Asymmetric Induction in the High-pressure Cycloaddition of 2,3-*O*-Isopropylidene-D-glyceraldehyde to 1-Methoxybuta-1,3-diene

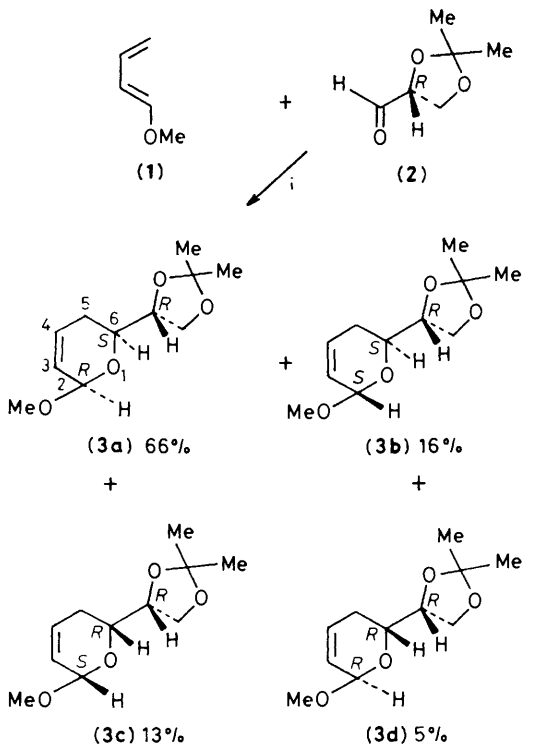
Janusz Jurczak,* Tomasz Bauer, Stanislaw Filipek, Marek Tkacz, and Krystyna Zygo

Institute of Organic Chemistry and Institute of Physical Chemistry, Polish Academy of Sciences, 01-224 Warszawa, Poland

The high-pressure cycloaddition of 2,3-*O*-isopropylidene-D-glyceraldehyde (**2**) to 1-methoxybuta-1,3-diene (**1**) afforded the diastereoisomeric cycloadducts (**3**) for which the diastereoisomeric excess and absolute configuration have been determined.

Recently we have described the high-pressure cycloaddition of simple representative carbonyl compounds to 1-methoxybuta-1,3-diene (**1**).[1] This process gives easy access to 6-substituted 2-methoxy-5,6-dihydro-2*H*-pyrans, which are important synthons for the synthesis of sugars[2] and other natural products.[3,4]

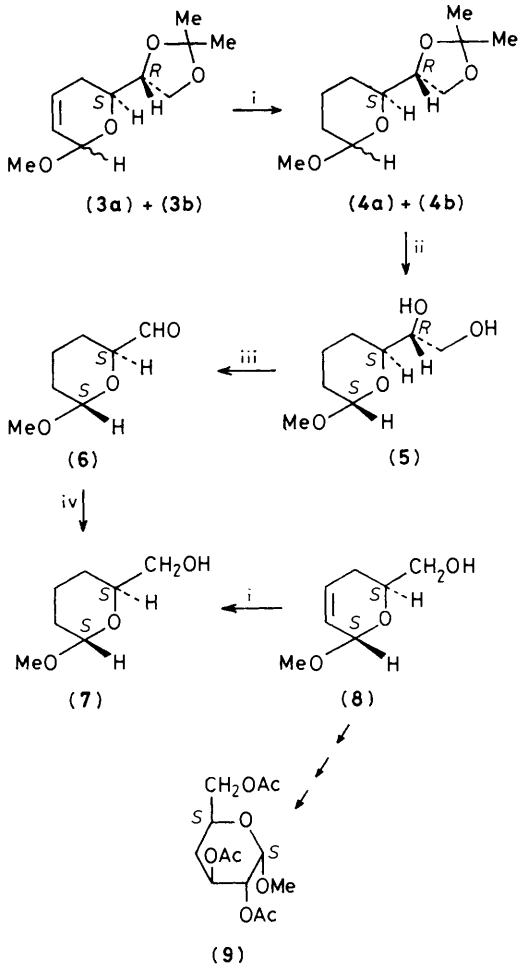
The cycloaddition of the aldehyde (**2**), bearing a chiral



Scheme 1. i, 22 kbar, 50 °C, diethyl ether, 80% yield.

centre located in the α-position with respect to the formyl group, to diene (**1**) gives rise to chiral cycloadducts (**3**). When the reaction is carried out under high-pressure conditions † (22 kbar,‡ 50 °C, diethyl ether as solvent), four diastereoisomeric adducts are formed: two *cis* diastereoisomers [(**3a**) and (**3c**)] by '*endo*' addition and two *trans* diastereoisomers [(**3b**) and (**3d**)] by '*exo*' addition,[5] in the proportions given in Scheme 1.

To establish the proportions of the diastereoisomers (**3**) formed, the reaction mixture was separated by column chromatography (silica gel Merck 60, 230—400 mesh, hexane–ethyl acetate 9 : 1 v/v as eluant), yielding two fractions which contained diastereoisomers (**3a**) + (**3b**) and (**3c**) + (**3d**), respectively. The ^{1}H n.m.r. spectra of both fractions exhibited differences in chemical shifts for the proton 2-H signals derived from *cis* [*i.e.* (**3a**) or (**3c**)] and *trans* [*i.e.* (**3b**) or (**3d**)] diastereoisomers.§ This differentiation (0.1—0.2 p.p.m.) was sufficient for precise integration, permitting the determination of the composition of both fractions. The diastereoisomeric composition was independently confirmed by hydrogenation of (**3a**) + (**3b**) over Adams catalyst, affording the tetrahydropyran derivatives (**4a**) + (**4b**) in an almost quantitative yield. This mixture of diastereoisomers was separated by column chromatography, and the resulting proportions of (**4a**) and (**4b**) were fully consistent with the spectrally determined



Scheme 2. i, H_2–Pt; ii, 1% HCl, MeOH; iii, $NaIO_4$; iv, $LiAlH_4$.

