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STEREOSELECTIVE ADDITION OF CYANIDE ION TO CHIRAL RHENIUM π-ALDEHYDE COMPLEXES OF THE FORMULAE $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^2\text{-}O{=}CHR)]^+\ BF_4^-$; A NEW SYNTHESIS OF OPTICALLY ACTIVE CYANOHYDRIN DERIVATIVES

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Abstract. Reaction of optically active aldehyde complexes (+)-($\underline{RS}$)-$[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^2\text{-}O{=}CHR)]^+\ BF_4^-$ and $(CH_3CH_2)_4N^+\ CN^-$ gives cyanohydrin alkoxide complexes (+)-$(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(CN)R)$ (78-95%) of 89-53% de. The alkoxide ligands are then converted to optically active MTPA esters (96-85%) of 90-56% de.

We recently reported that the chiral rhenium Lewis acid[1] $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)]^+\ X^-$ binds one enantioface of aliphatic aldehydes[2] and monosubstituted alkenes[3] with high apparent thermodynamic selectivities. We also reported that the resulting aldehyde complexes ($\underline{RS},\underline{SR}$)-$[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^2\text{-}O{=}CHR)]^+\ X^-$ (($\underline{RS},\underline{SR}$)-$\mathbf{1}^+\ X^-$) undergo stereoselective addition of deuteride to give, after workup, α-deuterated primary alcohols of high optical purities.[2] Hence, we sought to assay the stereoselectivities of analogous additions of *carbon* nucleophiles. In this communication, we report that cyanide ion adds to aldehyde complexes $\mathbf{1}^+\ BF_4^-$ to give cyanohydrin alkoxide complexes $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(CN)R)$ (**2**) in high yields and good to excellent diastereomeric purities. These are easily converted to optically active cyanohydrin derivatives, thus providing a valuable and convenient complement to existing methodologies[4] for the asymmetric synthesis of cyanohydrins.

Reaction of racemic methyl complex $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(CH_3)$ (**3**)[5] with $HBF_4{\cdot}OEt_2$ (CH_2Cl_2, -80 °C) and then aldehydes RCH=O gave π aldehyde complexes ($\underline{RS},\underline{SR}$)-$[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^2\text{-}O{=}CHR)]^+\ BF_4^-$ (($\underline{RS},\underline{SR}$)-$\mathbf{1}^+\ BF_4^-$, R = **a**, CH_3; **b**, CH_2CH_3; **c**, $CH(CH_3)_2$; **d**, $CH_2C_6H_5$; **e**, C_6H_5) in 82-97% yields after workup. Optically active methyl complex[5] (+)-($\underline{S}$)-(**3**) was similarly converted to optically active aldehyde complexes (+)-($\underline{RS}$)-**1a-e**$^+\ BF_4^-$ (90-98% after precipitation with ether). Aldehyde complexes were characterized analogously to the corresponding PF_6^- salts reported earlier.[2]

Racemic complexes ($\underline{RS},\underline{SR}$)-**1a-e**$^+\ BF_4^-$ were suspended in CH_2Cl_2 (150 mg/3 mL) at -80 °C, and treated with solid $(CH_3CH_2)_4N^+\ CN^-$ (1.05-1.10 equiv). The reactions were kept at -80 °C for 16-18 h, and then chromatographed on deactivated Florisil.[6] This gave cyanohydrin alkoxide complexes $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(CN)R)$ (**2a-e**) in 85-93% yields and as 81-94:19-6 mixtures of ($\underline{RS},\underline{SR}$)/($\underline{RR},\underline{SS}$) diastereomers, as assayed by ^1H NMR and summarized in Scheme I. Complexes **2a-e** were characterized by microanalysis, and IR and NMR (^1H, ^{13}C, ^{31}P) spectroscopy.[7] Solutions or solid samples of **2a-e** did not significantly decompose in air over periods of hours, in contrast to analogous alkoxide complexes lacking the cyano substituent.[2,8] Stereochemical assignments were made as described below, with the major diastereomers derived from a *formal* attack of cyanide ion on the aldehyde face *anti* to the rhenium.

