(d, 1 H, indole 6-H, J_{6-7} = 8.1 Hz), 7.10 (dd, 1 H, indole 4-H), 7.25 (s, 1 H, indole 2-H), 7.30 (d + dd, 2 H, indole 7-H + vinyl α-H), 7.45 (d, 1 H, pyridine 5-H), 8.00 (d, 1 H, pyridine 6-H), 10.95 (s, 1 H, NH); IR (KBr) 3400, 3200, 2980, 2930, 2880, 1610, 1545, 1460, 1410 cm^{-1}; MS (30 eV) calcd for $C_{17}H_{15}FN_2$ (266.32), m/z (rel intensity) 267 (14.6), 266 (M^+, 64.1), 265 (11.0), 252 (19.3), 251 (100), 249 (15.1), 236 (18.8), 144 (15.6), 117 (60.1).

3-[1-[4-(1-Ethoxyethenyl)-2-fluoro-3-pyridyl]ethyl]indole (41). A mixture of (1-ethoxyvinyl)tributyltin (0.95 g, 3 mmol), bromo derivative **35** (1.2 g, 3.3 mmol), and tetrakis(triphenylphospine)palladium(0) (0.07 g, 0.06 mmol) in toluene (20 mL) was refluxed until precipitation of black palladium. Filtration and evaporation to dryness afforded a crude solid, which was crystallized from diethyl ether/hexane (1.1) to yield 95% of **41**: mp >250 °C; ^1H NMR ($CDCl_3$) δ 1.40 (t, 3 H, ethyl CH_3), 1.70 (d, 3 H, CH_3), 3.97 (q, 2 H, CH_2), 4.45 (d, 1 H, vinyl β-H, $J_{\beta-\beta}$ = 2.5 Hz), 4.55 (q, 1 H, CHMe, J = 7 Hz, 4.65 (d, 1 H, vinyl β-H), 6.80 (dd, 1 H, indole 5-H, J_{4-5} = 7.9 Hz, J_{5-6} = 7.3 Hz), 7.00 (dd, 1 H, indole 6-H), 7.10 (d, 1 H, indole 4-H), 7.25 (s + d, 2 H, indole 2-H + pyridine 5-H), 7.30 (d, 1 H, indole 7-H, J_{6-7} = 8 Hz), 8.05 (d, 1 H, pyridine 6-H), 10.65 (s, 1 H, NH); IR (KBr) 3230, 3100, 3050, 3040, 2970, 2930, 1630, 1600, 1550, 1460, 1435, 1410 cm^{-1}; MS (30 eV) calcd for $C_{19}H_{19}FN_2O$ (310.38), m/z (rel intensity) 310 (58.4), 281 (69.8), 264 (100), 249 (56.9), 239 (22.5).

5,11-Dimethyl-1-fluoro-6*H*-pyrido[4,3-*b*]carbazole (42). Ethoxyvinyl derivative **41** (0.5 g, 1.6 mmol) was dissolved in a 1/1 mixture of acetic acid and acetic anhydride (20 mL). A 1/1 solution of aqueous concentrated hydrochloric acid in THF was slowly added under stirring until formation of a white precipitate. The resulting suspension was further stirred at room temperature for 30 min before addition of water in a sufficient amount to dissolve the solid. Neutralization by sodium carbonate, extraction by diethyl ether, drying of the organic extracts over $MgSO_4$, evaporation to dryness, and sublimation (200 °C/1 mmHg) afforded **42** in 54% yield: mp >250 °C; ^1H NMR (DMSO-d_6) δ 2.80 (s, 3 H, Me_5), 3.30 (d, 3 H, Me_{11}, J_{H-F} = 4 Hz), 7.30 (dd, 1 H, 9-H), 7.55 (dd, 1 H, 8-H, J_{7-8} = 8.1 Hz), J_{8-9} = 7.1 Hz), 7.60 (d, 1 H, 7-H), 7.85 (dd, 1 H, 4-H, J_{3-4} = 6.05 Hz, J_{4-F} = 1.3 Hz), 7.95 (dd, 1 H, 3-H, J_{3-F} = 2.1 Hz), 8.40 (d, 1 H, 10-H), 11.70 (s, 1 H, NH); IR (KBr) 3430, 3240, 3180, 3100, 1605, 1470, 1405 cm^{-1}; MS (30 eV) calcd for $C_{17}H_{13}FN_2$ (264.30), m/z (rel intensity) 265 (19.8), 264 (M^+, 100), 263 (29.9), 249 (23.5). Anal. Calcd for $C_{17}H_{13}FN_2$ (264.30): C, 77.57; H, 4.94; N, 10.65. Found: C, 77.6; H, 4.81; N, 10.4.

Registry No. **1**, 372-48-5; **2**, 36178-05-9; **3**, 128071-98-7; **4**, 137718-84-4; **5**, 137718-85-5; **6**, 111887-72-0; **7**, 137718-86-6; **8**, 137718-87-7; **9**, 137718-88-8; **10**, 137718-89-9; **11**, 137718-90-2; **12**, 137718-91-3; **13**, 137718-92-4; **14**, 137718-93-5; **15**, 137718-94-6; **16**, 137718-95-7; **17**, 79574-70-2; **18**, 137718-96-8; **19**, 137718-97-9; **20**, 137718-98-0; **21**, 137718-99-1; **22**, 137742-03-1; **23**, 137719-00-7; **24**, 40247-45-8; **25**, 137719-01-8; **26**, 137719-02-9; **27**, 137719-03-0; **27'**, 137719-04-1; **28**, 137719-05-2; **29**, 52200-48-3; **30**, 137719-06-3; **31**, 137719-07-4; **32**, 137719-08-5; **33**, 137719-09-6; **34**, 137719-10-9; **35**, 137719-11-0; **36**, 137719-12-1; **37**, 137719-13-2; **38**, 137741-91-4; **39**, 137719-14-3; **40**, 137719-15-4; **41**, 137719-16-5; **42**, 137719-17-6; HCO_2Et, 109-94-4; PhCHO, 100-52-7; MeCHO, 75-07-0; TMSC≡CH, 1066-54-2; CH_2=CHSnBu_3, 7486-35-3; CH_2=C(OEt)SnBu_3, 97674-02-7; *N*-(phenylsulfonyl)-3-indolecarbaldehyde, 80360-20-9; indole, 127-72-0.

Radical Cyclization Routes to Bridged Pyranosides as Precursors of Densely Functionalized Cycloalkanes[1]

R. A. Alonso,[2] G. D. Vite,[3] R. E. McDevitt, and B. Fraser-Reid*

Paul M. Gross Chemical Laboratory, Department of Chemistry, Duke University, Durham, North Carolina 27706

Received July 16, 1991

Glycals derived from hexopyranoses permit the incorporation of iodine at C-2 as well as elaboration of an olefinic residue via the C-5-hydroxymethyl group. Radical cyclization of these functionalities leads to bicyclic systems whose bridge sizes depend on the lengths of the olefinic appendages. Hydrolysis of the anomeric centers of the [2.2.1] structures leads spontaneously to cyclopentane derivatives. However, with [2.2.2] structures, the hemiacetal intermediates are stable in bicyclic forms but are opened readily upon mcerpatolysis with propane dithiol to give cyclohexane derivatives.

Introduction

In our continuing interest in the development of strategies for carbohydrate → carbocycle transformations,[4] radical cyclization methods have proved valuable as demonstrated by recent syntheses of phyllantocin,[5] pipitzol,[6] and silphiperfolene.[7] In all of these cases the strategy can be symbolized as shown in Scheme Ia, where functionalized branches were installed on a sugar precursor from which the key intermediate I could be generated. Cyclization then led to an annulated sugar, symbolized by II, which could be reduced, or react further in a serial episode.

Notably, the radical center in I is pendant to, rather than directly on, the sugar ring. However, the seminal work of Barton and McCombie on generating carbon-centered radicals on the pyranose ring,[8] coupled with the elegant studies of Giese and co-workers on conformational aspects of pyranosyl radicals,[9] have prompted us to investigate these systems further. For example, the powerful influence

(1) This project was supported by grants from NIH GM 37380 and GM 32569.

(2) R.A.A. gratefully acknowledges a fellowship from the Conselleria de Educación e Ordenación Universitaria (Xunta de Galicia, Spain) and from the Ministerio de Educación y Ciencia. Present address: Universidad de Santiago de Compostela, Departamento de Química Orgânica, 15706 Santiago de Compostela, Spain.

(3) Present address: Bristol-Myers Squibb Institute Pharmaceutical Research Institute, P.O. Box 4000, Princeton, NJ 08543-4000.

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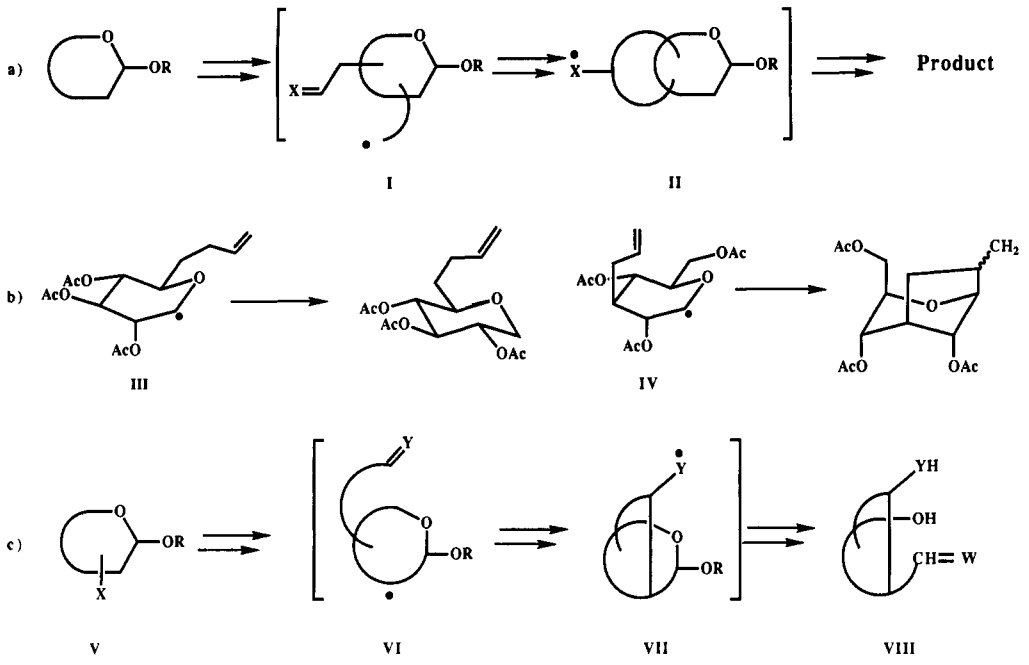
(9) (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, 969.

0022-3263/92/1957-0573$03.00/0

Scheme I

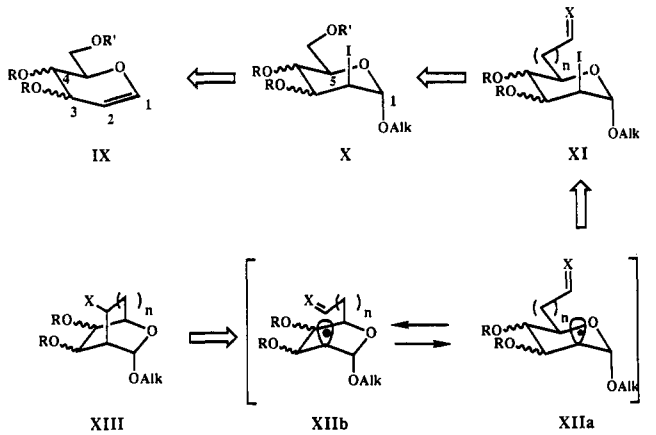


of conformations is dramatized by the difference in reactions of the glycosyl radicals III and IV (Scheme Ib), both of which exist as $B_{2,5}$ boat structures.[10] Thus, the olefin-bearing branch in the latter more easily adopts the axial orientation necessary for cyclization. These results are in keeping with the studies of Eliel and co-workers which show that the *A* value for alkyl substituents at C-5 is greater than that for other sites on the pyranose ring.[11]

Strategies for radical carbohydrate → carbocycle transformations have come recently from the laboratories of Wilcox,[12] RajanBabu,[13] and Bartlett.[14] However, an essential aim of our carbohydrate → carbocycle studies has been the optimal use of the glycosidic center as an NMR reference point, a stereocontrolling device via the anomeric effect, and as a versatile synthon.[4-7] Accordingly, we were interested in examining substrates, exemplified by VI (Scheme Ic), where the cyclization process does not involve the anomeric center. The resulting product would be the bridged bicyclic annulated pyranoside VII, where the size of the carbocylic ring would be controllable by the length of the olefin-bearing appendage. Subsequent reduction and hydrolysis of VII would then lead to VIII whose C-1 functional group is present as a (protected) aldehyde and ready for further elaboration.

The idea in Scheme Ic is developed more specifically in Scheme II. Attractive precursors for these investigations were the 2-deoxy-2-iodohexopyranosides XI.[15,16] The extensive work of Thiem[17] has shown that such *trans*-1,2-glycosides can be obtained with high stereochemical purity from commercially available glycals such as IX. The C-5 hydroxymethyl group would then become the implement for elaboration of the olefinic appendage as shown in XI.

Scheme II



For the cyclization to be successful conformational change, XIIa → XIIb, would be needed. However, the failure of III to cyclize had been attributed to the difficulty of such conformational changes (vide supra). Would XIIa be affected similarly? By varying the configurations and protecting groups at C-3 and C-4 of IX, we would be able to examine the effects upon the success of the cyclization. By changing the length of the pendant olefin in XI (n = 0, 1, 2, etc.) we would be able to assess the effect of the developing ring strain in the bicyclic product XIII.

In this manuscript we describe our recent work investigating the strategy outlined in Scheme II, which is geared to the synthesis of densely functionalized cyclopentane and cyclohexane derivatives.[15]

Results and Discussion

Synthesis of Precursors (Scheme III). The precursors were prepared from D-glucal **1a** and D-galactal **16a**,

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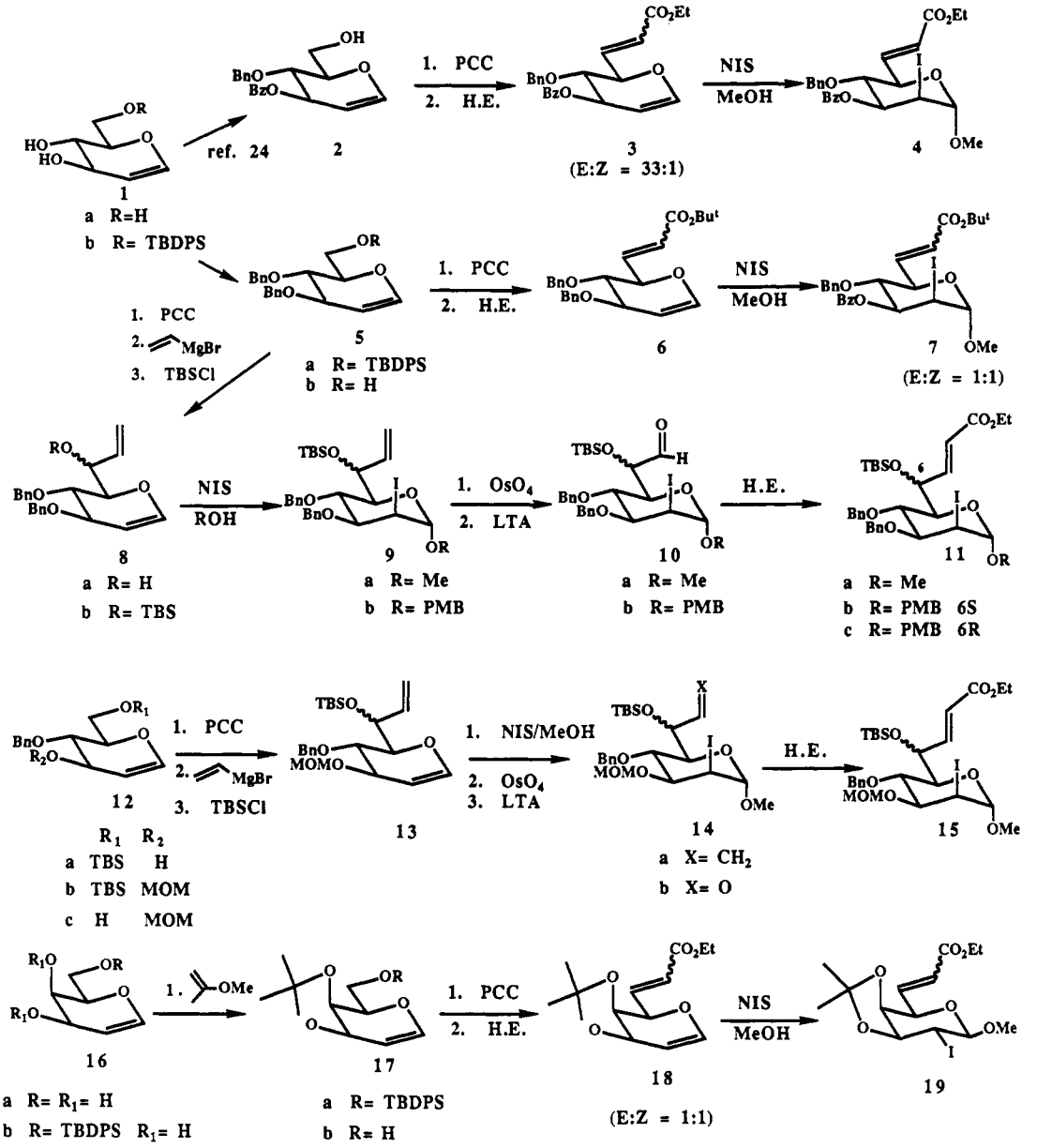
(14) Bartlett, P. A.; McLaren, K. L.; Ting, P. C. *J. Am. Chem. Soc.* **1988**, *110*, 1638.
(15) For a preliminary account of this work see: Vite, G. D.; Alonso, R. A.; Fraser-Reid, B. *J. Org. Chem.* **1989**, *54*, 2268.
(16) In the course of this study, two reports have appeared using this methodology for the generation of the radical precursor at C-2: Audin, C.; Lancelin, J.-M.; Beau, J.-M. *Tetrahedron Lett.* **1988**, *29*, 3691. Mesmacker, A. D.; Hoffmann, P.; Ernst, B. *Tetrahedron Lett.* **1989**, *30*, 57.
(17) (a) Thiem, J.; Karl, H. *Tetrahedron Lett.* **1978**, 4999. (b) Thiem, J.; Karl, H.; Schwentner, J. *Synthesis* **1978**, 696.

