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I am submitting herewith a thesis written by Jeremy L. Clark entitled "Synthesis of 1-*O*-cinnamoyl and benzoyl esters of D-glucopyranose as acyl donors for anthocyanins of the wild carrot." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemistry.

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David C. Baker, Major Professor

We have read this thesis and
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Don K. Dougall

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George W. Kabalka

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Associate Vice Chancellor and
Dean of the Graduate School

Synthesis of 1-*O*-cinnamoyl and benzoyl esters of D-glucopyranose as acyl donors for anthocyanins of the wild carrot

A Thesis

Presented for the

Master of Science

Degree

The University of Tennessee, Knoxville

Jeremy L. Clark

August 1998

DEDICATION

This thesis is dedicated to my mother, Jane Clark, and to the memory of my dad, Tommy Clark

ACKNOWLEDGMENTS

I wish to thank Dr. David Baker for his guidance and financial support that has helped me achieve this degree. I am also thankful to the other members of my committee: Dr. Don Dougall and Dr. George Kabalka for their commitment to science through research and teaching. Lastly, I would like to thank past and present members of the Baker research group. Steve Johnson, Shijia Yan, Ken Price, Sean Hamilton, Neil Whittemore, Michael Gaines, and Karen Terry all have provided valuable assistance.

ABSTRACT

This research develops 1-*O*-cinnamoyl and benzoyl esters of D-glucopyranose for use as acyl donors to anthocyanins from the wild carrot (*Daucus carota*).

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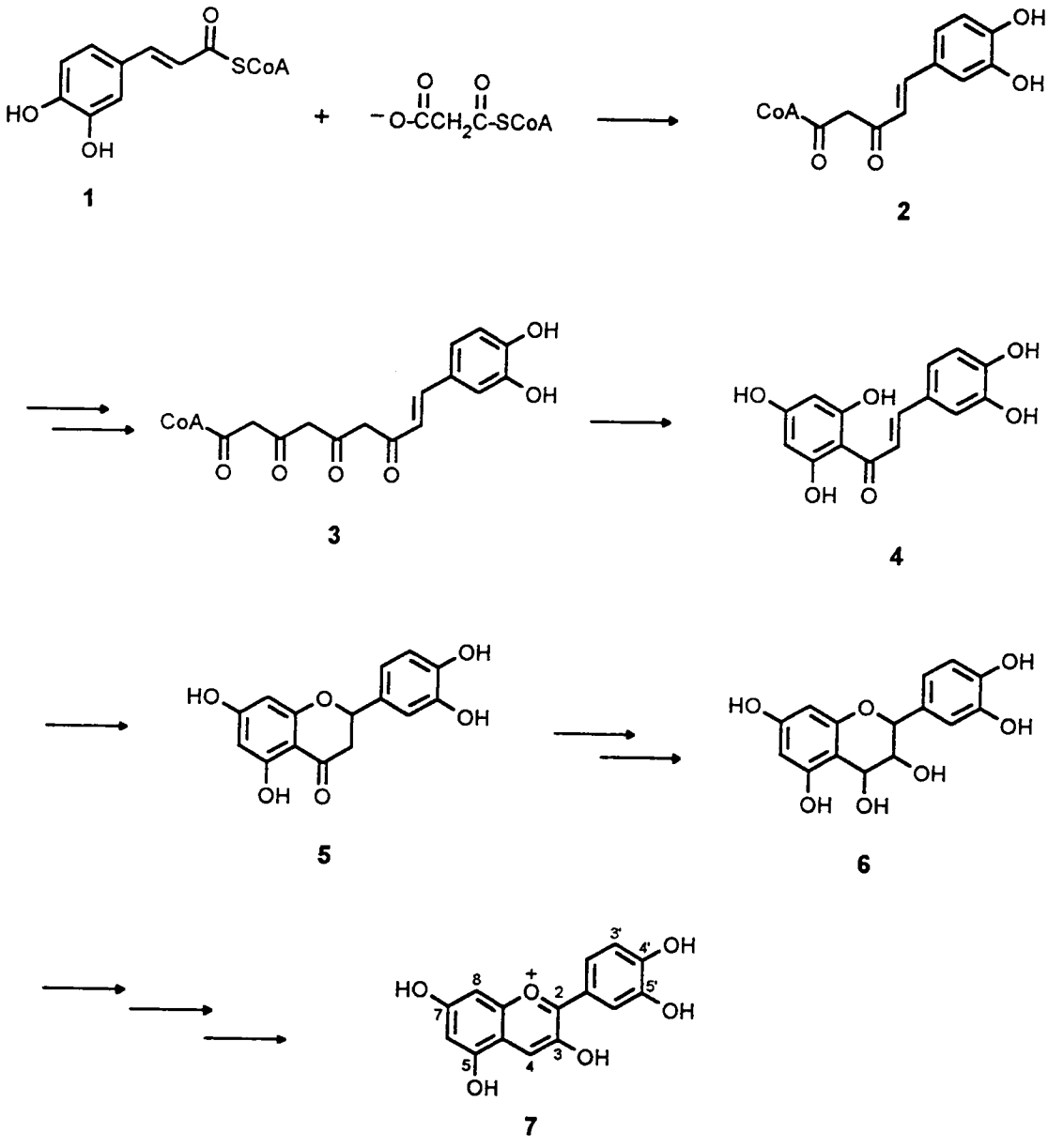
I. INTRODUCTION

Anthocyanins are plant pigments that are responsible for many of nature's brilliant colors. The orange, red, mauve, scarlet, violet, and blue colors of flower petals, fruits, roots, and leaves of higher plants are due, in large part, to anthocyanins.[1] Owing to the many colors they posses, anthocyanins represent a potential source for safe, natural coloring agents.

The unfortunate reality is that anthocyanins are not used extensively as food and pharmaceutical coloring agents due to their instability at or near neutral pH. Anthocyanins are generally red in color at acidic pH's (for example, pH 2–5),[2] but often lose their color as the pH approaches 7. A mechanism for this loss of color is hydration at C-2 which gives a colorless hemiacetal as the flavylium chromophore is destroyed (refer to **7** in Scheme 1).

The biosynthesis of anthocyanins proceeds through a coenzyme A-ester of hydroxycinnamic acid (Scheme 1 shows 3,4-dihydroxycinnamoyl-CoA, **1**). Accordingly, one molecule of the CoA-ester **1** and three molecules of malonyl-CoA are condensed in three chalcone synthase catalyzed reactions to afford **3** that is cyclized by chalcone synthase to afford the chalcone, **4**. Chalcone isomerase effects the formation of the C ring in the flavanone **5**.[3] The flavanone is then transformed to a flava-3,4-*cis*-diol **(6)** by dihydroflavonol 4-reductase. The enzymology of the last three steps of anthocyanidin formation are incomplete. But the diol **6** is probably hydrated at C-2 and subsequently

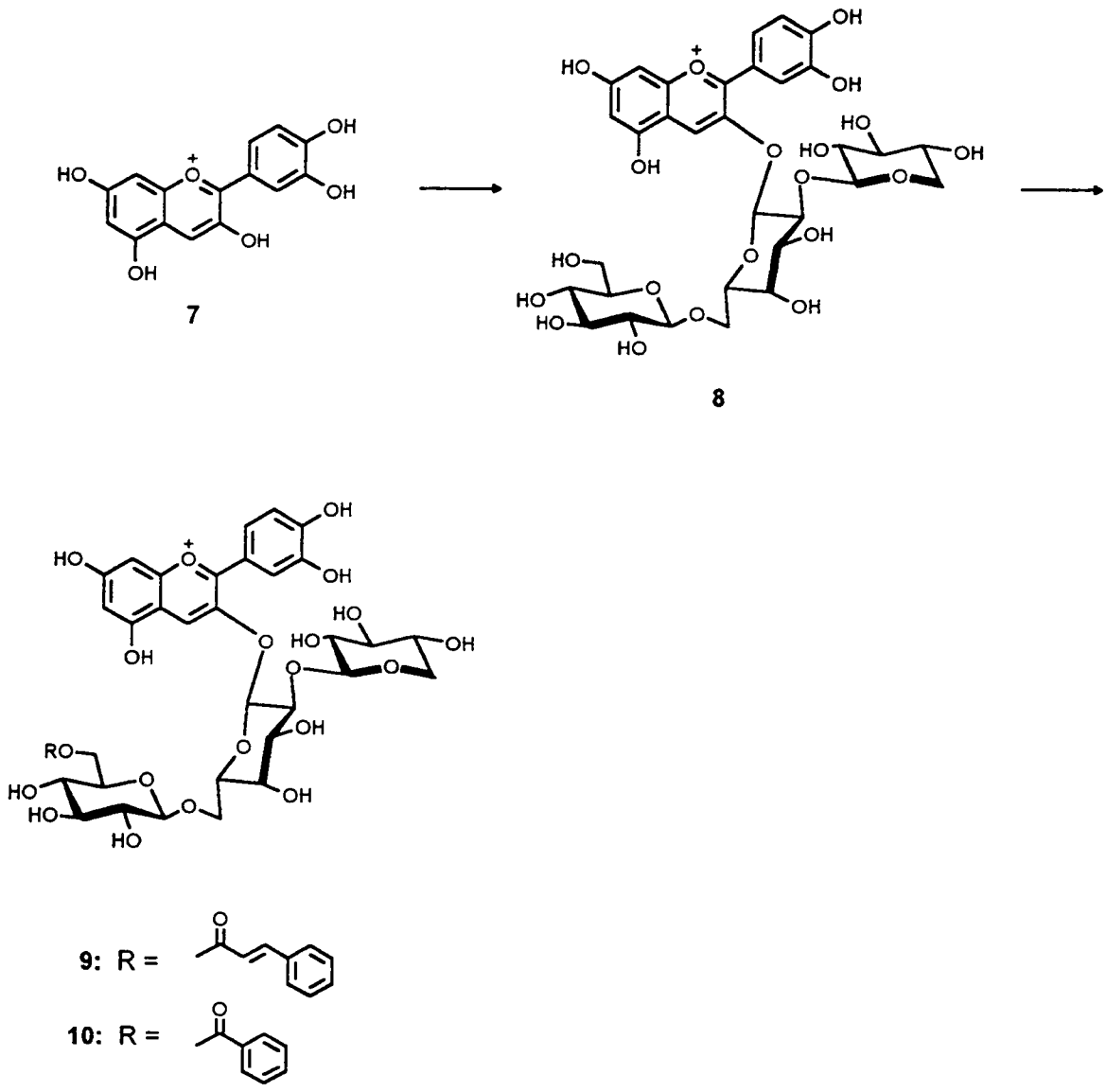


Scheme 1. Biosynthesis of anthocyanidin (7).

dehydrated at C-2 and C-4 to give the anthocyanidin 7.[12] Glycosylation and acylation, the final two steps in the formation of anthocyanins, are very specific for individual anothocyanins (Scheme 2).[4] The various glycosylations are catalyzed by uridine diphospate transferases with various diphosphate nucleotide carbohydrate substrates while acylations are catalyzed by specific acyl transferases[4] with either esters of D-glucopyranose or CoA thioesters as the acyl donors (Scheme 2).

Saylor and Mansell,[9] Kamsteeg et al.,[10] and Teusch et al.,[11] have demsonstrated that CoA esters of hydroxycinnamic acids are the acyl donors to anthocyanins from a variety of plants. Furthermore, CoA esters, have been identified as acyl donors to the glucose moiety in other flavonoids.[12] Until recently, CoA esters were the presumed acyl donors for the acylation of anthocyanins; but in 1992 Gläßgen and Seitz demonstrated that 1-*O* glucosyl esters are the acyl donors to an anthocyanin.[13]

Dougall and Baker have demonstrated that β-D-glucopyranosyl-(1→6)-[β-D-xylopyranosyl-(1→2)-β-D-galactopyranosyl-(1O^3)-cyanidin **(8)**, an anthocyanin from the wild carrot (*Daucus carota*), becomes acylated when fed cinnamic and benzoic acids in plant cell tissue cultures.[5] Furthermore, anthocyanins that are acylated with cinnamic acids have demonstrated a greater stability than the corresponding nonacylated anthocyanins.[2,6,7] Many explanations have been proposed to explain the added stabilization of these acylated anthocyanins.[6-8] But the focus of the project is to ascertain if glucosyl esters are intermediates in this acylation and to gain insight into the specificity of the acyltransferases that acylate the 6-hydroxyl group of the glucose moiety (Scheme 2).



Scheme 2. Biosynthesis of anthocyanins **(9)** and **(10)**.

II. STATEMENT OF THE PROBLEM

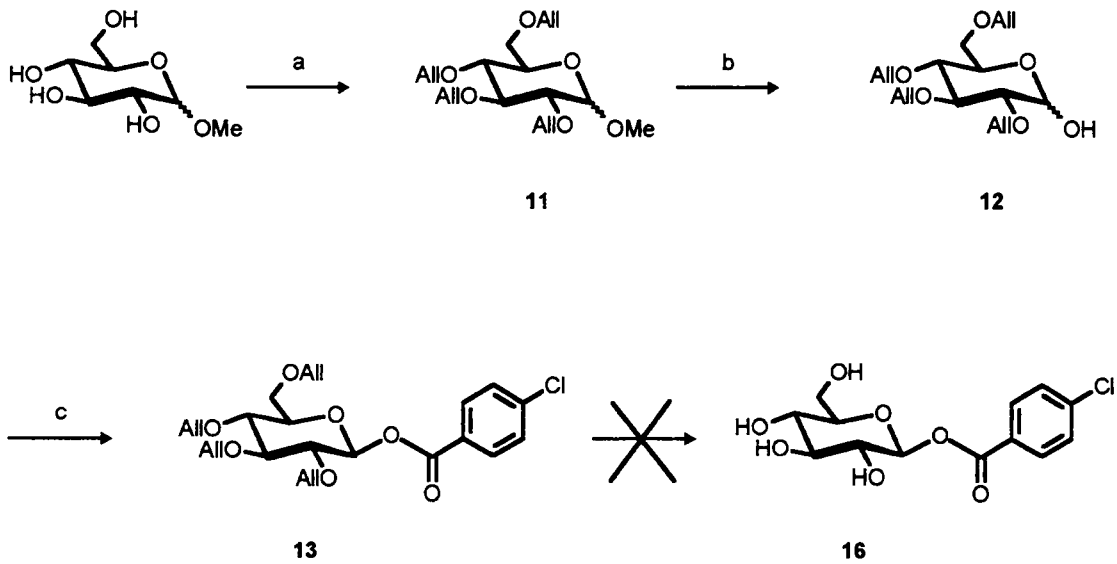
The goal of this project is to synthesize 1-*O*-cinnamoyl and benzoyl esters of β-D-glucopyranose. These compounds are evaluated as acyl donors to anthocyanins from the wild carrot.

III. RESULTS AND DISCUSSION

A. Attempted synthesis of 1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose (16) from 2,3,4,6 tetra-*O*-allyl glucopyranose (12).

A general synthetic method for the preparation of 1-*O*-cinnamoyl and benzoyl esters of D-glucopyranose requires protecting groups that can be removed without cleaving the sensitive 1-*O*-ester or reducing the conjugated double bond of a cinnamoate. Due to the mild methods for removing allyl ethers, the perallylated compound **12** was envisioned to be an appropriate starting material (Scheme 3). To obtain compound **12**, methyl α-D-glycopyranoside was treated with allyl bromide in anhydrous *N,N*-dimethylformamide, followed by portionwise addition of sodium hydride. Acetolysis in 1:1 acetic acid–acetic anhydride with a catalytic amount of sulfuric acid, followed by saponification with sodium methoxide in methanol, gave **12** in modest yield.

Diastereoselective formation of the β-D-glucosyl ester **13** was achieved by a slight modification to the procedure developed by Bols and Hansen.[14] The perallylated compound **12**, in CH_2Cl_2 and triethylamine, was treated with 4-chlorobenzoyl chloride in equal portions over 5 min at 0 °C. While the procedure by Bols calls for the portionwise addition of the acid chloride over 100 minutes, this procedure occasionally showed poor anomeric selectivity (e.g., ~1:2 α/β).



Reagents: (a) allyl bromide, NaH, DMF; (b) i. Ac_2O, AcOH, cat. H_2SO_4, ii. NaOMe, MeOH; (c) 4-chlorobenzoyl chloride, TEA, CH_2Cl_2.

Scheme 3. Attempted synthesis of 1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(16)** from 2,3,4,6-tetra-*O*-allyl-D-glucopyranose **(12)**

Bols and Hansen report that the rate of mutarotation of the perbenzylated glucopyranose **15** is approximately forty times faster in triethylamine than in pyridine.[14,15] This finding is not surprising given that a probable mechanism for mutarotation involves loss of the anomeric hydroxyl proton. Therefore, it should be anticipated that a stronger base such as triethlylamine should accomodate a faster rate of mutarotation than a weaker base such as pyridine. Given the relatively fast rate of mutarotation, the formation of either the α or β ester will be independent of the ratio of k_1 to k_{-1} (Figure 1). The preponderant formation of one product will be independent of the position of equilibrium; that is, only if k_2 is greater than k_3 will the β ester be formed preferentially.

Following the work with trichloroacetimidate esters, Schmidt and co-workers coined the term "kinetic anomeric effect" to account for the diastereoselective formation of 1-*O*-acylated glycopyranoses.[16] Essentially, this term implies that the β anomer is more nucleophilic than the α anomer due to steric repulsion of the lone pairs of electrons that make the anomeric oxygen's lone pair of electrons more accessible to an electrophile (Figure 1). Alternatively, if the anomeric hydroxy group were deprotonated and an oxy-anion were formed, the resulting β-oxide and the ring oxygen would have a unfavorable dipole interaction. The steric repulsion of the lone pair of electrons makes k_2 greater than k_3 and facilitates the kinetic formation of the β-glucosyl ester. Accordingly, 2,3,4,6-tetra-*O*-allyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(13)** was prepared in 71% yield with greater than 90% diastereoselectivity.

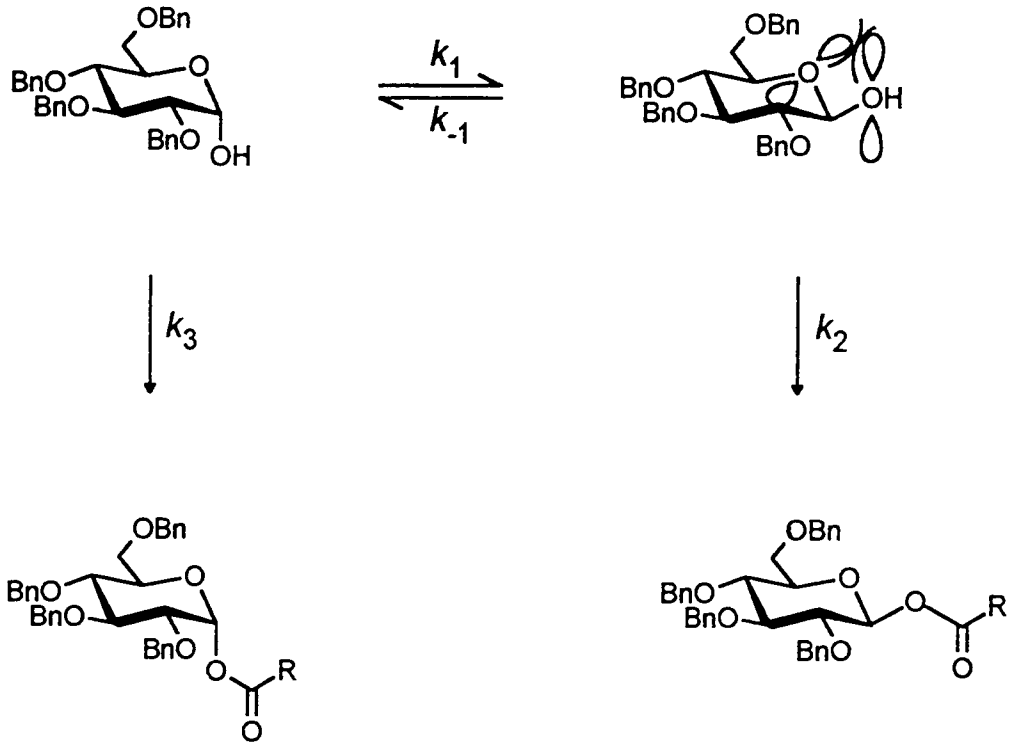


Figure 1. Diastereoselective formation of alpha and beta glucosyl esters.

Allyl ethers are cleaved by isomerization to the more thermodynamically stable 1-propenyl ethers, followed by mild acid- or base-catalyzed hydrolysis.[17] Isomerization can be effected by potassium *tert*-butoxide in dimethyl sulfoxide at elevated temperatures[18] or by transition metal complexes such as Wilkinson's catalyst, $(Ph_3P)_3RhCl$.[19b,c] Even under an improved procedure which employs an activated Wilkinson's catalyst, a $(Ph_3P)_3RhCl$/BuLi pair,[20] isomerization with Wilkinson's catalysts was not satisfactory. However, the iridium complex 1,5-cyclooctadiene-bis[methyldiphenylphosphine] iridium(I) hexafluorophosphate, $[Ir(cod)PMePh_2)_2]^+PF_6^-$, which was developed by Felkin[21] and co-workers readily isomerized the perallylated sugar to the 1-propenyl derivative.

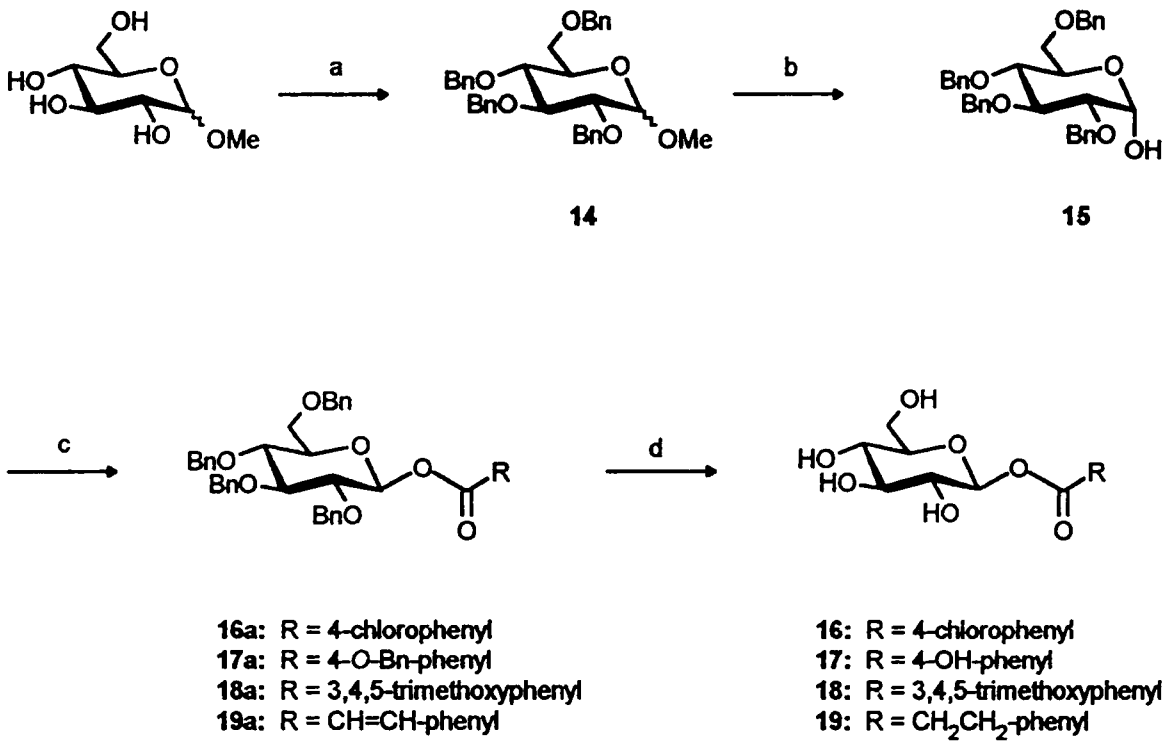
A simple method for activating the iridium complex has been used frequently in our laboratory.[22] The iridium complex, as a mixture with THF, is swirled under a balloon filled with hydrogen until the red color turns to a pale tan color. The mixture is then purged with N_2 to ensure complete removal of the H_2. This activated solution is then added to the perallylated sugar **(12)**, and the reaction is monitored by TLC whereby the 1-propenyl ether has a slightly higher R_f than the allyl ether starting material. Upon analyzing an an aliquot by ^1H NMR spectroscopy, the isomerization is confirmed to be complete. A tell-tale sign is the disappearance of the multiplet at δ 3.99–4.38 ($-OCH_2CH=CH_2$) and the appearance of a doublet at δ 6.10 ($-OCH=CHCH_3$). Additionally, the $-OCH_2CH=CH_2$ multiplet in the allyl ether changes to a doublet at δ 1.50 in the 1-propenyl ether ($-OCH=CHCH_3$).

Unfortunately, attempted cleavage of the 1-propenyl ether using I_2[23] $HgCl_2$[18] and acetone/1 M HCl[19b] gave spurious results, and no major spot was detected by TLC using any of the hydrolysis methods. In the latter case, a slow cleavage of the ester was observed at elavated temperatures.

