ORGANIC LETTERS

2000
Vol. 2, No. 8
1113−1116

An Efficient Synthesis of Cyclodextrin-Based Carbohydrate Cluster Compounds

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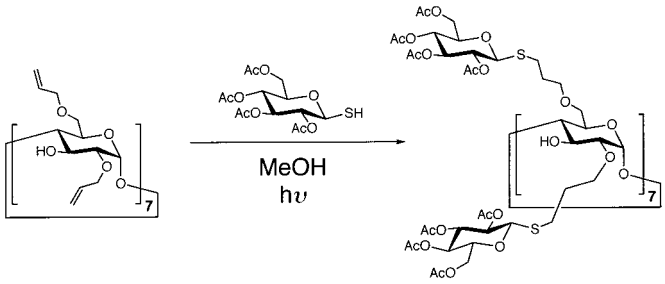
Received February 14, 2000

ABSTRACT



The photoaddition of the thiol 2,3,4,6-tetra-*O*-acetyl-β-D-1-thioglucopyranose to the allyl ether functions of per-2-allyl-, per-6-allyl-, and per-2,6-diallyl-β-cyclodextrin derivatives provides a remarkably simple and efficient way for attaching glucopyranose units onto (1) the secondary face, as well as (2) the primary face, of β-cyclodextrin—not to mention (3) both the primary and secondary faces, simultaneously—in yields of up to 70%.

The synthesis and protein binding characteristics of highly branched carbohydrate-containing compounds, designed to exploit the so-called "multivalent" and "glycoside-cluster effect", continue to receive much attention[1] in contemporary carbohydrate research. In addition, the preparation and characterization of compounds that not only possess multivalent carbohydrate recognition sites but also have the intrinsic potential to act as hosts for the complexation of guest molecules is gaining in importance in part because compounds of this type could act as the forerunners of "intelligent" drug delivery systems.[2] For example, research groups headed by Dondoni[3] and Roy[4] have reported the attachment of carbohydrate residues onto calixarene scaffolds. More recently, Aoyama and co-workers[5] have reported their findings on the synthesis and properties of calix[4]-resorcarene-based carbohydrate cluster compounds and have

(1) (a) Lee, Y. C.; Lee, R. T.; Rice, K.; Ichikawa, Y.; Wong, T.-C. *Pure Appl. Chem.* **1991**, *63*, 499−506. (b) Lee, Y. C.; Lee, R. T *Acc. Chem. Res.* **1995**, *28*, 321−327. (c) Sigal, G. B.; Mammen, M.; Dahmann, G.; Whitesides, G. M. *J. Am. Chem. Soc.* **1996**, *118*, 3789−3800. (d) Mann, D. A.; Kanai, M.; Maly, D. J.; Kiessling, L. L. *J. Am. Chem. Soc.* **1998**, *120*, 10575−10582. (e) Dimick, S. M.; Powell, S. C.; McMahon, S. A.; Moothoo, D. N.; Naismith, J. H.; Toone, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 10286−10296.

(2) (a) Parrot-Lopez, H.; Galons, H.; Coleman, A. W.; Mahuteau, J.; Miocque, M. *Tetrahedron Lett.* **1992**, *33*, 209−212. (b) Parrot-Lopez, H.; Leray, E.; Coleman, A. W. *Supramol. Chem.* **1993**, *3*, 37−42. (c) Attioui, F.; Al-Omar, A.; Leary, E.; Parrot-Lopez, H.; Finance, C.; Bonaly, R. *Biol. Cell.* **1994**, *82*, 161−167. (d) Leray, E.; Parrot-Lopez, H.; Auge, C.; Coleman, A. W.; Finance, C.; Bonaly, R. *J. Chem. Soc., Chem. Commun.* **1995**, 1019−1020. (e) García Fernández, J. M.; Mellet, C. O.; Maciejewski, S.; Defaye, J. *J. Chem. Soc., Chem. Commun.* **1996**, 2741−2742.

