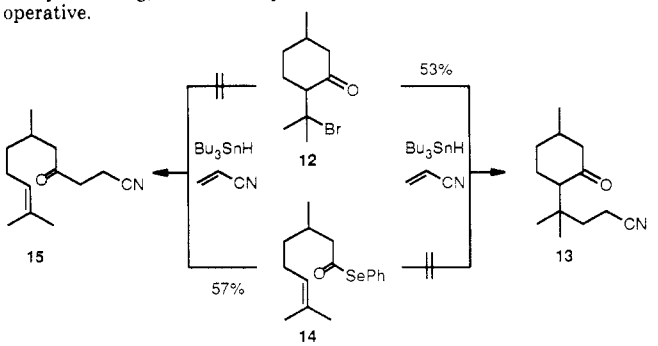
Thus, although the ring expansion rearrangement has proven operationally viable for the observed **1a** → **2a** cyclization, it cannot be operative in the observed conversion of **1b** → **2b**. These observations coupled with the lack of observation of reversible acyl radical-alkene addition reactions[17] suggest that **2a-b** are derived from a direct, kinetically and thermodynamically preferred 6-*endo-trig* acyl radical-alkene cyclization. However, as detailed herein, the free-radical ring expansion (rearrangement) has proven effective and when combined with a subsequent 5-*exo-dig* 5-hexynyl free radical cyclization provides a useful entry into the preparation of fused 5,6-, 5,7- and 5,8-bicyclic 1,4-diones.

(17) The potential of a reversible acyl radical-alkene addition reaction was experimentally addressed by subjecting **12** to standard free radical cyclization conditions (Bu_3SnH, catalytic AIBN, benzene, 80 °C) in the presence of 4 equiv of acrylonitrile. The lack of evidence for formation of **15** (the major product obtained by generation of the acyl radical derived from phenyl selenoester **14** under identical conditions) suggests that an equilibrating, reversible acyl radical-alkene addition reaction is not operative.



Acknowledgment. This work was assisted through the financial support of the National Institutes of Health (CA 42056).

Supplementary Material Available: Full details of the preparation and free-radical rearrangement-cyclization reactions of **6a-c** and **9** (8 pages). Ordering information is given on any current masthead page.

Linkage Position Determination in Oligosaccharides: MS/MS Study of Lithium-Cationized Carbohydrates

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Summary: Tandem mass spectrometry of the $[M + 2Li - H]^+$ ion of isomeric disaccharides is used to distinguish differences in the linkage position of the glycosidic bond. This technique can be applied to larger oligosaccharides with mixed linkages and still allow for correct determination of position and type of linkage.

Fast atom bombardment (FAB) combined with tandem mass spectrometry (MS/MS) has been shown to be useful for determining the sequence, and to a lesser extent, the pattern of branching of oligosaccharides.[1,2] The sequence-related fragment ions are produced from protonated molecular ions mainly by cleavage of the glycosidic bond with positive charge retained on either side of the molecule. Since the process of alkali metal ion attachment can strongly influence fragmentation of various organic molecules,[3,4] the fragmentation behavior of carbohydrates coordinated to lithium has been investigated in this study.

It is known that the alkali metal cationized species, compared to protonated molecular ions, undergo a larger number of structurally informative fragmentations of the sugar ring.[5] Our experiments with various oligosaccharides using collision-induced dissociation (CID) of lithiated molecular ions indicate that these structurally informative fragmentations can be greatly enhanced by using the dilithiated species, $[M + 2Li - H]^+$, as the precursor ion.[6] The CID spectra of dilithiated carbohydrates show predominantly fragmentations which are produced by ring cleavages of the sugar unit and provide important information for characterizing the glycosidic linkage position in oligosaccharides.

