Stereocontrolled Functionalization of Cycloheptatrieneiron Complexes. Synthesis of Polyhydroxylated Cycloheptane Derivatives

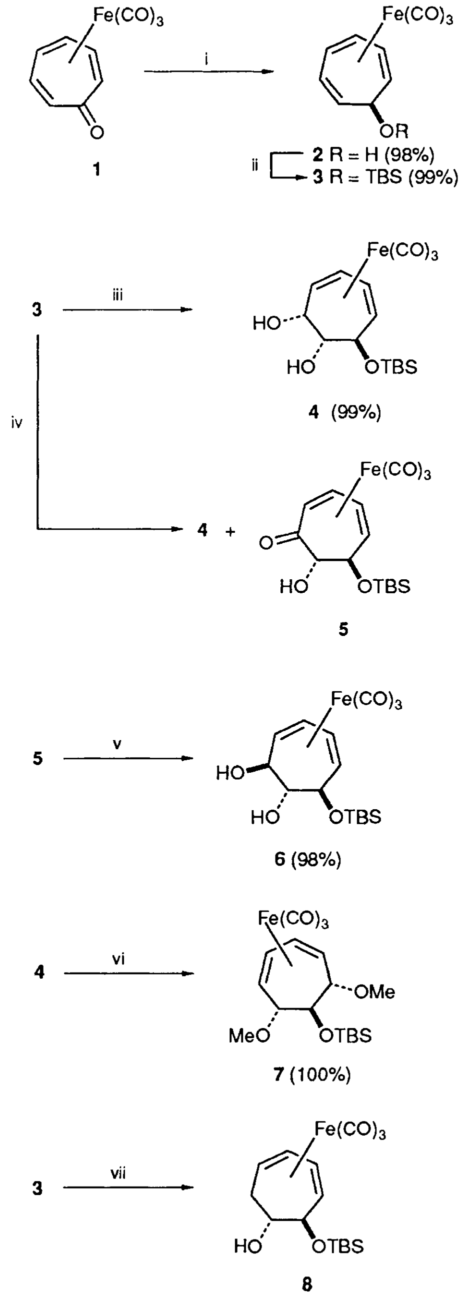
Anthony J. Pearson* and Kumar Srinivasan

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106, USA

Osmylation and hydroboration of η^4-cycloheptatriene–Fe(CO)$_2$L complexes [L = CO or P(OPh)$_3$] proceeds with excellent regio- and stereo-selectivity, owing to the profound directing effects of the Fe(CO)$_2$L group.

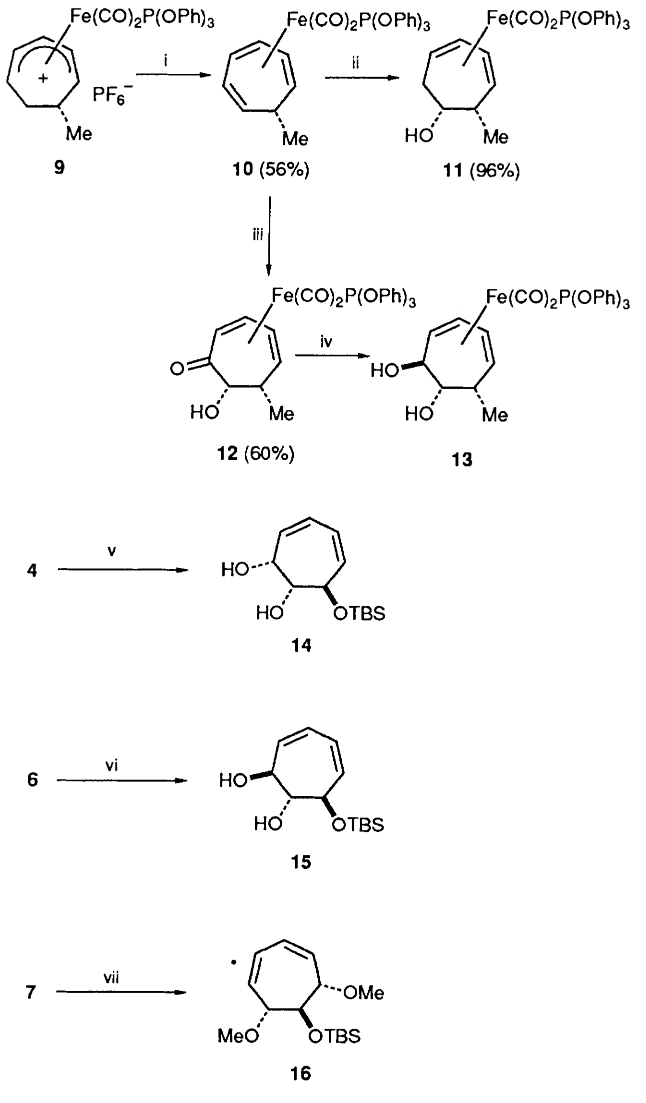
In recent years we have reported[1] methods for stereocontrolled attachment of carbon substituents to cycloheptadiene *via* nucleophile addition to cycloheptadienyl–Fe(CO)$_2$L cations [*e.g.*, L = P(OPh)$_3$]. This has resulted in syntheses of the Prelog–Djerassi lactone in optically pure form, as well as intermediates for synthesis of the macrolide antibiotics carbomycin B and tylosin.[2] We present herein methods for stereocontrolled hydroxylation of cycloheptatriene derivatives, which we anticipate will be useful for the construction of a variety of heptitol and aminoheptitol derivatives.[3]

