Ring Contraction *vs* Fragmentation in the Intramolecular Reactions of 3-*O*-(Trifluoromethanesulfonyl)pyranosides. Efficient Synthesis of Branched-Chain Furanosides

Mohamed Kassou and Sergio Castillón*

Departament de Química, Universitat Rovira i Virgili, Pça. Imperial Tarraco 1, 43005 Tarragona, Spain

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Intramolecular reactions of several methyl 3-*O*-triflylpyranosides of *gluco*, *manno*, *galacto*, and *arabino* (2-deoxy-*gluco*) configuration are studied. Triflates **1b**–**6b**, of *gluco*, *manno*, and 2-deoxy-*gluco* configuration, give rise to ring-contraction products (branched-chain furanosides) **12**, **15**, **16**, **17**, **19**, and **20**, respectively. Triflates **7b** and **10b** of *galacto* configuration give the fragmentation products **21** and **23**, whereas the 2-deoxy-*galacto* derivative **8b** leads to ring-contraction product **20**, which shows the decisive influence of the configuration at position 4 and the presence of a 2-alkoxy group on the reaction process. When the results from 4,6-*O*-benzylidene derivatives (**1b**–**8b**) and 4,6-di-*O*-benzyl derivatives (**9b**–**11b**) are compared, it turns out that the presence of a 4,6-*O*-benzylidene protecting group favors the formation of ring-contraction products. The use of 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) as the solvent and pyridine or 2,6-di-*tert*-butyl-4-methylpyridine as the base allowed us to obtain good to excellent yields of ring-contraction or fragmentation products.

Carbohydrates have been extensively used as chiral synthons for the synthesis of enantiomerically pure compounds,[1] and numerous stereoselective transformations have been developed in this field. In relation to this, triflate derivatives[2] have been successfully used for inter[3] and intramolecular[4] nucleophilic substitution. However, some triflate derivatives of appropriately protected carbohydrates have given rise to other reactions, such as triflate migration,[5] ring contraction in 2-*O*-triflyl[6] as well as in 3-*O*-triflyl derivatives,[7–9] or fragmentation reactions,[10] and these have interesting applications in synthesis. Recently, Binkley reported a study of the intramolecular reactions of triflates with a neighboring hydroxy group and found that epoxide formation, elimination, or ring-contraction reactions may be produced, depending on the triflate position and on the relative stereochemistry of hydroxy and triflate groups.[7]

It is well established that a *trans*-diequatorial arrangement between the triflate and a C–C bond is a necessary condition for ring contraction or fragmentation and that the presence of a nonbonded lone pair antiperiplanar to the C–C bond facilitates cleavage.[10b,11] However, minor structural differences in the starting material cause drastic changes in the reaction process (see Scheme 1). Thus, methyl 3-*O*-(trifluoromethanesulfonyl)-β-*lyxo*-pyranosides (2-deoxy-*galacto* derivatives) give fragmentation[10] or ring contraction[7b] depending on the protection of OH at position 4 (eqs 1 and 2). On the other hand, when the unprotected OH is at position 2, a different ring contraction takes place[8] (eq 3), but in the same reaction type the *gluco* derivative gives an S_N2 reaction[8] (eq 4), while partial ring contraction was observed for a fully protected *gluco* derivative during treatment with $Bu_4N^+BH_4^-$ (eq 5).[9]

As a part of a program aimed at transforming readily available carbohydrates into valuable chiral synthons, we report a systematic study of the reaction of different fully protected monocyclic and bicyclic methyl 3-*O*-triflylpyranoside derivatives under conditions leading to ring contraction and/or fragmentation.

Results and Discussion

In light of the above-mentioned examples, it appears that substituents adjacent to the triflate group can influence the course of the reaction.[5–10] However, the role of conformational rigidity caused by the traditional 4,6-*O*-benzylidene group and by the stereochemistry of positions 1, 2, and 4 has not been completely established.

In order to examine the influence of these variables, alcohols **1a**–**11a**[12–21] were synthesized according to

[⊗] Abstract published in *Advance ACS Abstracts,* June 1, 1995.

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(3) (a) Fleet, G. W. J.; Ramsden, N. G.; Witty, D. R. *Tetrahedron* **1989**, *45*, 319. (b) Tarara, G; Hoppe, D. *Synthesis* **1989**, 89. (c) Binkley, R. W.; Ambrose, M. G.; Hehemann, D. G. *J. Carbohydr. Chem.* **1987**, *6*, 203. (d) Broxterman, H. J. G.; Neefjes, J. J.; van der Marel, G. A.; Ploegh, H. L.; van Boom J. H. *J. Carbohydr. Chem.* **1988**, *7*, 593. (e) Blanc-Muesser, M; Driguez, H. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3345.

(4) (a) Pankiewicz, K. W.; Sochacka, E.; Kabat, M. M.; Ciszewsky, L. A.; Watanabe, K. A. *J. Org. Chem.* **1988**, *53*, 3473. (b) Binkley, R. W., Abdulaziz, M. A. *J. Org. Chem.* **1987**, *52*, 4713. (c) Binkley, R. W.; Sivik, M. R. *J. Org. Chem.* **1986**, *51*, 2619.

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(6) In pyranose ring: (a) Estevez, J. C.; Fairbanks, A. J.; Hsia, K. Y., Ward, P.; Fleet, G. W. J. *Tetrahedron Lett.* **1994**, *35*, 3361. (b) Charette, A. B.; Coté, B. *J. Org. Chem.* **1993**, *58*, 933. (c) Montell, S. J.; Ford, P. S.; Watkin, D. J.; Fleet, G. W. J.; Brown, D. *Tetrahedron Lett.* **1992**, *33*, 4503. (d) Charette, A. B.; Coté, B.; Marcoux, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 8166. (e) Baer, H. H.; Hernández-Mateo, F.; Siemsen, L. *Carbohydr. Res.* **1989**, *187*, 67. (f) Fleet, G. W. J.; Seymour, L. C. *Tetrahedron Lett.* **1987**, *28*, 3015. (g) Hanessian, S.; Tyler, P. C.; Demailly, G.; Chapleur, Y. *J. Am. Chem. Soc.* **1981**, *103*, 6243. In furanose ring: (h) Witty, D. R.; Fleet, G. W. J.; Vogt, K.; Wilson, F. X.; Wang, Y.; Storer, R.; Myers, P. L.; Wallis, C. J. *Tetrahedron Lett.* **1990**, *31*, 4787.

