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Synthesis of thromboxane A_2 models from glucose

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Abstract

Trans-opening of the 2,3-anhydro-6-deoxy-4-*O*-methyl-α-D-allopyranoside with lithium bromide yields the *altro* and *gluco* regioisomers methyl 2-bromo-2,6-dideoxy-4-*O*-methyl-α-D-altropyranoside and methyl 2-bromo-3,6-dideoxy-4-*O*-methyl-α-D-glycopyranoside which can be hydrolysed to give the sugar precursors 2-bromo-2,6-dideoxy-4-*O*-methyl-α/β-D-altropyranose and 3-bromo-3,6-dideoxy-4-*O*-methyl-D-glucopyranose. Under Mitsunobu conditions the *altro* compound yields the first 1,3-anhydro-altrose derivative. In case of the *gluco* derivative alkaline treatment does not give a 1,3-anhydro-glucose derivative but the 2,6-dideoxy-altrose via intermediate 2,3-epoxide formation. Methanolysis and reductive debromination under photolytic initiation were studied. © 1997 Elsevier Science Ltd.

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1. Indroduction

In thromboxane A molecules [1,2] the 2,6-dioxabicyclo[3.1.1]heptane system is the highly reactive oxetane substructure which causes the decisive vascular contraction. By hydrolysis of TXA_2 the more stable but physiologically non-active TXB_2 has been synthesized previously by several groups [3–5]. A number of heterosubstituted TXA_2 analogues with higher stability against hydrolysis have also been prepared [6]. The first racemic TXA_2 model compounds with enhanced hydrolytic stability were published by Fried et al. [7] employing fluoro-stabilized precursors. Another racemic model was described by Still et al. [8], and this group subsequently published the synthesis of TXA_2 itself by cyclisation of TXB_2 [9,10]. Previously Schuerch et al. were the first to describe syntheses of 2,6-dioxabicyclo[3.1.1]heptanes in the sugar series [11–14] in the course of their polymerisation studies to give 1,3-glycanes. Their systems were 2-substituted derivatives with D-*gluco* or D-*manno* configuration and later Kong et al. reported on the preparation of other 1,3-anhydro sugar derivatives [15–17]. We were interested in a sugar-based approach to enantiomerically pure TXA_2 mod-

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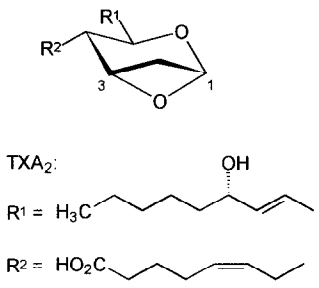
els which would require 2-deoxy compounds having the D-*ribo* configuration. Such a system in turn should be easily accessible from glucose according to a series of established reactions, and the final cyclisation to the 1,3-anhydro system should make use of an intramolecular nucleophilic substitution reaction.



2. Results and discussion

Methyl α-D-glucopyranoside was benzylidenated, mesylated and transformed into the *allo* epoxide [18]. Oxidative benzylidene ring opening with NBS, debenzoylation and reductive debromination gave the epoxide **1** [19] as a versatile precursor. For 1,3-anhydro sugar model the 4-position was methylated employing the old but very mild Purdie method with methyl iodide/silver oxide [20] to give the crystalline ether derivative **2** in over 90% yield.

