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ASYMMETRIC HYDROFORMYLATION OF DELTACYCLENE

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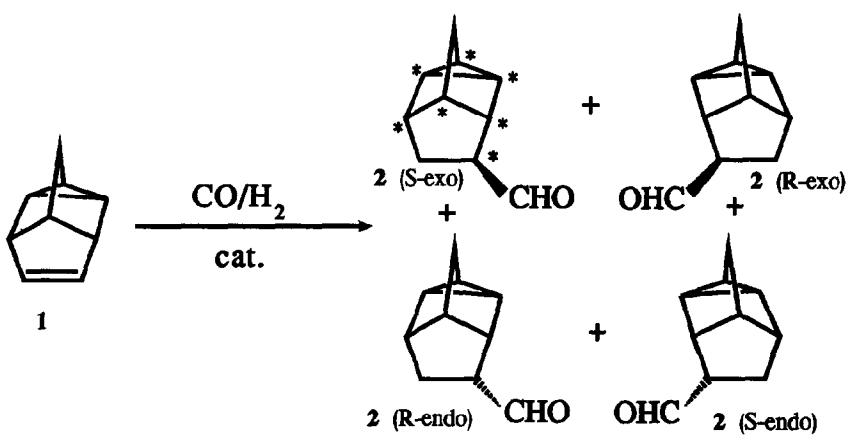
Abstract: Deltacyclene (tetracyclo[4,3,0,$0^{2,9}0^{3,7}$]non-4-ene was stereoselectively hydroformylated to *exo*-formyl-deltacyclane in the presence of rhodium and platinum catalysts. In the case of optically active bisphosphines up to 22 % e.e-s were achieved.

Although the asymmetric hydroformylation of olefins of various structure has been investigated in detail [1] little attention has been paid to that of polycyclic substrates. Among the favourite test substrates for asymmetric carbonylation reactions is norbornene, a bicyclic prochiral olefin. Growing interest in the synthesis of substituted deltacyclanes has arisen [2]. High optical yields have been obtained in the asymmetric [2+2+2] cycloaddition reaction of norbornadiene and terminal acetylenes [3].

In this communication we show that deltacyclene (1) obtained from a homo-Diels -Alder reaction [4] between norbornadiene and acetylene undergoes hydroformylation by optically active rhodium-phosphine and platinum-phosphine-tin(II)chloride catalysts.



The formyl-deltacyclane (**2**) contains seven new stereocenters which are created in one step. Exo and endo products are possible.

Table 1. Hydroformylation of deltacyclene with rhodium-containing catalysts

Catalyst	R.time [h]	R.temp. [°C]	Conversion [%]	Product distribution * [%]		
				2,exo (e.e.**, %)		**2**,endo
0.5 $[Rh(nbd)Cl]_2$ + 3 PPh_3	8	100	>99	93	—	7
0.5 $[Rh(nbd)Cl]_2$+1.5(2S,3S)-CHIRAPHOS	8	100	>99	96	22 (S)	4
0.5 $[Rh(nbd)Cl]_2$+1.5(2S,3S)-CHIRAPHOS	8	50	60	98	n.d.	2
0.5$[Rh(nbd)Cl]_2$+1.5 (2S,3S)-CHIRAPHOS	15	50	>99	98	3.5 (R)	2
0.5 $[Rh(nbd)Cl]_2$ + 1.5 (4S,5S)-DIOP	8	100	>99	98	3 (R)	2

*The amount of deltacyclane (**3**, hydrogenated product) is less than 1% in all cases. ** Determined by ^{1}H-NMR shift-technique using Eu(tfc)$_3$ ($\Delta\delta$=5.1 ppm, $\Delta\Delta\delta$= 0.12 ppm for CHO-proton of **2**) or Eu(dcm)$_3$ ($\Delta\delta$ =3.4ppm; $\Delta\Delta\delta$=0.07ppm for CHO-proton of **2** and $\Delta\delta$=1.75 ppm, $\Delta\Delta\delta$= 0.12 ppm for $COOCH_3$-proton of **5**) chiral shift reagent ; n.d.=not determined

Reaction conditions: 0.025mmol catalyst, 2 mmol substrate, 10 ml toluene, p(CO)=p(H_2)=40bar

Table 2. Hydroformylation of deltacyclene with platinum-containing catalysts

Catalyst	R.time [h]	R.temp. [°C]	Conversion [%]	Product distribution [%]			
				2,exo (e.e.**, %)		**2**,endo	**3**
$PtCl(SnCl_3)$[(S,S)-BDPP]	4	100	99	97	7.7 (R)	3	—
$PtCl(SnCl_3)$[(S,S)-BDPP]	60	25	98	98	16.3 (R)	2	—
$PtCl_2$[(S,S)-BPPM] + $SnCl_2$	10	100	57	97	18.6 (R)	2	<1
$PtCl_2$[(R)-PROPHOS] + $SnCl_2$	10	100	>99	93	1.2 (S)	3	4
$PtCl_2$[(R)-PROPHOS] + $SnCl_2$	115	25	93	96	0.9 (R)	2	2
$PtCl_2$[(R)-PROPHOS] + $SnCl_2$	20	25	19	96	n.d.	2	2

** See Table 1. n.d.= not determined

Reaction conditions: 0.025 mmol catalyst; 1mmol substrate; 20 ml toluene; p(CO)=p(H_2)=40bar

The hydroformylation reaction is highly chemoselective both in the presence of rhodium- and platinum-containing catalysts. Surprisingly, the amount of the hydrogenated product (deltacyclane,(3) [5]) is almost negligible in all cases even under severe reaction conditions. The *exo*-formyl-deltacyclane (2, exo) [6] was formed in excellent yields using both type of catalysts (Table 1, Table 2). The chemoselectivity is better in the rhodium-catalyzed reaction because of a small extent of hydrogenation. From the point of view of the stereoselectivity, chiral bisphosphines are superior to a monodentate one (PPh_3).

