terium and the differences due to the nonbonding interactions of H vs. D with $CF_3$ and Ph. Deuterium has a slightly smaller steric requirement than hydrogen which is manifest only under conditions of severe steric overcrowding.[8] We believe that this effect would be barely perceptible in the present case. The observed difference in stereoselectivity then must be a direct consequence of the hydrogen vs. deuterium transfer.

Three factors, not necessarily unrelated, associated with the direct transfer of hydrogen vs. deuterium may account for the observed stereochemical differences: (1) bond distance; the average C–H bond distance is about 0.008 Å longer than the C–D bond distance;[9] (2) the difference in rate of transfer per se; (3) tunneling. Evidence bearing on the second and third points can be obtained by a temperature study and this is in progress.[10] It may be that the stereoselectivity is extremely susceptible to the proximity of approach of the carbon centers in the C--H--C vs. C--D--C transition states. Hydrogen (hydride), with a de Broglie wavelength greater than that of deuterium, may be able to transfer from reagent to substrate from a greater distance than can deuterium (deuteride). The logical presumption is that the closer the proximity of the two carbon centers, the greater the steric compression in the transition state. This should lead to greater stereoselectivity for deuterium transfer, as observed.

The overall low kinetic isotope effect is consistent with a nonlinear hydride transfer. However, a larger kinetic isotope effect ($k^H/k^D = 1.92 \pm 0.04$) was found for the formation of $R_H$-**8** and $S_D$-**8** (the least favored products arising from *pro*-$R_H$-**10** and *pro*-$S_D$-**10**) compared to that ($k^H/k^D = 1.58 \pm 0.04$) for the favored products ($S_H$-**8** and $R_D$-**8** arising from *pro*-$S_H$-**10** and *pro*-$R_D$-**10**). These observations are qualitatively consistent with proton tunneling arguments.

(*R*)-(−)-Mandelic acid, **1**, was converted via the methyl ester, 70.5 g, mp 54–55 °C, $[\alpha]^{20}_D$ −174.2 (*c* 4.05, $CHCl_3$), >99% enantiomerically pure, into (*R*)-(−)-methyl *O*-mesylmandelate, **2**, mp 115–116 °C $[\alpha]^{20}_D$ −113.6 (*c* 6.67 $CHCl_3$), 77.6 g. Treatment of **2** (63 g in 800 mL of THF) with LAD (10.8 g in 600 mL of ether) for 4 h at room temperature gave crude **3** (73% crude yield of a 9–91 mixture of 1- and 2-phenylethanols). Fractionation through a 28-plate glass-helices column gave **3**, $\alpha^{20}_D$ −1.10 (neat, $l = 1$). Analysis by GLC showed 99.8% 2-phenylethanol and by NMR indicated 99 ± 1% 2-phenylethanol-*1,1,2-d*$_3$. This alcohol, 4.5 mg in $CDCl_3$ in the presence of 43 mg of the chiral shift reagent $Eu(dcm)_3$,[1a] showed signals for the benzylic protons of the *S* and *R* enantiomers at 1492 and 1520 Hz in the ratio of 86.8 to 13.1 (73.7 ± 1.5% ee). The enantiomer NMR chemical shift differences with the chiral $Eu(hfbc)_3$[11] reagent were observable but the signals were not completely separated.

*S*-(−)-**3**, 13 g, was converted into *S*-(+)-**4** ($PPh_3$, 7.7 g, NBS, 19.8 g, benzene, 65 mL, 0 °C) to give 13.7 g, 63.5%, of redistilled **4**, $\alpha^{20}_D$ +0.855° (neat $l = 1$), from which the Grignard reagent **5** was prepared (sublimed Mg, $Et_2O$). An aliquot was oxidized ($O_2$, −78 °C) to regenerate **3** which was purified by preparative GLC and shown[1] to be an 86.7:13.3 mixture of *S* and *R* enantiomers (73.4 ± 2% ee, i.e., no racemization in $\mathbf{3} \rightarrow \mathbf{4} \rightarrow \mathbf{5} \rightarrow \mathbf{3}$). An aliquot of the same Grignard solution was treated at 0 °C with **6**, to give a 66% yield of **8** (purified by GLC 20 ft × ⅜ in. Carbowax, 215 °C). The MTPA derivatives **9** were analyzed by $^{19}F$ NMR (Figure 1). Identity of signals and quantitative analysis were determined by samples of known configuration and composition.

