protonated carbonyl compounds can relax to their ground states. In this context, the photoreactions of **3** and **4** described here can perhaps be better compared to those of 1,3-dienes rather than conjugated enones.[7]

Secondly, it is of interest to consider the mechanism of the thermal isomerization about the C–O bonds. Several possibilities can be eliminated from consideration. Thus, the minimal effect of introducing a methyl group at $C_3$ on the rate of isomerization about the C–O bond renders a direct rotation process unlikely as this involves a large change in the charge distribution in the system. The absence of any appreciable medium effect eliminates any base addition route, while the substantially different activation energies for isomerism about the C–O and $C_2$–$C_3$ bonds rules out the intervention of a common *O*-methyloxetium ion in these two rearrangements. Rather, it appears that the most likely process occurring is an inversion or "lateral shift" mechanism[8] as has also been found with the isoelectronic aldimines and ketimines.[9]

**Acknowledgment.** This work was supported by the National Research Council of Canada.

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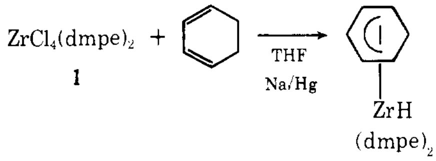
## Tertiary Phosphine Complexes of Low-Valent Zirconium and Their Properties

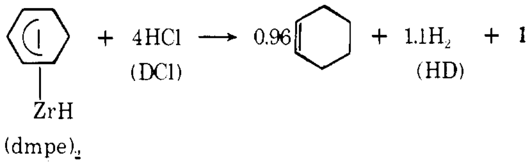
*Sir:*

The low-valent chemistry of the group 4 transition elements has been restricted to derivatives with carbocyclic ligands. Thus, Ti(II), Zr(II), and Ti(0) compounds containing ligated benzene,[1] cyclooctatetraene,[2] cyclopentadienyl,[3] and substituted cyclopentadienyl[4] ions and tropylium ion[5] are known. No stable derivatives of Zr(0) or Hf(0) have been reported. We report the preparation of Zr(0) and Zr(II) complexes of the chelating, bidentate phosphine 1,2-bis(dimethylphosphino)ethane and their activity as hydrogenation and hydrogen-transfer catalysts.

Treatment of $ZrCl_4$ with dmpe affords $ZrCl_4(dmpe)_2$[6] (**1**), analogous to dodecahedral $MCl_4(diars)_2$ (M = Ti,[7] Zr;[8] diars = 1,2-bis(dimethylarsino)benzene). Direct reduction of **1** (Cs in benzene, Na/Hg in THF) gives intractable products which are thermally unstable, reverting to **1** and a black deposit, presumed to be zirconium metal. However, reduction of **1** in the presence of excess 1,3-cyclohexadiene gives, after recrystallization from hexane, a red-brown crystalline solid, formulated as $Zr(H)(\eta^5\text{-}C_6H_7)(dmpe)_2$ (**2**) (eq 1) on the basis of spectroscopic and chemical data.[9] The ZrH unit in **2** was not located spectroscopically (IR, NMR);[10] its presence is inferred from the formation of 1 equiv of HD/1 equiv of Zr on treatment of **2** with DCl (eq 2).

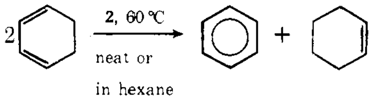


**2** (40%) (1)



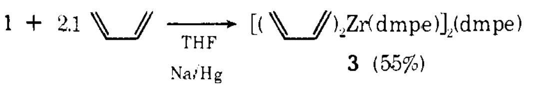
(2)

Although **2** is thermally stable at moderate temperatures, on photolysis, or at elevated temperatures (*T* > 130 °C), decomposition occurs with the deposition of black solids and the stoichiometric formation of 1 equiv each of hydrogen and benzene/1 equiv of Zr. At temperatures below its decomposition point, **2** is an efficient catalyst for the disproportionation of cyclohexadiene, as indicated in eq 3.[11,12] Less efficient rhodium- and iridium-based catalysts are known for this reaction.[13] Indeed, intermediates related to **2**, i.e., derived by insertion of the metal ion into a methylene C–H bond of cyclohexadiene, have been proposed in the disproportionation catalyzed by $(\eta\text{-}C_5Me_5)Rh(\eta^4\text{-}C_6H_8)$[13b] and $[Rh(norbornadiene)(\eta^4\text{-}C_6H_8)]BF_4$.[13c]

