



Pergamon

Tetrahedron Letters 41 (2000) 2479–2482

TETRAHEDRON
LETTERS

Preparation of a novel class of macrocycle and cryptand containing the 1,1'-disubstituted ferrocene unit

Alberto Tárraga,* Pedro Molina * and Juan Luis López

Departamento de Química Orgánica, Facultad de Química, Universidad de Murcia, Campus de Espinardo, E-30071 Murcia, Spain

Received 19 November 1999; revised 18 January 2000; accepted 25 January 2000

Abstract

Condensation of 1,1'-diacetylferrocene with *o*-azidobenzaldehyde under appropriate conditions leads either to the [5]-ferrocenophane **2** or the bis(azide) **3**, as the only reaction products. Compound **2** undergoes an intramolecular aza-Wittig reaction to give the new type of cryptand **4**. Bis(azide) **3** is converted into the macrocycle **5** by a Staudinger reaction with bis(diphenylphosphino)ethane; alternatively, thermally-induced azide decomposition provides the 1,1'-bis(indolyl)ferrocene derivative **6**. © 2000 Elsevier Science Ltd. All rights reserved.

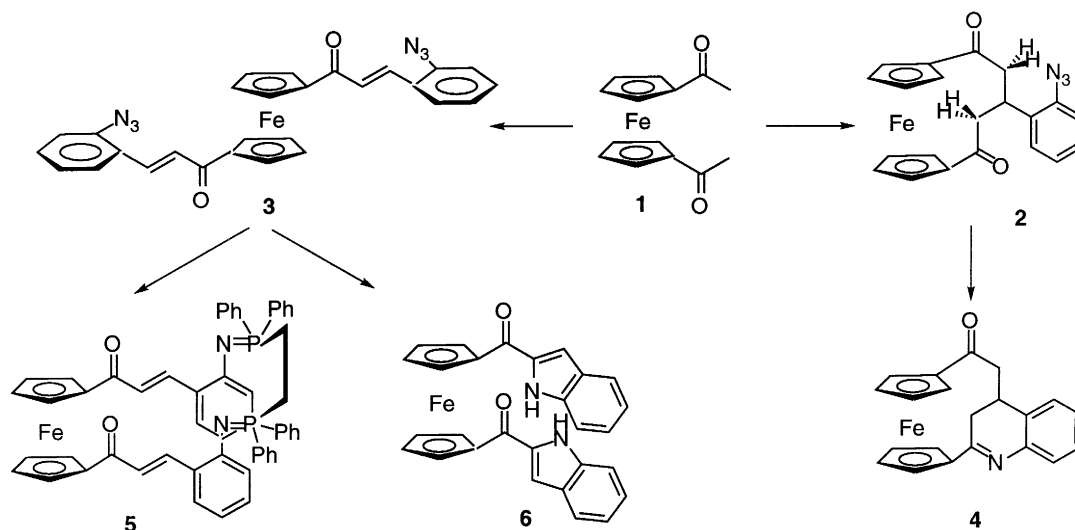
Keywords: ferrocene; aza-Wittig reaction; Staudinger reaction; macrocycle; cryptand.

Considerable attention has been paid over the last few years to systems containing a ferrocene unit and an R-aza complexing moiety able to act as a ligand towards transition metal ions. These ligands are of interest for the construction of heterobimetallic systems, which can behave as redox-active and photo-active receptors with the capability of selectively sensing ionic-guest species via electrochemical and/or optical methodologies.¹ In this context, a recent paper describing the preparation of the 1,1'-bis(4-diethylaminocinnamoyl)ferrocene (7% yield) as a rare molecule which is both electroactive and fluorescent,² prompted us to disclose our results on the synthesis of ferrocenyl-substituted azaheterocycles.³