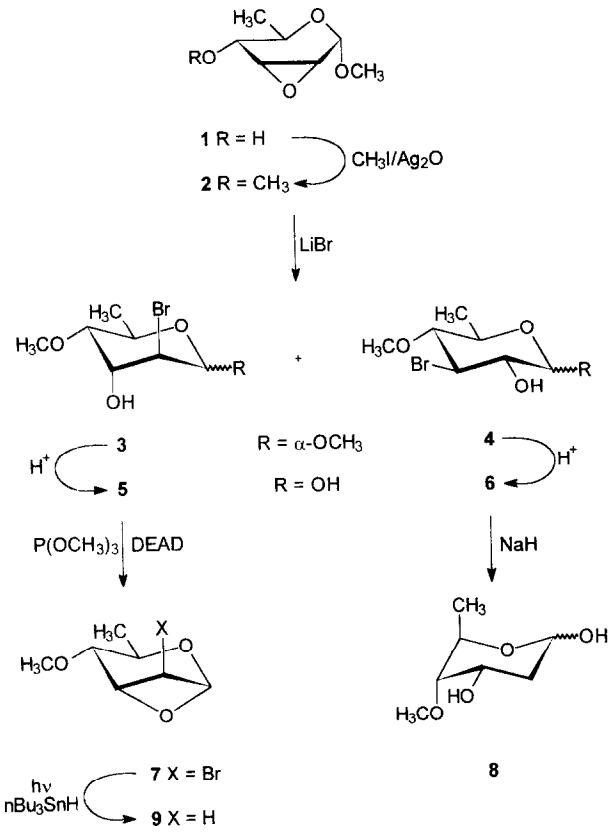
A favourable access to bromohydrines employing commercially available lithium bromide could be followed in analogy to epoxide openings with lithium iodide [21,22]. By trans-opening according to the Fürst–Plattner rule [23] both regioisomers with *altro* (**3**) and *gluco* configuration (**4**) were obtained as crystals in a ratio of about 1:1. As has been shown previously [22] the *altro* compound **3** is formed by S_N2 attack of bromide at C-2 of **2** in the $^0H_5$ (D) half-chair conformation. Similarly, **2** in the inverted $^5H_0$ (D) half-chair conformation would be preferentially attacked at C-3 to give the *gluco* compound **4** in the $^1C_4$ (D) conformation, which readily adopts the normal $^4C_1$ (D) chair conformation.

For cleavage of the methyl glycosides [24], treatment with strong acid ion exchange resin for four days at 80 °C proved to be mild enough to leave intact the 4-methyl ether function. However, the turnover was only about 50% which required chromatographic regeneration and reuse of the recovered glycoside. The altrose derivative **5** was obtained as a syrupy anomeric mixture (^{1}H NMR: $\alpha:\beta \sim 1:1$). Similarly, the glucose derivative **6** was obtained as an anomeric mixture and assigned (^{1}H NMR: $\alpha:\beta \sim 1:1.75$)

Attempts to construct a 1,3-anhydro sugar in the *gluco* series having an electron attracting 2-OH group were made with **6**, the α-anomer of which was expected to be converted by basic deprotonation of 1-OH and intramolecular S_N2 attack at C-3. With *n*-butyl- or methyllithium (cf. lit. [13,14]) complex mixtures resulted but treatment of **6** with sodium hydride under argon in benzene after 20 min at 0 °C gave exclusively an anomeric mixture ($\alpha:\beta = 2:1$) of 2,6-dideoxy-4-*O*-methyl-D-ribo-hexopyranose (**8**). Apparently, in this case the well known but undesired epoxide formation from vicinal halohydrines [25,26] dominated to give the intermediate 2,3-epoxide exclusively. This in turn would have been expected to readily undergo a hydride opening, both at C-2 and C-3 corresponding to the opening of **2** with bromide. We assume that the regiospecific nucleophilic attack by hydride at C-2 occured via the open chain 2,3-epoxide, in which the nucleophile enjoyed directionary effects from the aldehyde function.

Both anomers, **8**α and **8**β, exhibit coupling constants in the ^{1}H NMR spectra which deviate considerably from the normal $^4C_1$ (D) chair conformations as for instance in the corresponding digitoxose. Based on the coupling constants $J_{4,5} = 1.5$ Hz for a *lyxo* compound in virtually pure $^1C_4$ (D) form [27] and $J_{4,5} = 10.0$ Hz for digitoxose in practically pure $^4C_1$ (D) form the molar fractions of **8**α and **8**β could be calculated [28]. Both in **8**α and **8**β the $^1C_4$ (D) chair forms dominate by 70% and 90% in chloroform, respectively, which may be interpreted as a result of steric and polar interactions (Scheme 1).