(7) (a) Binkley, R. W. *J. Carbohydr. Chem.* **1994**, *13*, 111. (b) Binkley, R. W. *J. Org. Chem.* **1992**, *57*, 2353.

(8) Knapp, S.; Nauhgton, A. B. J.; Jaramillo, C.; Pipik, B. *J. Org. Chem.* **1992**, *57*, 7328.

(9) Sato, K.; Hoshi, Y.; Kajihara, Y. *Chem. Lett.* **1992**, 1469.

(10) (a) Binkley, R. W. *J. Org. Chem.* **1991**, *56*, 3892. (b) Binkley, R. W. *J. Carbohydr. Chem.* **1991**, *10*, 417.

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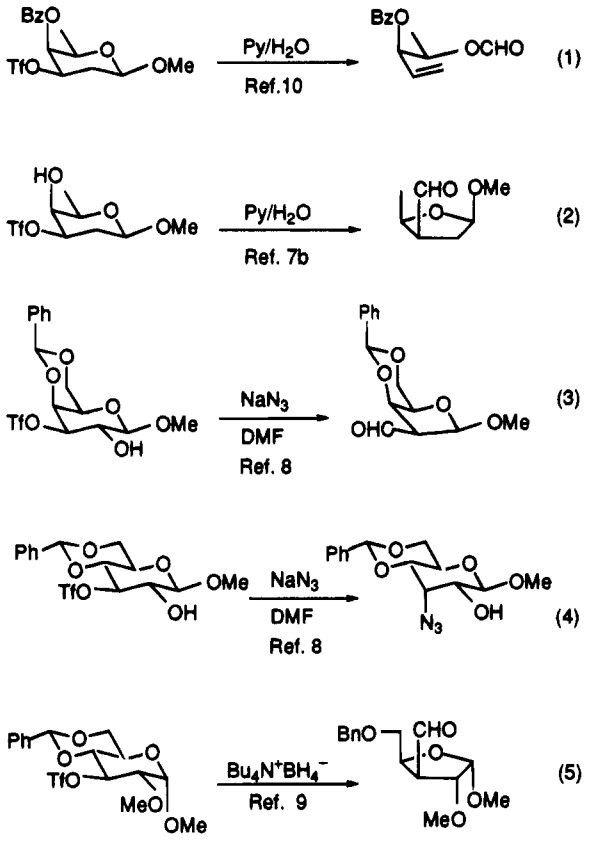
Scheme 1

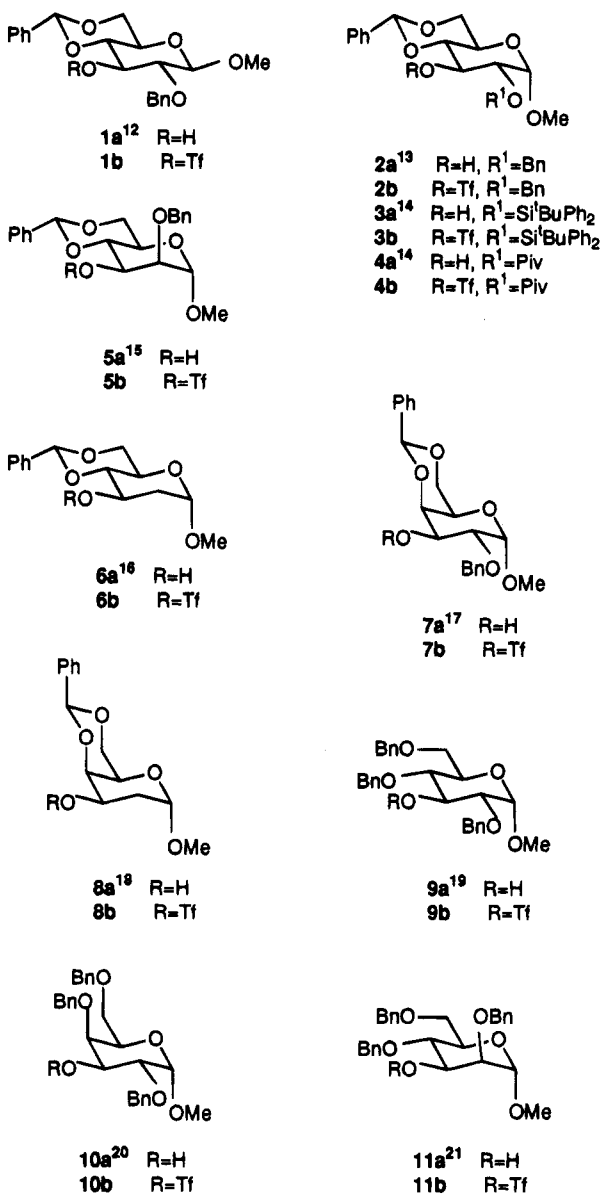


reported procedures and transformed into triflates **1b**–**11b** (Chart 1) by treatment with triflic anhydride in pyridine at low temperature.[7b] The triflates were characterized by their ^{1}H NMR spectra, but in general they proved to be rather unstable in storage. Consequently, the triflates were not purified but were subjected to rearrangement conditions, immediately after they were prepared.