(3) (a) Marra, A.; Scherrmann, M.-C.; Dondoni, A.; Casnati, A.; Minari, P.; Ungaro, R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2479−2481. (b) Marra, A.; Dondoni, A.; Sansone, F. *J. Org. Chem.* **1996**, *61*, 5155−5158. (c) Dondoni, A.; Marra, A.; Schermann, M.-C.; Casnati, A.; Sansome, F.; Ungaro, R. *Chem. Eur. J.* **1997**, *3*, 1774−1782. (d) Dondoni A.; Kleban M.; Marra A. *Tetrahedron Lett.* **1997**, *38*, 7801−7804.

(4) (a) Meunier, S. J.; Roy, R. *Tetrahedron Lett.* **1996**, *37*, 5469−5472. (b) Roy, R.; Kim, J. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 369−372.

(5) (a) Fujimoto, T.; Shimizu, C.; Hayashida, O.; Aoyama, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6676−6677. (b) Hayashida, O.; Shimizu, C.; Fujimoto, T.; Aoyama, Y. *Chem. Lett.* **1998**, 13−14. (c) Ariga, K.; Isoyama, K.; Hayashida, O.; Aoyama, Y. *Chem. Lett.* **1998**, 1007−1008. (d) Fujimoto, T.; Shimizu, C.; Hayashida, O.; Aoyama, Y. *J. Am. Chem. Soc.* **1998**, *120*, 601−602. (e) Hayashida, O.; Kato, M.; Akagi, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1999**, *121*, 11597−11598.

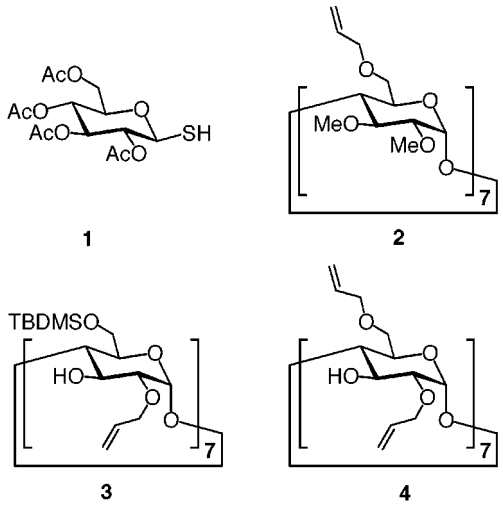
10.1021/ol005668x CCC: $19.00
Published on Web 03/24/2000

outlined how these hosts can be used to deliver guest molecules to surfaces[5a] and lectins.[5d]

The use of cyclodextrins[6] (CDs), a class of cyclic oligosaccharides capable of forming inclusion complexes with a wide variety of substrates in aqueous solution, as a core for the attachment of additional carbohydrate residues (1) presents arguably a more biocompatible alternative to the calixarenes and (2) offers increased water solubility and a promiscuous potential for guest inclusion. Since Djedaïni-Pilard and co-workers[7] reported the synthesis of perthioglucosylated derivatives of β-CD in 1995, several other groups[8] have recently described alternative synthetic strategies for the perfunctionalization of CDs—*but on their primary faces only*—with carbohydrate appendages. In at least one instance[8b] the ability of compounds of this type to interact with plant lectins has been demonstrated.