Scheme III



readily obtained by deacetylation[18] of the commercially available tri-*O*-acetyl derivatives. The routine transformations are shown in the Scheme III, the details of which are given in the Experimental Section. In all cases the hydroxymethyl group was oxidized to an aldehyde, the subsequent processing being dependent on the desired length of the olefin-bearing appendage, or more precisely on the size of the required carbocyclic product (See Schemes IV–VII). For cyclopentane products, the olefination was carried out by a Horner–Emmons process, some variation in the *E*/*Z* ratio of the olefinic products being achieved by changing the reagent[19] as well as the reaction conditions.[20]

The iodoalkoxylation reaction[17] in all cases gave one of the two possible 1,2-trans adducts overwhelmingly. Thus, in the glucal precursors **3**, **6**, **8b**, and **13**, the 2-deoxy-2-iodo glycosides obtained were all of the α-D-manno configuration. However, for the galactal precursor **18**, the product was the β-D-galactoside **19**. Although NIS glycosidation usually affords α-glycosides, an exception has been reported from Thiem's laboratory[21] for 3,4-*O*-isopropylidene galactal derivatives. The availability of **19** provided us with an opportunity to test whether the relative orientations at C-1 and C-5 (e.g., in **4** versus **19**) had an effect on the success of the intramolecular cyclization.

Free-Radical Cyclizations. The radical cyclizations were carried out by treatment of the precursors with tri-*n*-butyltin hydride and a catalytic amount of AIBN in refluxing toluene over 2–4 h. The oxabicyclic products were obtained in good to excellent yields.

Formation of 2-Oxabicyclo[2.2.1]heptanes (Scheme IV). The initial experiments were carried out with the 2-deoxy-2-iodopyranoside (*E*)-**4**, the bicyclic compounds **20a** and **21a** being obtained as a 1.8:1 isomeric mixture in 91% isolated yield. The products were easily separated by flash chromatography and crystallized readily. Their C-7 configurations were assigned on the basis of NOE experiments. In each case, irradiation of the more shielded

(18) (a) Roth, W.; Pigman, W. *Methods Carbohyd. Chem.* **1963**, *2*, 405. (b) Paquette, L.; Oplinger, J. A. *J. Org. Chem.* **1988**, *23*, 2953.
(19) Griffiths, G. F.; Kenner, G. W.; McCombie, S. W.; Smith, K. M.; Sutton, M. J. *Tetrahedron* **1976**, *32*, 275.
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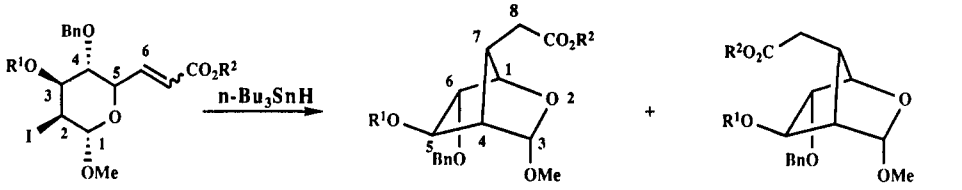
(21) Thiem, J.; Meyer, B. *Chem. Ber.* **1980**, *113*, 3067.

Scheme IV

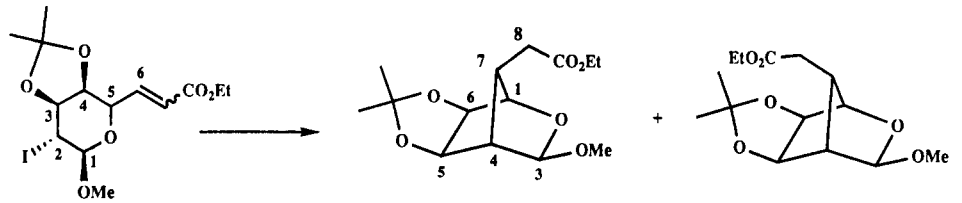


4 R^1= Bz, R^2= Et
7 R^1= Bn, R^2= t-Bu

20a R^1= Bz, R^2= Et
20b R^1= Bn, R^2= t-Bu

21a R^1= Bz, R^2= Et
21b R^1= Bn, R^2= t-Bu

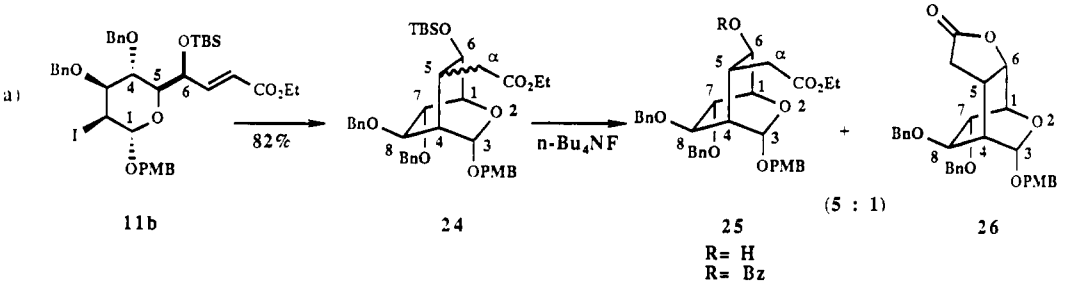
E-4 ⟶ 20a : 21a (1.8 : 1) (91%)
E-7 ⟶ 20b : 21b (4.5 : 1) (80%)
Z-7 ⟶ 20b : 21b (5.5 : 1) (80%)



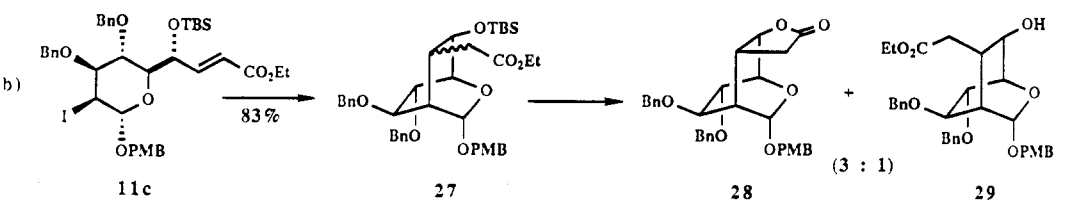
19 22 23

E-19 ⟶ 22 : 23 (8:1) (98%)
Z-19 ⟶ 22 (97%)

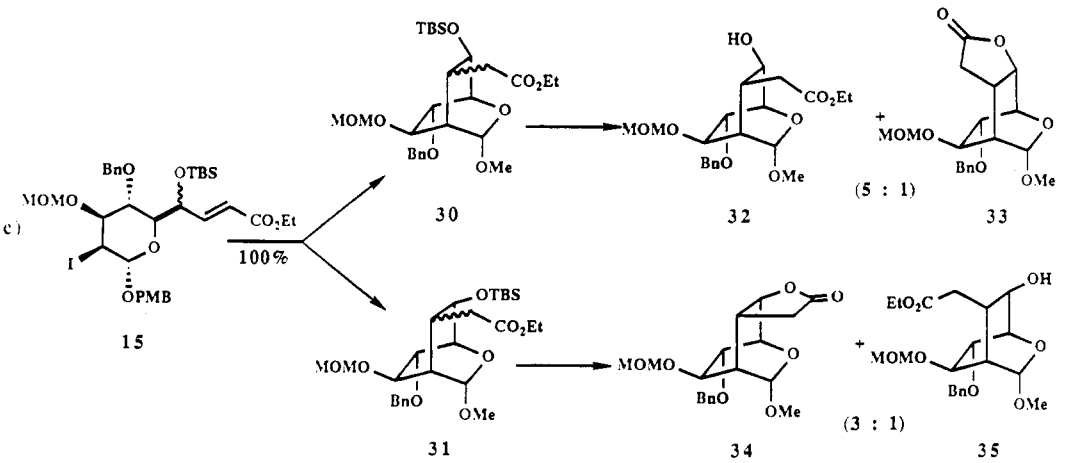
Scheme V



11b 24 25 (R= H, R= Bz) 26 (5 : 1)

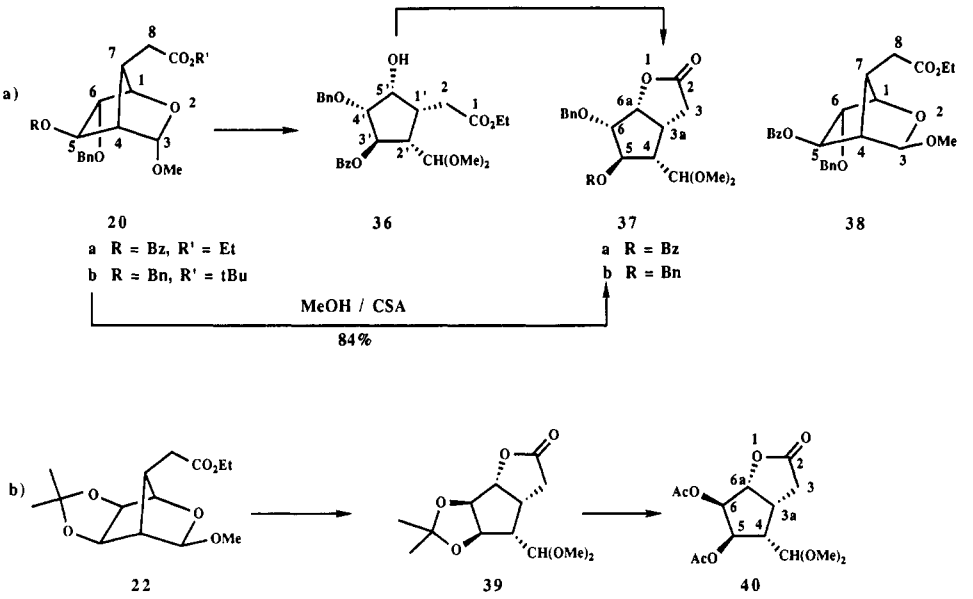


11c 27 28 29 (3 : 1)

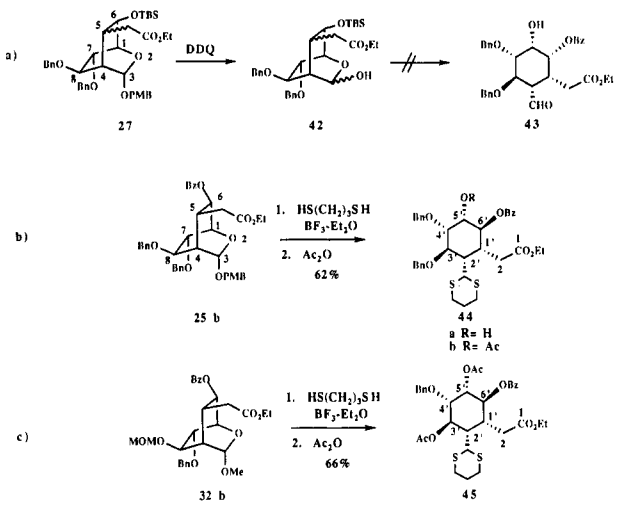


15 30 31 32 34 33 35 (5 : 1) (3 : 1)

Scheme VI



Scheme VII



of the two H-8 protons resulted in enhancement of the signal due to H-3 in the major epimer and H-6 in the minor. This indicated that the major isomer must have the structure **20a** in which the ester group lay on the less crowded side of the bicyclic structure.

We wished to assess the effect of olefinic geometry and size of the ester group on the stereochemical course of the cyclization. For this purpose we prepared the corresponding *tert*-butyl esters, (*E*)-**7** and (*Z*)-**7**. An increase in the stereoselectivity as compared with the above described ethyl ester was observed. With (*E*)-**7**, the bicyclic compounds **20b** and **21b** were obtained in 4.5:1 ratio, and with (*Z*)-**7** the ratio was changed only slightly being 5.5:1 (Scheme IV). It therefore appears that olefinic geometry does not have a profound effect on product formation. On the other hand, the results from (*E*)-**4** versus (*E*)-**7** suggest that the size of the ester derivative has a marked influence on the stereoselectivity of cyclization.

A similar, although more pronounced, trend was found in the cyclization of the galactal derivatives (*E*)-**19** and (*Z*)-**19**. In this case, the trans α,β-unsaturated ester, (*E*)-**19**, afforded a mixture of the oxabicycles **22** and **23** in 98% isolated yield and in an 8:1 ratio, as determined by GCMS (Scheme IV). With the cis isomer (*Z*)-**19**, only the bicyclic compound **22** (97% isolated yield) was obtained on the basis of GCMS and ^{13}C NMR evidence.

Comparison of the results with (*Z*)-**7** and (*Z*)-**19** in Scheme IV reveals the profound effect of the C-4 configuration of the substrate. In both cases the major products **20b** and **22**, respectively, have 7*R* configurations, and it is obvious from Scheme IV that the alternative 7*S* structures, **21b** and **23**, are more congested. This is consistent with the fact that the C-4 substituent on the β-face of the substrate as in **19** causes more congestion as compared to the α-orientation in the gluco derivative **7**.

However, it also appears from the results that the transition state which leads to **23** is more congested in the case of (*Z*)-**19** than with (*E*)-**19**.

Formation of 2-Oxabicyclo[2.2.2]octanes (Scheme V). We first examined the C-6 epimeric mixture of the methyl glycoside **11a** shown in Scheme III, and although radical cyclization proceeded in 85% yield, the rich mixture of 2-oxabicyclo[2.2.2]octyl isomers made it difficult to assess the effect of the configuration at C-6 upon the stereochemical outcome of cyclization.

Fortunately, the C-6 epimers of the *p*-methoxybenzyl glycosides **11b** and **11c** (Scheme V) were readily separated by flash chromatography, their configurations being assigned on the basis of the cyclization products to which they gave rise as described below. Thus, cyclization of the L-glycero ((C-6(*S*)) epimer **11b** resulted in an 82% yield of bicyclic compound **24** as a 5:1 mixture of stereoisomers which could not be separated by flash chromatography. However, cleavage of the silyl ether led to the readily separated hydroxyester **25a** and lactone **26**, the former being the major component (Scheme Va).

Likewise, cyclization of the D-glycero ((C-6(*R*)) epimer **11c** afforded the oxabicyclic system **27** in 83% yield as a 3:1 mixture of stereoisomers. Analogous desilylation gave the separable lactone **28** and hydroxy ester **29**. In this case, the lactone **28** was the major component (Scheme Vb).

As with the [2.2.1] systems described above, NOE experiments were used to deduce the relationship between the ester side chain and H-3 in the hydroxy esters **25a** and **29** and by corollary the configurations at C-5 in all related products. Thus, it was on the basis of these results that the configurations at C-6 of **11b** and **11c**, respectively, were assigned.

The above protocol was applied for studying the course of cyclization of the C-3 methoxymethylated analogue **15**.

Cyclization proceeded in quantitative yield (Scheme Vc), and the two sets of C-5 epimers **30** and **31**, produced in 7:1 ratio, were isolated by flash chromatography. Desilylation of **30** afforded hydroxy ester **32a** and lactone **33** in 5:1 ratio, while similar reaction of **31** gave lactone **34** and hydroxy ester **35** in 3:1 ratio.