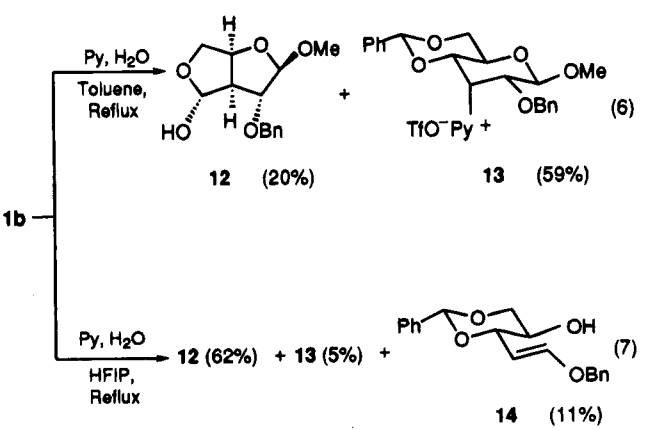
Four different major reactions can take place in the case of 3-*O*-triflyl carbohydrate derivatives, *viz.* substitution, elimination, ring-contraction, and fragmentation reactions. Usually, ring-contraction and fragmentation reactions are carried out by heating in solvents such as benzene,[7b] toluene[10] or DMF[6b,f] and in the presence of a base, to neutralize the triflic acid formed, and water to capture the resulting cabocation. In compounds **1b**–**11b** the triflate group is equatorial and the elimination reaction is unfavorable because it would require a conformation inversion (which is the case for *manno* and *galacto* derivatives), which is drastically hindered in compounds with a bicyclic structure. To avoid substitution reactions, a nonnucleophilic medium is mandatory.

We began the study by treating the *β-gluco* triflate **1b** in toluene/pyridine/water, but no reaction was observed

Chart 1



Scheme 2



after standing at room temperature for 24 h; however, when this solution was heated under reflux (procedure A) for 1 h, compound **13**[22] was obtained in 59% yield (in relation to **1a**) together with 20% of the ring-contraction product **12** (Scheme 2, eq 6; Table 1). During the search for milder reaction conditions, the reaction was performed in 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) (bp = 57–60

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(13) Ogawa, T.; Kaburagi, T. *Carbohydr. Res.* **1982**, *103*, 53.
(14) Rashid, A.; Mark Taylor, G.; Wood, W. W.; Alker, D. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1289.
(15) Boren, H. B.; Garegg, P. J.; Wallin, N. H. *Acta Chim. Scand.* **1972**, *26*, 1082.
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(17) Eby, R.; Schuerch, C. *Cabohydr. Res.* **1982**, *100*, C-41.
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(20) Flowers, H. M. *Carbohydr. Res.* **1975**, *39*, 245.
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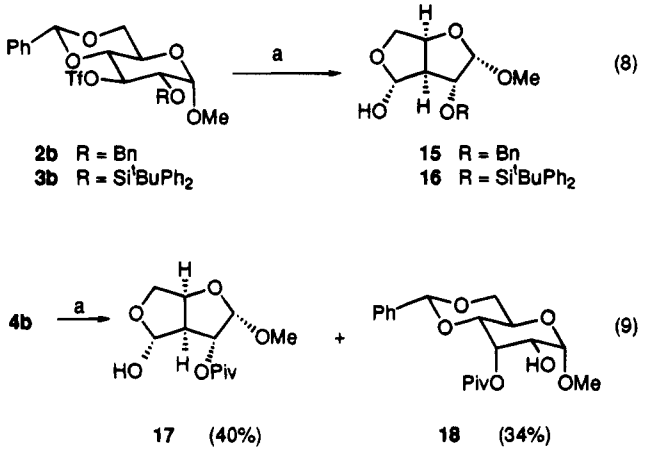
Table 1. Intramolecular Reactions of Triflates 1b–11b

triflate	conditions[a]	products (%)[b]	
1b	A	**12** (20)	**13** (59)
1b	B	**12** (62)[c]	**13** (5)
2b	A	**15** (68)	
2b	B	**15** (81)	
2b	C	**15** (92)	
3b	B	**16** (80)	
4b	B	**17** (40)	**18** (34)
5b	B	**19** (75)	
5b	C	**19** (84)	
6b	A[d]	**20** (54)	
6b	B[d]	**20** (91)	
7b	B	**21** (38)	**22** (26)
8b	A[d]	**20** (62)	
8b	B[d]	**20** (70)	
10b	A	**23** (38)	**24** (24)
10b	B	**23** (58)	
11b	B	**25** (27)	

[a] A = toluene/pyridine/H_2O, reflux. B = hexafluoro-2-propanol/pyridine/H_2O, reflux. C = hexafluoro-2-propanol/2,6-di-*tert*-butyl-4-methylpyridine/H_2O, reflux. [b] Relative to the alcohols **1a–11a**. [c] 11% of **14** was also obtained. [d] Room temperature.

Scheme 3



[a] Keys: (a) HFIP, pyridine, H_2O, reflux.

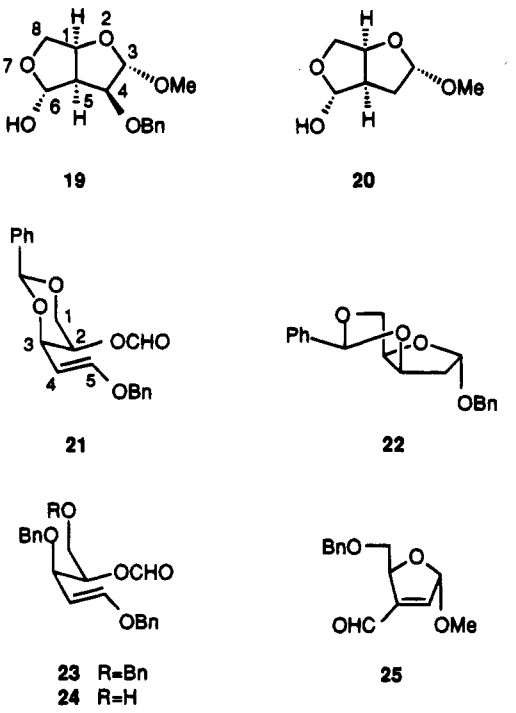
°C), an acidic alcohol with a nonnucleophilic conjugated base. When **1b** was refluxed in HFIP, in the presence of pyridine and H_2O (procedure B), compound **12** (62%) together with fragmentation product **14** (11%) and substitution product **13** (5%) was obtained (Scheme 2, eq 7).

However, when its α anomer (triflate derivative **2b**) followed reaction procedure A, it gave almost exclusively ring-contraction product **15**, which can also be considered as a branched-chain furanoside (Scheme 3, eq 8). The axial anomeric substituent, which hinders the approach of the nucleophile from the lower face of the carbohydrate ring, restricts substitution and the formation of fragmentation products. Yields could be improved by lowering the temperature (procedure B) and by using bulky base 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) (procedure C); in this last case compound **15** (92%) was obtained.

