Utility of Diene-Tricarbonyliron Complexes as Mobile Chiral Auxiliaries: Highly Diastereoselective 1,5-Nucleophilic Substitution with 1,2-Migration of the $Fe(CO)_3$ Moiety

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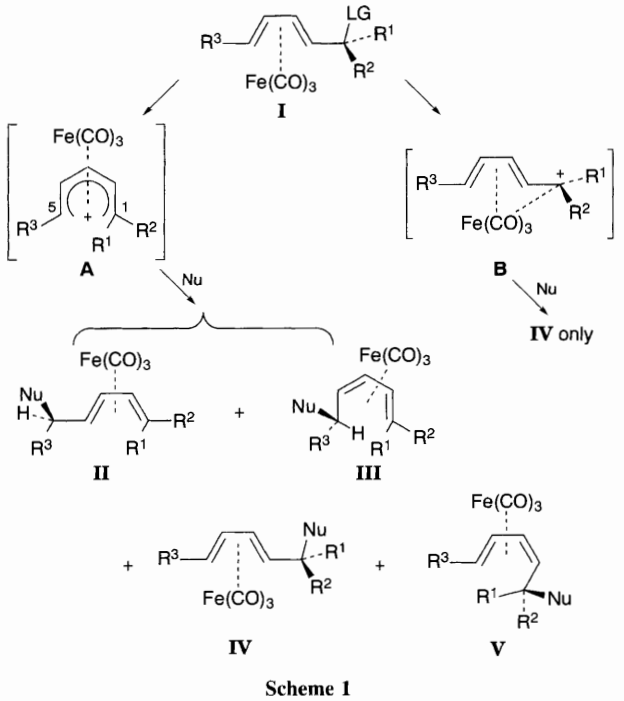
O-Acyl or *O*-phosphoryl cyanohydrin derivatives of the tricarbonyliron complex of hexa-2,4-dienal undergo regio- and stereo-selective 1,5-substitution reactions with several heteroatomic nucleophiles giving, with migration of the $Fe(CO)_3$ group, predominantly either (*E,E*)- or (*E,Z*)- products by appropriate selection of solvent and acid catalyst.

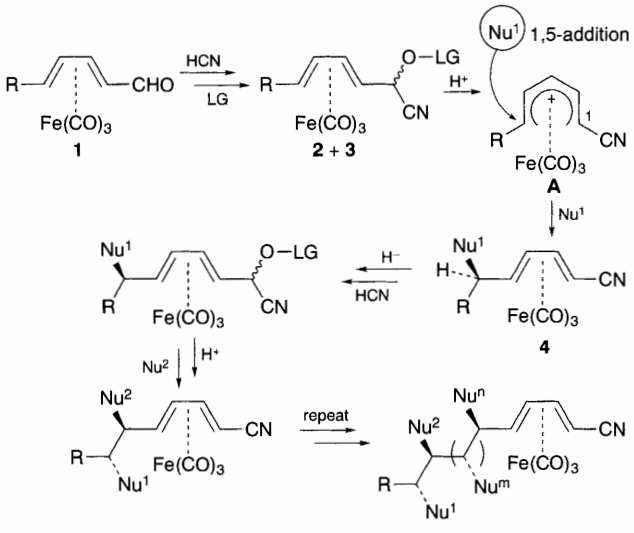
Over the past decade, η^5-dienyl tricarbonyliron(+1) cation complexes have proved extremely useful as intermediates in organic synthesis and highly diastereoselective addition reactions to the η^5-cation complexes are well documented.[1] Although U-shaped cation complexes **A** are conveniently generated from the corresponding alcohol or acetate complexes **I**, they are well-known to react with various nucleophiles in a stereoselective but non-regioselective manner, giving rise to four possible regiochemical isomers **II–V** in ratios depending on the electronic and steric effects of the R^1, R^2 and R^3 groups, even without considering the stereochemistry (Scheme 1).[2] Recently, two groups have reported the regio- and stereospecific nucleophilic substitutions *via* S-shaped cation complexes **B**, which open a route for (*E,E*)-1,1-substituted adducts **IV**.[3] However, there is still the serious problem of how to obtain the other type of isomers **II**, **III** and **V** predominantly. In particular, in view of an iterative chiral induction[4] with the aid of the iron–tricarbonyl moiety, the (*E,E*)- and (*E,Z*)-1,5-substituted adducts **II** and **III** are very promising intermediates, because in these products 1,2-migration of the $Fe(CO)_3$ in pentadienyl cations should occur. In the course of our studies on diene–iron complexes,[5] we became interested in the cyanohydrin derivatives **2** and **3** for the following reasons: (i) nucleophiles would predominantly attack the C-5 position of the cation complex **A**, owing to an electronic effect of the nitrile group;[6] (ii) the resulting nitriles **4** and **5** could be converted easily into aldehydes, from which another cyanohydrin would be prepared for the second manipulation (Scheme 2). Consequently, we wish to report here some regio- and diastereoselective 1,5-substitution reactions of the cyanohydrin derivatives **2** and **3** into the (*E,E*)- and (*E,Z*)-1,5-substituted adducts **4** and **5** along with concurrent migration of the $Fe(CO)_3$ group.



