Journal of Organometallic Chemistry, 413 (1991) 125–135
Elsevier Sequoia S.A., Lausanne
JOM 21666

Microbial resolution of organometallic planar chirality. Enantioselective reduction of *ortho*- and *meta*-substituted tricarbonylchromium benzaldehydes by bakers' yeast

Siden Top [a], Gérard Jaouen [a,*], Clara Baldoli [b], Paola Del Buttero [b] and Stefano Maiorana [b,*]

[a] *Ecole Nationale Supérieure de Chimie de Paris, UA CNRS 403, 11 rue Pierre et Marie Curie, 75231 Paris Cedex 05 (France)*
[b] *Dipartimento di Chimica Organica e Industriale dell'Università, Via C. Golgi 19, I-20133 Milan (Italy)*

(Received December 17th, 1990)

Abstract

ortho- and *meta*-substituted (η-benzaldehyde)tricarbonylchromium(0) complexes can be enantioselectively reduced by commercial bakers' yeast to give alcohols and unchanged aldehydes with good to high enantiomeric excesses.

ortho- and *meta*-substituted (η-benzaldehyde) and (η-aryl ketone)tricarbonylchromium(0) complexes have been extensively used in innovative asymmetric syntheses, especially in Grignard reactions [1]. These complexes possess a planar chirality and can be resolved into optically pure enantiomers. The conventional method for the resolution of these species involves the reaction of related acids with optically pure agents such as amines, the tedious separation of the diastereomers obtained by fractional crystallization, and a reduction step [2]. The use of semioxamazide derivatives enables separation by column chromatography [3]. However, the recognized value of these series in organic synthesis [4] has stimulated our search for an easier route to these useful chiral synthons [5].

The high specificity of reactions catalyzed by enzymes has now been well documented and more recently their application in organic syntheses has been shown to be a powerful technique for the preparation of chiral compounds [6]. This methodology, called bioconversion or microbial transformation, has been extensively used, especially by the pharmaceutical industry. The compatibility of reacting microorganisms with organometallic compounds together with their ability to perform stereospecific reactions has been little studied [7], but we [7c] and Yamazaki et al. [7e] have demonstrated that the planar chirality of chromium complexes can be

* Dedicated to Professor P.L. Pauson on the occasion of his retirement.

0022-328X/91/$03.50

resolved by bioconversion reactions. This method could provide a convenient and direct route to optically pure *ortho-* or *meta*-substituted chromiumtricarbonyl benzaldehydes and alcohols. We now report our recent results on the kinetic resolution of *ortho-* and *meta*-substituted (η-benzaldehydes)tricarbonylchromium(0) complexes by bakers' yeast reduction.

Results

Racemic (η-benzaldehyde)tricarbonylchromium(0) complexes *ortho-* and *meta*-substituted by methoxy, methyl, fluoro and trimethylsilyl groups (**1a,b,c,d,e** and **2a,b**) and (η-piperonal)tricarbonylchromium(0) (**3**) were selected for this study (Fig. 1). The yeast used in the reaction was a fresh bakers' yeast commercially supplied, which was washed with demineralized water prior to use. The washed yeast was suspended in demineralized water and fed with glucose. After 30 min stirring at an appropriate temperature a solution of the complex in the minimum of ethanol was added. The extent of reaction was monitored by HPLC and the reaction was stopped when the ratio of the being formed alcohol and the remaining aldehyde was ca. 1/1.

The resolution of the benzaldehyde complex depends on the power of the yeast to discriminate between the two enantiomers (Schemes 1 and 2). If the rate constants for the reduction are very different for the two enantiomers, one of them is preferentially reduced and at the mid-point the reaction will contain a mixture containing ideally one enantiomer of unchanged aldehyde and the other enantiomer of alcohol. If the reaction is continued the remaining enantiomer of benzaldehyde starts being reduced and produces the second enantiomer of alochol. In this situation, the benzaldehyde complex is still optically pure but the alcohol gradually becomes a mixture of enantiomers. Hence, it is important to stop the reaction at 50% transformation in order to isolate both benzaldehyde and alcohol in pure form or at least in very high enantiomeric excess (ee). Classical chromatography then permits the separation of optically active alcohol and aldehyde. This type of reaction can produce only one enantiomer of aldehyde or alcohol, but the second enantiomer can be obtained, if needed, by chemical reduction of the remaining aldehyde or oxidation of the formed alcohol.

