Cationic Mono- and Bi-nuclear Iron Complexes as Lewis Acid Catalysts in Mukaiyama Reactions

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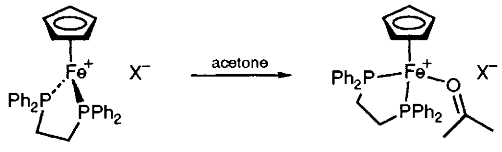
Organometallic Lewis acids derived from photolysis of mono- and bi-nuclear cationic iron carbonyl complexes function as excellent catalysts for the Mukaiyama aldol reaction.

The development of efficient catalysts for C–C bond-forming transformations continues to present organic chemists with a formidable challenge. Furthermore, the extension of such systems to effect enantioselective transformations is often problematical[1] and as a result, asymmetric versions of aldol reactions have been largely restricted to the stoichiometric use of chirality sources.[2]

We have been investigating the potential of cationic organometallic Lewis acids to mediate the Mukaiyama aldol reaction[3] of enol silanes with aldehydes by activation of the aldehyde component through coordination.[4,5] The Lewis acidity of such systems derives from a combination of their cationic nature and the fact that, as 16-electron complexes, they are inherently electron-deficient. The iron-based system **1**, shown in Scheme 1, was first synthesised by Sellmann *et al.* and characterised as the corresponding octahedral 18-electron acetone adduct **2**.[6]

IR spectroscopy of **2** indicated η^1-binding mode of the carbonyl to the iron centre and such an arrangement has been confirmed by X-ray crystallographic studies of related complexes.[7] It has been found that a solution of the acetone complex in dichloromethane at −78 °C undergoes rapid ligand exchange when treated with an excess of benzaldehyde to form the corresponding aldehyde adduct. This exchange is accompanied by a dramatic colour change from brown to deep-purple as well as a shift in the IR absorption from 1710 to 1696 cm^{-1}. It appears that the bound aldehyde is now activated towards nucleophilic attack since addition of the silyl ketene acetal **3**[8] at −78 °C and warming to −20 °C overnight allows isolation of the *O*-silylated aldol product **4** in 77% yield (Scheme 2). This reaction does not occur in the absence of the cationic iron complex **2** and the use of just 2 mol% of the catalyst is sufficient to effect clean conversion. The relatively high turnover number associated with this transformation is evidence for an efficient silyl transfer mechanism allowing release of the catalytic species back into the reaction medium.[9]

Having discovered an effective catalyst system, a direct and versatile route of access to the complex was sought. The method of choice became the procedure described originally by Sellmann *et al.*[6] involving photolytic decarbonylation of the corresponding 18-electron cationic iron carbonyl complex in acetone. Removal of the solvent under reduced pressure and replacement by dichloromethane at −78 °C provided convenient access to the active catalyst **2**, which could then be treated sequentially with benzaldehyde followd by a variety of nucleophile components. Warming to −20 °C and stirring for the stated period led to formation of the corresponding aldol product in the yields shown in Table 1, employing in each example less than 3 mol% of catalyst.[10]†

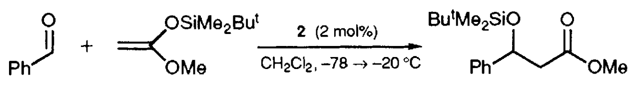


1
16 - electron

2
18 - electron

$X^- = PF_6^-, BF_4^-$

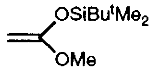
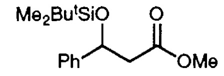
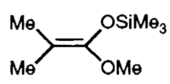
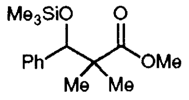
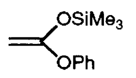
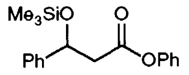
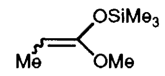
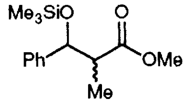
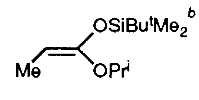
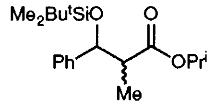
Scheme 1



3 **4**
77%

Scheme 2

Table 1

Entry	Nucleophile	Product	Reaction time/h	Yield (%)
1			20	77
2			18	90
3			24	55
4			6	70[a]
5			20	48[c]

[a] Product formed as a 1 : 1 diastereoisomeric mixture. [b] 88% Isomeric purity. [c] Product formed as a 1.2 : 1 diastereoisomeric mixture.

