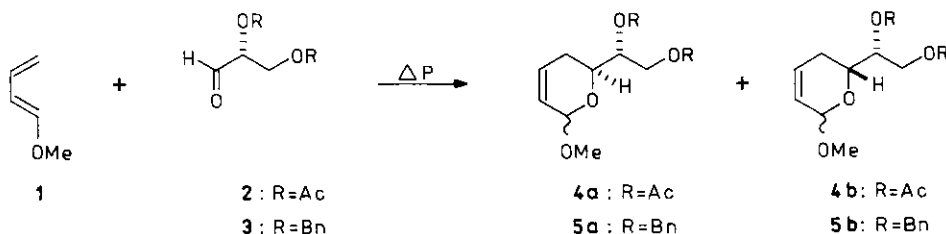


## NOVEL REDUCTIVE OPENING OF 5,6-DIHYDRO-2H-PYRAN RING

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**Abstract** — Oxidation of 2-methoxy-5,6-dihydro-2H-pyran derivatives (**4** and **5**), followed by reduction of the resulting peroxides with sodium borohydride afforded enantiomerically pure open-chained compounds **2**, **10**, **11**, and **12**, which can serve as chiral building blocks.

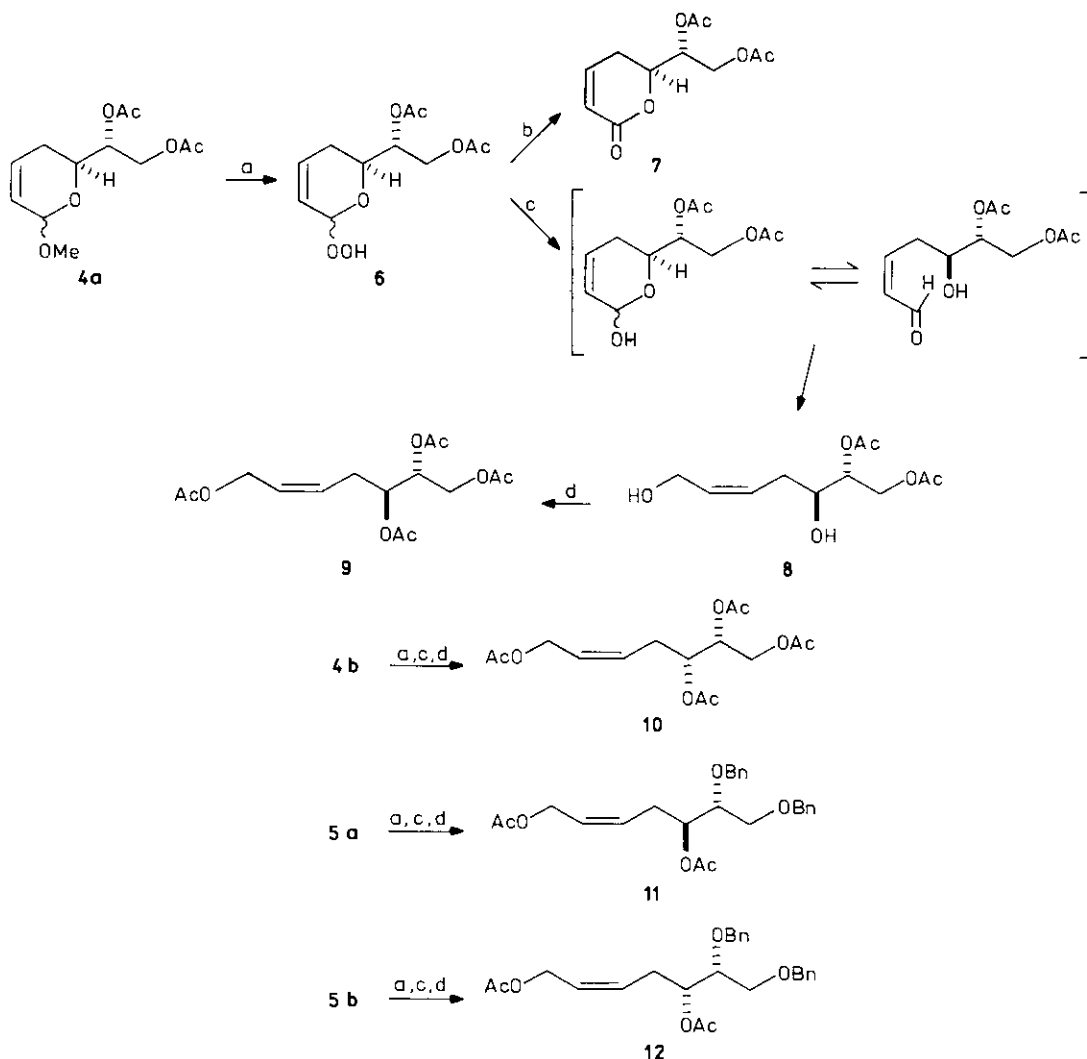
A few years ago we have described<sup>1</sup> a high-pressure asymmetric (4+2)cycloaddition of 1-methoxybuta-1,3-diene (**1**) to 2,3-O-isopropylidene-D-glyceraldehyde, leading with high stereoselectivity to 5,6-dihydro-2H-pyran derivatives. Recently, we have extended this approach to other derivatives of D-glyceraldehyde as dienophiles, e.g. compounds **2** and **3**. The reactions of **1** with 2,3-di-O-acetyl-D-glyceraldehyde (**2**)<sup>2</sup> and with 2,3-di-O-benzyl-D-glyceraldehyde (**3**),<sup>2,3</sup> carried out at 20 kbar and 50°C in methylene chloride,<sup>4</sup> gave - respectively - two pairs of diastereoisomers **4a**:**4b**=79:21 (66% yield), and **5a**:**5b**=71:29 (36% yield) (Scheme 1).



