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Synthesis of glucuronides of α,β-unsaturated carboxylic acids

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ABSTRACT

A practical synthetic method for glucuronides of α,β-unsaturated carboxylic acids is described. An essential point of this method is the use of groups removable using non-reducing conditions for the protection of the glucuronic acid.

INTRODUCTION

Many acidic drugs such as the non-steroidal anti-inflammatory drugs **1** are metabolised in the liver to form unstable 1-*O*-acyl-β-D-glucuronic acids **2**, which are readily excreted in the urine or bile[1] (Scheme 1). The synthesis of this kind of glucuronide is difficult due to their instability. For example, compound **2** rearranges to its 2-, 3-, and 4-*O*-acyl positional isomers, arising from intramolecular acyl migration in neutral or weakly basic conditions[1,2], and is easily hydrolysed compared to a normal ester[2–5].

Some synthetic methods for glucuronides **2** have been reported[4–6]. In general, they are prepared by condensation of a protected glucuronic acid derivative with an appropriate aglycon derivative, followed by removal of the protecting group, which may be, for example, a benzyl derivative[4]. However, this protecting group cannot be applied to the preparation of α,β-unsaturated carboxylic acid glucuronides. The trichloroethylcarbonyl group, which can be removed by treatment with zinc, has also been used as a protecting group removable under non-hydrogenating conditions, but this is inadequate in cases where the zinc complex of an acyl glucuronide can be formed[5]. Recently, a new protected form of glucuronic acid, using allyloxycarbonyl groups for O-protection and a benzyl ester for acid

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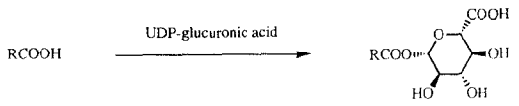
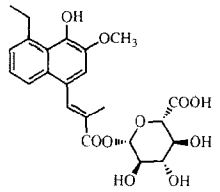


1 2

Scheme 1. Formation of 1-*O*-acyl-β-D-glucuronic acids **2**.

protection, has been reported[7]. Although this protected form is useful in several cases, it is difficult to deprotect the benzyl ester for the preparation of α,β-unsaturated carboxylic acid glucuronides. Furthermore, the introduction of allyloxycarbonyl groups requires a large excess of allyl chloroformate (25 equiv), and the yield for their deprotection step is low (35%)[7].

During our efforts to synthesise the labile α,β-unsaturated carboxylic acid glucuronide **3**, a metabolite of E5090[8] observed in rat and beagle bile, we have found a more efficient protected form (**10**) of glucuronic acid. In the present paper, we describe a practical preparative method for 1-*O*-acyl-β-D-glucuronic acids, using compound **3** as an example.



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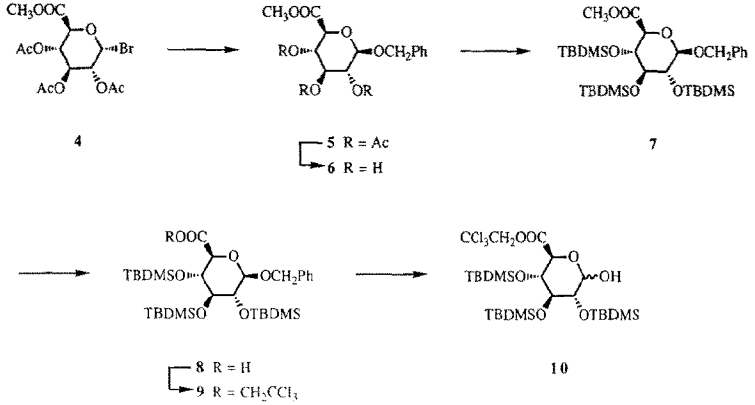
RESULTS AND DISCUSSION

The successful preparation of compound **3** depends on finding suitable hydroxyl and carboxyl protecting groups which can be easily removed under mild conditions. In our synthesis, we have chosen the *tert*-butyldimethylsilyl (TBDMS) group for protecting the hydroxyl groups and the trichloroethyl ester for protecting the acid group of glucuronic acid.