Figure 1 shows the CID spectra of the $[M + 2Li - H]^+$ of three isomeric disaccharides.[7] The differences among these isomers are quite obvious. The disaccharide with the 1→6 linkage shows characteristic ions at m/z 235, 265, and 295. However, the disaccharide with the 1→4 linkage shows the absence of m/z 265. All three of these ions are absent in the disaccharide possessing the 1→1 linkage. Although not shown here, the spectrum of the 1→3 isomer does not exhibit m/z 295 and the 1→2 isomer shows no m/z 265 (like the 1→4 isomer).[8] The latter isomer also produces an ion which is 18 units lower than the precursor ion and is absent in the spectra of all the other isomeric disaccharides.

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(2) Laine, R. A.; Pamidimukkala, K. M.; French, A. D.; Hall, R. W.; Abbas, S. A.; Jain, R. K.; Matta, K. L. *J. Am. Chem. Soc.* **1988**, *110*, 6931.
(3) Leary, J. A.; Williams, T. D.; Bott, G. *Rap. Commun. Mass Spec.* **1989**, *3*, 192.
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(6) CID spectra of the monolithiated disaccharides show large ion abundances from the nonreducing end with little differentiation between the various isomers of different linkages. The dilithiated spectra, however, show higher abundances of ions which characterize the linkage position and work from the reducing end back toward the nonreducing end. This applies as well to furanose moities at the reducing end (see the supplementary material).
(7) CID spectra were collected on a VG ZAB 2-EQ mass spectrometer of BEqQ geometry using argon as a collision gas at a cell pressure of 1×10^{-6} mbar and 40-110 eV collision energy (lab-frame of reference). The matrix used was 50:50 dithiothreitol:dithioerythritol with Li_2CO_3 as the source of lithium. All carbohydrates were purchased commercially, and no further purification steps were undertaken. Microgram quantities of the various sugars were diluted in 5 μL of Li_2CO_3/water and mixed with 5 μL of matrix.
(8) Both the 1→3 and the 1→2 compounds are also isomeric with the other three disaccharides shown in Figure 1.

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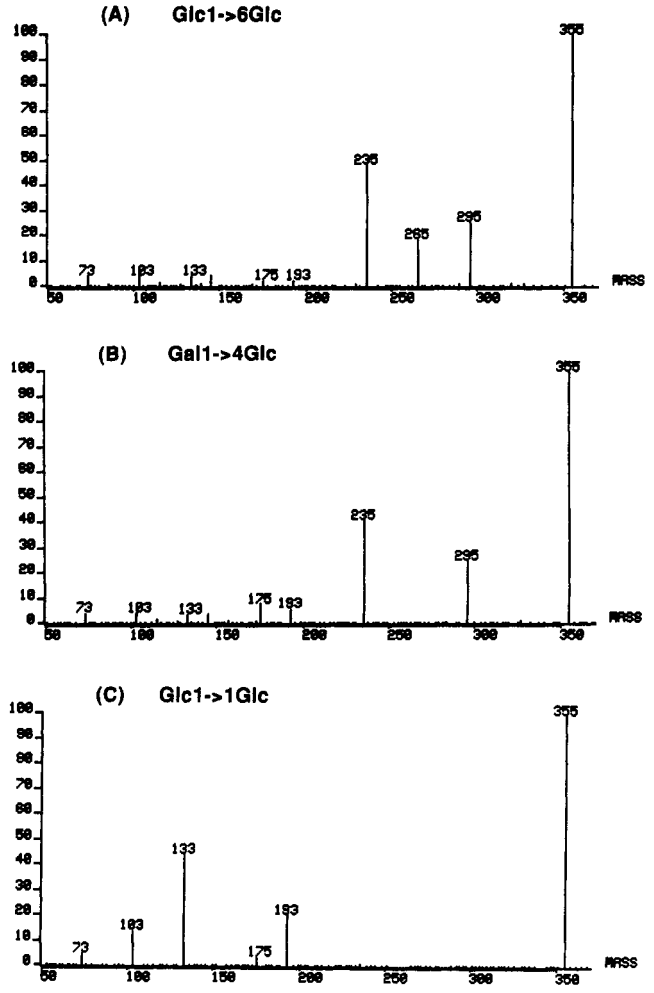
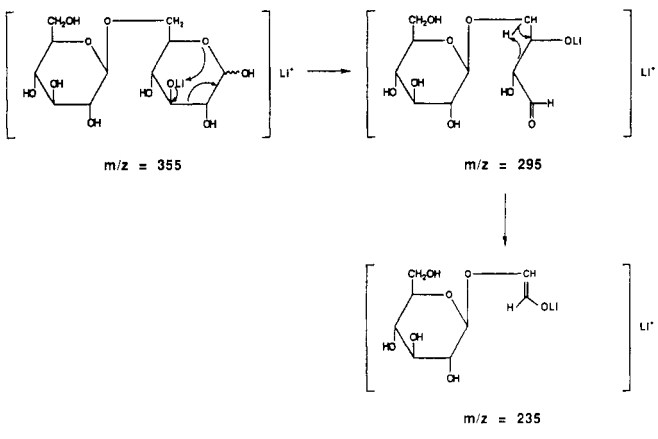


