ELSEVIER

Journal of Molecular Catalysis A: Chemical 179 (2002) 79–86

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

Synthesis of α,ω-epoxyaldehydes by hydroformylation of α,ω-epoxyalkenes

C. Botteghi [a], M. Marchetti [b,*], S. Paganelli [a], S. Scognamillo [b]

[a] *Dipartimento di Chimica, Università Ca' Foscari di Venezia, Calle Larga S. Marta 2137, I-30123 Venezia, Italy*
[b] *Istituto per l'Applicazione delle Tecniche Chimiche Avanzate ai Problemi Agrobiologici (ATCAPA), CNR, via Vienna 2, I-07100 Sassari, Italy*

Received 24 April 2001; received in revised form 10 September 2001; accepted 11 September 2001

Abstract

Linear α,ω-epoxyaldehydes with variable distance between the two functional groups, a class of interesting cross-linking agents for proteins, polysacharides and other polymeric compounds, can be conveniently prepared by hydroformylation of commercially available α,ω-epoxyalkenes catalyzed by rhodium/phosphine complexes. For example, 1,2-epoxyhex-5-ene (**2b**) was converted into 6,7-epoxyheptanal (**1b**) with 75–99% yields in the presence of the catalytic system $HRh(CO)(PPh_3)_3$/xantphos at 20 atm ($CO/H_2 = 1$) and at 40–100 °C. Operating at 40 °C practically regiospecific formation of the linear epoxyaldehyde was found. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: α,ω-Epoxyalkenes; α,ω-Epoxyaldehydes; Hydroformylation; Rhodium; Xantphos

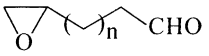
1. Introduction

The synthesis of bifunctional compounds, in which two reactive functions are located at the ends of a linear chain of several carbon atoms [1], has recently attracted a great attention, in connection with their application especially as cross-linking agents for polymers such as for example polyvinylalcohols, polysaccarides and polypeptides [2–5]. Particularly important are those compounds which embody in their molecules two functions displaying different reactivities: in this case they represent valuable intermediates for the synthesis of many substances, in which the crucial strategy relies in the fact that each function must be available at different steps of the preparative scheme. For example, fluorescent labels can be easily obtained by reaction of aminofluoresceine and an epoxyaldehyde followed by opening of the epoxide moiety and subsequent linking to an amino nucleotide [6]. Phosphorilated epoxides, a class of possible inhibitors for the phosphoglycerate mutase enzyme [7], can be in principle conveniently prepared from α,ω-epoxyaldehydes by transforming the aldehyde into phosphonate function by a few simple steps. Another example of application is the functionalyzation of β-cyclodextrin: epoxyammonium salts are used to prepare active cyclodextrin for capillary electrophoresis [8].

Owing to our interest in producing polyfunctional compounds of potential biological interest [9], we decided, among the numerous classes of bifunctional molecules, to study preparative routes to α,ω-epoxyaldehydes **1**, since both the aldehyde and oxirane groups are able to interact with a very large

* Corresponding author. Tel.: +39-79-210162; fax: +39-79-218479.
E-mail address: mauro@hpj.area.ss.cnr.it (M. Marchetti).

1381-1169/02/$ – see front matter
PII: S1381-1169(01)00395-8



1a, n = 1; **1b**, n = 3; **1c**, n = 5; **1d**, n = 7

Fig. 1. Structure of variable length chain epoxyaldehydes.

variety of other functions, but at the same time with very different reaction mode and rate (Fig. 1).

Epoxyaldehydes are scarcely described in the literature [10–12]: only the synthesis of epoxyaldehydes, in which the aldehyde group is adjacent to the oxirane ring, seems to have received a fairly high attention. We have found only one report on the preparation of β,γ-epoxyaldehyde dimethyl acetals [13].

Taking into account that α,ω-epoxyolefins **2** are rather accessible by one-sided epoxidation reaction of the corresponding α,ω-dienes [14], some of which are present on the petrochemical market [15,16], the hydroformylation of olefins **2** appeared to us one of the most promising ways to get the target compound **1** in kg-scale amounts (Scheme 1).

