Surprising stereochemical stability in a multistep organometallic transformation

Stephen A. Benyunes and Susan E. Gibson (née Thomas)*

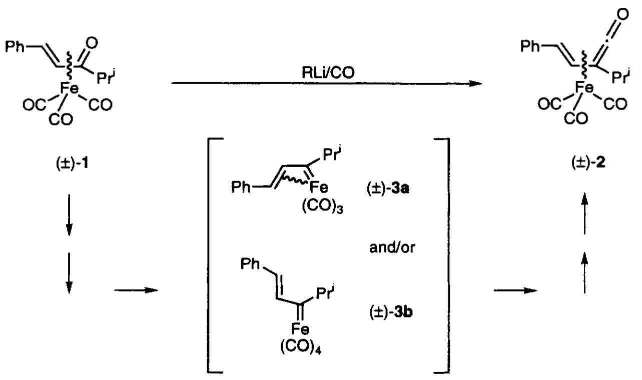
Department of Chemistry, Imperial College of Science, Technology and Medicine, South Kensington, London, UK SW7 2AY

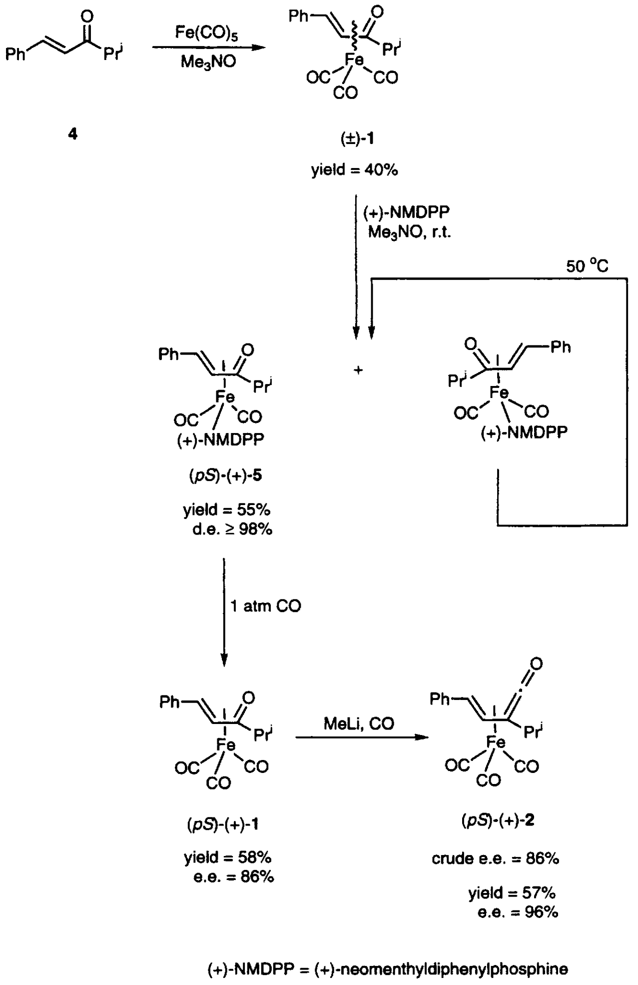
The alkyllithium/carbon monoxide mediated conversion of iron tricarbonyl complexes of vinylketones to iron tricarbonyl complexes of vinylketenes proceeds without loss of stereochemical integrity.

There is currently widespread interest in defining and controlling the stereochemical outcome of chemical reactions. To date this interest has focussed predominantly on organic reactions and, as a result, our control and understanding of these processes is now very sophisticated; in contrast, stereochemical studies of organometallic processes, particularly those in which both the metal centre and its ligands play a significant role, are still relatively rare.†

Some time ago we discovered that iron tricarbonyl complexes of vinylketones *e.g.* **1** are transformed into iron tricarbonyl complexes of vinylketenes *e.g.* **2** on addition of an alkyllithium reagent under an atmosphere of carbon monoxide.[5,6] We currently believe that this unique transformation proceeds *via* a multistep mechanism involving *inter alia* a vinylcarbene intermediate of type **3a** (η^3) and/or **3b** (η^1), based on (*i*) the isolation of RCO_2Li from the reaction mixture,[6] and (*ii*) precedents for the conversion of iron vinylcarbene complexes into vinylketene complexes in the presence of carbon monoxide.[7,8] The transformation of a chromium vinylcarbene complex into a vinylketene derivative is believed to be a key step in the widely studied reactions of chromium carbenes with alkynes.[9,10] In view of current stereochemical and mechanistic interest in this area,[1,2,9] and the continuing high levels of interest in stereochemistry in general, we thought it appropriate to define the stereochemical consequence of converting an iron tricarbonyl complex of a vinylketone into an iron tricarbonyl complex of a vinylketene. The way in which this was achieved and the result obtained, which in view of the multistep nature of the transformation was somewhat surprising, are reported herein.