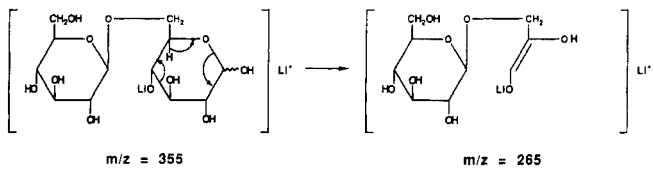
Figure 1. CID spectra of dilithiated molecular ions of (A) gentiobiose, (B) lactose, (C) trehalose.

The fragmentation mechanisms believed to be responsible for the ions observed in the spectrum of the 1→6 disaccharide are shown in pathways 1 and 2. The MS/MS experiment confirms that m/z 235 arises from m/z 355 via the first generation product ion m/z 295.[9] As shown in the mechanisms, it is proposed that replacement of hydrogen with lithium on one of the hydroxyl groups of the sugar ring is responsible for the ring cleavages. It is also interesting to note that the cleavages are analogous to major fragmentation pathways seen in the negative ion mode.[10] However, unlike the negative ion mode analysis, dilithiated oligomers of three and four rings only need to be run once to distinguish the different linkages from the reducing end to the first sugar ring.

Pathway 1:



Pathway 2:



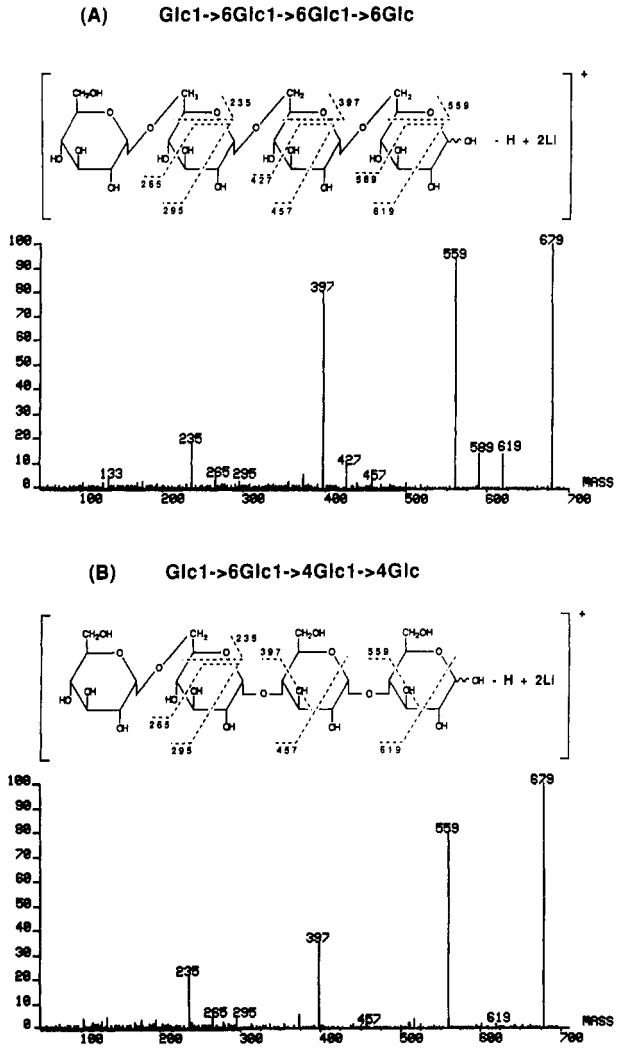


Figure 2. CID spectra of dilithiated molecular ions of (A) Glc1→6Glc1→6Glc1→6Glc, (B) Glc1→6Glc1→4Glc1→4Glc. The structure and the characteristic fragmentation are also shown for each compound.

This method was applied to two isomeric tetramers whose structures and CID spectra are shown in Figure 2. In Figure 2B one notices the absence of ions at m/z 589 and 427, thus indicating that the linkage position starting at the reducing end is 1→4, 1→4.[11] However, the presence of all three ions at m/z 235, 265, and 295 indicate that the third linkage position furthest from the reducing end is

(9) The ion at m/z 355 was transmitted into the MIKES cell where it underwent metastable decomposition. The first generation product ion m/z 295 was then selected and transmitted into the rf only quadrupole collision cell and underwent CID with argon at 1×10^{-6} mbar. The resulting second generation product ions were mass analyzed in the quadrupole mass analyzer.

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(11) Maltotetraose (1→4, 1→4, 1→4) also has very small intensity of the ions m/z 295, 457, and 619 but are definately present as determined from the peak widths of the raw data (see the supplementary material for comparison with isomaltotetraose.

1→6. Figure 2A contains all three characteristic ions for each linkage indicating a 1→6, 1→6, 1→6 pattern.

Investigations into using the dilithiated precursor as a method for determining linkage position in larger oligomers are currently underway. Semiempirical calculations on both mono- and dilithiated disaccharides and metastable decomposition studies are also underway in order to better access the position of lithium coordination to the molecule.

