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Preliminary communication

Highly stereoselective reduction of methyl ketone complexes of the chiral Lewis acid $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)]^+$ by $K(s\text{-}C_4H_9)_3BH$; synthesis of optically active secondary alcohols and derivatives

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Abstract

Reaction of optically active ketone complexes (+)-(*R*)-$[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^1\text{-}O{=}C(R)CH_3)]^+$ BF_4^- ($R = CH_2CH_3$, $CH(CH_3)_2$, $C(CH_3)_3$, C_6H_5) with $K(s\text{-}C_4H_9)_3BH$ gives alkoxide complexes (+)-(*RS*)-$(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(R)CH_3)$ (73–90%) in 80–98% de. The alkoxide ligand is then converted to Mosher esters (93–99%) of 79–98% de.

A number of methods have recently been reported for the asymmetric reduction of prochiral ketones to optically active alcohols [1,2]. The majority of these utilize chiral aluminum and borohydride reagents [2]. In this communication, we report the highly enantioselective reduction of methyl ketones with a commercially available, achiral borohydride. Control of absolute stereochemistry is achieved by prior ketone complexation to the chiral, transition metal Lewis acid $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)]^+$ (I).

Reaction of methyl complex $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(CH_3)$ (**1**) and $HBF_4 \cdot O(C_2H_5)_2$ in CH_2Cl_2 at −78°C gave the dichloromethane complex $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(ClCH_2Cl)]^+$ BF_4^- (**2**), which has been previously shown to serve as a functional equivalent of the chiral Lewis acid I [3]. Subsequent addition of (a) acetone, (b) 2-butanone, (c) 3-methyl-2-butanone, (d) 3,3-dimethyl-2-butanone, and (e) acetophenone (3 equiv.) gave σ-ketone complexes $[(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(\eta^1\text{-}O{=}C(R)CH_3)]^+$ BF_4^- (**3a**–**3e**) in 79–86% yields after workup. Complexes **3a**–**3e** were characterized analogously to the corresponding PF_6^- salts of **3a**, **3b** and **3e** reported earlier [4,5*]. In each case, IR ν(C=O) and ^{13}C NMR C=O chemical shifts characteristic of σ ketone binding were observed [6]. Complexes **3b**–**3e** appeared by

* Reference numbers with asterisks indicate notes in the list of references.

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low temperature NMR to be one C=O geometric isomer. However, acetone complex **3a** (PF_6^- salt) has been previously shown to undergo rapid intramolecular methyl group exchange [4]. Nonetheless, C=O geometric isomers with the rhenium and smaller methyl group *cis* would be expected to predominate. Two crystal structures have established the ligand conformation shown in formula II (Scheme 1) [4,6].

Dichloromethane solutions of **3a–3e** were treated with $K(s\text{-}C_4H_9)_3BH$ at $-80\,^\circ C$ (1.05–1.10 equiv., 1.0 *M* in THF; Scheme 1). Analysis by ^{31}P NMR showed reduction to secondary alkoxide complexes $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(OCH(R)CH_3)$ (**4a–4e**) to be complete within 3 min. In preparative experiments, solvents were subsequently removed by rotary evaporation. The residue was extracted with benzene and the extract was filtered through a 2×2 cm plug of CaO [7*]. Solvent was removed from the filtrate to give analytically pure alkoxide complexes in high yields as $> 99/1$ to 87/13 mixtures of diastereomers (Scheme 1). In all cases, diastereomers exhibited distinctive ^1H, ^{13}C, and ^{31}P NMR spectra, and mixtures enriched in the minor diastereomers could be generated by reductions at higher temperatures.

