Dimerizing or Cyclizing C−C Bond Formation via C−H Bond Activation by Prior Zirconation[1]

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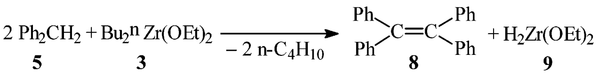
Summary: Benzylic hydrocarbons of the types Ar−CH_3 and Ar_2CH_2 undergo zirconation at their benzylic C−H bonds by $Bu^n{}_2Zr(OEt)_2$ at room temperature in Lewis basic solvents and catalyzed by lithium ethoxide. Upon heating, such benzylic organozirconium derivatives can undergo C−C bond formation, either intermolecularly or intramolecularly, with the elimination of zirconium(IV) hydrides of the type $H_2Zr(OEt)_2$. Such oxidative dimerizations or cyclizations are exemplified by the conversion of toluene into trans-stilbene or the formation of 9,10-dihydrophenanthrene from 2,2′-dimethylbibenzyl.

In furthering our current studies of the chemical reactivity of early-transition-metal alkyls,[2−4] we sought to extend the metalating action of group 4 metal alkyls from substrates such as cyclopentadienes and terminal alkynes[4] to weaker carbon acids such as diphenylmethane and even toluene. To this end we have employed the thermally more stable zirconium derivatives of the type $R_2Zr(OR')_2$, which can be readily generated, for example, by the treatment of zirconium(IV) ethoxide (**1**) in THF at −78 °C with 2 equiv of *n*-butyllithium (**2**) and warming the di-*n*-butylzirconium diethoxide (**3**) formed to 25 °C (eq 1). When 2 equiv of diphenylmethane (**5**) was added to the THF solution of **3** and the mixture then stirred at room temperature for 8 h, the solution turned deep orange. Treatment of the reaction mixture with D_2O and the usual workup led to the isolation of diphenylmethane consisting essentially of 100% of α-monodeuterated **6**, with only traces of **7** and residual **5** (eq 2).[5a] These results establish that reagent **3** is able to zirconate the methylene group of **5** and generate principally the zirconated precursor $Ph_2CH{-}ZrBu(OEt)_2$, with subsidiary amounts of $Ph_2C[ZrBu(OEt)_2]_2$.[5b]

$$\underset{\mathbf{1}}{Zr(OEt)_4} + \underset{\mathbf{2}}{2Bu^nLi} \xrightarrow{-78\ ^\circ C} \underset{\mathbf{3}}{Bu_2{}^nZr(OEt)_2} + \underset{\mathbf{4}}{2LiOEt} \qquad (1)$$

$$\underset{\mathbf{5}}{Ph_2CH_2} \xrightarrow[2.\ D_2O]{1.\ 0.5\ equiv.\ \mathbf{3}} \underset{\mathbf{6}}{Ph_2CHD} + \underset{\mathbf{7}}{Ph_2CD_2} \qquad (2)$$

As useful as this observation may prove to be,[6] the more exciting and most unexpected finding is the result obtained when such a 2:1 mixture of diphenylmethane (**5**) and di-*n*-butylzirconium diethoxide (**3**) in THF was allowed to react further at reflux for 8 h. Upon hydrolysis, hydrogen gas evolution was observed and up to 80% of tetraphenylethylene (**8**) was found to have resulted. The dihydrogen evolution indicated that a zirconium hydride, such as $H_2Zr(OEt)_2$ (**9**), was the other primary product formed in refluxing THF (eq 3).[7]



(3)

Thus, a most unusual and efficient C−C bond coupling between two molecules of diphenylmethane (**5**) had occurred with the transfer of hydrogen to zirconium.

Such a low-temperature coupling of sp^3-hybridized carbon centers in hydrocarbon **5** via dehydrogenation

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(1) Organic Chemistry of Subvalent Transition Metal Complexes. 30. Part 29: Eisch, J. J.; Otieno, P. O. *Eur. J. Org. Chem.*, in press.

(2) Eisch, J. J.; Shi, X.; Owuor, F. *Organometallics* **1998**, *17*, 5219.

(3) Eisch, J. J.; Owuor, F. A.; Shi, X. *Organometallics* **1999**, *18*, 1583.