Supplementary Material Available: CID spectra of mono- and dilithiated species for the five isomeric disaccharides discussed as well as CID of mono- and dilithiated precursors for three trimers, two tetramers, and two trimers with furanose reducing ends (11 pages). Ordering information is given on any current masthead page.

The Olefination of Functionalized Alkylidenemalonates by 1,1-Dimetalloalkanes: A New Chemo- and Stereoselective Preparation of Functionalized Olefins

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Summary: The polyfunctional alkylidenemalonates **1**, readily prepared by an addition–elimination reaction of FG-RCu(CN)ZnI to [(phenylsulfonyl)methylidene]-malonates of type **7**, were found to undergo a highly chemoselective and stereoselective olefination reaction with 1,1-dimetalloalkanes of zinc and magnesium. An application to the stereospecific preparation of an insect pheromone **8** is reported.

The reaction of aldehydes and ketones with phosphorus reagents,[1] arsenic and tellurium ylides,[2] α-metalated boranes and silanes,[3] various 1,1-dimetallic reagents, and transition metal carbenes[4] has proven to be one of the best methods for the preparation of olefins. We report herein a new stereoselective olefination of polyfunctional alkylidenemalonates **1** by 1-magnesio-1-zincioalkanes of type **2** leading to functionalized olefins **3**. The reaction proceeds under very mild conditions (−78 °C to −20 °C, 10 min),[5] shows a remarkable chemoselectivity, and gives excellent yields (76–91%; Scheme I and Table I). It can be formulated as being a Michael addition affording a γ-metalated enolate **4**, followed by a fragmentation of **4** furnishing the olefin **3** and a magnesium and zinc dienolate **5**. The starting 1,1-dimetalloalkanes **2** are readily obtained by the allylzincation of alkenylmagnesium bromides[6] (THF, 0–35 °C, 40 min; >90% yield), whereas the polyfunctional alkylidenemalonates **1a–j** were prepared[5] in high yields by the addition of copper–zinc organometallics[7] RCu(CN)ZnI **6a–f,h** and $PhMe_2SiCu(CN)Li$ **6g**[8] to the new reagents[9] [(phenylsulfonyl)methylidene]malonates **7a–c** (THF, −78 °C to −30 °C, 1 h, 40–90%; Scheme II and Table II). The fast rate of the reaction allows the successful olefination of alkylidenemalonates having ester, nitrile, chloride, or thioether functionalities (Table I). Even a function highly susceptible to olefination reactions[1-4] such as an aromatic aldehyde survives our mild reaction conditions, demonstrating clearly the *exceptional chemoselectivity* of this reaction (entry 14 of Table I). Thus diethyl (4-formylbenzylidene)malonate **1k** furnishes the desired alkyliden-