## References and Notes

(1) (a) The enantiomeric purity of **3** was determined by use of Whitesides' chiral shift reagent, $Eu(dcm)_3$. M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974). We wish to thank Dr. Whitesides for the sample of $Eu(dcm)_3$ used in these studies. (*b*) The absolute configuration of **3** is assigned assuming an $S_N2$ displacement of mesylate by deuteride. C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Am. Chem. Soc.*, **88**, 3347 (1966); P. K. Wong, K. S. Y. Lou, and J. K. Stille, *ibid.*, **96**, 5956 (1974); R. O. Hutchins, D. Kandasamy, C. A. Maryanoff, D. Masilamani, and B. E. Maryanoff, *J. Org. Chem.*, **42**, 82 (1977); L. M. Stephenson and D. L. Mattern, *ibid.*, **41**, 3614 (1976).

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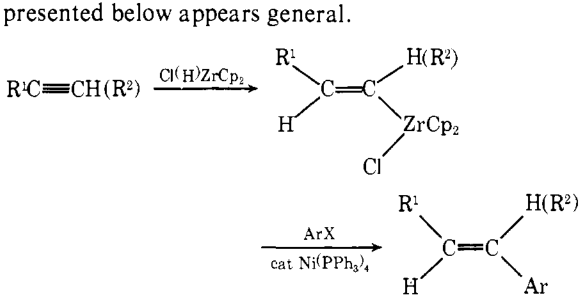
## Selective Carbon–Carbon Bond Formation via Transition Metal Catalysis. 4.[1] A Novel Approach to Cross-Coupling Exemplified by the Nickel-Catalyzed Reaction of Alkenylzirconium Derivatives with Aryl Halides

*Sir:*

We wish to report a novel approach to the selective cross-coupling which involves the reaction of organozirconium derivatives with organic halides under the influence of nickel complexes, such as $Ni(PPh_3)_4$. Although the scope of the present discussion is restricted to the alkenyl–aryl coupling represented by eq 1, the applicability of the methodology presented below appears general.



(1)

Within the past few years, hydrozirconation[2a] has emerged as a unique hydrometalation with some attractive features, such as the facile formation of terminally Zr-substituted derivatives from internal alkenes[2b] and high regioselectivity observed with alkynes[2c] and dienes.[2d] Moreover, our preliminary study indicates that the reaction can tolerate certain

**Table I.** The Ni-Catalyzed Reaction of Alkenylzirconium Derivatives with Aryl Halides[a]

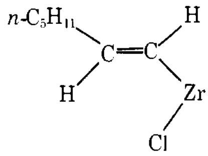
| Entry | Alkenyl group (R) of ($E$)-R(Cl)ZrCp$_2$ | ArX | Yield[b] of ArR, % |
|---|---|---|---|
| 1 | 1-Heptenyl | Iodobenzene | 96[c] |
| 2 | 1-Heptenyl | 1-Bromonaphthalene | 70[d] |
| 3 | $\beta$-Ethoxyethenyl | Iodobenzene | 99 (76)[e] |
| 4 | 4-Tetrahydropyranyloxy-1-butenyl | Iodobenzene | 84 |
| 5 | 1-Hexenyl | $p$-Chloroiodobenzene | 95 |
| 6 | 1-Hexenyl | $p$-Iodoanisole | 80[f] |
| 7 | 1-Hexenyl | $p$-Bromobenzonitrile | 92 |
| 8 | 1-Hexenyl | Methyl $p$-bromobenzoate | 92[g] |
| 9 | 2-Octenyl | Iodobenzene | 35[h] |

[a] Unless otherwise mentioned, the reaction was carried out over 12–24 h at room temperature in the presence of 10 mole % of Ni(PPh$_3$)$_4$ prepared in situ by the reaction of Ni(acac)$_2$ with diisobutylaluminum hydride and triphenylphosphine. [b] By GLC based on ArX. [c] The amount of biphenyl was 4%. [d] The yields observed in both the catalytic and the stoichiometric reactions are essentially identical. [e] By isolation. [f] A minor amount (<ca. 20%) of an unidentified by-product was present. [g] 6 h at room temperature then 13 h at 50 °C. [h] 6 h at room temperature then 48 h at 50 °C. The amount of biphenyl was 50% based on iodobenzene.

functional groups, in particular oxy-functional groups, that are incompatible with hydroalumination.[3] Unfortunately, their application to the carbon–carbon bond formation has been limited to only a few reactions, such as carbonylation[2] and the reaction with acyl halides.[2b,4] In light of our recent finding that the combined use of organometallics of low nucleophilicity, such as those containing Al[5] and Zn,[1] and Ni or Pd complexes provides highly chemo-, regio-, and/or stereoselective cross-coupling procedures, it became of interest to find out if organozirconium compounds could be utilized in a similar manner.

