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SYNTHESIS OF CARBOHYDRATE CONJUGATES. CHEMICAL MODIFICATION OF MONOSACCHARIDES *via* 2,4,6-TRICHLORO-1,3,5-TRIAZINE*

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ABSTRACT

Several monosaccharides and organic residues, including alkyl, spin-label and organometallic groups, have been linked in various combinations through nitrogen, oxygen, or sulfur atoms by treatment with 2,4,6-trichloro-1,3,5-triazine.

INTRODUCTION

For biochemical investigations, it is of interest to join several organic residues simultaneously to the same sugar molecule, for example when the carbohydrate residue acts as a recognition site and another group as a spectroscopic probe. In the present work, the use of the trivalent reagent 2,4,6-trichloro-1,3,5-triazine (**1**), was investigated. The chemistry of **1** has been extensively documented[2] and this compound has already found some use in carbohydrate chemistry[3,4], such as the dyeing of cellulosic fibers by the Procion dyes[5]. The nucleophilic displacement of the chlorine atoms from **1** by oxygen, nitrogen, or sulfur nucleophiles, is analogous to the nucleophilic, aromatic, substitution reaction of halonitrobenzenes. Thus, the ring nitrogen atoms help stabilize the carbanionic transition state and are responsible for the high activity of the displacement of the first chlorine atom. The relative rates for the subsequent displacements depend on an interplay between the remaining activating effects of the nitrogen atoms and the activating or deactivating effect of the heteroatoms by which the ring is primarily substituted. It is this interplay that introduces the possibility of tri-substitution of **1** with three different organic residues. The triazine residue is a convenient link for labelling carbohydrates with stable, nitroxide-free radicals and it is this use that is described herein.

*For a preliminary communication, see ref. 1.

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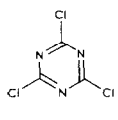
RESULTS AND DISCUSSION

In accord with the resistance to displacement of the three chlorine atoms of **1** by nitrogen nucleophiles, **1** reacted with 4-amino-2,2,6,6-tetramethylpiperidinyl oxide (**2**) at 0° in aqueous acetone with sodium hydrogencarbonate to form the monosubstituted derivative **4**. Replacement of the second chlorine atom by either 1-hexylamine to form **5**, or dodecylamine to form **6** and **7**, required reaction temperatures of 45 and 80°, respectively. The sequence in which these groups were incorporated was of critical importance, as attempts to condense the amino spin-label **2** with either the mono- or di-alkyl triazine chlorides failed. Replacement of a chlorine substituent of **1** by an oxygen or sulfur atom enhanced the reactivity of the remaining chlorine substituents, but the lack of any difference in sequential substitution made it difficult to avoid over-substitution, as shown by the reaction of **1**



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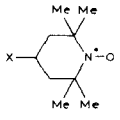
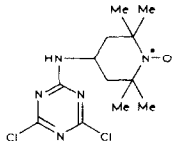


2 X = NH_2
3 X = OH



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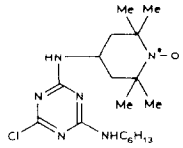

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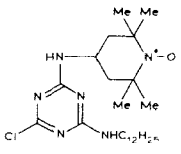

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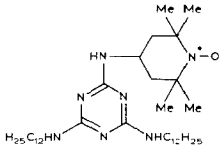

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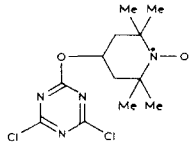

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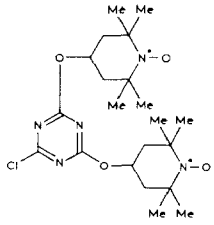

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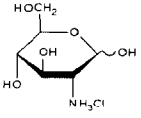

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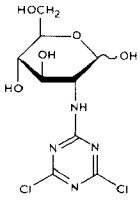

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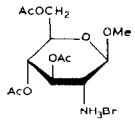

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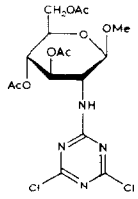