Optically active aldehyde complexes (+)-(RS)-**1a**-**e**$^+$ BF_4^- were more soluble than the racemates, and were similarly reacted with $(CH_3CH_2)_4N^+$ CN^- (-80 °C, 150 mg/3 mL CH_2Cl_2), but under homogeneous conditions. Identical workups gave optically active cyanohydrin complexes (+)-**2a**-**e** in 78-95% yields and as 77-95:23-5 mixtures of (RS)/(RR) diastereomers.[6] Chromatography on $(CH_3CH_2)_3N$-deactivated silica gel allowed isolation of the major diastereomers in pure form.

Attention was next turned to detaching the cyanohydrin alkoxide ligand from the rhenium. Complexes (+)-**2a**-**e** and 4-dimethylaminopyridine (DMAP, 1 equiv) were dissolved in benzene at room temperature. Then (-)-(R)-$(CH_3O)(C_6H_5)(CF_3)CCOCl$ ((-)-(R)-MTPA-Cl,[9] 2 equiv) was slowly added. The reactions were stirred for 16-18 h, and then chromatographed (silica gel, 2-5% v/v ethyl acetate in hexanes) to give Mosher cyanohydrin-MTPA esters **4a**-**e** in 96-85% yields and as 78-95:22-5 mixtures of (SS)/(RR) diastereomers (Scheme I; assayed by capillary GC and ^1H NMR). The rhenium fragment was converted to chloride complex $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(Cl)$, which is of moderate configurational stability under the reaction conditions.[10]

The MTPA esters **4d**-**e** have been reported previously,[4b,c] and the absolute configurations of **4a**-**e** were assigned from established NMR correlations.[9b,11] As a confirmation, alkoxide (+)-**2e** was treated with p-$CH_3C_6H_4SO_3H$. Silica gel chromatography gave benzaldehyde cyanohydrin (71%, ≥95% purity) that was strongly levorotatory ([α] -42° ± 1°, c 30 mg/mL, $CDCl_3$; lit (R):[4c] 49°), indicative of the S absolute configuration.[12] The configurations of the alkoxide carbons in **2a**-**e** (Scheme I) were assigned accordingly.

Several aspects of the preceding data merit note. First, the stabilities of rhenium cyanohydrin alkoxides **2a**-**e** markedly contrast with those of alkali metal cyanohydrin alkoxides. The latter compounds, which have been characterized only as reaction intermediates, rapidly decompose to alkali metal cyanides and aldehydes in aprotic media.[13] Second, our methodology should allow the asymmetric synthesis of cyanohydrin derivatives in cases where the cyanohydrins are thermodynamically inaccessible from free aldehydes. Third, although no attempt was made to recover the rhenium in optically active form following the generation of MTPA esters **4a**-**e**, studies with related secondary alkoxide complexes $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(R)CH_3)$ indicate that this can easily be achieved.[8] Fourth, any slight variations in the stereoselectivities for cyanide addition to racemic and optically active **1a**-**e**$^+$ BF_4^- (Scheme I) have several possible explanations,[14] including the difference in reaction homogeneity noted above. Fifth, appropriately substituted aromatic aldehyde complexes $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(O{=}CHAr)]^+$ BF_4^- have been found to exist as mixtures of η^1 (σ) and η^2 (π) isomers.[15] Hence, the possibility remains that cyanide addition to **1a**-**e**$^+$ BF_4^- might occur via σ transition states. Product stereochemistry would be expected to be identical to that from a π transition state, as analyzed elsewhere for σ ketone complexes.[8] Finally, Faller and coworkers have recently reported the intramolecular asymmetric addition of carbon nucleophiles to transient molybdenum aldehyde complexes.[16] Further examples of stereoselective additions of nucleophiles to aldehyde, ketone, and alkene complexes of the $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)]^+$ fragment will be described in the near future.