In order to test the effect of bulkier and electronically different protecting groups on the reaction process, triflates **3b** and **4b** were allowed to react by procedure B. 2-*O*-Si^{t}BuPh$_2$ derivative **3b** mainly gave the ring-contraction product **16** (80%) as in the case of triflate **2b** (Scheme 3, eq 8). Thus, compound **16** was obtained in

(22) Triflate substitution by pyridine in carbohydrates has been reported. (a) Ambrose, M. G.; Binkley, R. W. *J. Org. Chem.* **1983**, *48*, 674. (b) See also ref 10b.

Chart 2



three steps (74% overall yield) from commercially available methyl 4,6-*O*-benzylidene-α-D-*gluco*-pyranoside. However, 2-*O*-pivaloyl derivative **4b** led to a mixture of the ring-contraction product **17** (40%) and alcohol **18**, which arose from the pivaloyl migration and hydrolysis of the acyloxonium intermediate cation[4b,c] (Scheme 3, eq 9).

The effect of the stereochemistry of the triflate groups' neighboring substituents was also studied. 3-*O*-Triflyl-*manno* derivative **5b** principally gave ring-contraction product **19** (75%) (Chart 2) when subjected to conditions B. Small amounts of substitution product could also be detected. Using procedure C, the yield increased to 84% (Table 1).

With no substituent at position 2, as is the case of triflate **6b**, ring-contraction product **20**[23] was obtained even at room temperature. The more drastic conditions required in 2-alkoxy-3-*O*-triflyl carbohydrates must be related to the triflate stabilization caused by the electronegative 2-alkoxy group.[7b,24] The highest yields of **20** (91%) were obtained using HFIP as the solvent, in the presence of pyridine. Under these mild conditions, the use of DTBMP did not improve the yields.

3-*O*-Triflyl-*galacto* derivative **7b** led to a mixture of fragmentation product **21** and its derivative **22** when it was allowed to react according to procedure B. In fact, **22** is produced by formate hydrolysis of **21** and then by adding the resulting alcohol intramolecularly to the enol ether double bond; this process may be catalyzed by pyridinium triflate present in the reaction mixture.[25] Probably, cyclization which leads to the five-membered ring is also due to the rigidity caused by the 4,6-*O*-benzylidene group. This result is in sharp contrast to the case where the 2-OH was unprotected (Scheme 1, eq

(23) Compound **20** has already been synthesized by ring contraction of epoxide-containing pyranosides. Rehnberg, N.; Magnusson, G. *J. Org. Chem.* **1990**, *55*, 5467.

(24) Beard, C. D.; Baum, K.; Grakauskas, V. *J. Org. Chem.* **1973**, *38*, 3673.

(25) For the alcohol addition to enol ethers catalyzed by weak acids, see: Kaila, N.; Blumenstein, M.; Bielawska, H.; Franck, R. W. *J. Org. Chem.* **1992**, *57*, 4576.

3),[8] where ring contraction was produced by breaking the C_1-C_2 bond, and it is similar to the one shown by other 3-*O*-triflyl *galacto*- or 2-deoxy-*galacto*-pyranosyl derivatives (Scheme 1, eq 1).[10]

Curiously, the corresponding 2-deoxy-3-*O*-triflyl derivative **8b** gave ring-contraction product **20** in comparable yields to those obtained for triflate derivative **6b**. This behavior is completely different from other monocyclic, configurationally related compounds (Scheme 1, eq 1) and from the above-mentioned 2-*O*-benzyl derivative **7b**. Therefore, the influence of substituents in the ring and of the 4,6-*O*-benzylidene group on the reaction process is significant.

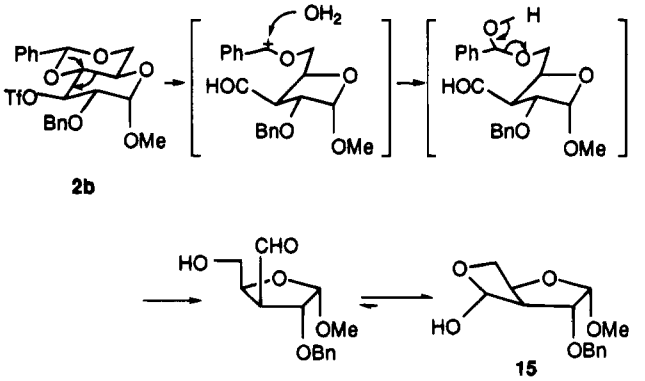
To evaluate the influence of the 4,6-*O*-benzylidene group, monocyclic triflates **9b**–**11b**, which do not contain this protecting group, were submitted to standard reaction conditions. Triflate **9b** gave a complex mixture of compounds when subjected to conditions B and C, suggesting that several alternative reactions have taken place. Compound **10b** afforded a mixture of fragmentation products **23** and **24**[26] (Table 1), when treated under conditions A. The formation of compound **24** was confirmed by treating the resulting mixture with NaH and benzyl bromide in THF, which afforded compound **23** exclusively. In this case no cyclized products were detected, as expected for a less rigid system. When triflate **10b** was treated under conditions B, only fragmentation product **23** was recovered.

Using procedure B, triflate **11b** also gave a mixture of compounds, from which compound **25**[27] was isolated in 27% yield. This compound may arise from a ring contraction followed by the elimination of benzyl alcohol.

