58. Asymmetric *Diels-Alder* Reaction of 1-Methoxybuta-1,3-diene with (2*R*)-*N*-Glyoxyloylbornane-10,2-sultam

Preliminary Communication

by **Tomasz Bauer, Christian Chapuis**[1])*, **Janusz Kozak**, and **Janusz Jurczak***

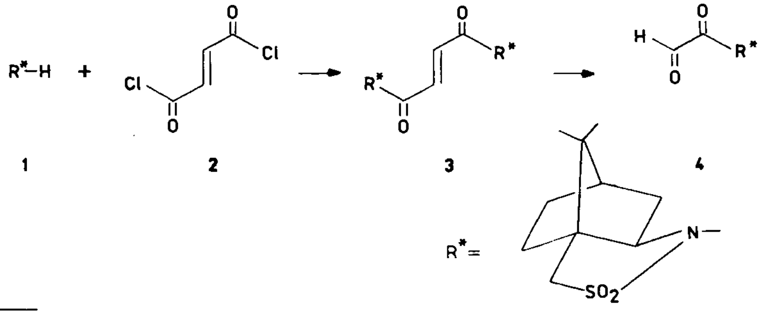
Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warszawa, Poland

(5.I.89)

Starting from sultam **1**, the chiral dienophile (2*R*)-*N*-glyoxyloylbornane-10,2-sultam (**4**) was readily prepared. Non-catalyzed atmospheric- and high-pressure as well as [Eu(fod)$_3$]-promoted [4 + 2] cycloadditions of 1-methoxybuta-1,3-diene (**5**) to chiral dienophile **4**, leading with high asymmetric induction to 6-methoxy-3,6-dihydro-2*H*-pyran-2-yl derivatives **6**–**9**, are described. The extent and direction of asymmetric induction in these reactions were established by ^{1}H-NMR analysis and chemical correlation, respectively. Stereochemical models for both non-catalyzed and [Eu(fod)$_3$]-promoted reactions are proposed.

The *Diels-Alder* reaction of 1-alkoxybuta-1,3-dienes with alkyl glyoxylates leads to formation of 2-alkoxy-5,6-dihydro-2*H*-pyran in racemic form [1]. These adducts are convenient substrates for stereoselective total syntheses of many monosaccharides [2] and other natural products [3] [4]. Attempts have been made to obtain these adducts in enantiomeric form by [4 + 2] cycloaddition of 1-methoxybuta-1,3-diene to optically active esters of glyoxylic acid [5]; however, the enantiomeric purities of the obtained adducts were low. Application of the high-pressure technique to the reaction of 1-methoxybuta-1,3-diene with (*R*)-menthyl glyoxylate has substantially improved asymmetric induction [6]. It appeared worthwhile to investigate the influence of the highly potent chiral auxiliary (2*R*)-bornane-10,2-sultam, introduced and successfully applied by *Oppolzer et al.* [7], on asymmetric induction in this type of *Diels-Alder* reaction.

Scheme 1



---

[1]) Present address: *Firmenich SA*, CH–1283 La Plaine.

In the present studies, the chiral dienophile *N*-glyoxyloylbornane-10,2-sultam (**4**) was obtained by reaction of fumaroyl dichloride **2** with 2 equiv. of sultam **1** (→diamide **3** in 60% yield; m.p. 247–248°; $[\alpha]_D = -135.6$ ($c = 1.18$, $CHCl_3$)) followed by ozonolysis *(Scheme 1)*. After usual workup, the crude **4** was obtained in quantitative yield and used as such in all further experiments.

The [4 + 2] cycloaddition of 1-methoxybuta-1,3-diene (**5**) to chiral dienophile **4** gave rise to the chiral cycloadducts **6**–**9** *(Scheme 2)*. The results of this reaction carried out under various conditions are presented in the *Table*.

