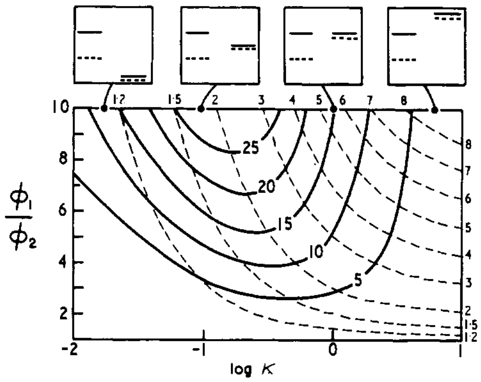

Figure 1. Contour diagram showing breakdown of the Swain–Schaad relation. The full lines are contours for different values of c (the percentage breakdown of the Swain–Schaad relation) as a function of ϕ_1/ϕ_2 (the ratio of fractionation factors for the two steps) and κ (which describes the extent to which one step is cleanly rate limiting). The dashed lines are contours for $\phi_1/\phi_{1,2}$ (which is approximately equal to the *observed* deuterium kinetic isotope effect) as a function of ϕ_1/ϕ_2 and κ. The square boxes show typical free energy levels (H, full lines; D, dashed lines) for the two transition states. Transition state 1 (on the left of the boxes) has a bound proton ($\phi_1 \simeq 1$) and there is a difference in the zero point energies; transition state 2 (on the right) has the proton in flight ($\phi_2 < 1$) and the H and D levels are much closer.

to 10. For the range $10 > \phi_1/\phi_2 > 1$, therefore, we construct Figure 1, which is a contour diagram for c calculated from eq 8. In addition, the broken lines show contours for $\phi_1/\phi_{1,2}$ (from eq 5). Since ϕ_1 does not involve a proton transfer, this ratio may be estimated from the experimental data:[8]

$$\frac{\phi_1}{\phi_{1,2}} = \frac{(k_{1,2})_H}{(k_{1,2})_D}\left(\frac{\phi_1}{\phi_S}\right) \simeq \frac{(k_{1,2})_H}{(k_{1,2})_D} \tag{9}$$

That is, $\phi_1/\phi_{1,2}$ is approximately equal to the *observed* deuterium isotope effect.

Thus Figure 1 displays how the breakdown of the Swain–Schaad relation and the *observed* deuterium isotope effect depend on the properties of the transition states. The insets illustrate typical free energies associated with the transition states and the isotope effects. On the right of the diagram ($\kappa = k_{-1}/k_2 \gg 1$) the proton transfer transition state is cleanly rate limiting. Under these conditions c tends to zero, and the ratio $\phi_1/\phi_{1,2}$ tends toward the ratio of the single factors ϕ_1/ϕ_2. On the left of the diagram ($\kappa \ll 1$) the first transition state is cleanly rate limiting. Again c tends to zero, but now $\phi_1/\phi_{1,2}$ tends to unity ($\phi_{1,2} \simeq \phi_1$). Along the bottom of the diagram c tends to zero because there is very litle difference between the fractionation in the two transition states. Over most of the diagram c is small, but significant values do occur where (as shown in the inset) isotopic substitution actually changes the rate limiting step.

From the experimental values of the deuterium and tritium isotope effects, we can calculate c and $\phi_1/\phi_{1,2}$ from eq 7 and 9. The intersection of the appropriate contours for c (Figure 1, full lines) and for $\phi_1/\phi_{1,2}$ (Figure 1, broken lines) therefore allows us *in principle* to determine the values of κ and ϕ_1/ϕ_2. (In obtaining $\phi_1/\phi_{1,2}$ from eq 9 we must assume a value of ϕ_1, but this assumption is not serious, since we have a good knowledge of fractionation factors for bound sites[9] and the location of the intersection of contours is not very sensitive to the position of the $\phi_1/\phi_{1,2}$ contour. This latter point is not true for broken contours close to unity and means that the approach will not work if the observed $\phi_1/\phi_{1,2}$ is less than about 1.2.)