B. Synthesis of β-Glucosyl esters (16–19) from 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (15).

Given the difficulties in removing the 1-propenyl ether protecting groups, a descision was made to use benzyl protecting groups that would at least provide the benzoate esters upon hydrogenolytic deprotection. Accordingly, 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose **(15)**[24] was prepared by benzylating methyl α-D-gluco-pyranoside to give methyl 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **(14)**. Sulfuric acid cleavage of the glycoside afforded **15** in a modest 31% yield overall yield.

Diastereoselective coupling to provide esters **16a–19a** was performed under the same conditions that provided **13**. The α/β selectivity of the crude reaction mixtures was ascertained by ^{1}H NMR intergration of the anomeric protons (see experimental section for specific α/β ratios). The α anomeric proton, having an equatorial configuration, appears downfield (ca. δ 6.5) with respect to the β anomeric proton (ca. δ 5.5), which has an axial configuration. This is to say that the α anomeric proton is deshielded from the effective magnetic field. Additionally, the H_1–H_2 interaction (axial–equatorial) in the α anomer gives rise to a much smaller coupling constant ($J_{1,2}$ ~ 3–4 Hz) than the H_1–H_2 (axial–axial) interaction in the β anomer ($J_{1,2}$ ~ 8–9 Hz).[25]



16a: R = 4-chlorophenyl
17a: R = 4-O-Bn-phenyl
18a: R = 3,4,5-trimethoxyphenyl
19a: R = CH=CH-phenyl

16: R = 4-chlorophenyl
17: R = 4-OH-phenyl
18: R = 3,4,5-trimethoxyphenyl
19: R = CH_2CH_2-phenyl

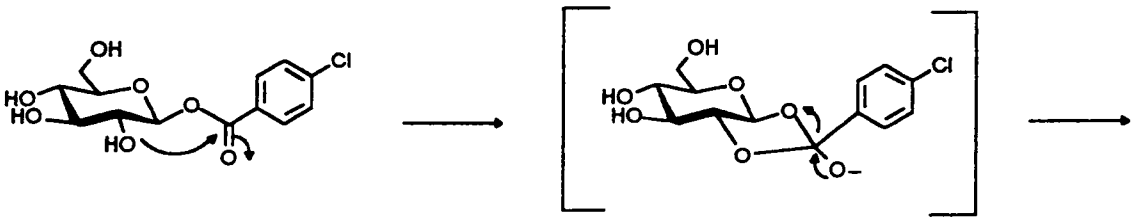
Reagents: (a) benzyl bromide, NaH, DMF; (b) AcOH, H_2SO_4, H_2O; (c) RCOCl, TEA, CH_2Cl_2; (d) 10% Pd/C, H_2, EtOAc/EtOH.

Scheme 4. Synthesis of 1-*O*-esters of β-D-glucopyranose **(16–19)** from 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose **(15).**

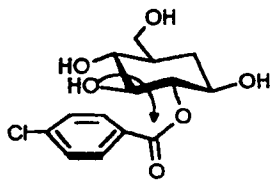
Initial attempts to debenzylate **16a** with either 10% Pd/C or 20% $Pd(OH)_2$, under 15 psi H_2 (~ 1 atm), and with moderate stirring at room temperature, consistently afforded a reaction mixture whose ^1H NMR spectrum indicated an additional multiplet in the aromatic region. HPLC (10% methanol–water) analysis of the crude reaction that was homogenous by TLC (1:10 EtOAc–methanol) indicated two widely separated components, t_R = 15 min and t_R = 30 min. Isolation of the components revealed that the earlier component was 1-*O*-benzoyl-β-D-glucopyranose (for **16**, R = phenyl): ^1H NMR data (CD_3OD, 400 MHz): δ 3.41–3.52 (m, 4H, H-2, H-3, H-4, H-5), 3.71 (dd, 1H, $J_{6b,5}$ 4.8 Hz, $J_{6b,6}$ 12.0 Hz, H-6b), 3.85 (dd, 1H, $J_{6,5}$ 2.4 Hz, H-6), 5.72 (d, 1H, $J_{1,2}$ 8.0 Hz, H-1), 7.51 (Ψt, 2H, *J* 8.4 Hz, Ph), 7.63 (d, 1H, *J* 8.4 Hz, Ph), 8.09 (d, 2H, Ph); ESIMS (positive-ion mode) calcd for $C_{13}H_{16}O_7$: $[M + H]^+$ 285.1; $[M + Na]^+$ 307.1; $[2M + H]^+$ 569.2; $[2M + Na]^+$ 591.2; Found: *m/z* 285.2, 307.2, 569.2; 591.3.

The observed dechlorination presumably ensues by an initial arylpalladium complex ("ArPdCl"), which is subsequently eliminated with the addition of hydrogen. The arylpalladium complex is the active species in the well-known and synthetically useful Heck coupling reaction.[26] Transfer hydrogenolysis using cyclohexene as the hydrogen source reportedly debenzylates without concomitant dechlorination.[27] However, transfer hydrogenolysis using 20% $Pd(OH)_2$ and cyclohexene proved unsuccessful in removing all four benzyl ethers. Performing the debenzylation at 0 °C with 10% Pd/C at ≤1 atm H_2 not only circumvented the observed dechlorination, but also avoided migration of the acyl group, a pervading complication in the initial debenzylation attempts.

Acyl migration was reported by Emil Fischer in 1920 when he oberved acetyl group migration in glycerol esters.[28] Prior to his death in 1919, Fischer proposed that acyl migration proceeds by a 1,2-orthoacid ester intermediate such as **A** (Scheme 5). While later investigations into this phenomenon confirmed the presence of an orthoester in glyerol[29] and ethlyene glycol,[30] a stable orthoester has not been isolated in a carbohydrate. Moreover, the extent of acyl migration in glucopyranoses under a variety of conditions has been reported[31,32] but due to time constraints, a thorough study of conditions which facilitate the observed acyl migrations in each compound was not performed. But one of the glucosyl esters, 1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose **(20)** underwent an extraordinary facile $C_1 \rightarrow C_2$ acyl migration as seen in the HPLC chromatograms and confirmed by the ^{1}H NMR spectrum. After 2.5 h at ca. 0 °C, the ^{1}H NMR spectra (Appendix, p. 65) revealed an additional doublet at δ 5.34 ($J_{1,2}$ 3.9 Hz) which corresponds to the anomeric proton of 2-*O*-(4-chlorobenzoyl)-α-D-glucopyranose **(21)**. An additional psuedo triplet multiplicity in the ^{1}H NMR spectrum at δ 3.98 (J 9.5 Hz) corresponds to the proton at C-2 and further supports the presence of a 2-*O* acylated carbohydrate. In this particular instance, the acyl group appears to stop at the 2-position as evidenced by the HPLC chromatogram that showed only one peak in addition to the starting material.



16 **A**



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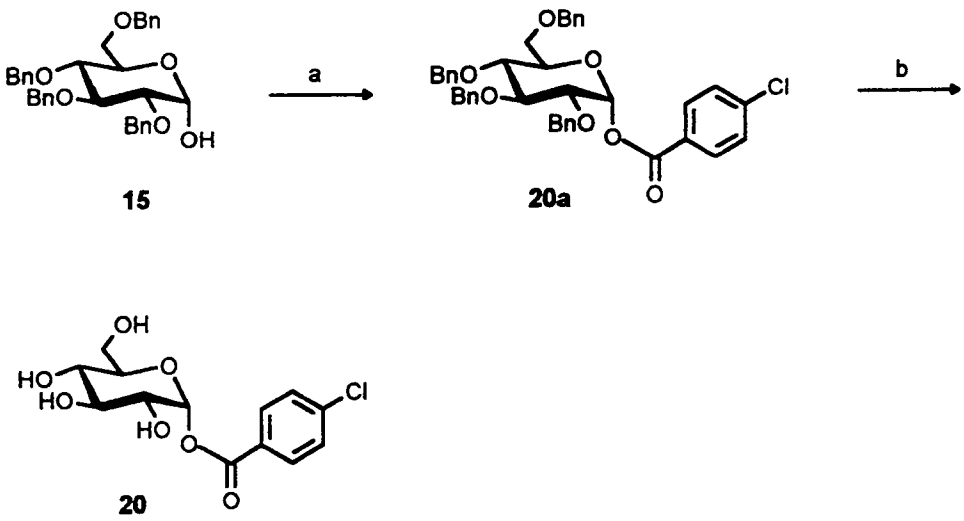
Scheme 5. Possible mechanism for observed 1,2-acyl migrations.

C. Synthesis of 1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose (20a).

Using pyridine as a base and cosolvent slows the rate of mutarotation of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose **(15)** such that the product distribution reflects the initial position of the equilibrium (refer to Figure 1).[14,33] In other words, given a slow rate of mutarotation of the pure α anomer starting material, the α-D-glucosyl ester should predominate over the β ester. Additionally, the addition of the acid chloride was done in portions to facilitate the formation of the thermodynamic product, **20a** (Scheme 6).

D. Synthesis of 1-*O*-(4-chlorocinnamoyl)-β-D-glucopyranose (25).

Due to the increased oxidation potential at the benzylic position, the *p*-methoxybenzyl ether can be removed with the mild oxidizing agent, cerric ammonium nitrate (CAN). Due to the electron-donating *para* methoxy group, the *p*-methoxybenzyl ether is also more sensitive than a benzyl ether to acid-catalyzed cleavage. Therefore, the allyl group was used to protect the anomeric hydroxyl group (Scheme 7). The allyl group can be isomerized to an acid-labile 1-propenyl ether that can be cleaved in the presence of the *p*-methoxybenzyl (PMB) ethers. Therefore, the allyl acetal **(22)** was prepared in 61% yield by the procedure used by Hecker and co-workers.[41] Allowing this acetal to react with excess PMBCl and sodium hydride under reflux afforded 2,3,4,6-tetra-*O*-(4-methoxy-benzyl)-D-glucoside **(23)**. Isomerization to the 1-propenyl group with potassium *tert*-butoxide in dimethyl sulfoxide at 90 °C, followed by mild acidic cleavage using 9:1 acetone–1 M HCl[19b] gave compound **24**.



Reagents: (a) 4-chlorobenzoyl chloride, TEA, pyridine/CH_2Cl_2; (b) 10% Pd/C, H_2, EtOAc/EtOH.

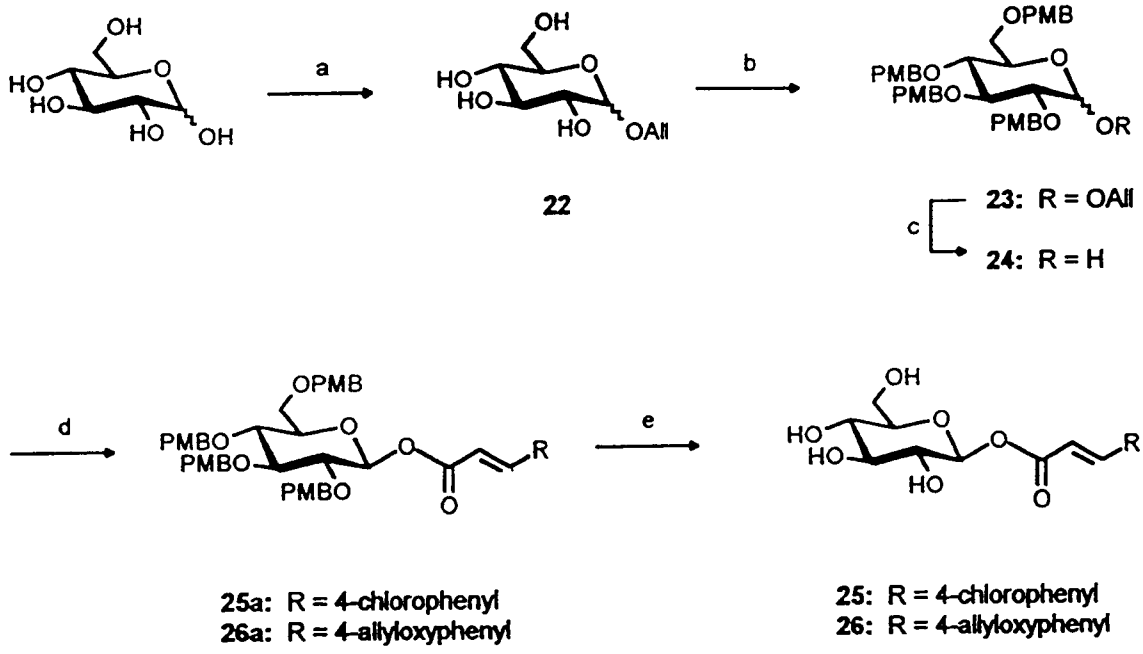
Scheme 6. Synthesis of 1-*O*-4-chlorobenzoyl-α-D-glucopyranose **(20).**

Compounds **25a** and **26a** were prepared by the acylation procedure used to provide compounds **13** and **16–19**. While **25a** was deprotected with CAN to provide **25** in good yield, deprotection of **26a** under identical conditions gave a complex reaction mixture. The crude reaction mixture did not show an anomeric proton resonance when analyzed by ^{1}H NMR spectroscopy. No further investigation was carried out on the compound.

E. Synthesis of 1-*O*-(3,4,5-trimethoxycinnamoyl)-β-D-glucopyranose (29) and 1-*O*-(4-hydroxycinnamoyl)-β-D-glucopyranose (31).

The method of Plusquellec[34] was used to provide compounds **29** and **31** (Scheme 8). This method exploits the increased acidity of the anomeric hydroxyl proton that, presumably, accounts for the regioselective 1-*O*-acylation of β-D-glucose.[35] The diastereoselectivity could arise due to the slow rate of mutaroatation of β-D-glucose in pyridine.[33] Additionally, compounds **27** and **28** are excellent acyl donors to the anomeric hydroxyl group as 8-hydroxyquinoline is an excellent leaving group.

The spurious regioselectivity observed in the reactions leading to **29** and **31** was evident by 40–50% of the alternative regioisomers as judged by HPLC. It was not determined whether the other regioisomers arose from the reaction's lack of selectivity or from acyl migration during workup. Essentially pure **31** was obtained by preparative C_{18} reversed-phase HPLC, while cystallization from EtOAc provided analytically pure **29**. Preparing β-glucosyl esters *via* unprotected β-D-glucose appears to be a general preparative method, but the recurring problem of acyl migration dampened this prospect.



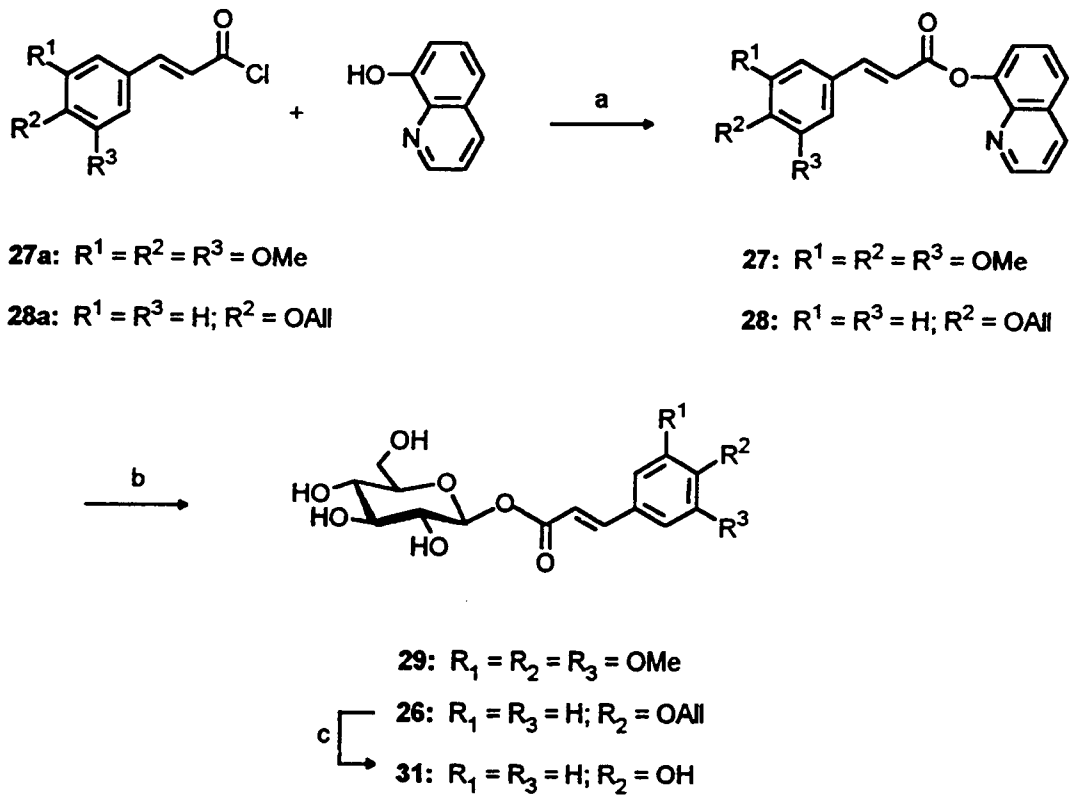
Reagents: (a) allyl alcohol, cat. BF_3·OEt_2; (b) 4-methoxybenzyl bromide, NaH, DMF; (c) i. *t*-BuOK, DMSO, ii. 1 M HCl, acetone; (d) RCH=CHCOCl, TEA, CH_2Cl_2; (e) cerric ammonium nitrate, CH_3CN.

Scheme 7. Synthesis of glycosyl esters **(25–26)** from 2,3,4,6-tetra-*O*-4-methoxybenzyl-D-glucopyranose **(24)**.

In many cases, the esters that were prepared using this method very quickly underwent acyl migrations during purification.

F. Acylation of anthocyanins

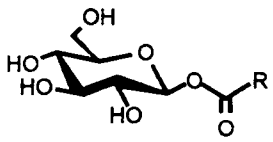
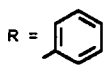
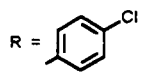
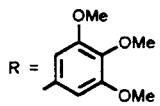
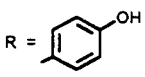
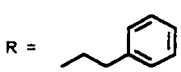
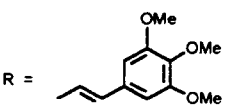
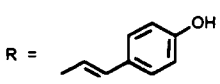
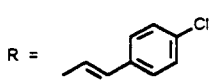
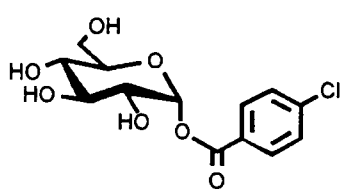
The enzyme assays were performed by Dr. Don Dougall (Deptartment of Botany at University of Tennessee, Knoxville) according to the method of Gläßgen and Seitz.[13] Enzyme activities were determined using reversed-phase HPLC, and the enzyme preparations were co-chromatographed with authentic anthocyanin samples.[5] Table 1 on page 22 summarizes the esters evaluated; of the nine esters assayed as acyl donors (**16–20**, **25**, **26**, 1-*O*-cinnamoyl-β-D-glucopyranose, and 1-*O*-benzoyl-β-D-glucopyranose), all but 1-*O*-(4-hydroxybenzoyl)-β-D-glucopyranose **(17)**, 1-*O*-(3,4,5-trimethoxybenzoyl)-β-D-glucopyranose **(18)**, 1-*O*-4-chlorobenzoyl-α-D-glucopyrnaose **(20)** acylated the anothocyanins.



Reagents: (a) triethlylamine, THF; (b) β-D-glucose, pyridine, cat. NaH; (c) i. $[Ir(cod)PMePh_2)_2]^+PF_6^-$, dioxane, ii. I_2.

Scheme 8. Synthesis of 1-*O*-(3,4,5-trimethoxycinnamoyl)-β-D-glucopyranose **(29)** and 1-*O*-(4-hydroxycinnamoyl)-β-D-glucopyranose **(31).**

Table 1. Summary of Methods of Preparation and Acyl Transfer Activity.

Compound	Method of Preparation[a]	Acyl transfer[b]
		
	A	Yes
	A	Yes
	A	No
	A	No
	A	Yes
	B	Yes
	B	Yes
	C	Yes
	D	No

[a] Method A: from 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (**15**) (Scheme 4).
Method B: from cinnamoyloxyquinoline esters (Scheme 8).
Method C: from 2,3,4,6-tetra-*O*-(4-methoxybenzyl)-D-glucopyranose (**24**) (Scheme 7).
Method D: same as method A, but shown in Scheme 5.
[b] For experimental details, see ref. 13. Enzyme assays were performed by Dr. Don Dougall.

IV. EXPERIMENTAL

^1H NMR spectra were obtained in the indicated solvent at 250 MHz or 400 MHz as approximately 5–10% (w/v) solutions using a Bruker AC 250 instrument or AMX 400 spectrometer. ^{13}C NMR spectra were obtained at 62.5 MHz or 100 MHz using a Bruker 250 MHz or 400 MHz spectrometer, respectively. ^1H and ^{13}C NMR chemical shifts are reported as δ (ppm) downfield with respect to an internal standard of tetramethylsilane. Peak multiplicities that are approximate first order are reported as: s, singlet; d, doublet; Ψt, "psuedo" triplet; t, triplet; dd, doublet of doublets; dt, doublet of triplets; m, multiplet. Melting points were determined using a Thomas–Hoover "Unimelt" capillary melting point apparatus coupled with a Cole–Parmer 8520-50 Digi-Sense digital themocouple. Optical rotations were measured with a Perkin–Elmer 241 automatic polarimeter at the sodium D line (589 nm) in a 1-dm cell at the indicated temperatures. Atlantic Microlab, Inc. of Norcross, GA provided the elemental analysis.

Positive-ion electrospray mass spectra were obtained using Fissions Quattro II triple quadruple instrument with a nominal mass range of 50–1000 Da. Data acquisition and manipulation were accomplished using the Microamps MassLynx software package. Sample solutions (approximately 16 μg/mL in 1:1 methanol–water containing 1% formic acid) were infused at a flow rate of 5 μL/min. Nitrogen was used as the nebulizing (20

L/H) and drying gas (300/h) while maintaining the source temperature of 80 °C.

Anhydrous solvents were reagent grade and used as supplied. Tetrahydrofuran (THF) was distilled as needed at atmospheric pressure from a potassium–benzophenone ketyl. *N,N*-Dimethlyformamide (DMF) was distilled *in vacuo* (ca. 20–30 torr) from calcium hydride and was stored over 4 Å molecular sieves. Dichloromethane, pyridine and acetonitrile were distilled as needed from calcium hydride. 1,4-Dioxane was distilled as needed from lithium aluminum hydride. Molecular sieves were activated before use by heating at ca. 200 °C for 3–4 h under high vacuum (ca. 1 torr). Solvents were evaporated with a Büchi rotary evaporator at 30–40 °C/30 torr. "Under high vacuum" means that rotary evaporation was done at a pressure of less than 5 torr. All nonaqueous reactions were carried out under a positive pressure of N_2.

E. Merck Silica Gel-60 products were used to carry out adsorption chromatography. All reactions were monitored with 0.2-mm aluminum-backed thin-layer chromatography (TLC) plates which were visualized by using a 254-nm UV light and by a spray–heat development using *p*-anisaldehyde–sulfuric acid reagent.[36] Column chromatography was carried out using either fine (40–63 μm particle size) or coarse (63–212 μm) silica gel.

Analytical high-performance liquid chromatography was conducted on a Beckman 100A instrument equipped with a Phenomenex C_{18} reversed-phase column (250 x 4.60 mm). All elutions were isocratic with a flow rate of 2 mL/min for analytical chromatograms and 5 mL/min for preparative chromatograms. Preparative HPLC was

performed on a Waters 500A/prep system equipped with a 25 x 10 cm C_{18} cartridge. All chromatograms were monitored at 254 nm.

General procedure for the preparation of acid chlorides. Acid chlorides were prepared by treating 5 mmol of the appropriate acid with an excess of thionyl chloride (20–25 mmol equivalent) and anhydrous pyridine (1–2 drops). The roundbottom flask was then equipped with a drying tube ($CaSO_4$) that contained a Pasteur pipet fitted with Tygon tubing to facilitate the safe emission of the gaseous byproducts. The reaction was allowed to stand at 45–50 °C until $SO_{2(g)}$ and $HCl_{(g)}$ evolution ceased (generally within 1 h). Removal of the excess thionyl chloride *in vacuo* at 50 °C left a residue which, after further drying *in vacuo* at room temperature, was used directly for the next step.

General acylation procedure: Preparation of protected 1-*O*-esters of β-D-glucopyranoses (13, 16a–19a, and 25a, 26a). The protected β-glucosyl esters were prepared according to the procedure of Bols and Hansen.[14] The appropriate pyranose **(12, 15, or 24)** (1.65 mmol) was dissolved in CH_2Cl_2 (20 mL) and was cooled to 0 °C prior to adding triethylamine (0.93 mL, 6.7 mmol). After 10 min of stirring at 0 °C, the desired acid chloride (5 mmol) was added portionwise over 5 min. The reaction was allowed to warm to room temperature, and stirring was continued under N_2 until TLC showed disappearance of the starting material (generally within 1–2 h after the addition of the acid chloride). The reaction was quenched by pouring into 1 M HCl (20 mL), followed by washing with saturated $NaHCO_3$ (30 mL) and water (30 mL). Drying the

organic extract with $MgSO_4$ and removal of the solvent left a residue that was analyzed by ^1H NMR spectroscopy to determine the anomeric ratio. Anomerically pure compounds were obtained by flash chromatography, followed by crystallization from ether–pentane or by careful column chromatography on fine silica gel (40–63 μm).