(4) Eisch, J. J.; Owuor, F. A.; Otieno, P. O. *Organometallics* **2001**, *20*, 4132.

(5) (a) Dibutylzirconium diethoxide (**3**) was prepared in THF by the slow addition of 2 equiv of *n*-butyllithium in hexane to a solution of zirconium(IV) ethoxide in THF previously cooled to −78 °C by a solid CO_2−acetone bath. To 1 equiv of **3** at −78 °C was then added 2 equiv of a hydrocarbon substrate, such as **5**, the temperature was brought to room temperature for 2−4 h, and finally the reaction solution was heated to reflux for 8 h. Identification of the reaction products and of the products of reactions worked up with D_2O, for their deuterium-labeled patterns, was achieved by a combination of ^1H, ^2H, and ^{13}C NMR and IR spectroscopy. In the case of the reaction in eq 2 the product **6** showed an integrated ratio of aromatic H to methylene H of 10.0:1.00 in its ^1H NMR spectrum. The byproduct, lithium ethoxide (**4**), is considered essential in catalyzing the zirconation of benzylic hydrocarbons. This conclusion is based upon the failure of $Bu^n{}_2ZrCl_2$, generated in THF from the reaction of $ZrCl_4$ with 2 equiv of **2**, to zirconate **5**. Apparently, the byproduct LiCl is an ineffectual adjuvant for zirconation. (b) The subsequent refluxing of such a reaction mixture leads to the coupling depicted in eq 3, but workup of such reactions by D_2O revealed that the residual diphenylmethane now consisted of about 75% of **7** and 25% of **6**. This finding indicates that further zirconation of **5** occurred upon heating.

(6) The zirconating action of **3** has been found to be effective for vinylic as well as benzylic C−H bonds. For example, anisole in a hexane solution of **3** underwent efficient and selective zirconation at 25 °C at a C_2 position: workup of the reaction product with D_2O and combined ^1H and ^2H NMR spectroscopy verified the presence of 2-deuterioanisole. The scope of such zirconations, as catalyzed by donor solvents (TMEDA, DME, HMPTA) and salts of secondary amines, is under active study.

(7) Upon the initiation of reflux for reaction 3, the large volume of gas evolved was passed into $CDCl_3$ and was shown by ^1H NMR to be principally butane. The gas evolved upon the hydrolysis of reactions 3, 5, and 6 was shown to be almost only dihydrogen by various means: mass spectrometry, noncondensability in a −78 °C cold trap, and no reaction on passing through a solution of Br_2 in CCl_4 (distinction from 1-butene). The amount of hydrogen gas formed could not be correlated with that expected from **9**, because at reflux **9** slowly cleaves THF, which was apparent from the varying amounts of 1-butanol obtained by subsequent hydrolysis.

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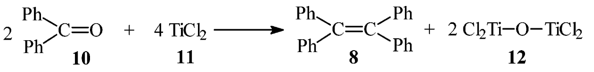
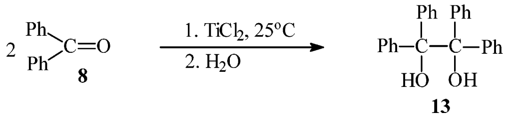
and the formation of its olefin dimer (**8**) is conceptually the chemical opposite of the *reductive dimerization* of aromatic ketones such as **10** to their olefin dimer (**8**), as has been achieved with subvalent titanium salts, $TiCl_n$, where $n < 3$. Although the exact oxidation state of the titanium reagent involved in such *reductive dimerization* of ketones was not defined in the three original and independent reports of this reaction,[8−10] a subsequent study employing analytically pure $TiCl_2$ (**11**) (as its bis-THF complex) has established the stoichiometry shown in eq 4. The carbonyl oxygen is incorporated into the byproduct tetrachlorodititanoxane(III) (**12**).[11]



$$2\,Ph_2C{=}O + 4\,TiCl_2 \longrightarrow Ph_2C{=}CPh_2 + 2\,Cl_2Ti{-}O{-}TiCl_2 \qquad (4)$$

In light of the differences between the *reductive dimerization* of eq 4 and the reaction exemplified by eq 3, this new-found coupling of carbon centers can fittingly be termed an *oxidative dimerization*. Moreover, there is a further parallel in such contrasting carbon−carbon coupling processes: just as the reductive coupling of ketones can stop at the single C−C bond or pinacol stage (**13**) (eq 5),[11] so shorter heating periods with certain carbon carbon acids such as toluene (**14**) can yield >70% of the oxidatively coupled dimer, bibenzyl (**15**) (eq 6). Prolongation of reflux leads principally to the olefin *trans*-stilbene (**16**) (eq 7).