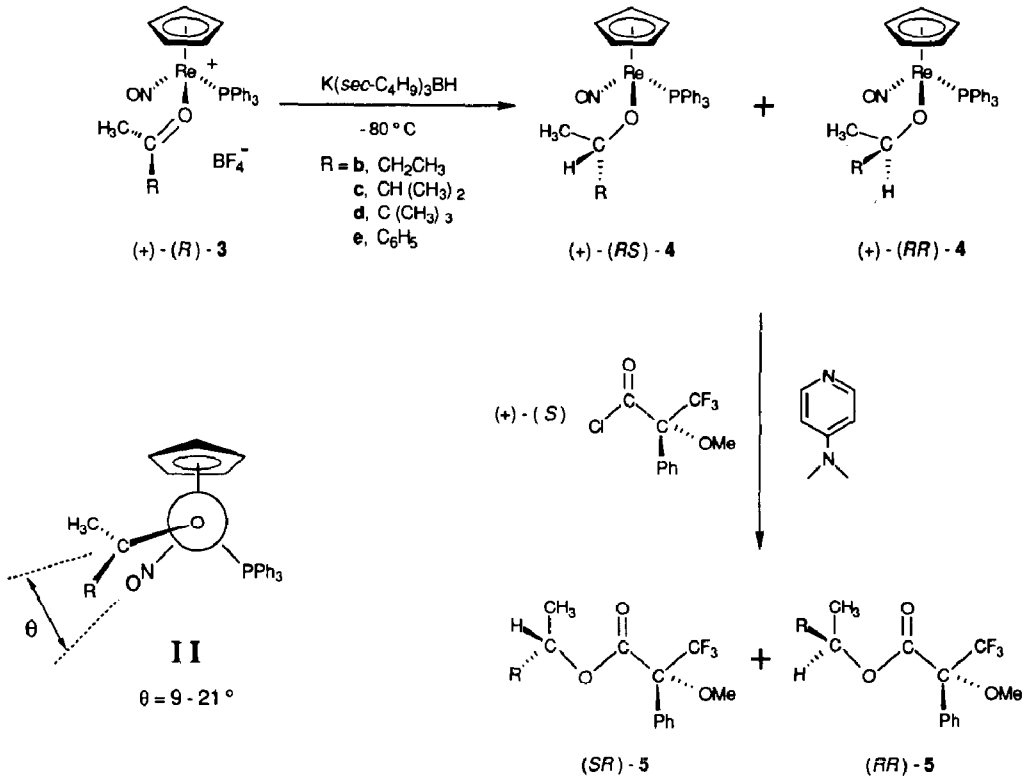
Optically active methyl complex (+)-(*S*)-**1** [8*] was similarly converted to optically active ketone complexes (+)-(*R*)-**3b–3e** [9*]. Analogous reduction of (+)-(*R*)-**3b–3e** with $K(s\text{-}C_4H_9)_3BH$ gave optically active alkoxide complexes (+)-(*RS*)-**4b–4e** in diastereomer ratios similar to those obtained above (Scheme 1) [10*].

We next sought to liberate the alkoxide ligands in (+)-(*RS*)-**4b–4e** from the rhenium, optimally in tandem with assays for the absolute configurations and optical purities of the alkoxide fragments. Accordingly, (+)-(*RS*)-**4b–4c**, acid chloride (+)-(*S*)-$(CH_3O)(C_6H_5)(CF_3)CCOCl$ ((+)-(*S*)-MTPA-Cl, Scheme 1; 1.5 equiv.) [11], and 4-dimethylaminopyridine (DMAP) were treated at $50\,^\circ C$ (benzene, 2 h). Chromatographic work-ups gave the previously synthesized Mosher esters (*SR*)-MTPA-$OCH(R)CH_3$ ((*SR*)-**5b–5c**) in 93–99% yields. The ester diastereomeric excesses (Scheme 1) were assayed by both NMR and GLC, and absolute configurations were assigned by NMR as reported by others previously [11*]. The absolute configurations of the alkoxide carbons confirmed the alkoxide complex diastereomer assignments (Scheme 1) and are consistent with a transition state for ketone reduction in which the carbonyl group in II is attacked on the face opposite the bulky PPh_3 ligand.

We have noted that the rate of alkoxide ligand acylation depends upon the number and bulk of the alkoxide carbon substituents (e.g., $1^\circ > 2^\circ > 3^\circ$). Also, certain alkoxide complexes have been shown to undergo epimerization at carbon above room temperature [12]. Accordingly, the corresponding acylation reactions of (+)-(*RS*)-**4d–4e** gave Mosher esters of somewhat lower diastereomeric excesses than (+)-(*RS*)-**4d–4e**. Hence, (+)-(*RS*)-**4d–4e** were treated with HCl (1.1 equiv., $-78\,^\circ C$) to give alcohols $HOCH(R)CH_3$. Then (+)-(*S*)-MTPA-Cl and DMAP (3 equiv.) were added and reaction and workup conducted as above. An analogous chromatographic isolation gave esters (*SR*)-**5d–5e** in high yields and diastereomer excesses (Scheme 1).

The above acylation reactions also give chloride complex $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(Cl)$, which is not very configurationally stable [13]. Hence, we have not assayed for optical purity. Rather, we have sought other means of alkoxide ligand removal that should deliver a more configurationally robust form of rhenium.

