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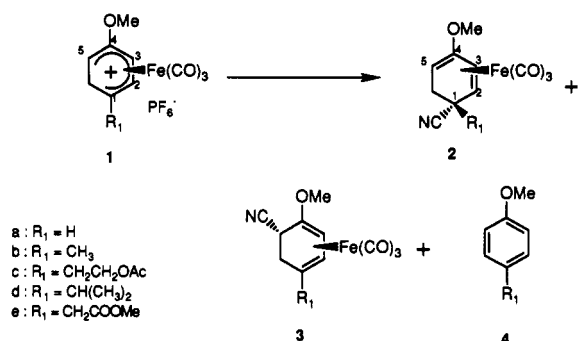
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Summary: By using a large excess of trimethylsilyl cyanide and a short reaction time, trimethyl isocyanide in sufficient amount is generated and added regioselectively at the C-1 terminus of the tricarbonyl cyclohexadienylum species 1, irrespective of steric hindrance and its α -proton acidity. Formation of the aromatic and trienyl complex is suppressed. Upon saponification or hydrolysis, addition product 2c is converted into the synthetically useful spirolactone 6. For the reaction mechanism, formation of phosphorus pentafluoride, trimethylsilyl fluoride, and free cyanide during the reaction between hexafluorophosphate anion and trimethylsilyl cyanide is suggested.

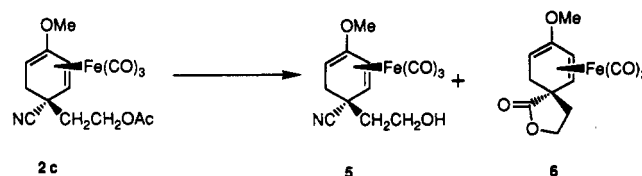
Tricarbonylcyclohexadienylumiron complexes have received increasing attention for their ability to react with a wide variety of nucleophiles which have led to their application as key intermediates in organic synthesis.¹ Unfortunately, substitution at the C-1 terminus of complexes 1 severely limits the range of suitable nucleophiles,



since in many cases competing deprotonation results in the formation of trienyl complexes,² together with decreasing regioselectivity.³ The metal cyanide anion has been used successfully only for unsubstituted C-1 dienylum complexes.⁴ Recently, it has been reported⁵ that trimethylsilyl cyanide is a reagent far superior to the metal cyanide. The scope for using trimethylsilyl cyanide has not been tested beyond the methyl substitution at C-1 of the dienylum complex 1.

We were interested in overcoming the limitation by steric effect of reaction of complexes of type 1 with cyanide anion. We now describe the results of studies designed to explore the synthetic potential and mechanistic implication of this reaction. The ability to effect cyanide addition regioselectively at the C-1 terminus of complex 1c will lead to the

facile construction of the spirolactone 6 upon hydrolysis, a valuable synthetic intermediate.



Results and Discussion

The cyclohexadienylum complex 1c was prepared according to the method of Pearson.⁶ The reaction of 1c with potassium cyanide was found to give poor yields of 2c, together with a small amount of regioisomer 3c and an aromatic product. Increasing the amount of potassium cyanide and using a longer reaction time have an adverse effect on the reaction, giving decreased regioselectivity with formation of equal amounts of 2c and 3c, together with the aromatic compound. Consequently, we turned our attention to the use of trimethylsilyl cyanide. Reaction of 1c under the reported conditions⁵ was found to yield a useful quantity of 2c with good regiocontrol. Unexpectedly, an initial attempt to improve the yield of 3c by a prolonged reaction time was unsuccessful; instead, aromatized products began to appear. In fact, the reaction of 1c with trimethylsilyl cyanide takes place only at elevated temperatures, due to the deactivating influence of the methoxy group. We thus conclude that the critical factors in this reaction are the higher concentration of trimethylsilyl cyanide and a shorter reaction time. Our results in Table I show that the best yield of 2c could be achieved with 10 equiv of trimethylsilyl cyanide in refluxing acetonitrile for 4 h. A further increase in the concentration of trimethylsilyl cyanide has no marked influence on the reaction. We next needed to examine the product distribution for the reaction of 1c with low concentrations of trimethylsilyl cyanide. When 1c was reacted with 1.5 equiv of trimethylsilyl cyanide, after the mixture was refluxed for 3 h it produced selectively 2c, albeit in poor yield. Refluxing for 7 h improved the yield of 2c slightly, and prolonged refluxing for 20 h decreased the yield of 2c but favored the formation of aromatic products. These results indicate that the synthetic value of this reaction could be improved if the appropriate excess of the required reagent to effect conversion in a specified period of time could be determined.