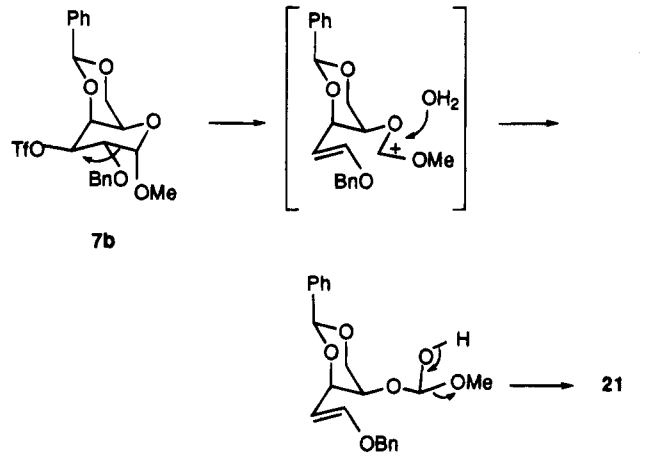
Structure Assignments. The presence of a pyridinium ring as a triflate salt in compound **13** was inferred from (i) the appearance of typical signals at δ 9.1–8.0 in the ^{1}H NMR spectrum, (ii) the appearance of a quadruplet at δ 120.6 ($J_{C,F}$ = 320 Hz) corresponding to the CF_3 group in the ^{13}C NMR spectrum, and (iii) the elemental analysis, which showed a sulfur content of 5.30%. The position of pyridinium was deduced from the δ value of H-3 (5.84 ppm) assigned on the basis of double resonance experiments. Coupling constants $J_{1,2}$, $J_{2,3}$, and $J_{3,4}$ showed an axial/equatorial/axial arrangement for H-2/H-3/H-4. NOE experiments confirmed this fact, showing that H-2 and H-4 signals increased when H-3 was irradiated. This suggests an *allo* configuration for compound **13**.

The ^{1}H NMR spectra of ring-contraction products **12**, **15**, **16**, **17**, and **20** showed the presence of only one isomer, which indicated that the expected equilibrium between anomers is fully shifted to one side. In compound **19** a small percentage of the open hydroxyaldehyde was observed in the equilibrium as well. The most significant spectroscopic features that allowed the proposed bicyclo[3.3.0] structures for compounds **12**, **15**, **16**, **17**, **19**, and **20** to be assigned were (i) the absence of the benzylidene group, (ii) the presence of two anomeric protons (~4.70–5.70 ppm) and carbons (~98–108 ppm), (iii) a large vicinal coupling constant $J_{1,5}$ = 7 Hz, which is characteristic of related bicyclic *cis*-fused compounds,[23,28,29] and (iv) a $J_{5,6}$ = 0 Hz for all compounds (δH-6 = ~5.3–5.7, singlet), which corresponds to a dihedral angle around 90°, so that 6-OH is in the exo face ((*R*)-configuration).

Scheme 4



Scheme 5



The ^{1}H and ^{13}C spectra of compounds **21**, **23**, and **24** showed the absence of OMe, the presence of a formate group (δ_{CHO} = ~161), and a *trans* enol ether group (δH-4 ~5.1, δH-5 ~6.50, $J_{4,5}$ = 12.7 Hz; δC-4 ~100, δC-5 ~151).

Mechanistic Considerations. On the basis of the above data, the following facts are evident: For 4,6-*O*-benzylidene derivatives: (i) elimination products have not been observed, (ii) β anomeric derivatives may give substitution reactions even with weak nucleophiles, especially at high temperature, (iii) for α anomeric derivatives, substitution is restricted, (iv) *gluco*, *manno*, 2-deoxy-*gluco*, and 2-deoxy-*galacto* derivatives (**2b**, **3b**, **4b**, **5b**, **6b**, and **8b**) give ring-contraction products (C_4-C_5 bond breaking) in good yields, and (v) *galacto* derivative **7b** leads to fragmentation products (C_1-C_2 bond breaking).

2,4,6-Tri-*O*-benzyl derivatives **9b**–**11b** afforded complex mixtures in general, except for the *galacto* derivative **10b** where the fragmentation process becomes more important.

The driving force for those ring-contraction and fragmentation processes in 4,6-*O*-benzylidene derivatives could be the formation of a stabilized carbocation in the benzylidene residue (Scheme 4) or the C-1 (Scheme 5) acetal carbons. In the case of monocyclic compounds, the carbocation at C-1 is more easily formed. There have been several reports dealing with ring contraction arising from the solvolysis of sulfonyl derivatives,[29,30] and a concerted mechanism for this process has been pro-

(26) A referee suggested that the capture by O-6 of a carbocation centered at C-1 at an intermediate stage of the process could explain the formation of compound **24**, which is a likely explanation.

(27) For the synthesis of closely related products, see ref. 22.

(28) Tatsuta, K.; Miyashita, S.; Akimoto, K.; Kinoshita, M. *Bull. Soc. Chim. Jpn.* **1982**, *55*, 3254.

posed.[28] Taking into account the fact that formation of a carbocation at C-1 has been demostrated for related carbohydrates,[10b] the process would be expected to be initially concerted involving the participation of a nonbonding electron pair antiperiplanar to the broken C–C bond, leading to stabilized carbocations (Schemes 4 and 5). Finally, water attack takes place and either benzaldehyde or methanol is lost.

The fundamental question remaining is why *galacto* derivatives **7b** and **10b** give fragmentation reactions while 2-deoxy-*galacto* derivative **8b** and the *gluco* and *manno* derivatives lead to ring-contraction reactions. An explanation for these competitive reactions must take into consideration the influence of the stereochemistry at position 4, the effect of electronegative substituents at position 2, and the stereochemistry of anomeric position in the relative stabilization of transition states leading to carbocations at benzylidene and anomeric positions.

Apparently, only in some cases, such as *β-galacto*[10] or hydroxy derivatives,[7b,28,29] is it possible to obtain good yields in fragmentation or ring-contraction products starting from monocyclic compounds.

On the other hand, the mechanism starting from hydroxy triflates (Scheme 1, eqs 2 and 3) must be different. The initial formation of the alcoholate and its tendency to be converted into a carbonyl group may favor ring contraction, as suggested by Magnusson[23] for related processes.

In conclusion, the 4,6-*O*-benzylidene group plays a crucial role in the reactivity of 3-*O*-triflylpyranoside derivatives, determining the preferable cleavage of the C-4/C-5 bond to give branched-chain furanosides in excellent yields. Compounds having a β configuration and electronegative substituents at C-2 give increasing amounts of the fragmentation product (C1–C2 bond cleavage), especially for *galacto* derivatives where this product is the most important one.