Treatment of the 2-bromo-*altro* derivative **5** with trimethyl phosphite and diethyl azodicarboxylate in a Mitsunobu reaction [29] was to generate an anomeric leaving group [8–12]. By reaction at 0 °C under argon for 30 min the cyclisation could be effected to give the 1,3-anhydro compound **7**. Quick workup and inspection of the novel material by ^{1}H NMR and 2 D-COSY spectroscopy revealed the oxetane substructure. In the spectrum the anomeric proton shows a triplet at δ 5.53 with a vicinal $J_{1,2}$ and a long-range $J_{1,3}$ coupling of 3.8 Hz each. Such long-range couplings are typical of oxetanes [30] as well as planar compounds with the coupling protons in a zig–zag arrangement [31,32]. Long-range couplings of comparable magnitude were observed in the NMR spectra of the corresponding bicyclo[1.1.0]butane [33] or bicyclo[2.1.1]hexane [34]. Further, the identity of **7**



Scheme 1.

could be underlined by a chemical ionisation mass spectrum.

Physiological tests of thromboxane derivatives make use of the Krebs–Henseleit approach with a rabbit aorta [2,35] and it was shown that often the physiological activity of these compounds runs parallel to the hydrolysis rate. Therefore, determination of methanolysis of **7** in dry deuterochloroform was performed to reveal a half life of about 20 min. This half life is in the same order of magnitude as that of comparable TXA_2 models [8,36,37], but relatively small in comparison with TXA_2 itself, yet much smaller than that of the fluoro-stabilized models of Fried et al. [7].

After complete methanolysis of **7** both the methyl 2-bromo-α-D-*altro* derivatives **3** and the corresponding methyl β-anomer of **3** (not depicted) could be determined in the ratio 1:1. Apparently, following protonation the resulting oxocarbenium intermediate was attacked from both faces. Such a mechanism is in keeping with that expected for anhydro sugars [38] and that of 1-hydroxy-oxetanes [39]. It was of interest to study the debromination of this enantiomerically pure 2,6-dioxabicyclo[3.1.1]heptane system, with *ribo* configuration **7**. The radical debromination of the axially disposed bromine atom was performed according to a protocol of previous communications [8–10] using tributylstannic hydride and catalytic amounts of a radical initiator (AIBN) under irradiation at 364 nm in deuterobenzene. The process was monitored by ^1H NMR spectroscopy but signals of the debrominated 2,6-dioxabicyclo[3.1.1]heptane **9** could not be unequivocally identified. Apparently, the system was extremely labil to hydrolysis and therefore after 30 min a mixture of compounds **5** and **8** in the ratio 1:2 was detected. Compound **5** is assumed to result from hydrolysis of the starting oxetane **7** the half life of which was about 20 min. The 2,6-dideoxy-*altro* compound **8** is supposed to be formed from the labile intermediate **9**, however, an alternative pathway directly via **5** cannot be excluded.

3. Experimental

General methods.—Melting points were determined with a Reichert hot-stage microscope. Specific optical rotations were measured with a Perkin–Elmer Polarimeter 241. NMR spectra were recorded with a Bruker WM 300 (^1H: 300 MHz; ^{13}C: 75.43 MHz) and a Bruker 360 (^1H: 360 MHz; ^{13}C: 90.52 MHz) instrument, for solutions in $CDCl_3$ unless otherwise specified. Thin-layer and column chromatography were performed on precoated silica gel plates (Merck 60 F_{254}) and on Kieselgel 60 (Merck 230–400 mesh), respectively. All reaction products were detected by TLC on silica gel 60 F_{254} (Merck) by quenching of fluorescence and/or charring with 10% ethanolic H_2SO_4.

Methyl 2,3-anhydro-6-deoxy-4-O-methyl-α-D-allopyranoside (**2**).—Alloepoxide **1** [19] (300 mg, 1.8 mmol) was dissolves in methyl iodide (7 mL) and after addition of freshly prepared silver oxide (2.5 g, 18 mmol) the mixture was heated under reflux for 3 h. After filtration and twofold extraction of the residue with hot $CHCl_3$ evaporation of the solvent gave a raw material which was purified by column chromatography on silica gel (1:3 EtOAc–toluene). Yield 290 mg (92%); mp 76.9 °C; $[\alpha]_D^{20}$ +194° (*c* 0.5, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ 4.82 (d, 1 H, $J_{1,2}$ 2.3 Hz, H-1), 3.50 (dd, 1 H, $J_{2,3}$ 2.7 Hz, H-2), 3.53 (dd, 1 H, $J_{3,4}$ 1.2 Hz, H-3), 3.24 (ddd, 1 H, $J_{4,5}$ 9.1 Hz, H-4), 3.85 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.23 (d, 3 H, CH_3-6), 3.44 and 3.51 (each s, each 3 H, OCH_3). Anal. Calcd for $C_8H_{14}O_4$ (174.2): C, 55.16; H, 8.10. Found: C, 55.29; H, 8.12.