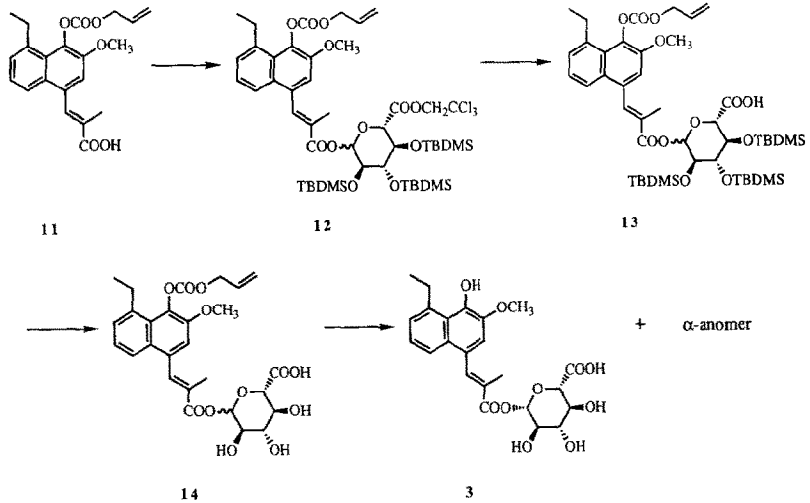
The synthetic route to the protected glucuronic acid derivative **10** is shown in Scheme 2. The hemiacetal hydroxyl group must be protected by an easily removable group. For example, a methyl glycoside cannot be cleaved in the presence of TBDMS groups. We have chosen the benzyl group which can be removed by catalytic hydrogenolysis. The Koenigs–Knorr reaction between benzyl alcohol and the bromide **4**[9] gave methyl (benzyl β-D-glucopyranosid)uronate **5**[10] after one recrystallisation from methanol. After deacetylation of **5** with sodium methoxide, the TBDMS groups were introduced in high yield. The methyl ester of compound **7** was hydrolysed under alkaline conditions to give the carboxylic acid **8**, which was



Scheme 2. Preparation of protected glucuronic acid derivative **10**.

then treated with diethyl phosphorochloridate and triethylamine followed by reaction with 2,2,2-trichloroethanol and 4-dimethylaminopyridine to afford the trichloroethyl ester **9**. Deprotection of the anomeric position was easily accomplished using catalytic hydrogenolysis to give the desired protected glucuronic acid derivative **10**, which was a fairly stable intermediate for the preparation of 1-*O*-acyl-β-D-glucuronic acids.

The synthetic route to compound **3** is shown in Scheme 3. The coupling of **10** with aglycon **11** was carried out by a Mitsunobu reaction using triphenylphosphine and diisopropyl azodicarboxylate[11] ($\alpha:\beta = 1:4$, ^{1}H NMR). The trichloroethyl ester must be cleaved before deprotection of the silyl ether, otherwise the zinc complex with the deprotected hydroxyl groups of the acyl glucuronide may be



Scheme 3. Preparation of α,β-unsaturated acid glucuronide **3**.

formed[5]. Compound **12** was treated with zinc dust in the presence of potassium dihydrogenphosphate[12] to yield the carboxylic acid **13**. Deprotection of the hydroxyl groups with tetrabutylammonium fluoride, which is widely used for the cleavage of silyl ethers, was accompanied by splitting of the anomeric ester. Therefore, the three TBDMS groups were removed by hydrofluoric acid in acetonitrile[13] which did not affect the anomeric center. Both the silylation and the desilylation reaction of the glucuronic acid were easily achieved in high yield. The allyloxycarbonyl group was removed by reaction with tributyltin hydride in the presence of tetrakis(triphenylphosphine)palladium(0)[14], to give a mixture of **3** and its α anomer, which was then fractionated by preparative HPLC, affording the target compound **3**. The HPLC retention time of **3** matched that of a metabolic sample.

It is thought that the protected glucuronic acid **10** may be generally applicable to the preparation of 1-*O*-acyl-β-D-glucuronic acids. Therefore, this synthetic method should be useful in the study of drug metabolism.

EXPERIMENTAL

General methods.—All melting points were determined on a YAZAWA BY-10 melting-point apparatus in open capillary tubes and are uncorrected. Specific rotations were determined at 25°C with a JASCO DIP-140 polarimeter. ^{1}H NMR spectra were recorded on a Varian UNITY 400 spectrometer with Me_4Si as an internal standard. All organic extracts were dried over anhyd $MgSO_4$, and the solvent was removed under reduced pressure with a rotary evaporator. Merck silica gel (Silica Gel 60, 70–230 mesh) or Wako silica gel (Wakogel C-200) was used for flash-column chromatography. Thin-layer chromatography (TLC) was developed using Merck Silica Gel 60F-254 precoated glass plates. Compounds were detected in TLC by UV light (254 nm).