Scheme 2

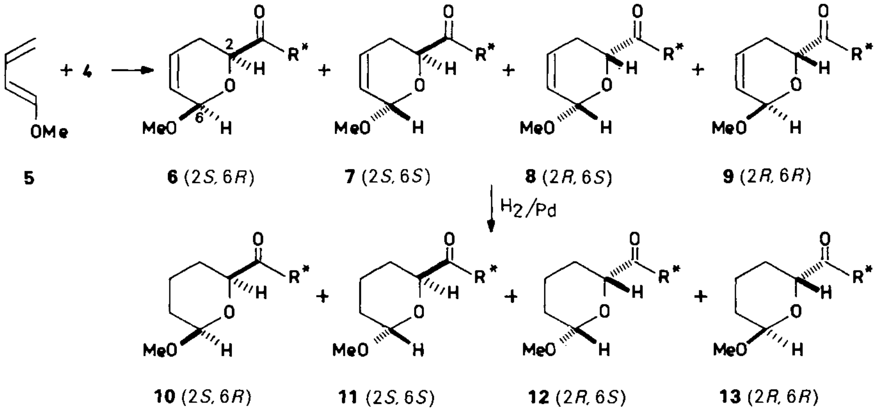


Table. *The Asymmetric* Diels-Alder *Reaction* **4** + **5**→**6**–**9**

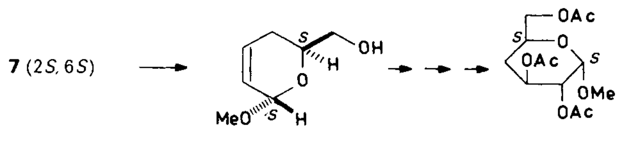
Entry	Pressure	Temperature [°]	Time [h]	Catalyst	Yield[a]) [%]	**6**/**7**	**8**/**9**	**6** + **7**/ **8** + **9**[b])
a	1 atm	20	20	–	73	3:2	1:1	73:27
b	10 kbar	20	20	–	76	3:2	1:1	71:29
c	10 kbar	20	20	2% $[Eu(fod)_3]$	80	2:3	3:7	75:25
d	1 atm	20	20	2% $[Eu(fod)_3]$	81	1:9	–[c])	89:11
e	1 atm	20	1	2% $[Eu(fod)_3]$	81	5:95	–	94:6
f	1 atm	–15	16	2% $[Eu(fod)_3]$	47	5:95	–	96:4
g	1 atm	–20	16	2% $[Eu(fod)_3]$	35	5:95	–	> 96:4
h	1 atm	–78	75	2% $[Eu(fod)_3]$	36	5:95	–	> 96:4

[a]) Isolated yield besides either polymers *(Entries a–e)* or starting material *(Entries f–h)*.
[b]) Corresponding to the (2*S*,6*S*)-**7**/(2*R*,6*R*)-**9** mixture obtained after acidic treatment [8].
[c]) **6** + **7**/**8** + **9** ratio inferior to enable a precise ^1H-NMR analysis.

When the reaction was effected at room temperature in CH_2Cl_2 as solvent *(Entry a)*, four diastereoisomeric adducts were formed: two *cis*-diastereoisomers (**6** and **8**) by *endo* addition, and two *trans*-diastereoisomers (**7** and **9**) by *exo* addition. To establish the proportions of the diastereoisomers, the mixture was separated by column chromatography (silica gel *Merck 60*, 230–400 mesh, hexane/AcOEt 9:1), yielding two fractions which contained pairs of diastereoisomers **6**/**7** and **8**/**9**, respectively. The ^1H-NMR spectra of all diastereoisomers exhibited differences in chemical shifts (0.05–0.35 ppm) for the H–C(2) and H–C(6) signals, allowing precise integration and, hence, determination of the composition of the crude reaction mixture. The composition was independently confirmed by hydrogenation of the reaction mixture over *Adams* catalyst affording, after chromatographic separation, two fractions containing mixtures of diastereoisomers **10**/**11** and **12**/**13**, respectively. The proportions found were fully consistent with those determined for the crude reaction mixture obtained from the [4 + 2] cycloaddition.

After the determination of the extent of asymmetric induction, we studied its direction by chemical correlation of pure diastereoisomer **7**²), readily available *via* acidic isomerization [8] of the mixture **6**/**7**, with compound **14**³) whose absolute configuration is known from an earlier correlation with the natural sugar derivative **15** [9] (see *Scheme 3*).