Preparation of 2,3,4,6-tetra-*O*-allyl-D-glucopyranose (12).[22b] According to the procedure of Crich and co-workers,[37] a solution of methyl α-D-glucopyranose (2.00 g, 10.3 mmol), DMF (25 mL), and allyl bromide (4.40 mL, 50.8 mmol) was cooled to 0 °C. To this stirring solution was added sodium hydride (2.47 g, 60% in mineral oil, 61.8 mmol) portionwise over 1 h, and the stirring was continued for 8 h. The white reaction mixture was poured into ice-water (150 mL) and extracted with ether (5 x 40 mL). The organic phase was dried ($MgSO_4$) and concentrated *in vacuo*. To the residual yellow oil was added petroleum ether, and the suspension was washed with acetonitrile (4 x 20 mL). Combining the acetonitrile layers and removing the solvents provided a pale yellow oil (3.5 g, 96%) with R_f 0.45 (1:3 EtOAc–hexanes). To the oil so obtained was added glacial acetic acid (7 mL) and acetic anhydride (7 mL), and the solution was cooled to 0 °C prior to adding concentrated H_2SO_4 (2 drops). After stirring for 8 h at 40 °C, ^1H NMR spectroscopy revealed complete conversion to 1-*O*-acetyl-2,3,4,6-tetra-*O*-allyl-D-glucopyranose. ^1H NMR data ($CDCl_3$, 250 MHz): δ 2.10 (s, 3H, $OCOCH_3$), 3.45–3.78 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6b), 3.99–4.38 (m, 8H, $OCH_2CH{=}CH_2$), 5.13–5.32 (m, 8H, $OCH_2CH{=}CH_2$), 5.48 (d, 0.2H, $J_{1,2}$ 7.9 Hz, H-1β), 5.80–5.98 (m, 4H, $OCH_2CH{=}CH_2$), 6.27 (d, 0.8H, $J_{1,2}$ 3.51 Hz, H-1α). The solvents were then evaporated

and the residue was chromatographed eluting with 1:3 EtOAc–hexanes. The compound with R_f 0.39 was collected, dissolved in methanol (50 mL) and treated with 1 M sodium methoxide (5 mL) at room temperature. Stirring was continued for 2.5 h at room temperature, whereby TLC showed conversion of the starting material to a single product with R_f 0.16 (1:3 EtOAc–hexanes). The reaction was quenched with Dowex-50W x 8 (H^+) resin. Removing the resin and solvents, followed by chromatography with 1:2 EtOAc–hexanes, gave **12** as a syrup (1.96 g, 56% for three steps): $[\alpha]_D^{24}$ +42.3° (*c* 1.0, $CHCl_3$), lit[22b] $[\alpha]_D^{20}$ +44.0° (*c* 1.00, $CHCl_3$) ^{1}H NMR data (DMSO-d_6, 250 MHz): δ 3.12–3.16 (m, 2H, H-2, H-4), 3.49–3.58 (m, 4H, H-3, H-5, H-6, H-6b), 3.91–4.28 (m, 9H, OCH_2CH=CH_2), 5.07–5.42 (m, 8H, $OCH_2CH=CH_2$), 5.79–5.97 (m, 4H, $OCH_2CH=CH_2$), 6.48 (d, 0.89H, *J* 4.6 Hz, α-OH_1,), 6.87 (d, 0.1H, *J* 6.6 Hz, β-OH_1,); ^{13}C NMR data (DMSO-d_6, 62.5 MHz): δ 69.0, 69.1, 70.4, 71.3, 72.7, 73.0, 77.5, 77.5, 79.6, 80.5, 89.6, 115.5, 115.9, 116.0, 116.3, 135.1, 135.1, 135.5, 135.9.

2,3,4,6-Tetra-*O*-allyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose (13). 2,3,4,6-Tetra-*O*-allyl-D-glucopyranose **(12)** (0.879 g, 2.58 mmol) upon acylation with 4-chlorobenzoyl chloride gave a 1:18 α/β mixture as judged by ^{1}H NMR integration. Flash chromatography (CH_2Cl_2) and subsequent crystallization from ether–pentane gave **13** as fine needles (0.614 g, 71%): mp 53–55 °C, $[\alpha]_D^{25}$ -21.2° (*c* 1.15, $CHCl_3$); ^{1}H NMR data ($CDCl_3$, 250 MHz): δ 3.46–3.74 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6b), 3.98–4.41 (m, 8H, OCH_2CH=CH_2), 5.08–5.33 (m, 8H, $OCH_2CH=CH_2$), 5.73 (d, 1H, $J_{1,2}$ 7.2 Hz, H-1), 5.77–6.05 (m, 4H, $OCH_2CH=CH_2$), 7.43 (d, 2H, *J* 8.5 Hz, Ar), 8.01 (d, 2H, Ar); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 72.4, 73.8, 74.4, 75.6, 76.7, 80.3, 84.2,

94.7, 116.8, 116.9, 117.2, 117.3, 127.9, 128.8, 131.3, 134.5, 134.6, 134.8, 135.0, 140.0, 164.8. Anal. Calcd for $C_{25}H_{31}ClO_7$: C, 62.69; H, 6.52. Found: C, 63.51; H, 6.88.

Preparation of 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranose (15).[24,38,39] A solution of methyl α-D-glucopyranoside (10.0 g, 51.5 mmol) and benzyl bromide (32.0 mL, 258 mmol) was cooled to 0 °C. To this stirring solution was added sodium hydride (12.4 g, 60% in mineral oil, 309 mmol) portionwise over 1.5 h. Upon conversion to a major spot on TLC (R_f 0.5, 1:3 EtOAc–hexanes), the reaction was poured into ice-water (50 mL), and extracted with ethyl acetate (3 x 50 mL). Drying ($MgSO_4$) and evaporation of the solvents under high vacuum left a syrup that was subjected to column chromatography (1:3 EtOAc–hexanes) to afford intermediate compound **14**, ^{1}H NMR data ($CDCl_3$, 250 MHz): δ 3.36 (s, 3H, OCH_3), 3.53–3.76 (m, 5H, H-2, H-3, H-4, H-5, H-6), 3.99 (Ψt, $J_{6b6} = J_{6b5}$ 9.4 Hz, H-6b), 4.42–5.00 (m, 10H, OCH_2Ph), 7.11–7.33 (m, 20H, Ph).

Compound **14** was dissolved in hot glacial acetic acid (500 mL) and was diluted with 1 M H_2SO_4 (100 mL). The solution was heated at 100 °C for 2.5 h, after which time an additional 110 mL of boiling 1 M H_2SO_4 was added, and heating was continued for an additional 24 h. The solution was cooled to room temperature and then poured into water (4 L) and allowed to stand at room temperature for 1.5 days. A portion of the product had precipitated and was collected by filtration. The filtrate was extracted with ethyl acetate (5 x 75 mL), dried ($MgSO_4$), and concentrated to afford an additional amount of hydrolyzed acetal. The precipitate and filtrate extractions were combined and crystallized from methanol to afforded **15** (9.65 g, 31% for 2 steps): mp 149–150 °C (lit[12]

mp 150–151 °C; lit[25] mp 149–149.5 °C; lit[26] mp 148 °C); $[\alpha]_D^{24}$ +19.8° (*c* 1.0, $CHCl_3$), lit[12] $[\alpha]_D^{20}$ +21.9° (*c* 2.19, $CHCl_3$); ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.53–3.66 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6b), 4.35–4.84 (m, 8H, OC*H*$_2$Ph), 5.09 (d, 1H, $J_{1,2}$ 3.1Hz, H-1), 7.09–7.30 (m, 20H, Ar).

Preparation of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose (16a).[14] 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (1.0 g, 1.85 mmol) upon acylation with 4-chlorobenzoyl chloride afforded a 1:15 α/β mixture that was subjected to careful column chromatography (1:2 Et_2O–petroleum ether) to afford **16a** (0.812 g, 65%) as a clear glass. Crystallization from ether–pentane gave **16a** as fine needles: mp 87–88 °C (lit[14] 87–88 °C), $[\alpha]_D^{22}$ -33.8° (*c* 1.0, $CHCl_3$), lit[14] $[\alpha]_D^{20}$ -34° (*c* 1.0, $CHCl_3$); ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.67–3.82, (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6a), 4.45–4.64 (m, 3H, OC*H*$_2$Ph), 4.77–4.94 (m, 5H, OC*H*$_2$Ph), 5.86 (d, 1H, $J_{1,2}$ 7.4 Hz, H-1), 7.1–7.3 (m, 20H, Bn), 7.41 (d, 2H, *J* 8.6 Hz, Ar), 7.97 (d, 2H, Ar); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 68.1, 73.5, 75.0, 75.6, 77.2, 80.8, 84.9, 84.7, 127.7–128.8, 131.4, 137.7–138.3, 140.0, 164.0. Anal. Calcd for $C_{41}H_{39}ClO_7$: C, 72.50; H, 5.79. Found: C, 72.53; H, 5.82.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(4-benzyloxybenzoyl)-β-D-glucopyranose (17a). 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (0.660 g, 1.22 mmol) upon acylation with 4-benzyloxybenzoyl chloride gave a 1:10 α/β mixture that was subjected to careful column chromatography (1:30 EtOAc–toluene) to obtain an anomerically pure compound. Compound **17a** was isolated as a white solid: mp 100–105 °C; $[\alpha]_D^{26}$ -30.9° (*c* 1.0, $CHCl_3$); ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.63–3.82 (m, 4H, H-2, H-3, H-4, H-5, H-

6a), 4.45–4.64 (m, 3H, OCH_2Ph), 4.81–4.93 (m, 5H, OCH_2Ph), 5.13 (s, 2H, PhOCH_2Ph), 5.86 (d, $J_{1,2}$ 7.5 Hz, H-1), 6.99 (d, 2H, J 8.8 Hz, Ar), 7.13–7.45 (m, 25H, Bn), 8.01 (d, 2H, J 8.8 Hz, Ar); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 68.2, 70.2, 73.5, 75.0, 75.6, 75.7, 77.2, 77.3, 81.0, 84.9, 94.5, 114.6, 121.9, 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.7, 132.2, 136.2, 137.9, 138.0, 138.1, 138.5, 164.5. Anal. Calcd. for $C_{48}H_{46}O_8$: C, 76.78; H, 6.17. Found: C, 76.19; H, 6.25.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(3,*4*,*5*-trimethoxybenzoyl)-β-D-glucopyranose (18a). 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (0.913 g, 1.69 mmol) upon acylation with 3,4,5-trimethoxybenzoyl chloride gave a 1:20 α/β mixture that was subjected to flash chromatography (1:2 Et_2O–petroleum ether) and then crystallized from Et_2O–pentane to give **18a** (0.722 g, 40%) as fine needles: mp 91 °C; $[\alpha]_D^{23}$ −31.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR data ($CDCl_3$, 250 MHz): δ 3.67–3.83 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6b), 3.87 (s, 6H, OCH_3), 3.92 (s, 3H, OCH_3), 4.46–4.67(m, 3H, OCH_2Ph), 4.79–4.94 (m, 5H, OCH_2Ph), 5.89 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 7.13 (d, 1H, H-2′), 7.16 (d, 1H, H-2′), 7.19–7.32 (m, 20H, Bn); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 56.3, 60.9, 68.0, 73.6, 74.9, 75.0, 75.6, 75.8, 77.2, 80.9, 84.9, 94.8, 107.4, 124.2, 127.9, 128.0, 128.4, 137.8, 137.8, 138.0, 138.4, 142.8, 152.9, 164.5, 193.2. Anal. Calcd. for $C_{44}H_{46}O_{10}$: C, 71.91; H, 6.31. Found: C, 71.81; H, 6.29.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-cinnamoyl-β-D-glucopyranose (19a). Compound **15** (0.990 g, 1.83 mmol) upon acylation with cinnamoyl chloride gave a 1:6 α/β ratio of products. Column chromatography (1:10 EtOAc–hexanes with ~0.5% 2-propanol) of this crude mixture gave pure **19a** (0.527 g, 43%) as a syrup: $[\alpha]_D^{25}$ −23.9° (*c* 1.0,

$CHCl_3$); ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.48–3.77 (m, 4H, H-2, H-3, H-4, H-5), 4.30–4.56 (m, 3H, OCH_2Ph), 4.66–4.87 (m, 5H, OCH_2Ph) 5.70 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 6.29 (d, 1H, J_{vic} 16 Hz, COCH=CHPh), 7.1–7.41 (m, 22H, Bn), 7.64 (d, 1H, COCH=CHPh); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 68.0, 73.4, 74.9, 75.4, 76.5, 77.2, 80.9, 84.8, 94.1, 117.1, 127.5, 127.6, 127.7, 127.8, 128.0, 128.1, 128.8, 130.5, 134.0, 137.8, 137.9, 138.0, 138.3, 146.3, 164.9. ESIMS (positive-ion mode): Calcd for $C_{43}H_{42}O_7$: $[M + H]^+$ 671.3; $[M + Na]^+$ 693.3; Found: *m/z* 671.1, 693.1.

2,3,4,6-Tetra-*O*-benzyl-1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose (20a). 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranose (0.700 g, 1.29 mmol) was dissolved in CH_2Cl_2 (10 mL) and pyridine (20 mL). The stirring solution was cooled to 0 °C and 4-chlorobenzoyl chloride (0.608 g, 3.88 mmol, dissolved in 8 mL CH_2Cl_2) was added in 2-mL portions over 1.5 h. After the final addition of the acid chloride, the solution was allowed to reach room temperature where stirring was continued for 1.5 h, after which time TLC (1:2 EtOAc–petroleum ether), indicated no remaining starting material. The reaction was quenched by pouring into 1 M HCl (20 mL), followed by washing with satd $NaHCO_3$ (20 mL) and H_2O (20 mL). Drying ($MgSO_4$) and evaporation of the solvents *in vacuo* gave a syrup that consisted of essentially an anomerically pure mixture. Flash chromatography (1:2 ether–petroleum ether), followed by crystallization from ethanol–pentane gave pure **20a** (0.837 g, 95%) as fine needles: mp 116–117 °C; $[\alpha]_D^{25}$ +74.4° (*c* 1.0, $CHCl_3$); ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.67–4.02 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6a), 4.45–4.77 (m, 3H, OCH_2Ph), 4.83–5.00 (m, 5H, OCH_2Ph), 6.58 (d, 1H, $J_{1,2}$ 3.4 Hz, H-1), 7.10–7.33 (m, 20H, Bn), 7.43 (d, 2H, *J* 8.5 Hz, Ar) 7.99 (d, 2H,

Ar); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 68.1, 73.1, 73.2, 73.6, 75.5, 75.7, 75.9, 77.2, 79.0, 81.8, 91.0, 122.7, 127.8, 127.9, 128.0, 128.1, 128.4, 128.5, 128.9, 131.3, 137.6, 137.8, 137.9, 138.6, 140.0, 164.1. Anal. Calcd. for $C_{41}H_{39}ClO_7$: C, 72.50; H, 5.79. Found: C, 72.41; H, 5.77.

General hydrogenolysis procedure: preparation of 16–20. The perbenzylated glucosyl ester **(16a–20a)** (0.56 mmol) was dissolved in ethyl acetate (8 mL) and diluted with absolute ethanol (3 mL). To the solution was added 10% Pd/C (ca. 15 mg), and the flask was equipped with an H_2-filled balloon. The mixture was allowed to stir gently at 0 °C until TLC (1:10 EtOAc–MeOH) showed a product with an R_f of ~ 0.3 (generally 6–8 h). The reaction mixture was filtered through a plug of Celite previously washed with water (10 mL), methanol (10 mL), acetone (10 mL), and ethanol (30 mL). Removal of the solvents under high vacuum afforded analytically pure compounds **16–20.**

Isolation of 1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose (16).[14] Compound **16a** (0.380 g, 0.559 mmol) was debenzylated to give **16** (0.168 g, 94%), which was isolated as a white solid after trituration with diethyl ether: mp 226–227 °C (dec), (lit[14] 226–228 °C), $[\alpha]_D^{24}$ -6.0° (*c* 1.0, EtOH), lit[14] $[\alpha]_D^{20}$ -6.2° (*c* 1.0, EtOH); ^1H NMR data (CD_3OD, 250 MHz): δ 3.43–3.51 (m, 4H, H-2, H-3, H-4, H-5), 3.77 (dd, 1H, $J_{6b,5}$ 4.1 Hz, $J_{6b,6}$ 13.3 Hz, H-6b), 5.71 (d, 1H, $J_{1,2}$ 7.8 Hz, H-1), 7.51 (d, 2H, *J* 8.6 Hz, Ar), 8.06 (d, 2H, Ar); ^{13}C NMR data (CD_3OD, 62.5 MHz): δ 62.3, 71.1, 74.0, 78.0, 78.9, 96.5, 129.5, 130.0, 132.5, 141.1, 165.8. ESIMS (positive-ion mode): Calcd for $C_{13}H_{15}ClO_7$: $^{35}Cl[M + Na]^+$ 341.7; $^{37}Cl[M + Na]^+$ 343.7; $^{35}Cl[2M + Na]^+$ 660.4; $^{37}Cl[2M + Na]^+$

662.4; Found: *m/z* 341.1, 343.1, 659.1, 661.0. Anal. Calcd for $C_{13}H_{15}ClO_7 \cdot 0.1H_2O$: C, 48.72; H, 4.81. Found: C, 48.71; H, 4.81.

1-*O*-(4-hydroxybenzoyl)-β-D-glucopyranose (17). Compound **17a** (0.400 g, 0.533 mmol) afforded **17** (0.080 g, 50%) as a white solid: mp 226–227 °C; $[\alpha]_D^{26}$ −8.8° (*c* 0.17, MeOH); ^{1}H NMR data (DMSO-d_6–D_2O, 250 MHz): δ 3.24–3.34 (m, 4H, H-2, H-3, H-4, H-5), 3.44 (dd, 1H, $J_{6b,5}$ 4.0 Hz, $J_{6b,6}$ 11.9 Hz, H-6b), 5.51 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 6.85 (d, 2H, J_{vic} 8.6 Hz, Ar), 7.85 (d, 2H, Ar); ^{13}C NMR data (DMSO-d_6, 62.5 MHz): δ 60.6, 69.6, 72.6, 76.4, 77.9, 94.6, 115.6, 119.9, 132.2, 162.5, 164.7; ESIMS (positive-ion mode): Calcd for $C_{13}H_{16}O_8$: $[M + Na]^+$ 323.3, $[2M + Na]^+$ 623.5; Found: *m/z* 322.6, 623.1. Anal. Calcd for $C_{13}H_{16}O_8 \cdot 0.2H_2O$: C, 51.39; H, 5.44. Found: C, 51.30; H, 5.52

Isolation of 1-*O*-(3,4,5-trimethoxybenzoyl)-β-D-glucopyranose (18).[40] Hydrogenolysis of **18a** (0.225 g, 0.601 mmol), followed by filtration through Celite and removal of the solvents, gave **18** (0.081 g, 71%) as a glass: mp 145–147 °C (lit[40] mp 94–95 °C); $[\alpha]_D^{23}$ −10.9° (*c* 1.0, EtOH), $[\alpha]_D^{26}$ −7.2° (*c* 1.0, acetone), lit value[40] $[\alpha]_D^{20}$ −6.4° (*c* 1.0, acetone); ^{1}H NMR data (CD_3OD, 250 MHz): δ 3.44–3.52 (m, 4H, H-2, H-3, H-4, H-5), 3.71 (dd, 1H, $J_{6b,5}$ 4.1 Hz, $J_{6b,6}$ 12.1 Hz, H-6b), 3.84 (s, 3H, OCH_3), 3.89 (s, 6H, OCH_3), 5.71 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 7.4 (s, 2H, Ar); ^{13}C NMR data (CD_3OD, 62.5 MHz): 56.8, 61.2, 62.3, 71.1, 74.0, 78.0, 78.9, 96.4, 108.5, 125.9, 144.1, 154.4, 166.4; ESIMS (positive-ion mode): Calcd for $C_{16}H_{22}O_{10}$: $[M + H]^+$ 375.3; $[M + Na]^+$ 397.3; Found: *m/z* 374.8, 396.9. Anal. Calcd. for $C_{16}H_{22}O_{10} \cdot 0.1\ H_2O$: C, 51.09; H, 5.95. Found: C, 51.07; H, 5.99.

1-*O*-(3-phenylpropanoyl)-β-D-glucopyranose (19). Hydrogenolysis of **19a** (0.245 g, 0.365 mmol) concomitantly saturated the conjugated double bond to afford **19** (0.087 g, 76%) as a syrup: $[\alpha]_D^{26}$ +9.0° (*c* 0.7, MeOH); ^{1}H NMR data (CD_3OD, 250 MHz): δ 2.71 (dt, 2H, J_{gem} 3.4 Hz, J_{vic} 7.6 Hz, COCH_2), 2.94 (t, 2H, CH_2Ph), 3.33–3.41 (m, 4H, H-2, H-3, H-4, H-5), 3.67 (dd, 1H, $J_{6b,5}$ 4.0 Hz, $J_{6b,6}$ 11.8 Hz, H-6b), 3.84 (d, 1H, $J_{5,6}$ 13.1 Hz, H-6), 5.50 (d, 1H, $J_{1,2}$ 7.8 Hz, H-1), 7.13–7.29 (m, 5H, Ph); ^{13}C NMR data (CD_3OD, 100 MHz): δ 31.6, 36.8, 62.8, 71.3, 73.9, 77.9, 78.7, 95.5, 127.0, 129.2, 141.6, 172.9; ESIMS (positive-ion mode): Calcd for $C_{15}H_{20}O_7$: $[M + H]^+$ 313.3; $[M + Na]^+$ 335.3; $[M + K]^+$ 351.3; Found: *m/z* 312.9, 334.9, 350.8. Anal. Calcd for $C_{15}H_{20}O_7 \cdot 0.2\ H_2O$: C, 57.69; H, 6.45. Found: C, 57.87; H, 6.29.

1-*O*-4-chlorobenzoyl-α-D-glucopyranose (20). By the same procedure used to provide **16–19**, compound **21** was isolated as a glass: $[\alpha]_D^{26}$ +63.8° (*c* 0.8, MeOH); ^{1}H NMR data (CD_3OD, 250 MHz): δ 3.44 (ψt, 1H, $J_{6,5} = J_{6,6b}$ 9.1 Hz, H-6), 3.61–3.87 (m, 5H, H-2, H-3, H-4, H-5, H-6b), 6.35 (d, 1H, $J_{1,2}$ 3.5 Hz), 7.52 (d, 2H, *J* 8.6 Hz, Ar), 8.06 (d, 2H, Ar). ^{13}C NMR data (CD_3OD, 62.5 MHz): δ 62.3, 71.1, 72.4, 74.9, 76.4, 94.5, 129.7, 129.9, 132.5, 140.9, 165.8; ESIMS (positive-ion mode): Calcd for $C_{13}H_{15}ClO_7$: ^{35}Cl$[M + Na]^+$ 341.7; ^{37}Cl$[M + Na]^+$ 343.7; Found: *m/z* 340.8, 342.7.

2,3,4,6-Tetra-*O*-(4-methoxybenzyl)-D-glucopyranose (24). The procedure used to provide **22** is a modification of a known procedure.[41] A mixture of glucose (19.95 g, 110.8 mmol) and allyl alcohol (200 mL, dried with $CaSO_4$) was treated with $BF_3 \cdot OEt_2$ (2.4 mL, 8.9 mmol) and was heated to reflux with good stirring. After refluxing for 4 h, ca.1.0 g of Dowex-50W x 8 (H^+) resin (prepared by washing with 1 M

HCl, water, methanol, and dried *in vacuo* at 60 °C for 5 h) was added and heating was continued for an additional 0.5 h. The slightly colored solution was filtered through glass wool, and the solvents were removed under high vacuum. The syrup was subjected to flash chromatography (1:10 MeOH–EtOAc) to give **22** (15.8 g, 61%) as a syrup. The product (R_f 0.28, 1:10 MeOH–EtOAc) was sufficiently pure, and a portion was used for the next step. The slightly impure allyl glucopyranoside (4.72 g, 21.4 mmol) was dissolved in DMF (75 mL) and was allowed to stir at 0 °C. Sodium hydride (5.28 g, 60% in mineral oil, 132 mmol) was added in four portions over 0.5 h, followed by the dropwise addition of *p*-methoxybenzyl chloride (20 mL, 147 mmol). The reaction was then heated with stirring at 50–60 °C for 5 h when TLC showed a major product (R_f 0.43, 1:1 EtOAc–hexanes). The reaction was poured into ice-water (50 mL) and extracted with ethyl acetate (3 x 25 mL). Drying ($MgSO_4$), evaporation of the solvents under high vacuum, and column chromatography gave **23**, which was isomerized to the 1-propenyl ether according to the procedure of Gigg and Warren.[42] Compound **23** was dissolved in anhydrous DMSO (120 mL) and potassium *tert*-butoxide (2.01 g, 17.9 mmol) was added. The mixture was placed in a bath that was at 90 °C and allowed to stand for 1 h when TLC (1:1 EtOAc–hexanes) showed a compound with R_f 0.45, which indicated a complete isomerization to the 1-propenyl ether. The dark-brown solution was allowed to cool to room temperature, and water (5 mL) was added to quench the excess potassium *tert*-butoxide. Concentration under high vacuum, followed by lyophilization, provided a waxy solid that was dissolved in acetone (90 mL) and 1 M HCl (10 mL). The solution was allowed to reflux with good stirring overnight. The solution

was then concentrated, and the product was extracted with EtOAc (4 x 30 mL), washed with satd $NaHCO_3$ (50 mL) and water (50 mL). Drying ($MgSO_4$), removal of the solvents, and crystallization from methanol afforded **24** (7.08 g, 50% for three steps): mp 127–128 °C, $[\alpha]_D^{24}$ -2.5° (*c* 1.0, $CHCl_3$), ^1H NMR data ($CDCl_3$, 250 MHz): δ 3.49–3.69 (m, 5H, H-2, H-3, H-4, H-5, H-6), 3.76 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.87 (d, *J* 9.2 Hz, H-6b), 4.34–4.88 (m, 10H, Bn), 5.15 (d, 1H, $J_{1,2}$ 3.0 Hz, H-1), 6.78–6.88 (m, 11H, Bn), 7.03 (d, 2H, *J* 8.5 Hz, Bn), 7.22–7.30 (m, 9H, Bn); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 55.2, 68.1, 70.3, 72.9, 73.1, 74.6, 75.3, 79.7, 81.5, 91.4, 113.8, 113.9, 129.4, 129.5, 129.6, 159.3. Anal. Calcd for $C_{38}H_{44}O_{10}$: C, 69.08; H, 6.71; Found: C, 68.96; H, 6.80.