Experimental Section

Melting points were determined in open capillaries and are uncorrected. Optical rotations were determined at 589 nm in $CHCl_3$ solutions at 22 °C. Infrared spectra were recorded in $CHCl_3$ solutions on a FT-spectrometer. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were determined in $CDCl_3$. Elemental analyses were performed by the Servei de Recursos Científics, Universitat Rovira i Virgili. Preparative-scale separations were carried out by flash column chromatography using a 2 × 15-cm column of 240–400 mesh silica gel 60 and by TLC on silica gel 60 PF_{254} plates. Pyridine for the triflate synthesis was dried by standard methods; commercial 1,1,1,3,3,3-hexafluoro-2-propanol was used directly as purchased.

General Procedure for Triflate Synthesis.[7b] Triflic anhydride (3.3 mmol) was added to a stirred solution of 3 mmol of sugar and 7 mmol of dry pyridine in 15 mL of methylene chloride at −20 °C. The cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and stirred at that temperature until TLC analysis showed complete consumption of the starting material (45–60 min). Saturated aqueous sodium bicarbonate solution (10 mL) was added to the reaction mixture, the phases were separated, and the aqueous phase was extracted with 2 × 20 mL of methylene chloride. The organic phase was dried with anhydrous magnesium sulfate and evaporated at low temperature in high vacuum. The triflates obtained were immediately submitted to the rearrangement conditions since extensive decomposition was observed upon standing.

General Procedures for Thermal Intramolecular Reactions of Compounds 1b–10b. The following general procedures were used.

Procedure A. To a solution of triflate derivative, obtained from 0.4 mmol of alcohol following the general procedure for triflate synthesis, in 2 mL of toluene were added 1.2 mL of pyridine and 0.3 mL of water. This mixture was heated to 100 °C. On completion, the reaction mixture was concentrated under vacuum. Azeotropical distillation by adding toluene allowed the elimination of pyridine and water from the reaction mixture, which was then purified by flash chromatography.

Procedure B. A solution of freshly prepared sugar triflate derivative, obtained from 0.32 mmol of alcohol, in 3 mL of dichloromethane, and 1.3 mL of pyridine was added to a mixture of 3 mL of 1,1,1,3,3,3-hexafluoro-2-propanol and 0.33 mL of water. The reaction mixture was heated at reflux for 30–90 min. The mixture was concentrated under vacuum and purified by flash chromatography.

Procedure C. This method is similar to method B but 2,6-di-*tert*-butyl-4-methylpyridine (0.5 mmol) was used instead of pyridine.

Intramolecular Reaction of Triflate 1b. Procedure A. The standard procedure using **1b** gave, after 2.5 h, in order of elution **12** (16 mg, 20%) as an oil and **13** (90 mg, 59%) following flash chromatography (CH_2Cl_2/MeOH 10:1).

12: $[\alpha]_D$ −38.0° (*c* 1, $CHCl_3$)$_2$. ^1H NMR: 7.45–7.25, 5.49 (s, 1H), 4.97 (dd, 1H, $J_{1,8}$ = 3.7 Hz, $J_{1,5}$ = 6.6 Hz), 4.99 (s, 1H), 4.58 (s, 2H), 4.09 (dd, 1H, $J_{8,8'}$ = 10.5 Hz), 4.00 (d, 1H), 3.31 (s, 3H), 3.25 (d, 1H, $J_{4,3}$ = 2.7 Hz), 2.84 (d, 1H), 1.90 (s, 1H). ^{13}C NMR: 137.3, 129.5, 128.5, 127.7, 108.4, 101.6, 85.8, 84.3, 73.2, 71.6, 56.5, 54.6. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.16; H, 6.77. Found: C, 62.93; H, 6.80.

13: mp = 154 °C. $[\alpha]_D$ = −3.0° (*c* 1.5, $CHCl_3$). ^1H NMR: 8.90 (d, 2H, *J* = 6 Hz), 8.21 (t, 1H, *J* = 7 Hz), 7.87 (t, 2H, *J* = 7 Hz), 7.14 (m, 10H), 5.84 (t, 1H, $J_{3,2}$ = 6.5 Hz), 5.55 (s, 1H), 5.32 (d, 1H, $J_{1,2}$ = 7.2 Hz), 4.76 (d, 1H, *J* = 12 Hz), 4.58 (d, 1H), 4.36 (dd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,6'}$ = 10.2 Hz), 4.28 (dd, 1H, $J_{4,5}$ = 10 Hz, $J_{4,3}$ = 5.7 Hz), 4.18 (dd, 1H), 3.88 (m, 1H), 3.68 (t, 1H), 3.61 (s, 3H). ^{13}C NMR: 146.3, 146.0, 136.9, 129.2–125.8, 101.7, 100.6, 74.6, 74.2, 73.7, 69.1, 69.0, 62.6, 56.9. Anal. Calcd for $C_{27}H_{28}O_8NF_3S$: C, 56.26; H, 4.80; N, 2.40; S, 5.49. Found: C, 55.98; H, 4.76; N, 2.32; S, 5.30.

Procedure B. The standard procedure using **1b** gave, after 2.5 h, in order of elution **14**, 11 mg (14%), **12**, 53 mg (62%), and **13**, 9 mg (5%), following flash chromatography (hexane/ethyl acetate 7:3).

14: mp = 117–118 °C. $[\alpha]_D$ = −25.8° (*c* 0.3, $CHCl_3$). ^1H NMR: 7.30–7.50 (10H), 6.79 (d, 1H, $J_{4,5}$ = 12.6 Hz), 5.53 (s, 1H), 4.95 (dd, 1H, $J_{4,3}$ = 8.9 Hz), 4.80 (s, 2H), 4.35 (d, 1H, *J* = 4.4 Hz), 3.91 (t, 1H, $J_{3,2}$ = 8.2 Hz), 3.65–3.55 (m, 3H). ^{13}C NMR: 151.8, 129.0–126.1, 101.4, 101.1, 81.4, 71.4, 70.7, 65.9. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.07; H, 6.41. Found: C, 72.88; H, 6.46.