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† *Typical procedure*: to a dried photolysis apparatus flushed with argon was added a solution of 0.05 mmol $[Fe(C_5H_5)(dppe)CO]PF_6$ in 25 ml dry, degassed acetone. The solution was then irradiated for 30 min to 1 h at 0 °C (quartz lamp TQ 150, duranfilter, Original Hanau). The resultant dark-brown solution was then transferred to a flame-dried flask, the acetone was removed under vacuum and collected in a cold trap (−78 °C). The solid obtained was dried under high vaccum and then cooled to −78 °C. Dry dichloromethane (10 ml) was then added to the complex followed by benzaldehyde (2.0 mmol). Within 10 min the reaction mixture became deep-purple and the appropriate nucleophile component (2.4 mmol) was added. The reaction was then allowed to warm to −20 °C and stirred for the period indicated in Table 1. The reaction, once complete, was diluted with saturated aqueous $NaHCO_3$, extracted with dichloromethane, dried over $MgSO_4$ and the product isolated by chromatography on silica gel.

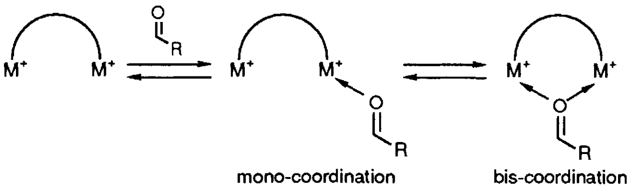
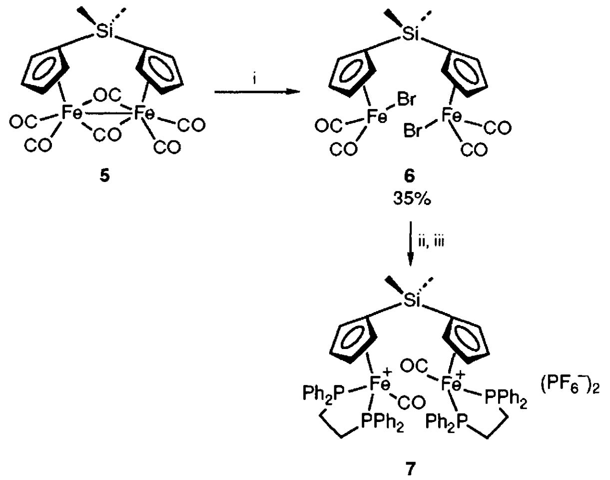


Fig. 1

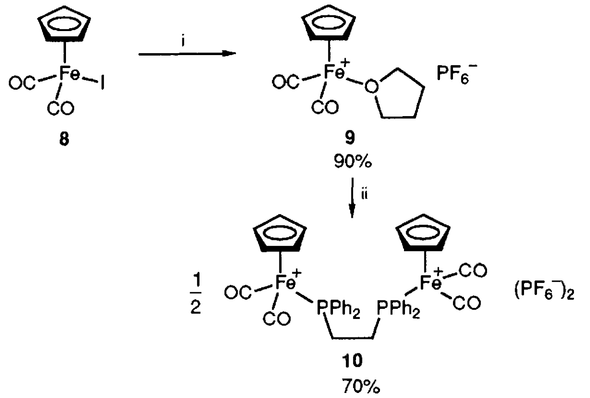


Scheme 3 *Reagents and conditions*: i, Br_2, $CHCl_3$; ii, dppe (2 equiv.), toluene, heat; iii, NH_4PF_4, $Me_3NO\cdot 2H_2O$, Me_2CO

This method for generating the catalyst was particularly attractive since routes to the photolysis substrates are well documented[11] and potentially amenable to chiral modification. Thus, replacement of the achiral diphosphine dppe [ethylenebis(diphenylphosphine)] by commercially available optically pure chiral diphosphines could open up further possibilities in the area of asymmetric C–C bond formation.