We have indeed found that ($E$)-alkenylzirconium compounds derived from terminal alkynes and Cl(H)ZrCp$_2$ react smoothly with aryl bromides and iodides in the presence of 10 mol % of Ni(PPh$_3$)$_4$ to provide the corresponding ($E$)-alkenylarenes in high yields. The experimental results are summarized in Table I.

No reaction is observed in the absence of the Ni catalyst. When the ($E$)-1-heptenylzirconium derivative (**1**) was reacted with 1 equiv of 1-naphthylnickel derivative (**2**) ($E$)-1-(1′-heptenyl)naphthalene was formed in 70% yield at a rate which was at least comparable to that for the corresponding catalytic reaction with 10 mol % of Ni(PPh$_3$)$_4$. These results indicate that the catalytic cycle suggested for other related reactions[6] which consists of the oxidative addition of organic halides to Ni(0) or Pd(0) complexes, transmetalation, and reductive elimination may also operate in the reaction reported here.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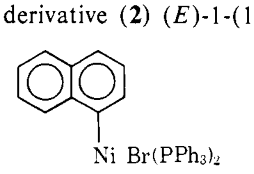
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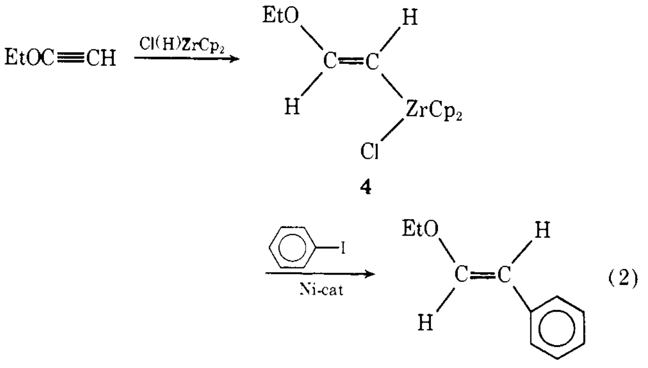
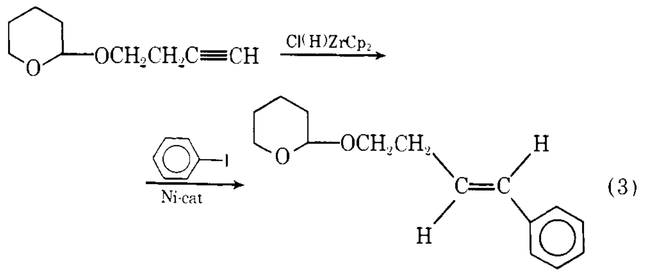
The stereochemistry of the product in each case is >98% $E$ by GLC, $^1$H and $^{13}$C NMR, and IR. In no case has there been any indication of regiochemical scrambling. In our hands the yields of the ($E$)-alkenylzirconium derivatives obtained by the reaction of Cl(H)ZrCp$_2$ with alkynes in a 1:1 molar ratio have been typically in the range 75–90% by $^1$H NMR. Thus, it has been necessary to use modest excesses of Cl(H)ZrCp$_2$ and alkynes for the complete conversion of aryl halides into the desired cross-coupled products. In all cases reported here the alkenylzirconium derivatives, formed in situ from 1.5 equiv[7] each of Cl(H)ZrCp$_2$ and an alkyne, are reacted with 1.0 equiv of aryl halides, upon which the yields are based. Under these conditions the reaction of the $\beta$-monosubstituted alkenylzirconium derivatives with aryl halides proceeds, in most cases, remarkably cleanly, producing the desired cross-coupled products in excellent yields as shown in Table I. Neither biaryls nor conjugated dienes are formed in any noticeable quantities (<2%) in all but one of the reactions of the $\beta$-monosubstituted alkenylzirconium derivatives. Only in the reaction of the ($E$)-heptenylzirconium reagent with iodobenzene has the formation of a minor but detectable amount (4%) of biphenyl been observed. It may also be worth noting that the transfer of the cyclopentadienyl group is not competitive.[8] Significantly, the presence of ether groups in alkynes which, in most cases, is incompatible with hydroalumination[3] can be tolerated in hydrozirconation. Thus, ethoxyacetylene was cleanly converted into >98% pure ($E$)-$\beta$-ethoxystyrene (**3**) in 99% yield via the ($E$)-2-ethoxyethenylzirconium derivative (**4**) (eq 2). Similarly, the tetrahydropyranyl derivative of ($E$)-4-phenyl-3-buten-1-ol was obtained in 84% yield as shown in eq 3.



