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ASYMMETRIC INDUCTION IN THE HIGH-PRESSURE REACTION BETWEEN 2,3-0-ISOPROPYLIDENE-D-GLYCERALDEHYDE AND 2,5-DIMETHYLFURAN

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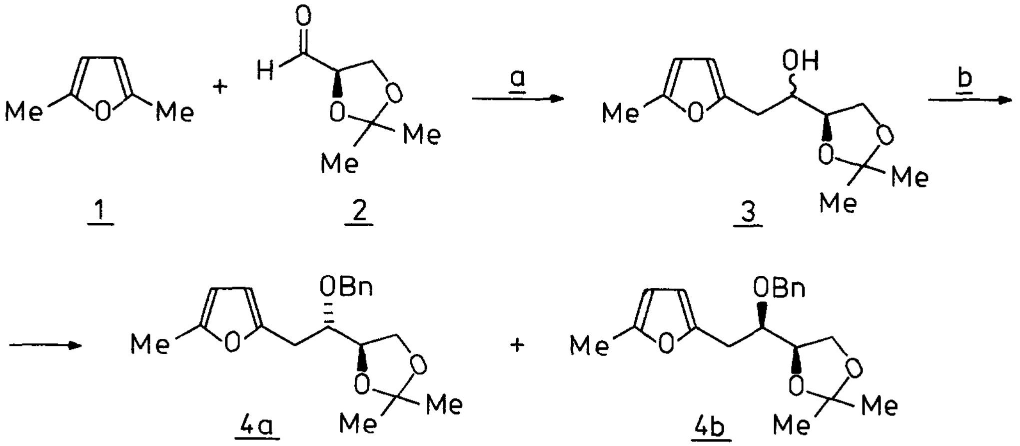
Abstract: High-pressure reaction of protected D-glyceraldehyde (2) with 2,5-dimethylfuran (1) and chemical transformation of the resulting product 3 to the 2-deoxy-D-pentitol derivatives (7, 8 and 9) is described.

Recent work in this laboratory resulted in a discovery of a new type of reaction between 2,5-dimethylfuran (1) and various carbonyl compounds.[1] Products of the reaction can constitute versatile synthons for synthesis of carbohydrates and other polyhydroxylated natural products. Compounds of this type have recently become objects of growing interest for synthetic chemists.[2] This prompted us to investigate the course of asymmetric induction using 2,3-0-isopropylidene-D-glyceraldehyde (2)[3] as a chiral carbonyl compound.

The reaction of 1 with 2 under high-pressure conditions[4] (Scheme I) gave the expected product 3[5] as a mixture of diastereoisomers [oil, ^{1}H NMR ($CDCl_3$), δ (ppm):1.42(3H,s), 1.49(3H,s), 2.32(3H,s), 2.83(2H,d,J=8Hz), 4.07(4H,m), 5.97(1H,d,J=2Hz), 6.09(1H, d,J=2Hz); $[\alpha]_D$ +3.5° (c=0.92, $CHCl_3$)] which was purified without separation of isomers in 22% yield.[6] In the reaction a new asymmetric centre is created via a 1,2-induction process. The ratio of diastereoisomers was determined from the ^{1}H NMR spectra of 3[7] as well as of its acetylated derivative[8] (in the presence of $Eu(fod)_3$ as a shift reagent), by intergration of the singlets originating from the methyl group adjacent to the furan ring . In both cases the diastereoisomeric excess was found to be 60%.

The protection of the hydroxyl group of 3 with benzyl bromide afforded separable diastereoisomeric benzyl ethers 4a and 4b. They were isolated by preparative TLC[9] to give less polar 4a [oil; $[\alpha]_{578}$-2°(c=1.61, $CHCl_3$)] and more polar 4b [oil; $[\alpha]_{578}$+29°(c=1.18, $CHCl_3$)] in diastereoisomerically pure forms. The ratio of 4a and 4b (8:2) thus obtained was fully consistent with that determined from the ^{1}H NMR spectra.[7,8]

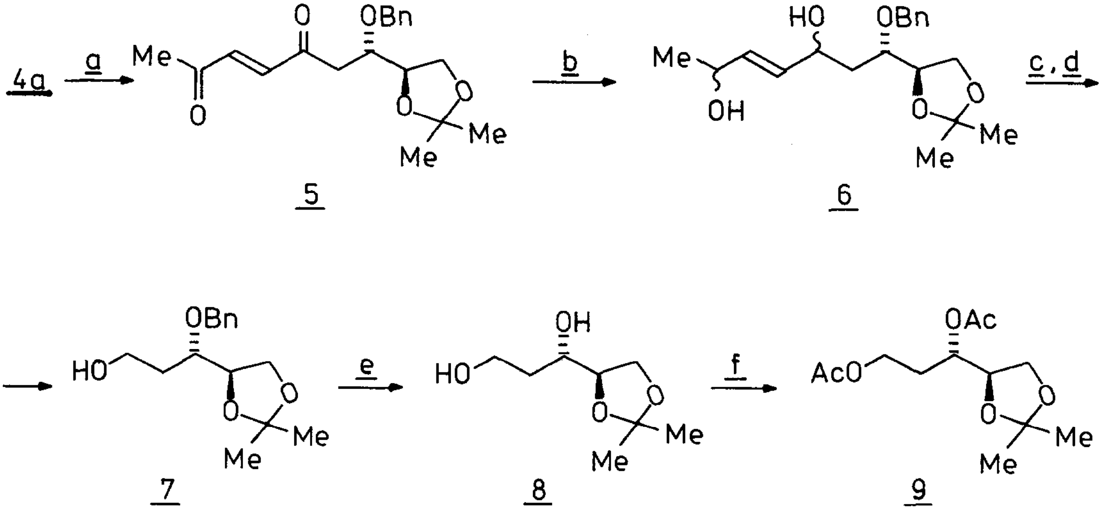
Scheme I



Reagents: a. 20 kbar, 55°C, CH_2Cl_2. b. $PhCH_2Br$, NaH, THF-DMF, RT.