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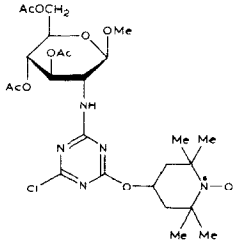

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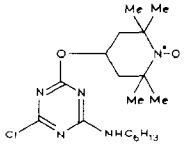

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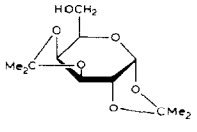

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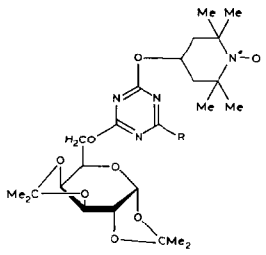
with the hydroxyl spin label **3**. Although one molar equivalent of **3** and **1** gave the monosubstituted spin-label **8**, and with two equivalents the bi-radical **9**, the reaction conditions must be carefully controlled to prevent mixtures of products being formed. The yields for both these reactions were low (10–16%), probably because both **1** and the products are hydrolyzed readily by sodium hydroxide, even at 0°; nevertheless, the products could be filtered directly from the reaction mixture and only required drying at ~50° (to sublime away any unreacted **1**) for purification. This ease of product isolation and the low cost of the starting materials helped to make these low yields acceptable.

Reactions of amino sugars with **1** also take place quite easily, such as the reaction of **10** with **1** to form **11**, previously described by Bishop and Chaudhari[3]. Reaction of the blocked amino sugar **12** to form **13** was performed in the same way and gave a yield of 76%. However, all attempts to treat **13** with the 4-amino-nitroxide **2** or to treat the spin-labelled triazine derivative **4** with the blocked amino sugar **12** failed. This seems to reflect the low nucleophilicity of both the amino



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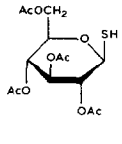
18 R = NHC_6H_{23}



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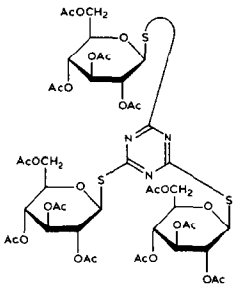

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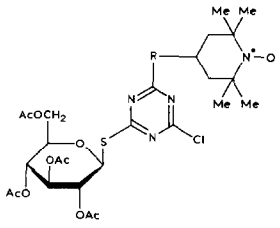
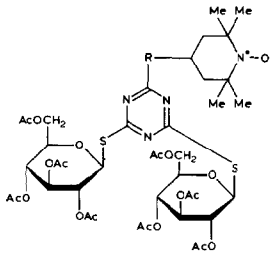


21 R = NH
22 R = O



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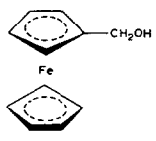

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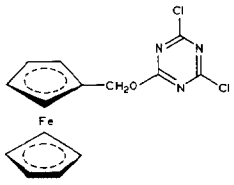

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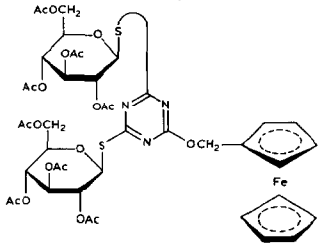

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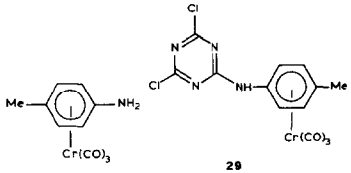

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sugar and the spin label; however, this same amino sugar **12** reacted readily with the oxygen-linked spin label derivative **8** to form **14**. Derivative **8** also reacted more readily under milder conditions with 1-hexylamine than did its nitrogen-linked counterpart **4** to form **15**.