The results leading to 2-oxabicyclo[2.2.2]octanes demonstrated clearly that the cyclization reaction is a high-yielding process that can tolerate a wide range of protecting groups. The results in Scheme V indicate that the configuration at C-6 of the precursor does NOT dramatically affect the stereochemistry of the cyclization, since in both cases the major product (**25a**, **28**, **32a**, or **34**) has the same configuration at C-5. Thus, a highly stereoselective preparation of either of the C-6 isomers of **11** or **15** would be advantageous for obtaining these major products in high yield.

Opening of the Bicyclic Compounds. Functionalized Cyclopentanes (Scheme VI). Cleavage of the pyranoside rings in the 2-oxabicyclo[2.2.1]heptanes to give the corresponding cyclopentanes succeeded under extremely mild conditions which is indicative of the inherent strain energy present in these systems. Thus, treatment of **20a** with methanol and pyridinium *p*-toluenesulfonate (PPTS)[22] at room temperature for 56 h afforded the hydroxy ester **36** (39%) and the corresponding lactone **37a** (45%), as well as the C-3 epimer **38** (8%).

Compound **36** was slowly converted into **37a** on standing. However, use of methanol and camphorsulfonic acid (CSA) led directly to lactone **37a** (95%) in a shorter period of time. Thus, the latter procedure is usually preferable since lactonization occurred quickly after opening of the bicyclic systems, and the isolated yields of the final lactones were always higher. Thus, by use of the latter procedure, **20b** was converted into lactone **37b** in 84% yield.

In the case of bicyclic compound **22**, treatment with CSA and methanol gave lactone **39** as an isolable intermediate. However, prolonged treatment followed by acetylation and chromatography afforded lactone **40** in 88% yield.

2-Oxabicyclo[2.2.1]octanes. (Scheme VII). The mild, acid-catalyzed methanolysis used for the 2-oxabicyclo-[2.2.1]heptyl systems (vide supra) was not successful with the 2-oxabicyclo[2.2.2]octyl analogues, and attempts to force the reaction by the use of mineral acids resulted in the formation of complex mixtures.

It was the failure of these solvolytic procedures with the methyl glycosides (e.g., **32–35**, Scheme V) that prompted us to prepare the *p*-methoxybenzyl (PMB) analogs. It was hoped that removal of the PMB protecting group under mild, neutral, oxidative conditions would lead to a hemiacetal that would open spontaneously to give the cyclohexane derivative—as had occurred with the corresponding cyclopentanes in Scheme VI. However, treatment of **27** (Scheme VIIa) with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) gave the lactol **42** which did not open to give **43** and resisted all attempts at transformation into a useful cyclohexane derivative.

Nevertheless, a suitable method was found that permitted ring opening of these substrates (Scheme VIIb and c). Thus, treatment of **25b** with 1,3-propanedithiol and boron trifluoride etherate afforded the cyclohexane derivative which was characterized as its acetate **44b**. Likewise, ring opening of **32b** under similar conditions, followed by direct acetylation of the product, afforded the diacetoxycyclohexane **45** in 66% yield, the methoxymethyl ether protecting group having been cleaved under the ring-opening conditions.

(22) Miyashita, N.; Yoshiokoshi, A.; Grieco, P. A. *J. Org. Chem.* 1977, *42*, 3773.

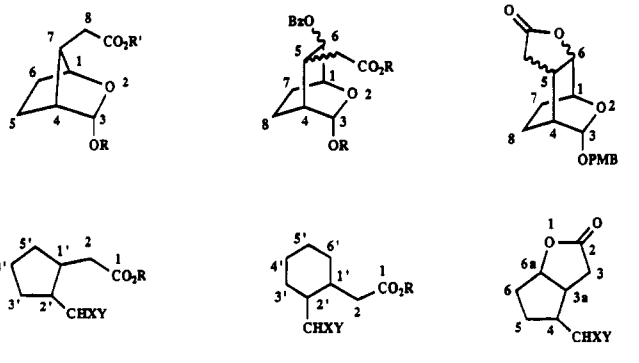
Conclusion

In summary, a new methodology for the formation of highly functionalized cyclopentanes and cyclohexanes, based on the intramolecular radical cyclizations of 2-deoxy-2-iodopyranoside derivatives, has been developed, the precursors being readily prepared from commercially available glycals. Iodide is an excellent radical progenitor and is stereoselectively introduced at C-2 by the well-established NIS-induced glycosidation procedure. α,β-Unsaturated carboxylic esters and other radical traps are readily incorporated via aldehydes derived from the C-5 hydroxymethyl group.

Radical cyclization to give 2-oxabicyclo[2.2.1]heptanes and 2-oxabicyclo[2.2.2]octanes proceed in excellent to quantitative yields in all cases, and good levels of stereoselectivity in the cyclization process can be achieved by selecting appropriate precursors, as demonstrated for the galactal derivative (*Z*)-**19**, where only the compound **22** was isolated in 97% yield.

Experimental Section

Tri-*O*-acetyl-D-glucal and D-galactal were purchased from commercial suppliers and used without further purification. All the reactions were performed under argon atmosphere and monitored by TLC using precoated silica gel aluminum plates containing a fluorescent indicator (5539, Merck). Anhydrous $MgSO_4$ or Na_2SO_4 were used to dry the organic solutions during workups, and the removal of the solvents was done under vacuum with a rotavapor. Flash column chromatography was performed using Kiessegel 60 (230–400 mesh, Merck) and mixtures of ethyl acetate–petroleum ether (EtOAc–PE) as eluant. Melting points were determined in capillary tubes and are uncorrected. Optical rotations were determined at the sodium D line. ^1H and ^{13}C NMR spectra were recorded with a Varian XL-300 (operating at 300.0 and 75 MHz) spectrometer, using tetramethylsilane (TMS) or $CDCl_3$ as internal standards and $CDCl_3$ as the solvent. Chemical shifts are reported in δ values, and coupling constants (J, Hz) where specifically assigned, were determined by double irradiation experiments. Chemical ionization mass spectroscopy was done with 10% NH_3 in methane with a source temperature of 150 °C. High-resolution mass spectra were recorded using NH_3 as the reagent gas and PFK for calibration.



Standard Procedures. Pyridinium Chlorochromate (PCC) Oxidations. A solution of the alcohol (0.5 mM) in dry CH_2Cl_2 (5 mL) was added dropwise via syringe over a suspension of powdered 4-Å molecular sieves (980 mg), which had been flame dried under vacuum, and PCC (0.5 g 2.5 mM, 5 equiv) in CH_2Cl_2 (15 mL) with good stirring under argon. When all of the starting material was consumed (TLC) diethyl ether (100 mL) was added and the resulting suspension was filtered through Florisil. Evaporation of the solvent afforded the crude aldehyde **5c**, aliquots of which were used for the next step without further purification.

Horner–Emmons Reactions. Triethyl phosphonoacetate (38 μL, 0.2 mM, 1.2 equiv) was added over a suspension of NaH (60%

suspension in mineral oil, 8.7 mg, 0.22 mM, 1.3 equiv) in dry THF (1.5 mL) at 0 °C. After 15 min, the reaction mixture was cooled to −78 °C (dry ice–acetone bath) and a solution of the crude aldehyde (0.17 mM) in dry THF (1 mL) was added via syringe. After completion of the reaction, the mixture was warmed to room temperature, a cold aqueous solution of NH_4Cl was added, and the THF was evaporated under reduced pressure. Extraction with diethyl ether, drying with $MgSO_4$, evaporation of the solvents, and filtration through silica gel gave the desired olefinic ester as a mixture of *E*/*Z* geometric isomers.

Iodoalkyloxylation of Glycals.[17] *N*-Iodosuccinimide (45 mg, 0.20 mM, 1.5 equiv) was added to a cooled (NaCl–ice bath) solution of the glycal (0.13 mM) and to the alcohol (0.54 mM, 4 equiv) in dry CH_3CN (1 mL). The reaction mixture was warmed to room temperature and monitored by ^1H NMR until the H-1 resonance at ~6.6 ppm had disappeared (~6 h). Diethyl ether was added, the solution was washed with 8% aqueous sodium metabisulfite and brine and dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. Flash chromatography then afforded the pure product.

Cleavage of Silyl Ethers. To an ice-cooled solution of the silyl ether (3.0 mM) in THF (10 mL) was added tetrabutylammonium fluoride (1.1 M solution in THF, 1.05 equiv) dropwise via syringe. After the mixture was stirred overnight at room temperature, an ice-cooled aqueous solution of ammonium chloride was added. The THF was evaporated, the aqueous phase was extracted with diethyl ether, and silica gel filtration afforded the corresponding alcohol.

Synthesis of Precursors (Scheme III). General Procedure for Radical Cyclization of the 2-Deoxy-2-iodo Substrates. A 5 mM solution of the iodide in dry toluene was degassed with argon and heated to reflux. Tri-*n*-butyltin hydride (1.3–1.5 equiv) and AIBN (10%) in toluene were added via syringe pump over 2–4 h. The solvent was evaporated under reduced pressure and the bicyclic products were isolated by flash chromatography (silica gel, EtOAc–PE mixtures). In some cases, the residue obtained after evaporation was stirred overnight with a diethyl ether–10% aqueous KF mixture,[23] prior to flash chromatography.

Ethyl 3-*O*-Benzoyl-4-*O*-benzyl-1,3,6,7-tetradeoxy-D-*arabino*-octa-1,6-dieno-1,5-pyranose Uronates (*E*)-3 and (*Z*)-3. A solution of alcohol **2**[24] (440 mg 1.3 mM) in dry CH_2Cl_2 (5 mL) was subjected to the Standard Procedures for PCC oxidation followed by the Horner–Emmons reaction to afford the ethyl ester **3** (480 mg, 90%) as a 33:1 *E*/*Z* mixture. The cis isomer (*Z*)-**3**, had slightly higher R_f (silica gel, 10% EtOAc–PE) and could be isolated. (*E*)-**3**: ^1H NMR δ 1.28 (t, *J* = 7.1, 3 H, CH_2CH_3), 3.84 (dd, $J_{4,3} \cong J_{4,5} \cong 4.5$, 1 H, H-4), 4.21 (t, *J* = 7.1, 2 H, CH_2CH_3), 4.74 (ABq, *J* = 11.8, Δδ = 0.08, 2 H, $ArCH_2$), 4.79 (m, 1 H, H-5), 5.02 (dd, $J_{2,1}$ = 6.1, $J_{2,3}$ = 4.0, 1 H, H-2), 5.60 (dd, $J_{3,2} \cong J_{3,4} \cong$ 4, 1 H, H-3), 6.11 (dd, $J_{7,6}$ = 15.8, $J_{7,5}$ = 1.9, 1 H, H-7), 6.58 (d, $J_{1,2}$ = 6.1, 1 H, H-1), 7.09 (dd, $J_{6,7}$ = 15.8, $J_{6,5}$ = 4.8, 1 H, H-6), 7.2–7.7 (m, 8 H, ArH), 7.9–8.1 (m, 2 H, ArH); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = −42.9° (*c* 0.94, $CHCl_3$); LRMS (CI/NH_3) *m*/*z* 426 (M + NH_4)$^+$. Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.58; H, 5.92. Found: C, 70.38; H, 5.89. (*Z*)-**3**: 1.27 (t, *J* = 7.1, 3 H, CH_2CH_3), 4.04 (m, 1 H, H-4), 4.16 (q, *J* = 7.1, 2 H, CH_2CH_3), 4.87 (ABq, *J* = 12.0, Δδ = 0.07, 2 H, $ArCH_2$), 5.13 (ddd, $J_{2,3} \cong J_{2,1} \cong 7$, $J_{2,4}$ = 1.5, 1 H, H-2), 5.37 (m, 1 H, H-3), 5.94 (dd, $J_{7,6}$ = 11.7, $J_{7,5}$ = 1.8, 1 H, H-7), 6.04 (m, 1 H, H-5), 6.45 (dd, $J_{6,7}$ = 11.7, $J_{6,5}$ = 7.6, 1 H, H-6), 6.60 (d, $J_{1,2}$ = 7.4, 1 H, H-1), 7.2–7.6 (m, 8 H, ArH), 7.9–8.0 (m, 2 H, ArH). Anal. Calcd for $C_{24}H_{24}O_6$: C, 70.58; H, 5.92. Found: C, 70.63; H, 5.89.

Ethyl (Methyl 3-*O*-benzoyl-4-*O*-benzyl-2,6,7-trideoxy-2-iodo-α-D-*manno*-oct-6(*E*)-eno-1,5-pyranosid)uronate (4). The glycal (*E*)-**3** (55 mg, 0.13 mM) was iodomethoxylated under the Standard Procedures, which afforded pure **4** (51 mg, 67%) as a colorless oil: ^1H NMR δ 1.32 (t, *J* = 7.1, 3 H, CH_2CH_3), 3.40 (s, 3 H, CH_3O), 3.84 (dd, $J_{4,3} \cong J_{4,5} \cong 9$, 1 H, H-4), 4.23 (q, *J* = 7.1, 2 H, CH_2CH_3), 4.46 (ddd, $J_{5,4}$ = 9.6, $J_{5,6}$ = 4.6, $J_{5,7}$ = 1.7, 1 H, H-5), 4.64 (ABq, *J* = 10.7, Δδ = 0.09, 2 H, $ArCH_2$), 4.66 (dd, $J_{2,1}$ = 1.5, $J_{2,3}$ = 4.3, 1 H, H-2), 4.97 (dd, $J_{3,4}$ = 8.8, $J_{3,2}$ = 4.3, 1 H, H-3), 5.11 (br s, 1 H, H-1), 6.25 (dd, $J_{7,6}$ = 15.8, $J_{7,5}$ = 1.6, 1 H, H-7), 7.09 (dd, $J_{6,7}$ = 15.8, $J_{6,5}$ = 4.6, 1 H, H-6), 7.15–7.64 (m, 8 H, ArH), 8.07 (m, 2 H, ArH); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = +41.3° (*c* 0.46, $CHCl_3$); LRMS (CI/NH_3) *m*/*z* 584 (M + NH_4)$^+$, 567 MH^+. Anal. Calcd for $C_{25}H_{27}O_7I$: C, 53.02; H, 4.80; I, 22.41. Found: C, 53.06; H, 4.83; I, 22.56.

6-*O*-(*tert*-Butyldiphenylsilyl)-D-glucal (1b). Tri-*O*-acetyl-D-glucal was deacetylated[18] to afford D-glucal **1a**. A solution of **1a** (3.00 g, 20.5 mM) in dry THF (75 mL) was cooled to 0 °C and treated with imidazole (1.55 g, 22.6 mM) and *tert*-butyldiphenylsilyl chloride (5.62 mL, 21.6 mM). The mixture was stirred for 1 h at 0 °C and for 4 h at room temperature. A solution of saturated sodium bicarbonate was added (100 mL) to the reaction mixture, followed by extraction with diethyl ether (2 × 50 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed by rotary evaporation. Flash chromatography (10% → 50% EtOAc–PE) of the residue (8.96 g) afforded **1b** (7.33 g, 93%) as a colorless oil: ^1H NMR δ 1.06 (s, 9 H, $(CH_3)_3CSi$), 3.02–3.19 (br s, 1 H, OH), 3.41–3.56 (br s, 1 H, OH), 3.75–4.02 (m, 4 H, H-4, H-5, H-6, H-6′), 4.22–4.29 (m, 1 H, H-3), 4.69 (dd, $J_{1,2}$ = 6.0, $J_{2,3}$ = 2.1, 1 H, H-2), 6.29 (dd, $J_{1,2}$ = 6.0, $J_{1,3}$ = 1.6, 1 H, H-1), 7.35–7.46 (m, 6 H, ArH), 7.66–7.72 (m, 4 H, ArH); ^{13}C NMR δ 19.2 ($(CH_3)_3CSi$), 26.8 ($(CH_3)_3CSi$), 63.7 (C-6), 69.7 and 71.3 (C-4, C-5), 77.1 (C-3), 102.3 (C-2), 127.73, 127.79, 129.83, 129.86, 132.7, 132.9, 135.5, 135.6, 144.2 (C-1); IR (neat) 3400, 1650, 1430, 1240 cm^{-1}; $[\alpha]^{20}_D$ = +7.5° (*c* 4.63, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m*/*z* 402 (M + NH_4)$^+$. Anal. Calcd for $C_{22}H_{28}O_4Si$: C, 68.71; H, 7.34. Found: C, 68.81; H, 7.33.

