21. Cycloaddition of 3,4-Dimethoxyfuran with 1,4-Benzoquinones under High Pressure[1])

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Summary

High-pressure cycloaddition of 3,4-dimethoxyfuran with 1,4-benzoquinone, toluquinone and 2,3-dimethoxy-1,4-benzoquinone show, at 7 kbar and room temperature, prevailing formation of *endo*-isomers. Raising pressure (or temperature) results in a surprising increase of the *exo*-isomer. By catalytic hydrogenation of a mixture **3a**/**4a**, followed by chromatography, the pure diastereomers **5** and **6** were obtained.

In one of our previous publications dealing with the cycloadditions of 3,4-dimethoxyfuran (**1**) we demonstrated the surprising ease of adduct formation with 1,4-benzoquinones **2** at room temperature and normal pressure [2]. The crystalline products from such *Diels-Alder* reactions were shown to possess the *endo*-structures **3a** (yield 68%), **3b** (86%), and **3c** (90%), respectively, except the single case of the addition with **2d** where the *exo*-structure **4c** (46%) appeared[2]).

As an explanation for this differential behaviour we assumed dissimilar solubilities or speed of crystallization of the stereoisomers, present in solution by addition and *retro-Diels-Alder* reactions typical for such systems.

In the present communication we report on the influence of both, high pressure and variation of temperature on the course of cycloadditions of **1** and **2**.

The 3,4-dimethoxyfuran (**1**) [3] was reacted with **2a**, **2b** and **2c** at 7–19 kbar and 25 or 50° in toluene as solvent during 20 h to give high yields of a mixture of the *exo*- and *endo*-adducts **3** and **4**, respectively. After completion of the reaction, the crystalline, pure *endo*-adducts **3** had precipitated from the solvent and were isolated by filtration. To the filtrate, ether was immediately added to yield a second

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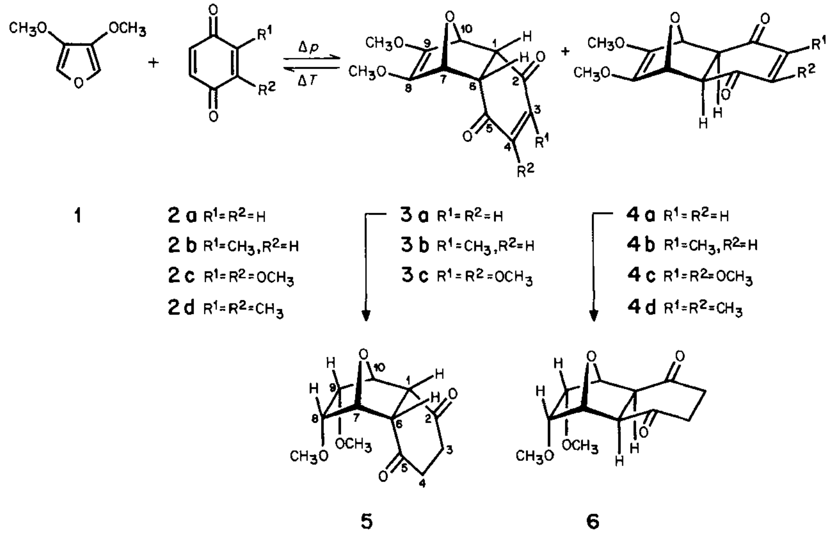
[1]) Organic Syntheses under High Pressure, Part V. For Part IV see [1].

[2]) Mother liquors were not examined for other stereoisomers. Solutions of **3a**, **3b** and **3c** slowly revert to starting materials and also recombine to **4a**, **4b**, and **4c**, respectively, except for solutions of **4d** which remained stable under these conditions [2].

Scheme



crop of pure **3**. The mother liquors, after evaporation *in vacuo*, were monitored by ^{1}H-NMR. The *endo/exo*-ratios of each reaction were estimated from the combination of weight of **3** and interpretation of the ^{1}H-NMR. spectrum at the signals of H–C(1)/H–C(6) and H–C(7)/H–C(10); see *Tables 1* and *2*.

Table 2 gives the results of high-pressure influence on the *endo/exo*-ratios in the reaction of **1** with the *p*-benzoquinones. At 7 kbar the general picture is in good accord with our earlier observations at normal pressure [2]. However, to our surprise, at higher pressure the amount of the *exo*-isomer increases. Whether differences in the volumes of the transition states under high pressure or acceleration of the *endo*→*exo*-isomerization speeded up by pressure (and also by temperature) play a role, has to be investigated [4].