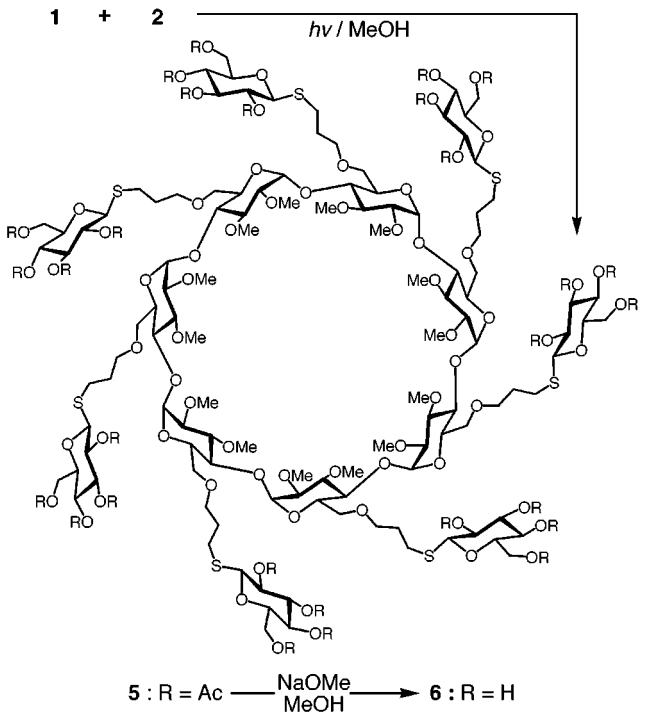
In furtherance of our own research[9] on glycodendrimers, we have been seeking an efficient strategy for attaching carbohydrate residues onto (1) *the secondary in addition to the primary faces* of CDs and then extending this strategy to the perfunctionalization of (2) *both the primary and secondary faces* of CDs simultaneously. Here, we report the efficient synthesis of some β-CD-based carbohydrate cluster compounds.

In view of its inherently divergent nature, any perfunctionalization of CDs is notoriously difficult to accomplish.[10] After a preliminary survey of possible reactions, we began to focus our attention on the well-known[11] photoadditon of thiols to allyl ethers in an anti-Markovnikov fashion to yield thioethers as the key step in the attachment of carbohydrate appendages to CD cores. The reaction's proven use in both carbohydrate[12] and CD[13] chemistry, coupled with the ease of introduction of (1) allyl ether functions onto the CD torus and (2) thiol groups onto the anomeric centers of saccharides, made it an appealing choice as the key step. β-D-Thioglucose[14] (**1**) was chosen as the model thiol to react with the allyl ether containing β-CD derivatives **2**,[15] **3**,[16] and **4**.[17]



Primary face modification of β-CD with seven carbohydrate appendages was achieved efficiently (Scheme 1) when

Scheme 1



a methanolic solution of a mixture of **1** (21 equiv) and **2** was irradiated[18] with UV light from an Hg lamp. After 5 h, TLC indicated an almost quantitative conversion to **5** when

(6) (a) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803−822. (b) Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743−1755. (c) Khan, A. R.; Forgo, P.; Stine, K. J.; D'Souza, V. T. *Chem. Rev.* **1998**, *98*, 1977−1996.

(7) Lainé, V.; Coste-Sarguet, A.; Gadelle, A.; Defaye, J.; Perly, B.; Djedaïni-Pilard, F. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1479−1487.

(8) (a) Mellet, C. O.; Benito, J. M.; García Fernández, J. M.; Law, H.; Chmurski, K.; Defaye, J.; O'Sullivan, M. L.; Caro, H. N. *Chem. Eur. J.* **1998**, *4*, 2523−2531. (b) García-López, J. J.; Hernández-Mateo, F.; Isac-García, J.; Kim, J. M.; Roy, R.; Santoyo-González, F.; Vargas-Berenguel, A. *J. Org. Chem.* **1999**, *64*, 522−531. (c) García-López, J. J.; Santoyo-González, F.; Vargas-Berenguel, A.; Giménez-Martínez, J. J. *Chem. Eur. J.* **1999**, *5*, 1775−1784. (d) Furuike, T.; Aiba, S. *Chem. Lett.* **1999**, 69−70.

(9) Ashton, P. R.; Hounsell, E. F.; Jayaraman, N.; Nielsen, T. M.; Spencer, N.; Stoddart, J. F.; Young, M. *J. Org. Chem.* **1998**, *63*, 3429−2437 and references therein.

(10) The challenge in perfunctionalizing α-, β-, or γ-CD is at least threefold. One is the need to identify bond-forming reactions that are high yielding over and over again so that, on repeating them 6, 7, or 8 (or perhaps 12, 14, or 16 or even 18, 21, or 24) times, the outcomes are high yields of pure products. The other is the need to obtain the pure products free from a multitude of undersubstituted compounds all with very similar properties to each other and to the pure products. Another challenge is the need to characterize the symmetrical products as being pure when the unsymmetrical impurities are so similar. The presence of axial symmetry (in the pure products) and the lack of it (in the impure compounds) can be simultaneously both a blessing and a curse!