3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-D-glucal (5a). Sodium hydride (3.76 g, 60% in mineral oil, 94 mM, 2.2 equiv) was placed in an oven-dried 1-L round-bottom flask purged with argon. After washing with petroleum ether (2 × 10 mL), dry THF (150 mL), benzyl bromide (20.3 mL, 170.7 mM, 4 equiv), and tetrabutylammonium iodide (0.3 g) were added. The mixture was cooled with an ice bath, and half of the solution of diol **1b** (16.41 g, 42.67 mM) in dry THF (100 mL) was added dropwise quickly via syringe. The ice bath was removed, and the other half of the solution of diol **1b** was added as before. After being stirred for 9 h at room temperature, the reaction mixture was cooled (0 °C) and quenched with methyl alcohol (10 mL). A saturated aqueous solution of ammonium chloride (200 mL) was added, and the organic solvents were evaporated under reduced pressure. Extraction with diethyl ether, drying with $MgSO_4$, evaporation of the solvent, and flash chromatography of the residue afforded the dibenzyl ether **5a** (15.77 g, 65%): ^1H NMR δ 1.05 (s, 9 H, $(CH_3)_3CSi$), 3.89–4.05 (m, 4 H, H-4, H-5, H-6, H-6′), 4.19–4.24 (m, 1 H, H-3), 4.61 (ABq, *J* = 11.8, Δδ = 0.04, 2 H, $ArCH_2$), 4.82 (ABq, *J* = 11.2, Δδ = 0.08, 2 H, $ArCH_2$), 4.84 (dd, $J_{1,2}$ = 6.1, $J_{2,3}$ = 1.2, 1 H, H-2), 6.39 (dd, $J_{1,2}$ = 6.1, $J_{1,3}$ = 1.1, 1 H, H-1), 7.21–7.44 (m, 16 H, ArH), 7.64–7.71 (m, 4 H, ArH); ^{13}C NMR δ 19.3 ($(CH_3)_3CSi$), 26.8 ($(CH_3)_3CSi$), 62.1 (C-6), 70.7 ($ArCH_2$), 73.9 ($ArCH_2$), 74.1 and 75.9 (C-4, C-5), 77.8 (C-3), 99.6 (C-2) 127.57, 127.62, 127.66, 127.77, 127.80, 128.4, 129.6, 133.1, 133.5, 135.6, 135.8, 138.3, 144.8 (C-1); IR (neat) 1650 cm^{-1}; $[\alpha]^{20}_D$ = −10.9° (*c* 4.28, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m*/*z* 582 (M + NH_4)$^+$. Anal. Calcd for $C_{36}H_{40}O_4Si$: C, 76.56; H, 7.14. Found: 76.72; H, 7.16.

3,4-Di-*O*-benzylglucal (5b). Cleavage of the silyl ether **5a** by use of the Standard Procedure afforded alcohol **5b** (0.885 g, 89%): mp 36–38 °C; ^1H NMR δ 1.95 (t, *J* = 6,7, 1 H, OH), 3.78–3.99 (m, 4 H, H-4, H-5, H-6, H-6′), 4.21–4.26 (m, 1 H, H-3), 4.63 (ABq, *J* = 11.5, Δδ = 0.05, 2 H, $ArCH_2$), 4.80 (ABq, *J* = 11.4, Δδ = 0.07, 2 H, $ArCH_2$), 4.90 (dd, $J_{1,2}$ = 6.0, $J_{2,3}$ = 2.7, 1 H, H-2), 6.41 (d, $J_{1,2}$ = 6.0, 1 H, H-1), 7.27–7.39 (m, 10 H, ArH); ^{13}C NMR δ 61.7 (C-6), 70.5 ($ArCH_2$), 73.7 ($ArCH_2$), 74.4 and 75.4 (C-4, C-5), 77.2 (C-3), 100.1 (C-2), 127.7, 127.9, 128.0, 128.42, 128.45, 137.9, 138.0, 144.5 (C-1); IR (neat) 3450, 1650 cm^{-1}; $[\alpha]^{20}_D$ = −34.8° (*c* 0.82, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m*/*z* 344 (M+NH_4)$^+$. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.72; H, 6.89.

***tert*-Butyl (Methyl 3,4-di-*O*-benzyl-2,6,7-trideoxy-2-iodo-α-D-*manno*-oct-6-eno-1,5-pyranosid)uronates (*E*)-7 and (*Z*)-7.** Alcohol **5b** (118 mg, 0.36 mM) was oxidized with PCC and subjected to the Horner–Emmons reactions as described in the Standard Procedures affording the α,β-unsaturated ester **6** (112 mg, 74%) as an inseparable mixture of *Z* and *E* isomers (*Z*:*E* = 1:1 according to ^1H NMR) that was used directly. Application

(23) (a) Milstein, D., Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636. (b) Leibner, J. E.; Jacobus, J. *J. Org. Chem.* **1979**, *44*, 449.

(24) Ireland, R. E., Wuts, P. M., Ernst, B. *J. Am. Chem. Soc.* **1981**, *103*, 3205.

of the Standard Procedure for iodomethoxylation afforded compound **7** (136 mg, 88%, $\alpha:\beta \approx 3:1$). Pure samples of the major α-anomers were obtained by flash chromatography. For α-(*Z*)-**7**: ^{1}H NMR δ 1.44 (s, 9 H, C(CH_3)$_3$), 3.37 (dd, $J_{3,4}$ = 8.5, $J_{3,2}$ = 4.4, 1 H, H-3), 3.41 (s, 3 H, CH_3O), 3.61 (dd, $J_{4,3} \cong J_{4,5} \cong 8.5$, 1 H, H-4), 4.51 (dd, $J_{2,1}$ = 1.9, $J_{2,3}$ = 4.4, 1 H, H-2), 4.60 (ABq, J = 11.3, $\Delta\delta$ = 0.14, 2 H, ArCH_2), 4.64 (ABq, J = 11.0, $\Delta\delta$ = 0.22, 2 H, ArCH_2), 5.06 (d, J = 1.9, 1 H, H-1), 5.55 (dd, $J_{5,4} \cong J_{5,6} \cong 8.5$, 1 H, H-5), 5.88 (dd, $J_{7,6}$ = 11.6, $J_{7,5}$ = 0.8, 1 H, H-7), 6.05 (dd, $J_{6,7}$ = 11.6, $J_{6,5}$ = 9.0, 1 H, H-6), 7.2–7.4 (m, 10 H, ArH); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = –62.9° (*c* 2.65, $CHCl_3$); LRMS (CI/NH_3) *m/z* 598 (M + NH_4)$^+$, 581 (MH)$^+$; HRMS calcd for $C_{27}H_{37}O_6NI$ (M + NH_4)$^+$ 598.1666, found 598:1677. For α-(*E*)-**7**: ^{1}H NMR δ 1.51 (s, 9 H, C(CH_3)$_3$), 3.31 (dd, $J_{3,2}$ = 4.2, $J_{3,4}$ = 8.3, 1 H, H-3), 3.32 (s, 3 H, CH_3O), 3.59 (dd, $J_{4,5} \cong J_{4,3} \cong 9$, 1 H, H-4), 4.28 (ddd, $J_{5,4}$ = 9.7, $J_{5,6}$ = 4.5, $J_{5,7}$ = 1.7, 1 H, H-5), 4.48 (dd, $J_{2,3}$ = 4.2, $J_{1,2}$ = 1.2, 1 H, H-2), 4.61 (ABq, J = 11.5, $\Delta\delta$ = 0.18, 2 H, ArCH_2), 4.72 (ABq, J = 10.5, $\Delta\delta$ = 0.28, 2 H, ArCH_2), 5.11 (br s, 1 H, H-1), 6.15 (dd, $J_{7,6}$ = 15.7, $J_{7,5}$ = 1.7, 1 H, H-7), 7.02 (dd, $J_{6,7}$ = 15.7, $J_{6,5}$ = 4.5, 1 H, H-6), 7.28–7.43 (m, 10 H, ArH); IR (neat) 1715 cm^{-1}; $[\alpha]^{20}_D$ = +40.3° (*c* 2.52, $CHCl_3$); LRMS (CI/NH_3) *m/z* 598 (M + NH_4)$^+$.

3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-1,2,7,8-tetradeoxy-L-*galacto*- and -D-*altro*-octa-1,7-dieno-1,5-pyranose (8b). Alcohol **5b** (797 mg, 2.44 mM) was oxidized using PCC according to the Standard Procedures. A solution of the resulting aldehyde (707 mg, 2.18 mM) in dry THF (5 mL) was added to a solution of vinylmagnesium bromide (10 mL, 1.0 M in THF, 10 mM) in 10 mL of dry THF at –78 °C. After 30 min, the solution was allowed to warm to 0 °C and stirred for 30 min. The reaction mixture was poured into saturated aqueous ammonium chloride (50 mL) and extracted with diethyl ether (2 × 25 mL). The combined extracts were washed with brine (25 mL), dried over $MgSO_4$, and rotary evaporated to give 802 mg of crude material. Flash chromatography (10% → 25% EtOAc–PE) afforded the alcohol **8a** (565 mg, 73%) as a 1.5:1 mixture of isomers, as determined by ^{1}H NMR. The material was dissolved in dry DMF (8 mL) and treated with imidazole (218 mg, 3.20 mM) and *tert*-butyldimethylsilyl chloride (362 mg, 2.40 mM). The mixture was stirred overnight at room temperature and then diluted with diethyl ether (60 mL). The mixture was washed with water (50 mL), and the organic layer was dried over $MgSO_4$. Rotary evaporation followed by flash chromatography (5% EtOAc–PE) of the residue gave glycal **8b** (686 mg, 92%) as a colorless oil: ^{1}H NMR δ 0.04 (s), 0.06 (s), 0.89 (s), 0.90 (s), 3.78–3.94 (m), 4.08 (br s), 4.20–4.25 (m), 4.45–4.93 (m), 5.08–5.30 (m), 5.83–6.01 (m), 6.39 (d, J = 6.3), 6.44 (d, J = 6.3), 7.27–7.37 (m); IR (neat) 1650, 1250, 1090, 840 cm^{-1}; GC/CIMS (*i*-C_4H_{10}) *m/z* 467 (M + H)$^+$. Anal. Calcd for $C_{28}H_{38}O_4Si$: C, 72.06; H, 8.21. Found: C, 71.89; H, 8.34.

α-Methyl 3,4-Di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-D-*manno*-D,L-*glycero*-oct-7-eno-1,5-pyranoside (9a). Glycal **8b** (659 mg, 1.41 mM) was converted to iodide **9a** (740 mg, 84%) by use of the Standard Procedure for iodomethoxylation: ^{1}H NMR δ 0.06 (s), 0.08 (s), 0.09 (s), 0.10 (s), 0.91 (s), 0.97 (s), 3.26 (s), 3.35 (s), 3.52–3.59 (m), 3.67–3.83 (m), 3.95–4.05 (m), 4.40–4.53 (m), 4.57–4.70 (m), 4.89 (d, J = 11.0), 4.97 (d, J = 11.0), 5.06–5.21 (m), 5.26 (br s), 5.95–6.19 (m), 7.23–7.43 (m); IR (neat) 1255, 1060 cm^{-1}; GC/CIMS (*i*-C_4H_{10}) *m/z* 625 MH$^+$. Anal. Calcd for $C_{24}H_{41}IO_5Si$: C, 55.76; H, 6.62; I. 20.32. Found: C, 55.81; H, 6.65; I, 20.42.

Oxidative Cleavage of Alkene 9a. A solution of iodide **9a** (696 mg, 1.11 mM) in acetone (16 mL) was treated with osmium tetroxide (0.3 mL, 2.5 wt % in *tert*-butyl alcohol) and *N*-methylmorpholine oxide (0.6 mL, 60 wt % in H_2O, 3.33 mM). The reaction was incomplete after 18 h, but addition of similar amounts of osmium tetroxide and *N*-methylmorpholine oxide, followed by 4 h of stirring, resulted in complete conversion (TLC). The mixture was diluted with EtOAc (50 mL) and washed with 5% aqueous sodium bisulfite (5 mL) and then water (10 mL). The combined aqueous layers were extracted with EtOAc. The combined organic layers were dried over Na_2SO_4, and rotary evaporation afforded the presumed mixture of diols (765 mg). The crude material was dissolved in dry CH_2Cl_2 (10 mL) and treated with anhydrous Na_2CO_3 (640 mg, 6.0 mM) and lead tetraacetate (541 mg, 1.22 mM) at 0 °C. After being stirred for 15 min at 0 °C, the mixture was warmed to room temperature and then passed through a column of Florisil. Elution with 5% EtOAc–PE gave aldehyde **10a** (590 mg, 85%): ^{1}H NMR δ 0.07 (s), 0.10 (s), 0.11 (s), 0.16 (s), 0.97 (s), 0.98 (s), 3.22 (s), 3.33 (s), 3.94–4.08 (m), 4.17 (br s), 4.34–4.66 (m), 4.89 (d, J = 10.7), 5.00–5.05 (2d), 7.15–7.38 (m), 9.40 (s), 9.68 (d, J = 1.6); IR (neat) 1735 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 644 (M + NH_4)$^+$. Anal. Calcd for $C_{30}H_{39}O_6I$: C, 53.76; H, 6.12; I, 20.28. Found: C, 53.59; H, 6.33; I, 20.49.

Ethyl (α-Methyl 3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-D-*manno*-D,L-*glycero*-non-7-eno-1,5-pyranos)uronate (11a). Aldehyde **10a** (233 mg, 0.372 mM) was subjected to the Standard Procedure for the Horner–Emmons reaction to obtain the ethyl ester **11a** (241 mg, 93%) as an inseparable mixture of C-6 epimers: ^{1}H NMR δ 0.06 (s), 0.07 (s), 0.15 (s), 0.96 (s), 0.97 (s), 1.22 (t, J = 7.1), 1.26 (t, J = 7.1), 3.24 (s), 3.34 (s), 3.60 (dd, J = 2.0, 9.3), 3.80–3.84 (m), 3.95–4.02 (m), 4.09 (q, J = 7.2), 4.17 (q, J = 7.2), 4.42–4.69 (m), 4.85 (d, J = 10.9), 4.99 (d, J = 11.1), 5.06 (br s), 5.11 (br s), 5.89 (dd, J = 1.0, 15.5), 6.00 (dd, J = 1.1, 15.8), 7.01 (dd, J = 4.7, 15.5), 7.13 (dd, J = 7.2, 15.8), 7.17–7.42 (m); IR (neat) 1715, 1660 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 714 (M + NH_4)$^+$. Anal. Calcd for $C_{32}H_{45}O_7ISi$: C, 55.17; H, 6.51; I, 18.21. Found: C, 55.11; H, 6.55; I, 18.31.

Ethyl (α-*p*-Methoxybenzyl 3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-D-*manno*-L-*glycero*-non-7-eno-1,5-pyranos)uronate (11b) and Ethyl (α-*p*-Methoxybenzyl 3,4-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-D-*manno*-D-*glycero*-non-7-eno-1,5-pyranos)uronate (11c). Glycal **8b** (1.27 g, 2.72 mM) was treated with NIS and *p*-methoxybenzyl alcohol as outlined in the Standard Procedures to provide iodide **9b** (1.64 g, 82%). The material was converted to aldehyde **10b** (1.27 g, 79%) as described for the preparation of aldehyde **10a** and thence to ethyl esters **11b** and **11c** (total 0.937 g, 83%) using the Standard Procedure for Horner–Emmons reactions. The esters were partially resolved using flash chromatography (2% → 10% EtOAc–PE) to give, in order of elution, **11b** (0.236 g), overlap of **11b** and **11c** (0.117 g), and **11c** (0.584 g). **For 11b**: ^{1}H NMR δ 0.09 (s, 6 H, $(CH_3)_2Si$), 0.97 (s, 9 H, $(CH_3)_3CSi$), 1.26 (t, J = 7.2, 3 H, CH_3CH_2O), 3.38 (dd, $J_{2,3}$ = 4.1, $J_{3,4}$ = 8.4, 1 H, H-3), 3.71 (dd, $J_{4,5}$ = 9.5, $J_{5,6}$ = 2.2, 1 H, H-5), 3.81 (s, 3 H, $ArOCH_3$), 4.01 (dd, $J_{3,4} \cong J_{4,5} \cong 9$, 1 H, H-4), 4.19 (q, J = 7.2, 2 H, CH_3CH_2O), 4.28 (d, J = 11.2, 1 H, ArCH), 4.41–4.50 (m, 3 H, H-2, ArCH, ArCH), 4.58–4.70 (m, 3 H, H-6, ArCH, ArCH), 4.97 (d, J = 10.8, 1 H, ArCH), 5.24 (br s, 1 H, H-1), 6.03 (dd, $J_{7,8}$ = 16.8, $J_{6,8}$ = 1.0, 1 H, H-8), 6.86 (d, J = 8.7, 2 H, ArH), 7.13–7.39 (m, 13 H, H-7, ArH); IR (neat) 1730, 1670, 1620 cm^{-1}; $[\alpha]^{20}_D$ = +9.5° (*c* 1.10, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 820 (M + NH_4)$^+$; HRMS calcd for $C_{39}H_{55}NO_8ISi$ (M + NH_4)$^+$ 820.2742, found 820.2730. For **11c**: ^{1}H NMR δ 0.07 (s, 3 H, CH_3Si), 0.16 (s, 3 H, CH_3Si), 0.97 (s, 9 H, $(CH_3)_3CSi$), 1.23 (t, J = 7.1, 3 H, CH_3CH_2O), 3.34–3.39 (m, 1 H, H-3), 3.82 (s, 3 H, $ArOCH_3$), 3.80–3.87 (m, 2 H, H-4, H-5), 4.08 (q, J = 7.1, 2 H, CH_3CH_2O), 4.40–4.49 (m, 4 H, H-2, H-6, ArCH, ArCH), 4.59 (d, J = 11.5, 1 H, ArCH), 4.64 (d, J = 11.2, 1 H, ArCH), 4.70 (ABq, J = 10.7, $\Delta\delta$ = 0.13, 2 H, $ArCH_2$), 5.22 (br s, 1 H, H-1), 5.88 (dd, $J_{7,8}$ = 15.6, $J_{6,8}$ = 1.9, 1 H, H-8), 6.89 (d, J = 8.8, 2 H, ArH), 6.97 (dd, $J_{7,8}$ = 15.6, $J_{6,7}$ = 4.7, 1 H, H-7), 7.18–7.40 (m, 12 H, ArH); IR (neat) 1730, 1655, 1620 cm^{-1}; $[\alpha]^{20}_D$ = +25.9° (*c* 1.02, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 820 (M + NH_4)$^+$; HRMS calcd for $C_{39}H_{55}NO_8ISi$ (M + NH_4)$^+$ 820.2742, found 820.2714.