After catalytic hydrogenation of a (54:46)-mixture of **3a** and **4a** with Pd/C, followed by chromatographic separation, the diastereomers **5** (31%, m.p. 117–120°) and **6** (42%, m.p. 147–150°) were obtained. Their structures depicted in the *Scheme* are based on X-ray structure determinations [5]. In accord with earlier observations on the stereochemistry of the hydrogenation of *Diels-Alder* adducts with 3,4-dimethoxyfuran (**1**) [1] [6], again exclusive addition of H_2 from the *exo*-side was observed.

Experimental Part

General Remarks. High-pressure experiments were performed in an apparatus of the piston-cylinder type described in our earlier papers [1] [7].

Melting points (m.p., uncorrected) were determined on a *Kofler* block. ^{1}H-NMR. spectra were recorded with a *Jeol-JNM-4H-100* spectrometer (δ scale, TMS at 0 ppm). IR. spectra (cm^{-1}) were recorded on a *Unicam-SP-200* spectrophotometer. Silica gel *G (Merck)* was used for TLC. and *Merck 60* silica gel for column chromatography. Typical TLC. systems were ligroin/ethyl acetate 7:3 (*v/v*) or 1:1 (*v/v*).

Table 1. *^{1}H-NMR. data of* endo- *and* exo-*adducts* **3** *and* **4**, *and of tetrahydro derivatives* **5** *and* **6**

Compound	Solvent	H–C(1), H–C(6)	H–C(3),H–C(4)	H–C(7), H–C(10)	CH_3O–C(8), CH_3O–C(9)	CH_3–C(3)	CH_3O–C(3), CH_3O–C(4)	H–C(8), H–C(9)
3a[a])	D_6-Acetone	3.36 (*m*, 2 H)	6.53 (*s*, 2 H)	5.01 (*m*, 2 H)	3.53 (*s*, 6 H)	–	–	–
3a[b])	$CDCl_3$	3.50 (*m*, 2 H)	6.71 (*s*, 2 H)	5.22 (*m*, 2 H)	3.68 (*s*, 6 H)	–	–	–
4a[b])	$CDCl_3$	3.06 (*s*, 2 H)	6.80 (*s*, 2 H)	4.99 (*s*, 2 H)	3.82 (*s*, 6 H)	–	–	–
3b[a])	$CDCl_3$	3.40 (*m*, 2 H)	– 6.43 (*qa*, 1 H)[c])	5.05 (*m*, 2 H)	3.56 (*s*, 6 H)	1.93 (*d*, 3 H)[c])	–	–
3b[b])	$CDCl_3$	3.50 (*m*, 2 H)	– 6.60 (*qa*, 1 H)[c])	5.18 (*m*, 2 H)	3.68 (*s*, 6 H)	2.00 (*d*, 3 H)[c])	–	–
4b[b])	$CDCl_3$	3.08 (*s*, 2 H)	– 6.81 (*qa*, 1 H)[c])	5.00 (*s*, 2 H)	3.83 (*s*, 6 H)	2.08 (*d*, 3 H)[c])	–	–
3c[a])	$CDCl_3$	3.43 (*m*, 2 H)	– –	5.13 (*m*, 2 H)	3.66 (*s*, 6 H)	–	3.95 (*s*, 6 H)	–
3c[b])	$CDCl_3$	3.48 (*m*, 2 H)	– –	5.18 (*m*, 2 H)	3.72 (*s*, 6 H)	–	4.02 (*s*, 6 H)	–
4c[a])	CCl_4	2.93 (*s*, 2 H)	– –	4.77 (*s*, 2 H)	3.73 (*s*, 6 H)	–	3.93 (*s*, 6 H)	–
4c[b])	$CDCl_3$	3.08 (*s*, 2 H)	– –	4.98 (*s*, 2 H)	3.83 (*s*, 6 H)	–	4.07 (*s*, 6 H)	–
5[b])	$CDCl_3$	3.50 (*m*, 2 H)	2.73, 3.03 (2 *m*, 4 H)	5.00 (*m*, 2 H)	3.43 (*s*, 6 H)	–	–	3.73 (*m*, 2 H)
5[b])	C_6D_6	3.18 (*m*, 2 H)	2.09 (*s*, 4 H)	4.86 (*m*, 2 H)	3.06 (*s*, 6 H)	–	–	3.26 (*m*, 2 H)
6[b])	$CDCl_3$	3.12 (*m*, 2 H)	2.60, 3.20 (2 *m*, 4 H)	5.10 (*m*, 2 H)	3.28 (*s*, 6 H)	–	–	3.75 (*m*, 2 H)
6[b])	C_6D_6	2.70 (*m*, 2 H)	1.64 (*s*, 4 H)	4.85 (*m*, 2 H)	2.95 (*s*, 6 H)	–	–	3.23 (*m*, 2 H)