(11) Griesbaum, K. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 273−287.

(12) For examples, see: (a) Lee, R. T.; Lee, Y. C. *Carbohydr. Res.* **1974**, *37*, 193−196. (b) Kieburg, C.; Dubber, M.; Lindhorst, T. K. *Synlett* **1997**, 1447−1449.

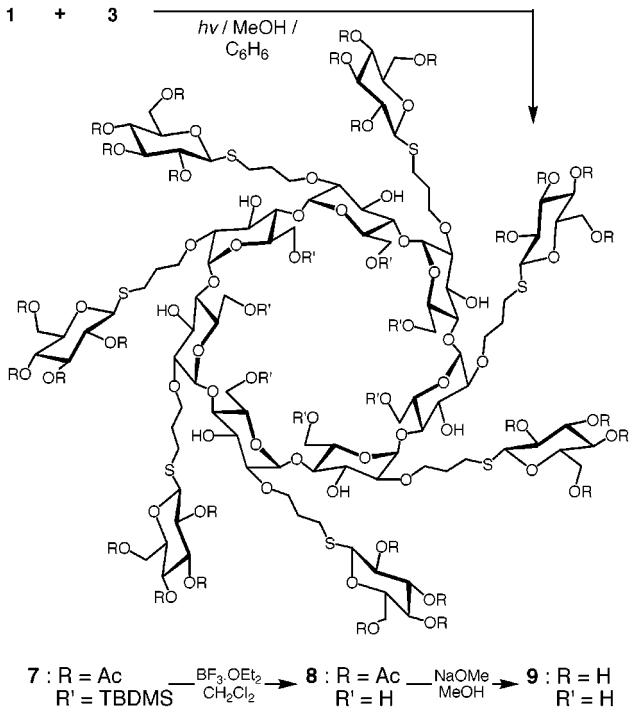
(13) (a) Hanessian, S.; Benalil, A.; Laferrière, C. *J. Org. Chem.* **1995**, *60*, 4786−4797. (b) Leydet, A.; Moullet, C.; Roque, J. P.; Witvrouw, M.; Pannecouque, C.; Andrei, G.; Snoeck, R.; Neyts, J.; Schols, D.; De Clerq, E. *J. Med. Chem.* **1998**, *41*, 4927−4932.

(14) Stanek, J.; Sindlerova, M.; Cerny, M. *Collect. Czech. Chem. Commun.* **1965**, *30*, 297−302.

the concentration of **2** in the reaction mixture was ca. 5 mM. At lower concentrations "under substitution" of **2** occurs; if the concentration of the reactants is too high, then the major product of the reaction is the disulfide formed by dimerization of two molecules of **1**. Purification of the crude product from the photochemical reaction by column chromatography (SiO_2) afforded a pure compound in 67% yield.[19] MALDI-TOF mass spectrometry of this compound revealed a peak at *m*/*z* 4185 $[M + Na]^+$, corresponding to a β-CD derivative **5**, which is fully adorned with seven β-D-thioglucose residues. The identity of **5**[20] was established unequivocally from its ^1H and ^{13}C NMR spectra.[21] Deprotection (NaOMe/MeOH) of **5** yielded (99%) **6**, which was also fully characterized by ^1H and ^{13}C NMR spectroscopies.[22]

The same synthetic strategy was applied to obtain a β-CD derivative perfunctionalized on its secondary face with seven carbohydrate appendages. Reaction (Scheme 2) of **1** with **3**,

Scheme 2



under essentially the same conditions as those[18] described above for the synthesis of **5**, gave the "fully substituted" compound[23] **7** in 42% yield after purification by silica gel column chromatography. O-Desilyation[24] of **7** afforded the intermediate **8**, which after deprotection (NaOMe/MeOH) furnished **9**.[25]

(15) (a) Per-2,3-dimethyl-β-cyclodextrin (Takeo, K.; Mitoh, H.; Uemura, K. *Carbohydr. Res.* **1989**, *187*, 203−221) was treated with allyl bromide (NaH/DMF) to afford **2** in a 42% yield.