1-*O*-(4-Chlorocinnamoyl)-2,3,4,6-tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranose (25a). 2,3,4,6-Tetra-*O*-(4-methoxybenzyl)-D-glucopyranose **(24)** (1.00 g, 1.51 mmol) upon acylation with 4-chlorocinnamoyl chloride afforded a 1:15 α/β mixture of products. The pure β anomer was obtained by careful column chromatography on fine silica gel (1:5 EtOAc–toluene) to afford **25a** as syrup (0.752 g, 61%): $[\alpha]_D^{24}$ -30.1° (*c* 1.0, $CHCl_3$); ^1H NMR data (DMSO-d_6, 250 MHz): δ 3.57–3.80 (m, 6H, H-2, H-3, H-4, H-5, H-6, H-6b), 3.70 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 4.37–4.44 (m, 2H, OCH_2Ar), 4.53–4.86 (m, 6H, OCH_2Ar), 6.32 (d, 1H, J_{vic} 16.1 Hz, $COCH$=CHAr), 6.76–6.87 (m, 10H, Bn), 7.03 (d, 2H, *J* 8.4 Hz, Ar), 7.17–7.25 (m, 9H, Bn), 7.26–7.46 (m, 10H, Bn and Ar), 7.65 (d, 1H, COCH=CHAr); ^{13}C NMR data (DMSO-d_6, 62.5 MHz): δ 55.3, 67.7, 73.1, 74.6, 75.4, 75.6, 80.6, 84.7, 94.2, 113.8, 117.9, 129.2, 129.4, 129.5, 129.7, 130.0, 130.2, 130.7,

132.6, 136.6, 144.8, 159.2, 164.8. Anal. Calcd for $C_{47}H_{49}ClO_{11}$: C, 68.40; H, 5.98. Found: C, 68.27; H, 6.10.

1-*O*-(4-Allyloxycinnamoyl)-2,3,4,6-tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranose (26a). 2,3,4,6-Tetra-*O*-4-methoxybenzyl-D-glucopyranose **(24)** (1.01 g, 1.53 mmol) upon acylation with 4-allyloxycinnamoyl chloride afforded **26a** (0.737 g, 57%) after column chromatography on fine silica gel (1:10 EtOAc–toluene). Crystallization from ether–pentane afforded a white solid: mp 84–85 °C; $[\alpha]_D^{24}$ -28.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR data (acetone-d_6, 250 MHz): δ 3.51–3.79 (m, 18H, H-2, H-3, H-4, H-5, H-6, H-6b overlapped with 4 OCH_3), 4.43–4.49 (m, 4H, OCH_2Ar), 4.52 (d, 2H, *J* 7.1 Hz, $OCH_2CH{=}CH_2$), 4.62–4.86 (m, 4H, OCH_2Ar), 5.24–5.46 (m, 2H, $OCH_2CH{=}CH_2$), 5.73 (d, 1H, $J_{1,2}$ 7.9 Hz, H-1), 5.99–6.10 (m, 1H, $OCH_2CH{=}CH_2$), 6.43 (d, 1H, J_{vic} 16.0 Hz, $COCH{=}CHAr$), 6.79–6.89 (m, 10H, Bn), 7.01 (d, 2H, *J* 8.7 Hz, Ar), 7.13–7.30 (m, 8H, Bn), 7.65 (d, 2H, Ar), 7.74 (d, 1H, $COCH{=}CHAr$); ^{13}C NMR data (acetone-d_6, 62.5 MHz): 55.4, 55.5, 69.1, 69.4, 73.3, 74.9, 76.3, 78.2, 81.7, 94.8, 114.4, 115.6, 117.7, 127.9, 130.1, 130.3, 130.4, 131.0, 131.3, 131.5, 131.6, 131.9, 134.2, 146.6, 160.1, 160.2, 161.7, 165.7. Anal. Calcd for $C_{50}H_{54}O_{12}$: C, 70.91; H, 6.43. Found: C, 70.81; H, 6.47.

1-*O*-(4-Chlorocinnamoyl)-β-D-glucopyranose (25). A solution of 1-*O*-4-chlorocinnamoyl-2,3,4,6-tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranose **(25a)** (0.200 g, 0.242 mmol) in 10:1 acetonitrile–water was cooled to 0 °C and treated with cerric ammonium nitrate (CAN) (1.51 g, 2.75 mmol) that was dissolved in acetonitrile (45 mL). After 1 h at room temperature, the solution was concentrated and poured onto a

silica gel column (eluted with acetonitrile, followed by 1:10 acetone–petroleum ether, then pure acetone). Removal of the solvents afforded **25** as a light-brown glass (0.053 g, 62 %): $[\alpha]_D^{24}$ -5.7° (*c* 1.0, MeOH); ^{1}H NMR data (CD_3OD, 250 MHz): δ 3.39–3.46 (m, 4H, H-2, H-3, H-3, H-4, H-5), 3.68 (dd, 1H, $J_{6b,6}$ 4.0 Hz, $J_{6b,5}$ 12.0 Hz), 3.84 (d, 1H, $J_{6,5}$ 11.6 Hz, H-6), 5.58 (d, 1H, $J_{1,2}$ 7.6 Hz, H-1), 6.58 (d, 1H, J_{vic} 16.1 Hz, COC*H*=CHAr), 7.42 (d, 2H, *J* 8.5 Hz, Ar), 7.62 (d, 2H, Ar), 7.77 (d, 1H, COCH=C*H*Ar); ^{13}C NMR data (CD_3OD, 62.5 MHz): 62.3, 68.1, 71.1, 74.0, 78.0, 78.8, 95.9, 119.1, 130.2, 130.2, 130.8, 134.3, 137.5, 146.1, 166.8; ESIMS (positive-ion mode): Calcd for $C_{15}H_{17}ClO_7$: $^{35}Cl[M + H]^+$ 344.7, $^{37}Cl[M + H]^+$ 346.7; $^{35}Cl[M + Na]^+$ 366.9; $^{37}Cl[M + Na]^+$ 368.9; Found: *m/z* 344.8, 347.0; 366.9, 368.8.

General procedure for preparation of 8-cinnamoyloxyquinolines. 8-Acyloxy-quinolines **(27, 28)** were prepared according to the procedure of Plusquellec.[34] To a stirring solution of 8-hydroxyquinoline (5 mmol) in THF (25 mL) at 0 °C was added TEA (1.0 mL, 7.2 mmol). After 5 min, the appropriate acid chloride (6 mmol in THF) was added, and stirring was continued at room temperature until TLC indicated disappearance of 8-hydroxyquinoline (generally 1–2 h). The solvent was removed, and the residual solid dissolved in CH_2Cl_2 (45 mL), washed with 1 M HCl (45 mL), followed by washing with 5% $NaHCO_3$ (50 mL). The organic layer was dried with $MgSO_4$, concentrated, and crystallized from 95% ethanol.

8-(3,4,5-Trimethoxycinnamoyloxy)quinoline (27). 3,4,5-Trimethoxycinnamic acid (1.51 g, 6.34 mmol) was treated with thionyl chloride to give trimethoxycinnamoyl chloride, which was used to acylate 8-hydroxyquinoline as described above. Crystallization afforded pure **27** (1.85 g, 80%) as spore-like crystals: mp 171–172 °C, ^{1}H NMR data ($CDCl_3$, 250 MHz): δ 3.92 (s, 9H, OCH_3), 6.81 (d, 1H, *J* 15.9 Hz, COCH=C*H*Ar), 6.87 (s, 2H, Ar), 7.45 (dd, 1H, $J_{3,2}$ 4.2 Hz , $J_{3,4}$ 8.3 Hz, H-3), 7.56–7.62 (m, 2H, H-5, H-6), 7.77 (dd, 1H, $J_{7,6}$ 7.2 Hz, $J_{7,5}$ 2.3 Hz, H-7), 7.9 (d, 1H, COC*H*=C*H*Ar), 8.21 (dd, 1H, $J_{4,3}$ 8.3 Hz, $J_{4,2}$ 1.6 Hz, H-4); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 56.2, 60.9, 76.5, 105.6, 116.4, 121.6, 121.7, 125.9, 126.2, 129.6, 129.8, 136.1, 140.4, 141.3, 146.9, 147.3, 150.6, 153.4, 165.6. Anal. Calcd for $C_{21}H_{19}NO_5$: C, 69.03; H, 5.24; N, 3.83. Found: C, 68.78; H, 5.20; N, 3.72.

8-(4-allyloxycinnamoyloxy)quinoline (28). 4-Hydroxycinnamic acid (1.50 g, 8.42 mmol) was dissolved in methanol (30 mL) and was treated with concd H_2SO_4 (5 drops). The solution was refluxed with vigorous stirring for 8 h, after which time the solvents were evaporated, and the residue was dissolved in EtOAc, washed with satd $NaHCO_3$ (20 mL), H_2O (20 mL), and dried ($MgSO_4$). Removal of the solvents afforded methyl 4-hydroxycinnamoate as a white solid which was dissolved in THF (20 mL) and treated with allyl bromide (1.10 mL, 12.6 mmol) at 0 °C. To this solution was added sodium hydride (0.340 g, 60% dispersion in mineral oil, 13.5 mmol) portionwise over 20 min, and the resulting mixture was stirred at room temperature for an additional 4 h. The reaction was then poured into ice-water, extracted with CH_2Cl_2 (3 x 20 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was saponified in 1:10 1,4-

dioxane–H_2O (50 mL) with NaOH (pH ~10) under reflux before was it was cooled to room temperature, acidified (pH ~2) with 1 M HCl, and extracted with EtOAc (3 x 20 mL). Drying ($MgSO_4$) and removal of the solvents afforded 4-allyloxycinnamic acid as an off-white solid. After drying *in vacuo* at 68 °C, the solid was treated with thionyl chloride as previously described to afford 4-allyloxycinnamoyl chloride as an oil. The oil so obtained was added to a stirring solution of 8-hydroxyquinoline (0.731 g, 5.03 mmol) in THF (25 mL) and TEA (1.0 mL, 7.2 mmol). The reaction was allowed to stir at room temperature until TLC indicated disappearance of 8-hydroxyquinoline (1.5 h). The solvent was removed, and the residual solid was dissolved in CH_2Cl_2 (45 mL) and washed with 5% $NaHCO_3$ (50 mL). Drying the organic layer ($MgSO_4$), concentration, and crystallization from 95% ethanol afforded **28** (1.74 g, 63% for four steps): mp 127–128 °C; ^{1}H NMR data ($CDCl_3$, 250 MHz): δ 4.58 (d, 2H, *J* 5.2 Hz, $OCH_2CH=CH_2$), 5.29–5.98 (m, 2H, $OCH_2CH=CH_2$), 6.00–6.14 (m, 1H, $OCH_2CH=CH_2$), 6.75 (d, 1H, J_{vic} 15.9 Hz, $COCH=CHAr$), 6.94, (d, 2H, *J* 8.7 Hz, Ar), 7.42 (dd, 1H, $J_{3,4}$ 8.3 Hz, $J_{3,2}$ 4.2 Hz, H-3), 7.50–7.59 (m, 4H, Ar), 7.71–7.75 (dd, 1H, $J_{7,6}$ 7.0 Hz, $J_{7,5}$ 2.6 Hz, H-7), 7.94 (d, 1H, $COCH=CHAr$), 8.18 (dd, 1H, $J_{4,3}$ 8.3 Hz, $J_{4,2}$ 1.5 Hz, H-4), 8.93 (dd, 1H, H-2); ^{13}C NMR data ($CDCl_3$, 62.5 MHz): δ 68.9, 114.6, 115.1, 118.0, 121.6, 121.7, 125.7, 126.3, 127.3, 129.6, 130.1, 132.8, 136.2, 141.3, 146.7, 147.4, 150.5, 160.7, 165.9. Anal. Calcd for $C_{21}H_{17}NO_3$: C, 76.12; H, 5.17; N, 4.23. Found: C, 74.79; H, 5.09; N, 4.15.

1-*O*-3,4,5-(Trimethoxycinnamoyl)-β-D-glucopyranose (29): Compound **29** was obtained according to the procedure of Plusquellec.[34] β-D-glucose (0.648 g, 3.60

mmol) in pyridine (35 mL) was heated at 90–100 °C for 1 h. After cooling to room temperature, **27** (0.384 g, 1.05 mmol) and a catalytic amount of sodium hydride (60% in mineral oil, previously washed with petroleum ether) were added and the solution was stirred at 30–35 °C for 6 h, after which time TLC (1:3 EtOAc–hexanes) indicated only a small amount of the ester starting material. The pyridine was removed under high vacuum, and the residual syrup was dissolved in butanol (25 mL) and was washed with a 0.1 N phosphate buffer (pH 7.0), followed by acetic acid (0.1 M, 30 mL). The butanol was removed under high vacuum. Column chromatography (1:1 petroleum ether–acetone, then pure acetone) afforded the title compound **(29)** along with 40% of the alternate regioisomers (0.097 g, 25% based on **27**). Crystallization from EtOAc afforded pure **29**: mp 105 °C (dec); $[\alpha]_D^{24}$ -9.1° (*c* 0.77, MeOH); ^{1}H NMR data (CD_3OD, 250 MHz): δ 3.39–3.52 (m, 4H, H-2, H-3, H-4, H-5), 3.71 (dd, 1H, $J_{6b,5}$ 4.3 Hz, $J_{6b,6}$ 11.9 Hz, H-6b), 3.79 (s, 3H, OCH_3), 3.87 (s, 6H, OCH_3), 5.58 (d, 1H, $J_{1,2}$ 7.7Hz, H-1), 6.52 (d, 1H, J_{vic} 15.9 Hz, COC*H*=CHAr), 6.94 (s, 2H, Ar), 7.73 (d, 1H, COCH=C*H*Ar). ^{13}C NMR data (CD_3OD, 62.5 MHz): δ 50.0, 56.8, 61.2, 62.4, 71.2, 74.1, 78.1, 78.9, 95.9, 107.0, 117.6, 131.4, 141.7, 147.7, 154.9, 167.2; ESIMS (positive-ion mode): Calcd for $C_{18}H_{24}O_{10}$: $[M + H]^+$ 401.3; $[M + Na]^+$ 423.3; Found: *m/z* 401.0, 423.0. Anal. Calcd. for $C_{18}H_{24}O_{10}\cdot 0.2H_2O$: C, 53.52; H, 6.09. Found: C 53.51; H, 5.98.

Preparation of 1-*O*-(4-hydroxycinnamoyl)-β-D-glucopyranose (31).[31,43]

1-*O*-4-allyloxycinnamoyl-β-D-glucopyranose **(26)** was prepared by the procedure that provided **29**. Compound **28** (0.890 g, 2.79 mmol) provided crude **26** (0.351 g,

34%) by the same procedure used to go from **27** to **29**. When analyzed by HPLC, the crude reaction mixture of **26** was found to contain ca. 40% of the undesired regioisomers but was subsequently deprotected.[22] A solution of 1,5-cyclooctadiene-bis(methyldiphenyl-phosphine) iridium hexafluorophosphate (35 mg, 41 μmol) in THF (5 mL) was swirled under an H_2-filled balloon at room temperature until the red suspension turned a light tan color (ca. 15 min). The tan solution, which contained the activated iridium catalyst, was then purged with dry N_2 for 15 min and transferred *via* syringe to a stirring solution of **26** (0.351 g, 0.958 mmol in 15 mL of 1,4-dioxane). After stirring at room temperature for 5 h, ^{1}H NMR spectroscopy indicated that the isomerization of the allyl group to the 1-propenyl group was complete. The solution containing the 1-propenyl ether was treated with solid I_2 (0.15 g, 0.59 mmol), and stirring was continued at room temperature until ^{1}H NMR spectroscopy revealed complete removal of the 1-propenyl ether (1 h). Solid sodium thiosulfate was added, and stirring was continued for an additional 15 min. Concentration of the solution, filtration through a silica gel column (packed with 1:1 petroleum ether–dioxane), and removal of the solvents gave crude **31,** which was further purified by C_{18} reversed-phase preparative HPLC (20% MeOH–H_2O). The title compound (0.031 g, 3.4% based on **28**) was obtained as a tan, flocculent solid: $[\alpha]_D^{24}$ −7.1° (*c* 0.9, MeOH), lit value[31] $[\alpha]_D^{20}$ −7.95° (*c* 0.9, MeOH) , lit value[43] $[\alpha]_D^{20}$ −8.22°, (*c* 0.9, MeOH); ^{1}H NMR data (DMSO-d_6, 250 MHz) δ 3.02–3.27 (m, 4H, H-2, H-3, H-4, H-5), 3.44 (dd, 1H, $J_{6b,6}$ 4.8 Hz, $J_{6b,5}$ 11.8 Hz, H-6b), 3.65 (d, 1H, $J_{6,5}$ 13.1 Hz, H-6), 5.44 (d, 1H, $J_{1,2}$ 7.7 Hz, H-1), 6.35 (d, 1H, J_{vic} 15.9 Hz, COC*H*=CHAr), 6.76 (d, 2H, *J* 8.5 Hz, Ar), 7.54 (d, 2H, Ar), 7.62 (d, 1H, COCH=C*H*Ar); ^{13}C NMR data

(DMSO-d_6, 62.5 MHz): δ 60.5, 69.5, 72.5, 76.5, 77.8, 94.2, 112.9, 116.0, 124.2, 130.3, 130.5, 146.1, 161.2, 165.4; ESIMS (positive-ion mode): Calcd for $C_{15}H_{18}O_8$: $[M + Na]^+$ 349.1, $[M + K]^+$ 365.0; Found: *m/z* 348.9, 364.7.

LIST OF REFERENCES

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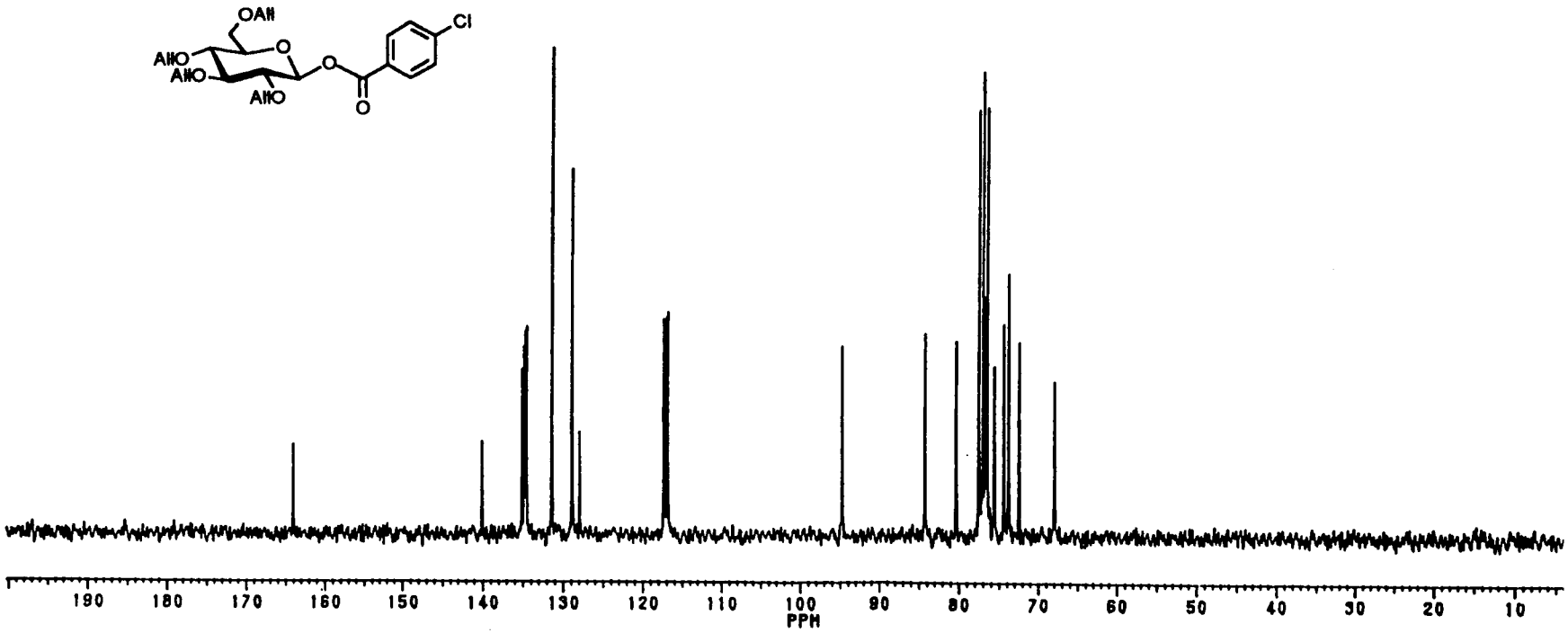
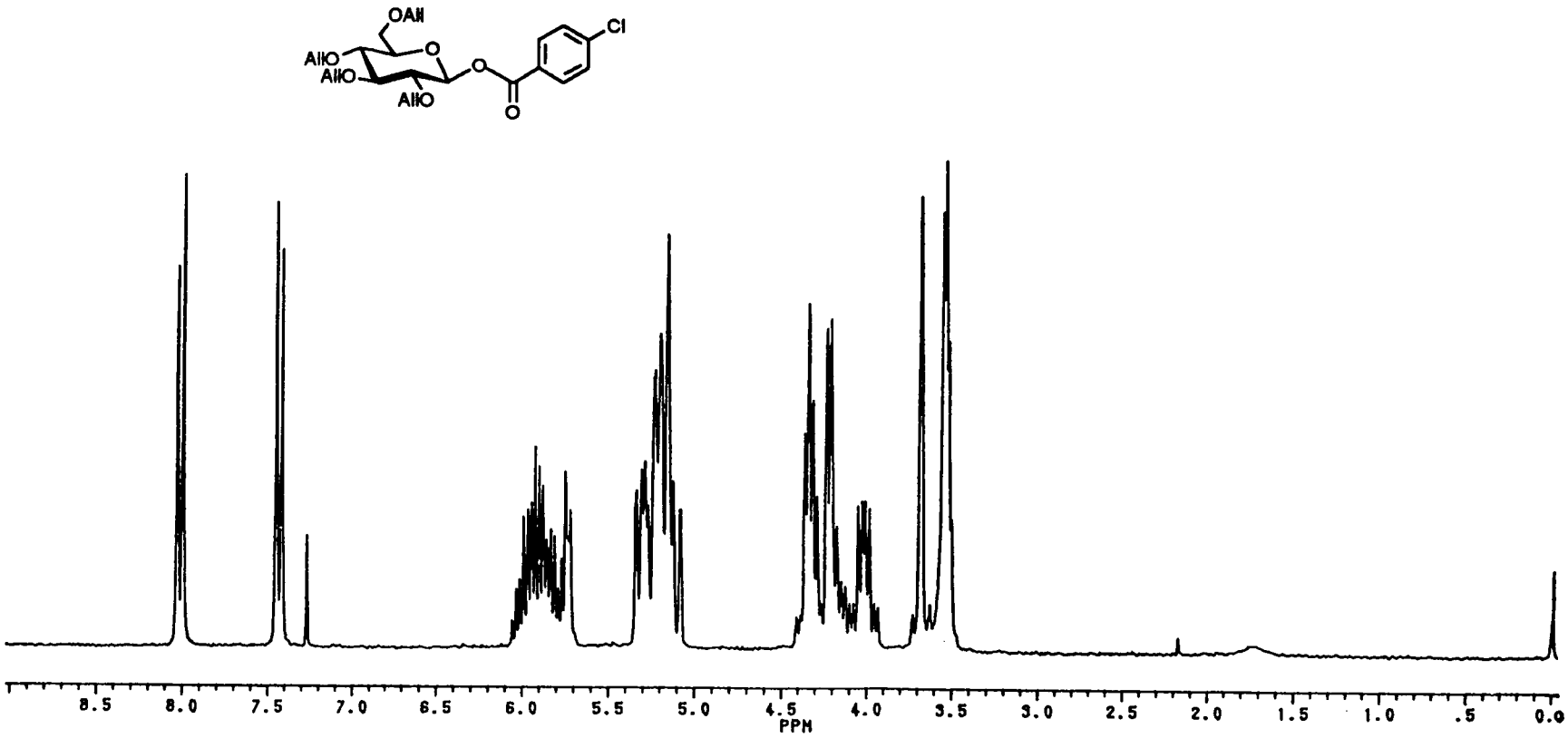
APPENDIX