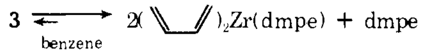


(3)

Presumably, **2** is formed by trapping of a $Zr^0P_4$ fragment, produced on reduction of **1**, with cyclohexadiene and insertion into the C–H bond of an allylic methylene group. Dienes lacking allylic C–H bonds should, therefore, lead to Zr(0) complexes. Accordingly, reduction of **1** in the presence of 2 equiv of butadiene proceeds as shown in eq 4. **3** may be isolated as purple crystals by recrystallization from hexane. The dmpe-bridged, dimeric formulation is suggested by analytic and $^1H$ NMR data;[14] the latter shows only coordinated butadiene and dmpe in the ratio 2.0/1.5. A parent ion is not present in the mass spectrum of **3**; however, an intense feature corresponding to $(C_4H_6)_2Zr(dmpe)^+$ is observed (calcd for $^{12}C_{14}{}^1H_{28}{}^{31}P_2{}^{90}Zr$, 348.0709; found, 348.0699), as well as features at lower mass corresponding to loss of dmpe and butadiene. No phosphorus couplings to the butadiene protons are observed in the $^1H$ NMR at 30 °C, suggesting rapid, reversible dissociation of dmpe as shown in eq 5. This proposal is consistent with molecular weight measurements (cryoscopic in benzene) (calculated for the three-particle system on the



(4)



(5)

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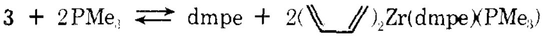
right-hand side of eq 5, 282; found, 280 ± 57). $^{31}P$ NMR observations are also consistent with the equilibrium proposed in eq 5.[15] The absence of metal hydrides is demonstrated by reaction of **3** with anhydrous HCl; 1- and 2-butenes are the only volatile products—no hydrogen is formed. Treatment of **3** with dry oxygen liberates butadiene. **3** reacts reversibly with $PMe_3$ at low temperatures. $^{31}P$ NMR spectra of **3** and excess $PMe_3$ (5 equiv/1 equiv of Zr) at −80 °C in toluene-$d_8$ show the presence of free dmpe (0.5 equiv/1 equiv of Zr) and an ABX pattern,[16] consistent with the formation of $(C_4H_6)_2$-Zr(dmpe)($PMe_3$) as shown in eq 6. That the interaction is reversible is shown by precipitation of the less soluble **3** on addition of hexane at −80 °C. Warming these solutions to room temperature results in irreversible decomposition.


(6)

In arene solvents, **3** reacts rapidly with hydrogen, forming butane and brown solutions.[17] These solutions catalyze the hydrogenation of olefins and alkynes under mild conditions. Thus, 1-octene, cyclohexene, and 2-pentyne are hydrogenated at moderate rates.[18] The trisubstituted olefin 2-methyl-2-butene is hydrogenated, at best, very slowly. $^{31}P$ NMR studies indicate that the toluene and benzene solutions formed on treatment of **3** with $H_2$ are complex.[19]

This work has two major ramifications: (1) formally di- and zerovalent zirconium complexes with electron-donating ligands are stable, particularly in the presence of π-accepting groups;[20] and (2) as shown by eq 3 and as suggested by the use of **3** as a hydrogenation catalyst, the Zr(IV) → Zr(II) and, possibly, Zr(II) → Zr(0) redox couples are not so endothermic that catalytic processes involving them are implausible.

**Acknowledgment** is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (CHE-75-19177) for support of this research.

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(10) The hydride resonance is, presumably, obscured by dmpe proton resonances: ZrH $^1H$ NMR resonances with chemical shifts near this and at lower fields are well documented: J. M. Manriquez, D. R. McAlister, R. D. Sanner, and J. E. Bercaw, *J. Am. Chem. Soc.*, **100,** 2716 (1978).

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(14) $^1H\{^{31}P\}$ NMR ($C_6D_6$) δ 5.36 (m, 4 H), 1.42 (m, 4 H), 1.24 (s, 6 H, dmpe), 0.76 (s, 18 H, dmpe methyl groups), −0.20 (m, 4 H). Anal. Calcd for $C_{17}H_{36}P_3Zr$: C, 48.09; H, 8.55; Zr, 21.48. Found: C, 47.62; H, 8.27; Zr, 21.91.