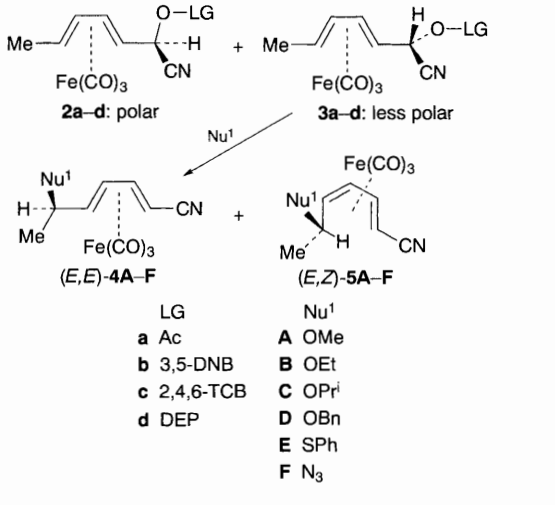
Scheme 1

At first, we studied the effect of the leaving groups (LG) of the cyanohydrin derivatives **2** and **3**. The cyano esters **2a–c** and **3a–c** were prepared from the racemic aldehyde complex **1**[7] in three steps: (i) Me_3SiCN, $ZnCl_2$, CH_2Cl_2; (ii) 10% HCl, MeOH; (iii) acetic anhydride or 3,5-dinitrobenzoyl (3,5-DNB) chloride or 2,4,6-trichlorobenzoyl (2,4,6-TCB) chloride, pyridine, CH_2Cl_2; yields:† 45 (**2a**), 45 (**3a**); 78 (**2b** + **3b**); 38 (**2c**), 40% (**3c**). The cyanophosphates **2d**‡ and **3d**‡ were obtained from **1** and diethyl phosphorocyanidate (DEP-CN) according to the reported procedure.[8]

A number of substitution reactions of **2** and **3** were examined using a variety of Brønsted acids and acidic ion-exchange resins



Scheme 2 Utility of the iron–tricarbonyl complex as a mobile chiral ligand



in MeOH, resulting in low to moderate yields of the substituted product, depending on the leaving groups (Table 1). In all cases except for runs 2 and 7, only one diastereoisomeric 1,5-substituted product **4A**† could be observed by 500 MHz ^{1}H NMR analysis. Table 1 indicates that 3,5-DNB, 2,4,6-TCB, and DEP are good leaving groups for the substitution reaction because both of their diastereoisomers, **2b–d** and **3b–d**, show the same reactivity, leading to the same product **4A**† irrespective of the chirality of the starting materials. Furthermore, we are interested in the different result of run 7, in which both **4A**† and **5A**† formed. In order to explain the generation of **5A**, the mixture of **4A** and **5A** obtained in run 7 was heated at 60 °C in MeOH in the presence of Dowex 50W, giving **4A**† as a single product in 91% yield (*cf.* run 8). This indicates that the (*E*,*E*)-isomer **4A** is a thermodynamically controlled product under the reaction conditions.

