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

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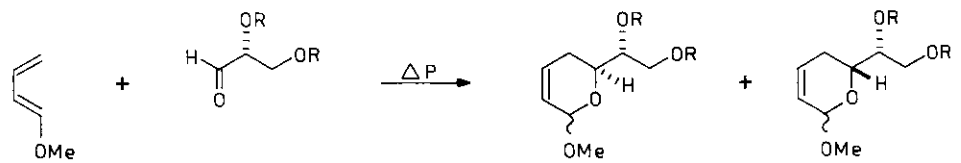
Abstract — Oxidation of 2-methoxy-5,6-dihydro-2H-pyran derivatives (4 and 5), followed by reduction of the resulting peroxides with sodium borohydride afforded enantiomerically pure open-chained compounds 9, 10, 11, and 12, which can serve as chiral building blocks.

A few years ago we have described[1] 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)[2] and with 2,3-di-O-benzyl-D-glyceraldehyde (3),[2,3] carried out at 20 kbar and 50°C in methylene chloride,[4] gave - respectively - two pairs of diastereoisomers 4a:4b=79:21 (66% yield), and 5a:5b=71:29 (36% yield) (Scheme 1).



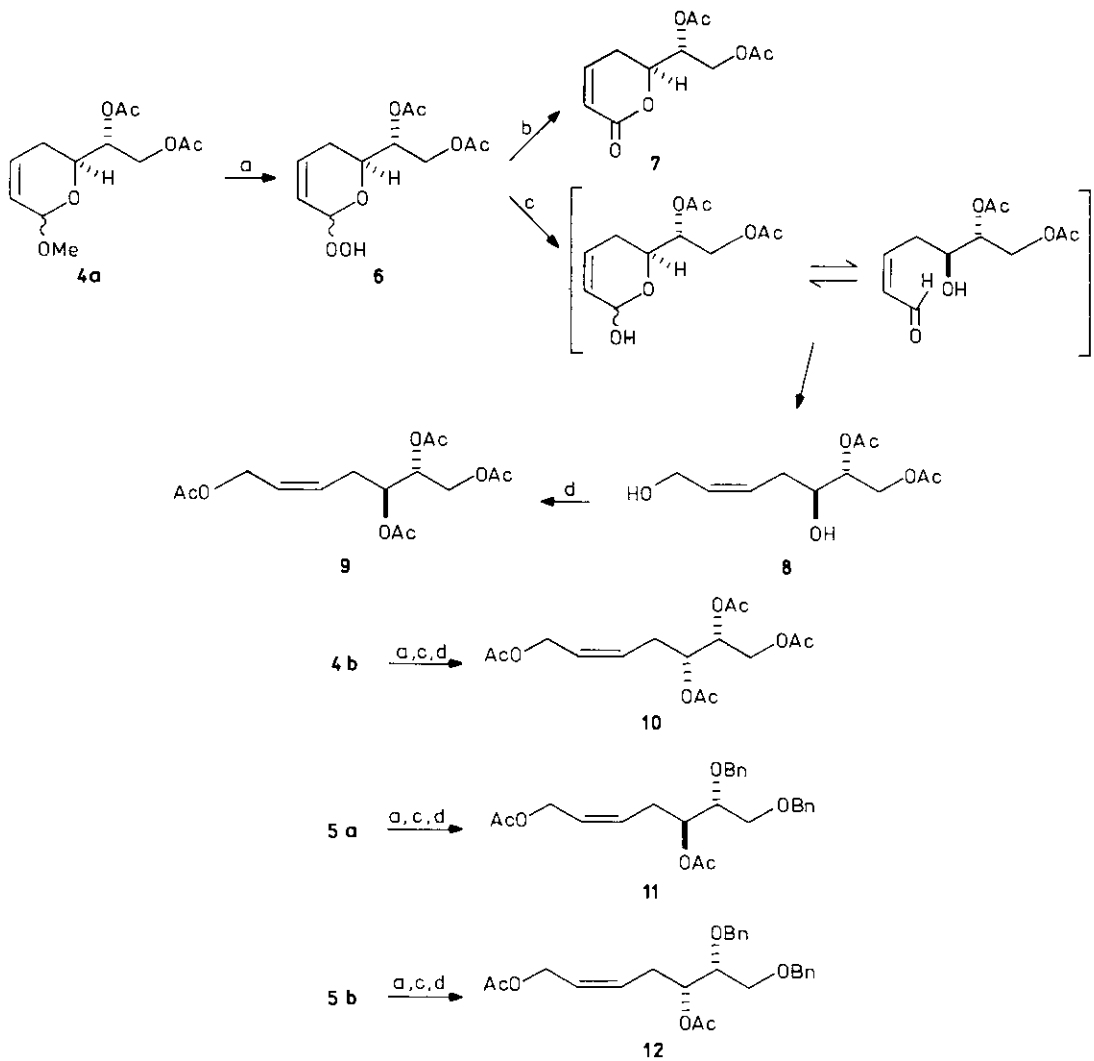
1 — 2: R=Ac, 3: R=Bn — 4a: R=Ac, 5a: R=Bn — 4b: R=Ac, 5b: R=Bn