An enantiomerically enriched sample of complex **1** was obtained (Scheme 1) from the alkyl styryl ketone **4** using a route based on a recently reported synthesis of enantiomerically enriched (benzylideneacetone)tricarbonyliron(0).[11]‡ Ketone **4**, readily prepared by condensation of benzaldehyde and 3-methylbutan-2-one was converted into its tricarbonyliron(0) complex (±)-**1** using $Fe(CO)_5$–Me_3NO–THF,§ and then reacted with (+)-neomenthyldiphenylphosphine [(+)-NMDPP][12]–Me_3NO in acetonitrile at room temperature. This gave a 1 : 1 mixture of two diastereoisomeric phosphine complexes one of which crystallised from the reaction mixture whilst the other remained in solution. The yield of the crystalline diastereoisomer was enhanced by thermal equilibration of the remainder of the complex mixture at 50 °C in acetonitrile.¶ The planar chirality of the crystalline diastereoisomer (d.e. ≥98%) was assigned as *pS*‖ by comparison of its optical rotation value $\{[\alpha]_D^{29.5}$ (*c* 0.156, CH_2Cl_2) = +1262 ± 30} with those of the (+)-NMDPP derivatives of (benzylideneacetone)tricarbonyliron(0) $\{[\alpha]_D^{20}$ (*c* 0.155, CH_2Cl_2) =





(+)-NMDPP = (+)-neomenthyldiphenylphosphine

Scheme 1

+1166 ± 50 (*pS*) and −1066 ± 50 (*pR*)}, the planar chirality of which had been determined by X-ray crystallography of the (+)-diastereoisomer.[11]

The phosphine complex (*pS*)-(+)-**5** was subsequently converted back to the tricarbonyliron(0) complex **1** by stirring it in toluene under an atmosphere of carbon monoxide for 2 days at room temperature. These optimised conditions gave a 58% yield of product with an e.e. of 86 ± 4% [as determined by ^{1}H NMR spectroscopy in the presence of the chiral shift reagent Eu(tfc)$_3$] {$[\alpha]_D^{27}$ (*c* 1.11, CH_2Cl_2) = +836 ± 20}. The enantiomeric purity of complex **1** generated in this reaction is dependent on time and temperature, with the loss of stereochemical purity observed here attributed to the racemisation of complex **1** under the reaction conditions *via* a series of steps involving decomplexation and recomplexation of the alkyl styryl ketone.[11] X-Ray crystallography of complex (+)-**1** revealed that its absolute configuration was (*pS*)** thereby demonstrating that phosphine/carbon monoxide exchange occurs with retention of planar chirality rather than inversion.

The enantiomerically enriched vinylketone complex (+)-**1** was then reacted with methyllithium under an atmosphere of carbon monoxide to give the vinylketene complex **2**.[5,6] A range of chiral shift reagents proved to be ineffective with complex **2** and so its enantiomeric purity was determined by chiral HPLC analysis [CHIRALCEL OB, Daicel Chemical Industries; *n*-hexane–isobutyl alcohol (98:2), 0.5 cm^3 min^{-1}] and found to be 86 ± 1%. Thus, the conversion of **1** to **2** had occurred without any leakage of stereochemical information whatsoever, a somewhat surprising result in view of the multistep nature of the transformation. Purification and crystallisation of the crude product gave material of 96% e.e. in 57% yield {$[\alpha]_D^{27}$ (*c* 0.5, CH_2Cl_2) = +1283 ± 30}. Comparison of this rotation data with that obtained from a sample of vinylketene complex **2** of 99% e.e. and absolute stereochemistry *pS* obtained by kinetic resolution of (±)-**2** using a phosphoramidate anion derived from (*S*)-α-methylbenzylamine {$[\alpha]_D^{25}$ (*c* 1.00, CH_2Cl_2) = +1312 ± 20}[15] revealed that the absolute stereochemistry of the sample of **2** derived from the vinylketone complex (+)-**1** was also *pS*.