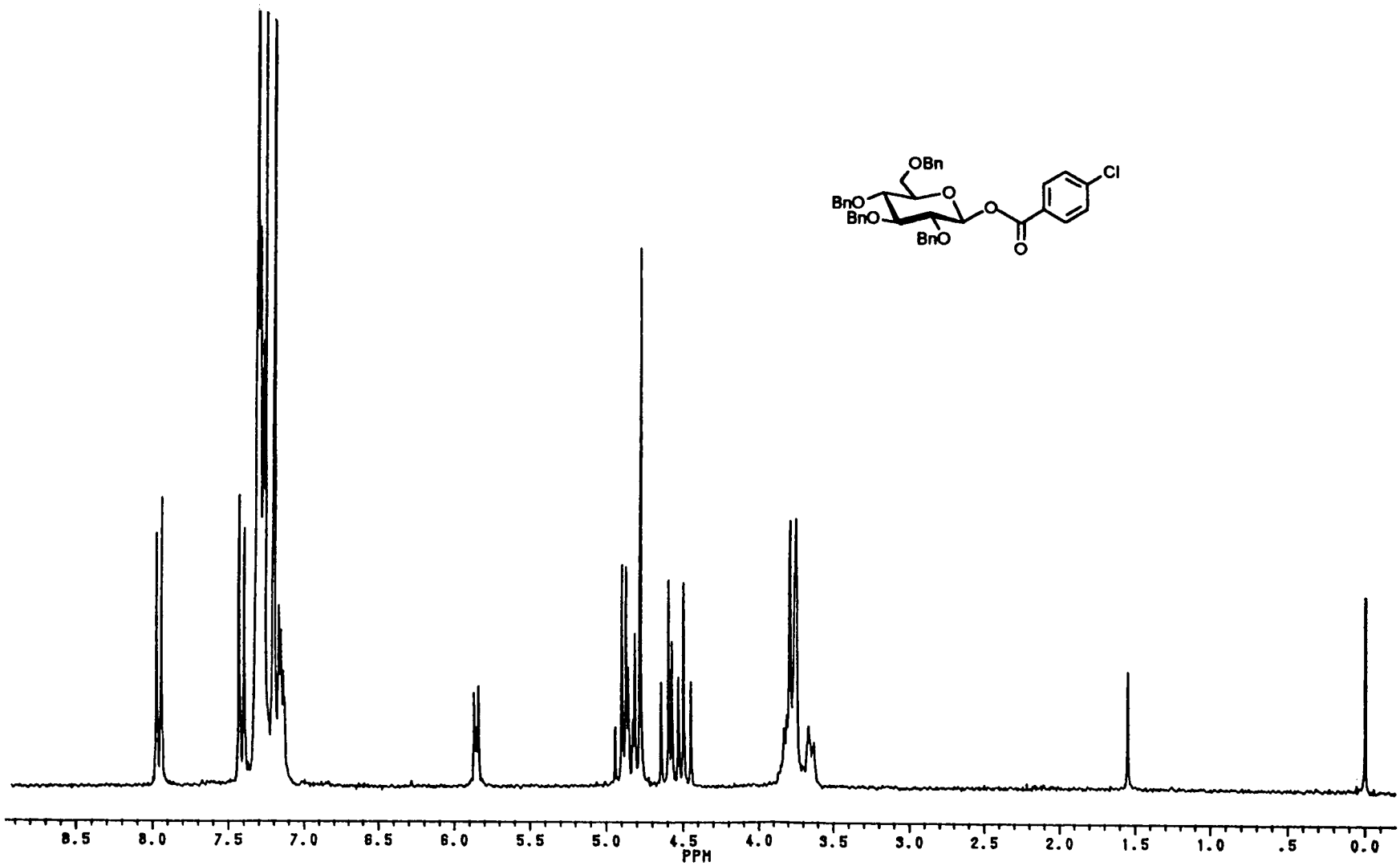
^{1}H AND ^{13}C NMR SPECTRA FOR SELECTED INTERMEDIATE AND TARGET COMPOUNDS



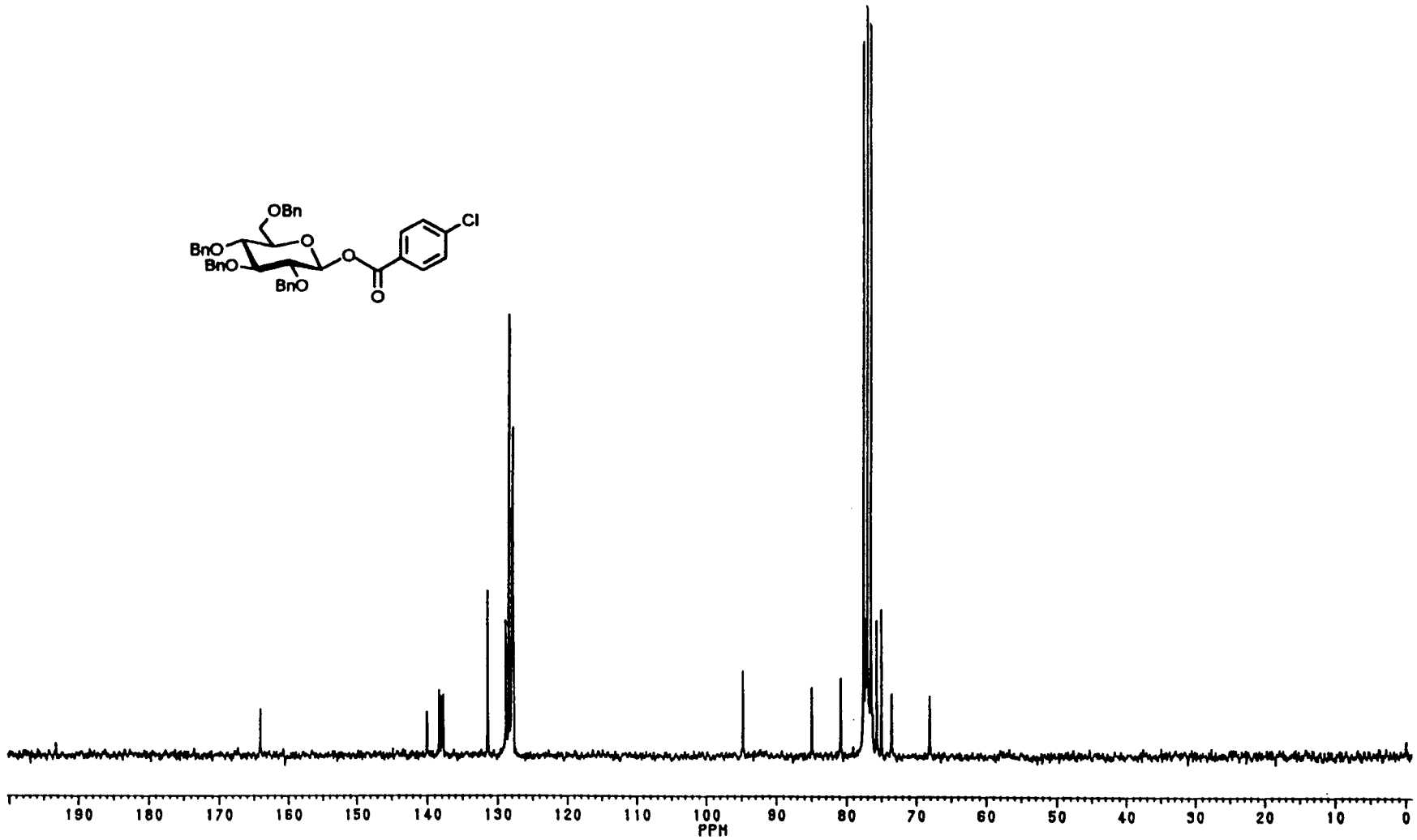
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 2,3,4,6-tetra-*O*-allyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(13)**.



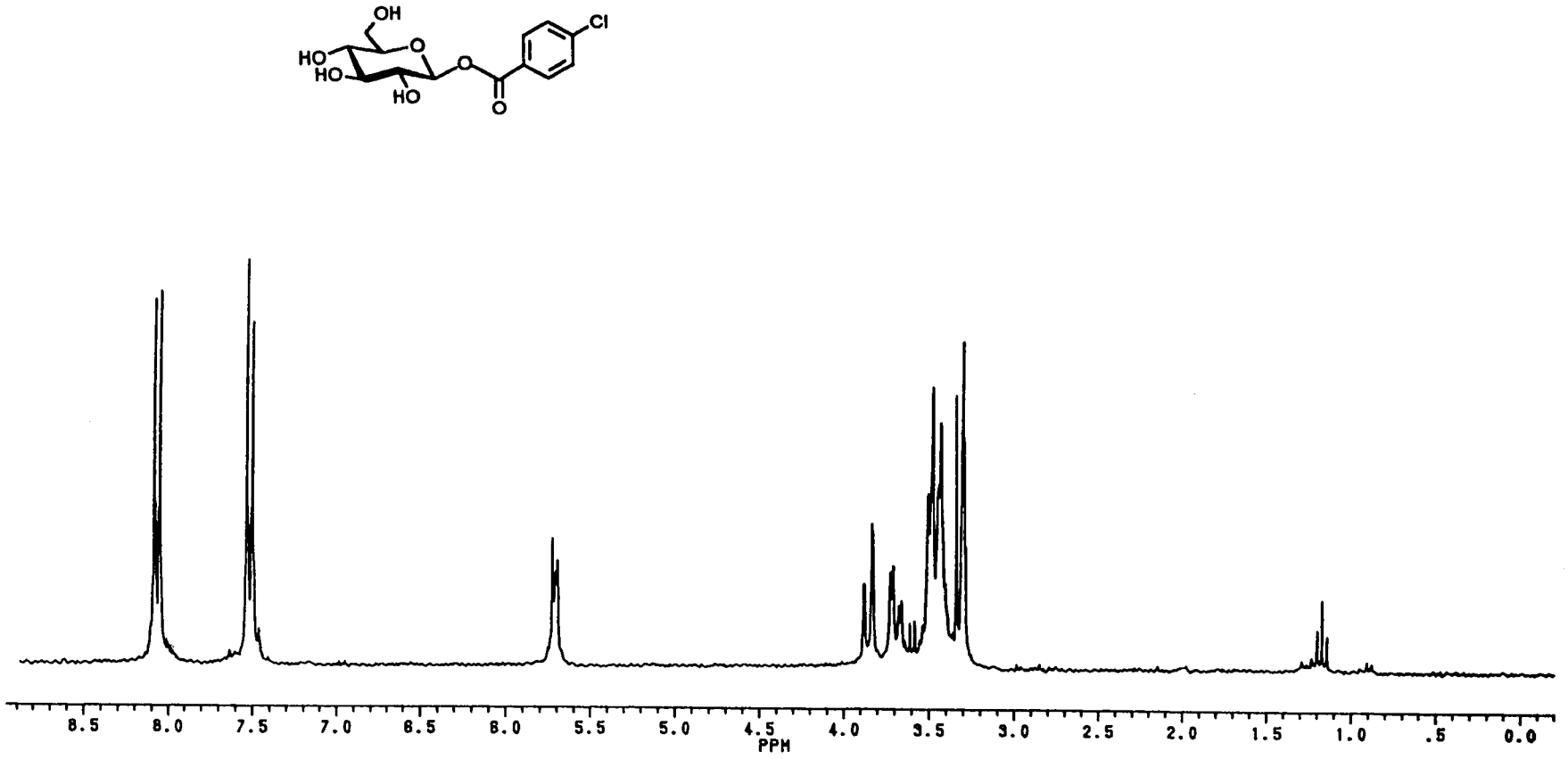
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 2,3,4,6-tetra-*O*-allyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(13)**.



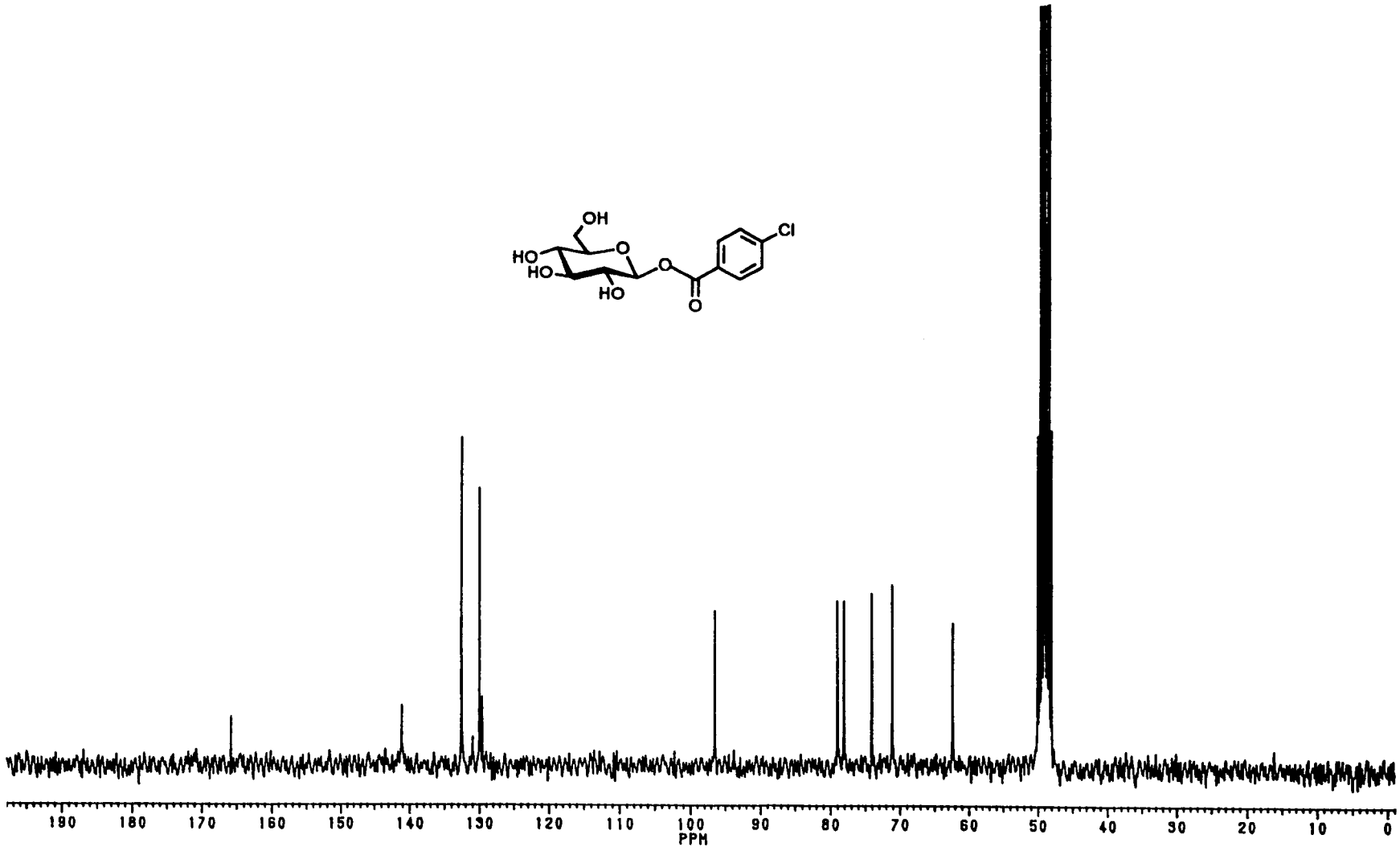
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(16a)**.



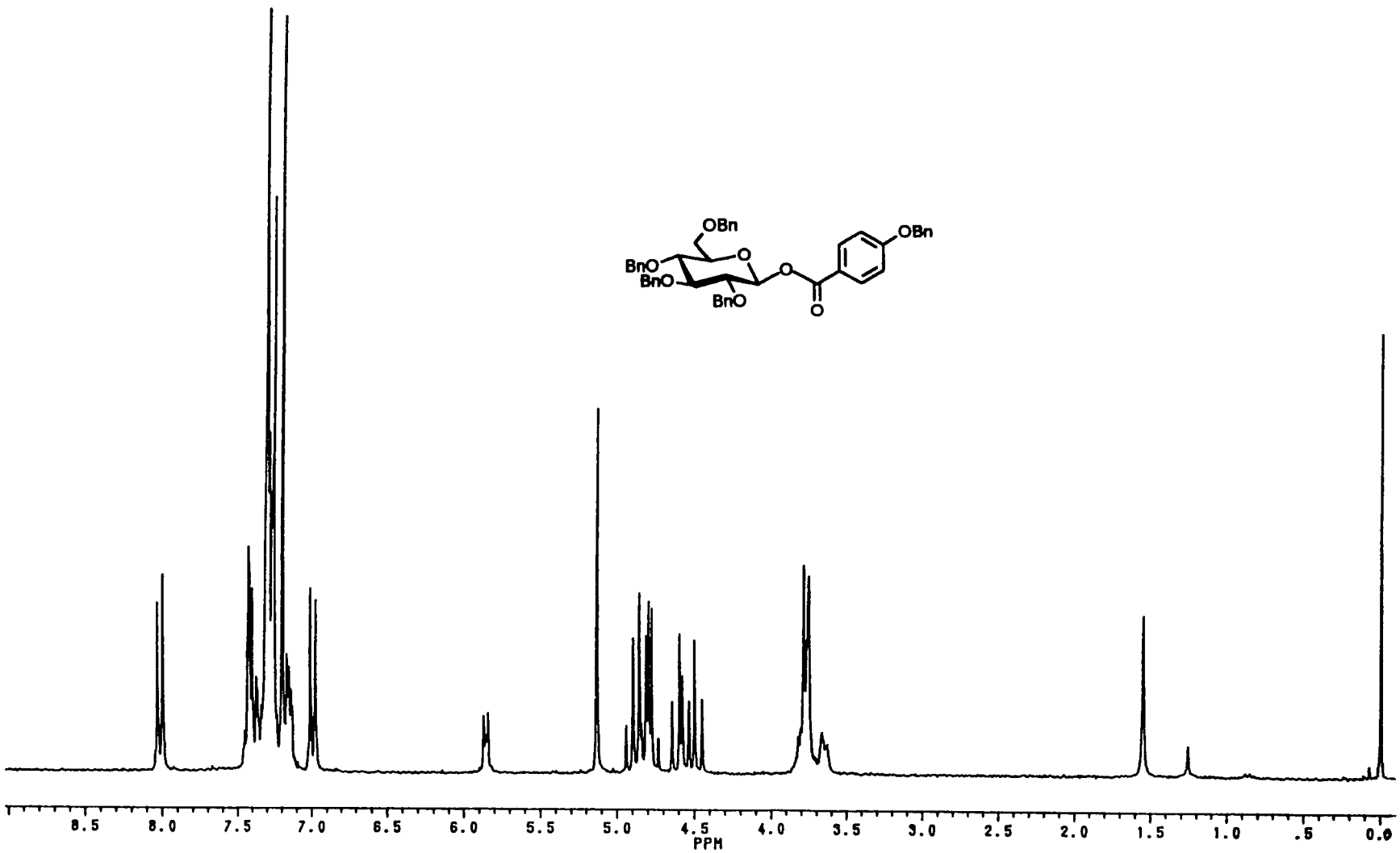
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(16a)**.



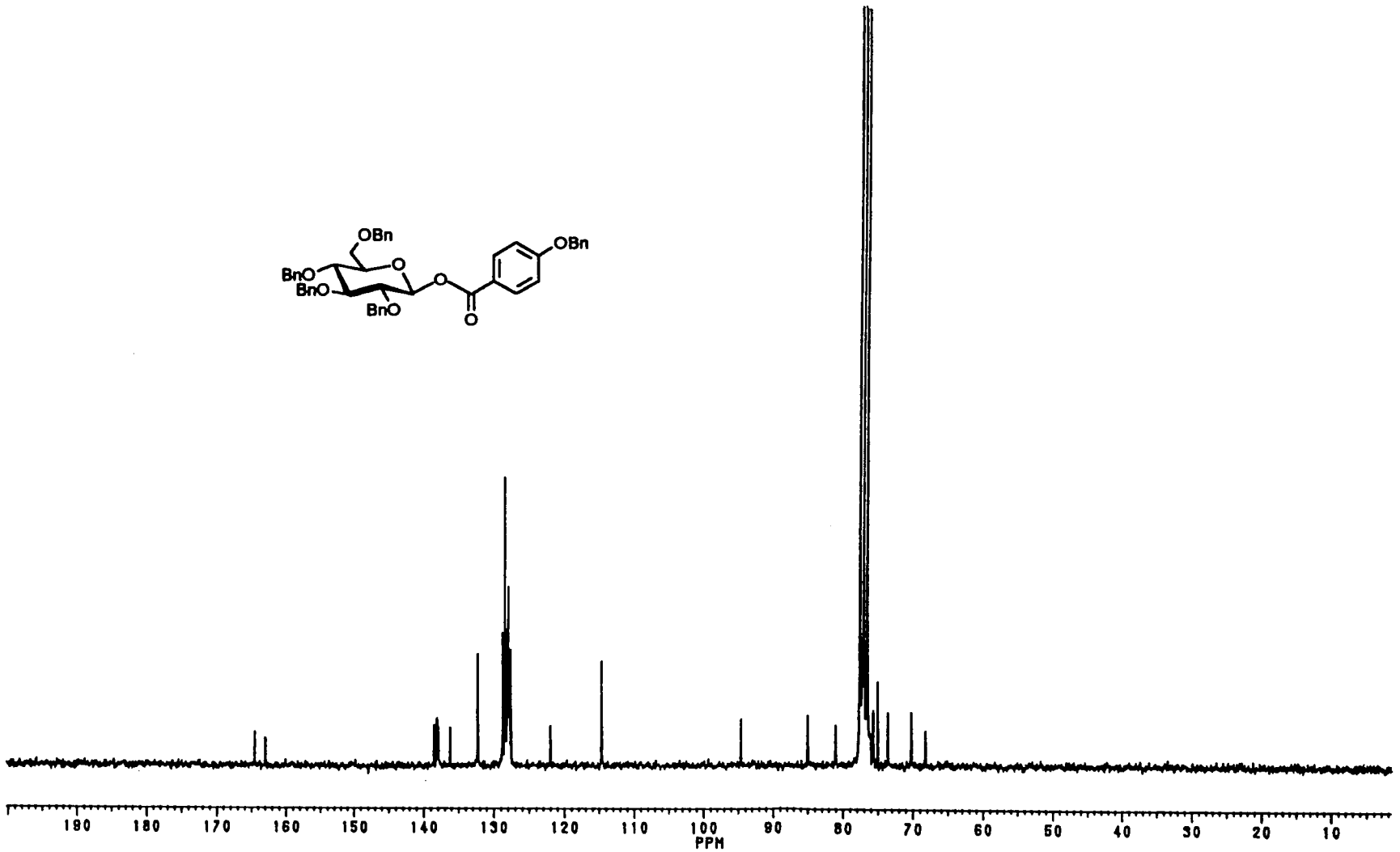
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(16)**.



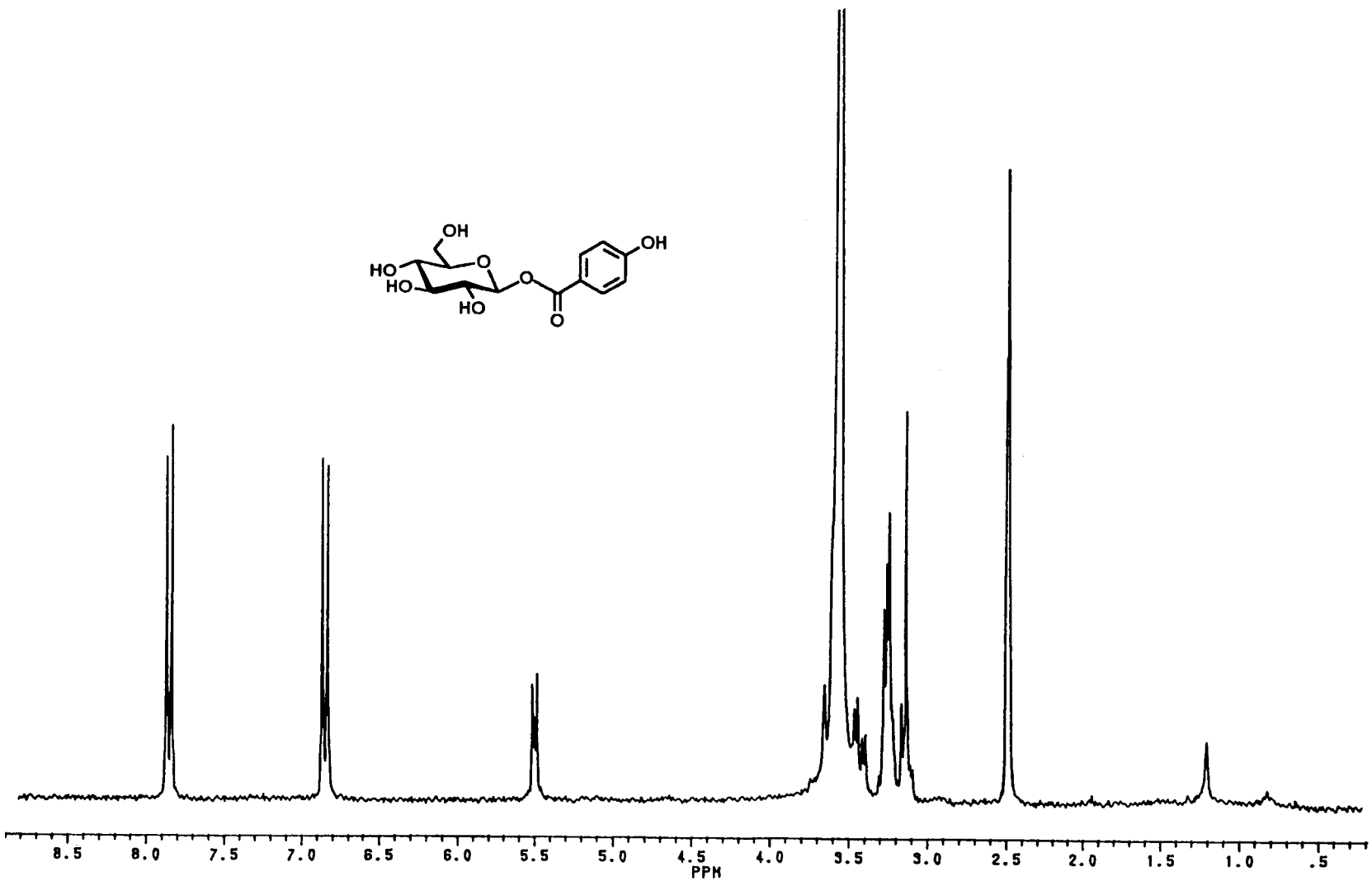
^{13}C NMR (CD_3OD, 62.5 MHz) spectrum of 1-*O*-(4-chlorobenzoyl)-β-D-glucopyranose **(16)**.