On the other hand, it is known that the oxirane ring is rather stable under standard hydroformylation conditions, when rhodium catalysts are used: for instance, styrene oxide subjected to oxo-reaction catalyzed by $HRh(CO)(PPh_3)_3$ (Rh-to-substrate molar ratio = 1:500) at 100 °C and 100 atm ($CO:H_2 = 1$) in toluene was practically recovered unchanged after 24 h [17]. Only cobalt catalysts are reported to display a satisfactory activity in the hydroformylation of various epoxides [18]: recently, the efficiency of cobalt complexes with hemilabile P–O chelating ligands was highlighted in the oxo-reaction of epoxides to give β-hydroxyaldehydes with high selectivities and yields [19].

In this paper, we are reporting the results obtained in the hydroformylation catalyzed by cobalt, rhodium or platinum carbonyl complexes of 1,2-epoxybut-3-ene (**2a**), 1,2-epoxyhex-5-ene (**2b**), 1,2-epoxyoct-7-ene (**2c**) and 1,2-epoxydec-9-ene (**2d**). As the linear α,ω-epoxyaldehydes are strongly desired for many purposes [20], most of our efforts were devoted to enhance the yield of the linear isomer as much as possible.

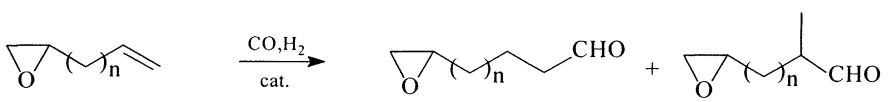
2. Experimental

2.1. Materials

The catalytic precursors $Co_2(CO)_8$, *cis*–bis(BZN) $PtCl_2$, $[Rh(COD)Cl]_2$ and $HRh(CO)(PPh_3)_3$, were purchased by Fluka and used without further purification. 1,2-Epoxybut-3-ene (**2a**), 1,2-epoxyhex-5-ene (**2b**), 1,2-epoxyoct-7-ene (**2c**) and 1,2-epoxydec-9-ene (**2d**) were Aldrich products. Xantphos was prepared as described by Kranenburg et al. [21]. $Rh(CO)_2(acac)$, triphenylphosphine (PPh_3), triphenylphosphite (TPPO), 1,3-bis(diphenylphosphinopropane) (DPP) were used as received from Aldrich. Solvents were purified following well-known procedures. Silica gel (70–230 mesh) was purchased by Merck. ^1H NMR spectra (300 MHz) were measured for solutions in $CDCl_3$ by a Varian VXR300s spectrometer.

2.1.1. Hydroformylation of epoxyalkenes catalyzed by Rh complexes

A 150 ml stainless steel reaction vessel was charged under a nitrogen purge with 10 mmol of the substrate, the rhodium catalyst, the ligand of choice and 10 ml of anhydrous toluene (for the molar ratio used, see Tables 3 and 5). The reactor was then pressurized with syngas ($CO/H_2 = 1$) and heated for the due time (see Tables 1–3). It was then cooled to room temperature and the residual gases released. The obtained oxo-mixture was analyzed by GC–MS. When



2
2a, n = 0; **2b**, n = 2;
2c, n = 4; **2d**, n = 6

1
1a, n = 0; **1b**, n = 2;
1c, n = 4; **1d**, n = 6

3
3a, n = 0; **3b**, n = 2;
3c, n = 4; **3d**, n = 6

Scheme 1. Hydroformylation of α,ω-epoxyalknes (cat. stands for cobalt, rhodium or platinum complexes).