Scheme 1. Reduction of racemic and optically active ketone complexes (±) - (*R,S*) - **3** and (+) - (*R*) - **3** by K(*sec*-C_4H_9)$_3$BH



starting material	ratio (±) - (*RS, SR*) - **4** / (±) - (*RR, SS*) - **4** or (+) - (*RS*) - **4** / (+) - (*RR*) - **4**		yield (%)	(*SR*) - **5** / (*RR*) - **5**		yield (%)
(±) - (*R, S*) - **3b**	87.0:13.0	(74 % de)	91	———		—
(±) - (*R, S*) - **3c**	91.0:9.0	(82 % de)	93	———		—
(±) - (*R, S*) - **3d**	99.5:0.5	(99 % de)	77	———		—
(±) - (*R, S*) - **3e**	99.0:1.0	(98 % de)	90	———		—
(+) - (*R*) - **3b**	90.0:10.0	(80 % de)	89	89.5:10.5	(79 % de)	99
(+) - (*R*) - **3c**	96.0:4.0	(92 % de)	90	96.5:3.5	(93 % de)	99
(+) - (*R*) - **3d**	98.0:2.0	(96 % de)	73	96.0:4.0	(92 % de)	93[a]
(+) - (*R*) - **3e**	99.0:1.0	(98 % de)	86	99.0:1.0	(98 % de)	98[a]

[a] In these experiments the (+) - (*RS*) - **4** / (+) - (*RR*) - **4** mixture was first treated with HCl at - 78 °C; see text.

Accordingly, reaction of (+)-(*RS*)-**4c**–**4e** directly with Mosher's acid, (+)-(*R*)-MTPA (1.0 equiv., CH_2Cl_2, −78°C, 5 min), liberated alcohols $HOCH(R)CH_3$ and gave the carboxylate complex (+)-(*RR*)-(η^5-C_5H_5)Re(NO)(PPh_3)(O(C=O)C(CF_3)-(OCH_3)(C_6H_5) ((+)-(*RR*)-**6**) in 88–95% d.e. [14*]. An authentic sample of (+)-(*RR*)-**6** was prepared by reaction of optically active dichloromethane complex (*S*)-**2**-BF_4^- and (+)-(*R*)-MTPA (3 equiv., −78°C; 52% after work-up), and an authentic sample of the mixture of diastereomers (+)-(*RR*)-**6** and (−)-(*SR*)-**6** was prepared by the corresponding reaction with racemic **2**.

In summary, we have shown that methyl ketone complexes of the chiral rhenium Lewis acid I are reduced with high stereoselectivity by a commercially available borohydride reductant. The alkoxide complex products can easily be elaborated to organic alcohols or esters, and the rhenium fragment can be recovered in optically active form. Further optimization of these protocols for application in asymmetric organic synthesis will be reported in future publications.

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References

1 Reviews: (a) M.M. Midland in J.D. Morrison (Ed.), Asymmetric Synthesis, Academic Press, New York, 1983, Vol. 2, p. 56; (b) E.R. Grandbois, S.I. Howard and J.D. Morrison, ibid., p. 71; (c) K.E. Koenig, ibid., 1985, Vol. 5, p. 79; (d) H.C. Brown, W.S. Park, B.T. Cho and P.V. Ramachandran, J. Org. Chem., 52 (1987) 5406.

2 See, inter alia, (a) R. Noyori, I. Tomino, Y. Tanimoto and M. Nishizawa, J. Am. Chem. Soc., 106 (1984) 6709; (b) R. Noyori, I. Tomino, M. Yamada and M. Nishizawa, ibid., 106 (1984) 6717; (c) G. Giacomelli, L. Lardicci and F. Palla, J. Org. Chem., 49 (1984) 310; (d) M.M. Midland and J.I. McLoughlin, ibid., 49 (1984) 4101; (e) T. Mukaiyama, K. Tomimori and T. Oriyama, Chem. Lett., (1985) 1359; (f) S. Itsuno, M. Nakano, K. Miyazaki, H. Masuda, K. Ito, A. Hirao and S. Nakahama, J. Chem. Soc., Perkin Trans. I, (1985) 2039; (g) P. Kvintovics, B.R. James and B. Heil, J. Chem. Soc., Chem. Commun., (1986) 1810; (h) H.W. Krause and A.K. Bhatnagar, J. Organomet. Chem., 302 (1986) 265; (i) E. Keinan, E.K. Hafeli, K.K. Seth and R. Lamed, J. Am. Chem. Soc., 108 (1986) 162; (j) M.B. Eleveld and H. Hogeveen, Tetrahedron Lett., 27 (1986) 635; (k) H.C. Brown, J. Chandrasekharan and P.V. Ramachandran, J. Am. Chem. Soc., 110 (1988) 1539; (l) T. Imai, T. Tamura, A. Yamamuro, T. Sato, T.A. Wollmann, R.M. Kennedy and S. Masamune, ibid., 108 (1986) 7402; (m) E.J. Corey, R.K. Bakshi, S. Shibata, C.P. Chen and V.K. Singh, ibid., 109 (1987) 7925; (n) M.M. Midland and A. Kazubski, J. Org. Chem., 47 (1982) 2495; (o) H.C. Brown, B.T. Cho and W.S. Park, ibid., 52 (1987) 4020; (p) H.C. Brown, B.T. Cho and W.S. Park, ibid., 53 (1988) 1231.

