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A REGIOSPECIFIC METHOD FOR THE HYDROCYANATION OF OLEFINS

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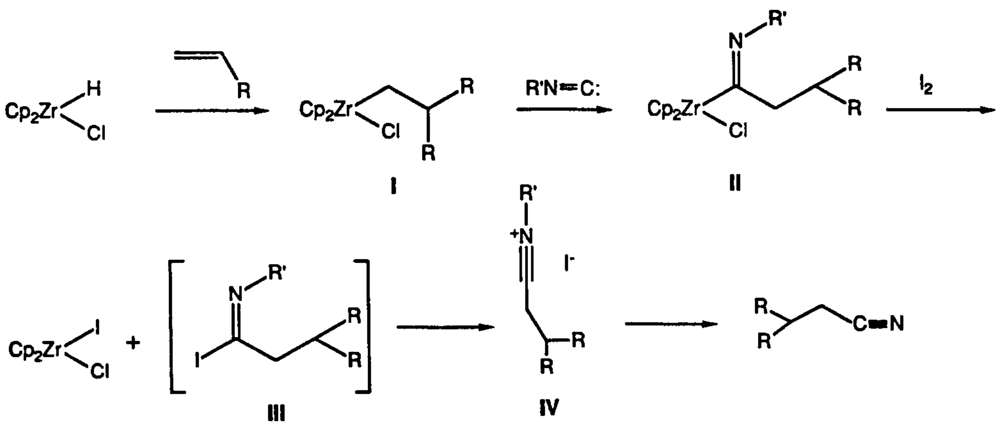
Summary: A convenient method for the anti-Markovnikov hydrocyanation of olefins utilizing organozirconium chemistry has been developed. This method has been shown to tolerate a wide range of functionality in the substrate olefin.

Recent years have seen a tremendous increase in the development and use of organometallic reagents for organic synthesis[1]. One transformation for which no reliable laboratory scale method exists is the hydrocyanation of olefins[2]. Hydrocyanation has been practiced commercially for many years, most notably by Dupont for the preparation of adiponitrile, utilizing a nickel-catalyzed hydrocyanation of butadiene. The Dupont work has been discussed in detail in a recent review[3]. Several other catalysts containing a variety of different transition metals also have been investigated[4]. Even with the many years of work on this problem, no general, high yield laboratory scale method for the anti-Markovnikov hydrocyanation of olefins exists.

The known methods for the hydrocyanation of olefins, although impressively efficient in particular cases, lack a generality and functional group compatability which would render them useful to synthetic organic chemists. Moreover methodology which employs hydrogen cyanide is not likely to see widespread use among synthetic chemists. Herein we report a method for olefin hydrocyanation which derives its regiospecificity from organozirconium precursors which are produced by the hydrozirconation of olefins [5,6].

The hydrozirconation of olefins is one of the most reliable organometallic methods used in organic synthesis[5,6]. The alkyl zirconocene chlorides I (Scheme I) so produced are known to be converted to

Scheme 1



aminoacyls II on treatment with an isocyanide[7]. We reasoned that treating II with one equivalent of iodine[5] should produce imidoyl iodide III[8]. III should spontaneously be converted, by loss of iodide, to the nitrilium ion IV[9]. We further reasoned that, if R' was chosen to be easily removable, either by nucleophilic attack of iodide or as a carbonium ion, that the R'-I and the desired nitrile would be formed. In practice, hydrozirconation of neohexene followed by successive additions of *t*-butyl isocyanide[10] (1.2 eq) and iodine (5 eq), leads to the formation of 4,4-dimethylvaleronitrile and *t*-butyl iodide. Subsequent work demonstrated that trimethylsilyl isocyanide (which is in equilibrium in solution with trimethylsilylcyanide)[11] converts I to II (R'= TMS), which is converted to the nitrile with concommitant production of trimethylsilyliodide upon treatment with iodine..

As is shown in Table 1, the reaction proceeds cleanly for a variety of different olefins. Importantly, the reaction tolerates a wide range of functional groups. Of particular interest are entries 6-8 in which, for the first time, a hydrozirconation reaction has been observed to proceed with less than complete regiospecificity for the terminal position. In fact, 2-vinyl furan gives only the secondary product, 2-furylpropionitrile[12]. We presume that the oxygen of the furan acts as an additional ligand and induces the zirconium to add (or migrate) to the internal carbon. In entries 6-8 the carbon β to the Cp_2ZrCl moiety in the internal regioisomer is sp^2-hybridized and the substituent is flat. This probably minimizes unfavorable steric interactions which normally cause the zirconium moiety to move to the terminal position.

As is evidenced by entries 10 and 11, this methodology is also suited for the hydrocyanation of alkynes[13].

In summary, we have developed a reliable, regiospecific hydrocyanation of olefins which, in general, gives products of anti-Markovnikov addition. This method, which uses isonitriles instead of hydrogen cyanide, can also be used to hydrocyanate alkynes.