As an example of the reaction of a free hydroxyl group of a suitably blocked monosaccharide with a chlorotriazine derivative, 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**16**) was treated with the oxygen linked, spin-labelled triazine **8** to yield **17**. When sodium hydroxide was replaced by sodium carbonate, there was no detectable reaction. Compound **17** was not isolated but treated directly with 1-hexylamine in aqueous acetone to give the trisubstituted derivative **18** in 45% overall yield. Thiols also reacted well with 2,4,6-trichloro-1,3,5-triazine as exemplified by the reaction of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**19**) with various chlorotriazines, but the weak deactivating effect of the sulfur substituent was not discernibly different from that of the alcohol substituent. Thus, **1** was treated with three equivalents of **19** in acetonitrile and triethylamine to form the trisaccharide derivative **20**. Reaction of **1** with one equivalent of **19** to form the monosubstituted, dichloro compound was unsuccessful owing to the high reactivity of that product and its decomposition, similar to that of the attempted mono-D-galactose preparation. The 1-thio-D-glucose derivative **19** was also treated with the nitrogen- and -oxygen-linked, spin-labelled triazine compounds **4** and **8** to form, respectively, the mono- (**21** and **22**) and bis-thiosugar (**23** and **24**) derivatives of each. These reactions all went readily at room temperature, and the products were isolated by filtration.

In a study to couple various organometallic groups to carbohydrates[6], 1-hydroxymethylferrocene (**25**) was treated with **1** similarly to the synthesis of the 4-hydroxy spin-label **8**. No disubstituted product was detected and synthesis of the disubstituted bisferrocene derivative was not attempted. The ferrocenetriazine derivative **26** reacted readily with **19** to form[6] the metal sugar conjugate **27**. Reactions with other organometallic complexes proceeded readily, as shown in the reaction of tricarbonyl(η-*p*-toluidine)chromium (**28**) with **1** to give **29**. This reaction proceeds as smoothly as that of the 4-amino spin-label reaction.

In this study, it has been shown that monosaccharides can be linked to the triazine ring through nitrogen, oxygen, and sulfur atoms. As well as monosaccharides, a variety of groups including alkyl, spin-label, and organo-metallic moieties have also been attached in various conbinations. The order of substitution onto the triazine ring is quite important, and a few general observations can be made: weakly basic amines, such as the spin label **2** and amino sugars, do not react well with aminochlorotriazines and should either be added first, or after an alkoxy or thio substitution. When strongly alkaline conditions to facilitate substitution with hydroxyl-containing compounds are used, substitution also should either be made first, or following an alkoxy or thio substitution, since elevated temperatures may cause competing hydrolysis. Relatively basic amines, such as alkylamines and also thio derivatives, can usually substitute the ring at any stage regardless of the substituents previously attached.

EXPERIMENTAL

General methods. — Melting points were determined with a Thomas–Hoover Unimelt instrument (model 6406-K) and are corrected. Optical rotations were measured with a Perkin–Elmer polarimeter (model 241-MC). ^{1}H-N.m.r. spectra were recorded at 270 MHz with a prototype of a home-built spectrometer based on a Bruker WP-60 console, a Nicolet 1180 computer (32K), a Nicolet 293A pulse controller unit, a Diablo Disk, and an Oxford Instruments Superconducting solenoid. All deuterated solvents were obtained from Merck Sharp and Dohme (Montreal, Canada) and tetramethylsilane was used as a standard. The mass spectra were recorded with an Atlas CH-4B mass spectrometer, and high-resolution determinations were obtained with an AE1 MS-9 or an MS-50 mass spectrometer. T.l.c. was performed on silica gel plates (Baker-flex Silica gel 1B2-F) in the following solvents: (*A*) 1:1 toluene–ethyl acetate, (*B*) 4:1 toluene–ethyl acetate, and (*C*) 1:5 methanol–chloroform; all compounds were checked for purity by t.l.c. in one of these solvent systems. Column chromatography was performed with 100–200 ASTM mesh silica (Fisher) packed in columns ~2.5 × 50 cm, and eluted with solvent (*A*), (*B*), or (*C*). For reactions requiring anhydrous solvents, the solvents were dried by standard methods, distilled, and stored under a N_2 atmosphere. All solutions were concentrated with a Büchi rotary evaporator. Microanalysis was performed by Mr. P. Borda of this department.