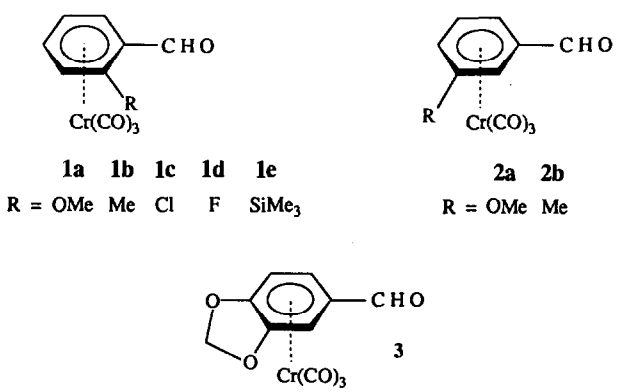
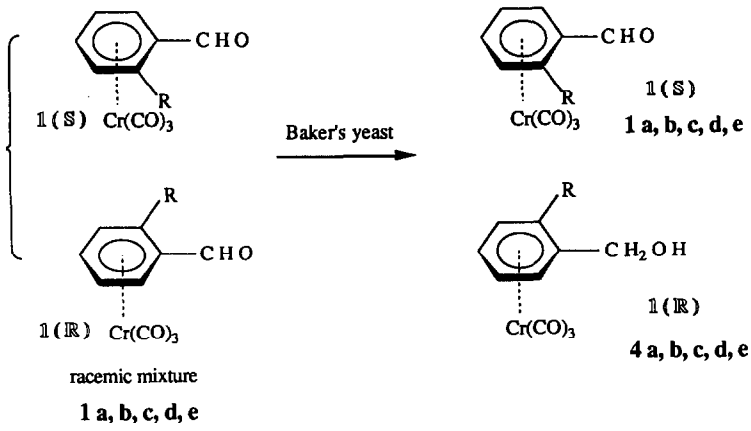
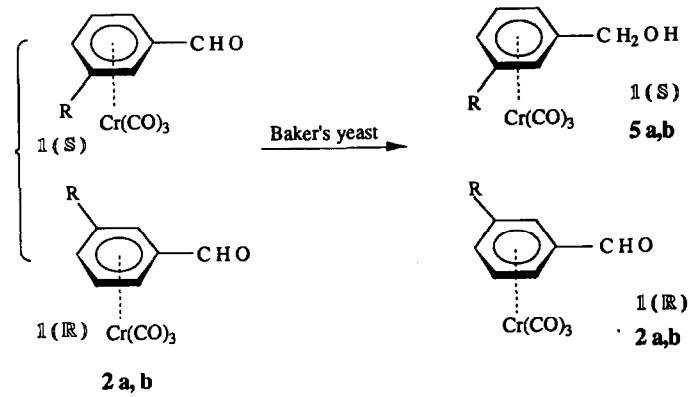


Fig. 1. Racemic complexes; only one of the enantiomers is shown.



Scheme 1



Scheme 2

The experimental results are summarized in Tables 1 and 2.

When the reaction was performed at ca. 35 or even at 30 °C (the usual temperatures for enzymatic reactions), the reduction was too fast and could not be stopped at the mid-point. The tricarbonylchromium group acts as an electron-withdrawing groups which increases the reactivity of the aldehyde carbonyl group. It was shown previously that (η-benzophenone)tricarbonylchromium is reduced at 30 °C in 24 h instead of 7 d for the uncomplexed benzophenone [7d]. In order to check this high reactivity we reduced the (η-α-deutero-benzaldehyde)tricarbonylchromium with the yeast at 30 °C (Scheme 3). The reduction was found to be very rapid, and complete within 20 min to give an 81% enantiomeric excess for the deuterated benzyl alcohol [8*]. The yeast was still active at 20 °C and the reduction slow enough to allow quenching of the reaction at about the mid-point. It is very difficult to stop the reaction at exactly 50% conversion owing to the time needed for the analysis by HPLC: 15 to 20 min was necessary for extracting the compound from the reaction

* Reference number with asterisk indicates a note in the list of references.