Stephenson⁷ has reported that, for all but the most unreactive dienylum complexes, the preequilibrium step between trimethylsilyl cyanide and isocyanide is rate-

(1) Pearson, A. J. *Pure Appl. Chem.* 1983, 55, 1767.

(2) Pearson, A. J. *J. Chem. Soc., Perkin Trans. 1* 1978, 495.

(3) Pearson, A. J.; Ham, P.; Ong, C. W.; Perrior, T. R.; Rees, D. C. *J. Chem. Soc., Perkin Trans. 1* 1982, 1525.

(4) Pearson, A. J.; Chardler, M. *J. Organomet. Chem.* 1980, 202, 175.

(5) Alexander, R. P.; Stephenson, G. R. *J. Organomet. Chem.* 1986, 299, C-1.

(6) Pearson, A. J.; Chandler, M. *J. Chem. Soc., Perkin Trans. 1* 1980, 2238.

(7) Alexander, R. P.; James, T. D.; Stephenson, G. R. *J. Chem. Soc., Dalton Trans.* 1987, 2013.

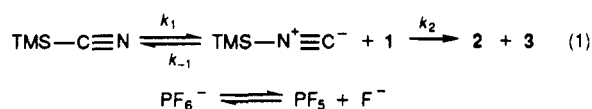
Table I. Reaction Conditions for (TMS)CN and KCN Addition to Cyclohexadienylum Salt 1

compd	amt of cyanide, equiv	solvent	reacn conditions	product yield ^a
1c	1.5 ((TMS)CN)	CH ₃ CN	reflux, 3 h	2c (20), 3c (0), 4 (0)
1c	1.5 ((TMS)CN)	CH ₃ CN	reflux, 7 h	2c (29), 3c (0), 4 (0)
1c	1.5 ((TMS)CN)	CH ₃ CN	reflux, 20 h	2c (10), 3c (0), 4 (40)
1c	5.0 ((TMS)CN)	CH ₃ CN	reflux, 4 h	2c (35), 3c (0), 4 (0)
1c	5.0 ((TMS)CN)	CH ₃ CN	room temp, 16 h	2c (45), 3c (0), 4, (10)
1c	10.0 ((TMS)CN)	CH ₃ CN	reflux, 4 h	2c (71), 3c (8), 4 (0)
1c	20.0 ((TMS)CN)	CH ₃ CN	reflux, 4 h	2c (73), 3c (8), 4 (0)
1c	(TMS)CN/Bu ₄ N ⁺ F ⁻	CH ₃ CN	0 °C, 1 h	2c (18), 3c (8), 4 (10)
1c	(TMS)CN/Bu ₄ N ⁺ F ⁻	CH ₃ CN	0 °C, 16 h	2c (25), 3c (30), 4 (40)
1d	10.0 ((TMS)CN)	CH ₃ CN	reflux, 4 h	2d (62), 3d (0), 4 (0)
1e	10.0 ((TMS)CN)	CH ₃ CN	reflux, 4 h	2e (40), 3e (10), 4 ^b (25)
1c	2 (KCN)	acetone/H ₂ O	0 °C, 1 h	2c (20), 3c (5), 4 (8)
1c	4 (KCN)	acetone/H ₂ O	0 °C, 16 h	2c (28), 3c (28), 4 (42)
1d	2 (KCN)	acetone/H ₂ O	0 °C, 1 h	2d (5), 3d (10), 4 (35)
1e	2 (KCN)	acetone/H ₂ O	0 °C, 1 h	2e (-), 3e (-), 4 ^b