Methyl 2-bromo-2,6-dideoxy-4-O-methyl-α-D-altropyranoside (**3**) and *methyl 3-bromo-3,6-dideoxy-*

4-O-methyl-α-D-glucopyranoside (**4**).—A soln of compound **2** (2.5 g, 14.3 mmol) in $CHCl_3$ (60 mL) was stirred with glacial acetic acid (0.86 g, 14.3 mmol), NaOAc (1.23 g, 15.0 mmol) and lithium bromide (3.5 g, 44.3 mmol) for 8 h at rt. The mixture was washed with aq sodium thiosulfate and $NaHCO_3$ soln, extracted with EtOAc, the extract dried ($MgSO_4$) and the solvent evaporated. Purification and separation of the regioisomers was on silica gel with 2:1 toluene–EtOAc. Compound **3**: yield 1.53 g (42%); mp 93 °C; $[\alpha]_D^{20}$ +86.4° (*c* 0.5, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.79 (d, 1 H, $J_{1,2}$ 1.4 Hz, H-1), 4.17 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 4.20 (ddd, 1 H, $J_{3,4}$ 3.0, $J_{3,OH-3}$ 7.1 Hz, H-3), 3.42 (dd, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 3.94 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.31 (d, 3 H, CH_3-6), 3.10 (d, OH-3), 3.37 and 3.40 (each s, each 3 H, OCH_3).

Compound **4**: yield 1.31 g (36%); mp 87 °C; $[\alpha]_D^{20}$ +74.5° (*c* 0.8, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.69 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 3.74 (ddd, 1 H, $J_{2,3}$ 10.4, $J_{2,OH-2}$ 8.7 Hz, H-2), 4.06 (dd, 1 H, $J_{3,4}$ 10.2 Hz, H-3), 2.99 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 3.63 (dq, 1H, $J_{5,6}$ 6.2 Hz, H-5), 1.33 (d, 3 H, CH_3-6), 2.47 (d, 1 H, OH-2), 3.44 and 3.61 (each s, each 3 H, OCH_3). Anal. Calcd for $C_8H_{15}BrO_4$ (255.1): C, 37.67; H, 5.93. Found: C, 37.91; H, 5.73.

2-Bromo-2,6-dideoxy-4-O-methyl-α/β-D-altropyranose (**5**).—A soln of compound **3** (225 mg, 0.88 mmol) in water (100 mL) was stirred with Lewatit SP 1080 (2 g) for 4 d at 80 °C. After filtration and evaporation the residue was purified on silica gel (2:3 toluene–EtOAc). The syrupy product (102 mg, 48%) was obtained as an α/β-mixture (1:1, ^{1}H NMR); $[\alpha]_D^{20}$ +19° (*c* 0.6, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): **5**α: δ 5.15 (dd, 1 H, $J_{1,2}$ 1.3, $J_{1,OH-1}$ 9.7 Hz, H-1), 4.30 (dd, 1 H, $J_{2,3}$ 3.5 Hz, H-2) 4.39 (ddd, 1 H, $J_{3,4}$ 3.2, $J_{3,OH-3}$ 7.2 Hz, H-3), 3.40 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 4.09 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.35 (d, 3 H, CH_3-6), 2.76 (d, 1 H, OH-1), 3.28 (d, 1 H, OH-3), 3.46 (s, 3 H, OCH_3); **5**β: δ 4.96 (dd, 1 H, $J_{1,2}$ 1.5, $J_{1,OH-1}$ 11.3 Hz, H-1), 4.39 (dd, 1 H, $J_{2,3}$ 3.6 Hz, H-2), 4.41 (ddd, 1 H, $J_{3,4}$ 3.0, $J_{3,OH-3}$ 7.4 Hz, H-3), 3.47 (dd, 1 H, $J_{4,5}$ 9.6 Hz, H-4), 3.82 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.32 (d, 3 H, CH_3-6), 1.76 (d, 1 H, OH-1), 3.35 (d, 1 H, OH-3), 3.43 (s, 3 H, OCH_3). Anal. Calcd for $C_7H_{13}BrO_4$ (241.1): C, 34.87; H, 5.44. Found: C, 34.96; H, 5.44.