Table 1
Hydroformylation of 1,2-epoxyhex-5-ene (**2b**)[a]

Run	Catalytic precursor	Solvent	*t* (h)	Conversion (%)[b]	Aldehyde yield (%)[b]	**1b**/**3b** (%)[b]
1	$Co_2(CO)_8$	Toluene	24	98	99	54/46
2[c]	*cis*–bis(BZN)$PtCl_2$/DPP	Toluene	21	98	70	72/28
3	$[Rh(COD)Cl]_2$	Toluene	20	99	99	60/40
4	$HRh(CO)(PPh_3)_3$	Toluene	24	98	98	68/32
5	$HRh(CO)(PPh_3)_3$	Heptanol	20	99	99	70/30
6	$Rh(CO)_2(acac)/PPh_3$	Toluene	20	99	99	76/24

[a] Reaction conditions: substrate = 10 mmol; solvent = 10 ml; temperature = 100 °C; catalyst/substrate molar ratio = 1/250; PPh_3/Rh = 3/1; $P(CO) = P(H_2) = 40$ atm. BZN: benzonitrile; acacH: acetylacetone; DPP: 1,3-bis(diphenylphosphino)propane; Pt/$SnCl_2$/DPP (molar ratio) = 1/2/1.
[b] Determined by GC analysis.
[c] A 28% of high boiling products were found in the reaction mixture.

Table 2
Hydroformylation of α,ω-epoxyolefins **2a**, **2c** and **2d**[a]

Run	Substrate	Catalytic precursor	*t* (h)	Conversion (%)[b]	Aldehyde yield (%)[b]	**1**/**3** (%)[b]
1[c]	**2a**	*cis*–bis(BZN)$PtCl_2/SnCl_2$/DPP	24	98	46	69/31
2	**2a**	$Rh(CO)_2(acac)/PPh_3$	24	99	99	58/42
3	**2a**	$Rh(CO)_2$(acac)/TPPO	24	98	98	50/50
4[d]	**2c**	*cis*–bis(BZN)$PtCl_2/SnCl_2$/DPP	20	99	63	51/49
5	**2c**	$[Rh(COD)Cl]_2$	21	98	98	53/47
6	**2c**	$Rh(CO)_2(acac)/PPh_3$	24	98	98	76/24
7[e]	**2d**	*cis*–bis(BZN)$PtCl_2/SnCl_2$/DPP	20	99	35	55/45
8	**2d**	$[Rh(COD)Cl]_2$	21	98	98	61/39
9	**2d**	$Rh(CO)_2(acac)/PPh_3$	24	99	99	70/30

[a] Reaction conditions: substrate = 10 mmol; solvent = toluene (10 ml); temperature = 100 °C; catalyst/substrate (molar ratio) = 1/250; PPh_3/Rh (molar ratio) = 3/1; TPPO/Rh (molar ratio) = 3/1; Pt/$SnCl_2$/DPP (molar ratio) = 1/2/1; $P(CO) = P(H_2) = 40$ atm. BZN: benzonitrile; acacH: acetylacetone; DPP: 1,3-bis(diphenylphosphino)propane; TPPO: triphenylphosphite.
[b] Determined by GC analysis.
[c] A 54% of unidentified high boiling products were found.
[d] A 36% of unidentified high boiling products were found.
[e] A 64% of unidentified high boiling products were found.

Table 3
Hydroformylation of 1,2-epoxyhex-5-ene (**2b**) catalyzed by $Rh(CO)_2$(acac) and phosphine ligands[a]

Run	Catalytic system	*t* (h)	*P* (atm)	Conversion (%)	**1b**/**3b**[b] (%)
1	$Rh(CO)_2(acac)/PPh_3$	5	20	35	62/38
2	$Rh(CO)_2(acac)/PPh_3$	20	80	>99	75/25
3	$Rh(CO)_2$(acac)/xantphos	22	80	96	56/44
4	$Rh(CO)_2$(acac)/xantphos	96	60	>99	55/45
5	$Rh(CO)_2$(acac)/xantphos	96	20	98	75/25

[a] Reaction conditions: substrate = 0.5 g (5 mmol); solvent = toluene (10 ml); temperature = 100 °C; catalyst/substrate molar ratio = 1/250; ligand/catalyst molar ratio = 3/1.
[b] The aldehyde yield was practically quantitative.

necessary the mixture of *iso*- and *n*-aldehyde was separated by flash chromatography using ethyl ether/*n*-hexane = 2:8 as eluent. Most of the aldehydes were characterized by GC–MS, ^{1}H NMR and ^{13}C NMR.