(16) König, W. A.; Icheln, D.; Runge, T.; Pfaffenberger, B.; Ludwig, P.; Hühnerfuss, H. *J. High Resolut. Chromatogr.* **1991**, *14*, 530−536.

(17) Bergeron, R. J.; Meeley, M. P.; Machidia, Y. *Bioorg. Chem.* **1976**, *5*, 121−126.

(18) **General Experimental.** The thiol **1** (21 or 42 equiv) and the CD (**2**, **3**, or **4**, all at 5 mM) were dissolved in distilled MeOH, and benzene was added dropwise to disslove the CD if required. A stream of Ar was bubbled through the solution for 20 min to thoroughly degas it. The solution, kept under an atmosphere of Ar, was placed in front of a Hg lamp and stirred for 5 h. Following removal of solvent(s), the residue was purified by column chromatography [SiO_2, EtOAc/Hexanes] to afford the product. Unreacted thiol **1** can be recovered and reused in subsequent reactions.

(19) Reported yields have not been optimized.

(20) **Data for 5.** ^1H NMR ($CDCl_3$, 500 MHz): δ 1.85−1.89 (14H, m, SCH_2CH_2), 1.98, 2.00, 2.04, 2.06 (84H, 4s, 4 × Ac), 2.64−2.73 (7H, m, SCH_a), 2.76−2.83 (7H, m, SCH_b), 3.12 (7H, dd, $^3J_{1,2} = 3.0$ Hz, $^3J_{2,3} = 9.5$ Hz, H-2), 3.46−3.64 (35H, m, H-3, H-4, H-6a, H-6b, OCH_a), 3.49 (21H, s OCH_3), 3.60 (21H, s, OCH_3), 3.66−3.69 (7H, m, H-5), 3.71−3.81 (7H, m, H-5′), 3.80−3.84 (7H, m, OCH_b), 4.09−4.12 (7H, m, H-6a′), 4.24 (7H, dd, $^3J_{5',6b'} = 4.6$ Hz, $^2J_{6a',6b'} = 12.4$ Hz, H-6b′), 4.53 (7H, d, $^3J_{1',2'} = 10.0$ Hz, H-1′), 4.98 (7H, t, $^3J_{1',2'} \approx {}^3J_{2',3'} = 9.8$ Hz, H-2′), 5.04−5.08 (14H, m, H-1, H-4′), 5.21 (7H, t, $^3J_{2',3'} \approx {}^3J_{3',4'} = 9.4$ Hz, H-3′). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 20.76, 20.79, 20.92, 20.96 (4 x CH_3CO), 27.3 (SCH_2), 30.4 (SCH_2CH_2), 58.8 (CH_3O), 61.5 (CH_3O), 62.3 (C-6′), 68.5 (C-4′), 69.7 (OCH_2), 70.0 (C-6), 70.1 (C-2′), 71.5 (C-5), 74.0 (C-3′), 75.9 (C-5′), 80.1 (C-3), 81.8 (C-4), 82.3 (C-2), 83.9 (C-1′), 99.1 (C-1), 169.5, 169.6, 170.3, 170.7 (4 × CH_3CO). MALDI-TOF: *m*/*z* = 4185 $[M + Na]^+$.

(21) The ^1H and ^{13}C NMR signals in the spectra of all of the protected CD-based carbohydrate cluster compounds, i.e. **5**, **7**, and **10**, were assigned fully using a combination of 2D-COSY and HMQC experiments. A common feature of the ^1H NMR spectra of these CD-based carbohydrate clusters is that they display broadened signals corresponding to their CD protons, while the signals for the protons of the glucose appendages are sharp. This phenomenon is revealed also in the ^{13}C NMR spectra, where the signals corresponding to the CD carbons are weaker and broader than those corresponding to the carbons in the glucose appendages. The reason for this signal broadening is most likely the outcome of a dynamic phenomenon; the glucose appendages start to cause the CD glucose residues to move on a time scale approaching that of the NMR time scale, thus causing the CD signals to broaden.