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(5) **Typical Procedure: (a) Formation of Functionalized Alkylidenemalonates 1.** To a solution of 11 mmol of the copper reagent FG-R-Cu(CN)ZnI, prepared according to ref 7, in 11 mL of THF, cooled to −78 °C was added dropwise a solution of 10 mmol of [(phenylsulfonyl)methylidene]malonate **7** in 3 mL THF. The reaction mixture was allowed to warm to −30 °C and was stirred until completion (1–2 h). The reaction was then quenched by addition to 100 mL of saturated aqueous NH_4Cl, diluted with 100 mL of ether and worked up as usual. The residual crude product was purified by flash chromatography, yielding colorless oils in 40–90% yields. **(b) Formation of Functionalized Olefins 3.** To a solution of 12 mmol of the 1-magnesio-1-zincioalkane **2** (prepared according to ref 6e) cooled to −78 °C, was added dropwise a solution of 10 mmol of the functionalized alkylidenemalonate **1** in 3 mL of THF. The solution was then warmed quickly to −20 °C and stirred for 10 min. The reaction was quenched in 100 mL of a saturated aqueous NH_4Cl solution and diluted with 100 mL of ether. The resulting organic layer was then washed with 100 mL of aqueous NH_4Cl, washed with 100 mL of water, and dried over $MgSO_4$, and the solvents removed by evaporation. The residual oils were then purified by flash column chromatography giving the functionalized olefins of type **3** in 72–91% yields.

(6) (a) Gaudemar, M. *C. R. Sceances Acad. Sci. Ser. C* **1971**, *273*, 1669. (b) Frangin, Y.; Gaudemar, M. *C. R. Sceances Acad. Sci. Ser. C* **1974**, *278*, 885. (c) Bellassoued, M.; Frangin, Y.; Gaudemar, M. *Synthesis* **1977**, 205. (d) Knochel, P.; Xiao, C.; Yeh, M. C. P. *Tetrahedron Lett.* **1988**, *29*, 6697. (e) Knochel, P.; Yeh, M. C. P.; Xiao, C. *Organometallics* **1989**, *8*, 2831. See also ref 4b.

(7) For the preparation and some of the typical aspects of the reactivity of the reagents FG-RCu(CN)ZnI, see: (a) Knochel, P.; Yeh, M. C. P.; Berk, S. C.; Talbert, J. *J. Org. Chem.* **1988**, *53*, 2390. (b) Berk, S. C.; Knochel, P.; Yeh, M. C. P. *J. Org. Chem.* **1988**, *53*, 5789. (c) Yeh, M. C. P.; Knochel, P. *Tetrahedron Lett.* **1989**, *30*, 4799 and references cited therein.

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(9) [(Phenylsulfonyl)methylidene]malonates **7** have been prepared by the oxidation of the corresponding (*S*)-(phenylmethylidene)malonate (Husinec, S.; Porter, A. E. A.; Strachan, C. H. *Collect. Czech. Chem. Commun.* **1987**, *52*, 207) in 95% yield; MCPBA (2.3 equiv); CH_2Cl_2, 0 °C, 10 h (see the supplementary material). Diethyl (chloromethylidene)- and (ethoxymethylidene)malonate were found to be unreactive with RCu(CN)ZnI; compare with: Cahiez, G.; Alami, M. *Tetrahedron* **1989**, *45*, 4163.

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