3 (a) J.M. Fernández and J.A. Gladysz, Inorg. Chem., 25 (1986) 2672; (b) J.M. Fernández and J.A. Gladysz, Organometallics, 8 (1989) 207.

4 J.M. Fernández, K. Emerson, R.D. Larsen and J.A. Gladysz, J. Chem. Soc., Chem. Commun., (1988) 37.

5 Commercial $HPF_6 \cdot O(C_2H_5)$ has been sporadically available since 1986, and samples have varied considerably in purity. Hence, we have switched from PF_6^- to BF_4^- as the counter-anion of choice for ketone complexes.

6 Y.-H. Huang and J.A. Gladysz, J. Chem. Ed., 65 (1988) 298.

7 More common supports (silica, alumina, florisil) effect rhenium–oxygen bond cleavage.

8 J.H. Merrifield, C.E. Strouse and J.A. Gladysz, Organometallics, 1 (1982) 1204. The preparation of enantiomeric alcohol derivatives from readily available (−)-(*R*)-1 will be described in our full paper.

9 $[\alpha]_{589}^{23}$ for (+)-(*R*)-**3b**–**3e**: 489°, 407°, 374°, and 501°, respectively. The values for (+)-(*R*)-**3d**–**3e** are provisional; enhanced solubilities have hampered the isolation of analytically pure samples.

10 $[\alpha]_{589}^{23}$ for the (+)-(*RS*)-**4b**–**4e**/(+)-(*RR*)-**4b**–**4e** mixtures: 511°, 521°, 452°, and 418°, respectively.

11 (a) J.A. Dale, D.L. Dull and H.S. Mosher, J. Org. Chem., 34 (1969) 2543; (b) The ester (*SR*)-**5e** was prepared earlier but its configuration was not assigned [11a]. We confirmed the assignment in Scheme 1 by synthesis of an authentic sample from (+)-(*R*)-MTPA and (−)-(*S*)-$C_6H_5CH(CH_3)OH$.

12 D.M. Dalton and C.M. Garner, University of Utah, unpublished results.

13 J.H. Merrifield, J.M. Fernández, W.E. Buhro and J.A. Gladysz, Inorg.Chem., 23 (1984) 4022.

14 Data on (+)-(*RR*)-**6** (isolated as an orange powder following chromatography): IR (cm^{-1}, KBr): ν(NO) 1758 s, ν(CO) 1648 s; ^1H NMR (δ, C_6D_6): 7.85–6.90 (m, $4C_6H_5$), 4.87 (s, C_5H_5), 3.25 (q, CH_3, J(HF) 1.1 Hz); $^{13}C\{^1H\}$ NMR (ppm, C_6D_6): 172.9 (s, CO), PPh_3 at 135.2 (d, J(CP) 52.3 Hz, *i*), 134.1 (d, J(CP) 11.0 Hz), 130.6 (s, *p*), 128.7 (d, J(CP) 10.2 Hz); CPh at 135.9 (s, *i*), 128.7 (s), 128.5 (s); 125.3 (q, CF_3, J(CF) 288 Hz), 90.8 (s, C_5H_5), 54.8 (s, CH_3) (one phenyl carbon and the quaternary carbon not observed); $^{31}P\{^1H\}$ NMR (ppm, C_6D_6): 20.3 (s). Anal Found: C, 51.04; H, 3.66. $C_{33}H_{28}F_3NO_4PRe$ calcd.: C, 51.03; H, 3.63%.