4-*O*-Benzyl-3-*O*-(methoxymethyl)-D-glucal (12c). Following the steps outlined above for the preparation of **1b**, the 6-*O*-*tert*-butyldimethylsilyl analogue was prepared from D-glucal **1a** (5.0 g, 34.2 mM) and *tert*-butyldimethylsilyl chloride (5.43 g, 36 mM) in THF (150 mL) containing pyridine (3.2 mL) and imidazole (2.7 g, 39.4 mM) at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was worked up in the usual way to afford 8.0 g (90%) of the 6-*O*-*tert*-butyldimethylsilylated product. The material was dissolved in pyridine (60 mL) and cooled to –40 °C, and benzoyl chloride (3.6 mL, 3.1 mM) was added gradually. The solution was warmed to –5 °C for 20 min and then was worked up affording 10.5 g of material which was chromatographed (using 25% ethyl acetate in petroleum ether) to afford 9.8 g of the desired 3-*O*-benzoyl derivative. This material was dissolved in THF (120 mL) containing potassium hydride (4 g of 35% dispersion) and stirred at 0 °C. After 15 min benzyl bromide (3.5 mL) in THF (10 mL) and a catalytic amount of tetra-*n*-butylammonium iodide were added. After being stirred for 6 h at room temperature, the

mixture was cooled in ice, poured into saturated ammonium chloride solution, and processed in the usual way. Flash chromatography using 2% ethyl acetate in petroleum ether afforded 9.2 g of **12a**. To a portion of this material (2.93 g, 8.36 mM) in dry CH_2Cl_2 (60 mL) at 0 °C was added diisopropylethylamine (5.8 mL, 33 mM) and chloromethyl methyl ether (2.4 mL, 32 mM). The mixture was stirred for 11 h at room temperature and then washed with 5% aqueous $NaHCO_3$ (50 mL), the aqueous layer was extracted with CH_2Cl_2 (50 mL), and the combined organic layers were washed with brine (50 mL), dried over Na_2SO_4, and rotary evaporated. Flash chromatography (2% → 5% EtOAc–PE) of the residue afforded **12b** (3.16 g, 96%). Desilylation of **12b** (3.03 g, 7.68 mM) by the Standard Procedure gave **12c** (2.07 g, 97%): ^{1}H NMR δ 1.99 (t, J = 6.4, 1 H, OH), 3.39 (s, 3 H, OCH_3), 3.78 (dd, $J_{3,4}$ = 6.4, $J_{4,5}$ = 8.6, 1 H, H-4), 3.83–3.89 (m, 2 H, H-6), 3.95 (dt, $J_{5,6}$ = 4.4, $J_{4,5}$ = 8.6, 1 H, H-5), 4.29–4.34 (m, 1 H, H-3), 4.69–4.78 (m, 3 H, CH_3OCH_2, ArC*H*), 4.81–4.87 (m, 2 H, H-2, ArC*H*), 6.38 (dd, $J_{1,2}$ = 6.1, $J_{1,3}$ = 1.4, 1 H, H-1), 7.29–7.38 (m, 5 H, Ar*H*); ^{13}C NMR δ 55.6 (OCH_3), 61.5 (C-6), 73.9 (ArCH_2), 74.2 and 74.8 (C-4, C-5), 77.4 (C-3), 95.8 (CH_3OCH_2), 101.1 (C-2), 127.91, 127.94, 128.5, 137.9, 144.3 (C-1); IR (neat) 3450, 1650 cm^{-1}; $[\alpha]^{20}_D$ = +10.2° (*c* 2.00, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 298 $(M + NH_4)^+$. Anal. Calcd for $C_{15}H_{20}O_5$: C, 64.27; H, 7.19. Found: C, 64.39; H, 6.20.

4-*O*-Benzyl-6-*O*-(*tert*-butyldimethylsilyl)-1,2,7,8-tetradeoxy-3-*O*-(methoxymethyl)-L-*galacto*-D-*altro*-octa-1,7-dieno-1,5-pyranose (13). Alcohol **12c** (1.94 g, 6.92 mM) was converted to the olefin **13** (1.30 g, 93%) as described above for the preparation of **8b**. The product was a 1:1 mixture of isomers, as determined by ^{1}H NMR: ^{1}H NMR δ 0.04 (s), 0.05 (s), 0.06 (s), 0.88 (s), 0.91 (s), 3.36 (s), 3.76–3.88 (m), 3.90–3.96 (m), 4.17–4.23 (m), 4.26–4.31 (m), 4.52–4.60 (m), 4.62–4.88 (m), 5.08–5.12 (m), 5.29 (d, J = 17.2), 5.82–6.02 (m), 6.37 (d, J = 6.1), 6.42 (d, J = 6.1), 7.23–7.44 (m); IR (neat) 1650 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 438 $(M + NH_4)^+$. Anal. Calcd for $C_{23}H_{36}O_5Si$: C, 65.68; H, 8.63. Found: C, 65.89; H, 8.69.

α-Methyl 4-*O*-Benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-3-*O*-(methoxymethyl)-D-*manno*-D,L-*glycero*-oct-7-eno-1,5-pyranoside (14a). Iodomethoxylation of **13** (1.02 g, 2.41 mM) by the Standard Procedure gave **14a** (1.32 g, 94%): ^{1}H NMR δ 0.06 (s), 0.08 (s), 0.09 (s), 0.11 (s), 0.92 (s), 0.97 (s), 3.27 (s), 3.36 (s), 3.42 (s), 3.43 (s), 3.43–3.53 (m), 3.55–3.61 (m), 3.68–3.84 (m), 4.02 (t, $J \cong 9$), 4.38–4.51 (m), 4.61–4.75 (m), 4.80–4.95 (m), 5.05–5.28 (m), 5.95–6.20 (m), 7.24–7.41 (m); IR (neat) 1460, 1250 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 596 $(M + NH_4)^+$. Anal. Calcd for $C_{24}H_{39}O_6ISi$: C, 49.82; H, 6.79; I, 21.93. Found: C, 49.87; H, 6.83; I, 21.84.

Oxidative Cleavage of 14a. Olefin **14a** (1.16 g, 2.00 mM) was converted to aldehyde **14b** (794 mg, 68%) as described for the preparation of **10a**: ^{1}H NMR δ 0.09 (s), 0.13 (s), 0.14 (s), 0.19 (s), 1.00 (s), 1.02 (s), 3.26 (s), 3.37 (s), 3.41 (s), 3.43 (s), 3.46–3.52 (m), 3.97–4.11 (m), 4.19 (s), 4.35–4.37 (m), 4.45–4.48 (m), 4.56–4.72 (m), 4.79 (d, J = 6.8), 4.86 (d, J = 11.0), 4.95–5.00 (m), 5.04 (s), 7.19–7.38 (m), 9.42 (s), 9.72 (d, J = 1.5); IR (neat) 1735 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 598 $(M + NH_4)^+$. Anal. Calcd for $C_{23}H_{37}O_7ISi$: C, 47.59; H, 6.42; I, 21.85. Found: C, 47.37; H, 6.44; I, 21.86.

Ethyl (α-Methyl 4-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-2,7,8-trideoxy-2-iodo-3-*O*-(methoxymethyl)-D-*manno*-D-*glycero*- and -L-*glycero*-non-7-eno-1,5-pyranos)uronate Mixture (15). Aldehyde **14b** (672 mg, 1.16 mM) was subjected to the standard Horner–Emmons reaction to give **15** (660 mg, 87%). The material (IR (neat) 1720, 1655 cm^{-1}; GC/CIMS (NH_3/CH_4) *m/z* 668 $(M + NH_4)^+$) was cyclized directly to give **30** and **31** as described below.

6-*O*-(*tert*-Butyldiphenylsilyl)galactal (16b). Tri-*O*-acetyl-D-galactal (1.25 g, 4.59 mM) was deacetylated to afford D-galactal **16a** which was then converted into the 6-O-silylated derivatve **16b** (1.45 g, 82%) as described above for the preparation of glucal analogue **1b**: ^{1}H NMR δ 1.07 (s, 9 H, C(CH_3)$_3$), 2.59 (d, J = 10.3, 1 H, (C-3)-O*H*), 2.97 (d, J = 5.3, 1 H, (C-4)-O*H*), 3.90 (dd, $J_{6,6'}$ = 11.6, $J_{6,5}$ = 4.0, 1 H, H-6), 3.91 (m, 1 H, H-5), 3.99 (dd, $J_{6',6}$ = 11.6, $J_{6',5}$ = 7.0, 1 H, H-6'), 4.14 (m, 1 H, H-4), 4.36 (m, 1 H, H-3), 4.73 (ddd, $J_{2,1}$ = 6.2, $J_{2,3} \cong J_{2,4} \cong$ 2.0, 1 H, H-2), 6.39 (dd, $J_{1,2}$ = 6.2, $J_{1,3}$ = 1.6, 1 H, H-1), 7.3–7.5 (m, 6 H, ArH), 7.6–7.8 (m, 4 H, ArH); IR (neat) 3400, 1640, 1420, 1230, 1110, 710 cm^{-1}; $[\alpha]^{20}_D$ = +2.45° (*c* 3.8, $CHCl_3$); LRMS (CI/NH_3-CH_4) *m/z* 402 $(M + NH_4)^+$. Anal. Calcd for $C_{22}H_{28}SiO_4$: C, 68.72; H, 7.34. Found: C, 68.31; H, 7.38.

6-*O*-(*tert*-Butyldiphenylsilyl)-3,4-*O*-isopropylidene-D-galactal (17a). To an ice-cooled solution of the diol **16b** (952 mg, 2.48 mM) in dry CH_2Cl_2 (10 mL) was added 2-methoxypropene (285 μL, 1.2 equiv) and pyridinium *p*-toluenesulfonate[22] (25 mg). After 30 min at 0 °C and 4 h at room temperature, additional 2-methoxypropene (237 μL, 1 equiv) was added and the reaction mixture was stirred for another 4 h. The solvent was evaporated, and the residue was treated with an ice-cooled aqueous solution of $NaHCO_3$ and extracted with diethyl ether. Flash chromatography afforded pure acetonide **17a** (758 mg, 72%) as a colorless oil: ^{1}H NMR δ 1.10 (s, 9 H, C(CH_3)$_3$), 1.40 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 3.9–4.1 (m, 3 H, H-5, H-6, H-6'), 4.49 (m, 1 H, H-4), 4.69 (dd, $J_{3,2}$ = 2.7, $J_{3,4}$ = 6.1, 1 H, H-3), 4.79 (ddd, $J_{2,1}$ = 6.3, $J_{2,3}$ = 2.7, $J_{2,4}$ = 1.6, 1 H, H-2), 6.36 (d, $J_{1,2}$ = 6.3, 1 H, H-1), 7.35–7.50 (m, 6 H, ArH), 7.65–7.80 (m, 4 H, ArH); IR (neat) 1650, 1240, 1110, 705 cm^{-1}; $[\alpha]^{20}_D$ = +16.3° (*c* 1.41, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 442 $(M + NH_4)^+$, 425 MH^+. Anal. Calcd for $C_{25}H_{32}SiO_4$: C, 70.72; H, 7.60. Found: C, 70.30; H, 7.62.

3,4-*O*-Isopropylidene-D-galactal (17b). Silyl ether **17a** (758 mg, 1.78 mM) was desilylated using the Standard Procedure to give alcohol **17b** (320 mg, 96%): ^{1}H NMR δ 1.33 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 2.38 (br s, 1 H, OH), 3.82 (m, 1 H, H-6), 3.97 (m, 2 H, H-5, H-6'), 4.28 (dd, $J_{4,3}$ = 6.2, $J_{4,2}$ = 1.4, 1 H, H-4), 4.66 (dd, $J_{3,4}$ = 6.2, $J_{3,2}$ = 2.7, 1 H, H-3), 4.79 (ddd, $J_{2,1}$ = 6.2, $J_{2,3}$ = 2.7, $J_{2,4}$ = 1.4, 1 H, H-2), 6.40 (d, $J_{1,2}$ = 6.2, 1 H, H-1); IR (neat) 3425, 1645 cm^{-1}; $[\alpha]^{20}_D$ = +29.2° (*c* 1.36, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 204 $(M + NH_4)^+$. Anal. Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.02; H, 7.63.

Ethyl 1,2,6,7-Tetradeoxy-3,4-isopropylidene-D-*lyxo*-octa-1,6-dieno-1,5-pyranosuronates (*E*)-18 and (*Z*)-18. Alcohol **17b** (306 mg, 1.7 mM) was converted to (*E*/*Z*)-18 by use of the Standard Procedures for PCC oxidation and Horner–Emmons reactions. The products were separated by flash chromatography as colorless oils (*Z*)-18 117 mg, 32%) and (*E*)-18 (136 mg, 38%). For (*Z*)-18 (higher R_f): ^{1}H NMR δ 1.30 (t, J = 7.1, 3 H, CH_2CH_3), 1.34 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 4.18 (q, J = 7.1, 2 H, CH_2CH_3), 4.46 (m, 1 H, H-4), 4.73 (dd, $J_{3,4}$ = 6.2, $J_{3,2}$ = 3.0, 1 H, H-3), 4.84 (ddd, $J_{2,1}$ = 6.3, $J_{2,3}$ = 3.0, $J_{2,4}$ = 1.4, 1 H, H-2), 5.58 (dd, $J_{5,6}$ = 7.7, $J_{5,7}$ = 1.5, 1 H, H-5), 5.97 (dd, $J_{7,6}$ = 11.7, $J_{7,5}$ = 1.5, 1 H, H-7), 6.40 (d, $J_{1,2}$ = 6.3, 1 H, H-1), 6.47 (dd, $J_{6,7}$ = 11.7, $J_{6,5}$ = 7.7, 1 H, H-6); ^{13}C NMR δ 14.2, 26.9, 28.0, 60.6, 68.6, 72.1, 74.8, 102.7, 110.5, 121.2, 144.6, 145.4, 165.7; IR (neat) 1715, 1645 cm^{-1}; GC/CIMS (CH_4/NH_3) *m/z* 272 $(M + NH_4)^+$, 255 MH^+; HRMS calcd for $C_{13}H_{18}O_5$ 254.1154, found 254.1158. (*E*)-18 (lower R_f): ^{1}H NMR δ 1.30 (t, J = 7.1, 3 H, CH_2CH_3), 1.35 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 4.20 (q, J = 7.1, 2 H, CH_2CH_3), 4.33 (ddd, $J_{4,3}$ = 6.1, $J_{4,5} \cong J_{4,2} \cong$ 1.4, 1 H, H-4), 4.56 (ddd, $J_{5,6}$ = 4.7, $J_{5,4} \cong J_{5,7} \cong$ 1.7, 1 H, H-5), 4.70 (dd, $J_{3,4}$ = 6.1, $J_{3,2}$ = 2.9, 1 H, H-3), 4.86 (ddd, $J_{2,1}$ = 6.3, $J_{2,3}$ = 2.9, $J_{2,4}$ = 1.4, 1 H, H-2), 6.20 (dd, $J_{7,6}$ = 15.7, $J_{7,5}$ = 1.9, 1 H, H-7), 6.43 (d, $J_{1,2}$ = 6.3, 1 H, H-1), 6.98 (dd, $J_{6,7}$ = 15.7, $J_{6,5}$ = 4.7, 1 H, H-6); IR (neat) 1720, 1650 cm^{-1}; $[\alpha]^{20}_D$ = +2.1° (*c* 2.59, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 272 $(M + NH_4)^+$, 255 MH^+.

