

**The Selective Activation of One Methyl Ketone Enantioface via  $\sigma$ -Binding to a Chiral Metal Template: Synthesis and Reactivity of Rhenium Ketone Complexes  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)(\eta^1\text{-Me}(\text{R})\text{C}=\text{O})]^+\text{PF}_6^-$**

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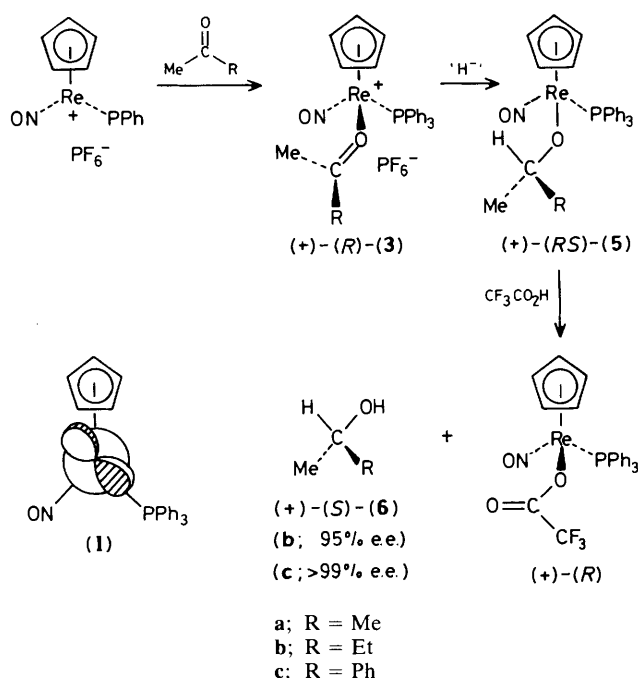
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The title compounds (R = Me, Et, Ph) are synthesized from ketones in high yield, structurally characterized, and shown to undergo highly stereoselective nucleophilic attack; secondary alcohols can be made with 95 to  $\geq 99\%$  enantiomeric excess (e.e.)

A general conversion of prochiral ketones to chiral secondary and tertiary alcohols of high optical purity would be of great value in organic synthesis. Accordingly, a number of creative approaches to this problem have recently been published.<sup>1,2</sup> We now report that the easily generated, chiral rhenium Lewis acid  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)]^+$  binds methyl ketones  $\text{Me}(\text{R})\text{C}=\text{O}$  in an  $\eta^1$  ( $\sigma$ ) fashion, with the metal *syn* to the smaller methyl substituent. These ketone complexes undergo essentially stereospecific nucleophilic attack, giving alkoxide

complexes that are easily converted to optically active alcohols.

The methyl complex  $(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)\text{Me}$  (**1**)<sup>3</sup> was treated with  $\text{HPF}_6 \cdot \text{Et}_2\text{O}$  ( $\text{CH}_2\text{Cl}_2$ ,  $-78^\circ\text{C}$ ) to give the co-ordinatively unsaturated, *pyramidal* cation  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)]^+\text{PF}_6^-$  (**2**), or a  $\text{CH}_2\text{Cl}_2$  adduct thereof.<sup>4</sup> Addition of acetone, butan-2-one, and acetophenone (3 equiv.,  $-78$  to  $20^\circ\text{C}$ ) gave  $\eta^1$  ketone complexes  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)(\eta^1\text{-CH}_3(\text{R})\text{C}=\text{O})]^+\text{PF}_6^-$  (**3a—c**) (see



Scheme 1. Formation and hydride reduction of optically active ketone complexes.