The spin label, 4-amino-2,2,6,6-tetramethylpiperidinyl oxide (**2**), 1-hexylamine, and 1-dodecylamine were purchased from Eastman Kodak Co. (Rochester, NY 14650); 2,4,6-trichloro-1,3,5-triazine (**1**) was purchased from Aldrich Chemical Co. (Milwaukee, WI 53233), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**26**) from Koch–Light Laboratories Ltd. (Colnbrook, Bucks, England), tricarbonyl(η-*p*-toluidine)chromium (**28**) from Strem Chemicals Inc. (Newburyport, MA 01950), and 2,2,6,6-tetramethyl-4-piperidinol from Aldrich. 2,3,4,6-Tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**19**) had previously been prepared by a standard procedure[7], and 4-hydroxy-2,2,6,6-tetramethylpiperidinyl oxide (**3**) was prepared by the method of Rozantsev[8] by oxidizing the secondary amine precursor.

4-(2,4-Dichloro-1,3,5-triazine-6-yl)amino-2,2,6,6-tetramethylpiperidinyl oxide (**4**). — Although this compound has been previously prepared[9], the method described herein is far more convenient. A solution of trichloro-1,3,5-triazine (**1**) (0.54 g, 2.9 mmol) in acetone (12 mL) was stirred at 0°, and an aqueous solution (20 mL) of 4-amino-2,2,6,6-tetramethylpiperidinyl oxide (**2**) (0.5 g, 2.9 mmol) and $NaHCO_3$ (0.24 g, 2.9 mmol) added. The mixture was further stirred for 1.5 h at 0°, and the precipitate filtered off and washed with cold water. The product was heated under vacuum to 50° in a sublimation apparatus (to remove unreacted **1**) to give **4** (75% yield), m.p. 195°.

Anal. Calc. for $C_{12}H_{18}Cl_2N_5O$: C, 45.17; H, 5.65; N, 21.96. Found: C, 45.38; H, 5.79; N, 21.70.

4-[2-Chloro-4-(1-hexylamino)-1,3,5-triazin-6-yl]amino-2,2,6,6-tetramethylpiperidinyl oxide (**5**). — A solution of **4** (0.2 g, 0.63 mmol) in acetone (5 mL) was added with stirring to water (5 mL) at 0°. To this stirred solution was added an aqueous solution (5 mL) of $NaHCO_3$ (60 mg, 0.7 mmol) and an acetone solution (5 mL) of 1-hexylamine (64 mg, 0.63 mmol). The mixture was then stirred for 20 min at 45°, and the product filtered, washed with cold water, and dried, to yield **5** (0.24 g, 83%), m.p. 160–161° (ethanol–water).

Anal. Calc. for $C_{18}H_{32}ClN_6O$: C, 56.32; H, 8.24; N, 21.90. Found: C, 56.34; H, 8.21; N, 21.90.

4-[2-Chloro-4-(1-dodecylamino)-1,3,5-triazin-6-yl]amino-2,2,6,6-tetramethylpiperidinyl oxide (**6**). — A solution of **4** (0.25 g, 0.78 mmol) in acetone (10 mL) was added with stirring to water (7 mL) at 0°. To this stirred solution was added an aqueous solution (10 mL) of $NaHCO_3$ (0.07 g, 0.83 mmol) and a hot acetone solution (10 mL) of dodecylamine (0.145 g, 0.78 mmol). The mixture was stirred for 40 min at 45°, and the pink precipitate filtered off, washed with water, and dried. The compound required no further purification and was obtained in 82% yield, m.p. 118–119°.

Anal. Calc. for $C_{24}H_{44}ClN_6O$: C, 61.63; H, 9.41; N, 17.96. Found: C, 61.66; H, 9.41; N, 18.16.