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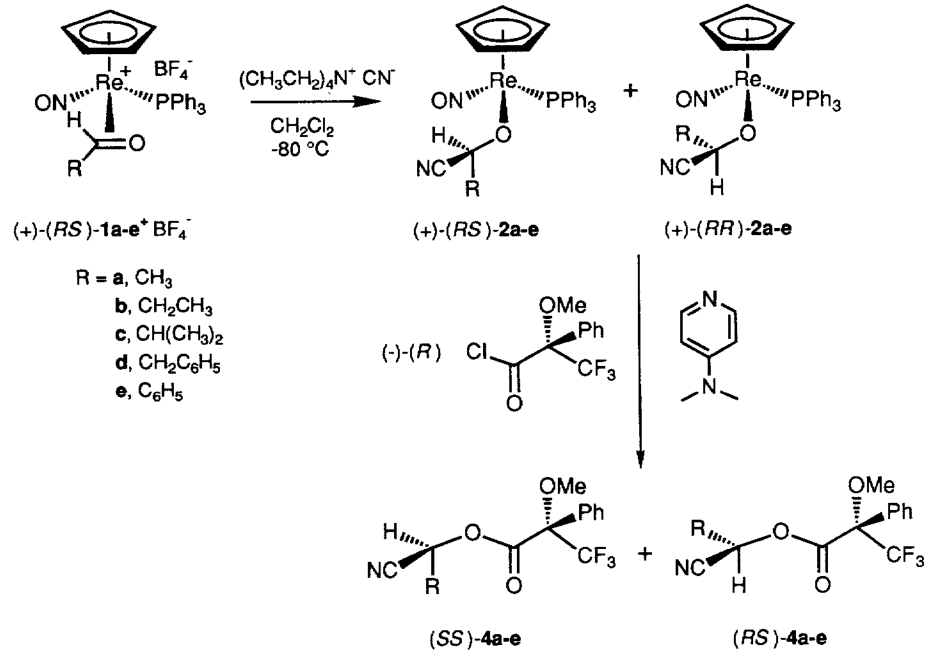
Scheme I. Addition of cyanide to racemic and optically active aldehyde complexes (±)-(*RS, SR*)-1^+ BF_4^- and (+)-(*RS*)-1^+ BF_4^-.



starting material	ratio (±) - (*RS, SR*) - **2** : (±) - (*RR, SS*) - **2** or (+) - (*RS*) - **2** : (+) - (*RR*) - **2**		yield (%)	(*SS*) - **4** / (*RS*) - **4**		yield (%)
(±) - (*RS,SR*) - **1a**	81.0:19.0	(62 % de)	87	—		—
(±) - (*RS,SR*) - **1b**	88.0:12.0	(76 % de)	88	—		—
(±) - (*RS,SR*) - **1c**	89.5:10.5	(79 % de)	90	—		—
(±) - (*RS,SR*) - **1d**	85.0:15.0	(70 % de)	85	—		—
(±) - (*RS,SR*) - **1e**	94.0: 6.0	(88 % de)	93	—		—
(+) - (*RS*) - **1a**	76.5:23.5	(53 % de)	84	78.0:22.0	(56 % de)	96
(+) - (*RS*) - **1b**	90.0:10.0	(80 % de)	92	90.0:10.0	(80 % de)	93[b]
(+) - (*RS*) - **1c**	91.0: 9.0	(83 % de)	93	91.5: 8.5	(83 % de)	94[b]
(+) - (*RS*) - **1d**	85.5:14.5	(71 % de)	78[a]	84.0:16.0	(68 % de)	85
(+) - (*RS*) - **1e**	94.5: 5.5	(89 % de)	95	95.0: 5.0	(90 % de)	87

a. Yield corrected for 4 mol % impurity.

b. Yield corrected for 15 wt. % of MTPA anhydride impurity.

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(6) Florisil was treated with 30% (v/w) concentrated NH_4OH. Without such deactivation (or on silica gel), variable amounts of **2a**-**e** were retained. Diastereomer ratios were not affected (within experimental error) by chromatography, as assayed by ^1H NMR analysis of crude (+)-**2a**,**b**,**e**.

(7) Spectroscopic properties of **2a**-**e** resemble those of other alkoxide complexes reported earlier.[2,8] Full data have been furnished to the reviewers; selected data on major diastereomers: IR (cm^{-1}, KBr) ν_{NO} 1627-1641; ^1H NMR (δ, C_6D_6) C_5H_5 5.00-5.07, OCH 4.43-5.60; ^{13}C NMR (ppm, C_6D_6) CN 123.4-125.0, C_5H_5 90.7-90.8, OCH 80.4-92.0; ^{31}P NMR (ppm, C_6D_6) 17.8-19.0.

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(11) The OCHRR' ^1H NMR resonance of one MTPA ester diastereomer is shielded, as rationalized by a syn orientation of the phenyl ring in a conformational model developed by Mosher.[9b] This correlation has been verified by many independent syntheses, and is used to assign configuration in **4a**-**d**. A second empirical correlation is found in **4a**-**e**: the OCH_3 ^1H NMR resonance of one diastereomer (syn to the cyanide in Mosher's model) is deshielded by 0.1-0.2 ppm.

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