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FACTORS AFFECTING THE *ENDO* : *EXO* RATIO IN DIELS-ALDER REACTIONS OF CYCLOPENTADIENE

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Abstract—The ratio of *endo*-CHO:*exo*-CHO in the Diels–Alder addition of a *trans*-$\alpha\beta$-unsaturated aldehyde to cyclopentadiene can be changed from 1:2 to 8:1, depending on temperature and BF_3-catalysis.

During recent investigations of synthetic routes to prostaglandins we required the compounds **2** and **3** as precursors. We report here (Tables 1 and 2) the striking dependence on the reaction conditions of the relative amounts of **2** and **3** from the Diels–Alder reaction of cyclopentadiene and *trans*-4-benzyloxybut-2-enal **1** and our conditions for optimum yields of either isomer. Also included are the results of a less extensive investigation of the effect of temperature on the uncatalysed reaction of cyclopentadiene and *trans*-10-oxodec-8-enoic acid **4** to give **5** and **6**. The isomer distributions were obtained by ^{1}H NMR spectroscopy of the reaction products from the relative magnitudes of the aldehydic hydrogen absorptions of the two isomers; there is ample evidence from ^{1}H and ^{13}C NMR[1] to show that the *exo*-hydrogen will be more deshielded and have an absorption at lower field than the *endo*-hydrogen. GLC analysis confirmed the isomer distribution.

The predominance of the *endo*-formyl adducts **2** and **5** (66 and 57% respectively) at low temperatures, in the uncatalysed reactions, doubtless arises from a kinetic preference for the isomer with a more favourable secondary interaction between the non-bonding formyl group and cyclopentadiene in the transition state.[2] However, as a consequence of the reversibility of the reaction it is possible to alter the product distribution to give mainly the *exo*-formyl adducts **3** and **6** (66 and 67% respectively) at high temperatures. These changes in the product distribution are analogous to the results obtained from the reaction of cyclopentadiene with some $\alpha\beta$-unsaturated acids.[3]

The Lewis acid catalyst, BF_3-etherate, dramatically accelerates the reaction of cyclopentadiene with the unsaturated aldehyde **1** and also increases the kinetic preference for the *endo*-formyl adduct **2**. Thus in the presence of the catalyst for a few minutes at 0° almost 90% of this adduct is formed. Comparable results for the catalysed reactions of cyclopentadiene with some unsaturated esters have been reported.[4]

EXPERIMENTAL

Preparation of trans-*4-benzyloxybut-2-enal* **1**. *Trans* - 4 - benzyloxybut - 2 - en - 1 - ol, prepared from *trans* - but - 2 - ene - 1,4 - diol by the method of Arai and Ichikizaki,[5] was oxidised with Jones reagent (CrO_3 in H_2SO_4aq). A soln of Jones reagent (CrO_3, H_2O, H_2SO_4; 26.7 g, 77 ml, 23 ml) was added dropwise to a cooled soln (0°) of the benzyloxybutenol (10.0 g) in acetone (50 ml). When the mixture maintained a permanent orange colour it was poured into water and extracted with ether. The combined ether solns were washed with water, dried ($MgSO_4$) and evaporated to give *trans* - 4 - benzyloxybut - 2 - enal (9.7 g, 97%), b.p. 112–115°/0.8 torr; (Found: C, 74.8; H, 6.7. Calc. for $C_{11}H_{12}O_2$ (M.Wt. 176.2); C, 75.0; H, 6.9%).

Preparation of trans - 10 - *oxodec* - 8 - *enoic acid* **4**. 7-Bromoheptanoic acid was prepared from 7-bromoheptanol by the method of Ames and Islip[6] and was converted into *cis* - 10 - hydroxydec - 8 - enoic acid following Ames *et al.*[7] The *cis*-hydroxy-alkenoic acid (6.0 g) was oxidised by stirring with activated MnO_2 (15.0 g) in benzene (200 ml) for 16 h. The insoluble material was removed by filtration and washed several times with chloroform, and the combined organic solns were evaporated to give crude *cis* - 10 - oxodec - 8 - enoic acid (3.8 g, 64%), m.p. 36–40°. Without further purification the material (2.6 g) was isomerised with 3M-HCl (1 ml) in tetrahydrofuran (100 ml) and after 1 h the mixture was poured into water. Ether extraction, followed by washing with water and evaporation, gave *trans*-oxodec-8-enoic acid **4** (2.3 g, 88.5%), m.p. 49–51° (ethyl acetate); (Found: C, 65.2; H, 8.75. Calc. for $C_{10}H_{16}O_3$ (M.Wt. 184.2); C, 65.2; H, 8.75%). ^{1}H NMR ($CDCl_3$): δ 9.5 (d, 1H, J 8 Hz, –CHO), 9.0 (s, 1H, $-CO_2H$), 7.2–5.8 (2t, 2H, J 6 Hz, 2d, J