Methyl (benzyl 2,3,4-tri-O-acetyl-β-D-glucopyranosid)uronate (**5**).—A mixture of methyl (2,3,4-tri-*O*-acetyl-α-D-glucopyranosyl bromide) uronate (**4**; 504 g, 1.27 mol), benzyl alcohol (206 g, 1.9 mol), silver carbonate (525 g, 1.9 mol), and 4A molecular sieves (1008 g) in benzene (3.36 L) was stirred at room temperature for 20 h. The precipitate was filtered off and the filtrate was evaporated. The solid residue was recrystallised from 1:1 MeOH—diisopropyl ether (2 L), to afford **5** (215 g, 40%) as colorless needles; mp 133–134°C; $[\alpha]_D$ −65° (*c* 1.0, $CHCl_3$) {lit.[10], mp 133–134°C, $[\alpha]_D$ −67° (*c* 1.0, $CHCl_3$)}. ^{1}H NMR data ($CDCl_3$): δ 2.00 (s, 3 H), 2.01 (s, 6 H), 3.77 (s, 3 H), 4.02 (d, 1 H, *J* 9.3 Hz), 4.59 (d, 1 H, *J* 7.7 Hz), 4.62 and 4.93 (ABq, 2 H, *J* 12.2 Hz), 5.06–5.11 (m, 1 H), 5.19–5.28 (m, 2 H), and 7.26–7.38 (m, 5 H). Anal. Calcd for $C_{20}H_{24}O_{10}$: C, 56.60; H, 5.70. Found: C, 56.38; H, 5.57.

Methyl (benzyl β-D-glucopyranosid)uronate (**6**).—To a suspension of **5** (135 g, 0.32 mol) in anhyd MeOH (850 mL) at −40°C was added a solution of Na (0.74 g, 32 mmol) in MeOH (32 mL). The mixture was allowed to warm to room temperature while stirring was continued, at the end of which time all of compound **5** had

dissolved. The mixture was recooled to 0°C and acidified with Dowex-50W (H^+) ion-exchange resin. The resin was filtered off and the filtrate was evaporated to give the crude product, which was purified by column chromatography on silica gel (elution with 19:1 $CHCl_3$–MeOH) to afford **6** (133 g, 88%) as a colorless solid; mp 130–131°C; $[\alpha]_D$ −84° (*c* 1.0, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 3.46–3.57 (m, 2 H), 3.70–3.86 (m, 2 H), 3.79 (s, 3 H), 4.37 (d, 1 H, *J* 7.1 Hz), 4.58 and 4.89 (ABq, 2 H, *J* 11.9 Hz), and 7.25–7.38 (m, 5H). Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.30; H, 5.97.

Methyl (benzyl 2,3,4-tri-O-tert-*butyldimethylsilyl-β-*D-*glucopyranosid)uronate* (**7**). —To a solution of **6** (133 g, 0.45 mol) in *N*,*N*-dimethylformamide (800 mL) at room temperature were added *tert*-butyldimethylsilyl chloride (303 g, 2.01 mol), imidazole (274 g, 4.0 mol), and 4-dimethylaminopyridine (27.4 g, 0.22 mol). After stirring the mixture at 80°C for 48 h, water was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 3:97 EtOAc–hexane) to afford **7** (270 g, 95%) as a colorless oil; $[\alpha]_D$ −29° (*c* 1.0, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ −0.04 (s, 3 H), 0.03 (s, 3 H), 0.06 (s, 3 H), 0.08 (s, 3 H), 0.09 (s, 3 H), 0.11 (s, 3 H), 0.82 (s, 9 H), 0.86 (s, 9 H), 0.87 (s, 9 H), 3.75 (s, 3 H), 3.71–3.77 (m, 2 H), 4.28–4.30 (m, 1 H), 4.39 (d, 1 H, *J* 1.1 Hz), 4.53 and 4.99 (ABq, 2 H, *J* 11.7 Hz), 4.92 (d, 1 H, *J* 6.8 Hz), 7.23–7.33 (m, 3 H), and 7.36–7.40 (m, 2 H). Anal. Calcd for $C_{32}H_{60}O_7Si_3$: C, 59.95; H, 9.43; Si, 13.1. Found: C, 59.79; H, 9.39; Si, 13.1.