It has been shown previously that a diene–Fe(CO)$_3$ system is stable during hydroboration and stoichiometric osmylation reactions of an attached alkene group.[4,5] We have now found that these reactions may be carried out on substituted



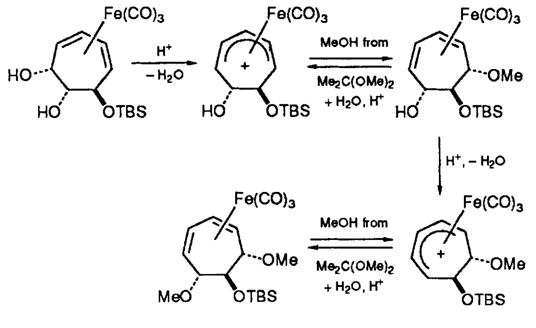
TBS = Bu^{t}Me$_2$Si

Scheme 1 *Reagents and conditions*: i, NaBH$_4$, CeCl$_3$·7H$_2$O, MeOH, 0 °C; ii, Bu^{t}Me$_2$SiOSO$_2$CF$_3$, pyridine, 4-*N*,*N*-dimethylaminopyridine (DMAP) catalyst, CH$_2$Cl$_2$; iii, OsO$_4$ (1 equiv.), pyridine, tetrahydrofuran (THF), then NaHSO$_3$, H$_2$O; iv, OsO$_4$ (catalyst), Bu^{t}OOH, Et$_4$NOAc, acetone; v, NaBH$_4$, MeOH; vi, CSA (catalyst), Me$_2$C(OMe)$_2$, acetone, 0 °C; vii, BH$_3$·THF, H$_2$O$_2$, NaOH, H$_2$O



TBS = Bu^{t}Me$_2$Si

Scheme 2. *Reagents and conditions*: i, Et$_3$N, CH$_2$Cl$_2$; ii, BH$_3$·THF, NaOH, H$_2$O$_2$, H$_2$O; iii, OsO$_4$ (catalyst), Bu^{t}OOH, Et$_4$NOAc, acetone; iv, NaBH$_4$; v, Me$_3$NO, MeCONMe$_2$, 0 °C, 4 h; vi, CuCl$_2$, EtOH; vii, CrO$_3$·2 pyridine, CH$_2$Cl$_2$



Scheme 3

η^4-cycloheptatriene–Fe(CO)$_2$L complexes with complete stereo- and regio-selectivity, attributable to the directing effects of the diene-metal moiety.[6] Thus, the protected alcohol **3**, readily prepared in high yield from the known tropone–Fe(CO)$_3$ complex **1**, was converted to a single diol **4** in 99% yield on osmylation under stoichiometric conditions.†

Catalytic osmylation, using the method of Sharpless,[7] also gave **4**, but this was usually contaminated by the ketol **5**, the ratio being dependent on reaction time. Thus, a shorter reaction time (6 h) gives a 4 : 1 mixture in favour of **4**, while a longer reaction time (overnight) give greater amounts of **5**. The regioselectivity during the overoxidation is interesting and potentially valuable, and the use of catalytic conditions is especially noteworthy in view of the usual sensitivity of

---

† All new compounds were obtained as racemic mixtures, were purified by preparative TLC or flash chromatography, and were fully characterized by 200 MHz ^{1}H NMR and IR spectroscopy. Elemental composition was confirmed by combustion analysis and/or high resolution mass spectrometry.

diene–$Fe(CO)_3$ complexes to, *e.g.*, alkaline hydroperoxides.[8] While complexes **4** and **5** are chromatographically inseparable, reduction with $NaBH_4$ gave a mixture of **4** and **6** which were readily separated. Treatment of **4** with a catalytic amount of camphorsulphonic (CSA) acid–methanol under anhydrous conditions afforded exclusively the symmetrically substituted complex **7**, easily recognized by its ^1H NMR spectrum.‡