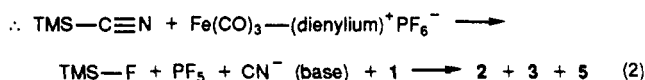
^a Yield obtained from starting dienylium salt. Unreacted dienylium salt may be recovered by filtration. Percent yields are given in parentheses.

^b Also obtained as the trienyl complex.⁶

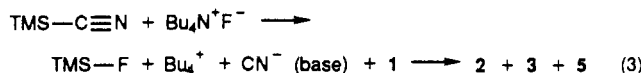
limiting (eq 1). The presence of steric hindrance at the



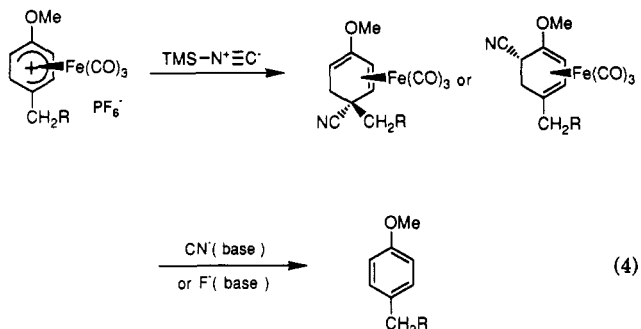
C-1 terminus and deactivation by the methoxy group in 1c has shifted the reaction toward the formation of aromatized product in higher yield. The mechanism outlined previously does not reflect on the formation of aromatized product. A second reaction pathway (eq 2)



which involved the reaction of trimethylsilyl cyanide with the hexafluorophosphate anion to generate trimethylsilyl fluoride, phosphorus pentafluoride, and free cyanide ion may take place, which accounts for the formation of aromatized product. The decomposition of hexafluorophosphate anion to phosphorus pentafluoride and fluoride anion at comparatively low temperature has been reported⁸ in the formation of 1-chloro-4-fluorobenzene from (*p*-chlorophenyl)diazonium hexafluorophosphate. The release of fluoride anion, which in turn reacts with trimethylsilyl cyanide to give basic cyanide anion, is expected to give poorer regioselectivity and aromatic product with 1c, similar to the case observed for reaction with potassium cyanide. Variation of the excess of trimethylsilyl cyanide indicates that the ratio of products obtained is proportional to the concentration of trimethylsilyl isocyanide and free cyanide ion present in the reaction mixture. Our work indicates that the concentration of trimethylsilyl isocyanide must be high enough for rapid addition to the dienylium complex prior to the dissociation of hexafluorophosphate anion to generate the fluoride anion followed by cyanide anion. This phenomenon may also account for the formation of the aromatic product after prolonged reaction time. It is suggested that the free fluoride and cyanide anions generated after prolonged reaction cause dehydrocyanation of the product 2c and 3c to give the aromatic product (eq 3). The postulated reaction between the hexafluorophosphate anion and trimethylsilyl cyanide may be easily mimicked using tetrabutylammonium



fluoride. Tetrabutylammonium fluoride is a widely used reagent for the desilylation of silyl enol ethers. As anticipated, the reaction of 1c with trimethylsilyl cyanide and tetrabutylammonium fluoride was found to give poorer regioselectivity, lower yields of 2c and 3c, and aromatized product even at lower temperature and shorter reaction time, which is consistent with our proposed mechanism (eq 4).