Table 1

Results of reduction of compounds **1a–e** (Alc = alcohol complex; Ald = aldehyde complex)

Complex (*R*,*S*)	Temperature and time of reaction	Alc/Ald by HPLC	Yield (by weight)	After isolation		After crystallization	
				$[\alpha]_D^{22}$ (°)	ee (%)	$[\alpha]_D^{22}$ (°)	ee (%)
1a (OMe)	22 °C 6 h	55/45	Alc: 48% Ald: 46% Alc/Ald = 51/49	+159 (+241 [a]) +823 (+1015 [b])	66 1 (*R*) 81 1(*S*)	+231 +1070	96 100
1b (Me)	22 °C 4.5 h	52/48	Alc: 41% Ald: 41% Alc/Ald = 50/50	−6.7 (−16 [a]) +631 (+665 [b])	42 1(*R*) 96 1(*S*)	−8.9 +704	56 100
1c (Cl)	21 °C 1 h 15 min	62/38	Alc: 48% Ald: 30% Alc/Ald = 61/39	+16.7 (+26.7) +971 (+1112)	62 1(*R*) 87 1(*S*)	+15.6 +1048	58 94
1d (F)	20 °C 25 min		Alc: 68% Ald: 27% Alc/Ald = 70/30	−4.9 (−25.3) +596 (+1148)	20 1(*R*) 52 1(*S*)	+782	68
1e ($SiMe_3$)	29 °C 14 h	60/40 [c]	Alc: 34% Ald: 26% Alc/Ald = 57/43	−3.2 (−5.1) +96.3 (+128.2)	61 [d] 1(*R*) 75 [d] 1(*S*)		66 [d] 81 [d]

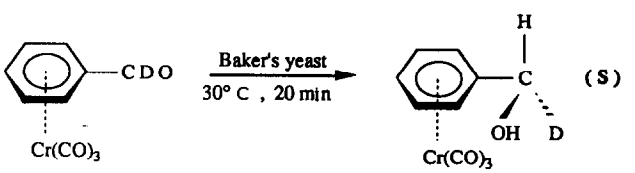
[a] $[\alpha]_D$ of optically pure complex from ref. 14. [b] $[\alpha]_D$ of optically pure complex from ref. 3. [c] Proportion determined by NMR. [d] Percentage determined by NMR using the Mosher's technique [10].

Table 2

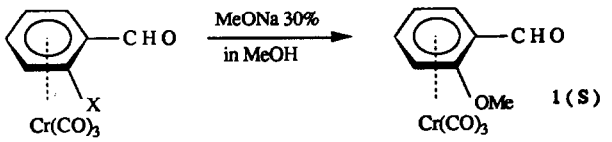
Results of reduction of compounds **2a**, **2b**, and **3**

Complex (*R*,*S*)	Temperature and time of reaction	Alc/Ald by HPLC	Yield (by weight)	After isolation		After crystallization	
				$[\alpha]_D^{22}$ (°)	ee (%)	$[\alpha]_D^{22}$ (°)	ee (%)
2a (OMe)	20 °C 30 min	45/55	Alc: 55% Ald: 44% Alc/Ald = 55/45	−4.6 (−8 [a]) +436 (+806 [a])	42 1(*S*) 54 1(*R*)	−3 +811	37 100
2b Me	17 °C 40 min		Alc: 44% Ald: 50% Alc/Ald = 47/53	−3.6 (−7 [a]) +164 (+316 [a])	52 1(*S*) 55 1(*R*)	+230	72
3	18 °C 2.5 h	56/44 [b]	Alc: 53% Ald: 47% Alc/Ald = 53/47	−6.7 (−15.5) +179 (+363)	43 (46 [c]) 49 (57 [c])		

[a] $[\alpha]_D$ of optically pure complex from ref. 16. [b] Proportion determined by NMR. [c] Percentage determined b NMR using the Mosher's technique [10].



Scheme 3



1c,d

1c (X = Cl) $[\alpha]_D = +1112°$
1d (X = F) $[\alpha]_D = +1148°$

1a

$[\alpha]_D = +1008°$
$[\alpha]_D = +800°$

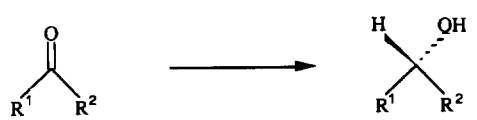
Scheme 4

mixture and elution from the column. At about the mid-point, the mixture was poured into water and the products were extracted with diethyl ether. After work-up, the crude products were chromatographed to separate the alcohol from the remaining aldehyde. The recovery of compounds was good, ranging from 78% for *o*-chloro complexes to 99% for *m*-methoxy derivatives. *o*-Trimethylsilylbenzaldehyde gave only 60% yields because the long reaction times led to partial decomplexation of the products.