But the real problem with the method lies in the small values of c. We cannot be certain that the Swain–Schaad relation itself holds[10] to better than 10% and, for instance, when $\kappa = 2$ (i.e., the proton transfer step is certainly not yet cleanly rate limiting) c is always less than 10%. We must therefore conclude that this method is *not* a general one for determining the relative free energies of two transition states which are both partially rate limiting.

In certain cases, however, interesting information *may* be found and having measured one isotope effect, we may use Figure 1 to see whether it is worthwhile to measure the other isotope effect. Two factors are relevant: the size of the observed isotope effect and the precision of the data. If the deuterium isotope effect is about 2 then one has the best chance of obtaining extra information from the breakdown of the Swain–Schaad relation. This is because the (broken) contour for $\phi_1/\phi_{1,2} = 2$ climbs up the "spur" where the breakdown is largest. It is interesting that many enzymes do have deuterium isotope effects between 2 and 3.[11]

The error on c, E_c, is given by $E_c = 1.6E_k$, where E_k is the percentage error on the kinetic data. If E_k is 10%, the error in c (±16) will cover the whole diagram and nothing can be deduced from measuring the second isotope effect. *The experimental error on the kinetic data must therefore be less than 3%.* Even so it is probable that the intersection will not be precisely located. Figure 1 can then be used to show the pairs of values of κ and ϕ_1/ϕ_2 that are consistent with the data.

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(6) If only one other transition state besides the proton transfer is rate limiting, then κ' describes the difference in free energy between that transition state and the jth transition state and $\bar{\phi}$ reduces to the fractionation factor for that transition state.

(7) R. P. Bell, "The Proton in Chemistry", Chapman and Hall, London, 1973, p 262.

(8) In many cases $\phi_1 \simeq \phi_S$, but for the general case if the relevant transition state occurs late in the reaction, it may be more appropriate to put $\bar{\phi} \simeq \phi_Z$ and thereby include the equilibrium isotope effect ϕ_Z/ϕ_A.

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(11) It is true, of course, that this approach can only be used when the isotope effect arises at least in part from a proton in flight. It is possible that observed deuterium isotope effects of 2 to 3 might arise from a combination of secondary isotope effects. In that case the whole approach is inoperative.

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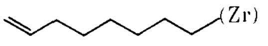
Transmetalation: Preparation of Organometallic Reagents for Organic Synthesis by Transfer of Organic Groups from One Metal to Another. Transmetalation from Zirconium to Aluminum

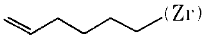
Sir:

Organozirconium(IV) complexes (**1**), produced by hydrozirconation of olefins or acetylenes using $Cp_2Zr(H)Cl$ (Cp =

η^5-C_5H_5), are of demonstrated value as readily obtainable intermediates in organic synthesis of use for preparing a variety of C–X bonds with a high degree of specificity;[1-5] however, with few exceptions[1,4] these compounds have not yet been shown to be effective reagents in a general sense for routine formation of C–C bonds. For example, some of these compounds (**1**) can undergo acylation by acyl halides (but very slowly) and in good yield only if steric congestion is minimal;[1] none has been observed to add to carbonyl groups of ketones or aldehydes nor to react with common alkylating agents such as alkyl halides, sulfates, or fluorosulfonates.[6] Accordingly, we are currently investigating the feasibility of transferring η^1-bound organic groups in **1** from Zr(IV) to another metallic element whose chemistry is already well established with regard to C–C bond formation processes. Through the sequence of hydrozirconation followed by transmetalation, it would be possible to take advantage of the ease and selectivity associated with hydrozirconation of olefins or acetylenes and the C–C bond forming propensity of this other metallic element in a "one-pot" reaction. We wish to report herein on our initial forays into this field which indicate that **1** can be the precursor of organoaluminum species. Furthermore, our results locate these organozirconium complexes in a transmetalation reactivity series for metal alkyls; this sequence can be used to predict transmetalation from **1** to other metals important in organic synthesis.