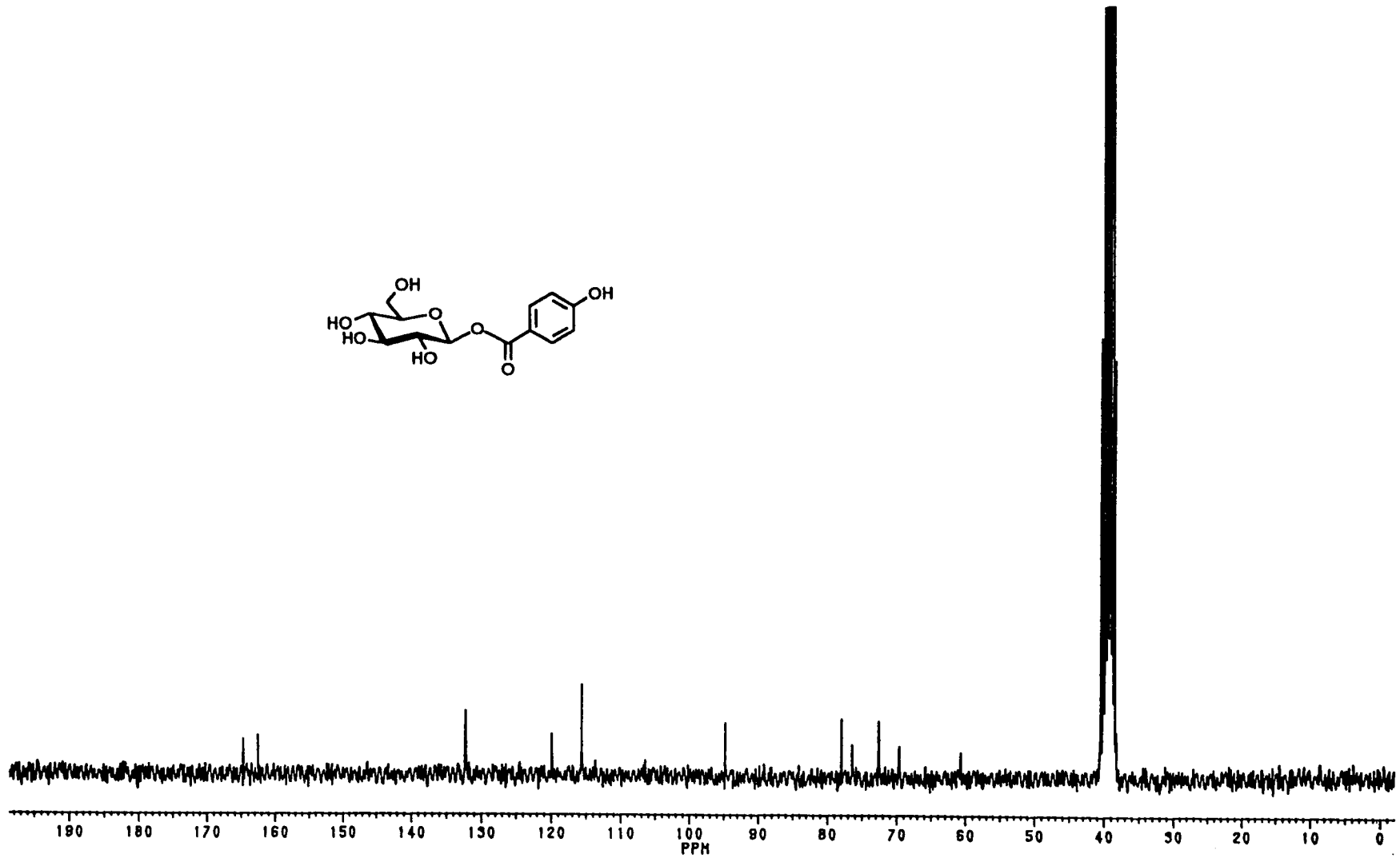
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(4-benzyloxybenzoyl)-β-D-glucopyranose **(17a)**.



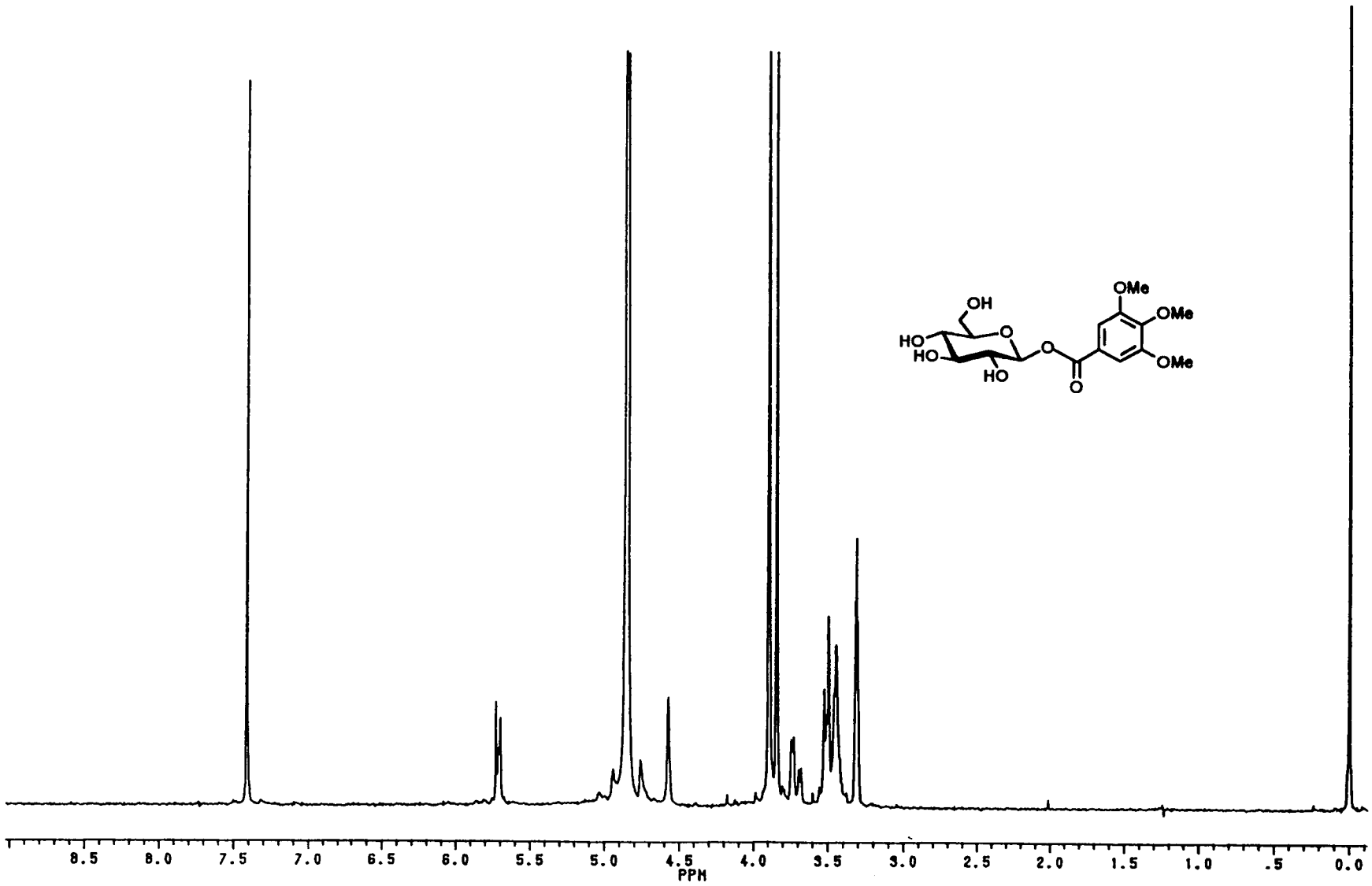
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 2,3,4,6-tetra-*O*-benzyl-1-*O*-(4-benzyloxybenzoyl)-β-D-glucopyranose (**17a**).



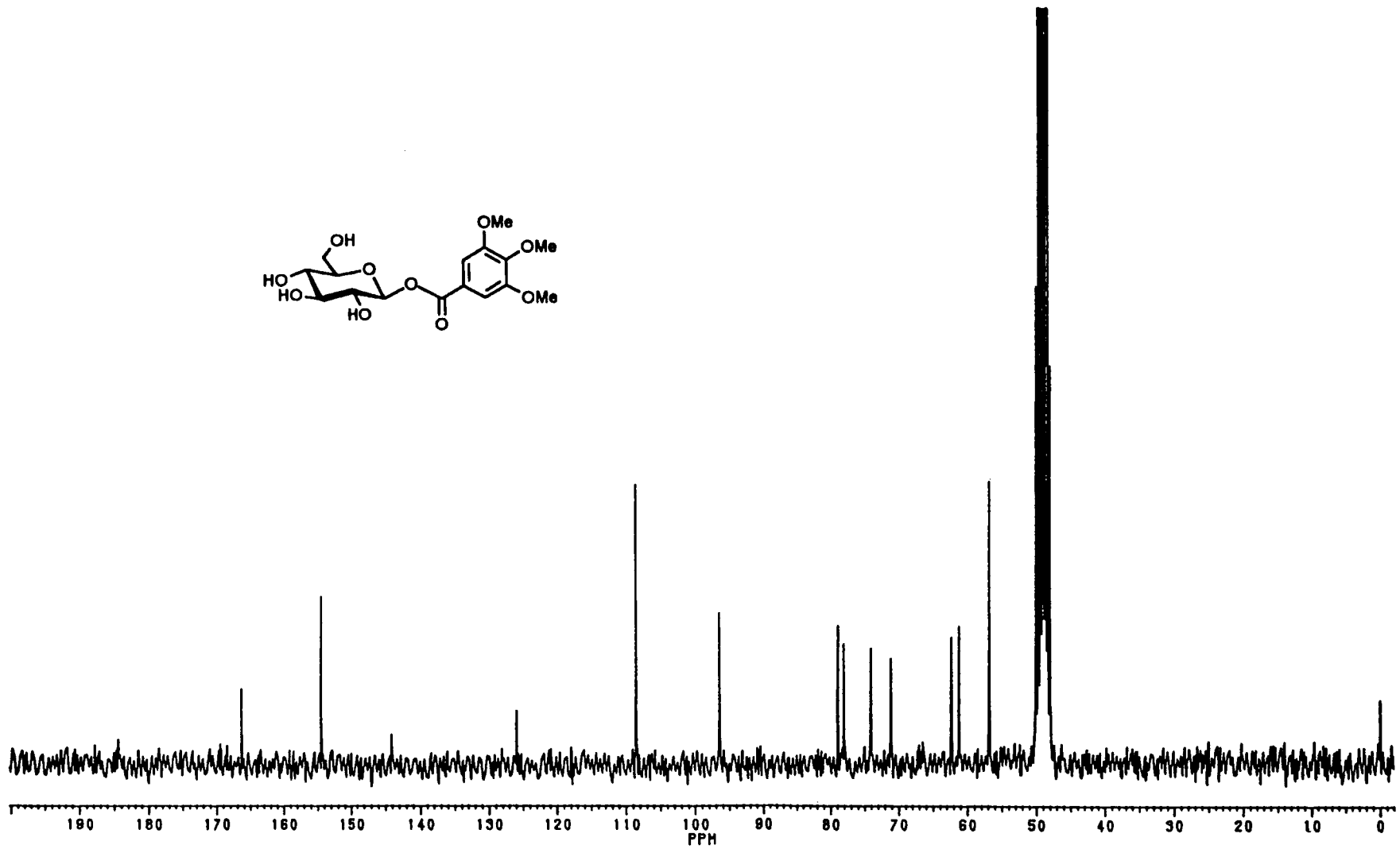
^{1}H NMR (DMSO-d_6, 250 MHz) spectrum of 1-*O*-(4-hydroxybenzoyl)-β-D-glucopyranose **(17)**.



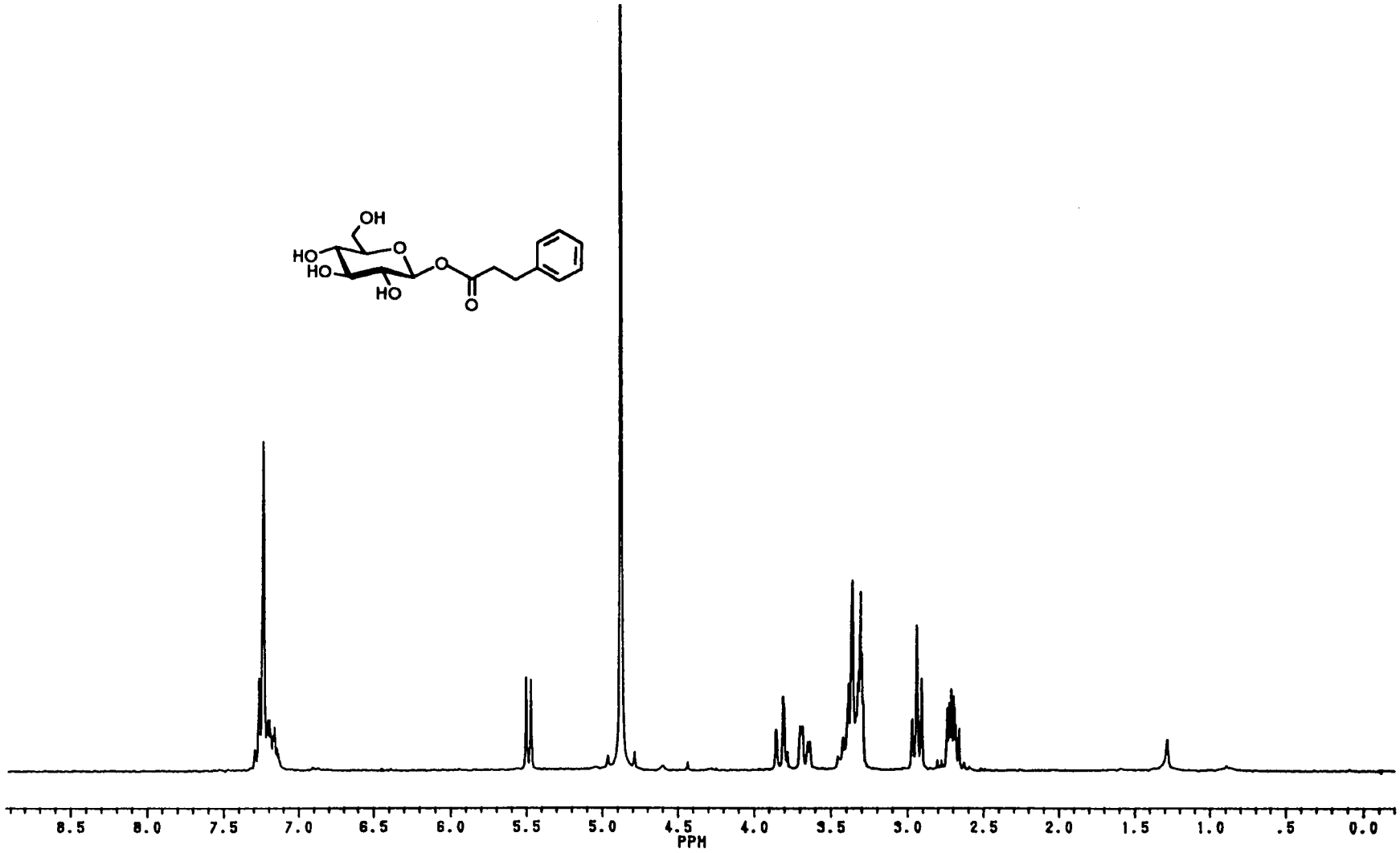
^{13}C NMR (DMSO-d_6, 62.5 MHz) spectrum of 1-*O*-(4-hydroxybenzoyl)-β-D-glucopyranose **(17)**.



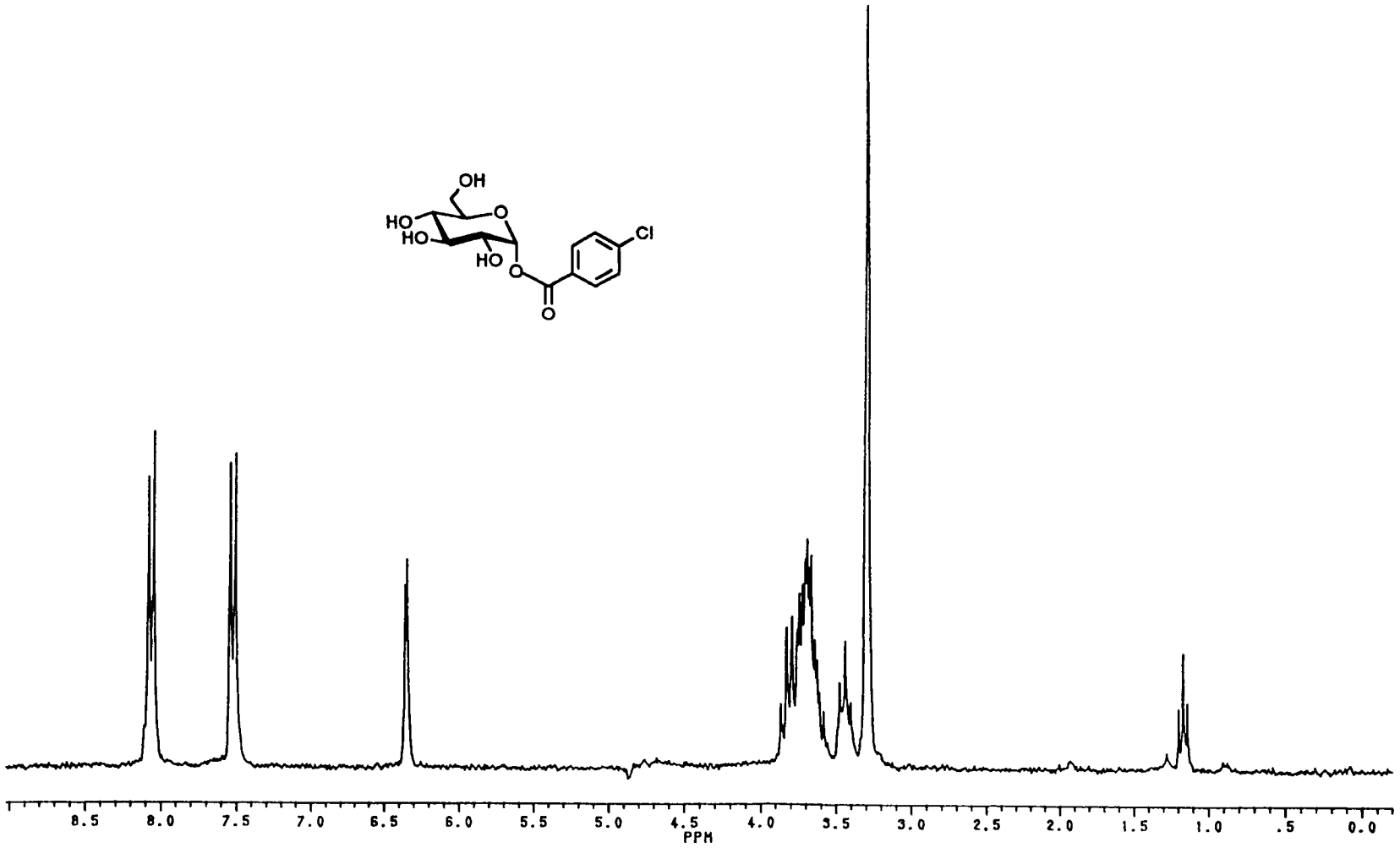
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-(3,4,5-trimethoxybenzoyl)-β-D-glucopyranose **(18)**.



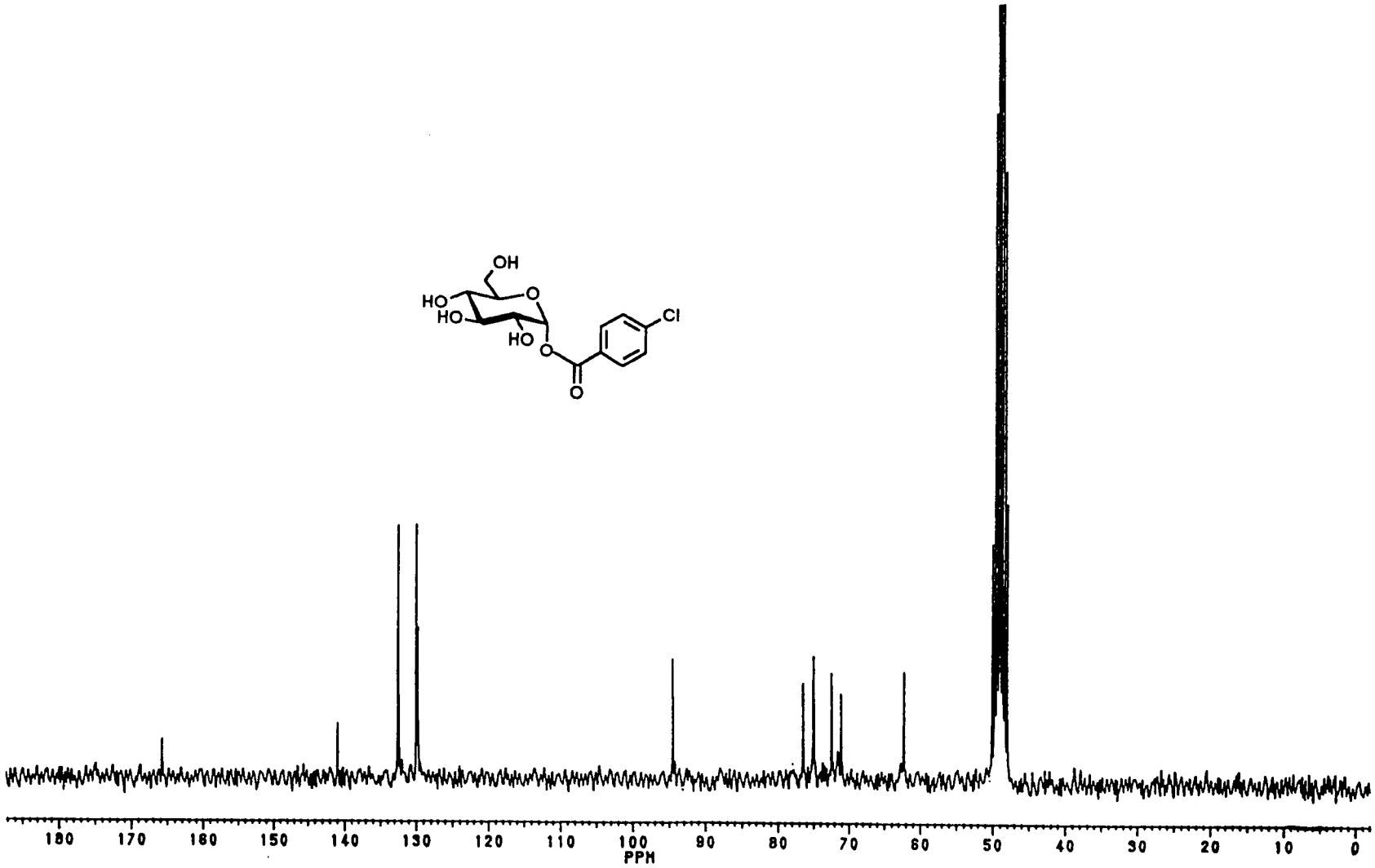
^{13}C NMR (CD_3OD, 62.5 MHz) spectrum of 1-*O*-(3,4,5-trimethoxybenzoyl)-β-D-glucopyranose **(18)**.