*2.1.2. Compound **1a***

Boiling point 121–123 °C. ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.62 (t, J = 1.7 Hz); 2.81 (d, J = 5.2 Hz); 2.75–2.69 (m); 2.30–2.25 (m); 1.66–1.60 (m). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 202.4; 51.7; 48.4; 38.3; 26.0. GC–MS (70 eV): *m/e* 101 [M + 1]; *m/e* 85; *m/e* 70; *m/e* 56; *m/e* 43.

*2.1.3. Compound **3a***

Boiling point 119–120 °C. The hydroformylation of **2a** gave a mixture of two diastereomeric epoxyaldehydes in a molecular ratio of about 70:30 (evaluated on the NMR signals related to the methyl group and the aldehyde proton of **3a**); the following NMR spectrum is referred to this mixture.^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.77 (d, J = 2.3 Hz); 9.68 (d, J = 2.1 Hz); 3.15–3.10 (m); 2.37–2.32 (m); 2.19–2.10 (m); 1.33 (d, J = 7.2 Hz); 1.23 (d, J = 7.2 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 200.1; 56.3; 43.1; 42.5; 5.7. GC–MS (70 eV): *m/e* 85; *m/e* 72; *m/e* 56; *m/e* 43.

*2.1.4. Compound **1b***

Boiling point 87–89 °C (10 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.70 (t, J = 1.8 Hz); 2.81–2.75 (m); 2.49 (d, J = 5.4 Hz); 2.33–2.26 (m); 1.66–1.33 (m). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 202.6; 51.2; 45.8; 44.6; 31.7; 24.7; 21.9. GC–MS (70 eV): *m/e* 128 [*M*]; *m/e* 112; *m/e* 97; *m/e* 84; *m/e* 71; *m/e* 56; *m/e* 43.

*2.1.5. Compound **3b***

Boiling point 80–82 °C (10 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.36 (d, J = 1.6 Hz); 3.03–2.95 (m); 2.80–2.65 (m); 2.50 (d, J = 5.4 Hz); 1.66–1.46 (m); 1.02 (d, J = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 204.4; 58.6; 46.2; 45.8; 29.8; 26.5; 13.5. GC–MS (70 eV): *m/e* 127 [M − 1]; *m/e* 109; *m/e* 84; *m/e* 71; *m/e* 55; *m/e* 43.

*2.1.6. Compound **1c***

Boiling point 130–133 °C (10 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.70 (t, J = 1.8 Hz); 2.81–2.77 (m); 2.50 (d, J = 5.0Hz); 2.32–2.27 (m); 1.55–1.17 (m). GC–MS (70 eV): *m/e* 156 [*M*]; *m/e* 125; *m/e* 112; *m/e* 97; *m/e* 85; *m/e* 71; *m/e* 56; *m/e* 43.

*2.1.7. Compound **3c***

Boiling point 119–121 °C (10 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.37 (d, J = 1.1 Hz); 2.78–2.67 (m); 2.61–2.54 (m); 2.52–2.49 (m); 1.50–1.18 (m); 1.02 (d, J = 7.1 Hz). GC–MS (70 eV): *m/e* 156 [*M*]; *m/e* 125, *m/e* 111; *m/e* 97; *m/e* 85; *m/e* 71; *m/e* 56; *m/e* 43.

*2.1.8. Compound **1d***

Boiling point 110–111 °C (0.1 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.75 (t, J = 1.7 Hz); 2.81–2.75 (m); 2.50 (d, J = 5.2 Hz); 2.33–2.28 (m); 1.81–1.12 (m). ^{13}C NMR ($CDCl_3$, 75 MHz), δ (ppm): 202.6; 51.2; 48.8; 32.3; 29.5; 29.1; 28.7; 26.0; 22.1. GC–MS (70 eV): *m/e* 184 [*M*]; *m/e* 141; *m/e* 125; *m/e* 112; *m/e* 97; *m/e* 85; *m/e* 71; *m/e* 56; *m/e* 43.