Next, expecting a diastereoselective preparation of (*E*,*Z*)-isomer **5**, we directed our attention to the reactivity of the cyanophosphates **2d** and **3d**, for which substitution proceeds at room temperature. After many experiments with various solvents and Lewis acids, we found that the $LiClO_4$-catalysed substitution of **2d** and **3d** in diethyl ether in the presence of 10 equiv. of nucleophiles gave a better result§ (Table 2). In these reactions, (*E*,*Z*)-isomers **5A** and **B**† bearing an oxygen atom could be always obtained as major isomers (*d.e.* 66–68% in runs 1 and 2), and isomers **5E** and **F**† bearing sulfur and nitrogen atoms were produced exclusively when benzenethiol and trimethylsilyl azide ($TMSN_3$) were used as nucleophiles (runs 3 and 4). Fortunately, we finally found that treatment of a mixture of **2d/3d** and several alcohols with a catalytic amount of $BF_3{\cdot}OEt_2$ in THF at 0 °C leads to the exclusive formation of the (*E*,*Z*)-isomers **5A–D**† in yields comparable with those of the $LiClO_4$-catalysed reaction, while in run 7 a small amount of **4C**† could be detected (runs 5–8).§

In conclusion, we have established the highly regio- and stereo-selective 1,5-substitution reactions of the cyanohydrin derivatives **2** and **3**, giving (*E*,*E*)-isomers **4A**† and (*E*,*Z*)-isomers **5A–F**† with concurrent migration of the $Fe(CO)_3$ group.

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Table 1 Reaction of the cyano esters **2a–d** and **3a–d** in MeOH under acidic conditions (Nu^1 = OMe)

Run	Substrate	Reaction conditions	Yield [**4A** : **5A**][a] (d.e.[%])[a]
1	**2a**	Dowex 50W, reflux, 48 h	23 [**4A** only] (0–50)
2	**3a**	Dowex 50W, reflux, 48 h	0
3	**2b**	Nafion NR-50, 60 °C, 6 h	50 [**4A** only] (>98)
4	**2c**	Nafion NR-50, 60 °C, 4 h	43 [**4A** only] (>98)
5	**2c**	HBF_4, 60 °C, 24 h	51 [**4A** only] (>98)
6	**3c**	Nafion NR-50, 60 °C, 10 h	52 [**4A** only] (>98)
7	**2d**	HBF_4 room temp., 6 h	53 [40 : 60] (>98)
8	**2d**	Nafion NR-50, 60 °C, 24 h	61 [**4A** only] (>98)

[a] Determined by 500 MHz ^{1}H NMR.

Table 2 Reaction of cyanophosphates **2d** and **3d** with various nucleophiles with Lewis acid catalysis

Run	Reaction conditions[a]	Nucleophile (Nu^1H or Nu^1TMS)	Yield (%) (d.e. [%])[b]	Ratio **4** : **5**[b]
1	**A**	MeOH	51 (>95)	16 : 84
2	**A**	EtOH	53 (>95)	17 : 83
3	**A**	PhSH	39 (>95)	<2 : >98
4	**A**	$TMSN_3$	60 (>95)	<2 : >98
5	**B**	MeOH	48 (>95)	<2 : >98
6	**B**	EtOH	54 (>95)	<2 : >98
7	**B**	Pr^iOH	45 (>95)	4 : 96
8	**B**	BnOH	39 (>95)	<2 : >98

[a] **A**: $LiClO_4$ (1.1 equiv.) and nucleophile (10 equiv.) were kept in diethyl ether at room temp. for 16 h. **B**: $BF_3{\cdot}Et_2O$ (0.1 equiv.) and nucleophile (10 equiv.) were kept in THF at 0 °C for 5 h. [b] Determined by 500 MHz ^{1}H NMR.

Footnotes

† The relative stereochemistry of **2** and **3** was estimated by R_f values according to Clinton and Lillya's report.[9] That of **4** and **5** was also elucidated from the reported examples[1] and the reaction mechanism.