Ethyl (Methyl 2,6,7-trideoxy-2-iodo-3,4-isopropylidene-β-D-*galacto*-oct-6-eno-1,5-pyranosid)uronates (*E*)-19 and (*Z*)-19. Glycals (*E*)-18 (110 mg, 0.43 mM) and (*Z*)-18 (70 mg, 0.28 mM) were converted to iodides (*E*)-19 (156 mg, 87%) and (*Z*)-19 (108 mg, 95%) by use of the Standard Procedure. For (*E*)-19: ^{1}H NMR δ 1.30 (t, J = 7.1, 3 H, CH_2CH_3), 1.36 (s, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 3.55 (s, 3 H, OCH_3), 3.79 (dd, $J_{2,1} \cong J_{2,3} \cong$ 9, 1 H, H-2), 4.02 (dd, $J_{4,3}$ = 5.0, $J_{4,5}$ = 2.3, 1 H, H-4), 4.22 (q, J = 7.1, 2 H, CH_2CH_3), 4.43 (dd, $J_{1,2}$ = 9.3, 1 H, H-1), 4.51 (ddd, $J_{5,6}$ = 4.3, $J_{5,7} \cong J_{5,4} \cong$ 2, 1 H, H-5), 4.57 (dd, $J_{3,2}$ = 9.8, $J_{3,4}$ = 5.0, 1 H, H-3), 6.21 (dd, $J_{7,6}$ = 15.7, $J_{7,5}$ = 1.9, 1 H, H-7), 6.97 (dd, $J_{6,7}$ = 15.7, $J_{6,5}$ = 4.3, 1 H, H-6); ^{13}C NMR δ 14.3, 26.1, 28.2, 32.0, 57.2, 60.7, 72.2, 75.1, 81.9, 103.1 (C-1), 110.6 ($(CH_3)_2C$), 122.9, 141.2, 165.9; IR (neat) 1720, 1660, 1380 cm^{-1}; $[\alpha]^{20}_D$ = −16.0° (*c* 1.71, $CHCl_3$); GC/CIMS (NH_3/CH_4) *m/z* 430 $(M + NH_4)^+$; HRMS Calcd for $C_{14}H_{21}IO_6$ 412.0383, found 412.0380. For (*Z*)-19: ^{1}H NMR δ 1.30 (t, J = 7.2, 3 H, CH_2CH_3), 1.33 (s, 3 H, CH_3), 1.52, (s, 3 H, CH_3), 3.53 (s, 3 H, OCH_3), 3.78 (dd, $J_{2,3} \cong J_{2,1} \cong$ 9, 1 H, H-2), 4.18 (dd, $J_{4,5}$ = 2.2, $J_{4,3}$ = 5.1, 1 H, H-4), 4.19 (q, J = 7.2, CH_2CH_3), 4.41 (d, $J_{1,2}$ = 9.4, 1 H, H-1), 4.59 (dd, $J_{3,2}$ = 8.8, $J_{3,4}$ = 5.1, 1 H, H-3), 5.52 (ddd, $J_{5,6}$ = 7.4, $J_{5,4}$ = 2.2, $J_{5,7}$ = 1.5, 1 H,

H-7), 5.96 (dd, $J_{7,6}$ = 11.6, $J_{7,5}$ = 1.5, 1 H, H-7), 6.38 (dd, $J_{6,7}$ = 11.6, $J_{6,5}$ = 7.4, 1 H, H-6); ^{13}C NMR δ 14.2, 26.1, 28.3, 32.6, 57.3, 60.6, 70.3, 75.3, 82.2, 102.8 (C-1), 110.3, 120.9, 144.2, 165.8; IR (neat) 1710 cm^{-1}; $[\alpha]^{20}_D$ = −47.3° (c 0.67, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 430 (M + NH_4)$^+$, 413 MH^+. Anal. Calcd for $C_{14}H_{21}IO_6$: C, 40.79; H, 5.13. Found: C, 41.21; H, 5.19.

Formation of 2-Oxabicyclo[2.2.1]heptanes 20–23. (1*R*,3*S*,4*S*,5*R*,6*R*,7*R*)-5-(Benzoyloxy)-6-(benzyloxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid Ethyl Ester (20a) and (1*R*,3*S*,4*S*,5*R*,6*R*,7*S*)-5-(Benzoyloxy)-6-(benzyloxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid Ethyl Ester (21a). Cyclization of iodopyranoside **4** (390 mg, 0.69 mM) carried out as described in the Standard Procedure afforded the easily separable bicyclic compounds **20a** (178 mg, 59%) and **21a** (98 mg, 32%) as white solids. For **20a** (higher R_f): mp 86 °C; ^{1}H NMR δ 1.24 (t, J = 7.1, 3 H, CH_2CH_3), 2.45 (dd, $J_{8,8'}$ = 21.0, $J_{8,7}$ = 10.2, 1 H, H-8), 2.6–2.8 (m, 3 H, H-4, H-7, H-8′), 3.55 (s, 3 H, OCH_3), 3.96 (br s, 1 H, H-6), 4.13 (q, J = 7.1, 2 H, CH_2CH_3), 4.32 (br s, 1 H, H-1), 4.69 (ABq, J = 12.3, Δδ = 0.09, 2 H, $ArCH_2$), 5.21 (d, $J_{3,4}$ = 2.7, 1 H, H-3), 5.56 (s, 1 H, H-5), 7.2–7.6 (m, 8 H, ArH), 8.00 (m, 2 H, ArH); ^{13}C NMR δ 14.2 (CH_2CH_3), 30.5 (C-8), 42.5 (C-7), 50.1 (C-4), 56.7 (CH_3O), 60.7 (CH_2CH_3), 71.3 ($ArCH_2$), 74.4 (C-5), 80.3 (C-1), 85.5 (C-6), 103.8 (C-3), 127.6, 127.9, 128.28, 128.34, 129.6, 129.9, 133.1, 137.8, 165.4 ($PhCO_2R$), 172.1 (CO_2Et); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = +16.7° (c 0.93, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 458 (M + NH_4)$^+$, 441 MH^+. Anal. Calcd for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41. Found: C, 68.11; H, 6.56. For **21a** (lower R_f): mp 74 °C; ^{1}H NMR δ 1.12 (t, J = 7.1, 3 H, CH_2CH_3), 2.54 (dd, $J_{8,8'}$ = 15.9, $J_{8,7}$ = 7.5, 1 H, H-8), 2.65 (dd, $J_{8',8}$ = 15.9, $J_{8',7}$ = 8.6, 1 H, H-8′), 2.7–2.9 (m, 2 H, H-4, H-7), 3.54 (s, 3 H, OCH_3), 4.02 (dq, J = 7.1 and 1.3, 2 H, CH_2CH_3), 4.16 (dd, J = 3.7 and 2.01, 1 H, H-6), 4.36 (br s, 1 H, H-1), 4.69 (ABq, J = 12.3, Δδ = 0.11, 2 H, $ArCH_2$), 5.19 (d, $J_{3,4}$ = 2.7, 1 H, H-3), 5.7 (br s, 1 H, H-5), 7.2–7.6 (m, 8 H, ArH), 7.98 (m, 2 H, ArH); ^{13}C NMR δ 14.0 (CH_2CH_3), 31.8 (C-8), 44.6 (C-7), 49.0 (C-4), 56.4 (OCH_3), 60.7 (CH_2CH_3), 71.8 ($ArCH_2$), 74.8 (C-5), 80.6 (C-1), 85.2 (C-6), 105.2 (C-3), 127.7, 128.0, 128.3, 128.4, 129.5, 129.9, 133.1, 137.8, 165.2 ($PhCO_2R$), 171.5 (CO_2Et); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = +35.2° (c 0.58, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 458 (M + NH_4)$^+$, 441 MH^+. Anal. Calcd for $C_{25}H_{28}O_7$: C, 68.17; H, 6.41. Found: C, 68.16; H, 6.31.

(1*R*,3*S*,4*S*,5*R*,6*R*,7*R*)-5,6-Bis(benzyloxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid *tert*-Butyl Ester (20b) and (1*R*,3*S*,4*S*,5*R*,6*R*,7*S*)-5,6-Bis(benzyloxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid *tert*-Butyl Ester (21b). The title compounds were obtained by use of the Standard Procedure for radical cyclization, starting from either (*Z*)-**7** (80%, **20b**:**21b** = 5.5:1) or (*E*)-**7** (80%, **20b**:**21b** = 4.5:1). The products were readily separated by flash chromatography. For **20b** (higher R_f): ^{1}H NMR δ 1.43 (s, 9 H, $C(CH_3)_3$), 2.33 (dd, $J_{8,8'}$ = 15.8, $J_{8,7}$ = 5.8, 1 H, H-8), 2.53 (br s, 1 H, H-4), 2.55 (dd, $J_{8',8}$ = 15.8, $J_{8',7}$ = 9.0, 1 H, H-8′), 2.66 (dd, $J_{7,8'}$ = 9.0, $J_{7,8}$ = 5.8, 1 H, H-7), 3.49 (s, 3 H, CH_3O), 3.79 (d, J = 1.7, 1 H, H-6), 4.14 (br s, 1 H, H-5), 4.29 (br s, 1 H, H-1), 4.45 (ABq, J = 11.5, Δδ = 0.05, 2 H, $ArCH_2$), 4.59 (ABq, J = 12.2, Δδ = 0.13, 2 H, $ArCH_2$), 5.15 (d, $J_{3,4}$ = 2.9, 1 H, H-3), 7.2–7.4 (m, 10 H, ArH); ^{13}C NMR δ 28.1 ($C(CH_3)_3$), 31.9 (C-8), 42.8 (C-7), 49.2 (C-4), 56.7 (CH_3O), 71.0 and 71.1 ($ArCH_2$), 78.8 (C-5), 79.8 (C-1), 80.7 ($C(CH_3)_3$), 86.8 (C-6), 104.1 (C-3), 127.62, 127.65, 127.7, 128.0, 128.3, 128.4, 138.3, 171.6 (COOR); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = −9.6° (c 1.77, $CHCl_3$); LRMS (CI/NH_3) m/z 472 (M + NH_4)$^+$; HRMS calcd for $C_{27}H_{35}O_6$ (M + H)$^+$ 455.2434, found 455.2454. For **21b** (lower R_f): ^{1}H NMR δ 1.39 (s, 9 H, $C(CH_3)_3$), 2.45 (dd, $J_{8,8'}$ = 19.1, $J_{8,7}$ = 10.3, 1 H, H-8), 2.6–2.7 (m, 3 H, H-4, H-7, H-8′), 3.47 (s, 3 H, CH_3O), 4.00 (br s, 1 H, H-6), 4.24 (br s, 1 H, H-5), 4.31 (br s, 1 H, H-1), 4.46 (ABq, J = 11.7, Δδ = 0.08, 2 H, $ArCH_2$), 4.60 (ABq, J = 12.3, Δδ = 0.08, 2 H, $ArCH_2$), 5.12 (d, J = 2.9, 1 H, H-3), 7.27–7.40 (m, 10 H, ArH); ^{13}C NMR δ 28.1 ($C(CH_3)_3$), 32.8 (C-8), 45.2 (C-7), 47.5 (C-4), 56.4 (CH_3O), 71.4 and 71.5 ($ArCH_2$), 79.5 (C-5), 80.0 (C-1), 86.7 (C-6), 105.5 (C-3), 127.47, 127.51, 127.6, 128.0, 128.32, 128.33, 169.8 (COOR); IR (neat) 1720 cm^{-1}; $[\alpha]^{20}_D$ = −8.9° (c 0.18, $CHCl_3$); LRMS (CI/NH_3) m/z 472 (M + NH_4)$^+$, 455 MH^+; HRMS calcd for $C_{27}H_{35}O_6$ MH^+ 455.2434, found 455.2436.

(1*R*,3*R*,4*S*,5*R*,6*S*,7*R*)-5,6-(Isopropylidenedioxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid Ethyl Ester (22) and (1*R*,3*R*,4*S*,5*R*,6*S*,7*S*)-5,6-(Isopropylidendioxy)-3-methoxy-2-oxabicyclo[2.2.1]heptane-7-acetic Acid Ethyl Ester (23). A. Cyclization of iodide (*E*)-**19** (147 mg, 0.357 mM), effected by the Standard Procedure (KF treatment before chromatography was employed), afforded bicyclic compounds **22** and **23**, which were inseparable by flash chromatography (100 mg, 98% (**22**:**23**, 8:1), determined by GC): ^{1}H NMR δ 1.2–1.35 (m, 6 H, CH_2CH_3, CH_3), 1.47 (s, 3 H, CH_3 major isomer), 1.51 (s, 3 H, CH_3, minor isomer), 2.5–2.9 (m, 4 H, H-4, H-7, H-8, H-8′), 3.34 (s, 3 H, OCH_3), 4.0–4.3 (m, 5 H, H-5, H-6, H-1, CH_2CH_3), 4.29 (s, 1 H, H-3, major isomer), 4.36 (s, 1 H, H-3, minor isomer); GC/CIMS (CH_4/NH_3) major isomer (**30**) retention time = 5.3 min, m/z 304 ((M + NH_4)$^+$, 100), 287 (MH^+, 68), 272 (11); minor isomer (**31**) retention time = 5.5 min, m/z 304 ((M + NH_4)$^+$, 60), 287 (MH^+, 33), 272 (11), 214 (100).

B. Similar cyclization of iodide (*Z*)-**19** (85 mg, 0.706 mM) afforded bicyclic **22** (58 mg, 97%) exclusively: ^{1}H NMR δ 1.25 (t, J = 7.1, 3 H, CH_2CH_3), 1.29 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.56 (br s, 1 H, H-4), 2.59 (m, 1 H, H-7), 2.71 (dd, $J_{8,8'}$ = 12.9, $J_{8,7}$ = 5.9, 1 H, H-8), 2.76 (dd, $J_{8',8}$ = 12.9, $J_{8',7}$ = 8.8, 1 H, H-8′), 3.34 (s, 3 H, OCH_3), 4.1–4.2 (m, 5 H, H-5, H-6, H-1, CH_2CH_3), 4.29 (br s, 1 H, H-3); ^{13}C NMR δ 14.3, 24.3, 25.6, 30.7, 37.1, 48.1, 55.4, 60.3, 77.8, 79.6, 79.7, 103.3, 111.9, 173.0; IR (neat) 1725 cm^{-1}; $[\alpha]^{19}_D$ = −39.4° (c 1.64, $CHCl_3$); GC/CIMS (CH_4/NH_3) m/z 304 ((M + NH_4)$^+$, 100), 287 (MH^+, 54), 272 (1), 255 (73).

Formation of 2-Oxabicyclo[2.2.2]octanes. Compounds 25a and 26. Iodide **11b** (195 mg, 0.243 mM) was cyclized following the Standard Procedure to afford bicyclic compound **24** (total 134 mg, 82%) after flash chromatography (10% → 20% diethyl ether–PE) as an inseparable mixture in a 5:1 ratio as determined by integration of the signal for H-3: major isomer δ 5.06 (d, J = 1.6, 1 H, H-3); minor isomer δ 4.89 (d, J = 2.0, 1 H, H-3); IR (neat, mixture) 1730, 1615, 1515 cm^{-1}; GC/CIMS (NH_3/CH_4) m/z 694 (M + NH_4)$^+$. To a solution of the mixture (30.6 mg, 0.452 mM) in THF (2 mL) was added tetra-*n*-butylammonium fluoride (0.05 mL, 1.1 M in THF). After the mixture was stirred for 4 h at room temperature, silica gel was added and the solvent was removed by rotary evaporation. Flash chromatography (25% → 50% EtOAc–PE) afforded, in order of elution, hydroxy ester **25a** (16.9 mg, 66%) and lactone **26** (3.8 mg, 16%). For **25a**: ^{1}H NMR δ 1.25 (J = 7.2, 3 H, CH_2CH_3), 2.01 (br s, 1 H, H-4), 2.31–2.58 (m, 3 H, H-5, H-9, H-9′), 3.71 (dd, $J_{OH,6}$ = $J_{6,5}$ = 4.3, 1 H, H-6), 3.78 (s, 3 H, $ArOCH_3$), 3.99 (d, $J_{3,4}$ = 2.4, 1 H, H-4), 4.11 (br s, 1 H, H-8), 4.15 (q, J = 7.2, 2 H, CH_2CH_3), 4.27 (dd, $J_{4,8} \cong J_{8,7} \cong 3$, 1 H, H-8), 4.48 (s, 2 H, $ArCH_2$), 4.61 (ABq, J = 12.0 Δδ = 0.10, 2 H, $ArCH_2$), 4.61 (ABq, J = 11.5, Δδ = 0.41, 2 H, $ArCH_2$), 4.97 (d, $J_{3,4}$ = 1.6, 1 H, H-3), 6.80 (d, J = 8.6, 2 H, ArH), 7.21–7.39 (m, 12 H, ArH); IR (neat) 3475, 1730, 1615, 1590, 1515 cm^{-1}; $[\alpha]^{18}_D$ = +42.4° (c 1.69, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 580 (M + NH_4)$^+$; HRMS calcd for $C_{33}H_{42}O_8N$ (M + NH_4)$^+$ 580.2910, found 580.2907. For **26**: ^{1}H NMR δ 2.40 (br s, 1 H, H-4), 2.57–2.71 (m, 2 H, H-5, H-9), 2.89–3.02 (m, 1 H, H-9′), 3.79 (s, 3 H, $ArOCH_3$), 3.91 (br s, 1 H, H-7), 4.31 (br s, 1 H, H-8), 4.47 (ABq, J = 11.5, Δδ = 0.11, 2 H, $ArCH_2$), 4.52 (br s, 1 H, H-1), 4.58 (ABq, J = 11.6, Δδ = 0.12, 2 H, $ArCH_2$), 4.63 (ABq, J = 11.4, Δδ = 0.39, 2 H, $ArCH_2$), 4.78–4.89 (m, 2 H, H-3, H-6), 6.79 (d, J = 8.6, 2 H, ArH), 7.20–7.39 (m, 12 H, ArH); IR (neat) 1790, 1615, 1590, 1515 cm^{-1}; $[\alpha]^{20}_D$ = +48.0° (c 0.64, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 534 (M + NH_4)$^+$; HRMS calcd for $C_{31}H_{36}O_7N$ (M + NH_4)$^+$ 534.2492, found 534.2494.