The absolute configurations of the optically-active complexes were ascertained by comparison of their optical rotations with the literature data [2]. However the absolute configuration of chlorobenzaldehyde (**1c**) and fluorobenzaldehyde (**1d**) were unknown, and were determined by chemical correlation as shown in Scheme 4.

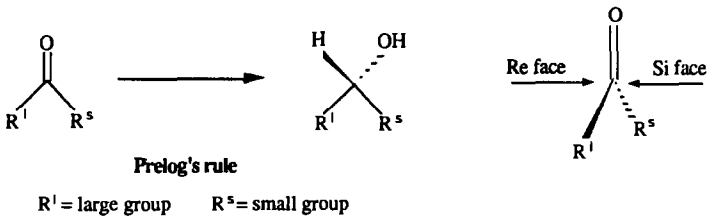
MeONa reacts with enantiomer **1c**, $[\alpha]_D = +1112°$, to give methoxybenzaldehyde 1(*S*), $[\alpha]_D = +1008°$ [18]. Hence the obtained chlorobenzhydrol **4c** is 1(*R*). The same experiment carried out on fluorobenzaldehyde (**1d**), $[\alpha]_D = +1148°$, gave methoxybenzaldehyde 1(*S*), $[\alpha]_D = +800°$ (the $[\alpha]_D$ has been calculated on the crude but sufficiently pure product). Interestingly, this transformation does not involve significant racemization, in strong contrast to a similar reaction involving *o*-fluoromethyl benzoate tricarbonylchromium [9]. The absolute configuration of the piperonal complex was not determined. The optical purities of the complexes were calculated from the $[\alpha]_D$ of the optically pure authentic samples or from the ^1H NMR spectra by Mosher's technique [10].

Of note is the inversion of the configuration of the major enantiomers with bakers' yeast on going from the *ortho* to the *meta* series. All the *ortho*-substituted benzaldehydes tested give an excess of 1(*R*) alcohols in contrast to the *meta*-substituted benzaldehydes, which give mainly 1(*S*) alcohols. This may be rationalized in terms of Prelog's rule [11]. Prelog [11] and MacLeod et al. [12] undertook the yeast reduction of a variety of ketones flanked by disymmetric substituents and concluded that steric factors played a dominant role. With rare exceptions, secondary alcohols were preferentially formed with the *S*-configuration (Scheme 5). If we consider a prochiral ketone flanked by a large group R^l and a small group R^s,



R^1, R^2 = alkyl with $R^2 > R^1$

Scheme 5

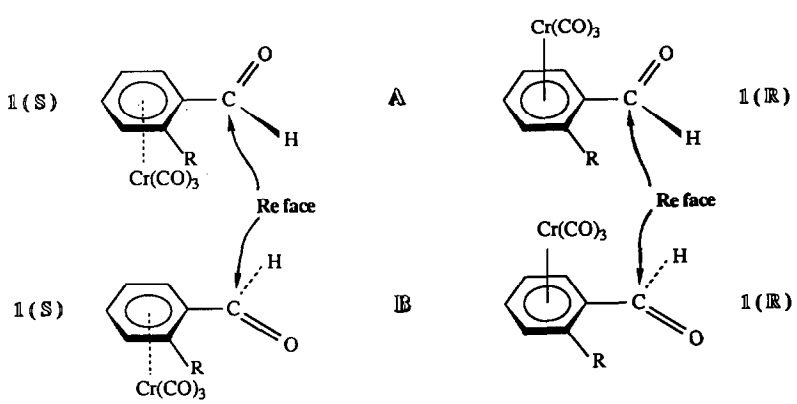


Scheme 6

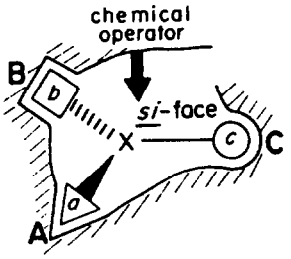
Prelog's rule predicts the formation of alcohol with configuration determined by the transfer of hydrogen to the Re-face of the ketone (Scheme 6).