Having established the extent of asymmetric induction in the high-pressure reaction of 1 with 2, we decided to study its direction by chemical correlation. The way adopted, which can equally serve as a method for synthesis of 2-deoxypentitols, is represented in Scheme II.

Scheme II



Reagents: a. PCC, AcONa, CH_2Cl_2, RT. b. DIBAL, CH_2Cl_2-hexane, -78°C. c. OsO_4-$NaIO_4$, aq. dioxane, RT. d. $NaBH_4$, MeOH, 0°C → RT. e. H_2, Pd/C, MeOH, RT. f. Ac_2O, Py, RT.

The sequence of reactions started from the major isomer, optically pure 4a. Furan ring opening in order to give enedione 5 [oil; IR(film): 1690cm^{-1}] was effected with PCC by Piancatelli method.[10] Trans-configuration of the double bond was based on the work of Williams and LeGoff.[11] DIBAL reduction gave diol 6 which was directly subjected to OsO_4-$NaIO_4$ reaction[12] followed by $NaBH_4$ reduction. 3-0-benzyl-4,5-0-isopropylidene-2-deoxy-D-ribitol (7) [oil; ^1H NMR ($CDCl_3$), δ (ppm): 1.38(3H,s), 1.45(3H,s) 1.86(2H,m), 2.72(1H,bs), 3.70-4.30(6H,m), 4.75(2H,s), 7.46(5H,s); $[\alpha]_D$+2^o(c=3.65, $CHCl_3$)] thus obtained was debenzylated by catalytic hydrogenation (10% Pd/C as a catalyst) to give diol 8 [$[\alpha]_D$+15^o(c=0.67, $CHCl_3$)]. Acetylation of 8 afforded 1,3-di-0-acetyl-4,5-0-isopropylidene-2-deoxy-D-ribitol (9) [oil; ^1H NMR($CDCl_3$), δ (ppm): 1.35(3H,s), 1.42(3H,s), 1.95(2H,m), 2.05(3H,s), 2.08(3H,s), 3.70-4.30(5H,m), 5.10(1H,m); $[\alpha]_D$-21^o(c=0.66, $CHCl_3$)] for which $[\alpha]_D$-23.2^o(c=0.63, $CHCl_3$) was reported.[2b] For identically protected 2-deoxy-D-xylitol, the optical rotation $[\alpha]_D$+36.7^o(c=0.29, $CHCl_3$) was also reported.[2b] This established the absolute configuration at the newly created centre of chirality shown in Schemes I and II.

The high-pressure reaction reported in the present Communication offers an access to optically pure synthons which have considerable potential applications in the synthesis of natural products. Studies directed towards the synthesis of carbohydrates and related compounds as well as the influence of high pressure on the asymmetric induction are in progress and will be reported in the near future.

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References and Notes

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3. 2,3-0-isopropylidene-D-glyceraldehyde (2) was prepared according to H.O.L.Fischer, E.Baer, J.Biol.Chem., 1939, 128, 463. For the high-pressure reaction of 2 with 1-methoxybuta-1,3-diene see: J.Jurczak, T.Bauer, S.Filipek, M.Tkacz, K.Zygo, J.Chem.Soc.,Chem.Commun., 1983, 540.

4. For the high-pressure experiments we used the piston-cylinder type apparatus described earlier: J.Jurczak, M.Chmielewski, S.Filipek, Synthesis, 1979, 41.
5. Satisfactory analytical and spectral data were obtained for all new compounds described in this paper. Polarimetric measurements were performed with a Perkin-Elmer 141 automatic polarimeter. ^{1}H NMR spectra were measured with a Jeol JNM-4H-100 spectrometer (100 MHz), with TMS as internal reference. IR spectra were recorded with a Beckman Acculab 1 spectrophotometer.
6. Only about 40% of 2 was consumed during the high-pressure reaction.
7. ^{1}H NMR ($CDCl_3$) spectrum of 3 (25.9 mg) with $Eu(fod)_3$ (11 mg) shows two singlets corresponding to CH_3-furan at δ=2.23(0.6H) and 2.36ppm (2.4H).
8. Similar spectrum as in Ref.7 for acetyl derivative of 3 (16.7 mg) with $Eu(fod)_3$ 16mg) shows for CH_3-furan δ=2.33(0.6H) and 2.43 ppm (2.4H).
9. PTLC plates: silica-gel 60 F_{254}, Merck; hexane-ethyl ether 95:5 ^{v}/v as an eluent, 5 developments.
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