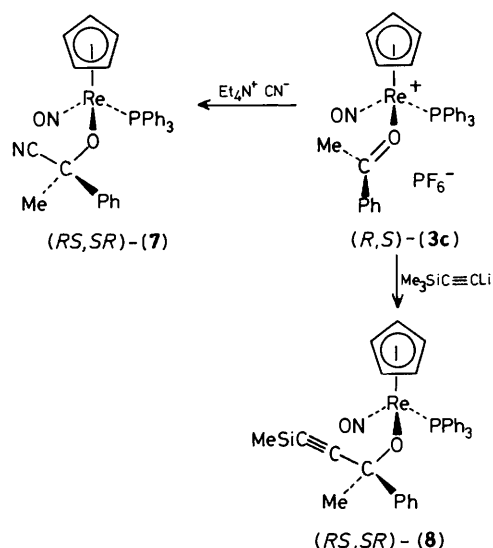
Scheme 1) in 85–88% yields after recrystallization.<sup>5†</sup> The  $\eta^1$  co-ordination mode was assigned on the basis of the CO  $^{13}\text{C}$  n.m.r. resonances ( $\delta$  214–236) and the i.r.  $\nu_{\text{C=O}}$  (1558–1623  $\text{cm}^{-1}$ , KBr).<sup>5</sup> Interestingly, we find that common types of aldehydes bind  $\eta^2$  ( $\pi$ ) to (2),<sup>6</sup> and we suggest that ketones bind  $\eta^1$  due to their greater steric bulk and poorer  $\pi$ -acidity.<sup>‡</sup>

Acetone complex (3a) exhibited only one  $^1\text{H}$  and  $^{13}\text{C}$  n.m.r. Me resonance at  $-92$  to  $-85^\circ\text{C}$ . The acetone ligand slowly exchanged with  $^2\text{H}_6$ -acetone (5–15 equiv.,  $\text{CD}_2\text{Cl}_2$ ,  $35^\circ\text{C}$ ), and application of the McKay equation<sup>8</sup> to rate data indicated a dissociative mechanism with  $k_{\text{diss}} 2.2 \pm 0.3 \times 10^{-4} \text{ s}^{-1}$  ( $t_{1/2}$  52 min), too slow to account for the equivalent resonances. One

† New compounds were characterized by microanalysis, i.r., and n.m.r. ( $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$ ).

Crystal data for (3c),  $\text{C}_{31}\text{H}_{28}\text{F}_6\text{NO}_2\text{P}_2\text{Re}$ , monoclinic,  $a = 14.348(2)$ ,  $b = 15.206(2)$ ,  $c = 14.770(2)$  Å,  $\beta = 108.44(1)^\circ$ ,  $U = 3057.0(6)$  Å<sup>3</sup>, space group  $P2_1/n$ ,  $Z = 4$ ,  $M = 808.9$ ,  $D_c = 1.76 \text{ g cm}^{-3}$ ,  $D_m = 1.81 \text{ g cm}^{-3}$ ,  $\mu(\text{Mo-K}\alpha) 43.9 \text{ cm}^{-1}$ ; data were collected on a Nicolet R3m/E four circle diffractometer, Mo-K $\alpha$  radiation,  $\lambda = 0.71069$  Å; 10615 independent reflections  $3^\circ < 2\theta < 64^\circ$ , of which 5273 unique reflection with  $I > 3\sigma(I)$  were used for structure refinement, corrected for Lorentz and polarization effects and absorption; solution by Patterson analysis, refinement by full-matrix least-squares to  $R = 0.0416$  and  $R_w = 0.0408$ . All crystallographic calculations were performed on a Data General Eclipse computer using the SHELXTL program package.<sup>13</sup> The largest peaks of the final  $F_o - F_c$  difference map were about  $0.8 \text{ e Å}^{-3}$  and were located  $1.58 \pm .15$  Å from P(2), indicating slight disorder of the  $\text{PF}_6^-$  anion. The large fluorine thermal parameters and the range of defined P–F distances (1.49–1.57 Å) also indicate some disorder. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

‡ Calculated energies of key orbitals in acetaldehyde and acetone (eV):  $\pi - 13.46, -13.00$ ;  $\eta - 11.31, -10.93$ ;  $\pi^* 4.39, 4.53$ .



Scheme 2. Reactions of (3c) with carbon nucleophiles.