Compound 25b. A a solution of **25a** (18.9 mg, 0.0339 mmol) in pyridine (2 mL) at 0 °C was added benzoyl chloride (0.05 mL). The reaction mixture was stirred for 1 h at 0 °C and for 2 h at room temperature and diluted with diethyl ether (50 mL). The resulting mixture was washed in succession with saturated aqueous sodium bicarbonate (2 × 25 mL), water (25 mL), and brine (25 mL). The organic layer was dried over Na_2SO_4, and the solvent was removed by rotary evaporation. Flash chromatography (10% → 25% EtOAc–PE) of the residue afforded the benzoate **25b** (23.1 mg, 97%): ^{1}H NMR δ 1.17 (t, J = 7.1, 3 H, CH_3CH_2O), 2.41–2.54 (m, 2 H, H-4, H-9), 2.77–2.90 (m, 2 H, H-5, H-9′), 3.81 (s, 3 H, CH_3O), 3.91 (br s, 1 H, H-7), 4.06 (q, J = 7.1, 2 H, CH_3CH_2O), 4.25 (d, $J_{5,6} \cong 4$, 1 H, H-1), 4.36 (dd, $J_{4,8} \cong J_{8,7} \cong 3$, 1 H, H-8), 4.54 (ABq, J = 11.6, Δδ = 0.11, 2 H, $ArCH_2$), 4.61 (ABq, J = 12, Δδ ≅ 0.03, 2 H, $ArCH_2$), 4.67 (ABq, J = 11.4, Δδ = 0.21, 2 H, $ArCH_2$), 4.99 (dd, $J_{1,6}$ = $J_{6,5}$ = 4.5, 1 H, H-6), 5.18 (d, $J_{3,4}$ = 1.7, 1 H, H-3), 6.84 (d, J = 8.7, 2 H, ArH), 7.20–7.45 (m, 14 H, ArH),

7.54–7.60 (m, 1 H, ArH), 7.88–7.92 (m, 2 H, ArH); GC/CIMS (NH_3/CH_4) m/z 684 $(M + NH_4)^+$; HRMS calcd for $C_{40}H_{46}NO_9$ 684.3173, found 684.3153.

Compounds 28 and 29. Iodide **11c** (143 mg, 0.178 mM) was cyclized to bicyclic compound **27** (total 89.5 mg, 83%) following the Standard Procedure. Flash chromatography (5% → 25% diethyl ether–PE) provided **27** as an inseparable mixture in a ratio of 3:1 as determined by integration of the signal for H-3: major isomer δ 5.10 (d, J = 1.0, 1 H, H-3); minor isomer δ 5.06 (d, J = 2.4, 1 H, H-3); IR (neat, mixture) 1730, 1615, 1515 cm^{-1}; GC/CIMS (NH_3/CH_4) m/z 694 $(M + NH_4)^+$. To a solution of the mixture (28.2 mg, 0.0417 mM) in THF (2 mL) was added tetra-*n*-butylammonium fluoride (0.05 mL, 1.1 M in THF). After the mixture was stirred for 2 h at room temperature, silica gel was added and the solvent was removed by rotary evaporation. Flash chromatography (30% → 70% EtOAc–PE) afforded, in order of elution, lactone **28** (15.2, mg, 71%) and hydroxy ester **29** (5.4 mg, 23%). For **28**: ^1H NMR δ 2.35–2.40 (m, 1 H, H-4), 2.50 (dd, $J_{5,9}$ = 4.4, $J_{9,9'}$ = 19.0, 1 H, H-9), 2.79 (dd, $J_{5,9'}$ = 12.0, $J_{9,9'}$ = 19.0, 1 H, H-9′), 3.08–3.19 (m, 1 H, H-5), 3.45 (br s, 1 H, H-7), 3.80 (s, 3 H, ArOCH_3), 4.31 (br s, 1 H, H-8), 4.38 (br s, 1 H, H-1), 4.47 (ABq, J = 11.4, $\Delta\delta$ = 0.05, 2 H, ArCH_2), 4.52 (dd, $J_{1,6}$ = 1.9, $J_{6,5}$ = 9.4, 1 H, H-6), 4.63 (ABq, J = 11.8, $\Delta\delta$ = 0.10, 2 H, ArCH_2), 4.63 (ABq, J = 11.2, $\Delta\delta$ = 0.45, 2 H, ArCH_2), 5.12 (d, $J_{3,4}$ = 2.2, 1 H, H-3), 6.80 (d, J = 8.6, 2 H, ArH), 7.20–7.40 (m, 12 H, ArH); IR (neat) 1775, 1615, 1590, 1515 cm^{-1}; $[\alpha]^{20}_D$ = +17.9° (*c* 1.52, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 534 $(M + NH_4)^+$; HRMS calcd for $C_{31}H_{36}O_7N$ $(M + NH_4)^+$ 534.2492, found 534.2483. For **29**: ^1H NMR δ 1.24 (t, J = 7.1, 3 H, CH_2CH_3), 1.92–1.98 (m, 1 H, H-5), 2.27 (br s, 1 H, H-4), 2.61 (dd, $J_{5,9}$ = 4.2, $J_{9,9'}$ = 18.0, 1 H, H-9), 2.96 (dd, $J_{5,9}$ = 10.8, $J_{9,9'}$ = 18.0, 1 H, H-9′), 3.45 (br s, 1 H, H-7), 3.56 (d, $J_{6,5}$ = 2.7, 1 H, H-6), 3.79 (s, 3 H, ArOCH_3), 4.13 (q, J = 7.1, 2 H, CH_2CH$_3$), 4.23 (br s, 1 H, H-1), 4.25 (br s, 1 H, H-8), 4.45 (ABq, J = 11.5, $\Delta\delta$ = 0.11, 2 H, ArCH_2), 4.63 (ABq, J = 12.1, $\Delta\delta$ = 0.13, 2 H, ArCH_2), 4.66 (ABq, J = 11.4, $\Delta\delta$ = 0.43, 2 H, ArCH_2), 5.05 (d, $J_{3,4}$ = 2.4, 1 H, H-3), 6.80 (d, J = 8.7, 2 H, ArH), 7.22–7.40 (m, 12 H, ArH); IR (neat) 3450, 1730, 1615, 1590, 1515 cm^{-1}; $[\alpha]^{20}_D$ = +16.3° (*c* 0.51, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 580 $(M + NH_4)^+$; HRMS calcd for $C_{33}H_{42}O_8N$ $(M + NH_4)^+$ 580.2910, found 580.2907.

Compounds 32a → 35. Iodide **15** (102.8 mg, 0.158 mM) was cyclized to give a mixture of bicyclic compounds (total 85 mg, 100%) following the Standard Procedure. Flash chromatography (5% → 20% EtOAc–PE) provided the two sets of epimers **30** (53 mg) and **31** (31 mg) in a 1:3 ratio. The C-6 configurations were determined by the following transformations.

Compounds 32a and 33. Desilylation of the mixture **30** (53 mg) as described for the preparation of **28** provided the hydroxy ester **32a** (23.1 mg) and the lactone **33** (4.8 mg). For **32a**: ^1H NMR δ 1.28 (t, J = 7.1, 3 H, CH_3CH$_2$O), 2.01 (br s, 1 H, H-4), 2.33–2.43 (m, 1 H, H-5), 2.47 (dd, $J_{9,9'}$ = 17.3, $J_{5,9}$ = 3.9, 1 H, H-9), 2.61 (dd, $J_{9,9'}$ = 17.3, $5_{5,9'}$ = 12.0, 1 H, H-9′), 3.36 (s, 3 H, CH_3O), 3.43 (s, 3 H, CH_3O), 3.61 (br s, 1 H, OH), 3.72 (dd, $J_{1,6} \approx J_{OH,6} \approx 4$, 1 H, H-6), 3.93 (d, $J_{8,7}$ = 2.7, 1 H, H-7), 4.06 (d, $J_{1,6}$ = 3.7, 1 H, H-1), 4.18 (q, J = 7.1, 2 H, CH$_3$CH_2O), 4.30 (dd, $J_{4,8} \approx J_{8,7} \approx 3$, 1 H, H-8), 4.60–4.70 (m, 4 H, ArCH_2, CH$_3$OCH_2), 4.79 (d, $J_{1,2}$ = 1.7, 1 H, H-3), 7.23–7.42 (m, 5 H, ArH); IR (neat) 3450, 1730 cm^{-1}; $[\alpha]^{20}_D$ = +45.9° (*c* 0.64, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z; HRMS calcd for $C_{21}H_{30}O_8$ 410.1941, found 410.1929. For **33**: ^1H NMR δ 2.35 (br s, 1 H, H-4), 2.62–2.75 (m, 2 H, H-5, H-9), 2.97 (dd, $J_{9,9'}$ = 15.9, $J_{5,9'}$ = 8.0, 1 H, H-9′), 3.34 (s, 3 H, CH_3O), 3.44 (s, 3 H, CH_3O), 3.80 (br s, 1 H, H-7), 4.34–4.42 (m, 2 H, H-8, H-1), 4.56–4.70 (m, 4 H, ArCH_2, CH$_3$OCH_2), 4.71 (d, $J_{3,4}$ = 2.4, 1 H, H-3), 4.84 (dd, $J_{1,6}$ = 5.6, $J_{6,5}$ = 8.3, 1 H, H-6), 7.25–7.43 (m, 5 H, ArH); IR (neat) 1790 cm^{-1}; GC/CIMS (NH_3/CH_4) m/z 382 $(M + NH_4)^+$; HRMS calcd for $C_{19}H_{24}O_7$ 364.1522, found 364.1522.

Similar treatment of the diastereoisomers **31** (31 mg) led to lactone **34** and hydroxy ester **35** as a chromatographically inseparable mixture (10.7 mg, 3:1 ratio): ^1H NMR (partial) δ 4.85 (d, J = 2.5, H-3 of **34**), 4.89 (d, J = 2.2, H-3 of **35**); IR (neat) 3450, 1785, 1730 cm^{-1}; GC/CIMS (NH_3/CH_4) m/z 428 (**35** $(M + NH_4)^+$), 382 (**34** $(M + NH_4)^+$); HRMS calcd for $C_{21}H_{30}O_8$ (**35**) and $C_{19}H_{24}O_7$ (**34**) 410.1941 (**35**), 364.1522 (**34**), found 410.1929 (**35**), 364.1522 (**34**).

Compound 32b. As described above for **25a** affording the benzoate **32b** (16.9 mg): ^1H NMR δ 1.17 (t, J = 7.1, 3 H, CH_3CH$_2$O), 2.27 (br s, 1 H, H-4), 2.48 (dd, $J_{9,9'}$ = 15.4, $J_{5,9}$ = 9.5, 1 H, H-9), 2.67–2.77 (m, 1 H, H-5), 2.86 (dd, $J_{9,9'}$ = 15.4, $J_{5,9'}$ = 6.1, 1 H, H-9′), 3.39 (s, 3 H, CH_3O), 3.46 (s, 3 H, CH_3O), 3.84 (d, $J_{8,7}$ = 2.3, 1 H, H-7), 4.04 (q, J = 7.1, 2 H, CH$_3$CH_2O), 4.13–4.15 (m, 1 H, H-1), 4.37 (dd, $J_{4,8}$ = $J_{8,7}$ = 2.3, 1 H, H-8), 4.64 (s, 2 H, CH$_3$OCH_2), 4.69 (ABq, J = 6.9, $\Delta\delta$ = 0.02, 2 H, ArCH_2), 4.89–4.94 (m, 2 H, H-3, H-6), 7.19–7.44 (m, 7 H, ArH), 7.52–7.60 (m, 1 H, ArH), 7.82–7.89 (m, 2 H, ArH); IR (neat) 1730 cm^{-1}; $[\alpha]^{20}_D$ = +44.9° (*c* 1.62, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 532 $(M + NH_4)^+$; HRMS calcd for $C_{28}H_{38}O_9N$ $(M + NH_4)^+$ 532.2547, found 532.2530.

Solvolysis of Bicyclic Compounds. Method A. A solution of bicyclic compound **20a** (24 mg, 0.05 mM) and camphorsulfonic acid (CSA) (cat.) in dry MeOH (0.5 mL) was stirred under argon at room temperature for 4 h. One drop of triethylamine was added, and the reaction mixture was concentrated to dryness. Purification by flash chromatography afforded lactone **37a** as a white solid (22 mg, 95%).