We next turn our attention to the series of hindered cyclohexadienylum complexes 1d,e, and the results are summarized in Table I. Reaction of 1d with trimethylsilyl cyanide (10 equiv) under reflux for 4 h was found to give exclusively 2c in high yield. Conversely, reaction of 1d with potassium cyanide was found to give very poor yields of 2c and 3c, but mainly aromatic products. The increase in α -proton acidity in 1e did not hamper nitrile addition with trimethylsilyl cyanide. A reasonable yield of 2e was obtained in this case, with increasing amounts of trienyl and aromatized products.

Next we investigated the spirocyclization of complex 2d. Table II summarizes the results of studies for the conversion of 2d to spiro lactone 6 under both basic and acidic conditions. It became apparent that these reactions favored the simple saponification of the acetate to the corresponding alcohol 5 in a shorter reaction time. A high yield of the spiro lactone 6 was eventually obtained after prolonged acid hydrolysis of the acetate, formed by the intramolecular condensation of the hydroxy complex 5 with the nitrile to give an imine which was further hydrolyzed to the ketone.

There are two noteworthy features of these results. First, the yields obtained during nitrile addition to the

(8) Corbridge, D. E. C. *Phosphorus: An outline of its Chemistry, Biochemistry and Technology*, 3rd Ed.; Elsevier: Amsterdam, 1985; p 102.

Table II. Hydrolysis of Complex 2c under Basic and Acidic Conditions

hydrolysis conditions	temp	reacn time	yield, %	
			5	6
K ₂ CO ₃ (1.02 equiv)/MeOH	0 °C	30 min	65	15
K ₂ CO ₃ (1.02 equiv)/MeOH	0 °C	2 h	15	37
K ₂ CO ₃ (1.02 equiv)/MeOH	room temp	15 h	4	64
H ₂ SO ₄ (cat.)/MeOH	room temp	9 h	19	44
H ₂ SO ₄ (cat.)/MeOH	room temp	1 day	0	76
NaOMe (1 equiv)/THF/MeOH	0 °C	30 min	32	16
NaOMe (1 equiv)/THF/MeOH	-78 °C		0	0

cyclohexadienylium complex are generally high with minimum proton abstraction, irrespective of the substituents at the C-1 terminus in 1. Second, the regioselectivity during the reaction is more pronounced, which gives mainly the desired C-1 addition product. The results presented here indicate that significant changes in reactivity occur when a large excess of trimethylsilyl cyanide is used together with a shorter reaction time. A clear understanding of all the reaction pathways among the reagents involved can lead to successful modifications of the reaction in favor of the required product.

Experimental Section

The organoiron complexes 1c,⁶ 1d,⁹ and 1e⁶ were prepared using published methods. Acetonitrile was distilled from calcium hydride under nitrogen. IR spectra were measured with a Digilab FTS-40 spectrometer. ¹H NMR spectra were obtained using a Varian VXR-300 (300 MHz) spectrometer. Chemical shifts are reported in ppm relative to TMS. Mass spectra were obtained using a Hitachi m-52 spectrometer. Elemental analyses were performed using a Heraeus CHNO-rapid analyzer. Radial chromatography was performed on a Harrison Research Chromatotron using 2.0 mm layer thickness silica gel 60FP-254 with calcium sulfate binder.

General Procedure for Nitrile Addition to the Tricarbonyl Cyclohexadienylium Salt. (a) **Sodium Cyanide Method.** To a stirred solution of potassium cyanide in 20% aqueous acetone at 0 °C under nitrogen was added the hexafluorophosphate salt in acetone. The reaction was carried out for the period indicated in Table I, and the mixture was then poured into ethyl acetate and washed successively with brine, cold 5% hydrochloric acid, aqueous sodium bicarbonate, and water. The organic layer was dried (Na₂SO₄) and evaporated under reduced pressure to give crude products. The mixture was separated by radial chromatography using hexane/ethyl acetate (5:1) as eluent.

(b) **Trimethylsilyl Cyanide Method.** Trimethylsilyl cyanide was added to a stirred solution of the hexafluorophosphate salt in acetonitrile and refluxed for a given period. The reaction mixture was cooled to room temperature and poured into water. The product was extracted with ethyl acetate and washed with brine and water. The organic layer was dried (Na₂SO₄) and evaporated under reduced pressure to give a crude product. It was purified as above.