‡ Due to the instability of **2d** and **3d** towards column chromatography, these compounds were used as a diastereomixture (**2d** : **3d** = 2 : 3 or 3 : 2) without purification.

§ At this stage, the reason why these two reaction conditions gave only the (*E*,*Z*)-isomer **5** is not clear but, owing to the mild Lewis acidity of $LiClO_4$ and the strong coordination ability of THF to $BF_3{\cdot}OEt_2$, the *Z* to *E* isomerization of **5** into **4** might be supressed effectively.

References

1 C. Quirosa-Guillou and J.-P. Lellouche, *J. Org. Chem.*, 1994, **59**, 4693; H.-J. Knölker, A.-A. El-Ahl and G. Weingärtner, *Synlett*, 1994, 194; W. A. Donaldson, M.-J. Jin and P. T. Bell, *Organometallics*, 1993, **12**, 1174; A. J. Pearson, S. Balasubramanian and K. Srinivasan, *Tetrahedron*, 1993, **49**, 5663; A. J. Pearson and K. Srinivasan, *Synlett*, 1992, 983; G. R. Stephenson and D. A. Owen, *Tetrahedron Lett.*, 1991, **32**, 1291; A. Teniou, L. Toupet and R. Grée, *Synlett*, 1991, 195; R. Grée, *Synthesis*, 1989, 341; A. J. Birch, L. F. Kelly and A. S. Narula, *Tetrahedron*, 1982, **38**, 1813.

2 W. A. Donaldson and M. Ramaswamy, *Tetrahedron Lett.*, 1988, **29**, 1343; A. J. Pearson, T. R. Perrior and D. C. Rees, *J. Organomet. Chem.*, 1982, **226**, C39; R. S. Bayoud, E. R. Biehl and P. C. Reeves, *J. Organomet. Chem.*, 1979, **174**, 297; 1978, **150**, 75.

3 W. R. Roush and C. K. Wada, *Tetrahedron Lett.*, 1994, **35**, 7347; *J. Am. Chem. Soc.*, 1994, **116**, 2151; M. Uemura, T. Minami, Y. Yamashita, K. Hiyoshi and Y. Hayashi, *Tetrahedron Lett.*, 1987, **28**, 641.

4 G. R. Stephenson, H. Finch, D. A. Owen and S. Swanson, *Tetrahedron*, 1993, **49**, 5649; A. J. Pearson, *Synlett*, 1990, 10; G. R. Stephenson, R. P. Alexander, C. Morley and P. W. Howard, *Philos. Trans. R. Soc. London, A*, 1988, **326**, 545.

5 Y. Takemoto, S. Ueda, J. Takeuchi, T. Nakamoto and C. Iwata, *Tetrahedron Lett.*, 1994, **35**, 8821; Y. Takemoto, J. Takeuchi and C. Iwata, *Tetrahedron Lett.*, 1993, **34**, 6067; 6069.

6 G. R. Stephenson, P. W. Howard and S. C. Taylor, *J. Organomet. Chem.*, 1991, **419**, C14; D. A. Owen, G. R. Stephenson, H. Finch and S. Swanson, *Tetrahedron Lett.*, 1990, **31**, 3401; W. A. Donaldson and M. Ramaswamy, *Tetrahedron Lett.*, 1989, **30**, 1339; R. Grée, M. Laabassi, P. Mosset and R. Carrié, *Tetrahedron Lett.*, 1985, **26**, 2317.

7 M. Franck-Neumann, D. Martina and M. P. Heitz, *Tetrahedron Lett.*, 1982, **23**, 3493.

8 S. Harusawa, R. Yoneda, T. Kurihara, Y. Hamada and T. Shioiri, *Tetrahedron Lett.*, 1984, **25**, 427; S. Harusawa, S. Nakamura, S. Yagi, T. Kurihara, Y. Hamada and T. Shioiri, *Synth. Commun.*, 1984, **14**, 1365.

9 N. A. Clinton and C. P. Lillya, *J. Am. Chem. Soc.*, 1970, **92**, 3058.