[1*S*,3*S*,4*R*,5*S*,6*R*]-4-(Benzyloxy)-6-hydroxy-3-methoxy-2,7-dioxabicyclo[3.3.0]octane (15). By the general procedure C described above using **2b**, compound **15** (78 mg, 92%) was obtained, after 1.5 h, as an oil following flash chromatography (hexane/ethyl acetate 6:4). $[\alpha]_D$ +37.5° (*c* 2.65, $CHCl_3$). IR: 3600–3200 cm^{-1} (ν_{OH}). ^1H NMR: 7.28–7.25 (m, 5H), 5.25 (s), 4.75 (m, 2H), 4.56 (d, 1H, *J* = 12 Hz), 4.54 (d, 1H), 3.98 (dd, 1H, $J_{8,8'}$ = 10.2 Hz, $J_{8,1}$ = 3.9 Hz), 3.81 (d, 1H), 3.63 (dd, 1H, $J_{4,5}$ = 7.2 Hz), 3.33 (s, 3H), 2.83 (t, 1H, $J_{5,1}$ = 7.2 Hz), 2.11 (s, 1H). ^{13}C NMR: 102.7, 102.0, 81.8, 80.3, 72.5, 71.1, 54.6, 54.5. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.16; H, 6.77. Found: C, 63.28; H, 6.85.

[1*S*,3*S*,4*R*,5*S*,6*R*]-4-((*tert*-Butyldiphenylsilyl)oxy)-6-hydroxy-3-methoxy-2,7-dioxabicyclo[3.3.0]octane (16). The general procedure B was followed using **3b**; compound **16** (106 mg, 80%) was obtained, after 1 h, as an oil following flash chromatography (hexane/ethyl acetate 7:2). $[\alpha]_D$ +20.45° (*c* 3, $CHCl_3$). IR: 3600–3200 cm^{-1} (ν_{OH}). ^1H NMR: 7.80–7.30

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(m, 10H), 5.03 (s, 1H), 4.79 (dd, 1H, $J_{1,8}$ = 4.2 Hz, $J_{1,5}$ = 7.2 Hz), 4.27 (d, 1H, $J_{3,4}$ = 4.2 Hz), 3.95 (dd, 1H, $J_{8,8'}$ = 10.5 Hz), 3.86 (dd, 1H, $J_{4,5}$ = 6.9 Hz), 3.78 (d, 1H), 3.30 (s, 3H), 2.90 (t, 1H), 2.74 (s, 1H), 1.10 (s, 9H). ^{13}C NMR: 135.9, 133.4, 130.0, 127.8, 104.0, 102.0, 80.3, 77.0, 71.2, 56.6, 54.8. Anal. Calcd for $C_{23}H_{30}O_5Si$: C, 66.67; H, 7.24. Found: C, 66.84; H, 7.31.

[1*S*,3*S*,4*R*,5*S*,6*R*]-4-(Pivaloyloxy)-6-hydroxy-3-methoxy-2,7-dioxabicyclo[3.3.0]octane (17) and methyl 4,6-*O*-Benzylidene-3-*O*-pivaloyl-α-D-*allo*-pyranoside (18). The general procedure B was followed using **4b**; compounds **17** (33.5 mg, 40%) and **18** (40, 34%) were obtained, after 2 h, following flash chromatography (light petroleum ether/ethyl ether 3:1).

17: $[\alpha]_D$ +124.2° (*c* 0.25, $CHCl_3$). IR: 3600−3200 cm^{-1} (ν_{OH}). ^{1}H NMR: 5.58 (s, 1H), 5.10 (d, 1H, $J_{3,4}$ = 4.2 Hz), 4.85 (dd, 1H, $J_{1,8}$ = 4.2 Hz, $J_{1,5}$ = 7.2 Hz), 4.62 (dd, 1H, $J_{4,5}$ = 6.9 Hz), 4.09 (dd, 1H, $J_{8,8'}$ = 10.5 Hz), 4.01 (d, 1H), 3.35 (s, 3H), 2.93 (t, 1H), 2.61 (s, 1H), 1.22 (s, 9H). ^{13}C NMR: 178.2, 102.9, 102.0, 80.3, 76.5, 71.1, 55.0, 53.7, 38.0 −29.0. Anal. Calcd for $C_{12}H_{20}O_6$: C, 55.38; H, 7.69. Found: C, 55.51; H, 7.76.

18: mp = 162−163 °C. $[\alpha]_D$ +133.0° (*c* 0.3, $CHCl_3$). IR: 3600−3200 cm^{-1} (ν_{OH}). ^{1}H NMR: 7.41−7.30 (5H), 5.63 (t, 1H, $J_{3,2}$ = $J_{3,4}$ = 3 Hz), 5.52 (s, 1H), 4.75 (d, 1H, $J_{1,2}$ = 4.2 Hz), 4.33 (dd, 1H, $J_{6,5}$ = 4.8 Hz, $J_{6,6'}$ = 10.2 Hz), 4.08 (dt, 1H, $J_{5,6}$ = $J_{5,4'}$ = 10.0 Hz, $J_{5,6'}$ = 5.0 Hz), 3.86 (ddd, 1H, $J_{2,OH}$ = 10.2 Hz), 3.72 (t, 3H), 3.64 (dd, 1H), 4.48 (s, 3H), 2.54 (d, 1H), 1.24 (s, 9H). ^{13}C NMR: 178.2, 128.9−126.1, 101.4, 99.2, 76.5, 69.1, 68.7, 67.3, 58.1, 56.0, 38.7, 27.1. Anal. Calcd for $C_{19}H_{26}O_7$: C, 62.29; H, 7.10. Found: C, 62.06; H, 7.15.

[1*S*,3*S*,4*S*,5*S*,6*R*]-4-(Benzyloxy)-6-hydroxy-3-methoxy-2,7-dioxabicyclo[3.3.0]octane (19). Following the general procedure C starting from **5b** for 1.5 h and after flash chromatography (hexane/ethyl acetate 6:4), compound **19** was obtained (71.5 mg, 84%) as a mixture where the open hydroxy aldehyde could be detected. ^{1}H NMR: 7.27 (m, 5H), 5.75 (s, 1H), 4.87 (d, 1H, $J_{3,4}$ = 1.5 Hz), 4.70 (ddd, $J_{1,5}$ = 6.6 Hz, $J_{1,8}$ = $J_{1,8'}$ = 2.0 Hz), 4.61 (d, 1H, J = 12.0 Hz), 4.47 (d, 1H), 4.02 (m, 2H), 4.00 (dd, 1H, $J_{4,5}$ = 7.8 Hz), 3.26 (s, 3H), 2.93 (dd, 1H), 2.78 (s, 1H). ^{13}C NMR: 137.4, 128.4, 127.8, 127.7, 108.4, 98.3, 82.8, 82.6, 72.7, 71.4, 54.9, 53.4. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.16; H, 6.77. Found: C, 62.97; H, 6.68.