Compounds 2c, 3c, and 2e were obtained as yellowish orange oils, whereas 2d was obtained as a yellow solid.

Tricarbonyl[2-acetoxy-1-((2-5-η)-1-cyano-4-methoxycyclohexa-2,4-dienyl)ethane]iron (2c): ν_{\max} (CHCl₃) 2231, 2061, 1981, 1732, 1485 cm⁻¹; ¹H NMR (CDCl₃) δ 5.18 (1 H, dd, J = 6.3 and 1.8 Hz, 3-H), 4.24 (2 H, t, J = 6.6 Hz, CH₂OAc), 3.69 (3 H, s, OMe), 3.48 (1 H, m, 5-H), 2.66 (1 H, d, J = 6.3 Hz, 2-H), 2.39 (1 H, dd, J = 15.6 and 3 Hz, endo 6-H), 2.06 (3 H, s, OAc), 2.1–1.8 (2 H, obscured, CH₂), 1.84 (1 H, dd, J = 15.6 and 3 Hz, exo 6-H); mass m/e 361 (M⁺), 335 (M⁺ - CN), 305 (M⁺ - 2CO). Anal. Calcd for C₁₅H₁₅NO₆Fe: C, 49.89; H, 4.19; N, 3.88. Found: C, 50.08; H, 4.23; N, 4.01.

Tricarbonyl[(2,5-η)-2-methoxy-5-(2-acetoxyethyl)cyclohexa-2,4-dienyl cyanide]iron (3c): ν_{\max} (CHCl₃) 2234, 2048, 1980, 1736 cm⁻¹; ¹H NMR (CDCl₃) δ 5.41 (1 H, d, J = 4.0 Hz, 3-H), 5.14 (1 H, d, J = 4.0 Hz, 4-H), 4.14 (2 H, t, J = 6 Hz, CH₂OAc), 3.49 (3 H, s, OMe), 3.39 (1 H, dd, J = 11.0 and 10.0 Hz, 1-H), 2.34 (1 H, dd, J = 15.0 and 11.0 Hz, endo 6-H), 2.10 (3 H, s, OAc), 2.03 (2 H, obscure, CH₂); mass m/e 361 (M⁺), 335 (M⁺ - CN), 305 (M⁺ - 2CO), 277 (M⁺ - 3CO).

Tricarbonyl[1-((2-5-η)-1-cyano-4-methoxycyclohexa-2,4-dienyl)-1-methylethane]iron (2d): mp 101–102 °C; ν_{\max} (CHCl₃) 2226, 2055, 1986, 1490 cm⁻¹; ¹H NMR (CDCl₃) δ 5.78 (1 H, dd, J = 6.3 and 2.4 Hz, 3-H), 3.68 (3 H, s, OMe), 3.48 (1 H, m, 5-H), 2.73 (1 H, d, J = 6.3 Hz, 2-H), 2.31 (1 H, dd, J = 16.0 and 4.0 Hz, endo 6-H), 1.80 (1 H, dd, J = 16.0 and 4.0 Hz, exo 6-H), 1.54 (1 H, hept, J = 6.3 Hz, CHMe₂); mass m/e 317 (M⁺), 291 (M⁺ - CN), 289 (M⁺ - CO), 263 (M⁺ - CO - CN). Anal. Calcd for C₁₄H₁₅NO₄Fe: C, 53.02; H, 4.77; N, 4.42. Found: C, 52.98; H, 4.80; N, 4.40.