*2.1.9. Compound **3d***

Boiling point 103–105 °C (0.1 mmHg). ^{1}H NMR ($CDCl_3$, 300 MHz), δ (ppm): 9.60 (d, J = 1.5 Hz); 2.81–2.72 (m); 2.62–2.53 (m); 2.50 (t, J = 3.0 Hz); 1.46–1.16 (m); 1.01 (d, J = 7.1 Hz). GC–MS (70 eV), 1,2-epossi-9-metildecanale (tr = 14.86 min, 8%): *m/e* 184 [*M*]; *m/e* 141; *m/e* 125; *m/e* 112; *m/e* 97; *m/e* 85; *m/e* 71; *m/e* 56; *m/e* 43.

*2.1.10. Hydroformylation of **2b** catalyzed by $Co_2(CO)_8$*

A 150 ml stainless steel reaction vessel was charged under a nitrogen purge with 10 mmol of substrate, 0.04 mmol of $Co_2(CO)_8$ and 10 ml of anhydrous toluene (see Table 1). The reactor was then pressurized to 100 atm with syngas (CO/H_2 = 1) and heated at 100 °C for the due time (see Table 1). The reactor was then cooled to room temperature and the residual gases released. The reaction mixture was analyzed by GC to determine the conversion and the normal to branched aldehyde ratio.

2.1.11. Hydroformylation of epoxyalkenes catalyzed by Pt complexes

A 150 ml stainless steel reaction vessel was charged under a nitrogen purge with 10 mmol of substrate, 0.04 mmol of Pt complex, 0.08 mmol of $SnCl_2$,

Table 4
Hydroformylation of 1,2-epoxyhex-5-ene (**2b**) catalyzed by $RhH(CO)(PPh)_3$/xantphos[a]

Run	*t* (h)	Temperature (°C)	Conversion (%)	**1b**/**3b**[b] (%)
1	22	40	21	>99
2	48	40	48	>99
3	60	40	75	>99
4	24	50	76	97/3
5	24	60	93	96/4
6	24	100	>99	86/14

[a] Reaction conditions: substrate = 0.5 g (5 mmol); solvent = toluene (10 ml); $P(CO) = P(H_2) = 10$ atm; catalyst/substrate molar ratio = 1/600; ligand/catalyst molar ratio = 2.2/1.
[b] The chemo-selectivity was practically quantitative.

0.04 mmol of 1,2-bis(diphenylphosphino)propane and 10 ml of anhydrous toluene (see Tables 1 and 2). The reactor was then pressurized to 80 atm with syngas ($CO/H_2 = 1$) and heated at 100 °C for the due time (see Tables 1 and 2). The reactor was then cooled to room temperature and the residual gases released. The reaction mixture was analyzed by GC to determine the conversion and the normal-to-branched aldehyde ratio.

2.1.12. Hydroformylation of α,ω-epoxyalkenes catalyzed by Rh/xantphos complex

A 150 ml stainless steel reaction vessel was charged under a nitrogen purge with 5 mmol of substrate, 0.0083 mmol of $RhH(CO)(PPh_3)_3$ and 0.018 mmol of xantphos in 10 ml of anhydrous toluene (see Tables 4 and 5). The reactor was then pressurized to 20 atm with syngas ($CO/H_2 = 1$) and heated at the desired temperature for the due time (see Tables 4 and 5).

Table 5
Hydroformylation of various α,ω-epoxyalkenes catalyzed by $RhH(CO)(PPh)_3$/xantphos[a]

Run	Substrate	*t* (h)	Conversion (%)	**1**/**3**[b] (%)
1	**5**	44	85	>99
2	**6**	60	75	>99
3	**7**	20	67	>99
4	**8**	48	76	94/6

[a] Reaction conditions: substrate = 5 mmol; solvent = toluene (10 ml); $P(CO) = P(H_2) = 10$ atm; temperature = 40 °C; catalyst/substrate molar ratio = 1/600; ligand/catalyst molar ratio = 2.2/1.
[b] The chemo-selectivity was practically quantitative.

The reactor was then cooled to room temperature and the residual gases released. The reaction mixture was first analyzed by GC to determine the conversion and the normal-to-branched aldehyde ratio and then the linear isomer was purified by careful distillation.