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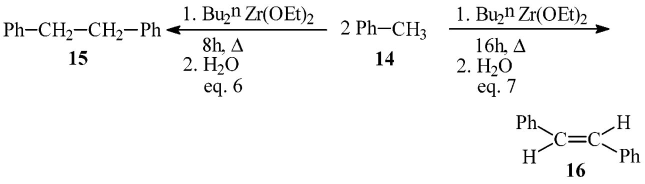
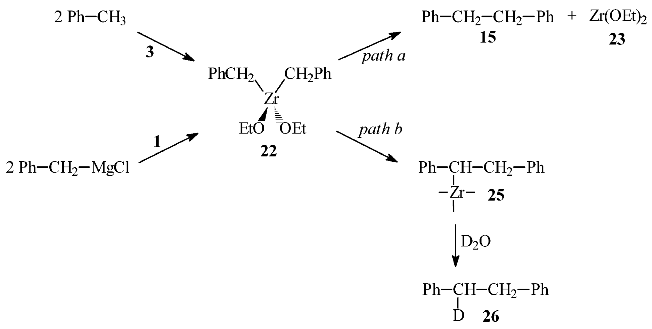
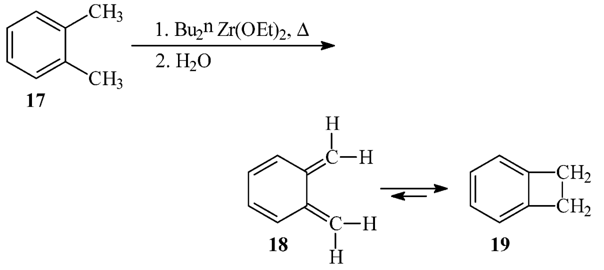


In preliminary studies of the scope of such benzylic carbon−carbon coupling processes, it has been established that the reaction can occur not only intermolecularly, as with diphenylmethane (**5**; eq 3) and toluene (**14**; eq 6), but also intramolecularly, as exemplified by *o*-xylene (**17**) leading to *o*-xylylene (**18**) and eventually to benzocyclobutene (**19**, eq 8)[12] and by 2,2′-dimethylbiphenyl (**20**) yielding 9,10-dihydrophenanthrene (**21**, eq 9). The yields of cyclized products, now in the range of 50−60%, have not yet been optimized by the use of bases such as piperidine and TMEDA or of higher boiling ethers such as DME and 2-ethoxyethyl ether, which have been shown to increase the yields of the C−C and C═C coupling products formed in eqs 3, 6, and 7.[6]

Scheme 1





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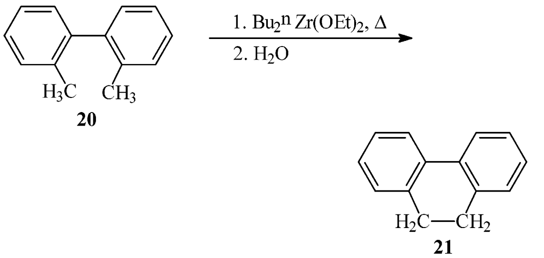

(9)

Parallel attempts to cyclize *p*-xylene to [2.2]paracyclophane, even with high dilution, have thus far produced only a 65% yield of (*E*)-4,4′-dimethylstilbene. The failure to obtain any [2.2]paracyclophane may be due to the excessive ring strain involved in such a closure.[13]