In the case of benzaldehyde complexes the carbonyl function is not prochiral but Prelog's rule is still applicable. It is known that CO tends to be planar with respect to the arene ring; the steric or stereoelectronic effect caused by the *ortho*-group should favor a conformation in which the carbonyl and the *ortho*-substituent are remote from one another [1]. Hence, model **A** is the preferred conformation for both enantiomers 1(*S*) and 1(*R*) (Scheme 7). In addition it is clear that the Re-face of 1(*S*) enantiomer is blocked by the chromium group, while the Re-face of the 1(*R*) enantiomer is still accessible and its reduction gives the 1(*R*) alcohol, in agreement with the experimental results. The equilibrium between conformations **A** and **B** must play an important role in the resolution of complexes. The optical purities of the aldehydes 1(*S*) are good, but those of the alcohols 1(*R*) are only medium. However, the first crystallization gave pure enantiomers in the case of **1a** and **1b**.

In the case of *meta*-substituted benzaldehydes, the steric effect of a *meta*-substituent is not so important as in *ortho* series, and the two conformers **A** and **B** should both exist in about the same proportions. The experiments gave a good enantiomeric excess for methoxy **2a** and a medium excess for methyl **2b** and acetal **3**, but in this *meta* series there is an inversion of reactivity for the preferred enantiomers relative to that for the *ortho*-substituted aldehydes: the enantiomer 1(*S*) of the aldehydes is first reduced giving rise to alcohols 1(*S*). Since the discrimination between the less bulky Re faces can be expected to be weak, reduction should give racemic alcohols or little enantioselectivity. In the light of the



Scheme 7



Scheme 8

results, the discrimination between the two enantiomers might be thought to come from the recognition of the arene tricarbonylchromium part of the molecule by the yeast in addition to that of the CO face. In this case the molecular recognition of the planar chirality by the active site of the enzyme seems an important factor to consider. The ability of enzymes to discriminate between paired groups that are both stereoheterotropic and homomorphic at a prochiral center has been explained by Ogston in terms of a three point interaction of the substrate, as illustrated in Scheme 8 [13].

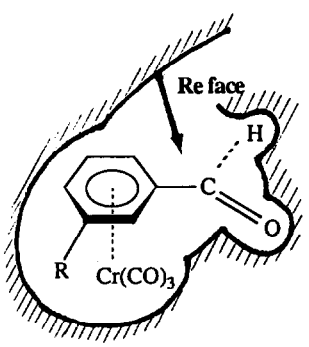
We suggest that the recognition of the planar chirality of complexes involves the same type of interaction as that proposed by Ogston (Scheme 9).

In addition, the nature of the *ortho*-group has an important influence on the rate of the reaction. The mid-point of reaction was reached at 25 min, 1 h 15 min, 4 h 30 min and 6 h for fluoro, chloro, methyl and methoxy compounds, respectively, while the trimethylsilyl benzaldehyde complex did not react at 20 °C during 7 h (the mid-point was reached only after 14 h at 29 °C). It is clear that electron-withdrawing groups increase the rate of the reaction (in addition to the effect of $Cr(CO)_3$ group).

In the *meta* series, reduction is much faster than for the *ortho*-substituted benzaldehydes; for example, it takes only 30 min to reduce *meta*-methoxy benzaldehyde. This may be a result of the difference in steric effects around the reduction sites.

These results demonstrate that there is no restriction on enzymatic reactions using organometallic complexes in terms of stability, molecular recognition, veloc-

1(S)



Scheme 9

ity, or penetration into the cells. The planar chirality of tricarbonylchromium complexes can be resolved by the yeast, providing an easy access to these optically-active complexes. It will be interesting to examine other enzymatic reactions such as hydrolysis, oxygenation, condensation and formation of C–C bonds in order to study the scope and limitation of this approach in organometallic chemistry.