(22) **Data for 6.** Selected NMR data. ^1H NMR (D_2O, 500 MHz): δ 1.91−2.40 (14H, m, CH_2), 2.81−2.93 (14H, m, SCH_2), 3.21 (7H, dd, J = 2.9, 9.6 Hz, H-2), 3.54 (21H, s, OCH_3), 3.64 (21H, s, OCH_3), 4.43 (7H, d, J = 9.6 Hz, H-1′), 5.20 (7H, d, J = 2.9 Hz, H-1). ^{13}C NMR (CD_3OD, 125 MHz): δ 28.7, 32.1, 59.9, 62.6, 63.8, 71.6, 71.9, 72.3, 73.5, 75.2, 80.4, 81.4, 82.7, 83.9, 84.3, 88.1, 100.4.

(23) **Data for 7.** ^1H NMR ($CDCl_3$, 500 MHz): δ 0.029 (21H, s, $SiCH_3$), 0.037 (21H, s, $SiCH_3$), 0.879 (63H, s, $C(CH_3)$), 1.92−1.94 (14H, m, SCH_2CH_2), 2.02, 2.04, 2.07, 2.10 (84H, 4s, 4 × Ac), 2.77−2.91 (14H, m, SCH_2), 3.25 (7H, dd, $^3J_{1,2} = 3.1$ Hz, $^3J_{2,3} = 9.6$ Hz, H-2), 3.48 (7H, t, $^3J_{3,4} \approx {}^3J_{4,5} = 9.0$ Hz, H-4), 3.54 (7H, d, $^3J_{5,6a} = 9.6$ Hz, H-5), 3.68 (7H, d, $^2J_{6a,6b} = 10.8$ Hz, H-6a), 3.77−3.83 (14H, m, H-5′, OCH_a), 3.90−3.94 (14H, m, H-3, H-6b), 4.04−4.10 (7H, m, OCH_b), 4.17 (7H, dd, $^3J_{5',6a'} = 2.3$ Hz, $^2J_{6a',6b'} = 12.0$ Hz, H-6a′), 4.31 (7H, dd, $^3J_{5',6a'} = 4.8$ Hz, $^2J_{6a',6b'} = 12.0$ Hz, H-6b′), 4.64 (7H, d, $^3J_{1',2'} = 10.1$ Hz, H-1′), 4.91 Hz (7H, d, $^3J_{1,2} = 3.1$ Hz, H-1), 5.05 (7H, t, $^3J_{1',2'} \approx {}^3J_{2',3'} = 10.1$ Hz, H-2′), 5.13 (7H, $^3J_{3',4'} \approx {}^3J_{4',5'} = 9.8$ Hz, H-4′), 5.28 (7H, t, $^3J_{2',3'} \approx {}^3J_{3',4'} = 9.4$ Hz, H-3′). ^{13}C NMR ($CDCl_3$, 125 MHz): δ −4.9, −4.8 ($Si(CH_3)_2$), 18.5 ($SiC(CH_3)_3$), 20.8−21.1 (4 × CH_3CO), 26.1 ($SiC(CH_3)_3$), 27.6 (SCH_2CH_2), 30.5 (SCH_2), 61.9 (C-6), 62.4 (C-6′), 68.6 (C-3′), 70.3 (C-2′), 71.3 (OCH_2), 71.9 (C-5), 73.3 (C-3), 74.2 (C-3′), 75.9 (C-4′), 81.2 (C-2), 82.4 (C-4), 84.3 (C-1′), 101.4 (C-1), 169.6, 169.7, 170.4, 170.8 (4 × CH_3CO). MALDI-TOF: *m*/*z* 4789 $[M + Na]^+$.