3. Results and discussion

In the first phase of our research work we subjected 1,2-epoxyhex-5-ene (**2b**) to the oxo-reaction under various experimental conditions and in the presence of different catalytic systems in order to find the best operative parameters for achieving the desired chemo- and regio-selectivity. Table 1 summarizes the most representative outcomes obtained in the first set of oxo-experiments.

As expected, rhodium complexes show a good catalytical activity towards the hydroformylation of epoxyolefin **2b** and ensure a very high selectivity under different reaction conditions. It is noteworthy that also in this case only the double bond is involved in the catalytic reaction, the oxirane ring remaining substantially unreacted under the reaction conditions adopted. Platinum catalysts gave satisfactory aldehyde yields, but in all cases the formation of variable amounts of tars was observed (Table 1, run 2). In our opinion the presence in the platinum based catalytic systems of $SnCl_2$, which acts as a Lewis acid in the reaction solution, is responsible for the lower chemo-selectivity found: it is conceivable that the cleavage of the epoxy ring is involved in the formation of these undesired by-products.

Among the rhodium complexes those containing the PPh_3 ligand showed to be the most active and selective. The value of the regio-selectivity towards the production of the linear aldehyde is unsatisfactory, reaching in the best case 76% of the normal regioisomer in the hydroformylation of **2b** catalyzed by $Rh(CO)_2(acac)/PPh_3$ (1:3 M ratio) (Table 1, run 6).

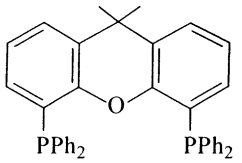
Other epoxyolefins, 1,2-epoxybutene (**2a**), 1,2-epoxyoct-7-ene (**2c**) and 1,2-epoxydec-9-ene (**2d**), were subjected to hydroformylation in the presence of various platinum or rhodium carbonyl complexes under analogous reaction conditions: the results of these experiments are collected in Table 2. Again, the most favorable combination between catalytic activity and chemo-selectivity was provided by rhodium

complexes with PPh_3 or triphenylphosphite ligands (Table 2, runs 2, 4, 7).

$Pt/SnCl_2$ complexes gave rise again to the formation of substantial amount of high boiling unidentified by-products. The regio-selectivity values resulted to be comparable with those obtained in the hydroformylation of substrate **2b**; only in the case of 1,2-epoxybut-3-ene (**2a**) the selectivity towards the formation of linear epoxyaldehyde, using the catalytic system $Rh(CO)_2(acac)/PPh_3$, is significantly lowered with respect to the other substrates (Table 2, run 2).

In a previous paper, Lazzaroni et al. [22] reported some interesting results on unmodifed rhodium carbonyl complexes catalyzed hydroformylation of allyl ethyl ether, where the distance between the oxygen atom and the olefinic double bond is the same as in the olefin epoxide **5**. They found that the linear-to-branched aldehyde ratio, which in the case on 1-hexene is about 70/30 decreased up to 52/48 under the same oxo-conditions, when allyl ethyl ether was employed [23]. The peculiar behavior of this unsaturated ether was attributed to the fact that the branched σ-alkyl rhodium intermediate species **I** is slightly more stabilized by delocalization of the negative charge on the $–CH_2OC_2H_5$ group with respect to the linear σ-complex **II**. This effect of the heteroatom is practically ineffective for the species **II** and it is slightly destabilizing in the branched σ-rhodium complex deriving from 1-hexene **III** (Fig. 2).

Since 1,2-epoxybut-3-ene (**2a**) is structurally related to allyl ethyl ether (the oxygen atom is bound in both compounds with the carbon atom adjacent to the olefinic linkage) it is conceivable that the similar effect is working in substrate **2a**, so shifting the oxo-epoxyaldehydes distribution towards the more branched product.



Bite angle 109.8°

Fig. 3. Xantphos.