Experimental

The known benzaldehyde complex derivatives were prepared by use of a conventional complexation method involving the refluxing of a solution of the arene and $Cr(CO)_6$ in a di-n-butyl ether/THF mixture [15]. The purities of the complexes were checked by comparison of their physical and spectroscopic data with those for authentic samples. The alcohols obtained were identified in the same way. α-Deuterio-benzaldehyde was prepared from benzil by the method described by Burgstahler et al. [17]. (*o*-Trimethylsilylbenzaldehyde)tricarbonylchromium (**1e**) was made by a published method [18]. The bakers' yeast was purchased from local bakers. HPLC was used to monitor the progress of the reduction by determination of the ratio of the product alcohol and remaining aldehyde. The ratio was calculated from the height of peaks, taking into consideration the difference between the peak heights for benzaldehyde and alcohol at the same concentration. The HPLC Beckman "Gold System" was used with a Rosil Silica column and CH_2Cl_2–heptane as eluant. Mosher's technique was used to determine the enantiomeric purity of the alcohols by an NMR method [10].

Synthesis of (η-o-chlorobenzadehyde)tricarbonylchromium(0) (1c)

A solution of (*o*-chlorobenzaldehyde)diethylacetal (93 mmol) (prepared from *o*-chlorobenzaldehyde and triethyl orthoformate) and $Cr(CO)_6$ (100 mmol) in a 4/1 mixture of dioxane/diglyme was refluxed at 115 °C for 20 h under an inert atmosphere in a Strohmeier apparatus. The solvent was distilled off under vacuum and the yellow residue was dissolved in diethyl ether and the solution filtered through Celite. After evaporation of the solvent the acetal complex obtained (m.p. 48–50 °C) was hydrolysed in acidic aqueous dioxane for 3 h. Racemic complex **1c** was isolated in 55% overall yield as dark red crystals by chromatography (eluant: light petroleum/diethyl ether (3/1)), m.p. 66–67 °C (^{i}PrOH). ^{1}H NMR (δ, $CDCl_3$) 5.1 (t, 1H), 5.35 (d, 1H, *J* 6.6 Hz), 5.7 (dt, 1H, J_o 6.6, J_m 1.2 Hz), 6.2 (dd, 1H, J_o 6.6, J_m 1.2 Hz), 10.0 (s, 1H, CHO). IR (ν, cm^{-1}, $CHCl_3$) 2000, 1940 (CO); 1690 (CHO). Anal.: Found: C, 43.51; H, 1.79. $C_{10}H_5ClCrO_4$ calc: C, 43.39; H, 1.8%.

Chemical resolution: racemic (η-*o*-chlorobenzadehyde)tricarbonylchromium (**1c**) was resolved by the Solladié-Cavallo method [3]. Racemic **1c** was treated with (*S*)-(−)-5-(α-phenylethyl)semioxamazide to give a mixture of two diasteromeric semioxamazones, which were separated by chromatography with diethyl ether/light petroleum (4/1) as eluant. First diastereomer: R_f = 0.38, m.p. 177–178 °C dec. (EtOH), $[\alpha]_D$ = +1263° (*c* = 0.35, $CHCl_3$). ^{1}H NMR (δ, $CDCl_3$) 1.6 (d, 3H, *J* 6 Hz), 5.0–5.2 (m, 1H + 1H, arom.), 5.3–5.6 (m, 2H, arom.), 6.4 (d, 1H, arom.), 7.3 (s, 5H, arom.), 7.8 (s, broad, 1H, NH), 8.4 (s, 1H), 10.7 (s, 1H, NH). IR (ν, cm^{-1}, $CHCl_3$) 3390, 3300 (NH), 1990, 1930 (CO); 1680 (CON). Anal.: Found: C, 51.98; H, 3.50; N, 9.05. $C_{20}H_{16}ClCrN_3O_5$ calc: C, 51.56; H, 3.44; N, 9.02%

Second diastereomer: $R_f = 0.26$, m.p. 172–174°C dec. (EtOH), $[\alpha]_D = -1297$ ($c = 0.32$, $CHCl_3$). The ^1H NMR and IR data were identical with those for the first diastereomer. Anal.: Found: C, 51.72; H, 3.41; N, 9.08. Hydrolysis of the first diastereomer gave (+)-**1c**, $[\alpha]_D = +1112°$ ($c = 0.2$, $CHCl_3$) and that of the second diastereomer gave (−)-**1c**, $[\alpha]_D = -1120°$ ($c = 0.2$, $CHCl_3$).