[1*S*,3*S*,5*S*,6*R*]-6-Hydroxy-3-methoxy-2,7-dioxabicyclo-[3.3.0]octane[23] (20). By general procedure C using **6b** and after 1.5 h at room temperature, compound **20** was obtained (46.5 mg, 91%) following flash chormatography (hexane/ethyl acetate 6:4). ^{13}C NMR: 106.5, 103.7, 82.3, 71.6, 54.4, 49.4, 37.0.

(2*R*,3*R*,4*E*)-1,3-*O*-Benzylidene-5-(benzyloxy)-2-*O*-formyl-4-pentene-1,2,3-triol (21) and Benzyl 3,5-*O*-Benzylidene-2-deoxy-α-D-*threo*-pentofuranoside (22). The standard procedure B using **7b** gave, after 1 h, a mixture which was purified by TLC (hexane/ethyl acetate 7:1), obtaining compounds **21** (41 mg, 38%) and **22** (26 mg, 26%).

21: mp = 99−100 °C. $[\alpha]_D$ −25.8 (*c* 0.3, $CHCl_3$). ^{1}H NMR: 8.19 (s, 1H), 7.40−7.24 (m, 10H), 6.52 (d, 1H, $J_{5,4}$ = 12.7 Hz), 5.59 (s, 1H), 5.12 (dd, 1H, $J_{4,3}$ = 7.7 Hz), 4.79 (bs, 1H), 4.74 (d, 1H, J = 11.6 Hz), 4.67 (d, 1H), 4.44 (d, 1H), 4.28 (d, 1H, $J_{1,1'}$ = 13.1 Hz) 4.09 (d, 1H). ^{13}C NMR: 160.6, 150.8, 129.0−126.0, 101.6, 101.4, 72.5, 71.2, 69.2, 68.2. Anal. Calcd for $C_{20}H_{20}O_5$: C, 70.58; H, 5.88. Found: C, 70.40; H, 5.94.

22: mp = 104−105 °C. $[\alpha]_D$ +36.6 (*c* 0.6, $CHCl_3$). ^{1}H NMR: 7.43−7.18 (m, 10H), 5.51 (dd, 1H, $J_{1,2}$ = 5.7 Hz, $J_{1,2'}$ = 4.0 Hz), 5.39 (s, 1H), 4.76 (d, 1H, J = 11.7 Hz), 4.52 (d, 1H), 4.49 (m, 1H), 4.42 (d, 1H, $J_{5,5'}$ = 13.2 Hz), 4.12 (dd, 1H, $J_{5',4}$ = 2.4 Hz), 3.90 (m, 1H), 2.42 (dd, 1H, $J_{2,2'}$ = 14.7 Hz), 2.11 (ddd, 1H, $J_{2',3}$ = 4.4 Hz). ^{13}C NMR: 128.9−126.1, 103.8, 99.5, 76.7, 72.5, 70.1, 66.9, 41.3. Anal. Calcd for $C_{19}H_{20}O_4$: C, 73.08; H, 6.41. Found: C, 72.90; H, 6.53.

(2*R*,3*R*,4*E*)-5-(Benzyloxy)-1,3-di-*O*-benzyl-2-*O*-formyl-4-pentene-1,2,3-triol (23). By the general procedure B using **10b**, after 4 h compound **23** was obtained (80 mg, 58%) as an oil following flash chormatography (hexane/ethyl acetate 6:1): mp = 123−124 °C. $[\alpha]_D$ −1.05 (*c* 0.84, $CHCl_3$). ^{1}H NMR: 8.18 (s, 1H), 7.40−7.24 (m, 15H), 6.51 (d, 1H, J = 12.6 Hz), 5.13 (m, 1H), 4.78 (d, 1H, J = 12 Hz), 4.73 (dd, 1H, $J_{4,3}$ = 9.3 Hz), 4.72 (d, 1H), 4.58 (d, 1H), 4.51 (d, 1H), 4.42 (d, 1H), 4.32 (d, 1H), 3.96 (dd, 1H, $J_{3,2}$ = 6.0 Hz), 3.64 (dd, 1H, $J_{1,2}$ = 4.1 Hz, $J_{1,1'}$ = 10.6 Hz), 3.57 (dd, 1H, $J_{1',2}$ = 5.8 Hz). ^{13}C NMR: 160.8, 150.8, 128.6−127.5, 100.1, 75.4, 74.9, 73.3, 71.2, 69.3, 68.5. Anal. Calcd. for $C_{27}H_{28}O_5$: C, 75.00; H, 6.48. Found: C, 74.70; H, 6.52.

(2*S*,5*S*)-2-((Benzyloxy)methyl)-5-methoxy-2,5-dihydrofuran-3-carbaldehyde (25). The standard procedure B was followed using triflate **11b**. After 30 min, purification by TLC (hexane/ether 10:3) gave compound **25** (21.5mg, 27%) as an oil. $[\alpha]_D$ +13.3° (*c* 1.2, $CHCl_3$). ^{1}H NMR: 9.89 (s, 1H), 7.33−7.25 (m, 5H), 6.73 (dd, 1H), 5.96 (dd, 1H, $J_{5,4}$ = 4.2 Hz, J = 1.3 Hz), 5.24 (qd, 1H), 4.57 (d, 1H, J = 12.3 Hz), 4.50 (d, 1H), 3.84 (dd, 1H, J = 2.4 Hz, J_{gem} = 10.5 Hz), 3.74 (dd, 1H, J = 3.9 Hz), 3.46 (s, 3H). ^{13}C NMR: 187.0, 145.6, 142.7, 128.3−127.5, 107.9, 83.2, 73.5, 69.9, 55.1. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.74; H, 6.45. Found: C, 67.96; H, 6.50.

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