4-[4,6-Di-(1-dodecylamino)-1,3,5-triazin-6-yl]amino-2,2,6,6-tetramethylpiperidinyl oxide (**7**). — A solution of **6** (0.2 g, 0.43 mmol) in acetone (5 mL) was added with stirring to water (5 mL). To this stirred solution was added an aqueous solution (5 mL) of $NaHCO_3$ (0.04 g, 0.48 mmol) and a hot acetone solution (10 mL) of dodecylamine (0.08 g, 0.43 mmol). The mixture was stirred overnight at 80°, and the pink precipitate filtered off, washed with water, and dried. The product needed no further purification and was obtained in 85% yield, m.p. 78–79°.

Anal. Calc. for $C_{36}H_{70}N_7O$: C, 70.15; H, 11.36; N, 15.90. Found: C, 70.46; H, 11.20; N, 15.74.

4-[2,4-Dichloro-1,3,5-triazin-6-yl]oxy-2,2,6,6-tetramethylpiperidinyl oxide (**8**). — 4-Hydroxy-2,2,6,6-tetramethylpiperidinyl oxide (**3**) (2.0 g, 12 mmol) was dissolved in a mixture of water (50 mL) and 4% NaOH (12 mL), and added dropwise to a stirred, ice-cold acetone solution (40 mL) of **1** (1.8 g, 9.8 mmol) over a period of 1 h. The orange precipitate was filtered off, washed with water, and heated to 50° in a sublimation apparatus to remove unreacted **1**. The product required no further purification and was obtained in a 16% yield, m.p. 108–109°.

Anal. Calc. for $C_{12}H_{17}Cl_2N_4O_2$: C, 45.05; H, 5.31; N, 17.50. Found: C, 44.74; H, 5.42; N, 17.56.

2-Chloro-4,6-di-(2,2,6,6-tetramethyl-4-piperidinyloxy oxide)1,3,5-triazine (**9**). — 4-Hydroxy-2,2,6,6-tetramethylpiperidinyl oxide (**3**) (2 g, 12 mmol) was dissolved in a mixture of water (50 mL) and 4% NaOH (13 mL) and added dropwise, over a period of 40 min, to an ice-cold, stirred acetone solution (40 mL) of **1** (1 g, 5.4 mmol). The mixture was stirred for 1.5 h at room temperature, and the orange precipitate filtered off, washed with water, and dried at 50° to remove any unreacted **1**, giving **9** in 10% yield, m.p. 194–195°.

Anal. Calc. for $C_{21}H_{34}ClN_5O_4$: C, 55.36; H, 7.46; N, 15.36. Found: C, 55.10; H, 7.31; N, 15.08.

*Methyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-(2,4-dichloro-1,3,5-triazin-6-yl)amino-β-*D*-glucopyranoside (***13***).* — To an ice-cold, stirred solution of **1** (0.12 g, 0.65 mmol) in acetone (3 mL) were added an aqueous solution (8 mL) of methyl 3,4,6-tri-*O*-acetyl-2-amino-2-deoxy-β-D-glucopyranoside hydrobromide (**12**) (0.25 g, 0.63 mmol) and $NaHCO_3$ (0.12 g, 1.4 mmol). The mixture was stirred for 1 h at 0° and the precipitate filtered off to give **13** in a 76% yield, m.p. 190–191°, $[\alpha]_D^{22}$ −30.0° (*c* 1, chloroform).

Anal. Calc. for $C_{16}H_{20}Cl_2N_4O_8$: C, 41.13; H, 4.28; N, 12.00. Found: C, 41.36; H, 4.50; N, 11.90.

*4-[4-Chloro-6-(methyl 3,4,6-tetra-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside 2-yl)amino-1,3,5-triazin-2-yl]-2,2,6,6-tetramethylaminopiperidinyl oxide* (**14**). — A mixture of **8** (0.1 g, 0.31 mmol), **12** (0.125 g, 0.31 mmol), and Na_2CO_3 (0.1 g, 0.94 mmol) was stirred in acetonitrile (30 mL) overnight at room temperature. The mixture was filtered and the filtrate evaporated to dryness. The residue was purified by silica column chromatography in solvent (*A*). The orange compound crystallized from ethanol–water to give a 53% yield, m.p. 90–91°, $[\alpha]_D^{22}$ +39.0° (*c* 1, chloroform).