*Synthesis of (η-o-fluorobenzadehyde)tricarbonylchromium(0) (**1d**)*

A similar procedure to that used for **1c** gave in 48% overall yield, m.p. 101–102°C. ^1H NMR (δ, $CDCl_3$) 4.8 (dt, 1H, J_o 6.2, J_m 2.2 Hz), 5.34 (t, 1H, J 6 Hz), 5.72–5.78 (m, 1H), 6.10–6.14 (m, 1H), 9.9 (s, 1H, CHO). IR (ν, cm^{-1}, CH_2Cl_2) 2000, 1940 (CO); 1690 (CHO). Anal. Found: C, 46.54; H, 1.90. $C_{10}H_5FCrO_4$ calc: C, 46.16; H, 1.92%.

Chemical resolution: separation of diastereomers by chromatography with CH_2Cl_2/AcOEt (4/1) as eluant. First diastereomer: $R_f = 0.6$, m.p. 174–175°C dec. (EtOH), $[\alpha]_D = +1374°$ ($c = 0.3$, $CHCl_3$). ^1H NMR (δ, $CDCl_3$) 1.8 (d, 3H, J 8 Hz), 4.93–5.02 (dt, 1H, arom. J_o 6.1, J_m 1.8 Hz), 5.04–5.19 (m, 1H, CH.), 5.37 (t, 1H, arom., J 6.5 Hz), 5.55–5.65 (m, 1H, arom.), 6.4–6.49 (m, 1H, arom.), 7.31 (s, 5H, arom.), 7.8 (d, 1H, NH, J 8 Hz), 8.2 (s, 1H), 10.7 (s, 1H, NH). IR (ν, cm^{-1}, CH_2Cl_2) 3390, 3300 (NH), 1990, 1920 (CO); 1680 (CON). Anal.: Found: C, 53.53; H, 3.58; N, 9.32. $C_{20}H_{16}FCrN_3O_5$ calc: C, 53.45; H, 3.56; N, 9.35%.

Second diastereomer: $R_f = 0.35$, m.p. 160°C dec., $[\alpha]_D = -1358°$ ($c = 0.3$ $CHCl_3$). Hydrolysis of the first diastereomer gave (+)-**1d**, $[\alpha]_D = +1148$ ($c = 0.2$, $CHCl_3$) and that of the second diastereomer gave (−)-**1d**, $[\alpha]_D = -1139°$ ($c = 0.2$, $CHCl_3$).

*Synthesis of (η-piperonal)tricarbonylchromium(0) (**3**)*

A solution of piperonal acetal (93 mmol) (prepared from piperonal and triethyl orthoformate) and $Cr(CO)_6$ (100 mmol) in a 4/1 mixtures of dioxane/diglyme was refluxed at 115°C for 20 h in the Strohmeier apparatus. The solvent was distilled off under vacuum and the yellow residue was dissolved in diethyl ether. After filtration of the solution over Celite and evaporation, the residual acetal complex was hydrolysed in an acidic aqueous dioxane for 1 h. Finally from column chromatography with light petroleum/diethyl ether (4/1), racemic (η-piperonal)tricarbonylchromium(0) (**3**) was isolated in 40% overall yield as dark orange crystals, m.p. 99–100°C. ^1H NMR (δ, $CDCl_3$) 5.4 (d, 1H, J_o 6.6 Hz), 5.6 (dd, 1H, J_o 6.6, J_m 1 Hz), 5.8 (s, 1H), 6.05 (s, 1H), 6.1 (s, 1H), 9.3 (s, 1H). IR (ν, cm^{-1}, Nujol) 1970, 1890 (CO); 1680 (CHO); 1260–1030 (C=C); 910, 730 (–O–CH_2–O–). Anal.: Found: C, 47.45; H, 2.16. $C_{11}H_6CrO_6$ calc: C, 46.17; H, 2.11%.