As a conceptual variation, we have also been investigating the use of dicationic species as dinuclear Lewis acid catalysts. As depicted in general terms in Fig. 1, the opportunity for either mono- or bis-coordination exists and the mode of coordination could have a profound influence on reactivity as well as on the stereochemical course of the ensuing addition.[12]

In designing the bidentate Lewis acids, it was decided to exploit the catalytic activity of the mononuclear iron complexes described above and as a result, two such centres were incorporated into one molecule by bridging. Initially, the possibility of bridging two cationic iron centres through the cyclopentadienyl rings was considered and the ready accessibility of the dimethylsilyl-bridged tetracarbonyl complex **5**[13] enabled this approach to be realised. Treatment of **5** with one equivalent of bromine in chloroform effected conversion to the dibromide **6** in moderate yield (Scheme 3).[14]‡ It was then possible to apply the methodology employed in the mononuclear series equally successfully to the dinuclear systems to access the bis-dppe-ligated dicationic complex **7**.



Scheme 4 *Reagents and conditions*: i, $AgPF_6$, tetrahydrofuran (thf); ii, dppe (0.5 equiv.), MeOH, heat

Photolysis of **7** in acetone over a period of 30 min resulted in a complex with a carbonyl IR absorption at 1700 cm^{-1}. This relatively low value (*cf.* **2**) may be seen as tentative evidence for bis-coordination and indeed a solution of the complex in dichloromethane exhibited enhanced catalytic activity compared with the analogous mononuclear complex. Thus, Mukaiyama reaction of **3** with benzaldehyde occurred within 3 h at −78 °C providing **4** in 80% yield.

As an alternative approach to bridging the two iron centres, systems were examined where the diphosphine ligand performed this task. The dppe-bridged complex **9** shown in Scheme 4 has been synthesised previously in modest yield by Treichel *et al.*[15]

Such a complex, under photolytic conditions in acetone, should lose at least one carbon monoxide ligand from each iron centre in an analogous fashion to the complexes already described. The resulting acetone adduct would be expected to exhibit increased Lewis acidity compared with **2** based on electronic and steric considerations. The synthesis of the thf-ligated complex **9** was achieved in an efficient manner by adaptation of the procedure reported by Reger *et al.*[16] Combination with dppe in refluxing methanol led to the required bridged dicationic complex **10** which precipitated from the reaction mixture and could be isolated in pure form simply by filtration.§ The light-yellow complex formed on subsequent photolysis in acetone for 30 min proved to exhibit very high catalytic activity with 1 mol% effecting clean addition of **3** to benzaldehyde within 2 h at −78 °C in 70% isolated yield.

In conclusion, this work describes the discovery of an efficient catalyst system involving cationic iron-based Lewis acids derived from easily handled iron carbonyl complexes. Photolytic triggering of the active species is a further aspect of the system that could have applications in other processes such as polymerisation. The success of dinuclear Lewis acids to effect efficient aldol reaction would appear to mark a new departure in the area of catalytic C–C bond formation. Work continues in our laboratories to assess the potential of these catalyst systems in stereoselective C–C bond-forming transformations.

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‡ All new compounds gave satisfactory elemental analyses and were characterised by NMR, IR and mass (FD or FAB) spectroscopy.

§ The use of higher-boiling solvent (*e.g.* toluene) led to the loss of a further CO ligand and the formation of the mono-iron complex **5**.