We have found that the reaction of 1,1'-diacetylferrocene with *o*-azidobenzaldehyde in a basic medium may be driven towards the formation of 3-(*o*-azidophenyl)[5]-ferrocenophane-1,5-dione **2** or 1,1'-bis(*o*-azidocinnamoyl)ferrocene **3** as the only reaction products simply by changing the sequence of addition of the reagents as well as the amount of base (Scheme 1). Addition of *o*-azidobenzaldehyde (1 equiv.) to an ethanolic solution of 1,1'-diacetylferrocene containing an excess of KOH gave **2** in 70% yield, which was separated as a stable red solid. However, addition of a stoichiometric amount of ethanolic KOH to a mixture of 1,1'-diacetylferrocene and *o*-azidobenzaldehyde (1:5) provided **3** in 61% yield as a stable

* Corresponding authors.

solid. In this case, the use of stoichiometric amounts of base prevents the conversion **3**→**2** by a reverse aldol condensation⁴



Scheme 1.

The ^1H and ^{13}C NMR spectra of [5]-ferrocenophane **2** clearly revealed the highly ordered and asymmetric conformation of the molecule. In the ^1H NMR spectrum the protons of the Cp rings appeared as well-separated four broad singlets at $\delta=4.92$, 4.89, 4.62 and 4.55 (2:2:2:2), whereas the two protons within the two equivalent methylene groups of the bridge are magnetically non-equivalent (at 318 K a broad doublet at $\delta=2.54$ and a broad triplet at $\delta=2.99$ are detected for both methylene groups). The signal of the methine proton is embedded in the ferrocene region and, hence, cannot be seen. However, in the analogue 3-(4-methylphenyl)[5]-ferrocenophane-1,5-dione, prepared in 50% yield in the same way, the methine proton appeared at $\delta=4.31$ ppm as a broad triplet.

Probably, the anisochrony of the two protons within each of the two equivalent methylene groups in **2** could be due to the fact that the ferrocene develops a diamagnetic anisotropy.⁵ Thus, the signal of the two quasi-axial hydrogen atoms in the *endo*-position directed towards the iron atom are shifted downfield, whereas the signals of the two quasi-equatorial hydrogen atoms in the *exo*-position that point away from the iron atom, are shifted to higher magnetic fields. As regards the asymmetry observed for the Cp ring protons, it is known that in [5]-ferrocenophanes the iron-to-ring distance is the same as in ferrocene⁶ since the bridge is long enough to span the rings without strain. In the [5]-ferrocenophane **2** the four signals for the two Cp rings strongly suggest a staggered conformation of the two rings as the bridge forces them out of coplanarity, with the two rings now being magnetically non-equivalent.

The ^1H and ^{13}C NMR spectra of compound **3** reveals high symmetry, only showing one set of signals for the two cinnamoyl substituents which are almost identical to those found in the monosubstituted analogue.^{3d} These data suggest that the two substituents in compound **3** are constrained to an *anti* geometry.⁷

Compounds **2** and **3** have proven to be useful building blocks for the preparation of new macrocycles and cryptands containing the ferrocene unit. [5]-Ferrocenophane **2** underwent intramolecular aza-Wittig reaction by the action of *n*- Bu_3P at room temperature to give the cryptand **4** in 55% yield. The unusual structure of **4**, which can be considered either as a [5]-ferrocenophane bearing a 2,4-bridged dihydroquinoline ring or [4](2,4)-quinolinophane containing a 1,1'-disubstituted ferrocene bridge, was deduced from NMR spectroscopic data as well as mass spectrometry. The ^1H NMR spectrum of **4** clearly

showed the asymmetry of the molecule, showing the two methylene groups as two double doublets and two doublets.⁸ The signals corresponding to the two Cp rings were very illustrative. The ¹H NMR spectrum displayed seven singlets for the eight ring protons and the ¹³C NMR spectrum gave ten signals for the ferrocene carbon atoms.