Chemical resolution: racemic (η-piperonal)tricarbonylchromium(0) (**3**) was resolved by the Solladié–Cavallo method [3]. Racemic **3** was reacted with (*S*)-(−)-5-(α-phenylethyl)semioxamazide to give a mixture of two diastereomeric semioxamazones which were separated by chromatography with CH_2Cl_2/ethyl acetate (7/1) as eluant. First diastereomer: $R_f = 0.53$, m.p. 145°C dec., $[\alpha]_D = +372.6°$ ($c = 0.21$, $CHCl_3$). ^1H NMR (δ, $CDCl_3$) 1.6 (d, 3H, J 7 Hz), 5.1 (m, 2H), 5.4 (d, 1H, J 6.8 Hz), 5.8 (s, 1H), 6.0 (s, 1H), 6.1 (s, 1H), 7.3 (s, 5H, arom.), 7.8 (s, broad, 1H, NH), 8.0 (s, 1H), 10.9 (s, broad, 1H, NH). Anal.: Found: C, 53.01; H, 3.58; N, 8.82. $C_{21}H_{17}CrN_3O_7$ calc: C, 53.20; H, 3.60; N, 8.86%. Second diastereomer: $R_f = 0.40$, m.p. 105–106°C, $[\alpha]_D = -412°$ ($c = 0.23$, $CHCl_3$). Hydrolysis of the first dia-

stereomer gave (+)-**3**, $[\alpha]_D = +363°$ ($c = 0.192$, $CHCl_3$) and that of the second diasteromer gave (−)-**3**, $[\alpha]_D = -352°$ ($c = 0.205$, $CHCl_3$).

Synthesis of (η-α-deuterio-benzaldehyde)tricarbonylchromium(0)

α-Deuterio-benzaldehyde, prepared from benzil [17] was converted into diethyl-acetal by reaction with triethyl-*ortho*-formate as described previously [19]. A solution of the acetal (1.36 g, 0.0075 mol) and $Cr(CO)_6$ (4.4 g, 0.02 mol) in dibutyl ether (130 ml) and THF (10 ml) was refluxed for 15 h. After filtration and solvent removal, the crude product was purified on a silica gel column with diethyl ether/pentane (1/4) as eluant. The acetal complex was isolated as an yellow oil, 0.9 g, 42% yield. ^1H NMR (δ, $CDCl_3$) 5.56 (m, 2H), 5.32 (m, 3H), 3.64 (m, CH_2), 1.24 (t, CH_3). The acetal complex (2 g, 0.0063 mol) was dissolved in 50 ml of ethanol and 10 ml of concentrated HCl was added. After 15 min the mixture was poured into cold water and the product extracted with diethyl ether. Work-up gave (η-α-deuterio-benzaldehyde)tricarbonylchromium(0), 1.6 g, 100% yield, m.p. 78 °C. ^1H NMR (δ, $CDCl_3$) 5.89 (m, 2H), 5.63 (m, 1H), 5.25 (m, 2H). MS *m/z*: 243 (M^+), 215 ($M^+ - CO$), 187 ($M^+ - 2CO$), 159 ($M^+ - 3CO$).

Yeast preparation

Fresh bakers' yeast (10 g) was stirred with demineralized water (100 ml) and the mixture was centrifuged for 10 min at 2500 rev min^{-1}. After removal of water, the washing was repeated. The bakers' yeast so treated was suspended in demineralized water (100 ml) and after addition of glucose (2.5 g) the mixture was stirred at the temperature chosen for the reduction reaction for 30 min before the reaction with aldehyde.

General procedure for reduction

Reduction of (η-*o*-methoxybenzaldehyde)tricarbonylchromium(0) (**1a**). After the yeast mixture had been kept at the appropriate temperature, as described above a solution of racemic **1a** (109 mg, 0.4 mmol) in ethanol (5 ml) was added. The progress of the reaction was monitored by HPLC and the reaction was stopped after 6 h. Extraction of the mixture with diethyl ether afforded the crude product (108 mg, 99%), which was purified by preparative chromatography on silica gel plates (eluant Et_2O/pentane (2/1)). (+)-1*S*-(η-*o*-methoxybenzaldehyde)tricarbonylchromium(0) (**1a**) (49 mg) was isolated as a red solid $[\alpha]_D^{22} = +823°$ ($c = 0.43$, $CHCl_3$); ee = 81% and (+)-(1*R*)-(η-*o*-methoxybenzyl alcohol)tricarbonylchromium(0) (**4a**) (52 mg) as a yellow solid, $[\alpha]_D^{22} = +159°$ ($c = 0.81$, $CHCl_3$); e.e. = 66%. A single crystallization from ether/pentane gave alcohol with e.e. = 96% and aldehyde in e.e. = 100%.

Acknowledgement

We thank Prof. I.S. Butler and Prof. J.A.S. Howell for helpful discussions, and CNRS and CNR Rome for financial support.

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