2,2,2-Trichloroethyl (benzyl 2,3,4-tri-O-tert-*butyldimethylsilyl-β-*D-*glucopyranosid)uronate* (**9**).—To a solution of **7** (273 g, 0.43 mol) in tetrahydrofuran (2340 mL) at room temperature was added 0.2 M NaOH (2340 mL). After stirring the reaction mixture at 50°C for 10 h, 1 M HCl (470 mL) was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated to give 265 g of crude glucopyranosiduronic acid **8** as a pale-yellow oil, which was used in the next step without further purification. To a mixture of this crude acid and diethyl phosphorochloridate (87.5 g, 0.51 mol) in benzene (1500 mL) at 0°C under N_2 was added triethylamine (118 mL, 0.85 mol) over a period of 20 min. After stirring the mixture at room temperature for 1 h, 2,2,2-trichloroethanol (81.1 mL, 0.85 mol) and 4-dimethylaminopyridine (25.8 g, 0.21 mol) were added and stirring was continued at the same temperature for 6 h. The mixture was poured into water and extracted with benzene. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 3:97 EtOAc–hexane) to afford **9** (271 g, 84%) as a colorless oil; $[\alpha]_D$ −18° (*c* 1.0, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ −0.03 (s, 3 H), 0.04 (s, 3 H), 0.06 (s, 3 H), 0.09 (s, 3 H), 0.10 (s, 3 H), 0.14 (s, 3 H), 0.83 (s, 9 H), 0.86 (s, 9 H), 0.88 (s, 9 H), 3.75 (d, 1 H, *J* 6.6 Hz), 3.78 (d, 1 H, *J* 3.6 Hz), 4.34–4.36 (m, 1 H), 4.54 and 5.00 (ABq, 2 H, *J* 11.5 Hz), 4.54 (d, 1 H, *J* 0.7 Hz), 4.62 and 4.86 (ABq, 2 H, *J* 11.9 Hz), 4.96 (d, 1 H, *J* 6.6 Hz), 7.27–7.34 (m, 3 H), and 7.35–7.40 (m, 2 H). Anal. Calcd for

$C_{33}H_{59}Cl_3O_7Si_3$: C, 52.26; H, 7.84; Cl, 14.0; Si, 11.1. Found: C, 52.58; H, 7.86; Cl, 13.4; Si, 11.2.

2,2,2-Trichloroethyl 2,3,4-tri-O-tert-*butyldimethylsilyl*-D-*glucopyranuronate* (**10**). —A solution of **9** (271 g, 0.36 mol) in EtOAc (2000 mL) was hydrogenated over 10% Pd–C (water content ~50%; 13.5 g) at 1 atm for 17 h. The catalyst was filtered off and the filtrate was evaporated to give the crude product, which was purified by column chromatography on silica gel (elution with 3:97 EtOAc–hexane) to afford **10** (191 g, 80%) as a colorless solid; mp 78°C; $[\alpha]_D$ +30° (*c* 1.0, $CHCl_3$). ^1H NMR data ($CDCl_3$): δ 0.07 (s, 3 H), 0.09 (s, 3 H), 0.14 (s, 6 H), 0.15 (s, 3 H), 0.16 (s, 3 H), 0.85 (s, 9 H), 0.93 (s, 9 H), 0.94 (s, 9 H), 3.60–3.64 (m, 1 H), 3.79 (d, 1 H, *J* 12.6 Hz), 3.90–3.94 (m, 1 H), 4.16–4.20 (m, 1 H), 4.63 (br s, 1 H), 4.45 and 4.96 (ABq, 2 H, *J* 11.9 Hz), and 5.50 (dd, 1 H, *J* 2.7, 12.8 Hz). Anal. Calcd for $C_{26}H_{53}Cl_3O_7Si_3$: C, 46.72; H, 7.99; Cl, 15.9; Si, 12.6. Found: C, 46.69; H, 7.95; Cl, 15.5; Si, 12.3.