Thus, it can be concluded that the alkyllithium/carbon monoxide mediated conversion of iron tricarbonyl complexes of vinylketones to iron tricarbonyl complexes of vinylketenes proceeds with retention of configuration; symmetrical intermediates such as vinylcarbene **3b** can now be eliminated entirely from mechanistic speculation about this reaction and can be considered unlikely in the conversion of iron/chromium vinylcarbene complexes to vinylketene complexes.

The authors thank Dr D. Lathbury, Mr K. Sutcliffe and Mr D. Ross of SmithKline Beecham Pharmaceuticals, Tonbridge for invaluable initial help with the HPLC analysis. They also gratefully acknowledge support from the EPSRC/DTI Link Initiative on Asymmetric Synthesis for a post-doctoral fellowship (S. A. B.).

Footnotes

† Recent studies in this area include the first stereoselective synthesis of arene chromium tricarbonyl complexes from chromium carbene complexes and alkynes (the Dötz benzannulation reaction),[1,2] a stereospecific three- to five-carbon ring expansion of 2-alkenylcyclopropylcarbenechromium complexes,[3] and a study of the fate of a stereogenic centre linked to palladium upon reaction with an alkyne which provides evidence for a concerted alkyne insertion into the palladium–carbon bond.[4]

‡ An identical study to the one reported herein based on (benzylideneacetone)tricarbonyliron(0) gave an identical stereochemical result; for the sake of brevity, however, and as the methyl analogue of (*pS*)-(+)-**5** proved relatively difficult to obtain in acceptable yield, we have confined out report here to the study based on the isopropyl substituted complex **1**.

§ 0.1 Mol of complex (±)-**1** may be generated readily by this method.

¶ The two analogous benzylideneacetone (+)-NMDPP diastereoisomers were found to be stable with respect to epimerisation in toluene at 45 °C.[11] Similar dicarbonyl(diene)[(+)-NMDPP]iron(0) complexes, however, have been shown to epimerise in benzene and toluene at higher temperatures (70–100 °C).[13]

‖ Application of the Cahn–Ingold–Prelog convention for π complexes[14] to the iron-bound carbon bearing the phenyl group leads to the *pS* designation.

** Details of this analysis will be reported in the full account of this work.

References

1 R. P. Hsung, W. D. Wulff and A. L. Rheingold, *J. Am. Chem. Soc.*, 1994, **116**, 6449.

2 R. L. Beddoes, J. D. King and P. Quayle, *Tetrahedron Lett.*, 1995, **36**, 3027.

3 J. W. Herndon, D. K. Hill and L. A. McMullen, *Tetrahedron Lett.*, 1995, **36**, 5687.

4 J. Spencer and M. Pfeffer, *Tetrahedron Asymmetry*, 1995, **6**, 419.

5 C. J. Richards and S. E. Thomas, *J. Chem. Soc., Chem. Commun.*, 1990, 307.

6 N. W. Alcock, C. J. Richards and S. E. Thomas, *Organometallics*, 1991, **10**, 231.

7 J. Klimes and E. Weiss, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 205.

8 T. Mitsudo, H. Watanabe, T. Sasaki, Y. Takegami, Y. Watanabe, K. Kafuku and K. Nakatsu, *Organometallics*, 1989, **8**, 368.

9 J. Barluenga, F. Aznar, A. Martin, S. Garcia-Granda and E. Pérez-Carreno, *J. Am. Chem. Soc.*, 1994, **116**, 11191 and references therein.

10 W. D. Wulff, A. M. Gilbert, R. P. Hsung and A. Rahm, *J. Og. Chem.*, 1995, **60**, 4566 and references therein.

11 A. Marcuzzi, A. Linden, D. Rentsch and W. von Philipsborn, *J. Organomet. Chem.*, 1992, **429**, 87.

12 J. D. Morrison and W. F. Masler, *J. Org. Chem.*, 1974, **39**, 270.

13 J. A. S. Howell, A. G. Bell, D. Cunningham, P. McArdle, T. A. Albright, Z. Goldschmidt, H. E. Gottlieb and D. Hezroni-Langerman, *Organoemtallics*, 1993, **12**, 2541.

14 R. S. Cahn, C. Ingold and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, 1966, **5**, 385.

15 S. A. Benyunes, S. E. Gibson (née Thomas) and M. F. Ward, *Tetrahedron Asymmetry*, in the press.

Received, 3rd October 1995; Com. 5/06508I