It is worth noting that the transformation **2**→**4**, involving an intramolecular aza-Wittig reaction, constitutes the first example of the conversion of a ferrocenephane into a cryptand bearing a ferrocene moiety and also shows the applicability of this reaction for forming strained carbon–nitrogen double bonds.⁹

On the other hand, the Staudinger reaction between the bis(azide) **3** and 1,2-bis(diphenylphosphino)ethane in dry dichloromethane at room temperature afforded the 18-membered macrocycle **5** in 20% yield after chromatographic purification. The *syn* spatial arrangement in compound **5** is induced by the diphosphine in an optimal manner by the ‘ball bearing’¹⁰ motion of the two Cp rings of the ferrocene unit. The proposed structure **5** was deduced from NMR spectroscopic data (¹H, ¹³C, ³¹P) and m.s. in FAB mode. The ¹H and ¹³C NMR spectra of **5** do not show significant differences with respect to the precursor bis(azide) **3** and the resonances corresponding to the diphosphine framework are in good agreement with the proposed structure. Macrocycle **5** could be of valuable interest for the construction of heterobimetallic ferrocene-based complexes because the iminophosphorane group has demonstrated its versatility towards forming M–N bonds to transition metals.¹¹

Bis(azide) **3** was converted in 30% yield into the 1,1'-bis(2-indolylcarbonyl)ferrocene **6** by heating at reflux temperature in a mixture of toluene:*o*-xylene (1:1). All attempts to improve the yield of **6** by changing the solvent and reaction time failed.

The ¹H and ¹³C NMR spectra of **6** clearly revealed that the top and bottom parts of the molecule are magnetically inequivalent. The ¹H NMR spectrum showed two distinct N–H resonances at 9.63 and 7.79 ppm, respectively, and in the ferrocene region appeared four broad singlets at δ =5.10, 4.95, 4.63 and 4.52 ppm (2:2:2:2) respectively, due to the α , α' , β and β' protons¹² in contrast to the N–H signal at 9.60 ppm and the two triplets at δ =5.15 and 4.63 ppm exhibited by the 2-ferrocenylcarbonyl indole.^{3d} The ¹³C NMR spectrum also displayed two sets of signals for all carbon atoms, one of them being identical to the observed one in the above-mentioned ferrocene derivative. The IR spectrum also showed two strong absorption bands due to the carbonyl groups.

All the data indicate intramolecular hydrogen bonding between the carbonyl group of one substituent and the N–H group of the opposing one as suggested by the structural drawing **6**. In addition, as the substituents possess π -stacking interaction sites, they could act simultaneously to give **6** a highly ordered conformation. This kind of interaction has been found in 1,1'-bis(azaaryl)-substituted ferrocenes^{12,13} and bis(amino acid)derivatives of 1,1'-ferrocenedicarboxylic acid,¹⁴ and has been successfully used for nucleobase recognition.¹⁵

In conclusion, we have prepared a new class of macrocycle and cryptand bearing a 1,1'-disubstituted ferrocene moiety from the condensation product between 1,1'-diacetylferrocene and *o*-azidobenzaldehyde. The electrochemical study of these products is in progress as well as an examination of their potential ability for cation recognition and formation of heterobimetallic complexes.

Acknowledgements

We gratefully acknowledge the financial support of DGES (PB95-1019). J.L.L. also thanks the Fundación Séneca (CARM) for a studentship.