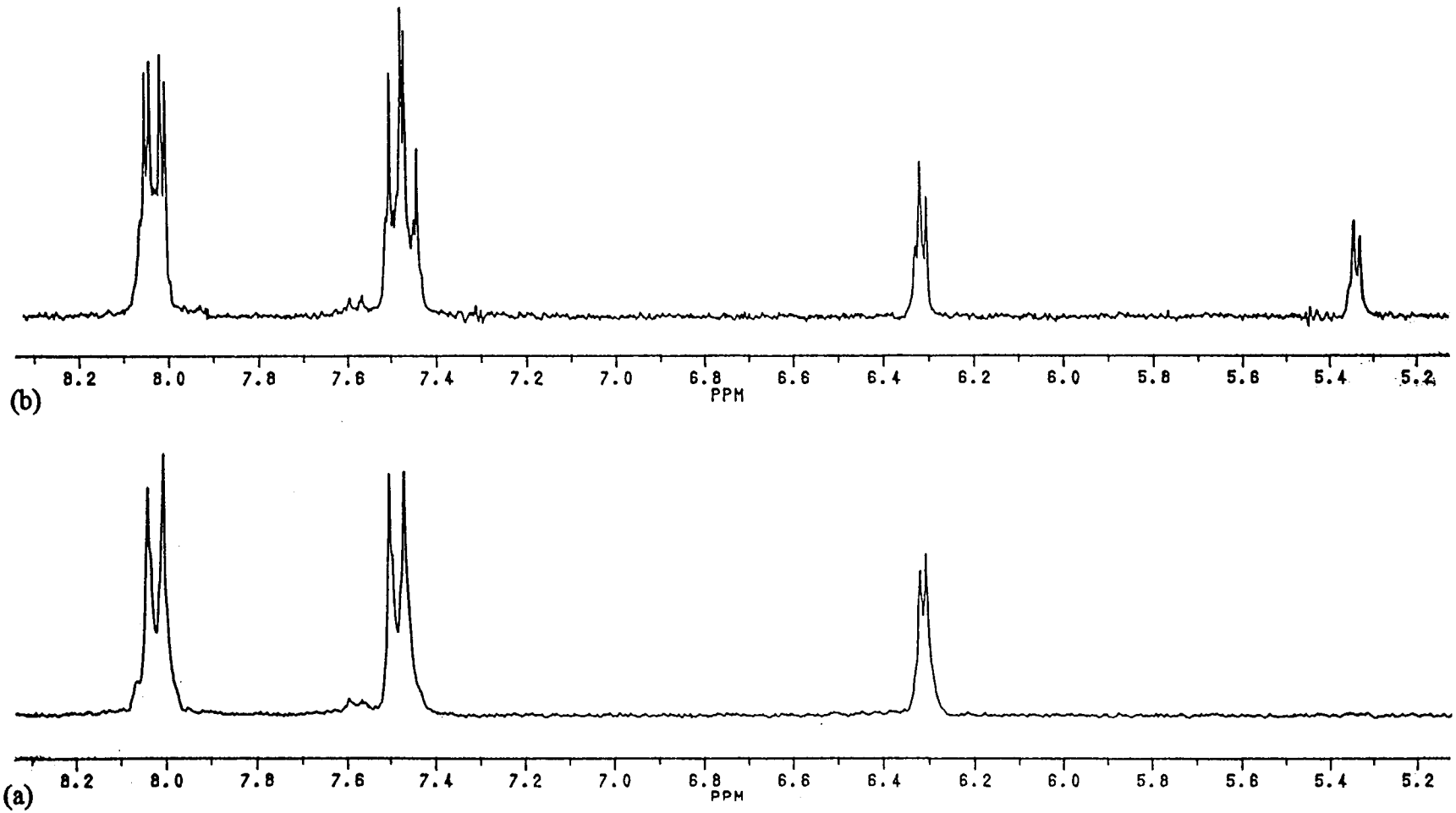
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-(3-phenylpropanoyl)-β-D-glucopyranose **(19)**.



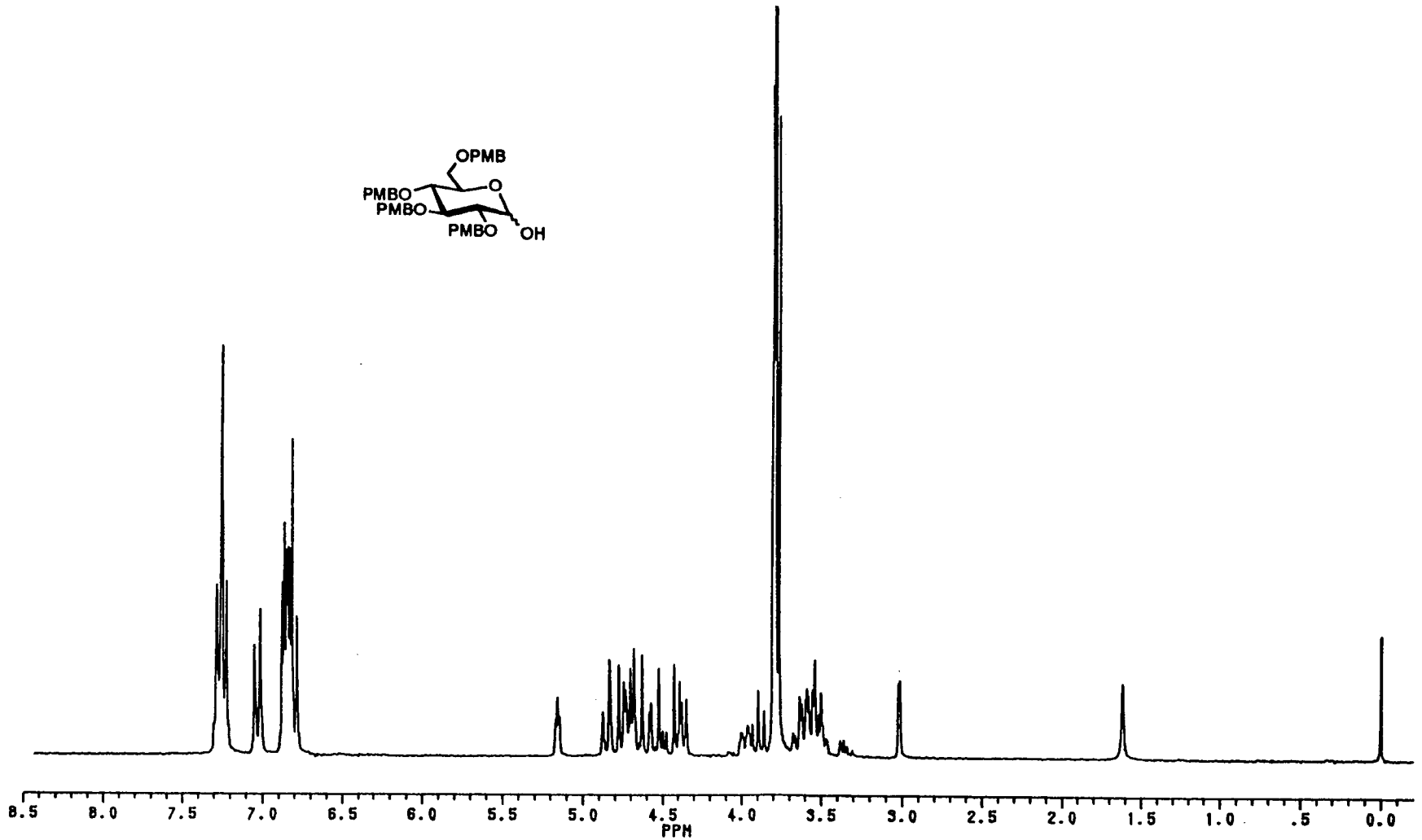
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose **(20)**.



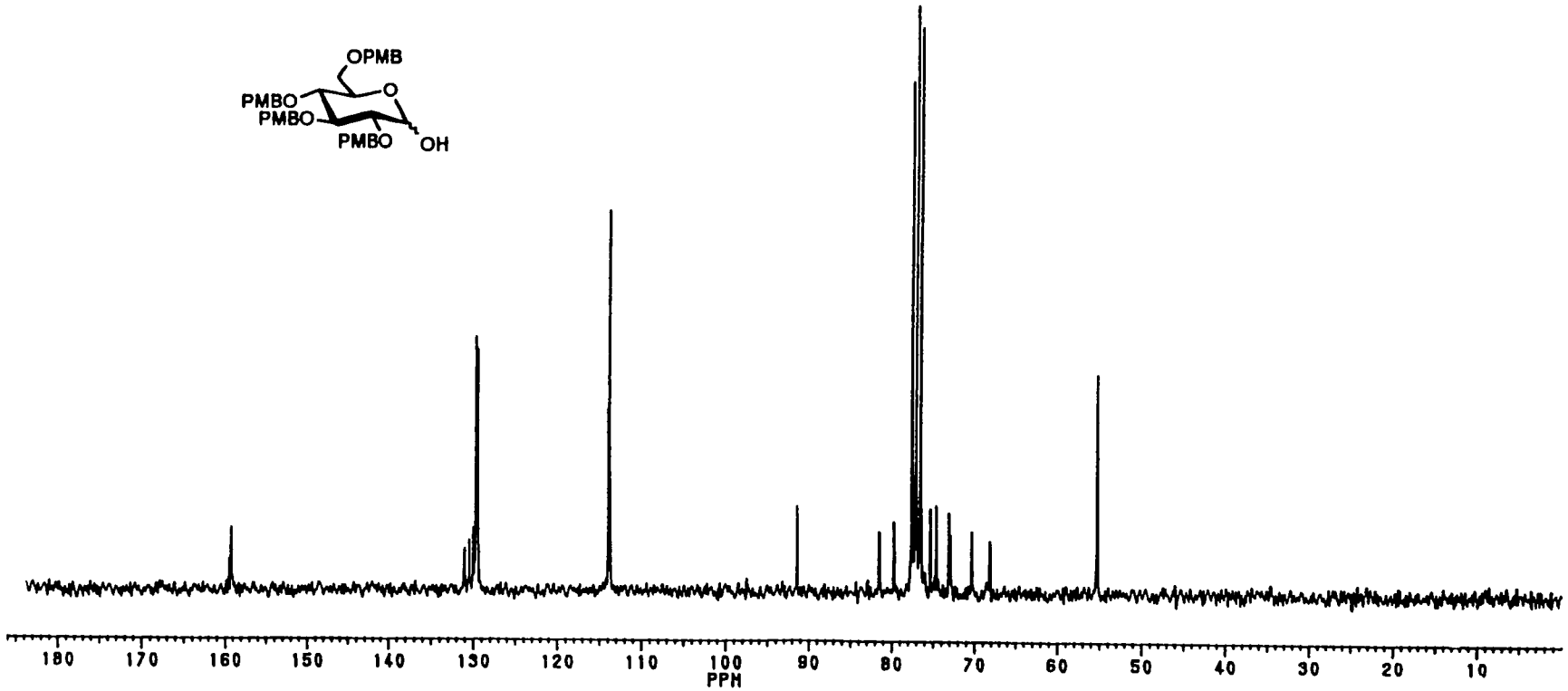
^{13}C NMR (CD_3OD, 62.5 MHz) spectrum of 1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose **(20)**.



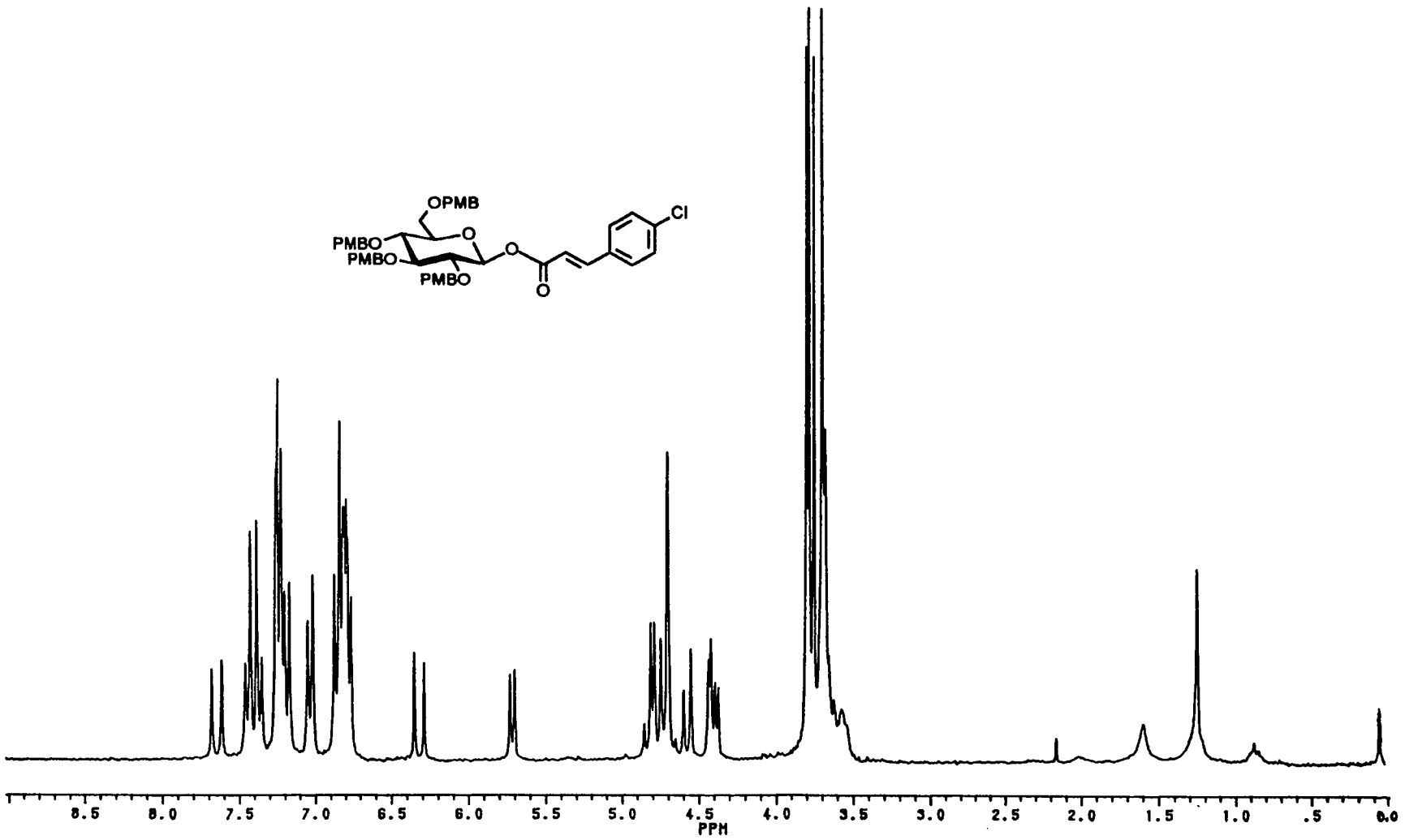
Partial ^{1}H NMR (CD_3OD, 250 MHz) spectra of 1-*O*-(4-chlorobenzoyl)-α-D-glucopyranose (**20**): (a) at t = 0 h; (b) at t = 2.5 h.



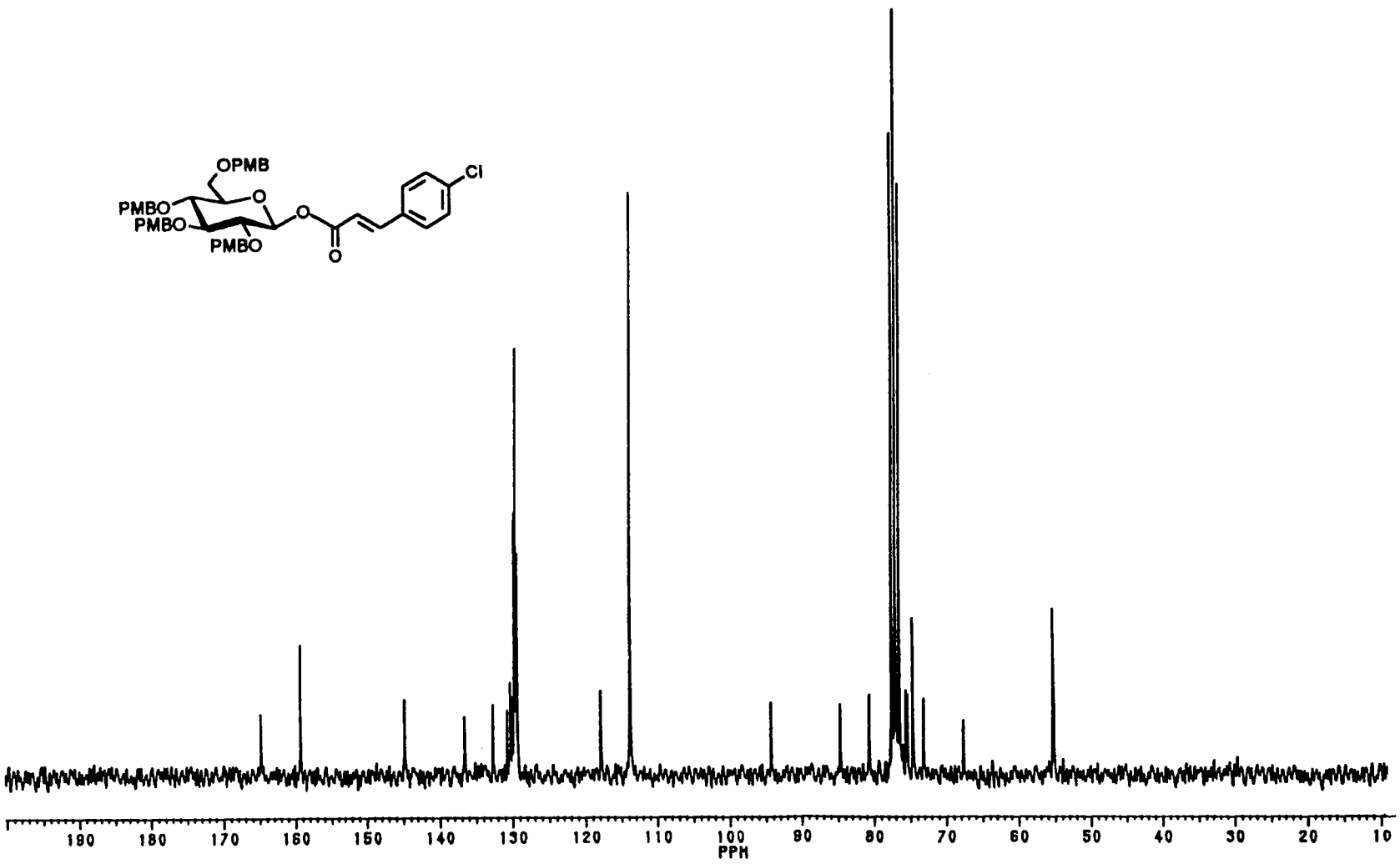
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 2,3,4,6-tetra-*O*-(4-methoxybenzyl)-D-glucopyranose **(24)**.



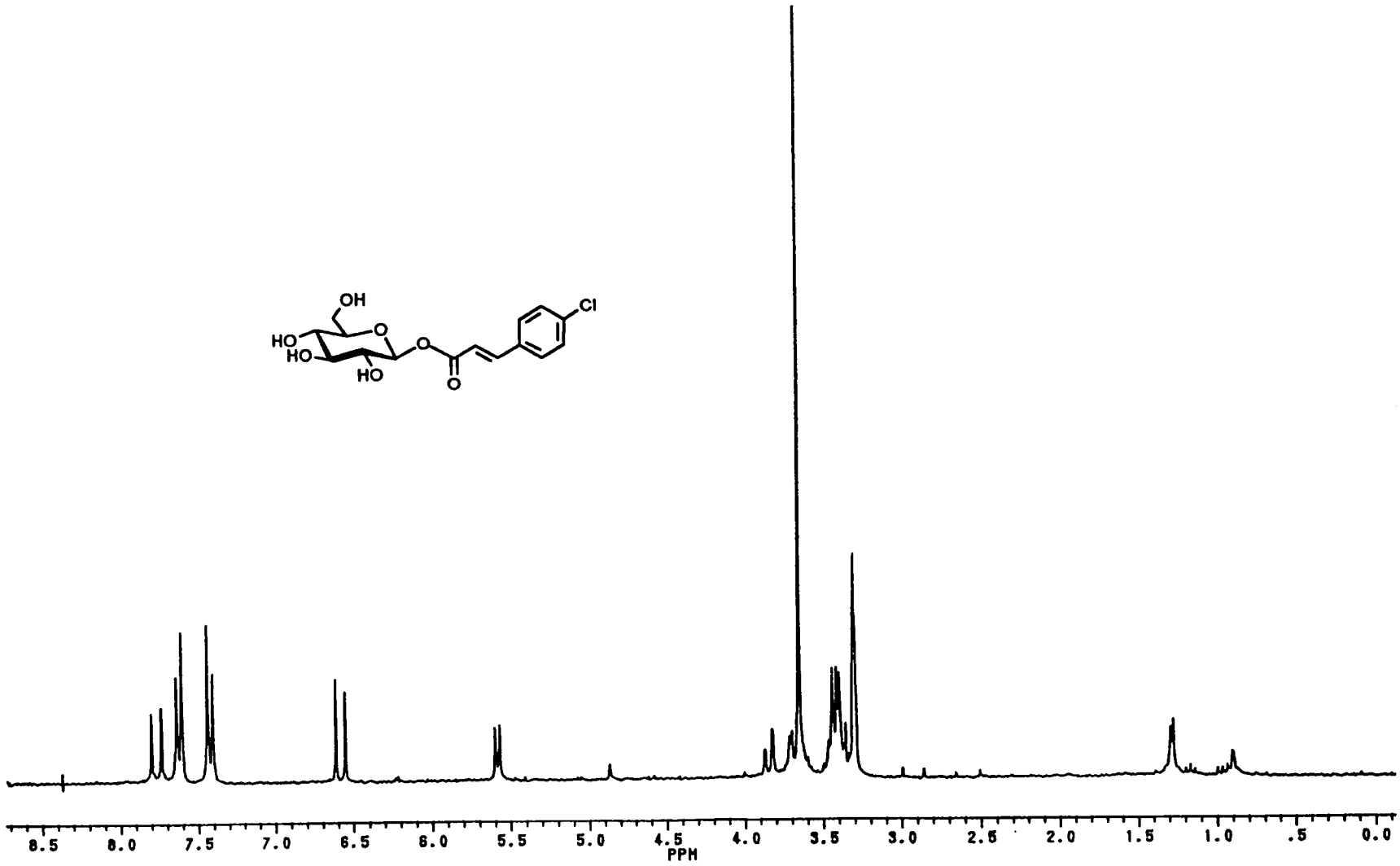
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 2,3,4,6-tetra-*O*-(4-methoxybenzyl)-D-glucopyranose **(24)**.



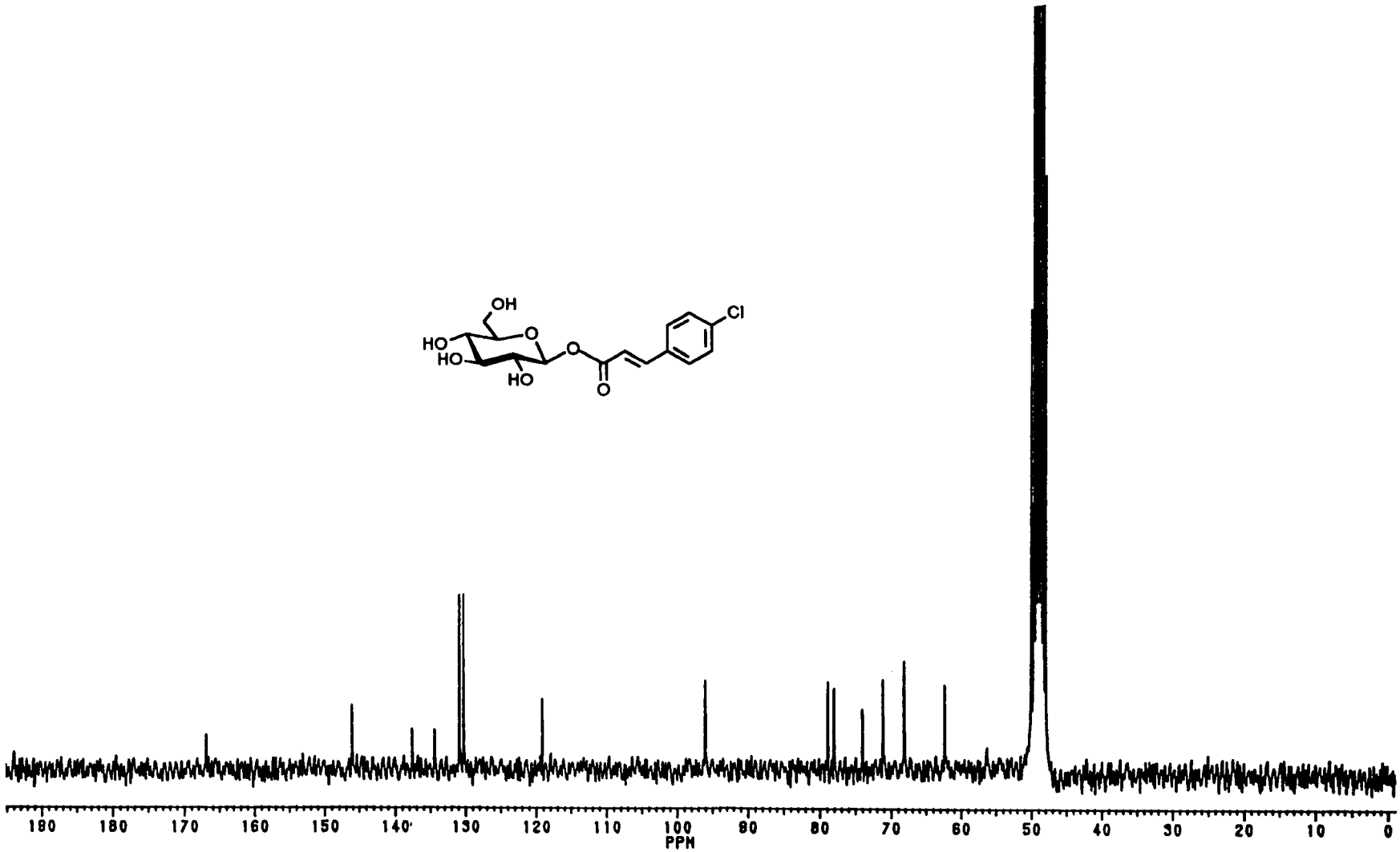
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 1-*O*-(4-chlorocinnamoyl)-2,3,4,6-tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranose (**25a**).