Scheme 3

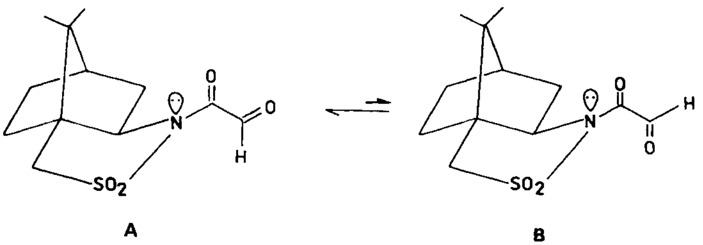


14 **15**

Several aspects of the data shown in the *Table* are noteworthy. The reaction carried out at ambient temperature and pressure afforded the diastereoisomeric cycloadducts in a good yield, but with rather low (46% d.e.) asymmetric induction *(Entry a)*. Therefore, we decided to enhance asymmetric induction by application of the high-pressure technique [6] and/or by [Eu(fod)$_3$] [10] as catalyst. The application of high pressure or both high pressure and [Eu(fod)$_3$] [11] failed to substantially change the yield and the diastereoisomeric composition of the product (*Entries b* and *c*). The best results in terms of both chemical (81%) and optical (88%) yield were obtained, when the reaction was performed at ambient temperature and pressure in the presence of 2% [Eu(fod)$_3$] during 1 h *(Entry e)*. Even better asymmetric induction was obtained at lower temperatures *(Entries f–h)* albeit with a much lower chemical yield. *Entry d* as compared with *Entry e* requires a few words of explanation. Lower asymmetric induction found for the reaction shown in *Entry d* probably resulted from the slightly lower stability of diastereoisomer **7** as compared with **9**; this fact causes the time-dependent change in the diastereoisomeric ratio.

Rationalization of our results can be based on earlier work of *Oppolzer et al.* [7] [12] and *Curran et al.* [13]. As suggested by X-ray analysis of *N*-acryloyl- and *N*-crotonoylsultam [7] [12] [13], for *N*-glyoxyloylsultam **4**, the sterically more stable SO$_2$/CO antiperipla-

Scheme 4



A **B**

---

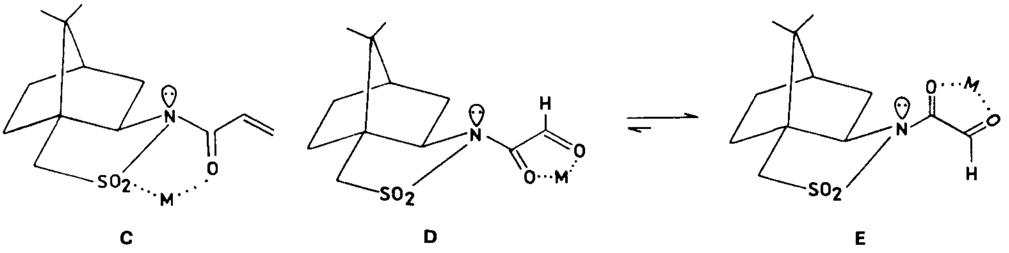
[2] Available in 95–98% yield from **6**/**7**: m.p. 215–217° from hexane/CH$_2$Cl$_2$, $[\alpha]_D = -113.4$ (c = 1.2, CHCl$_3$).

[3] $[\alpha]_D = -79.9$ (c = 1.55, benzene).

nar, CO/CHO s-*cis* planar conformation **A** should be preferred over conformation **B** *(Scheme 4)*. It is also noteworthy that under high pressure, the CO/CHO s-*cis* conformation of glyoxylates is favored [6] [14]. Therefore, the approach of diene **5** to dienophile **4** should occur from the top side of the bornane skeleton (*si* attack), as it has been observed for noncatalyzed addition of cyclopentadiene to the corresponding *N*-acryloyl- and *N*-crotonoylsultam [12] [15].