(^{1}H n.m.r.) diastereoisomeric composition of the fraction containing (**3a**) + (**3b**). Hydrogenation of the mixture of diastereoisomers (**3c**) + (**3d**) afforded analogous results.

The determination of the diastereoisomeric composition made possible the establishment of the diastereoisomeric excess (d.e.) for both addition types ('*endo*' and '*exo*').¶ It is interesting that in the reaction (**1**) + (**2**) → (**3**), carried out under high-pressure conditions (22 kbar, 50 °C), the asymmetric induction was different for the two types of addition; 67 and 52%, for '*endo*' and '*exo*', respectively. Moreover, the diastereoisomeric yield of cycloaddition was found to depend on both the pressure and the temperature. For example, for the reaction carried out at the same temperature (50 °C), but under much lower pressure (14.5 kbar), the diastereoisomeric yields for '*endo*' and '*exo*' additions were 61 and 40%, respectively. On the other hand, when the reaction was performed at lower temperature (25 °C) and high pressure (22 kbar), the diastereoisomeric yields were found to be 74 and 63% for '*endo*' and '*exo*' additions, respectively.

After the determination of the extent of asymmetric induction we decided to study its direction by the chemical correlation of a (**3a**) + (**3b**) diastereoisomer mixture with compound (**7**) which has known absolute configuration, having been correlated with the natural sugar (**9**). This correlation is represented in Scheme 2.

† For the high-pressure experiments we used the piston-cylinder type apparatus described earlier.[1]

‡ 1 bar = 10^5 Pa.

§ ^{1}H N.m.r. (100 MHz, $CDCl_3$): (**3a**) + (**3b**), δ, 6.20—5.60 (m, 2H, 3-H, 4-H), 5.03 [s, 0.8H, 2-H from (**3a**)], 4.90 [s, 0.2H, 2-H from (**3b**)], 4.40—3.60 (m, 4H, 6-H, $-OCH-CH_2O-$), 3.48 (s, 3H, OMe), 2.40—2.00 (m, 2H, 5-H, 5′-H), 1.42, 1.32 (2s, 6H, Me–C–Me); (**3c**) + (**3d**), δ, 6.20—5.60 (m, 2H, 3-H, 4-H), 5.20 [s, 0.7H, 2-H from (**3c**)], 4.97 [s, 0.3H, 2-H from (**3d**)], 4.50—3.80 (m, 4H, 6-H, $-OCH-CH_2O-$), 3.51 (s, 3H, OMe), 2.40—1.80 (m, 2H, 5-H, 5′-H), 1.48, and 1.42 (2s, 6H, Me–C–Me).

¶ d.e. ('*endo*') = {[(**3a**)] − [(**3c**)]}/{[(**3a**)] + [(**3c**)]}; d.e. ('*exo*') = {[(**3b**)] − [(**3d**)]}/{[(**3b**)] + [(**3d**)]}.

Hydrogenation of (**3a**) + (**3b**) afforded a mixture of compounds (**4a**) + (**4b**), which was treated, without chromatographic separation, with 1% HCl in methanol; this removed the isopropylidene protection, with simultaneous equilibration at the acetal centre to give the almost diastereoisomerically pure *trans* diol (**5**). Compound (**5**) was split with $NaIO_4$ (diethyl ether–water) to the aldehyde (**6**) which upon reduction with $LiAlH_4$ gave alcohol (**7**).** The specific rotation of (**7**) {$[\alpha]_D^{20}$ + 129.7°(*c* 4.3, benzene)} was almost identical with that found for alcohol (**7**) obtained by the hydrogenation of the unsaturated alcohol (**8**) whose 2*S*:6*S* absolute configuration was established by chemical correlation[2] with known methyl 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-*xylo*-hexopyranoside (**9**).[6]

The present results offer a new and effective method for obtaining interesting, optically pure, versatile synthons useful in the syntheses of natural products, such as optically active 2-deoxyribose[7] and 6-aminoheptose derivatives found in aminoglycoside antibiotics.[8] High-pressure conditions enable the title cycloaddition, which could not be performed under atmospheric pressure, to be carried out in high yield; moreover, the effect of pressure on asymmetric induction is perceptible. It is noteworthy that the present approach gave very high asymmetric induction, never achieved before in non-catalysed Diels–Alder reactions.

This work was supported by a Polish Academy of Sciences grant.

Received, 1st February 1983; Com. 163

** Satisfactory analyses and spectral data were obtained for all new compounds.

References

1 J. Jurczak, M. Chmielewski, and S. Filipek, *Synthesis*, 1979, 41.
2 A. Konował, J. Jurczak, and A. Zamojski, *Tetrahedron*, 1976, **32**, 2957.
3 M. Chmielewski, J. Jurczak, and A. Zamojski, *Tetrahedron*, 1978, **34**, 2977.
4 M. Chmielewski and J. Jurczak, *J. Org. Chem.*, 1981, **46**, 2230.
5 S. M. Weinreb and R. R. Staib, *Tetrahedron*, 1982, **38**, 3087, and references quoted therein.
6 S. D. Gero and R. D. Guthrie, *J. Chem. Soc. C*, 1967, 1761.
7 J. Jurczak and T. Bauer, manuscript in preparation.
8 J. Yoshimura, *J. Antibiot.*, 1979, **32**, Suppl., S-205.