(15) At 30 °C in toluene-$d_8$, two resonances are observed (−13.4 and 48.5 ppm). The high-field signal is near the chemical shift of free dmpe (49.5 ppm); addition of free dmpe shifts this line to higher field, but does not result in the appearance of a separate resonance. When the solution is cooled to −40 °C, the high-field resonance broadens and moves to lower field (~4.8 ppm). At lower temperatures, both resonances become complex; we were unable to obtain a limiting spectrum. This data is consistent with the equilibrium in eq 5: at low temperatures the exchange rate slows and the anticipated positive $\Delta S_{rxn}$ shifts the equilibrium to the left-hand side. More complex equilibria involving butadiene exchange may also occur.

(16) $\delta_A$ 10.0, $\delta_B$ 8.3, $\delta_x$ −10.3 ppm ($|J_{AB}| = 3.3$, $|J_{AX}| = 9.8$, $|J_{BX}| = 9.8$ Hz.

(17) In aliphatic solvents, a zirconium mirror is deposited on the walls of the apparatus. Presumably, an arene–Zr interaction is necessary to stabilize the product.

(18) Rates are 4.3, 5.7, and 10.1 mol of substrate hydrogenated/h•mol of Zr at 27 °C and 760 mm$H_2$ for 1-octene, cyclohexene, and 2-pentyne, respectively. In the latter case *cis*-2-pentene is a detectable intermediate.

(19) $ZrH_3(dmpe)_2$ has been claimed by treatment of $Zr(benzyl)_4$/dmpe mixtures with high pressures of hydrogen: F. N. Tebbe, U.S. Patent 3 933 876; *Chem. Abstr.*, **84,** 165021e (1976).

(20) Indeed, a limiting zirconium(IV) metallocyclopentene resonance structure for **3** may be written, an expression of extensive π interaction. However, the similarity of the $^1H$[21a] and $^{13}C$[21b] NMR chemical shifts of the butadiene portion of **3** (39.1 and 105.6 ppm for methylene and methine carbons, respectively, relative to $Me_4Si$) to those for butadieneirontricarbonyl[21] suggest similar resonance forms. In particular, the values of $J_{^{13}CH}$ (146 and 156 Hz for **3,** 160 and 170 Hz for butadieneirontricarbonyl,[21b] 158 and 158 Hz for butadiene[21b]) indicate significant $sp^2$ character for the terminal methylene carbons in all cases, and, therefore, significant Zr(0) character in **3.**

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*Received July 25, 1978*

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## Total Synthesis of α-Amino-3-chloro-4,5-dihydro-5-isoxazoleacetic Acid (AT-125), an Antitumor Antibiotic

*Sir:*

Recently Martin et al.[1] described the isolation and structure of a novel antitumor antibiotic, (α*S*,5*S*)-α-amino-3-chloro-4,5-dihydro-5-isoxazoleacetic acid (**1,** AT-125). This material, isolated from *Streptomyces sviceus*, significantly increased the life span of tumor (L-1210 or P388) bearing mice[2] and, of even greater interest, it significantly increased the life span of immune deficient mice implanted with a solid human mammary tumor.[3] The biological activity of this material and its novel structure have already elicited a report by Baldwin et al. on an approach to its synthesis which produced nonstereospecifically a methylated analogue.[4] We report here a stereoselective, total synthesis of the racemic and optically pure isomers of AT-125.

In planning the synthesis we decided to pursue a path to AT-125 through derivatives of the known amino acid tricholomic acid (**2**).[5] In order to obtain relay material for such a route, AT-125 was hydrolyzed with 2 N NaOH to tricholomic acid identical by TLC and NMR with an authentic sample.[6] The hydrolyzed material was converted to its phthalimide methyl ester **3** (*N*-carboethoxyphthalimide[7] followed by diazomethane) which we found could be chlorinated in 65–70% yields with $(Me_2N)_3PCl_2$ in THF[8,9] to produce a material identical with the phthalimide methyl ester of AT-125. Encouraged by these results we turned our attention toward the synthesis of tricholomic acid or a suitably protected derivative thereof.

Since the synthesis of tricholomic acid previously described

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