In these last years Kranenburg et al. [21] developed diphosphines based on xanthene-type backbones such as xantphos, which showed to promote an exceptionally high regio-selectivity towards the formation of linear aldehydes in the rhodium catalyzed hydroformylation of olefins. This peculiar behavior of xantphos (Fig. 3) was ascribed to the large "natural" bite angle formed by coordination with the metal [24,25].

1,2-Epoxydec-9-ene (**2d**) behaves, under the same oxo-conditions, in an analogous way with respect to substrate **2b**: the L/B ratio, which is 45/55 at total substrate conversion, in the presence of $Rh(CO)_2acac/PPh_3$, reaches the value of 94/6 using $HRh(CO)(PPh_3)_3$/xantphos (Table 5).

The reaction temperature exerts a rather strong influence on the linear-to-branched isomer distribution: the regio-selectivity decreases from practically 100 to 86% with increasing temperature from 40 to 100 °C (runs 1–6, Table 4).

The data reported in the Table 5 point out that the catalytic system formed modifying $HRh(CO)(PPh_3)_3$ with xantphos (1–2.2 M ratio) works excellently for all the substrates hydroformylated at low pressure and low temperature giving high epoxyaldehyde yields and generally regiospecific formation of the linear oxo-product, even if the reaction runs rather slowly under these very mild conditions.

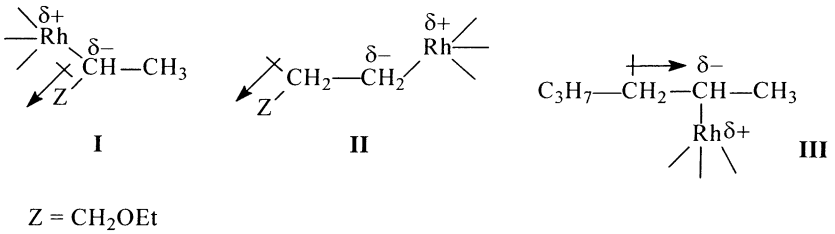
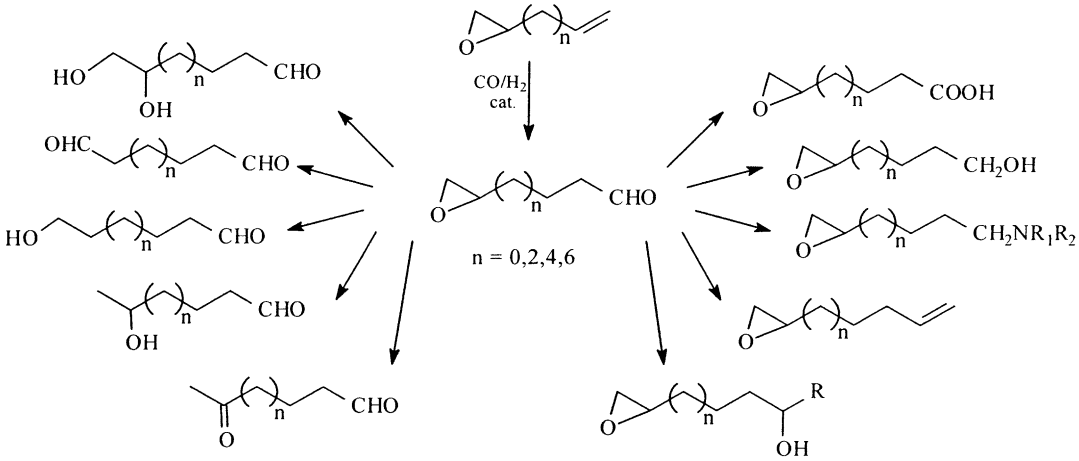


Fig. 2. The σ-rhodium complexes.



Scheme 2. Bifunctional compounds obtainable from linear variable length chain epoxyaldehdes.

4. Conclusive remarks

In conclusion, the hydroformylation of α,ω-epoxyolefins, employing rhodium complexes with phosphine ligands, has been successfully carried out giving high yields of α,ω-epoxyaldehydes (up to >99%). The use of large bite angle diphosphines like xantphos can exclusively afford, if the reaction conditions are carefully controlled, exclusively the linear epoxyaldehyde.