[a]) At 100 MHz [2]. [b]) This paper, 100 MHz. [c]) $^4J = 2$ Hz.

Table 2. *Influence of high pressure on* endo/exo-*ratio of the cycloadducts* **3** *and* **4**

p [kbar]	*T* [°C]	Yield [%] (**3a**+**4a**)	*endo/exo* (**3a/4a**)	Yield [%] (**3b**+**4b**)	*endo/exo* (**3b/4b**)	Yield [%] (**3c**+**4c**)	*endo/exo* (**3c/4c**)
7.0	25	90	89:11	95	89:11	91	79:21
7.0	50	95	84:16	97	84:16	–	–
11.0	25	92	83:17	91	76:24	90	79:21
19.0	25	93	54:46	89	68:32	91	74:26
19.0	50	91	34:66	92	48:52	92	70:30

1. *7,10-Epoxy-8,9-dimethoxy*-cis-*1*-transoid-*1,10*-cis-*10-bicyclo[4.4.0]-deca-3,8-dien-2,5-dione* (**3a**) *and 7,10-Epoxy-8,9-dimethoxy*-cis-*1*-cisoid-*1,10*-cis-*10-bicyclo[4.4.0]deca-3,8-dien-2,5-dione* (**4a**). Typical high-pressure procedure: 216 mg (2 mmol) of **2a** and 256 mg (2 mmol) of **1** were dissolved in 3.5 ml of toluene. The mixture was placed in a *Teflon* ampoule [1] which was inserted into the high-pressure vessel filled with hexane as transmission medium and closed by a mobile piston. Then the high-pressure unit was placed between the pistons of a hydraulic press and the pressure raised to 6.8 kbar. After stabilization of the pressure, the heater was switched on, whereupon the temp. was raised to 50° and the pressure to 7.0 kbar. The mixture was kept under these conditions for 20 h, cooled to r.t. and decompressed. After decompression, crystalline **3a** which precipitated under high-pressure was immediately filtered off, and 5 ml of ether was added to the filtrate, and this mixture was cooled to – 10° to give the second crop of crystalline **3a**. The residue obtained after evaporation of ether and toluene was examined by ^{1}H-NMR. The integral showed the ratio **3a**/**4a** to be 1:4. From combination of the weights and integration, the yield of **3a** and **4a** was calculated as 447 mg (95%).

2. *7,10-Epoxy-8*endo, *9*endo-*dimethoxy*-cis-*1*-transoid-*1,10*-cis-*10-bicyclo[4.4.0]decane-2,5-dione* (**5**) *and 7,10-Epoxy-8*endo, *9*endo-*dimethoxy*-cis-*1*-cisoid-*1,10*-cis-*10-bicyclo[4.4.0]decane-2,5-dione* (**6**). The mixture of 472 mg **3a** and **4a** (54:46) was dissolved in 20 ml of methanol, and 30 mg of 10% Pd/C was added; hydrogenation at 4 atm for 3 h at r.t. gave, after filtration and evaporation of the solvent, a mixture which was separated by column chromatography (silica gel, ligroin/ethyl acetate 9:1) to give 148 mg (31%) of **5**; m.p. 117–120°. – IR. (KBr): 1705 (C=O), 1190, 1145, 1022 (C–O–C). – ^{1}H-NMR.: s. *Table 1*. – MS.: 240 (M^+).

Moreover 200 mg (42%) of **6** were isolated, m.p. 147–150°. – IR. (KBr): 1700 (C=O), 1195, 1150, 1110, 1015 (C–O–C). – ^{1}H-NMR.: s. *Table 1*. – MS.: 240 (M^+).

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