Scheme 1

Both reaction mixtures were separated by high-performance liquid chromatography, yielding in each case two fractions containing *cis-trans* diastereoisomers of S (**4a** and **5a**) and R (**4b** and **5b**) absolute configuration on the C-6 chiral center. Whereas these adducts are very interesting synthons, their conversion to open-chained

forms would increase their synthetic utility. The 2-alkoxy-5,6-dihydro-2H-pyran system can be opened by acidic hydrolysis,<sup>5</sup> but in this case there is simultaneous Z - E isomerisation of the double bond. In this communication we describe a new method for ring opening with preservation of the Z configuration of the double bond. Our concept is based on a known approach to the synthesis of  $\alpha,\beta$ -unsaturated  $\delta$ -lactones.<sup>6</sup> Upon use of this method to adduct **4a** (oxidation with 30% hydrogen peroxide in the presence of molybdenum trioxide, followed by treatment of the resulting hydroperoxide **6**<sup>7</sup> with an equimolar mixture of acetic anhydride and pyridine), lactone **7**<sup>8,9</sup> was obtained in 67% yield (Scheme 2).



Scheme 2. Reagents and reaction conditions: (a) 30%  $\text{H}_2\text{O}_2$ ,  $\text{MoO}_3 \cdot 2\text{H}_2\text{O}$ , RT, 3 h; (b)  $\text{Ac}_2\text{O}/\text{Py}$ ; (c)  $\text{NaBH}_4$ ,  $(\text{CH}_3)_2\text{CHOH}$ ,  $0^\circ\text{C}$ , 6 h; (d)  $\text{Ac}_2\text{O}$ ,  $\text{Et}_3\text{N}$ , DMAP,  $\text{CH}_2\text{Cl}_2$ , RT, 3 h.

For opening of the 5,6-dihydro-2H-pyran ring, hydroperoxide **6** was reduced with sodium borohydride in isopropanol. Under these conditions there was no isomerisation of the double bond. After acetylation of the resulting diol **8**, compound **9** was obtained in 81% yield. By means of the same method, compounds **10**, **11**, and **12** were obtained in 57, 75, and 58% yield, respectively.<sup>8</sup> The structures of above-mentioned compounds as well as the Z configuration of the double bond were confirmed by analysis of their <sup>1</sup>H NMR spectra.