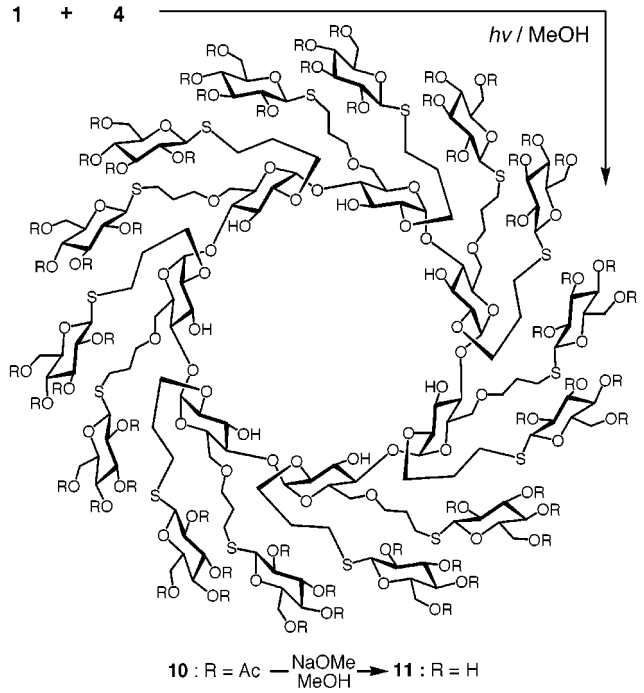
(24) Kelly, D. R.; Roberts, S. M.; Newton, R. F. *Synth. Commun.* **1979**, *9*, 295−299.

(25) **Data for 9.** Selected NMR data. ^1H NMR (D_2O, 500 MHz): 1.85−1.92 (14H, m, CH_2), 2.71−2.77 (7H, m, SCH_a), 2.80−2.86 (7H, m, SCH_b), 3.25 (7H, t, J = 9.8 Hz, H-2′), 3.37 (7H, dd, J = 2.0, 5.7 Hz, H-2), 3.41 (7H, t, J = 9.0 Hz, H-3′), 4.45 (7H, d, J = 9.8 Hz, H-1′), 5.12, (7H, s, H-1). ^{13}C NMR (D_2O, 125 MHz): δ 26.3, 29.4, 60.0, 60.8, 69.4, 70.4, 71.1, 72.1, 73.5, 79.7, 80.9, 85.2, 99.6.

(26) **Data for 10.** ^1H NMR ($CDCl_3$, 500 MHz): δ 1.82−1.90 (28H, m, SCH_2CH_2), 1.99, 2.00, 2.04, 2.06, 2.07 (168H, 5s, Ac), 2.56−2.85 (28H, m, SCH_2), 3.27 (7H, d, $^3J_{2,3} = 9.2$ Hz, H-2), 3.39 (7H, t, $^3J_{2,3} = 9.0$ Hz, H-4), 3.45−3.54 (28H, m, H-6a, H-6b, OCH_2), 3.56−3.68 (7H, m, H-5), 3.70−3.78 (21H, m, H-5′, OCH_a), 3.81 (7H, t, $^3J_{2,3} = 9.0$ Hz, H-3), 3.97−4.04 (7H, m, OCH_b), 4.11 (14H, d, $^2J_{6a',6b'} = 10.9$ Hz, H-6a′), 4.24 (14H, dd, $^3J_{5',6b'} = 3.5$ Hz, $^2J_{6a',6b'} = 11.5$ Hz, H-6b′), 4.54 (7H, d, $^3J_{1',2'} = 10.0$ Hz, H-1′), 4.57 (7H, d, $^3J_{1',2'} = 10.0$ Hz, H-1′), 4.82 (7H, bs, H-1), 4.98 (14H, t, $^3J_{2',3'} = 9.2$ Hz, H-2′), 5.06 (7H, t, $^3J_{3',4'} = 9.7$ Hz, H-4′), 5.07 (7H, t, $^3J_{3',4'} = 9.7$ Hz, H-4′), 5.22 (7H, t, $^3J_{3',4'} = 9.3$ Hz, H-3′). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 20.4, 20.66 (CH_3CO), 26.9, 27.0 (SCH_2CH_2), 29.5, 30.0 (SCH_2), 62.2 (C-6′), 68.4 (C-4′), 69.1 (C-6), 69.9 (OCH_2), 70.0, 70.1 (C-2′), 70.6 (C-5), 71.3 (OCH_2), 73.1 (C-3), 73.9, 74.0 (C-3′), 75.7, 75.8 (C-5′), 80.7 (C-2), 83.3 (C-4), 83.7, 83.9 (C-1′), 101.9 (C-1), 169.20, 169.23, 169.29, 169.77, 169.96, 170.02, 170.37, 170.47 (8 × CH_3CO). MALDI-TOF: *m*/*z* 6820 $[M + Na]^+$.