Mechanistic insight into the nature of electrophilic cleavage[7] of the C–Zr bond suggests that transmetalation might be accomplished by treatment of **1** with a Lewis acidic metal halide, and we have found that simply mixing **1** with $AlCl_3$ rapidly yields the corresponding organoaluminum dichloride (reaction 1). Transmetalation from Zr to Al is accomplished as shown in the following illustration. To a suspension of 775 mg of $AlCl_3$ (5.8 mmol, from which HCl has been removed by evacuation) in 5 ml of CH_2Cl_2 cooled to 0 °C, is added a solution of 1.37 g (4.0 mmol) of **1a**[8] in CH_2Cl_2. Here,[9] an instantaneous color change from bright yellow to orange accompanies the transmetalation reaction which can also be conveniently monitored by NMR[10] (in the case of alkylzirconium precursors the NMR spectrum of the resulting compound is analogous to those observed for known alkylaluminum dichlorides[10]). In this way we have found in each case studied that transmetalation occurs nearly quantitatively and in less than 10 min at 0 °. It is important to note that organoaluminum dichlorides in which a remote double bond is present can undergo intramolecular cyclization.[11] Thus NMR analysis shows that **1f** gives (7-octenyl)$AlCl_2$ but that **1g** affords (cyclopentylmethyl)$AlCl_2$;[12] oxygenation of these latter species followed by hydrolysis gives the corresponding alcohols.

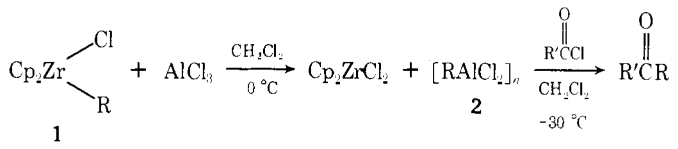

1f


1g

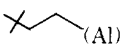
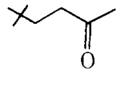
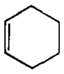
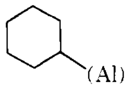
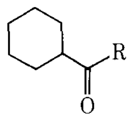
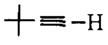
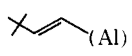
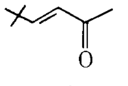
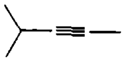
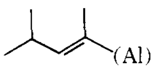
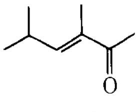
Organoaluminum dichlorides can act as mild alkylating agents;[13] for example, several of them have been reported[14] to be preferred precursors of ketones through acylation with acid chlorides. We find that this acylation proceeds well only for primary, saturated alkyl- and alkenylaluminum dichlorides (reaction 1).[14] To effect ketone synthesis, the reaction mixture containing the organoaluminum dichloride is cooled to −30 °C and a small excess of acyl chloride is added slowly. Only a slight color change occurs, but acylation of the organoaluminum compound is rapid and is usually complete in 15 min. This reaction can also be monitored conveniently by NMR; it gives $AlCl_3$-coordinated ketone from which free ketone can be obtained simply by hydrolysis and extraction. Results for this procedure and for those using other organozirconium complexes are shown in reaction 1.[14] It is especially noteworthy that since hydrozirconation of internal (or terminal) olefins gives the terminal zirconium alkyl exclusively,[1] hydrozirconation-transmetalation effectively provides a simple method to convert a mixture of isomeric olefins to a single ketonic product. For example, treatment of 2.91 g (7.85 mmol) of **1b**, prepared from a mixture of linear octenes, first with 1.23 g (9.25 mmol) of $AlCl_3$, and then with 0.73 g (9.25 mmol) of acetyl chloride as described above, gave, on aqueous workup, uniquely, 2-decanone (98% by VPC).