Hydroboration of **3** was also completely stereo- and regio-selective, giving complex **8** as the only product. In all these functionalization reactions, the stereodirecting power of the $Fe(CO)_3$ group is reinforced by the *tert*-butyldimethylsilyloxy substituent, and the regiochemistry of hydroboration is controlled by both the neighbouring diene-$Fe(CO)_3$ group§ and the ether.[9] A more stringent test of the directing power of the organometallic system was therefore sought. Deprotonation of the methyl-substituted dienyl complex **9** afforded **10** in 56% yield. Hydroboration of **10** afforded a single complex **11** in 96% yield, the structure of which was confirmed by comparison with an authentic sample.[10] Osmylation of **10**, under catalytic conditions, afforded exclusively the ketol **12**. Formation of ketol in the latter transformation is consistent with the observation that osmylation of **10** is much slower than osmylation of **3**, as expected, so that competing oxidation of the initially formed diol cannot be prevented. Borohydride reduction of **12** afforded a single diol **13**. These functionalizations of the uncomplexed double bond of **10** demonstrate the profound stereo- and regio-control that may be expected from the $Fe(CO)_2L$ unit, and contrast with effects observed during reactions of conformationally less rigid cycloheptadienone complexes discussed in the accompanying communication.[10]

Decomplexation of the products of these reactions provides access to a range of cycloheptadiene derivatives, such as **14**, **15** and **16**. Functionalization of the diene, using methods established during our earlier studies,[2] coupled with ring cleavage is expected to give a range of stereochemically defined heptitols, and this is currently under investigation in our laboratory.

We are grateful to the National Science Foundation for financial support (grant CHE-8921944).

Received, 12th November 1990; Com. 0/05088A

References

1 A. J. Pearson, S. L. Kole and T. Ray, *J. Am. Chem. Soc.*, 1984, **106**, 6060.
2 A. J. Pearson and T. Ray, *Tetrahedron Lett.*, 1986, **27**, 3111; A. J. Pearson and Y. S. Lai, *J. Chem. Soc., Chem. Commun.*, 1988, 442; A. J. Pearson, Y. S. Lai, W. Lu and A. A. Pinkerton, *J. Org. Chem.*, 1989, **54**, 3882.
3 N. Sakairi, M. Hayashida, A. Amano and H. Kuzuhara, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1301; J. G. Buchanan, K. W. Lumbard, R. J. Sturgeon, D. K. Thompson, and R. H. Wightman, *J. Chem. Soc., Perkin Trans. 1*, 1990, 699; I. Bruce, G. W. J. Fleet, I. Cenci di Bello and B. Winchester, *Tetrahedron Lett.*, 1989, **30**, 7257; G. W. J. Fleet, N. M. Carpenter, S. Petursson and N. G. Ramsden, *Tetrahedron Lett.*, 1990, **31**, 409, and references cited therein.
4 D. V. Banthorpe, H. Fitton and J. Lewis, *J. Chem. Soc., Perkin Trans. 1*, 1973, 2051; G. Evans, B. F. G. Johnson and J. Lewis, *J. Organomet. Chem.*, 1975, **102**, 507; D. H. R. Barton, A. A. L. Gunatilaka, T. Nakanishi, H. Patin, D. A. Widdowson and B. R. Worth, *J. Chem. Soc., Perkin Trans. 1*, 1976, 821.
5 A. J. Pearson and Y. S. Chen, *J. Org. Chem.*, 1986, **51**, 1939; R. Grée, *Synthesis*, 1989, 341.
6 See also: M. Rosenblum and J. C. Watkins, *J. Am. Chem. Soc.*, 1990, **112**, 6316; M. Franck-Neumann and D. Martina, *Tetrahedron Lett.*, 1975, 1759; J. H. Rigby and C. O. Ogbu, *Tetrahedron Lett.*, 1990, **31**, 3385.
7 K. Akashi, R. E. Palermo and K. B. Sharpless, *J. Org. Chem.*, 1978, **43**, 2063.
8 M. Franck-Neumann, D. Heitz and D. Martina, *Tetrahedron Lett.*, 1983, **24**, 1615.
9 G. M. L. Cragg, *Organoboranes in Organic Synthesis*, Marcel Dekker, New York, 1973; H. C. Brown, *Organic Synthesis via Boranes*, Wiley-Interscience, New York, 1975; D. A. Evans, G. C. Fu and A. H. Hoveyda, *J. Am. Chem. Soc.*, 1988, **110**, 6917.
10 A. J. Pearson and K.-Y. Chang, accompanying communication.

---

‡ A plausible mechanism for this transformation is shown in Scheme 3. The interesting selectivity observed suggests that this type of procedure can be used in a stepwise fashion to introduce substituents other than methoxy.

§ Stabilization of a partial positive charge α to a diene–$Fe(CO)_3$ group accounts for the regiochemistry of hydroboration. See also ref. 10.