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,[5] 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 α,β-unsaturated δ-lactones.[6] Upon use of this method to adduct 4a (oxidation with 30% hydrogen peroxide in the presence of molibdenium trioxide, followed by treatment of the resulting hydroperoxide 6[7] with an equimolar mixture of acetic anhydride and pyridine), lactone 7[8,9] was obtained in 67% yield (Scheme 2).



Scheme 2. Reagents and reaction conditions: (a) 30% H_2O_2, $MoO_3 \cdot 2H_2O$, RT, 3 h; (b) Ac_2O/Py; (c) $NaBH_4$, $(CH_3)_2CHOH$, 0°C, 6 h; (d) Ac_2O, Et_3N, DMAP, CH_2Cl_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.[8] The structures of above-mentioned compounds as well as the Z configuration of the double bond were confirmed by analysis of their ^{1}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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REFERENCES AND NOTES

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2. T. Bauer, *Ph. D. Thesis*, Warszawa, 1985.
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.
5. A. Konował, J. Jurczak, and A. Zamojski, *Roczniki Chem.*, 1968, 42, 2045.
6. J. Mieczkowski, J. Jurczak, M. Chmielewski, and A. Zamojski, *Carbohydr. Res.*, 1977, 56, 180.
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8. For all new compounds satisfactory elemental analyses or exact masses were obtained.
9. The selected data of compound 7: $[\alpha]_D^{20}$ -44.0° (c 0.66 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$ as solvent, TMS as standard), δ (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 (2×s, 6H, 2×$COCH_3$).
10. The selected data of compounds 9, 10, 11, and 12:
9: $[\alpha]_D^{20}$ +19.5° (c 1.00 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, TMS = 0), δ (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 (4×s, 12H, 4×$COCH_3$),

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

10: $[\alpha]_D^{20}$ -6.7° (c 0.67 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, TMS = 0), δ (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 (4×s, 12H, 4×$COCH_3$), $J_{2,3}$ = 12.5 Hz.

11: $[\alpha]_D^{20}$ +8.2° (c 1.11 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, TMS = 0), δ (ppm) 7.32 (m, 10H, 2×C_6H_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×CH_2Ph), 3.58 (m, 2H, H-7, H-7′), 2.48 (m, 2H, H-4, H-4′), 2.03, 1.98 (2×s, 6H, 2×$COCH_3$), $J_{2,3}$ = 11.2 Hz.

12: $[\alpha]_D^{20}$ -21.6° (c 0.49 in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, TMS = 0), δ (ppm) 7.33 (m, 10H, 2×C_6H_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×CH_2Ph), 3.68 (m, 1H, H-6), 3.58 (m, 2H, H-7, H-7′), 2.03, 2.00 (2×s, 6H, 2×$COCH_3$), $J_{2,3}$ = 10.8 Hz.

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

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