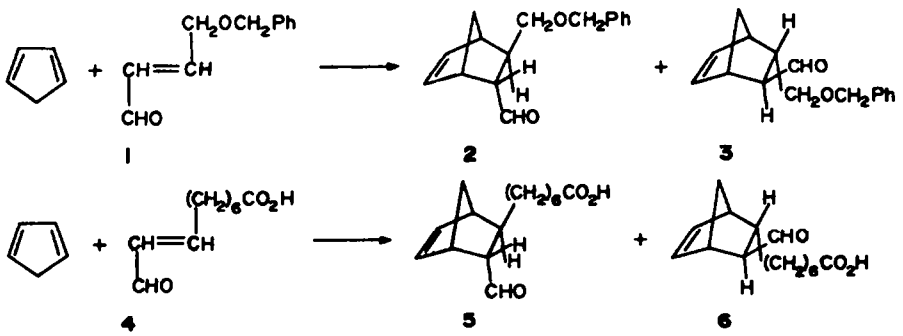

Table 1. The influence of reaction conditions on the yields and product distribution from the uncatalysed Diels–Alder reaction of cyclopentadiene with *trans*-4-benzyloxybut-2-enal 1 or *trans*-10-oxodec-8-enoic acid 4

Reaction conditions		Dienophile 1			Dienophile 4		
Temp. (°C)	Time (h)	Product Distribution (%) 2	3	Yield (%)[a]	Product Distribution (%) 5	6	Yield (%)[a]
0	240	66	34	57			
25	48	58	42	68			
100	16	51	49	91	57	43	66
150	16	45	55	92	42	58	75
175	16	39	61	91	39	61	80
200	2	42	58	74	33	67	50
200	6	34	66	73	37	63	60
200	16	Decomposition			Decomposition		

[a]Yield based on dienophile.

Table 2. Influence of reaction conditions on the yield and product distribution from the BF_3-etherate catalysed Diels–Alder reaction of cyclopentadiene and *trans*-4-benzyloxybut-2-enal 1

Solvent	molar ratio catalyst: 1	Temp (°C)	time (min)	product distribution (%) 2	3	Yield (%)[a]
Benzene	10	0	1	80	20	74
Benzene	10	0	2	85	15	100
Benzene	50	0	1	83	17	95
Benzene/Toluene	10	-15	5	90	10	100
Benzene/Toluene	10	-20	5	90	10	100
Dichloromethane	10	0	2	86	14	100
Dichloromethane	10	0	1.5	89	11	100
Dichloromethane	10	-15	5	no reaction		
Ethanol	10	-15	3	no reaction		

[a] Yield based on dienophile.

6 Hz, –CH=CH–), 2.6–2.1 (m, 4H, $-CH_2CO$ and $-CH_2C$=C), 1.8–1.1 (m, 8H, $-CH_2-$).

Procedure for uncatalysed Diels–Alder reactions. Cyclopentadiene (0.115 g, 1.7×10^{-3} mol) (produced by thermal depolymerisation of dicyclopentadiene at 180°) and the dienophile (1.6×10^{-3} mol) were dissolved in benzene (1 ml) and maintained at the required temp. for the selected time. For experiments at 100, 150, 175 and 200° the reactions were carried out in sealed glass ampoules. The reactions were worked up by removing the volatile materials by evaporation to give a residue which was analysed by ^{1}H NMR, GLC and GLC-mass spectrometry [glass columns (0.4 cm i.d. × 1.5 m) packed with DEGA (1% w/w) on Celite (100–120 mesh); adducts 2 and 3 at 160° and 70 ml min^{-1} (nitrogen) and adducts 5 and 6 at 200° and 60 ml min^{-1}].

Procedure for BF_3-etherate catalysed Diels–Alder reactions. A cooled soln of cyclopentadiene (0.079 g, 1.2×10^{-3} mol), 4-benzyloxybut-2-enal (0.2 g, 1.1×10^{-3} mol) and $BF_3 \cdot Et_2O$ (1.43 ml, 1.1×10^{-4} mol) in the selected solvent (10 ml) was stirred for the required time before being poured into $NaHCO_3$aq. Ether extraction, followed by drying ($MgSO_4$) and evaporation, gave adducts 2 and 3 as a residue.

The benzyloxynorbornene derivatives 2 and 3 had: mass spectrum: *m/e* (relative intensity) 242 (M^+, 0.9), 151 (3.8), 121 (8.1), 107 (5.6), 105 (6.2), 92 (14), 91 (100), 79 (13), 77 (13), 66 (80), 65 (23); ^{1}H NMR ($CDCl_3$): δ 9.6 (d, J 1.5 Hz, *exo*-CHO), 9.2 (d, J 1.5 Hz, *endo*-CHO), 7.1 (s, $5H_{arom}$), 6.2–5.7 (m, 2H, –CH=CH–), 4.35 (s, *exo*-Ar-CH_2–), 4.31 (s, *endo*-Ar-CH_2–), 3.35 (d, 2H, J 7 Hz, $ArCH_2O\underline{CH_2}$–), 3.2–1.2 (m, 6H, $-CH_2-$ and –CH–). The norbornenehexanoic acid derivatives 5 and 6 had ^{1}H NMR ($CDCl_3$): δ 10.1 (s, 1H, $-CO_2H$), 9.75 (d, J 2 Hz, *exo*-CHO), 9.4 (d, J 2 Hz, *endo*-CHO), 6.4–5.95 (m, 2H, –CH=CH–), 3.5–1.1 (m, 18H, $-CH_2-$ and –CH–).

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