Tricarbonyl[methyl ((2-5-η)-1-cyano-4-methoxycyclohexa-2,4-dienyl)acetate]iron (2e): ν_{\max} (CHCl₃) 2235, 2060, 1993, 1743 cm⁻¹; ¹H NMR (CDCl₃) δ 5.13 (1 H, dd, J = 6.3 and 2.4 Hz, 3-H), 3.73 (3 H, s, COOMe), 3.70 (3 H, s, OMe), 3.46 (1 H, m, 5-H), 2.74 (1 H, d, J = 6.3 Hz, 2-H), 2.67 (2 H, s, CH₂COOMe), 2.50 (1 H, dd, J = 15.0 and 3.0 Hz, endo 6-H), 1.82 (1 H, dd, J = 15.0 and 3.0 Hz, exo 6-H); mass m/e 319 (M⁺ - CO), 291 (M⁺ - 2CO), 263 (M⁺ - 3CO). Anal. Calcd for C₁₄H₁₃NO₆Fe: C, 48.44; H, 3.78; N, 4.04. Found: C, 48.40; H, 3.75; N, 4.00.

Basic Hydrolysis. To a stirred solution of potassium carbonate (1.02 equiv) in methanol at 0 °C was added 1d. The reaction mixture was stirred at 0 °C for the time indicated in Table II, after which it was neutralized with acetic acid. The solvents were evaporated, the residue was dissolved in ether, and this solution was washed successively with water and brine and dried (Na₂SO₄). The crude product was chromatographed on a silica gel column (with petroleum ether/ethyl acetate (4:1) as eluent) to afford 5 and 6.

Acidic Hydrolysis. To a stirred solution of concentrated sulfuric acid (catalytic amount) in methanol was added 1d. The reaction mixture was stirred at room temperature for 1 day, after which it was neutralized with a dilute solution of sodium bicarbonate. The solvents were evaporated, the residue was dissolved in ether, and this solution was washed successively with water and brine and dried (Na₂SO₄). Pure 6 was obtained in 76% yield.

Compound 5 was obtained as a yellowish orange gum, and 6 was obtained as a yellow solid.

Tricarbonyl[(6,9-η)-1-oxo-8-methoxy-2-oxaspiro[4.5]deca-6,8-diene]iron (6): mp 144–145 °C; ν_{\max} (CHCl₃) 2050, 1985, 1760, 1490 cm⁻¹; ¹H NMR (CDCl₃) δ 5.10 (1 H, dd, J = 6.3 and 2.4 Hz, 3-H), 4.25 (2 H, m, CH₂O-), 3.68 (3 H, s, OMe), 3.49 (1 H, m, 5-H), 2.51 (1 H, d, J = 6.3 Hz, 2-H), 2.23 (1 H, dd, J = 15.0 and 3.0 Hz, endo 6-H), 2.28 (1 H, m, -CH₂), 2.08 (1 H, m, CH₂), 1.75 (1 H, dd, J = 15.0 and 3.0 Hz, exo 6-H); mass m/e 320 (M⁺), 292 (M⁺ - CO), 264 (M⁺ - 2CO), 236 (M⁺ - 3CO). Anal. Calcd for C₁₂H₁₂O₆Fe: C, 48.78; H, 3.75. Found: C, 48.74; H, 3.75.

Tricarbonyl[(2-5-η)-1-cyano-4-methoxycyclohexa-2,4-dienyl]ethanol iron (5): ν_{\max} (CHCl₃) 3620, 2223, 2057, 1990, 1491 cm⁻¹; ¹H NMR (CDCl₃) δ 5.17 (1 H, dd, J = 6.3 and 2.5 Hz, 3-H), 3.87 (2 H, t, J = 6 Hz, CH₂OH), 3.69 (3 H, s, OMe), 3.47 (1 H, m, 5-H), 2.72 (1 H, d, J = 6.3 Hz, 2-H), 2.52 (1 H, dd, J = 15.0 and 3.0 Hz, endo 6-H), 2.10–1.70 (4 H, CH₂, exo 6-H and OH exchangeable with D₂O).

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(9) Prepared according to: Pearson, A. J.; Perrior, T. R. *J. Organomet. Chem.* 1985, 285, 254 (for the methoxy-substituted complex).