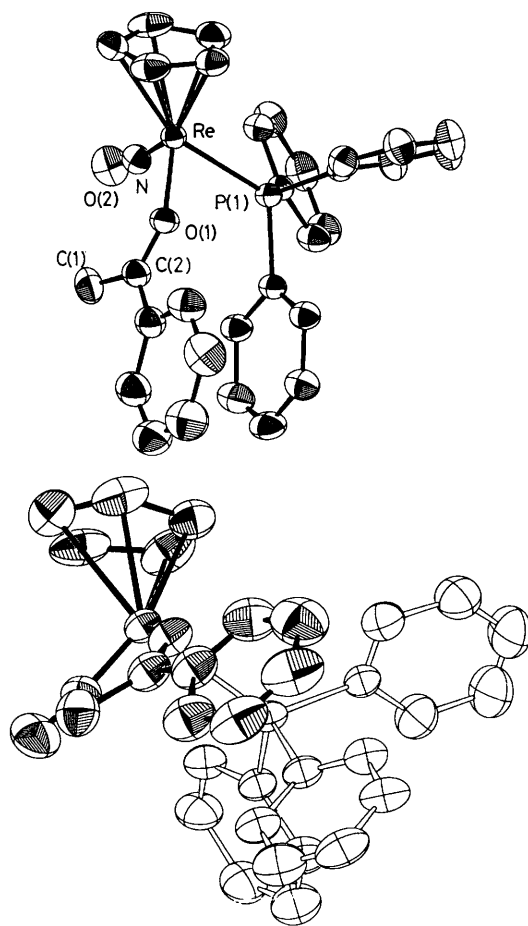


Figure 1. Structure of the cation of  $[(\eta^5\text{-C}_5\text{H}_5)\text{Re}(\text{NO})(\text{PPh}_3)(\eta^1\text{-MePhC=O})]^+\text{PF}_6^-$  (3c). Key bond lengths (Å) and angles ( $^\circ$ ): Re–O(1) 2.080(5), C(2)–O(1) 1.245(8), Re–N 1.758(5), Re–P(1) 2.397(2), N–O(2) 1.199(7); Re–O(1)–C(2) 138.3(4), N–Re–P(1) 91.3(2), N–Re–O(1) 103.0(2), P(1)–Re–O(1) 85.8(1), Re–N–O(2) 171.4(5); O(1)–C(2)–C(1) 117.5(5).

possibility is that the methyl groups equilibrate by an intramolecular  $\eta^1 = \eta^2 \rightleftharpoons \eta^1$  isomerization.

Subject to the caveat posed by the n.m.r. spectra of (3a), unsymmetrical ketone complexes (3b) and (3c) existed as single C=O geometric isomers ( $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{31}\text{P}$  n.m.r.  $-92$  to  $25^\circ\text{C}$ ), both as initially formed and after work-up. It was expected that rhenium would preferentially bind *syn* to the smaller methyl substituent. This was confirmed by an X-ray crystal structure of the acetophenone complex (3c) (Figure 1). The ON-Re-O-C torsion angle ( $\theta$ ) was found to be  $9^\circ$ . Thus, the methyl substituent is directed towards the smallest ligand (NO), with a slight cant towards the  $\eta^5\text{-C}_5\text{H}_5$  ligand. This orientation also allows overlap of the rhenium fragment HOMO I (Scheme 1)<sup>9</sup> with the C=O  $\pi^*$  lobes on oxygen. A possible phenyl-phenyl  $\pi$  interaction is evident in Figure 1, but an X-ray structure of acetone complex (3a) shows a similar  $\theta$  ( $21^\circ$ ).