**3** (99%)



**5** (84%)

The procedure reported here appears capable of tolerating various other functional groups as well. Thus, no difficulty has been encountered in the use of aryl iodides and bromides containing chloro, methoxy, cyano, and methoxycarbonyl groups[9] (entries 5–8).

We have been less fortunate in utilizing the alkenylzirconium derivatives formed from internal alkynes. For example, the reaction of the ($E$)-2-octenylzirconium derivative derived from 2-octyne and Cl(H)ZrCp$_2$ with iodobenzene was sufficiently slower than the corresponding reaction of the $\beta$-monosubstituted alkenylzirconium compounds so that the known homodimerization of aryl halides under the influence of Ni complexes[10] becomes competitive. The yields of 2-phenyl-2-octene and biphenyl were 35 and 50%, respectively.[11]

The following procedure for the preparation of ($E$)-$\beta$-ethoxystyrene is representative. To 3.87 g (15 mmol) of Cl(H)ZrCp$_2$[2b] suspended in 30 mL of dry benzene was added 1.05 g (15 mmol) of ethoxyacetylene. After stirring the reaction mixture for 2 h at room temperature, benzene and other volatile compounds were removed in vacuo,[12] and THF (10 mL) was added to the residue. In a separate flask $Ni(PPh_3)_4$ was prepared from anhydrous $Ni(acac)_2$ (1 mmol), diisobutylaluminum hydride (1 mmol), triphenylphosphine (4 mmol), and 15 mL of THF. To the mixture containing the $\beta$-ethoxyethenylzirconium derivative prepared above were added sequentially the supernatant solution of $Ni(PPh_3)_4$ and 2.04 g (10 mmol) of iodobenzene. After stirring the reaction mixture for 12 h at room temperature, GLC examination of a quenched aliquot indicated the formation of (*E*)-$\beta$-ethoxystyrene in 99% yield. After extraction with diethyl ether, washing with water, and drying, distillation provided 1.12 g (76%) of essentially pure (*E*)-$\beta$-ethoxystyrene: bp 70–72 °C (1.6 mm); $^1H$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 1.27 (t, $J$ = 7 Hz, 3 H), 3.80 (q, $J$ = 7 Hz, 2 H), 5.83 (d, $J$ = 13 Hz, 1 H), 6.97 (d, $J$ = 13 Hz, 1 H), and 7.20 (broad s, 5 H) ppm; $^{13}C$ NMR ($CDCl_3$, $Me_4Si$) $\delta$ 14.80, 65.40, 106.03, 125.11, 125.56, 128.58, 136.68, and 147.96 ppm; IR (neat) 1630 (s), 1180 (s), 930 (m), 920 (m), 750 (s), 690 (s) $cm^{-1}$.

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(6) References 1 and 5 and references cited therein.

(7) The use of 1 equiv each of these reagents has resulted in somewhat diminished and variable yields.

(8) A minor amount (<ca. 20%) of a by-product having a slightly shorter GLC retention time (SE-30) than that of (*E*)-*p*-(1-hexenyl)anisole was detected in the reaction mixture obtained by the reaction of *p*-iodoanisole and the (*E*)-1-hexenylzirconium reagent. Although this by-product, which is neither bianisyl nor 5,7-dodecadiene, may well be a cyclopentadiene derivative, its isolation and identification have not yet been successful. Interestingly, it was readily and completely destroyed during the workup. Consequently, it did not interfere with the isolation of the desired product.

(9) Other functional groups have not so far been tested. However, it has been reported that organozirconium derivatives obtained by the hydrozirconation with $Cl(H)ZrCp_2$ are generally inert to ketones, aldehydes, and alkyl halides, sulfates, and sulfonates.[4]

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(11) Our preliminary results indicate that the difficulty observed with internal alkynes may be overcome by adding a suitable second catalyst such as $ZnCl_2$. This possibility is being investigated in detail in our laboratory.

(12) In most cases the remaining alkynes were removed in this step. However, we have also found that the presence of alkynes does not interfere with the cross-coupling reaction.

