Tetrahedron Letters No. 51, pp 5217 - 5220, 1972. Pergamon Press. Printed in Great Britain.

FUNDAMENTAL STUDIES IN SUBSTITUTED FERROCENE SYSTEM. V
ORIENTATION IN ELECTROPHILIC SUBSTITUTION OF METHOXYFERROCENE

D. W. Slocum and C. R. Ernst

Department of Chemistry and Biochemistry
Southern Illinois University
Carbondale, Illinois 62901

(Received in USA 3 July 1972; received in UK for publication 14 November 1972)

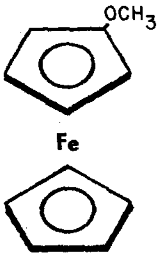
During our investigation of electronic effects in substituted ferrocenes[1], inconsistencies in literature reports of electrophilic site reactivities for methoxyferrocene (1) and related compounds have come to our attention. We wish to demonstrate herein that these contradictions have arisen because of incorrect assignments of the homoannular proton resonances in the pmr spectrum of methoxyferrocene and that surprising consistency actually exists among the data in this area.

The Table summarizes the site reactivities for methoxyferrocene, phenylferrocene and p-methoxyphenylferrocene recorded in the literature. Electrophilic substitution studies of Pauson and co-workers[2,3] indicate a greater reactivity for methoxyferrocene at the 2,5-positions. Such findings were in accordance with the activating effect of the methoxy group at the 2,5-positions in p-methoxyphenylferrocene observed by Rosenblum[5].

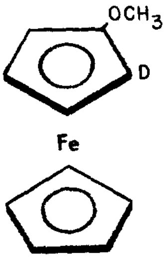
TABLE

Substituted Ferrocene	Relative Site Reactivity Position			Type of Reaction	Reference
	2	3	1'		
Methoxyferrocene	1.6	1.0	0.43	Aminomethylation	2,3
Methoxyferrocene	1.0	1.6	0.71	D-H Exchange	4
Phenylferrocene	1.64	1.00	2.13	Acetylation	5
p-Methoxyphenylferrocene	1.94	1.00	1.68	Acetylation	5

However, electrophilic D-H exchange data for methoxyferrocene has recently become available[4] indicating a greater rate of exchange at the 3,4-positions as compared to the 2,5-positions. The authors of this study commented that such observations were at variance with the site reactivities obtained by Pauson[2,3] and attributed these differences to the low accuracy of their experimental technique. Deuterium incorporation at the various positions in the D-H exchange study was analyzed by relative integration of the respective proton resonances in the pmr spectra of the recovered methoxyferrocene. Assignments of the resonances in the spectrum of methoxyferrocene utilized in the investigation of Kursanov et al placed the 2,5-position proton resonance at higher field strength (δ 3.69 ppm) than that of the 3,4-position protons (δ 3.95 ppm). These assignments were based on tentative literature assignments known at that time.[6,7]



1



2

Continuing nmr spectral studies in these laboratories of monosubstituted ferrocene derivatives have not yielded unequivocal demonstration that previous assignments[6,7] for the homoannular ring proton resonances of ferrocenes containing strong electron-donating groups are in error.[8,9] Contrary to initial assignments, the 3,4-position protons resonate at higher field than the 2,5-position protons. Our assignments are based on the comparative pmr spectra of methoxyferrocene and a specifically deuterated methoxyferrocene. The deuteromethoxyferrocene was prepared by a metalation-deuteration technique[9] which has recently been demonstrated to produce the 2-deutero derivative(2). Chemical shift assignments for the resonances in methoxyferrocene recorded at 100 MHz are: (CCl_4) δ3.52 ppm (3.0 proton singlet, $-OCH_3$), δ3.68 ppm (2.0 proton triplet, $H_{3,4}$), δ3.94 ppm (2.0 proton triplet, $H_{2,5}$)* and δ 4.03 ppm (5.0 proton singlet, C_5H_5 ring). The enhanced shielding of the 3,4-position protons in methoxyferrocene parallels the observed shielding trends in the spectra of other ferrocenes containing electron donating substituents such as amino[8], urethanyl[8] and alkyl[10] groups.

It is to be concluded that the assignments of the substituted ring protons of methoxyferrocene are reversed from that used in the D-H exchange study of Kursanov and coworkers.[4] This reassignment now allows reversal of the site reactivities of the 2,5- and 3,4-positions of methoxyferrocene in this same study(row two of the Table). This corrected data correlates exactly with electrophilic site reactivities observed by Pauson and co-workers[2,3] and brings unanimity to the data supporting activation towards electrophilic substitution of the 2,5-positions of ferrocene by the methoxy group.

It is of special interest to note that the relative ordering of shielding at the various positions in the spectrum of methoxyferrocene does not parallel the observed order of electrophilic site reactivity at these same positions. Rosenblum and Howells have formulated valance bond transition state structures and have calculated localization energies on model compounds which predict an activating effect toward electrophilic substitution at the 2-position for ferrocenes containing electron-donating groups.[5] On the other hand π-electron density calculations are lacking for the ferrocene system, pmr chemical shift shielding values providing the only estimate of electron density available at present. In so far as proton shielding values provide true estimation of electron density distribution in substituted ferrocenes, the ferrocene system parallels five-membered heterocyclic systems in that it exhibits a lack of correlation between electrophilic site reactivity and electron density.[11]

*This resonance attenuated by 1.0 proton in the 2-deuterated sample of methoxyferrocene.

Acknowledgment:

Support of this research by the Office of Research and Projects, Southern Illinois University, Carbondale, Illinois, is gratefully acknowledged.

1. For reviews cf. D. W. Slocum and C. R. Ernst, Organomet. Chem. Revs. A., 6 (1970) 337; D. W. Slocum and C. R. Ernst in "Advances in Organometallic Chemistry", v. 10, F.G.A. Stone and R. West, eds., Academic Press, New York, N.Y. (1972) pp. 79-114.
2. P. L. Pauson, G. R. Knox and I. G. Morrison, J. Chem. Soc. C, 1847 (1967).
3. P. L. Pauson, G. R. Knox, I. G. Morrison, M. A. Sandha and W. E. Watts, J. Chem. Soc. C, 1843 (1967).
4. D. N. Kursanov, V. N. Setkina, E. I. Fedin, M. N. Nefidova and A. I. Khatami, Dokl. Akad. Nauk. SSSR, 192, 339 (1970).
5. M. Rosenblum and W. G. Howells, J. Am. Chem. Soc., 84, 1167 (1962).
6. G. G. Dvoryantseva, S. L. Portnova, K. I. Grandberg, S. R. Gubin and Y. N. Sheinker, Dokl. Akad. Nauk SSSR, 160, 1075 (1965).
7. G. G. Dvoryantseva, Y. N. Sheinker and S. P. Gubin, Peaks. Sposobnost. Org. Soedin, Tartu. Gos. Univ., 3, 86 (1966); Chem. Abst. 68, 110006(1968).
8. D. W. Slocum, P. S. Shenkin, T. R. Engelmann and C. R. Ernst, Tetrahedron Lett.,4429 (1971).
9. D. W. Slocum, B. P. Koonsvitsky and C. R. Ernst, J. Organomet. Chem., 38, 125 (1972).
10. D. W. Slocum, W. E. Jones and C. R. Ernst, J. Org. Chem., 37, 0000 (1972).
11. R. H. Acheson, "An Introduction to the Chemistry of Heterocyclic Compounds," Interscience, New York, N.Y. (1967) pp 65 and 211.