References

1. Constable, E. C. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 407–408. Beer, P. D. *Adv. Inorg. Chem.* **1992**, *39*, 79–157. Medina, J. C.; Goodnow, T. T.; Rojas, M. T.; Atwood, J. L.; Lynn, B. C.; Kaifer, A. E.; Gokel, G. W. *J. Am. Chem. Soc.* **1992**, *114*, 10583–10595. Delavaux-Nicot, B.; Guari, Y.; Douziech, B.; Mathieu, R. *J. Chem. Soc., Chem. Commun.* **1995**, 585–587. Beer, P. D.; Graydon, A. R.; Sutton, L. R. *Polyhedron* **1996**, *15*, 2457–2461. Beer, P. D.; Szenes, F.; Balzani, V.; Sala, C. M.; Drew, M. G. B.; Dent, S. W.; Maestri, M. *J. Am. Chem. Soc.* **1997**, *119*, 11864–11875. Chesney, A.; Bryce, M. R.; Batsanov, A. S.; Howard, J. A. K.; Goldenberg, L. M. *Chem. Commun.* **1998**, 677–678.
2. Delavaux-Nicot, B.; Fery-Forgues, S. *Eur. J. Inorg. Chem.* **1999**, 1821–1825.
3. (a) Molina, P.; Pastor, A.; Vilaplana, M. J.; Ramírez de Arellano, M. C. *Tetrahedron Lett.* **1996**, *37*, 7829–7832. (b) Molina, P.; Pastor, A.; Vilaplana, M. J.; Velasco, M. D.; Ramírez de Arellano, M. C. *Organometallics* **1997**, *16*, 5836–5843. (c) Molina, P.; Tárraga, A.; Curiel, D.; Ramirez de Arellano, M.C. *Tetrahedron* **1999**, *55*, 1417–1426. (d) Molina, P.; Tárraga, A.; López, J. L.; Martínez, J. C. *J. Organomet. Chem.* **1999**, *584*, 147–158. (e) Tárraga, A.; Molina, P.; Curiel, D.; López, J. L.; Velasco, M. D. *Tetrahedron* **1999**, *55*, 14701–14718.
4. Winstead, J. A. *J. Org. Chem.* **1972**, *37*, 1271–1272.
5. Fuchs, B.; Fröhlich, R.; Musso, H. *Chem. Ber.* **1985**, *118*, 1968–1982.
6. Hillman, M.; Fujita, E.; Dauplaise, H.; Kuick, A.; Kerber, R. C. *Organometallics* **1984**, *3*, 1170–1177.
7. Luke, W. D.; Streitwieser Jr., A. *J. Am. Chem. Soc.* **1981**, *103*, 3241–3243.
8. Characterization data: ^1H NMR (300 MHz, CDCl_3) δ 2.26 (dd, 1H, $J=13.5$ Hz, $J=6.6$ Hz), 2.60 (dd, 1H, $J=14.7$ Hz, $J=5.1$ Hz), 3.00 (d, 1H, $J=14.7$ Hz), 3.10 (d, 1H, $J=13.5$ Hz), 3.46–3.53 (m, 1H), 4.41 (bs, 2H, Cp), 4.60 (s, 1H, Cp), 4.65 (s, 1H, Cp), 4.8 (s, 1H, Cp), 4.90 (bs, 2H, Cp), 5.31 (s, 1H, Cp), 7.90–7.11 (m, 2H), 7.25–7.33 (m, 2H); ^{13}C NMR (50 MHz, CDCl_3) δ 29.9 (CH_2), 35.3 (CH_2), 41.6 (CH), 66.7 (CH), 62.3 (CH), 70.8 (CH), 72.1 (CH), 72.9 (CH), 74.0 (CH), 74.4 (CH), 75.3 (q, C_{ipso} Fc), 83.7 (q, C_{ipso} Fc), 125.6 (CH), 125.8 (CH), 126.5 (CH), 128.2 (CH), 131.5 (q), 143.05 (q), 169.1 (C=N), 207.6 (C=O); MS (EI) m/z (%): 355 (M^+ , 100), 353 (13), 312 (18), 248 (51), 222 (16), 164 (15).
9. Sasaki, T.; Eguchi, S.; Okano, T. *J. Am. Chem. Soc.* **1983**, *105*, 5912–5913. Kanomata, N.; Nitta, M. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1119–1126.
10. Medina, J. C.; Li, C.; Bott, S. G.; Atwood, J. L.; Gokel, G. W. *J. Am. Chem. Soc.* **1991**, *113*, 366–367.
11. Molina, P.; Arques, A.; García, A.; Ramírez de Arellano, M.C. *Eur. J. Inorg. Chem.* **1998**, 1359–1368.
12. Saweczko, P.; Kraatz, M.B. *Coordination Chem. Rev.* **1999**, *190–192*, 185–198.
13. Gelin, F.; Thummel, R. P. *J. Org. Chem.* **1992**, *57*, 3780–3783.
14. Merrick, R. S.; Jarret, R. M.; Curran, T. P.; Dragoli, D. R.; Flaherty, M. B.; Lindyberg, S. E.; Slate, R. A.; Thornton, L. *Tetrahedron Lett.* **1996**, *37*, 5289–5292.
15. Onouye, M.; Hyodo, Y.; Nakazumi, H. *J. Org. Chem.* **1999**, *64*, 2704–2710.