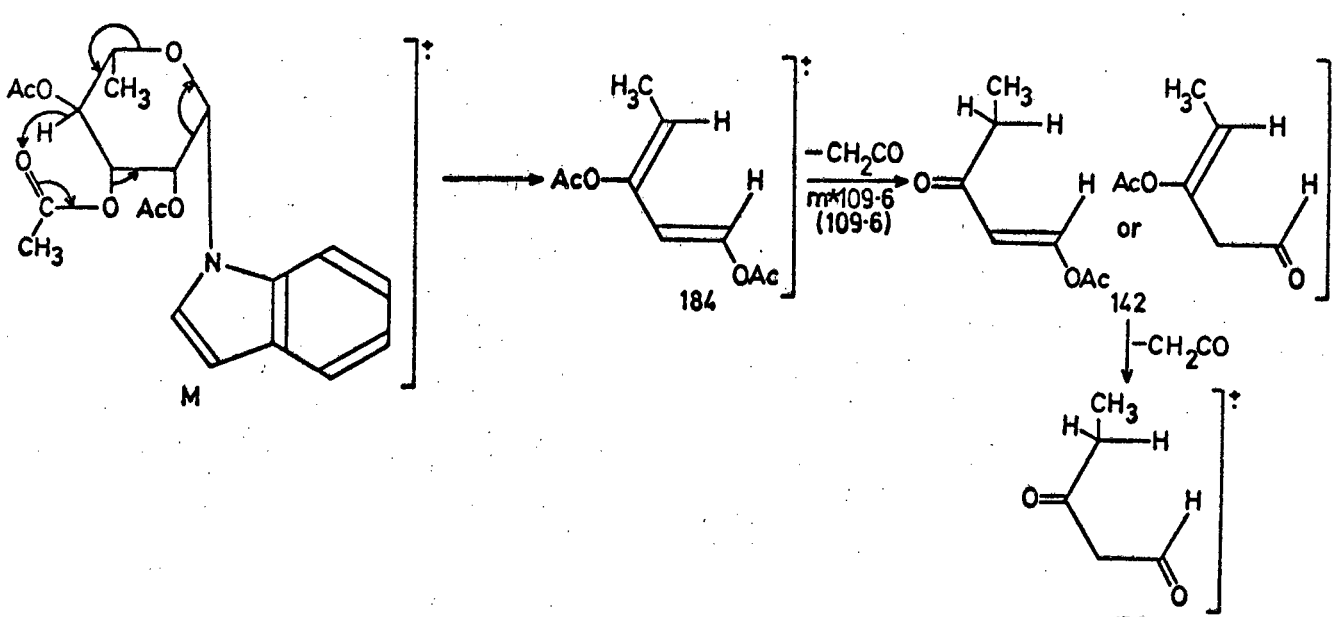

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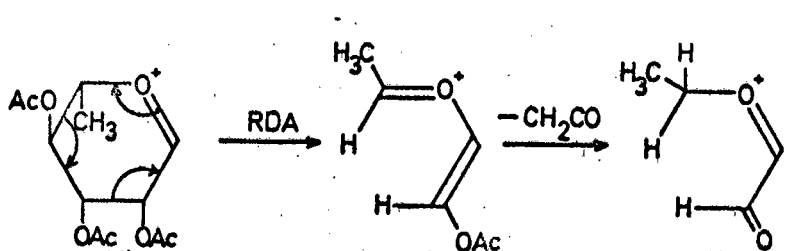

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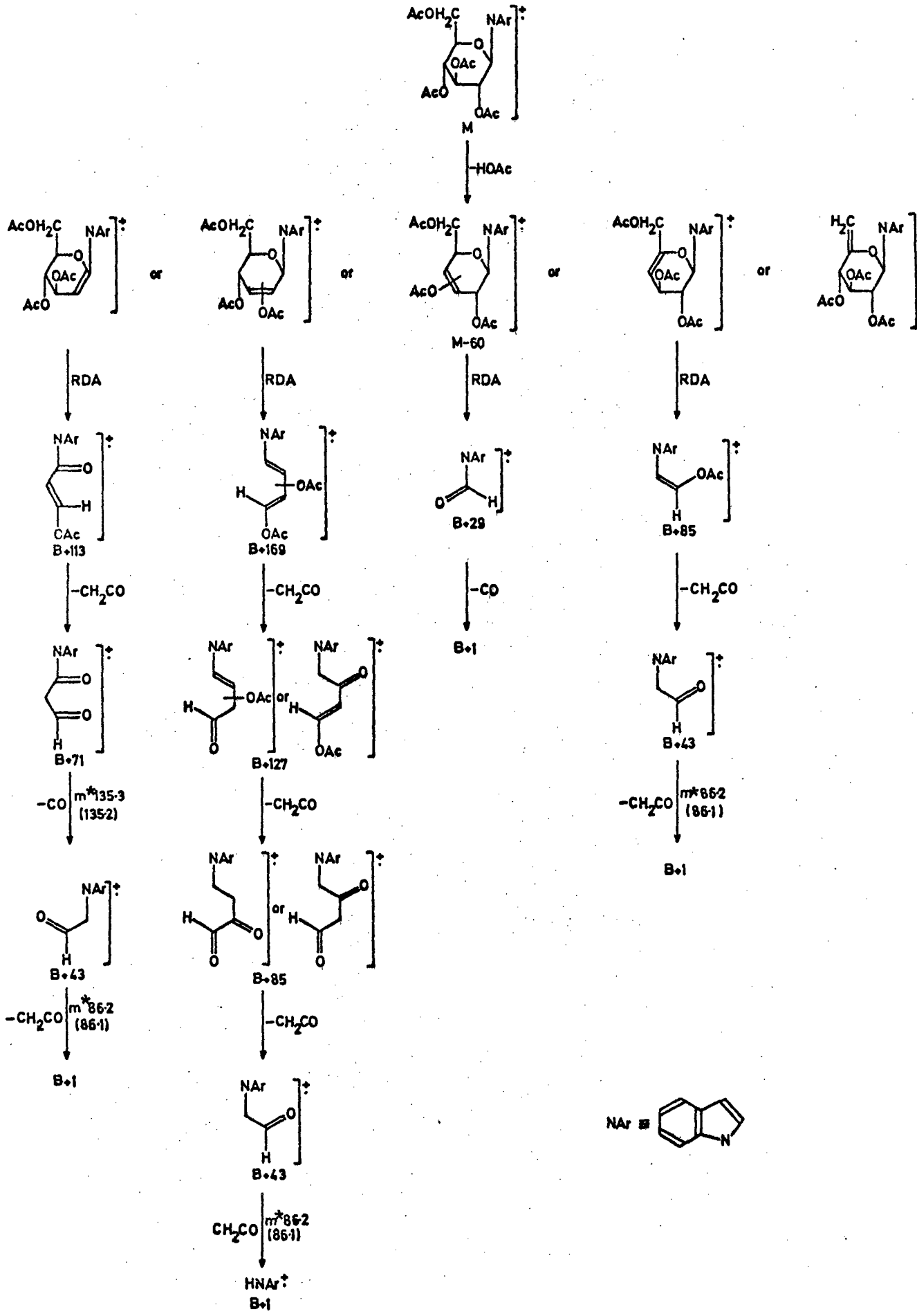
M
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