Attempts to directly acylate vinylic complexes such as **1d** or **1e** failed; however, by transmetalation to the corresponding (alkenyl) aluminum dichlorides (which themselves cannot be

Reaction I



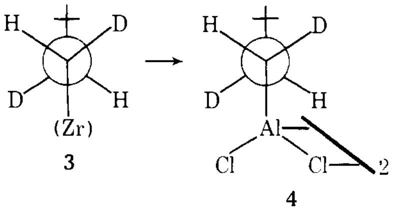
$$\underset{\mathbf{1}}{Cp_2Zr(Cl)R} + AlCl_3 \xrightarrow[0\ °C]{CH_2Cl_2} Cp_2ZrCl_2 + \underset{\mathbf{2}}{[RAlCl_2]_n} \xrightarrow[CH_2Cl_2,\ -30\ °C]{R'CCl(=O)} R'C(=O)R$$

	olefin/ acetylene →	RAlCl₂ →	product	Yield (%) (Based on RZr)[a] Zr only	Yield (%) (Based on RZr)[a] Zr → Al
a				60 (29 h)	98 (30 min)
b	*n*-octenes[c]		2-decanone	80 (>2 days)[1]	98 (60 min)
c				8 (48 h) R = CH_3	64[b] (45 min) R = Ph
d				—	97 (45 min)
e				—	98 (45 min)

[a] Yield determined by VPC. [b] Isolated yield. [c] 1-Octene, *cis*-2-octene, *trans*-2-octene, *cis*-4-octene, *trans*-4-octene (1:0.5:0.5:1:1).

prepared directly from acetylenes) followed by acylation, a high yield of α,β-unsaturated ketones is obtained. Through this sequential use of two reactive organometallic species, ketone is formed stereospecifically by overall cis addition of acyl-H to an alkyne; regioselectivity in the ketone prepared is the same as that in its Zr precursor.[2,12]

The mechanism of transmetalation from Zr to Al has been briefly investigated. In a competitive procedure involving equimolar amounts of alkyl complex **1a,** vinylic complex **1d,** and a deficiency of $AlCl_3$, we have found that transmetalation occurs faster for the vinylic substituent than for the alkyl one. In addition, results involving stereospecifically labeled dideuterio complex **3**[7] indicate that transmetalation from Zr to Al proceeds predominantly with retention of configuration at carbon[15,16] (as it does with vinylic substrates). These results suggest a mechanism for transmetalation which is indeed analogous to the one reported[7] for electrophilic cleavage of alkylzirconium complexes; the transition state (or intermediate) for this reaction involves a transition metal–main group metal complex containing a bridging alkyl (or vinylic) group. Such bridging alkyl or vinylic groups are well known in main group chemistry[13] and have been postulated to occur in intermediates[17,18] or in isolable species[19,20] in transition metal chemistry as well. Shuttling of a σ-bonded substituent from one metal to another via such a bridged intermediate could be expected to proceed more rapidly for the bridging vinylic compared to the bridging alkyl case; it is well known in organoaluminum chemistry, for example, that vinylic bridges between two Al atoms are more stable than are alkyl ones.[21,22]



3

4

$(Zr) = (\eta^5 - C_5H_5)_2Zr(Cl)—$

The sequence shown in reaction 1 suggests that acylation of **1** by acid chlorides could be *catalyzed* by $AlCl_3$. Transmetalation succeeds, however, only if $AlCl_3$ is not complexed with a Lewis base. Unfortunately, the ketonic product of acylation is a strong enough Lewis base to coordinate an equivalent amount of $AlCl_3$; this slows further transmetalation. Using 15% $AlCl_3$ (based on **1a,** 0 °C, 10 h), a 40% yield of ketone is produced; heating this reaction mixture (70 °C, 0.5 h) results in a higher yield (83%). Transmetalation does not proceed readily in Lewis basic solvents (such as ethers) for similar reasons.