The results presented here offer a new method for preparing versatile, optically pure building blocks, potentially useful for the synthesis of natural products.

#### ACKNOWLEDGMENT

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3. J. Jurczak and T. Bauer, *Tetrahedron Lett.*, submitted.
4. For high-pressure experiments we used the piston-cylinder type apparatus described earlier: J. Jurczak, M. Chmielewski, and S. Filipek, *Synthesis*, 1979, 41.
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8. For all new compounds satisfactory elemental analyses or exact masses were obtained.
9. The selected data of compound **9**: ( $\alpha$ )<sub>D</sub><sup>20</sup> -44.0° (c 0.66 in CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub> as solvent, TMS as standard),  $\delta$  (ppm) 6.92 (m, 1H, H-4), 6.06 (d, 1H, H-3), 5.22 (m, 1H, H-7), 4.63 (m, 1H, H-6), 4.52 (q, 1H, H-8), 4.20 (q, 1H, H-8'), 2.48 (m, 2H, H-5, H-5'), 2.21, 2.08 (2xs, 6H, 2xCOCH<sub>3</sub>).
10. The selected data of compounds **9**, **10**, **11**, and **12**:  
**9**: ( $\alpha$ )<sub>D</sub><sup>20</sup> +19.5° (c 1.00 in CHCl<sub>3</sub>); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS = 0),  $\delta$  (ppm) 5.66 (m, 1H, H-2), 5.60 (m, 1H, H-3), 5.14 (m, 2H, H-5, H-6), 4.60 (m, 2H, H-1, H-1'), 4.24 (m, 2H, H-7, H-7'), 2.46 (m, 2H, H-4, H-4'), 2.09 - 2.05 (4xs, 12H, 4xCOCH<sub>3</sub>),

$J_{2,3} = 11.0 \text{ Hz.}$

10:  $(\alpha)_D^{20} -6.7^\circ$  (c 0.67 in  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS = 0),  $\delta$  (ppm)  
5.69 (m, 1H, H-2), 5.60 (m, 1H, H-3), 5.21 (m, 1H, H-6), 5.14 (m, 1H, H-5),  
4.59 (m, 2H, H-1, H-1'), 4.29 (m, 1H, H-7), 4.03 (m, 1H, H-7'), 2.42 (m, 2H,  
H-4, H-4'), 2.10 - 2.05 (4xs, 12H,  $4\times\text{COCH}_3$ ),  $J_{2,3} = 12.5 \text{ Hz.}$

11:  $(\alpha)_D^{20} +8.2^\circ$  (c 1.11 in  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS = 0),  $\delta$  (ppm)  
7.32 (m, 10H,  $2\times\text{C}_6\text{H}_5$ ), 5.60 (m, 2H, H-2, H-3), 5.13 (m, 1H, H-5), 4.68 - 4.52  
(m, 6H, H-1, H-1',  $2\times\text{CH}_2\text{Ph}$ ), 3.58 (m, 2H, H-7, H-7'), 2.48 (m, 2H, H-4, H-4'),  
2.03, 1.98 (2xs, 6H,  $2\times\text{COCH}_3$ ),  $J_{2,3} = 11.2 \text{ Hz.}$

12:  $(\alpha)_D^{20} -21.6^\circ$  (c 0.49 in  $\text{CHCl}_3$ );  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS = 0),  $\delta$  (ppm)  
7.33 (m, 10H,  $2\times\text{C}_6\text{H}_5$ ), 5.60 (m, 1H, H-2), 5.52 (m, 1H, H-3), 5.11 (m, 1H, H-5),  
4.64 - 4.50 (m, 6H, H-1, H-1',  $2\times\text{CH}_2\text{Ph}$ ), 3.68 (m, 1H, H-6), 3.58 (m, 2H, H-7,  
H-7'), 2.03, 2.00 (2xs, 6H,  $2\times\text{COCH}_3$ ),  $J_{2,3} = 10.8 \text{ Hz.}$

In each case, the assignment of chemical shifts was confirmed by 2D-spectrum.

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