The mechanism of this remarkable *oxidative dimerization* remains to be elucidated, but from the known chemistry of early-transition-metal alkyls, a straightforward explanation might be considered to be based on reductive elimination. As applied to the formation of bibenzyl (**15**) from toluene (**14**) in eq 4, one could propose a bis-zirconation of **14** by **3** to produce $Bn_2Zr(OEt)_2$ (**22**). A reductive elimination of **15** from **22** should produce zirconium(II) ethoxide (**23**), which, like other known Zr(II) salts, should be black (*path a*, Scheme 1). To test the congruence of this proposal under the actual reaction conditions, the supposed intermediate **22** was prepared by another route, the reaction of $Zr(OEt)_4$ (**1**)

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(8) Mukaiyama, T.; Sato, T.; Hanna, *J. Chem. Lett.* **1973**, 1041.

(9) Tyrlik, S.; Wolochowicz, I. *Bull. Soc. Chim. Fr.* **1973**, 2147.

(10) McMurry, J. E.; Fleming, M. P. *J. Am. Chem. Soc.* **1974**, *96*, 4708.

(11) Eisch, J. J.; Shi, X.; Lasota,. *Z. Naturforsch.* **1995**, *50b*, 342.

(12) The organic product initially obtained upon hydrolysis consisted of a 2:1 mixture of benzocyclobutene (^1H NMR ($CDCl_3$) (δ) 3.10 (s, 4H), 7.01 (m, 4H); ^{13}C NMR (δ) 29.7 (4C), 122.5 (2C), 126.8 (2C), 145.8 (2C) (CH_2 confirmed by PENDANT experiment)) and *o*-xylylene (^1H NMR ($CDCl_3$) (δ) 5.6 (2H), 6.0 (2H), 6.3 (2H)). After 24 h the absorptions for *o*-xylylene had disappeared. Peaks for dibenzo-1,5-cyclooctadiene were *not* observed (^1H NMR ($CDCl_3$) (δ) 2.92 (s, 8H), 6.9 (s, 8H); ^{13}C NMR (δ) 35.2, 126.1, 129.7, 140.6). NMR data: Commita, P. B.; Bergman, M. R.; Moore, C. B.; Bergman, R. G. *J. Phys. Chem.* **1981**, *85*, 3266. Trahanovsky, W. S.; Chou, C. H.; Fischer, D. R.; Gerstein, B. C. *J. Am. Chem. Soc.* **1988**, *110*, 6579.

(13) An indication of such strain in [2.2]paracyclophane is that a suspension of this hydrocarbon in THF undergoes slow cleavage when stirred with **3** at room temperature for 24 h. Hydrolysis of the resulting orange-brown mixture gave about 15% of 4,4′-dimethylbibenzyl.

with 2 equiv of benzylmagnesium chloride in THF at 25 °C. Heating **22** in refluxing THF and hydrolytic workup did lead to the isolation of 80% of bibenzyl (**15**). However, the refluxing THF solution did not turn black but remained a light tan, a color inconsistent with the presence of **23**. Furthermore, when the refluxed solution of **22** was then cooled and hydrolyzed with D_2O, the isolated bibenzyl was now found to be principally α-deuteriobibenzyl (**26**).[14] This finding requires that its precursor formed by the thermolysis of **22** must have been an α-zirconiobibenzyl (**25**) (*path b*, Scheme 1). With this intriguing and tantalizing determination, we can conclude that a simple reductive elimination is *not* involved in *oxidative dimerization* and that an more exotic explanation must be sought.

In summary, by the metalating action of dialkylzirconium dialkoxides on benzylic C−H bonds, novel and useful C−C and C═C bonds can be formed in either an intermolecular or intramolecular manner with partial hydrogen transfer to the original zirconium(IV) center. Such *oxidative dimerizations* and cyclizations should prove most useful in organic synthesis.

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[14] An isolated sample of **26** was dissolved in $CDCl_3$, and its ^1H NMR spectrum was recorded. Integration of the aromatic proton signals at 7.1−7.3 ppm and the benzylic proton signals at 2.9 ppm gave an observed ratio of 10.0:3.13, compared with an expected ratio of 10.0:3.0 for pure **26**. Thus, the sample of **26** had an isotopic purity of at least 87% of α-deuteriation. Furthermore, an ^2H NMR signal was observed at 2.8 ppm.