(E)-3-[4-(Allyloxycarbonyloxy)-5-ethyl-3-methoxynaphthalen-1-yl]-2-methyl-2-propenoic acid (**11**).—To a solution of (*E*)-3-(5-ethyl-4-hydroxy-3-methoxynaphthalen-1-yl)-2-methyl-2-propenoic acid[8] (5.0 g, 17.5 mmol) in pyridine (10 mL)–ethyl ether (20 mL) at 0°C was added allyl chloroformate (7.38 mL, 70 mmol). After stirring at room temperature for 1 h, water was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. To a solution of the residue in MeOH (200 mL) at room temperature was added 1 M NaOH (52.5 mL, 52.5 mmol). After stirring for 24 h, 1 M HCl (52.5 mL, 52.5 mmol) was added at 0°C and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 3:7 EtOAc–hexane) to afford **11** (2.28 g, 35%) as a colorless solid; mp 154–155°C. ^1H NMR data ($CDCl_3$): δ 1.33 (t, 3 H, *J* 7.3 Hz), 2.01 (d, 3 H, *J* 1.5 Hz), 3.17 (q, 2 H, *J* 7.3 Hz), 3.97 (s, 3 H), 4.80–4.82 (m, 2 H), 5.35 (dd, 1 H, *J* 1.3, 10.6 Hz), 5.47 (dd, 1 H, *J* 1.5, 17.2 Hz), 5.99–6.10 (m, 1 H), 7.24 (s, 1 H), 7.30–7.37 (m, 2 H), 7.71 (dd, 1 H, *J* 1.8, 7.9 Hz), and 8.27 (br s, 1 H). Anal. Calcd for $C_{21}H_{22}O_6$: C, 68.09; H, 5.99. Found: C, 68.01; H, 6.01.

2,2,2-Trichloroethyl 1-O-*{(E)-3-[4-(allyloxycarbonyloxy)-5-ethyl-3-methoxynaphthalen-1-yl]-2-methyl-2-propenoyl}-2,3,4-tri*-O-tert-*butyldimethylsilyl*-D-*glucopyranuronate* (**12**).—To a solution of triphenylphosphine (2.42 g, 9.2 mmol) in anhyd tetrahydrofuran (15 mL) at −50°C under N_2 was added diisopropyl azodicarboxylate (1.82 mL, 9.2 mmol). After stirring the mixture at the same temperature for 30 min, a solution of **10** (4.11 g, 6.1 mmol) in anhyd tetrahydrofuran (10 mL) was added and stirring was continued for 30 min. Compound **11** (2.28 g, 6.1 mmol) was added and the mixture was then allowed to warm to room temperature. After stirring for 2 h, water was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 1:19 EtOAc–hexane) to afford **12** (3.0 g, 48%) as a pale-yellow amorphous powder. ^1H

NMR data ($CDCl_3$) of anomeric proton: δ 6.26 (d, 0.8 H, *J* 6.8 Hz, β) and 6.62 (d, 0.2 H, *J* 1.5 Hz, α). Anal. Calcd for $C_{47}H_{73}Cl_3O_{12}Si_3$: C, 55.30; H, 7.21. Found: C, 54.17; H, 7.05.

1-O-{(E)-3-[4-(Allyloxycarbonyloxy)-5-ethyl-3-methoxy-naphthalen-1-yl]-2-methyl-2-propenoyl}-2,3,4-tri-O-tert-butyldimethylsilyl-D-glucopyranuronic acid (**13**).—To a solution of **12** (2.90 g, 2.8 mmol) in tetrahydrofuran (40 mL) at room temperature were added Zn powder (8.0 g, 122 mmol) and 1 M potassium dihydrogenphosphate (4.0 mL, 4.0 mmol). After stirring the mixture at the same temperature for 2 h, the Zn powder was filtered off, then the filtrate was poured into water and extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 19:1 $CHCl_3$–MeOH) to afford **13** (2.14 g, 85%) as a pale-yellow amorphous powder. ^1H NMR data (CD_3OD) of anomeric proton: δ 6.29 (d, 0.8 H, *J* 6.8 Hz, β) and 6.50 (d, 0.2 H, *J* 2.2 Hz, α). Anal. Calcd for $C_{45}H_{72}O_{12}Si_3$: C, 60.77; H, 8.16; Si, 9.5. Found: C, 60.24; H, 8.08; Si, 9.3.

1-O-{(E)-3-[4-(Allyloxycarbonyloxy)-5-ethyl-3-methoxynaphthalen-1-yl]-2-methyl-2-propenoyl}-D-glucopyranuronic acid (**14**).—To a solution of **13** (2.10 g, 2.4 mmol) in acetonitrile (50 mL) at 0°C was added HF (46%; 2.5 mL, 57.5 mmol). After stirring the mixture at room temperature for 5 h, water was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 9:1:0.1 $CHCl_3$–MeOH–formic acid to afford **14** (1.03 g, 80%) as a yellow amorphous powder. ^1H NMR data (CD_3OD) of anomeric proton: δ 5.70 (d, 0.8 H, *J* 8.1 Hz, β) and 6.34 (d, 0.2 H, *J* 3.6 Hz, α) Anal. Calcd for $C_{27}H_{30}O_{12}$: C, 59.33; H, 5.53. Found: C, 58.34; H, 5.56.