This method offers a very convenient route to get a widespread variety of α,ω-epoxyaldehydes with variable distance between the two functions. By selectively transforming these two functional groups it is possible to create a library of other bifunctional compounds, which can find wide application in various biological research areas (Scheme 2).

References

[1] C. Botteghi, C. Dei Negri, S. Paganelli, M. Marchetti, J. Mol. Catal. A: Chemical 175 (2001) 17.
[2] H. Yamamoto, H. Tanisho, S. Ohara, A. Nishida, Int. J. Biol. Macromol. 14 (1992) 66.
[3] J.P. Draye, B. Delaey, A. Van de Voorde, A. Van den Bulke, E. Bogdano, Biomaterials 19 (1998) 99.
[4] J.Z. Knaul, S.M. Hudson, K.A.M. Creber, J. Polym. Sci. B: Polym. 37 (1999) 1079.
[5] V. Crescenzi, G. Paradossi, P. Desideri, M. Dentini, F. Cavalieri, E. Amici, R. Lisi, Polym. Gels Networks 5 (1997) 225.
[6] A. Serra, Tesi di Laurea, Università degli Studi di Sassari, 1998–1999.
[7] P. De Mando Puyan, J.J. Perie, Phosphorous, sulfur and silicon and the related elements, submitted for publication.
[8] A. Deratani, G. Lelievre, T. Maraldo, B. Sebille, Carbihydr. Res. 192 (1989) 215.
[9] C. Botteghi, M. Marchetti, S. Paganelli, in: M. Beller, C. Bolm (Eds.), Transition Metals for Organic Synthesis, Wiley, Weinheim, 1998, p. 25 and references therein.
[10] H. Urabe, T. Matsuka, F. Sato, Tetrahedron Lett. 29 (1992) 4179.
[11] A. De Mico, R. Margarita, L. Parlanti, A. Vescovi, G. Piancatelli, J. Org. Chem. 62 (1997) 6974.
[12] H. De, V. Finch, G.W. Hearne, D.S. La France, Shell Dev. Co., US Patent 2.887.498 (1959).
[13] O.G. Kulinkovich, I.G. Tishchenko, Yu.N. Romanshin, J. Org. Chem. USSR 22 (12) (1986) 2221.
[14] H.G. Alt, M. Jung, J. Organometal. Chem. 580 (1999) 1.
[15] G.W. Parshall, W.A. Nugent, CHEMTECH (1988) 314 and references therein.
[16] C.U. Pittmann, R.M. Hanes, J.J. Yang, J. Mol. Catal. 17 (1982) 377.
[17] C. Botteghi, M. Marchetti, S. Paganelli, unpublished results.
[18] B. Cornils, in: J. Falbe (Ed.), New Syntheses with Carbon Monoxide, Springer, Berlin, 1980, pp. 131–132 and references therein.
[19] R. Weber, U. Englert, B. Ganter, W. Keim, M. Mothrath, J. Chem. Soc., Chem. Commun. (2000) 1419.
[20] S. Scognamillo, Dissertation, University of Sassari, 1998 and references therein.
[21] M. Kranenburg, Y.E.M. van der Burgt, P.C.J. Kamer, P.W.N.M. van Leeuwen, Organometallics 14 (1995) 3081.

[22] R. Lazzaroni, R. Settambolo, G. Uccello-Barretta, Organometallics 14 (1995) 4644.
[23] R. Lazzaroni, R. Settambolo, A. Caiazzo, in: P.W.N.M. van Leeuwen, C. Claver (Eds.), Rhodium Catalyzed Hydroformylation, Kluwer Academic Publishers, Dordrecht, 2000, p. 15 and references therein.
[24] P. Dierkes, P.W.N.M. van Leeuwen, J. Chem. Soc., Dalton Trans. II (1999) 1519 and references therein.
[25] P.W.N.M. van Leeuwen, C.P. Casey, G.T. Whiteker, in: P.W.N.M. van Leeuwen, C. Claver (Eds.), Rhodium Catalyzed Hydroformylation, Kluwer Academic Publishers, Dordrecht, 2000, p. 63 and references therein.