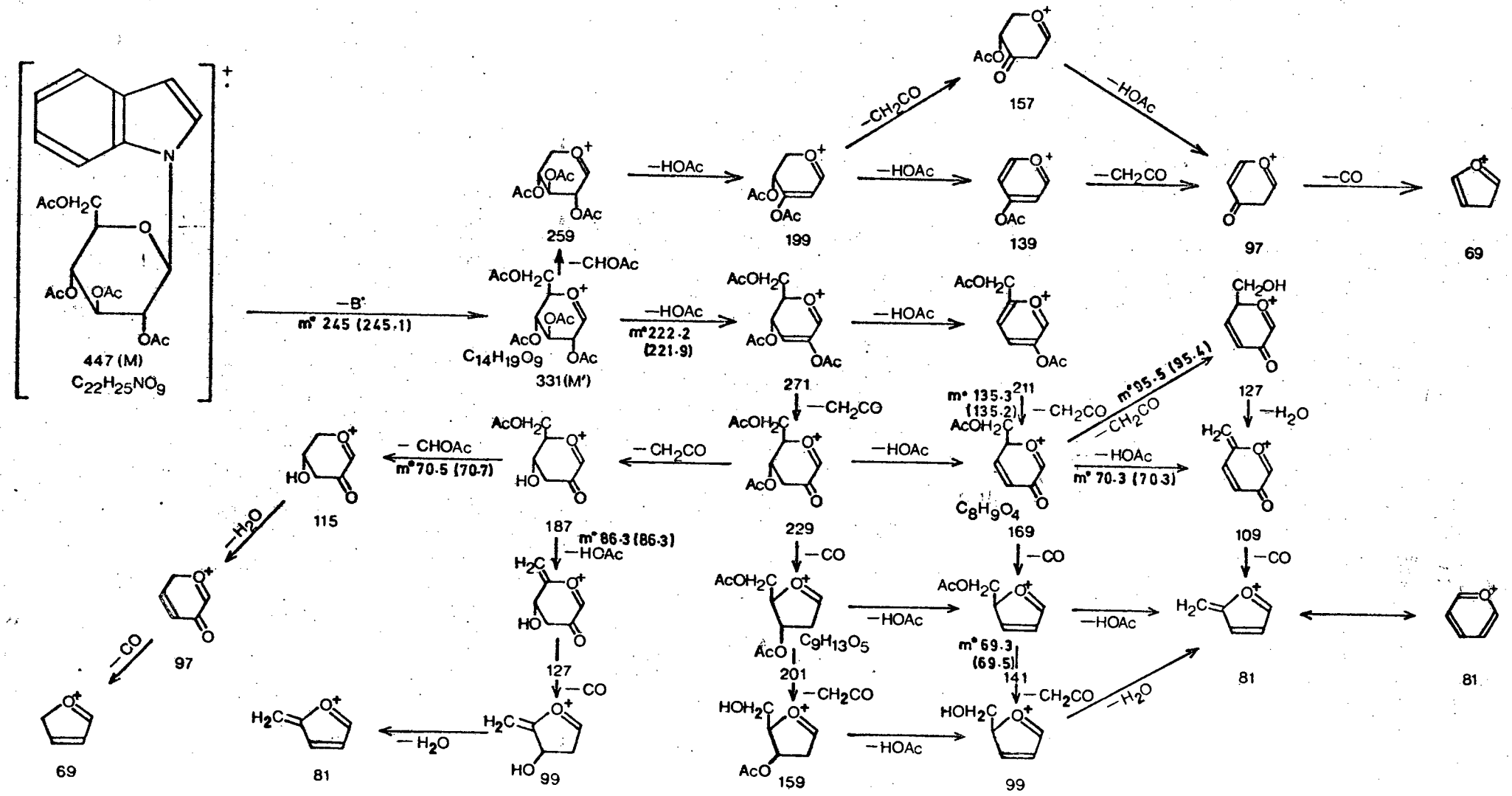
M-60
RDA
B+113
B+169
B+29
B+85
-CH2CO
B+71
B+127
B+43
-CO
m*135·3 (135·2)
m*86·2 (86·1)
-CD
B+1
B+85
NAr ≡

Appendix 8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−B·
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331(M')
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m* 222.2 (221.9)
199
271
157
−CH2CO
139
97
69
−CO
−HOAc
m* 135.3 (135.2)
m* 95.5 (95.4)
127
109
81
C8H9O4
169
229
187
m* 86.3 (86.3)
115
m* 70.5 (70.7)
m* 70.3 (70.3)
−H2O
C9H13O5
201
m* 69.3 (69.5)
141
159
99

APPENDIX 1