The enantioselectivity was also explored in the presence of rhodium and platinum complexes. Enantioselective control was achieved by using the optically active bisphosphines, PROPHOS [7], CHIRAPHOS [8], DIOP [9], BDPP [10] and BPPM [11]. The platinum catalysts containing phosphines forming 6- or 7-membered chelate ring result in higher optical yields than that of forming a 5-membered ring. For further characterization and additional determination of e.e. (see comments to Table 1) *exo*-formyl-deltacyclane was oxidized to the carboxylic acid (4)[12] by silver oxide and esterified with methanol to *exo*-carbomethoxy-deltacyclane (5)[13].

For the determination of the absolute configuration of the *exo*-formyl products, 5 was transesterified with (1R,2S,5R)-menthol. The absolute stereochemistry of the products can be assigned by the widely used configurational correlation model[14]. Due to through-space interaction of one of the diastereotopic methylene protons ($CHOCHCH_2$) with the $CH(CH_3)_2$ protons of the menthyl-moiety one of the methylene protons is slightly upfield in (S)-*exo*-2. The assignment of absolute stereochemistry by X-ray christallography failed.

Although the e.e-s obtained are rather low, an interesting phenomenon has been observed. While at low temperature one enantiomer is preferred, at high temperature the other enantiomer predominates using CHIRAPHOS (in rhodium-catalyzed reaction) and PROPHOS (in platinum-catalyzed reaction). Previously, a similar effect of the temperature on optical yield was described for the asymmetric hydroformylation of styrene [15].

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6. Spectroscopic data for **2** (4-*exo*-formyl-tetracyclo[4,3,0,$0^{2,9}0^{3,7}$]nonane): ^{1}H-NMR (δ,$CDCl_3$): 9.66 (1H, d, 1.4Hz, **CHO**); 2.78 (1H, ddd, 1.4Hz, 4.7Hz, 9.1Hz, **CHCHO**); 2.29 (1H, m, **CHCHCHO**); 1.9-2.1 (3H, m, **CH_aH_bCHCHO**+2CH-protons); 1.78 (1H, dd, 9.5Hz, 15Hz, **CH_aH_bCHCHO**); 1.56 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.54 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.1 (1H, m, cyclopropane-ring); 0.9-1.05 (2H, m, cyclopropane-ring); ^{13}C-NMR (δ,$CDCl_3$): 203.8(**CHO**); 52.9 (**CHCHO**); 44.1; 42.6; 39.6; 31.7; 27.7; 15.5; 14.8; 13.7; MS (m/z/rel.int.): 148/350(M^+); 119/440; 117/600; 91/1000

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12. Spectroscopic data for **4** (4-*exo*-carboxyl-tetracyclo[4,3,0,$0^{2,9}0^{3,7}$]nonane): ^{1}H-NMR (δ,$CDCl_3$): 11.1 (1H, brs, **COOH**); 2.78 (1H, dd, 5.7Hz, 9.2Hz, **CHCOOH**); 2.27 (1H, m, **CHCHCHO**); 1.9-2.05 (4H, m, **CH_2CHCHO**+2**CH**-protons); 1.56 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.54 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.1(1H,m,cyclopropane-ring); 0.9-1.05 (2H, m, cyclopropane-ring); ^{13}C-NMR (δ,$CDCl_3$): 183.0 (**COOH**); 46.8 (**CH**) ; 44.6 (**CH**); 42.4 (**CH**); 40.0 (**CH**); 31.5 (2xCH_2); 15.1 (**CH**); 14.9 (**CH**); 13.7 (**CH**); MS(m/z/rel.int.): 164/210(M^+); 119/1000; 91/720

13. Spectroscopic data for **5** (4-*exo*-carbomethoxy-tetracyclo[4,3,0,$0^{2,9}0^{3,7}$]nonane): ^{1}H-NMR (δ,$CDCl_3$): 3.66 (3H, s, **OCH_3**); 2.76 (1H, dd, 5.6Hz, 8.8Hz, **$CHCOOCH_3$**); 2.2 (1H, m, **CHCHCOOCH**$_3$); 2.03 (1H, brs, CH); 1.85-2.00 (4H, m, **CH_2CHCHO**+2CH-protons); 1.56 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.54 (1H, d, 12Hz, **$CHCH_aH_bCH$**); 1.08 (1H, m, cyclopropane-ring); 0.88-0.98 (2H, m, cyclopropane-ring); ^{13}C-NMR(δ,$CDCl_3$): 176.9 (COO); 51.6 (CH_3); 46.9 (CH); 44.6 (CH); 42.5 (CH); 40.1 (CH); 31.7 (CH_2); 31.6 (CH_2); 15.2 (CH); 15.0 (CH); 13.8 (CH); MS (m/z/rel.int.): 178/180 (M^+); 119/1000; 118/640; 91/800

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