3-Bromo-3,6-dideoxy-4-O-methyl-α/β-D-glucopyranose (**6**).—A soln of compound **4** (30 mg, 1.17 mmol) in water (120 mL) was stirred with Lewatit SP 1080 (2 g) for 4 d at 50–80 °C. After filtration and evaporation the residue was purified on silica gel (2:1 toluene–EtOAc). The syrupy material (152 mg, 54%) was obtained as an α/β-mixture (1:1.75, ^{1}H NMR); $[\alpha]_D^{20}$ +28° (*c* 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): **6**α: δ 4.51 (d, 1H, $J_{1,2}$ 3.7 Hz, H-1), 3.70 (ddd, 1 H, $J_{2,3}$ 10.0, $J_{2,OH-2}$ 9.8 Hz, H-2), 3.79 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.01 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 3.34 (dq, 1 H, $J_{5,6}$ 6.1 Hz, H-5), 1.31 (d, 3 H, CH_3-6), 2.72 (s, 1 H, OH-1), 3.45 (d, 1 H, OH-2), 3.57 (s, 3 H, OCH_3); **6**β: δ 5.15 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 3.45 (dd, 1 H, $J_{2,3}$ 10.2 Hz, H-2), 4.60 (dd, 1 H, $J_{3,4}$ 9.6 Hz, H-3), 2.93 (dd, 1 H, $J_{4,5}$ 9.2 Hz, H-4), 3.88 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.26 (d, 3 H, CH_3-6), 2.44 (s, 1 H, OH-1), 3.01 (s, 1 H, OH-2), 3.53 (s, 3 H, OCH_3). Anal Calcd for $C_7H_{13}BrO_4$ (241.1): C, 34.87; H, 5.44. Found: C, 34.78; H, 5.31.

1,3-Anhydro-2-bromo-2,6-dideoxy-4-O-methyl-α-D-altropyranoside (**7**).—Under argon trimethylphosphite (0.1 mL, 0.82 mmol) was dissolved in dry $CHCl_3$ (2 mL) and at 0 °C diethylazodicarboxylate (0.1 mL, 0.6 mmol) was added and the mixture stirred at rt for 5 min. The altro derivative **5** (12 mg, 0.05 mmol) was dissolved in dry $CHCl_3$ (1 mL) and 0.2 mL of the above soln was added at 0 °C under argon and stirred for 30 min. The reaction mixture was evaporated to dryness, the residue dissolved in dry 1:2 EtOAc–toluene and quickly purified on silica gel by flash chromatography (2:1 EtOAc–toluene). The product (8 mg, 70%) was obtained in about 80% purity as indicated by ^{1}H NMR. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.53 (dd, 1 H, $J_{1,2}$ 3.8, $J_{1,3}$ 3.8 Hz, H-1), 4.91 (dd, 1 H, $J_{2,3}$ 6.3 Hz, H-2), 4.87 (dd, 1 H, $J_{3,4}$ 0 Hz, H-3), 3.59 (dd, 1 H, $J_{4,5}$ 6.2 Hz, H-4), 4.06 (dq, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 1.46 (d, 3 H, CH_3-6), 3.32 (s, 3 H, OCH_3). MS: $C_7H_{11}BrO_3$ (223.1); $m/z = 241$ $[M + 18]^+$.

2,3-Dideoxy-4-O-methyl-α/β-D-ribohexopyranose (**8**).—Under argon the 3-bromo altro derivative **6** (12.1 mg, 0.048 mmol) was dissolved in anhyd deuterobenzene (1 mL) and treated at 0 °C with sodium hydride (3 mg, 0.1 mmol, obtained from the paraffin suspension by washing with deuterobenzene) for 20 min. The crude reaction mixture (α/β = 2:1, ^{1}H NMR) was studied by ^{1}H NMR (300 MHz, C_6D_6): **8**α: δ 5.36 (ddd, 1 H, $J_{1,2a}$ 5.1, $J_{1,2e}$ 0.4, $J_{1,OH-1}$ 9.9 Hz, H-1), 1.56 (ddd, 1 H, $J_{2a,2e}$ 13.4, $J_{2a,3}$ 5.2 Hz, H-2a),1.77 (ddd, 1 H, $J_{2e,3}$ 2.2 Hz, H-2e), 2.99 (ddd, 1 H, $J_{3,4}$ 6.4, $J_{3,OH-3}$ 9.0 Hz, H-3), 2.98 (dd, 1 H, $J_{4,5}$ 2.1 Hz, H-4), 4.31 (dq, 1 H, $J_{5,6}$ 6.6 Hz, H-5), 0.91 (d, 3 H, CH_3-6), 3.01 (d, 1 H, OH-1), 3.00 (m, 1 H, OH-3), 2.79 (s, 3 H, OCH_3); **8**β: δ 5.30 (ddd, 1 H, $J_{1,2a}$ 4.1, $J_{1,2e}$ 3.1, $J_{1,OH-1}$ 8.2 Hz,