The same direction of induction was observed for the *Lewis*-acid-catalyzed addition of cyclopentadiene to *N*-enoylsultams. This has earlier been rationalized by *Oppolzer et al.* [7] as a bottom C(α)-*re* attack of the diene on the SO_2/CO synperiplanar, CO/ $CH{=}CH_2$ s-*cis* planar conformation **C**, where the catalyst chelates both the SO_2 and CO groups to rigidify the side-chain *(Scheme 5)*. This is in accord with the observed bathochromic shift of both the CO and symmetric SO_2 stretchings in the IR spectra of the 1:1 complex of $TiCl_4$ and *N*-acryloylsultam [7]. In contrast, the 1:1 complex of $TiCl_4$ and *N*-glyoxyloylsultam **4** displayed a bathochromic shift of both CO stretchings (1702–1580 cm^{-1}) and hypsochromic shifts of both asymmetric and symmetric SO_2 stretchings (1345–1375 and 1140–1155 cm^{-1}, resp.). These facts suggest that the metal chelates both CO groups [16], as shown in conformations **D** and **E** *(Scheme 5)*. Therefore, the approach of diene **5** to dienophile **4** in conformation **E** from the top side of the bornane skeleton (*si* attack) should be preferred. However, in both non-catalyzed and *Lewis*-acid-catalyzed reactions, the participation of *si* attack from the sterically less hindered bottom side (conformer **B** in *Scheme 4* and conformer **D** in *Scheme 5*) cannot be excluded, since the chelating properties of [Eu(fod)$_3$] compared to $TiCl_4$ may be different in analogous systems [12] [15].

Scheme 5



M = Metal

The present results open a convenient and efficient route to optically pure 2-alkoxy-5,6-dihydro-2*H*-pyrans, *eo ipso* to the synthesis of optically pure monosaccharides from non-carbohydrate precursors.

This work was supported by the *Polish Academy of Sciences* (grant CPBP 01.13).

REFERENCES

[1] A. Konował, J. Jurczak, A. Zamojski, *Tetrahedron* **1976,** *32,* 2957.

[2] A. Zamojski, A. Banaszek, G. Grynkiewicz, *Adv. Carbohydr. Chem. Biochem.* **1982,** *40,* 1; A. Zamojski, G. Grynkiewicz, in 'The Total Synthesis of Natural Products', Ed. J. W. ApSimon, J. Wiley, Chichester, 1984, Vol. 6, pp. 141–235.

[3] M. Chmielewski, J. Jurczak, A. Zamojski, *Tetrahedron* **1978,** *34,* 2977.

[4] M. Chmielewski, J. Jurczak, *J. Org. Chem.* **1981,** *46,* 2230.

[5] J. Jurczak, A. Zamojski, *Tetrahedron* **1972,** *28,* 1505.

[6] J. Jurczak, *Pol. J. Chem.* **1979,** *53,* 2539.

[7] W. Oppolzer, C. Chapuis, G. Bernardinelli, *Helv. Chim. Acta* **1984,** *67,* 1397.

[8] J. Jurczak, T. Bauer, A. Gołebiowski, *Bull. Pol. Acad. Chem.* **1985,** *33,* 397.

[9] S. D. Gero, R. D. Guthrie, *J. Chem. Soc. (C)* **1967,** 1761.

[10] M. Bednarski, S. Danishefsky, *J. Am. Chem. Soc.* **1983,** *105,* 3716.

[11] J. Jurczak, A. Gołebiowski, T. Bauer, *Synthesis* **1985,** 928.

[12] W. Oppolzer, G. Poli, C. Starkemann, G. Bernardinelli, *Tetrahedron Lett.* **1988,** *29,* 3559.

[13] D. P. Curran, B. H. Kim, J. Daugherty, T. A. Heffner, *Tetrahedron Lett.* **1988,** *29,* 3555.

[14] J. Jurczak, M. Tkacz, *J. Org. Chem.* **1979,** *44,* 3347.

[15] C. Chapuis, Thesis, Université de Genève, 1984, No. 2144, p. 46, 51, 55, 56.

[16] M. F. Lappert, *J. Chem. Soc.* **1961,** 817.