Anal. Calc. for $C_{25}H_{37}ClN_5O_{10}$: C, 49.82; H, 6.14; N, 11.61. Found: C, 49.69; H, 6.35; N, 11.32.

4-[2-Chloro-4-(1-hexylamino)-1,3,5-triazin-6-yl]oxy-2,2,6,6-tetramethylpiperidin oxide (**15**). — A solution of **8** (0.1 g, 0.32 mmol) in acetone (3 mL) was added to a solution of 1-hexylamine (0.032 g, 0.32 mmol) and $NaHCO_3$ (0.03 g, 0.36 mmol) in 2:5 acetone–water (7 mL). The mixture was stirred for 20 min at room temperature and extracted with chloroform. The chloroform layer was washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue was chromatographed on a short silica gel column in solvent (*A*) to give an orange syrup (75% yield).

Anal. Calc. for $C_{18}H_{31}ClN_5O_2$: C, 56.20; H, 8.06; N, 18.20. Found: C, 56.22; H, 7.85; N, 17.90.

*4-[4-(1,2:3,4-Di-*O*-isopropylidene-α-*D*-galactopyranosyloxy)-6-(1-hexylamino)-1,3,5-triazin-2-yl]oxy-2,2,6,6-tetramethylpiperidinyl oxide* (**18**). — A mixture of **8** (0.1 g, 0.31 mmol), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**16**) (0.08 g, 0.31 mmol), and one crushed NaOH pellet (0.15 g) was stirred overnight at room temperature in benzene (10 mL). The mixture was filtered and the filtrate evaporated to dryness. To the syrup was added an ice-cold solution (10 mL) of $NaHCO_3$ (0.03 g, 0.36 mmol) and 1-hexylamine (0.03 g, 0.3 mmol) in 1:3 water–acetone. The mixture was allowed to warm to room temperature and then stirred for an additional 2 h. The pink precipitate was purified by silica gel column chromatography in solvent (*A*) and crystallized from ethanol–water to give a 40% overall yield, m.p. 170–171°, $[\alpha]_D^{22}$ −55.0° (*c* 1.4, chloroform).

Anal. Calc. for $C_{30}H_{50}N_5O_8$: C, 59.23; H, 8.22; N, 11.51. Found: C, 59.44; H, 8.25; N, 11.40.

2,4,6-Tri-(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosyl)-1,3,5-triazine (**20**). — A solution of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (**19**) (0.4 g, 1.1 mmol) in acetonitrile (6 mL) was added to a stirred acetonitrile solution (6 mL) of **1** (67 mg, 0.36 mmol), and then triethylamine (0.11 g, 1.1 mmol) was added. The mixture was stirred at room temperature for 0.5 h, and then poured into ice–water (50 mL). The precipitate was filtered off, washed with water, and dried. The compound required no further purification and was obtained in 66% yield, m.p. 122–124°, $[\alpha]_D^{22}$ +9.37° (*c* 0.32, chloroform).

Anal. Calc. for $C_{45}H_{57}N_3O_{27}S_3$: C, 46.29; H, 4.88; N, 3.60; S, 8.24. Found: C, 46.10; H, 4.82; N, 3.52; S, 8.05.

4-[4-Chloro-6-(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosyl)-1,3,5-triazin-2-yl]amino-2,2,6,6-tetramethylpiperidinyl oxide (**21**). — To a solution of **4** (0.2 g, 0.63 mmol) in acetone (5 mL) was added with stirring an acetone solution (5 mL) of **19** (0.23 g, 0.63 mmol) and an aqueous solution (10 mL) of $NaHCO_3$ (0.06 g, 0.71 mmol). The mixture was stirred for 20 min at room temperature and then extracted with chloroform. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a syrup that was purified on a silica gel column in solvent (*A*). After crystallization from ethanol–water, **21** was obtained in 72% yield, m.p. 105–106°, $[\alpha]_D^{22}$ +3.4° (*c* 5, chloroform).