H-1), 1.84 (ddd, 1 H, $J_{2a,2e}$ 13.2, $J_{2a,3}$ 5.4 Hz, H-2a), 1.99 (ddd, 1 H $J_{2e,3}$ 2.5 Hz, H-2e), 3.49 (ddd, 1 H, $J_{3,4}$ 6.0, $J_{3,OH-3}$ 8.3 Hz, H-3), 2.90 (dd, 1 H, $J_{4,5}$ 4.1 Hz, H-4), 4.20 (dq, 1 H, $J_{5,6}$ 6.5 Hz, H-5), 1.26 (d, 3 H, CH_3-6), 3.24 (d, 1 H, OH-1), 3.00 (m, 1 H, OH-3), 2.98 (s, 3 H, OCH_3).

Methanolysis of compound **7**.—In an NMR tube compound **7** (8 mg, 0.03 mmol) was dissolved in dry deuterochloroform (1 mL) and treated with dry MeOH (0.1 mL). The solvolysis rate was determined by integration of the ^{1}H NMR signal monitoring the decreasing amount of starting material **7** (4 min: 92%; 10 min: 77%; 17 min: 58%; 30 min: 30%). After completion of the reaction *methyl 2-bromo-2,6-dideoxy-4-O-methyl-α-* (**3**) and the corresponding *-β-D-altropyranoside* (no number) could be assigned by ^{1}H NMR analysis in a ratio of 1:1. In the mixture the ^{1}H NMR spectrum showed typical signals for *methyl 2-bromo-2,6-dideoxy-4-O-methyl-β-D-altropyranoside*: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.52 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 3.84 (dq, 1 H, $J_{4,5}$ 9.2, $J_{5,6}$ 6.3 Hz, H-5), 1.38 (d, 3 H, CH_3-6).

Photolysis of compound **7**.—To a soln of 1,3-anhydro-2-bromo derivative **7** (8 mg, 0.03 mmol) in dry deuterobenzene (1 mL) under argon tri-*n*-butylstannic hydride (12.0 mL, 0.045 mmol) and a catalytic amount of azobisisobutylnitrile were added. The mixture was irradiated at 364 nm for 30 min and the resulting mixture directly monitored by ^{1}H NMR. NMR signals of compounds **5** and **8** could be unequivocally assigned in a ratio of **5**:**8** = 1:2.