It is known that trialkylaluminum,[23] alkylmagnesium halide,[23] or alkyllithium[23] compounds will alkylate Cp_2ZrCl_2, and preliminary results show that **1** will alkylate $ZnCl_2$[24] or $HgCl_2$.[6] On the basis of these observations, the following reactivity sequence of alkylating abilities of organometallic alkyls toward metal halides is derived: RLi, RMgX, or $R_3Al > Cp_2Zr(Cl)R > RAlCl_2$; $Cp_2Zr(Cl)R > RZnCl$ or RHgCl. Transmetalation results presented herein suggest that, as a general rule, **1** should be able to alkylate metal salts in which the metal (with its complement of ligands) is more electronegative than is the Cp_2ZrCl-moiety (for example, Cu(I) halides) and that alkenyl complexes should be more reactive in this regard than alkyl ones. It is important to note here that, notwithstanding the utility of organoaluminum species in their own right, our results presented herein are significant in that they demonstrate that an easily prepared transition metal complex can serve as the convenient precursor of other reactive organometallic species. These studies, therefore, represent a point of departure for the rational development of new types of sequential organometallic reagent *systems,* be they stoichiometric or catalytic ones, in which the ability to transfer organic ligands readily from one metal to another provides a pathway to accomplish a synthetic transformation which is impossible (or is at best tedious) for any one given type of organometallic species alone.

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(8) All reactions were performed under an atmosphere of dry argon. All solvents were dried by distillation from an appropriate drying agent under inert atmosphere. Organozirconium complexes could be purified by crystallization from hexane.

(9) For **1c** a color change from orange to yellow was observed. NMR analysis and not color is, of course, a more reliable method for monitoring the transmetalation reaction.

(10) For **1a,** for example, in CH_2Cl_2, δ_{Cp} 6.25, δ_{Zr-CH_2} 1.08, δ_{Al-CH_2} 0.25; for example, for $(CH_3CH_2AlCl_2)_2$, in CH_2Cl_2, δ_{Al-CH_2} 0.58. The *Zr* product formed by transmetalation depends on the amount of $AlCl_3$ present relative to **1.** A stoichiometric amount of $AlCl_3$ reacts with **1** to give free Cp_2ZrCl_2. If an excess of $AlCl_3$ is used (<100% excess), free Cp_2ZrCl_2 is not produced; the product obtained is a rapidly interconverting mixture of free Cp_2ZrCl_2 and $AlCl_3$-complexed Cp_2ZrCl_2. For varying amounts of excess $AlCl_3$, only a single sharp Cp resonance is observed (35 °C); the position of this resonance, with regard to free Cp_2ZrCl_2 (δ 6.52) and the deep orange complex (δ 7.10) formed from equimolar amounts of $AlCl_3$ and Cp_2ZrCl_2, depends upon the amount of excess $AlCl_3$ present. This $Cp_2ZrCl_2 \cdot AlCl_3$ complex is weak; it is readily destroyed (as evidenced by NMR) by weak Lewis bases such as ethers, acyl chlorides, or ketones.

(11) This reaction is closely analogous to the known cyclization of, for example, dialkyl(5-hexenyl)aluminum complexes; Houben-Weyl, "Methoden der Organischen Chemie", Vol. 13/4, Georg Thieme Verlag, Stuttgart, 1970.

(12) $Cp_2Zr(Cl)$(3-pentenyl), upon treatment with $AlCl_3$ followed by acetyl chloride, affords 3-cyclopropyl-3-methylpropan-2-one (79%).

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(14) This acylation reaction has not, to the best of our knowledge, been reported except for primary, saturated alkylaluminum dichlorides. We find that secondary alkylaluminum dichlorides react with aliphatic acid chlorides with extensive deprotonation. Such deprotonation by alkylaluminum dichlorides has been observed in other contexts (H. Reinheckel, K. Haage, and D. Jahnke, *Organomet. Chem. Rev., Sect. A*, **4,** 47 (1969)).

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(16) For *erythro*-**3,** $^3J_{HH} = 9$ Hz. We are unable, because of broadened lines in aluminum compound **4,** to determine, *quantitatively*, the percent retention of configuration at carbon.

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(22) Transmetalation of vinylic groups can proceed with a different stoichiometry, too, than that observed for alkyl groups: using a Zr:Al ratio of 3:1, $Al(alkenyl)_3$ is formed. For alkyl complexes, for varying ratios of Zr:Al, transmetalation has a stoichiometry of 1:1. Since highest yields of ketones are realized from $RAlCl_2$,[13] it is important, with vinylic complexes, to use a 1:1 ratio of Zr:Al.

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