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References

1 Recent examples of catalytic asymmetric transformations include: addition of dialkylzinc reagents to aldehydes: M. Kitamura, S. Suga, K. Kawai and R. Noyori, *J. Am. Chem. Soc.*, 1986, **108**, 6071; Diels–Alder cycloadditions: K. Narasaka, N. Iwasawa, M. Inoue, T. Yamada, M. Nakashima and J. Sugimori, *J. Am. Chem. Soc.*, 1989, **111**, 5340; E. J. Corey, R. Imwinkelried, S. Pikul and Y. B. Xiang, *J. Am. Chem. Soc.*, 1989, **111**, 5493; K. Furuta, S. Shimizu, Y. Miwa and H. Yamamoto, *J. Org. Chem.*, 1989, **54**, 1481; aldol additions: T. Mukaiyama, S. Kobayashi, H. Uchiro and I. Shiina, *Chem. Lett.*, 1990, 129; S. Kobayashi, Y. Fujishita and T. Mukaiyama, *Chem. Lett.*, 1990, 1455; K. Furuta, T. Masuyama and H. Yamamoto, *J. Am. Chem. Soc.*, 1991, **113**, 1041; E. R. Parmee, Y. Hong, O. Tempkin and S. Masamune, *Tetrahedron Lett.*, 1992, **33**, 1729; Y. Ito, M. Sawamura and T. Hayashi, *J. Am. Chem. Soc.*, 1986, **108**, 6405.

2 C. H. Heathcock, in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1984, vol. 3; I. Paterson, J. M. Goodman, M. A. Lister, R. C. Schumann, C. K. McClure and R. D. Norcross, *Tetrahedron*, 1990, **46**, 4663 and references cited therein; M. Braun, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 24.

3 For a review on the Mukaiyama aldol reaction, see: T. Mukaiyama, *Org. React.* (*N.Y.*), 1982, **28**, 203.

4 The use of cationic rhodium complexes as catalysts in aldol reactions has been reported from our laboratories: M. T. Reetz and A. E. Vougiokas, *Tetrahedron Lett.*, 1987, **28**, 793.

5 For a review of organometallic Lewis acids, see: W. Beck and K. Sünkel, *Chem. Rev.*, 1988, **88**, 1405.

6 D. Sellmann and E. Kleinschmidt, *J. Organomet. Chem.*, 1977, **140**, 211. For alternative routes to **2**, see: M. L. H. Green and R. N. Whiteley, *J. Chem. Soc. A*, 1971, 1943; G. Balavoine, M. L. H. Green and J. P. Sauvage, *J. Organomet. Chem.*, 1977, **128**, 247.

7 B. M. Foxman, P. T. Klemarczyk, R. E. Liptrot and M. Rosenblum, *J. Organomet. Chem.*, 1980, **187**, 253; J. W. Faller and Y. Ma, *J. Am. Chem. Soc.*, 1991, **113**, 1579.

8 C. H. Heathcock, S. K. Davidson, K. T. Hug and L. A. Flippin, *J. Org. Chem.*, 1986, **51**, 3027.

9 Neutral iron halide complexes have also been shown to catalyse Mukaiyama additions, albeit with diminished activity: L. Colombo, F. Ulgheri and L. Prati, *Tetrahedron Lett.*, 1989, **30**, 6435.

10 Photolysis of **5** in the presence of the reaction components led to side products resulting from photocycloaddition: T. Bach, *Tetrahedron Lett.*, 1991, **32**, 7037.

11 S. G. Davies, J. Hibberd, S. J. Simpson, S. E. Thomas and O. Watts, *J. Chem. Soc., Dalton Trans.*, 1984, 701.

12 Evidence for bis-coordination with bidentate Lewis acids has been described: H. E. Katz, *Organometallics,* 1987, **6**, 1134; A. L. Beauchamp, M. J. Olivier, J. D. Wuest and B. Zacharie, *Organometallics,* 1987, **6**, 153.

13 J. Weaver and P. Woodward, *J. Chem. Soc., Dalton Trans.*, 1973, 1439.

14 The corresponding diiodide has been reported: G. O. Nelson and M. E. Wright, *Organometallics,* 1982, **1**, 565.

15 P. M. Treichel, R. L. Shubkin, K. W. Barnett and D. Reichard, *Inorg. Chem.*, 1966, **5**, 1177.

16 D. L. Reger and C. Coleman, *J. Organomet. Chem.*, 1977, **131**, 153.