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2. The standard sequence for this transformation is hydroboration-oxidation, mesylation, cyanide displacement, cf. Roush, W. R. *Tetrahedron Lett.* **1985**, *26*, 4327.

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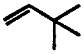
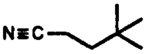
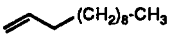
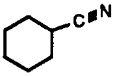
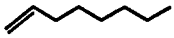
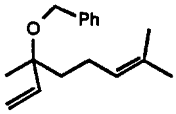
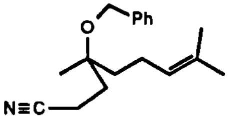
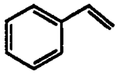
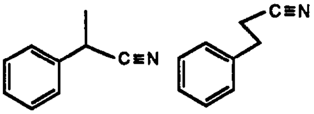
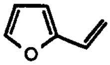
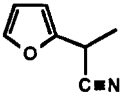
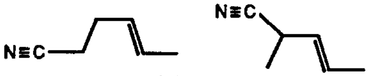
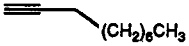
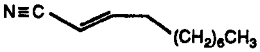
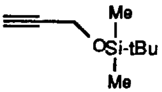
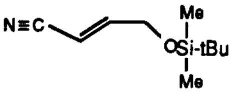
Table 1

	Olefin or acetylene	Nitrile	RNC	Yield	Z/E
(1)			t-Bu	84%	
			TMS	55	
(2)			t-Bu	73	
(3)			TMS	45	
(4)			TMS	65	
(5)			TMS	59[a]	
(6)		 1:2.6	t-Bu	97	
(7)			t-Bu	45[b]	
(8)		 6.5:1	t-Bu	50[b]	
(9)			t-Bu	70	
(10)			t-Bu	90	3.5-8.5:1
			TMS	55	28:1
(11)			t-Bu	62	6.5:1

a. Little or no benzyl group cleavage was observed.

b. Yields determined by quantitative gas chromatography. All other yields are of isolated material.

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10. For an example of conjugate hydrocyanation using t-butyl isocyanide cf. Ito, Y.; Kato, H.; Imai, H.; Saegusa, T. *J. Am. Chem. Soc.* **1982**, *104*, 6449.

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12. Less than 5% of the regioisomeric nitrile was formed.

13. For examples of methods for the hydrocyanation of alkynes, Cf. Jackson, W.R.; Permutter, P. *Chem. in Brit.* **1986**, *22*, 338 and references therein.

14. Typical experimental procedures are given below.

Using t-butyl isocyanide: To a suspension of $Cp_2Zr(H)Cl$ (0.97g, 3.76 mmol) in dry benzene (40 mL) under Ar was added via syringe 1-dodecene (0.84 mL, 3.76 mmol) and the reaction mixture was allowed to stir at RT for 14h yielding a clear red-brown solution. To this solution was added *t*-butyl isocyanide (0.49 mL, 4.14 mmol) and the mixture was allowed to stir for an additional 1 h. To the solution cooled to 5°C was added a solution of iodine (2.86g, 11.28 mmol) in benzene (40 mL) and the reaction mixture was stirred an additional 15 min at 5°C. It was then rinsed into a separatory funnel with methylene chloride, diluted with ether, washed with saturated sodium bisulfite, water, brine, dried ($MgSO_4$), filtered and concentrated to a volume of 5 mL. This was loaded onto a 60 mL fritted Buchner funnel containing a 1:2 mixture of celite and flash silica gel and was eluted with ether/pentane (100 mL) to yield a gold solution which was concentrated *in vacuo*. The resulting golden oil was purified by flash chromatography on silica gel using ether/pentane as solvent to yield 1-cyanododecene (0.541g, 73%), pure by ^1H and ^{13}C NMR, IR and capillary GC.

Using trimethylsilylcyanide: To a suspension of $Cp_2Zr(H)Cl$ (0.61g, 2.36 mmol) in dry benzene (40 mL) under Ar was added 6-benzyloxy-2,6-dimethyl-2,7-octadiene (0.62 mL, 575 mg, 2.36 mmol) and the reaction mixture was allowed to stir at RT for 13 h. To the resulting clear yellow solution was added TMSCN (0.35 mL, 2.60 mmol) and the reaction mixture was heated at 55°C for 24 h. The reaction mixture was cooled to 5°C and a solution of iodine (0.89 g, 3.54 mmol) in benzene (30 mL) was added via cannula and the reaction mixture was allowed to stir for 20 min at 5°C. The mixture was rinsed into a separatory funnel with methylene chloride, diluted with ether and the resulting organic layer was washed successively with saturated $NaHCO_3$, water, saturated brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The resulting golden oil was purified by flash chromatography on silica gel using ether/pentane as solvent to give the desired nitrile (0.378 g, 59%) as determined by ^1H and ^{13}C NMR, IR and high resolution mass spectroscopy.

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