When the above reactions were repeated with (+)-(S)-(1)<sup>10</sup> [ $\geq 98\%$  enantiomeric excess (e.e.)] ketone complexes (+)-(R)-(3a-c) formed with  $[\alpha]_{589}^{25}$  493, 516, and  $625^\circ$ .<sup>¶</sup>

The formyl complex ( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)(CHO) (4),<sup>3</sup> (CH<sub>2</sub>Cl<sub>2</sub>, 1.0 equiv.,  $-78$  to  $20^\circ\text{C}$ ) reduced (3a-c) to alkoxide complexes (RS,SR)-( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)-(OCH(R)Me) (5a-c), (67–69% after recrystallization).<sup>†</sup> A  $^1\text{H}$  n.m.r. assay showed crude (5b) and (5c) to be 96–98 and  $\geq 99\%$  diastereomeric excess, respectively.<sup>§</sup> Complex (4) did not react with acetone or butan-2-one (24 h, CDCl<sub>3</sub> or CD<sub>2</sub>Cl<sub>2</sub>,  $25^\circ\text{C}$ ), thus demonstrating that (2) activates ketones towards nucleophilic attack. Treatment of (5a-c) with CF<sub>3</sub>CO<sub>2</sub>H (1.0 equiv., CH<sub>2</sub>Cl<sub>2</sub>,  $0^\circ\text{C}$ ) gave alcohols HOCH-(R)Me (6a-c) in 89–91% yields (by  $^1\text{H}$  n.m.r.) and 53–56% yields following bulb-to-bulb distillation.

Complex (4) reduced optically active ketone complexes (+)-(R)-(3a-c) (Scheme 1) to optically active alkoxide complexes (+)-(RS)-(5a-c),  $[\alpha]_{589}^{23}$  223, 258, and  $272^\circ$ .<sup>¶</sup> When these were treated with CF<sub>3</sub>CO<sub>2</sub>H, the trifluoroacetate complex (+)-(R)-( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)(O<sub>2</sub>CCF<sub>3</sub>)<sup>11</sup> was isolated in 88–95% yields and  $\geq 99$ –98% enantiomeric excess (e.e.) This bounds the ketone and alkoxide complexes as  $\geq 98\%$  e.e., and establishes the expected<sup>6</sup> overall retention of configuration from methyl complex (+)-(S)-(1). Alcohols (+)-(S)-(6b) and (–)-(S)-(6c) were isolated as above and shown to be of 95 and  $>99\%$  e.e. by published  $^1\text{H}$  n.m.r. methods.<sup>12</sup> To our knowledge, this is the highest e.e. reported for the hydride reduction of butan-2-one.<sup>2k</sup> The absolute configurations are consistent with a transition state in which the nucleophile attacks the C=O face that is opposite the bulky PPh<sub>3</sub> ligand (Figure 1).

Similarly stereospecific reactions were found with carbon nucleophiles (Scheme 2). Reactions of (3c) with Et<sub>4</sub>N<sup>+</sup>CN<sup>–</sup> and Me<sub>3</sub>SiC≡C<sup>–</sup>Li (–78 to  $20^\circ\text{C}$ , 1.0 equiv., CH<sub>2</sub>Cl<sub>2</sub> or tetrahydrofuran) gave tertiary alkoxide complexes (RS,SR)-( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)(OC(CN)PhMe)[(RS,SR)-(7)] and (RS,SR)-( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)(OC(C≡CSiMe<sub>3</sub>)PhMe)-[(RS,SR)-(8)], in 86 and 68% yields, respectively, after recrystallization. No traces of the opposite diastereomers were found in the crude reaction mixtures, and configurations were assigned by analogy to the above hydride reductions.

In summary, we have developed an efficient procedure for the elaboration of methyl ketones to optically active second-

dary alcohols and tertiary alkoxides. This methodology is probably applicable to any ketone bearing two sterically differentiated substituents.

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§ Authentic samples of both diastereomers of (5b) and (5c) have been prepared from the triflate complex ( $\eta^5\text{-C}_5\text{H}_5$ )Re(NO)(PPh<sub>3</sub>)-(OSO<sub>2</sub>CF<sub>3</sub>)<sup>11</sup> and the corresponding alkoxides.

¶  $c$  0.0010 g ml<sup>-1</sup> (CHCl<sub>3</sub>, unless noted) for all  $[\alpha]$ .