1-O-[(E)-3-(5-Ethyl-4-hydroxy-3-methoxynaphthalen-1-yl)-2-methyl-2-propenoyl]-β-D-glucopyranuronic acid (**3**).—To a solution of **14** (980 mg, 1.8 mmol) in anhyd tetrahydrofuran (25 mL) at −20°C were added tetrakis(triphenylphosphine)palladium(0) (41 mg, 35 μmol) and tributyltin hydride (0.58 mL, 2.2 mmol). After stirring the mixture at the same temperature for 20 min, water was added and the mixture was extracted with EtOAc. The organic extract was washed with water and brine, dried, and evaporated. The crude residue was purified by column chromatography on silica gel (elution with 19:1 $CHCl_3$–MeOH) to afford a mixture of **3** and its α anomer (730 mg, 88%) as a yellow amorphous powder. This anomeric mixture (100 mg) was then separated by preparative HPLC (column: Merck LiChrospher RP-18, 10 mm × 250 mm; eluent: 60:20:20:0.1 water–MeOH–acetonitrile–acetic acid; flow rate: 5 mL/min; detection: UV at 240 nm) to afford **3** (70 mg, 70%) as a yellow amorphous powder; $[\alpha]_D$ +34° (*c* 0.6, MeOH). ^1H NMR data (CD_3OD): δ 1.30 (t, 3 H, *J* 7.3 Hz), 2.04 (d, 3 H, *J* 1.5 Hz), 3.37 (q, 2 H, *J* 7.3 Hz), 3.50–3.64 (m, 3 H), 3.96 (s, 3 H), 3.99 (d, 1 H, *J* 9.2 Hz), 5.69 (d, 1 H, *J* 7.5 Hz), 7.16–7.26 (m, 2 H), 7.29 (s, 1 H), 7.66 (dd, 1 H, *J* 1.3, 8.4 Hz), and 8.30 (br s, 1 H). High-resolution mass spectrum (M^+) calcd for $C_{23}H_{26}O_{10}$: 462.1526. Found: 462.1523.

REFERENCES

1 J. Hansen-Møller, C. Cornett, L. Dalgaard, and S.H. Hansen, *J. Pharm. Biomed. Anal.*, 6 (1988) 229–240, and references therein.
2 E.M. Faed, *Drug Metab. Rev.*, 15 (1984) 1213–1249.
3 N. Pravdic and D. Keglevic, *Croat. Chem. Acta*, 36 (1964) 73–79.
4 D. Keglevic, N. Pravdic, and J. Tomasic, *J. Chem. Soc. C.*, (1968) 511–514.
5 R. Bugianesi and T.Y. Shen, *Carbohydr. Res.*, 19 (1971) 179–187.
6 A.B. Barua and J.A. Olson, *J. Lipid Res.*, 26 (1985) 1277–1282.
7 A.D. Mesmaeker, P. Hoffmann, and B. Ernst, *Tretrahedron Lett.*, 30 (1989) 3773–3776.
8 M. Tanaka, K. Chiba, M. Okita, T. Kaneko, K. Tagami, S. Hibi, Y. Okamoto, H. Shirota, M. Goto, H. Sakurai, Y. Machida, and I. Yamatsu, *J. Med. Chem.*, 34 (1991) 2647–2649.
9 G.N. Bollenback, J.W. Long, D.G. Benjamin, and J.A. Lindquist, *J. Am. Chem. Soc.*, 77 (1955) 3310–3315.
10 N. Pravdic and D. Keglevic, *J. Chem. Soc.*, (1964) 4633–4635.
11 A.B. Smith, III, K.J. Hale, and R.A. Rivero, *Tetrahedron Lett.*, 27 (1986) 5813–5816.
12 G. Just and K. Grozinger, *Synthesis*, (1976) 457–458.
13 R.F. Newton, D.P. Reynolds, M.A.W. Finch, D.R. Kelly, and S.M. Roberts, *Tetrahedron Lett.*, (1979) 3981–3982.
14 F. Guibe and Y.S. M'leux, *Tetrahedron Lett.*, 22 (1981) 3591–3594.