Anal. Calc. for $C_{26}H_{37}ClN_5O_{10}S$: C, 48.28; H, 5.72; N, 10.82. Found: C, 48.49; H, 5.85; N, 10.53.

4-[4-Chloro-6-(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosyl)-1,3,5-triazin-2-yl]oxy-2,2,6,6-tetramethylpiperidinyl oxide (**22**). — A mixture of **8** (0.1 g, 0.31 mmol), **19** (0.114 g, 0.31 mmol), and Na_2CO_3 (0.05 g, 0.48 mmol) was stirred in acetonitrile (30 mL) overnight at room temperature, and then filtered. The filtrate was evaporated to dryness and the pink residue purified by silica gel column chromatography in solvent (*A*). Crystallization from light petroleum–ether gave **22** (57% yield), m.p. 85–86°, $[\alpha]_D^{22}$ −0.5° (*c* 6, chloroform).

Anal. Calc. for $C_{26}H_{36}ClN_4O_{11}S$: C, 48.20; H, 5.56; N, 8.64. Found: C, 48.27; H, 5.67; N, 8.55.

4-[4,6-Di-(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosyl)-1,3,5-triazin-2-yl]amino-2,2,6,6-tetramethylpiperidinyl oxide (**23**). — To a solution of **4** (0.1 g, 0.31 mmol) in acetone (5 mL) was added with stirring an acetone solution (5 mL) of **19** (0.23 g, 0.63 mmol) and an aqueous solution (10 mL) of $NaHCO_3$ (0.06 g, 0.7 mmol). The mixture was stirred overnight at room temperature and the orange precipitate processed and purified, as described for **22**, by column chromatography in solvent (*A*). The product crystallized from 2:1 water–ethanol to give **23** (85% yield), m.p. 108–109°, $[\alpha]_D^{22}$ +6.6° (*c* 5, chloroform).

Anal. Calc. for $C_{40}H_{56}N_5O_{19}S_2$: C, 49.30; H, 5.75; N, 7.18; S, 6.58. Found: C, 49.52; H, 5.98; N, 6.75; S, 6.31.

4-[4,6-Di-(2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranosyl)-1,3,5-triazin-2-yl]oxy-2,2,6,6-tetramethylpiperidinyl oxide (**24**). — This compound was prepared in the same way as **22**, except that two equivalents of **19** (0.228 g) were used. After

column chromatography in solvent (*A*), the compound crystallized from ethanol–water to give **24** (78% yield), m.p. 110–111°, $[\alpha]_D^{22}$ +5.55° (*c* 1.8, chloroform).

Anal. Calc. for $C_{40}H_{55}N_4O_{20}S_2$: C, 49.25; H, 5.64; N, 5.74; S, 6.57. Found: C, 49.35; H, 5.58; N, 5.65; S, 6.33.

*2,4-Dichloro-6-[tricarbonyl-(η-*p*-toluidine)chromium]-1,3,5-triazine* (**29**). — A solution of **1** (0.4 g, 2.2 mmol) was dissolved in acetone (8 mL) at 0°, and to this stirred solution was added an acetone solution (7 mL) of tricarbonyl(η-*p*-toluidine)chromium (**28**) (0.53 g, 2.2 mmol) and an aqueous solution (45 mL) of $NaHCO_3$ (0.3 g, 3.6 mmol). The mixture was stirred for 2 h at 0° and filtered to give **29** (yield 85%) which was recrystallized from ethanol–hexane, m.p. 160–161° (dec); ν_{max}^{Nujol} (C–O stretch) 1950 and 1850 cm^{-1}.

Anal. Calc. for $C_{13}H_8Cl_2CrN_4O_3$: C, 39.93; H, 2.05; N, 14.32. Found: C, 40.26; H, 2.22; N, 14.06.

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