Method B. A solution of bicyclic compound **20a** (50 mg, 0.11 mM) and pyridinium *p*-toluenesulfonate (PPTS)[22] (2 mg) in dry MeOH (1.5 mL) was stirred under argon at room temperature for 56 h. A cold 5% aqueous solution of $NaHCO_3$ (~4 mL) was added, and the mixture was extracted with EtOAc. After drying with $MgSO_4$ and evaporation of the solvents under reduced pressure, flash chromatography afforded, in order of elution, **38** (4 mg, 8%), **36** (21 mg, 39%), and **37a** (22 mg, 45%). Total yield: 92%. Compound **26** was converted into **37a** spontaneously upon standing. For **38**: ^1H NMR δ 1.24 (t, J = 7.1, 3 H, CH$_2$CH_3), 2.48–2.62 (m, 3 H, H-4, H-7, H-8), 2.92 (dd, $J_{8',8}$ = 17.2, $J_{8',7}$ = 9.1, 1 H, H-8′), 3.44 (s, 3 H, CH_3O), 3.90 (m, 1 H, H-6), 4.12 (q, J = 7.1, 2 H, CH_2CH$_3$), 4.42 (m, 1 H, H-5), 4.64 (s, 2 H, ArCH_2), 4.73 (s, 1 H, H-3), 4.79 (br s, 1 H, H-5), 7.24–7.35 (m, 5 H, ArH), 7.46 (m, 2 H, ArH), 7.59 (m, 1 H, ArH), 8.01 (m, 2 H, ArH); GC/CIMS (*i*-C_4H_{10}) m/z 441 MH^+, 431 $(M - CH_3O)^+$; HRMS calcd for $C_{25}H_{29}O_7$ MH^+ 441.1913, found 441.1921. For **36**: ^1H NMR δ 1.27 (t, J = 7.1, 3 H, CH$_2$CH_3), 2.51 (ddd, $J_{2',H} \cong J_{2',3'} \cong J_{2',1'} \cong 5$, 1 H, H-2′), 2.56 (dd, $J_{2a,2b}$ = 16.9, $J_{2a,1'}$ = 6.3, 1 H, H-2a), 2.78 (dd, $J_{2b,2a}$ = 16.9, $J_{2b,1'}$ = 8.6, 1 H, H-2b), 2.87 (m, 1 H, H-1′), 3.30 (s, 3 H, CH_3O), 3.34 (d, J = 7.9, 1 H, O*H*), 3.49 (s, 3 H, CH_3O), 4.00 (dd, $J_{4',3'}$ = 6.4, $J_{4',5'}$ = 4.6, 1 H, H-4′), 4.11 (ddd, $J_{5',4'}$ = 4.6, $J_{5',1'} \cong J_{5',OH} \cong 8$, 1 H, H-5′), 4.13 (q, J = 7.1, 2 H, CH_2CH$_3$), 4.68 (ABq, J = 12.5, $\Delta\delta$ = 0.09, 2 H, ArCH_2), 4.76 (d, $J_{H,2'}$ = 5.1, 1 H, C*H*(OMe)$_2$), 5.45 (dd, $J_{3',4'}$ = 6.4, $J_{3',2'}$ = 4.6, 1 H, H-3′), 7.2–7.6 (m, 8 H, ArH), 8.00 (m, 2 H, ArH); ^{13}C NMR δ 14.3 (CH$_2$*C*H$_3$), 31.1 (C-2), 37.7 (C-1′), 46.6 (C-2′), 55.1 and 56.0 (CH_3O), 60.2 (*C*H$_2$CH$_3$), 71.7 (ArCH_2), 72.2 (C-5′), 80.3 (C-3′), 83.9 (C-4′), 106.1 (*C*H(OMe)$_2$), 127.73, 127.76, 127.8, 128.4, 129.7, 130.0, 133.1, 137.7, 166.1 (PhCOOR), 173.0, (COOEt); IR (neat) 3450, 1720 cm^{-1}; $[\alpha]^{20}_D$ = −22.3° (*c* 1.28, $CHCl_3$); LRMS (CI/NH_3) m/z 490 $(M + NH_4)^+$. Anal. Calcd for $C_{26}H_{32}O_8$: C, 66.09; H, 6.83. Found: C, 66.29; H, 6.86. For **37a**: ^1H NMR δ 2.55 (dd, $J_{3,3'}$ = 18.4, $J_{3,3a}$ = 10.4, 1 H, H-3), 2.56 (ddd, $J_{4,3a}$ = 9.5, $J_{4,H} \cong J_{4,5} \cong 7$, 1 H, H-4), 2.82 (dd, $J_{3',3}$ = 18.4, $J_{3',3a}$ = 6.9, 1 H, H-3′), 3.19 (m, 1 H, H-3a), 3.28 (s, 3 H, CH_3O), 3.37 (s, 3 H, CH_3O), 4.03 (dd, $J_{6,6a} \cong J_{6,5} \cong 5.5$, 1 H, H-6), 4.52 (d, $J_{H,4}$ = 7.7, 1 H, C*H*(OMe)$_2$), 4.71 (ABq, J = 12.1, $\Delta\delta$ = 0.09, 2 H, ArCH_2), 4.95 (dd, $J_{6a,6}$ = 5.1, $J_{6a,3a}$ = 7.6, 1 H, H-6a), 5.61 (dd, $J_{5,4} \cong J_{5,6} \cong 5.5$, 1 H, H-5), 7.2–7.7 (m, 8 H, ArH), 8.00 (m, 2 H, ArH); ^{13}C NMR δ 30.7 (C-3), 36.9 (C-3a*), 45.1 (C-4*), 54.2 and 54.3 (OCH_3), 72.4 (ArCH_2), 77.3 (C-5*), 80.1 (C-6a*), 80.9 (C-6*), 104.1 (*C*H(OMe)$_2$), 127.7, 127.8, 128.4, 129.6, 129.7, 133.2, 137.4, 165.5 (PhCO_2R), 177.1 (*C*O$_2$R lactone); IR (neat) 1780, 1720 cm^{-1}; $[\alpha]^{20}_D$ = −27.05° (*c* 1.9, $CHCl_3$); LRMS (CI/NH_3) m/z 444 $(M + NH_4)^+$. Anal. Calcd for $C_{24}H_{26}O_7$: C, 67.59; H, 6.14. Found: C, 67.70; H, 6.35.

[3a*R*-(3aα,4α,5β,6β,6aα)]-5,6-Bis(benzyloxy)hexahydro-4-(1,1′-dimethoxymethyl)-2*H*-cyclopenta[*b*]furan-2-one (37b). The bicyclic compound **20b** (8 mg) was converted to lactone **37b** (white solid, 6.1 mg, 84%) as reported for the opening of bicyclic compound **20a** (Method A): mp 103 °C; ^1H NMR δ 2.42 (ddd, $J_{4,3a}$ = 9.5, $J_{4,H} \cong J_{4,5} \cong 6.8$, 1 H, H-4), 2.48 (dd, $J_{3',3}$ = 18.3, $J_{3',3a}$ = 10.3, 1 H, H-3′), 2.84 (dd, $J_{3,3'}$ = 18.3, $J_{3,3a}$ = 6.7, 1 H, H-3), 3.0–3.1 (m, 1 H, H-3a), 3.31 (s, 3 H, CH_3O), 3.34 (s, 3 H, CH_3O), 3.9 (dd, $J_{6,5} \cong J_{6,6a} \cong 5$, 1 H, H-6), 4.01 (dd, $J_{4,5}$ = 6.7, $J_{5,6}$ = 5.3, 1 H, H-5), 4.38 (d, $J_{H,4}$ = 6.8, 1 H, C*H*(OMe)$_2$), 4.63 (ABq, J = 11.8, $\Delta\delta$ = 0.23, 2 H, ArCH_2), 4.70 (ABq, J = 11.6, $\Delta\delta$ = 0.10, 2 H, ArCH_2), 4.91 (dd, $J_{6a,3a}$ = 7.3, $J_{6a,6}$ = 4.9, 1 H, H-6a), 7.2–7.4

(m, 10 H, ArH); ^{13}C NMR δ 31.1 (C-3), 36.5 (C-3a*), 45.9 (C-4*), 54.4 and 55.3 (CH_3O), 72.4 and 72.6 ($ArCH_2$), 80.9 (C-5*), 82.6 (C-6a*), 82.7 (C-6*), 104.8 ($CH(OMe)_2$), 127.8, 127.95, 127.99, 128.4, 128.5, 137.6, 138.1, 177.7 (COOR lactone); IR (neat) 1755, 1215, 775 cm^{-1}; $[\alpha]^{20}_D = -34.34°$ (c 0.82, $CHCl_3$); GC/CIMS (CH_4) m/z 441 ($M + C_2H_5$)$^+$, 381 ($MH - CH_3OH$)$^+$; HRMS calcd for $C_{24}H_{32}NO_6$ ($M + NH_4$)$^+$ 430.2230, found 430.2233.

[3a*S*-(4*S*,5*R*,6*S*,6a*R*)]-5,6-Diacetoxyhexahydro-4-(dimethoxymethyl)-2*H*-cyclopenta[*β*]furan-2-one (40). A solution of bicyclic compound **22** (33 mg, 0.115 mM) and CSA (12 mg) in MeOH (3 mL) was stirred at 40 °C under argon until all of the starting material and the intermediate lactone **39** had been consumed. Addition of triethylamine and evaporation of the solvents gave the crude diol which was dissolved in EtOAc and treated with (dimethylamino)pyridine (cat.) and Ac_2O (excess) at room temperature. An ice-cooled solution of $NaHCO_3$ was added, and the aqueous phase was extracted with EtOAc. Drying and evaporation of the organic solvent followed by filtration through silica gel afforded lactone **40** (32 mg, 88%) as a colorless oil: ^1H NMR δ 2.04 (s, 3 H, CH_3CO_2R), 2.09 (s, 3 H, CH_3CO_2R), 2.59 (dd, $J_{3,3'}$ = 18.9, $J_{3,3a}$ = 10.9, 1 H, H-3), 2.69 (ddd, $J_{4,3a}$ = 9.6, $J_{4,5}$ = 7.5, $J_{4,H}$ = 5.4, 1 H, H-4), 2.95 (dd, $J_{3',3}$ = 18.9, $J_{3',3a}$ = 4.3, 1 H, H-3'), 3.23 (m, 1 H, H-3a), 3.39 (s, 3 H, CH_3O), 3.41 (s, 3 H, CH_3O), 4.40 (d, $J_{H,4}$ = 5.4, 1 H, $CH(OMe)_2$), 4.79 (dd, $J_{6a,3a}$ = 8.0, $J_{6a,6}$ = 1.9, 1 H H-6a), 5.3-5.4 (m, 2 H, H-5, H-6); ^{13}C NMR δ 20.69, 20.73, 30.2 (CH_2CO_2R), 35.2, 45.7, 55.6 and 55.8 (OCH_3), 72.5, 75.1, 84.0, 104.8 ($CH(OMe)_2$), 169.3 and 169.7 (CH_3CO_2R), 176.4 (CO_2R lactone); IR (neat) 1790, 1750 cm^{-1}; $[\alpha]^{18}_D = -32.0°$ (c 1.5, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 334 (($M + NH_4$)$^+$, 100), 317 (MH^+, 2).

Formation of Functionalized Cyclohexanes. Ethyl 6-(Benzoyloxy)-3,4-bis(benzyloxy)-5-hydroxy-2-[2-(1,3-dithianyl)]cyclohex-1-ylacetate (44b). Stock solutions of boron trifluoride etherate (0.07 mL) in dry CH_2Cl_2 (0.93 mL) and 1,3-propanedithiol (0.06 mL) in dry CH_2Cl_2 (0.94 mL) were prepared. To a solution of benzoate **25b** (25.1 mg, 0.0376 mmol) in dry CH_2Cl_2 (1 mL) at -15 °C (ice-salt bath) was added 1,3-propanedithiol stock solution (0.1 mL, 0.05 mmol) and boron-trifluoride etherate stock solution (0.1 mL, 0.05 mmol). The resulting solution was stirred at -15 °C for 1 h; TLC (20% EtOAc-PE) showed the appearance of a spot with higher R_f. Another aliquot (0.1 mL) of each stock solution was added to the reaction mixture, and after an additional 15 min, no change was observed by TLC. The reaction contents were warmed to 0 °C and stirred for 30 min. TLC showed the apparance of a spot with lower R_f. The reaction mixture was diluted with EtOAc (30 mL) and washed in succession with saturated aqueous sodium bicarbonate (25 mL) and brine (25 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed by rotary evaporation. Flash chromatography (10% → 30% EtOAc-PE) of the residue afforded **44a** (14.9 mg, 62%): ^1H NMR δ 1.25 (t, J = 7.1, 3 H, CH_2CH_3), 1.81-1.97 (m, 1 H, $SCH_2CH_2CH_2S$), 2.04-2.16 (m, 1 H, $SCH_2CH_2CH_2S$), 2.58-2.99 (m, 7 H, SCHS, H-2', H-2a, $SCH_2CH_2CH_2S$), 3.22-3.66 (m, 1 H, H-2b), 3.82 (dd, $J_{3',4'}$ = 8.0, $J_{4',5'}$ = 3.5, 1 H, H-4'), 4.05-4.25 (m, 4 H, H-3', H-5', CH_2CH_3), 4.66 (ABq, J = 11.3, $\Delta\delta$ = 0.11, 2 H, $ArCH_2$), 4.77 (d, $J_{H,2'}$ = 5.7, 1 H, SCHS), 4.94 (ABq, J = 10.4, $\Delta\delta$ = 0.08, $ArCH_2$), 5.45 (t, $J_{5',6'} = J_{6',1'}$ = 3.7, 1 H, H-6'), 7.23-7.48 (m, 12 H, ArH), 7.53-7.64 (m, 1 H, ArH), 7.94-8.00 (m, 2 H, ArH); IR (neat) 3475, 1725 cm^{-1}; $[\alpha]^{20}_D = +6.4°$ (c 1.49, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 654 ($M + NH_4$)$^+$; HRMS calcd for $C_{35}H_{40}NO_7S_2$ ($M + NH_4$)$^+$ 654.2559, found 654.2530. A small sample of **44a** was acetylated to give **44b** (Ac_2O/EtOAc/cat. DMAP): ^1H NMR δ 1.28 (t, J = 7.1, 3 H, CH_2CH_3), 1.80-1.97 (m, 1 H, $SCH_2CH_2CH_2S$), 2.06-2.17 (m, 1 H, $SCH_2CH_2CH_2S$), 2.20 (s, 3 H, CH_3CO_2), 2.67-2.98 (m, 7 H, H-2', H-1', H-2a, $SCH_2CH_2CH_2S$), 3.38-3.45 (m, 1 H, H-2b), 3.90 (dd, $J_{3',4'}$ = 8.8, $J_{4',5'}$ = 3.7, 1 H, H-4'), 4.01 (dd, $J_{2',3'}$ = 10.6, $J_{3',4'}$ = 8.8, 1 H, H-3'), 4.12-4.25 (m, 2 H, CH_2CH_3), 4.61 (ABq, J = 10.9, $\Delta\delta$ = 0.16, 2 H, $ArCH_2$), 4.81 (d, $J_{H,2'}$ = 5.4, 1 H, SCHS), 4.96 (ABq, J = 10.2, $\Delta\delta$ = 0.19, 2 H, $ArCH_2$), 5.30 (dd, $J_{4',5'} \approx J_{5'6'} \approx$ 3, 1 H, H-5'), 5.55 (dd, $J_{5',6'} \approx J_{6',1'} \approx$ 3, 1 H, H-6'), 7.23-7.48 (m, 12 H, ArH), 7.53-7.61 (m, 1, ArH), 7.90-7.96 (m, 2 H, ArH); IR (neat) 1745, 1725 cm^{-1}; GC/CIMS (NH_3/CH_4) m/z 696 ($M + NH_4$)$^+$; HRMS calcd for $C_{37}H_{46}NO_8S_2$ ($M + NH_4$)$^+$ 696.2665, found 696.2648.

Ethyl 3,5-Diacetoxy-6-(benzoyloxy)-4-(benzyloxy)-2-[2-(1,3-dithianyl)]cyclohex-1-ylacetate (45). The bicyclic benzoate **32b** (15.1 mg, 0.0293 mmol) was ring opened to give a diol which was acetylated directly to give the diacetate **45** (12.3 mg, 66%), following the method described for the preparation of **44b**: ^1H NMR δ 1.23 (t, J = 7.1, 3 H, CH_3CH_2O), 1.73-1.93 (m, 1 H, $SCH_2CH_2CH_2S$), 1.98-2.20 (m, 1 H, $SCH_2CH_2CH_2S$), 2.12 (s, 6 H, CH_3CO_2), 2.61-3.01 (m, 7 H, H-2', H-2a, $SCH_2CH_2CH_2S$, H-1'), 3.17 (dd, $J_{2a,2b}$ = 15.8, $J_{1',2b}$ = 5.4, 1 H, H-2b), 3.74 (dd, $J_{3',4'}$ = 8.4, $J_{4',5'}$ = 3.5, 1 H, H-4'), 4.05-4.19 (m, 2 H, CH_3CH_2O), 4.39 (d, $J_{2',H}$ = 5.8, 1 H, SCHS), 4.55 (ABq, J = 12.2, $\Delta\delta$ = 0.07, 2 H, $ArCH_2$), 5.29-5.37 (m, 1 H, H-6'), 5.49 (dd, $J_{4',5'} \cong J_{5',6'} \cong$ 4, 1 H, H-5'), 5.55 (dd, $J_{2',3'} \cong J_{3',4'} \cong$ 9, 1 H, H-3'), 7.22-7.33 (br s, 5 H, ArH), 7.41-7.50 (m, 2 H, ArH), 7.56-7.63 (m, 1 H, ArH), 7.91-7.97 (m, 2 H, ArH); IR (neat) 1730 cm^{-1}; $[\alpha]^{20}_D = +6.0°$ (c 1.23, $CHCl_3$); GC/CIMS (NH_3/CH_4) m/z 648 ($M + NH_4$)$^+$; HRMS calcd for $C_{32}H_{42}O_9NS_2$ ($M + NH_4$)$^+$ 648.2301, found 648.2285.

A New Way toward *Z* α,β Unsaturated Esters: A Pyrethroid Application

Didier Babin,* Jacques Demassey, Jean Pierre Demoute, Phillipe Dutheil, Isabelle Terrie, and Jean Tessier

Roussel-Uclaf, Agrochemical Division, Chemical Research Department, 102 Route de Noisy, 93230 Romainville, France

Received June 3, 1991

Use of the stereospecific condensation of β carbalkoxysulfones with aldehydes, followed by the stereospecific reduction of the afforded sulfonyl acrylate with sodium dithionite allows us to propose this method as a new way to prepare *Z* α,β unsaturated esters. Steric hindrance seems to be the reason for the selectivity of the reduction and the mechanism was proved, by X-ray of an intermediate, to be a cis Michael addition of HSO_2^-, followed by an anti elimination of SO_2 and the sulfinate group. This method discovered in the pyrethroid series for the synthesis of acrinathrin 1 could have general application.

Introduction

RU 38702 (acrinathrin) 1 is a new miticide/insecticide recently introduced on the market. It belongs to the Roussel family of norpyrethrates characterized by their *Z* α,β unsaturated ester group. This geometry is the only one which gives good biological activity.[1] While searching for an industrial synthesis of this compound, we were in-

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0022-3263/92/1957-0584$03.00/0