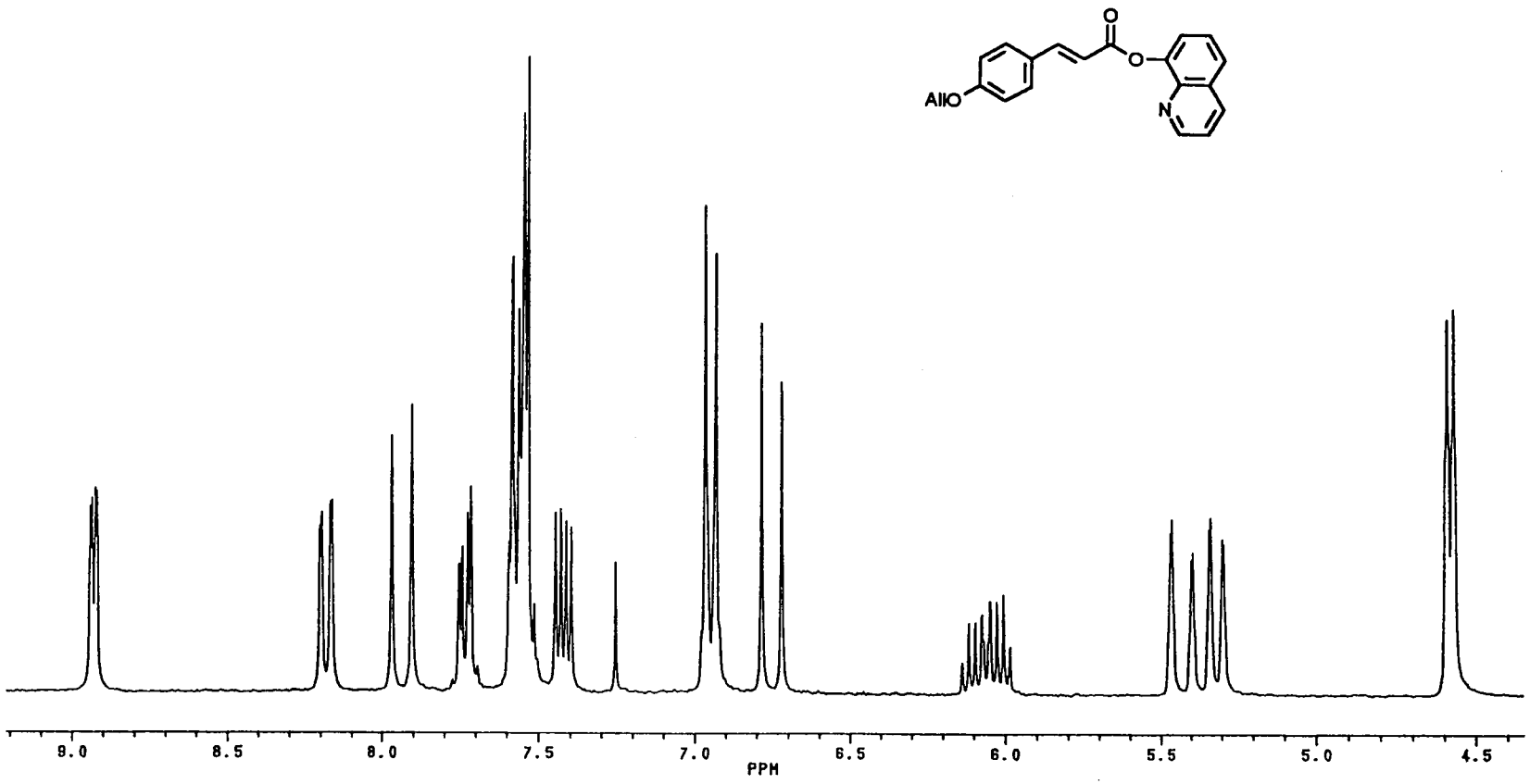
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 1-*O*-(4-chlorocinnamoyl)-2,3,4,6-tetra-*O*-(4-methoxybenzyl)-β-D-glucopyranose **(25a)**.



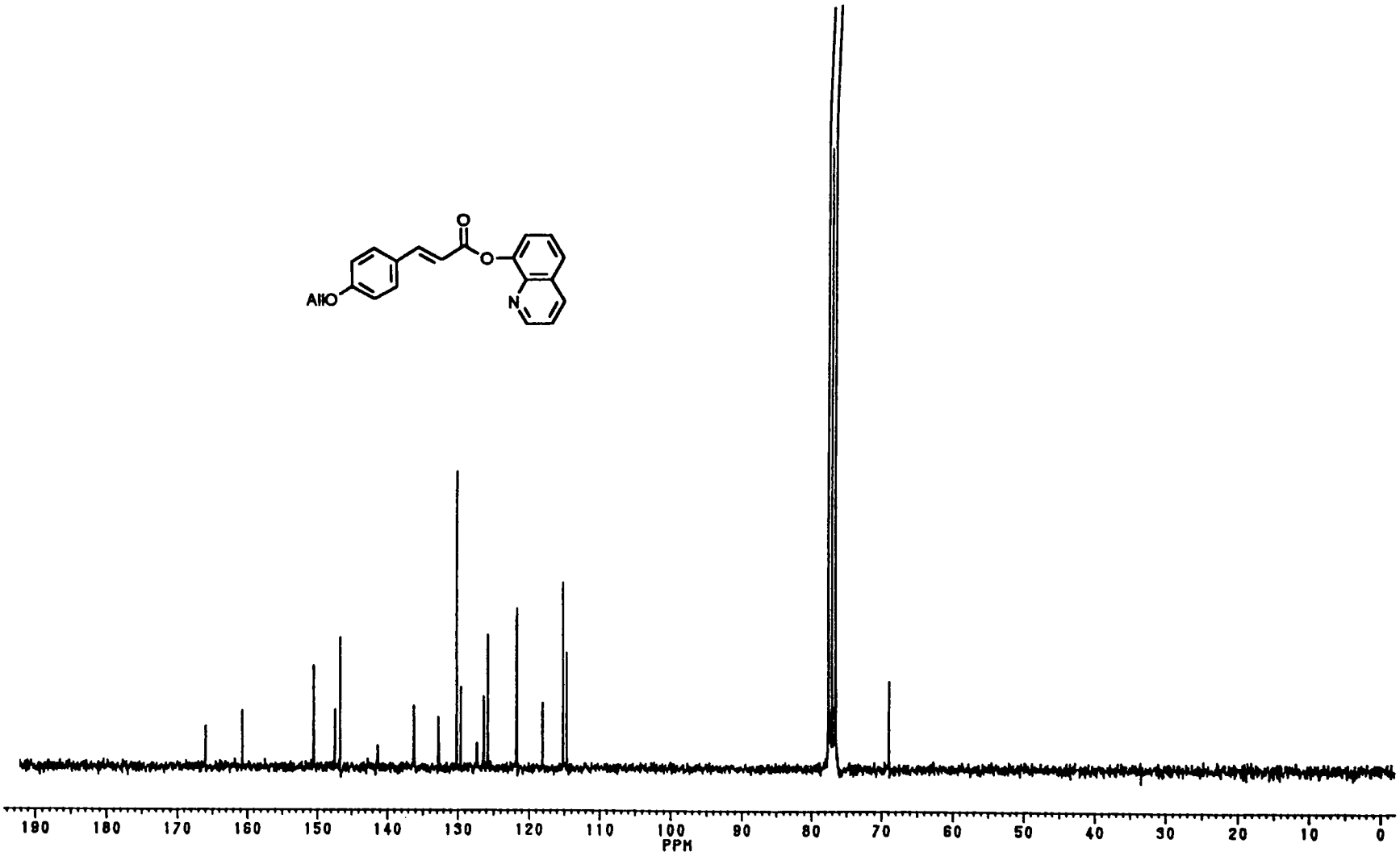
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-(4-chlorocinnamoyl)-β-D-glucopyranose **(25)**.



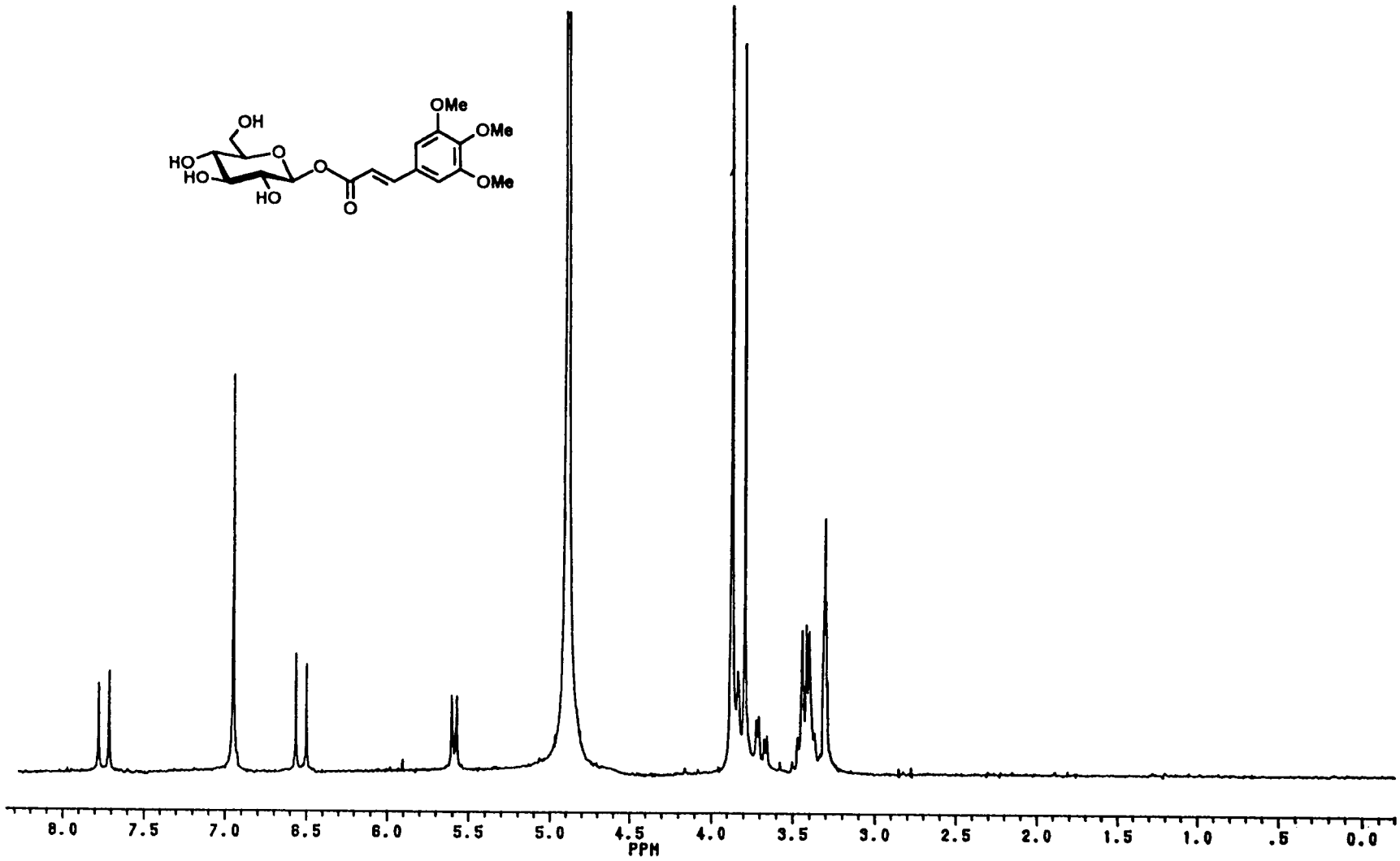
^{13}C NMR (CD_3OD, 62.5 MHz) spectrum of 1-*O*-(4-chlorocinnamoyl)-β-D-glucopyranose **(25)**.



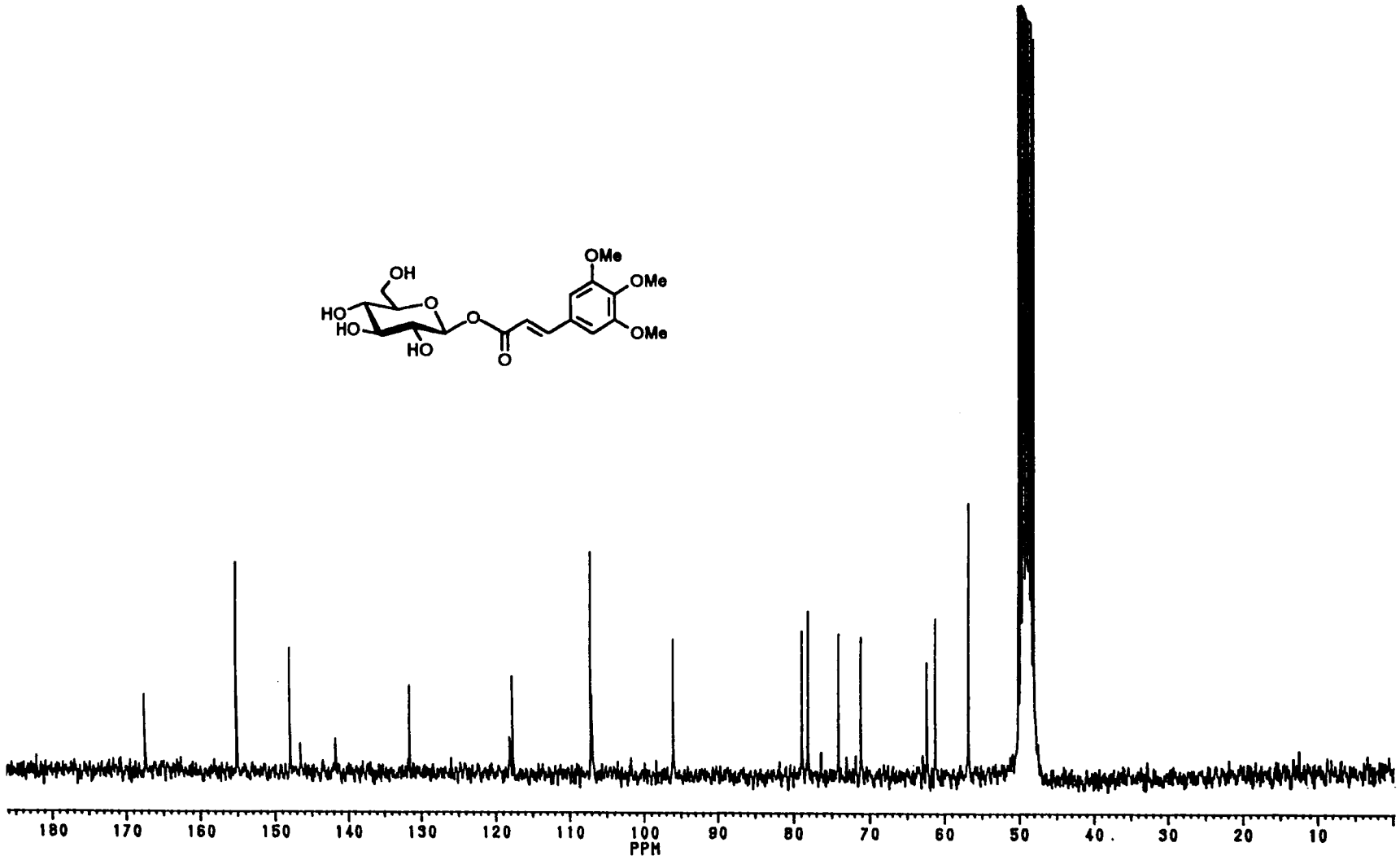
^{1}H NMR ($CDCl_3$, 250 MHz) spectrum of 8-(4-allyloxycinnamoyloxy)quinoline **(28)**.



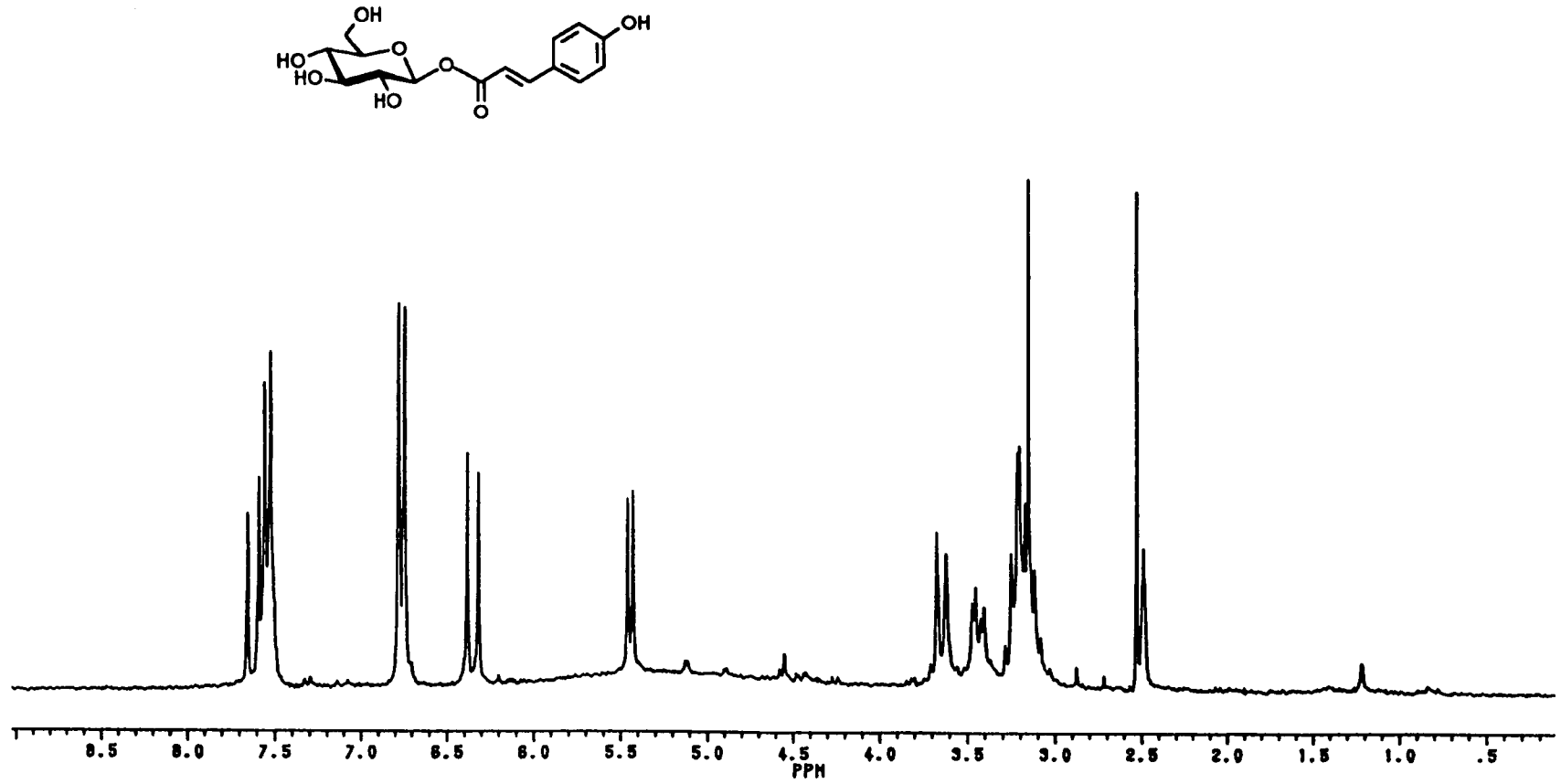
^{13}C NMR ($CDCl_3$, 62.5 MHz) spectrum of 8-(4-allyloxycinnamoyloxy)quinoline **(28)**.



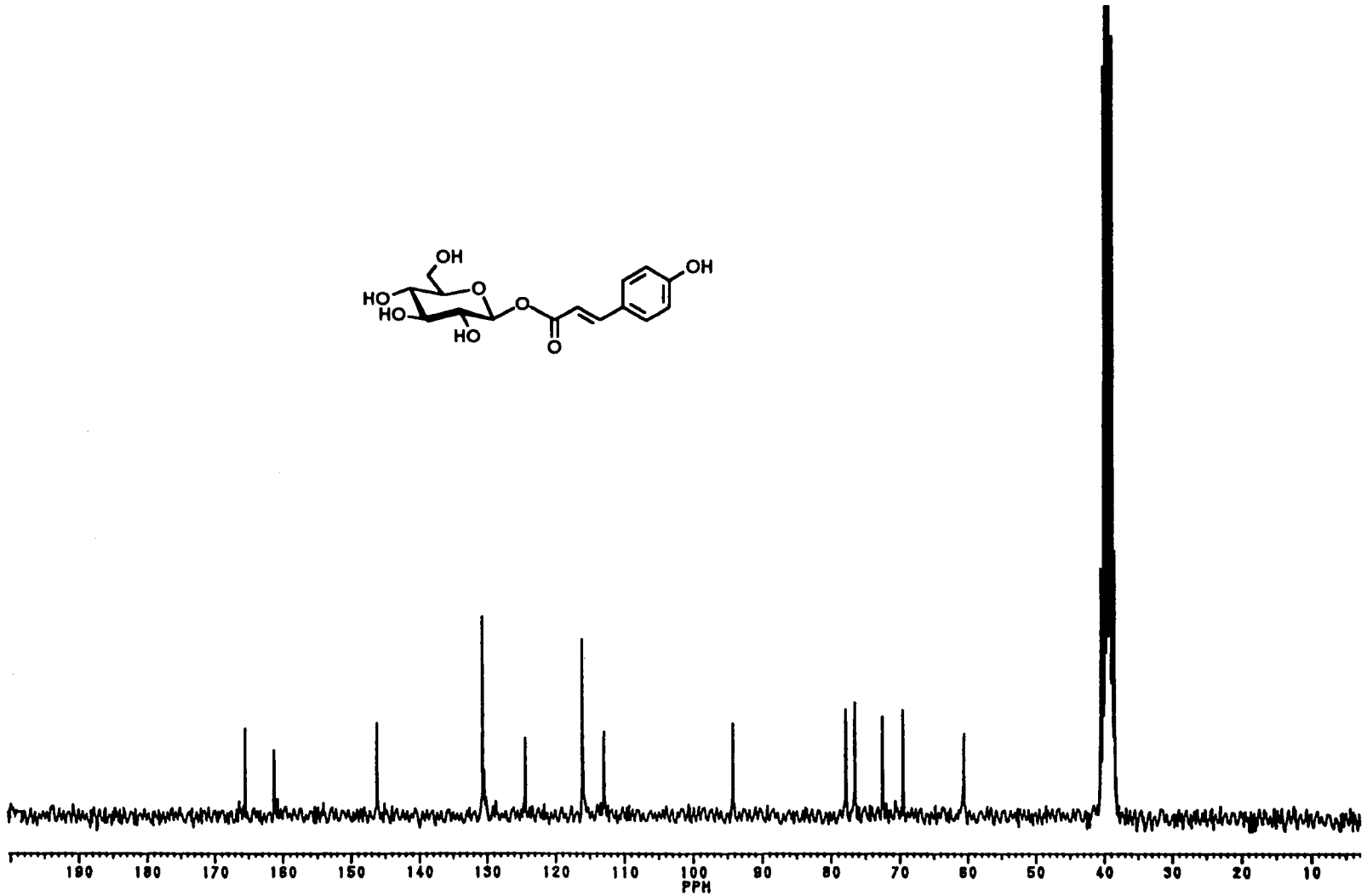
^{1}H NMR (CD_3OD, 250 MHz) spectrum of 1-*O*-3,4,5-(trimethoxycinnamoyl)-β-D-glucopyranose **(29)**.



^{13}C NMR (CD_3OD, 62.5 MHz) spectrum of 1-*O*-3,4,5-(trimethoxycinnamoyl)-β-D-glucopyranose **(29)**.



^{1}H NMR (DMSO-d_6, 250 MHz) spectrum of 1-*O*-(4-hydroxycinnamoyl)-β-D-glucopyranose **(31)**.



^{13}C NMR (DMSO-d_6, 62.5 MHz) spectrum of 1-*O*-(4-hydroxycinnamoyl)-β-D-glucopyranose **(31)**.

VITA

Jeremy Clark was born in Cullman, Alabama where he graduated from Cullman High School in 1989. In 1994, he graduated from Shorter College in Rome, Georgia with a Bachelor of Science degree in biology and chemistry. After working for one year, he entered the University of Tennessee Graduate School where he was a graduate teaching assistant.