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References

[1] M. Hamberg, J. Svenson, and B. Samuelson, *Proc. Natl. Acad. Sci. USA*, 72 (1975) 2994–2998.
[2] R. Needleman, S. Moncada, S. Bunting, J.R. Vane, M. Hamberg, and B. Samuelson, *Nature*, 261 (1976) 558–560.
[3] E.J. Corey, M. Shibasaki, J. Knolle, and T. Sugahara, *Tetrahedron Lett.*, (1977) 785–788.
[4] S. Hanessian and P. Lavallee, *Can. J. Chem.*, 55 (1997) 562–565.
[5] S. Hanessian and P. Lavallee, *Can. J. Chem.*, 59 (1981) 870–877.
[6] R.F. Newton, S.M. Roberts, and J.K. Taylor, *Synthesis* (1984) 449–478, and literature cited therein.
[7] J. Fried, E.A. Hallinan, and M.J. Szwedo, Jr., *J. Am. Chem. Soc.*, 106 (1984) 3871–3872.
[8] S.S. Bhagwat, P.R. Hamann, and W.C. Still, *Tetrahedron Lett.*, 26 (1985) 1955–1958.
[9] S.S. Bhagwat, P.R. Hamann, W.C. Still, S. Bunting, and F.A. Fitzpatrick, *Nature*, 315 (1985) 511–513.
[10] S.S. Bhagwat, P.R. Hamann, and W.C. Still, *J. Am. Chem. Soc.*, 107 (1985) 6372–6376.
[11] H. Ito, R. Eby, S. Kramer, and C. Schuerch, *Carbohydr. Res.*, 86 (1980) 193–202.
[12] A.J. Varma and C. Schuerch, *J. Org. Chem.*, 46 (1981) 799–803.
[13] F. Kong and C. Schuerch, *Carbohydr. Res.*, 112 (1983) 141–147.
[14] F. Good and C. Schuerch, *Carbohydr. Res.*, 125 (1984) 165–171.
[15] X. Wu, F. Kong, D. Lu, and P. Zhang, *Carbohydr. Res.*, 224 (1992) 75–87.
[16] C. Yang, F. Kong, and L. Cao, *J. Carbohydr. Chem.*, 11 (1992) 379–395.
[17] Z. Gan and F. Kong, *Carbohydr. Res.*, 270 (1995) 211–215.
[18] N.K. Richtmyer and C.S. Hudson, *J. Am. Chem. Soc.*, 63 (1941) 1727–1731.
[19] H. Paulsen and V. Sinnwell, *Chem. Ber.*, 111 (1978) 879–889.
[20] T. Purdie and J.C. Irvine, *J. Chem. Soc.*, 83 (1903) 1021–1037.
[21] R.U. Lemieux, E. Fraga, and K.A. Watanabe, *Can. J. Chem.*, 446 (1968) 61–69.
[22] J. Thiem, H. Karl, and U. Ellermann, *Chem. Ber.*, 112 (1979) 3139–3148.
[23] A. Fürst and P.A. Plattner, *Helv. Chim. Acta*, 32 (1949) 275–283.
[24] E.J. Bourne and S. Peat, *Advan. Carbohydr. Chem.*, 5 (1950) 145–190.
[25] S. Winstein and H.J. Lucas, *J. Am. Chem. Soc.*, 61 (1939) 1576–1581.
[26] R.G. Kadesch, *J. Am. Chem. Soc.*, 68 (1946) 41–45.
[27] E.-F. Fuchs, D. Horton, and W. Weckerle, *Carbohydr. Res.*, 57 (1977) C36–C39.
[28] G. Adiwidjaja, B. Meyer, H. Paulsen, and J. Thiem, *Tetrahedron*, 35 (1979) 373–384.
[29] O. Mitsunobu, *Synthesis* (1981) 1–28.
[30] C.L. Khetrapal, A.C. Kunwar, and A. Saupe, *Mol. Phys.*, 25 (1973) 1405–1413.
[31] S. Sternhell, *Quart. Rev. Chem. Soc.*, 23 (1969) 236–270.
[32] G. Kotowycz and R.U. Lemieux, *Chem. Rev.*, 73 (1973) 669–698.
[33] K.B. Wiberg, G.M. Lampman, R.P. Ciula, D.S. Connor, P. Schertler, and J. Lavanish, *Tetrahedron*, 21 (1965) 2749–2769.
[34] K. Tori, M. Ohtsuru, Y. Hata, and H. Tanida, *J. Chem. Soc., Chem. Commun.* (1968) 1096.
[35] H.A. Krebs and K. Hensleit, *Hoppe-Seyler's Z. Physiol. Chem.*, 210 (1932) 33–66.

[36] R.M. Burch, D.E. Mais, D.L. Saussy, and P.V. Halushka, *Proc. Natl, Acad. Sci. USA*, 82 (1985) 7434–7438.
[37] P.W. Sprague, J.E. Heikes, J.Z. Gougoutas, M.F. Malley, D.N. Harris, and R. Greenberg, *J. Med. Chem.*, 28 (1985) 1580–1590.
[38] M. Cerny and J. Stanek, Jr., *Advan. Carbohydr. Chem. Biochem.*, 34 (1977) 23–177.
[39] R.F. Atkinson and T.C. Bruice, *J. Am. Chem. Soc.*, 96 (1974) 819–825.