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## Dimeric Copper(II) Complexes Derived from 2,9-Bis(methoxymethyl)-2,9-dimethyl-4,7-dioxydecanedioic Acid. Formation of a Macrocyclic Chelate

*Sir:*

The complexation of multivalent cations by polyoxygenated ligands, including polyhydroxy derivatives,[1] multidentate macrocyclic compounds,[2,3] and carboxylates has been the subject of extensive studies, in particular because of the biological interest of such systems, and possible technological applications. However, relatively little work appears to have been done on ether-carboxylic acids.[4-9] Since the ether function(s) in such ligands would usually be expected to form rather labile bonds to metal cations, the resulting complexes, even if sufficiently stable to be isolated, might dissociate readily to yield coordinatively unsaturated species having catalytic activity.

Scheme I. Synthesis of 2,9-Bis(methoxymethyl)-2,9-dimethyl-4,7-dioxydecanedioic Acid.

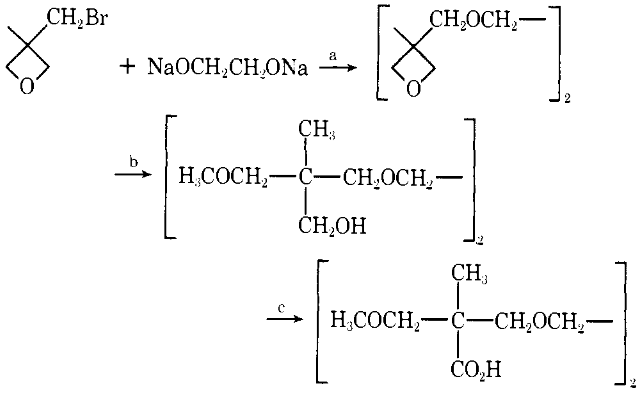

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Table I

| | 3ai | 3bii | 3cii |
|---|---|---|---|
| *a* | 11.506 (4) Å | 11.230 (4) Å | 14.593 (1) Å |
| *b* | 7.149 (2) | 9.940 (4) | 10.747 (1) |
| *c* | 13.085 (3) | 10.954 (4) | 11.894 (2) |
| $\alpha$ | 101.01 (1)° | 112.16 (3)° | 75.025 (6)° |
| $\beta$ | 114.06 (2)° | 107.26 (3)° | 115.011 (6)° |
| $\gamma$ | 90.85 (2)° | 81.22 (3)° | 99.567 (6)° |
| Formula | $C_{28}H_{52}Cu_2O_{18}$ | $C_{38}H_{58}Cu_2N_2O_{16}$ | $C_{64}H_{78}Cu_2O_{16}P_2$ |
| Z | 1 | 1 | 1 |
| No. of obsd ($>3\sigma$) reflections | 2681 | 2368 | 3038 |
| Current *R* factor | 0.085 | 0.104 | 0.094 |

[a] Δ, *tert*-amyl alcohol solvent. [b] Reflux in methanol–$H_2SO_4$ catalyst. [c] $HNO_3$. The product was purified as the dimethyl ester, bp 123 °C (0.01 mmHg). Subsequent reactions were performed on the acid obtained as a viscous gum on hydrolysis of the ester.

In the course of a study of complexes of ether-carboxylic acids, we have prepared 2,9-bis(methoxymethyl)-2,9-dimethyl-4,7-dioxydecanedioic acid (**1**; $H_2Y$) as a mixture of diastereoisomers by the route outlined in Scheme I. Heating **1** with an equimolar quantity of copper(II) acetate monohydrate in refluxing benzene, followed by distillation to azeotrope water and acetic acid gave a greenish blue-black solution. Column chromatography (silica gel) of this solution, and fractional crystallization (aqueous acetone) of the material eluted with benzene and with ether–benzene (1:3) gave two products, both of which have empirical formula $CuY{\cdot}H_2O$.[10] The major product (**3ai**) crystallized as thin green parallelograms (mp ~183 °C),[11] while the minor product (**3aii**) gave irregular blue prisms (mp ~170 °C).[11] Both products separately dissolved in refluxing benzene to give blue-black solutions from which the water could be removed by azeotropic distillation. Addition of acetonitrile followed by cyclohexane to these solutions resulted in the slow deposition of the appropriate $CuY{\cdot}H_2O$ on standing in air for 1 or 2 days. The crystals of the major isomer **3ai** thus produced were better