The next obvious question was whether this photochemical approach could be used to modify, simultaneously and fully, *both* the primary and secondary faces of a β-CD derivative in a reaction that would involve the formation of 14 thioether bonds per molecule. Reaction (Scheme 3) of per-2,6-diallyl-

Scheme 3



β-CD[17] (**4**) with 42 equiv of **1** in MeOH gave the desired compound[26] **10** in 70% yield, following purification by column chromatography on silica gel. Analysis of the carbohydrate region of the ^{13}C DEPT NMR spectrum (Figure 1) of **10** reveals signals corresponding to all of the carbons on the primary and secondary face glucose appendages and

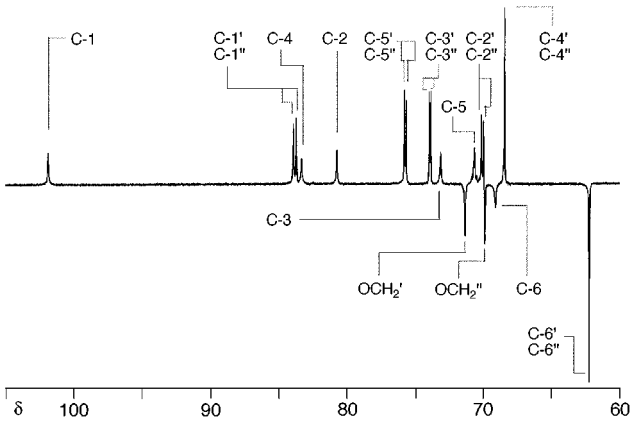


Figure 1. ^{13}C DEPT NMR spectrum of **10** showing the carbohydrate region.

the cyclodextrin torus. The signals corresponding to the carbons on both the primary and secondary face glucose appendages appear at a very similar or, for all intents and purposes, the same chemical shift. Deprotection (NaOMe/MeOH) of **10** afforded the free cluster compound **11**, which was fully characterized by both ^{1}H and ^{13}C NMR spectroscopies.[27]

In conclusion, we have described a novel synthetic strategy for the per-modification of *either* or *both* faces of β-CD. It utilizes the photoadditon of thiols to allyl ethers. We believe this method could be of great utility in the preparation of CD-based carbohydrate clusters, as it should work equally well with any monosaccharide thiol substrate and oligosaccharides. We are currently (1) investigating the binding abilities of these cluster compounds and (2) studying their interactions with plant lectins.

Acknowledgment. We thank UCLA for generous financial support.

Supporting Information Available: ^{1}H and ^{13}C NMR data for compounds **5**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(27) **Data for 11.** Selected NMR data. ^{1}H NMR (D_2O, 360 K, 500 MHz): δ 2.33−2.41 (28H, m, CH_2), 3.19−3.35 (28H, m, SCH_2), 4.91 (7H, d, J = 9.9 Hz, H-1′), 4.93 (7H, d, J = 9.9 Hz, H-1″), 5.56 (7H, d, J = 3.0 Hz, H-1). ^{13}C NMR (D_2O, 345 K, 125 MHz): δ 23.7, 26.9, 27.1, 29.9, 30.1, 61.59, 61.66, 69.4, 70.1, 70.3, 70.9, 71.3, 71.6, 72.89, 72.97, 77.82, 77.89, 80.30, 80.35, 81.96, 85.81, 85.88, 100.4.