A Theoretical Study on (η^5-C$_5$H$_5$)Fe(CO)(PPh$_3$)(C(O)CHMe) Anion Structure and Stereoselectivity

by V. Anisimov[1], E. Bartnicka[2], A. Dybała-Defratyka[3] and P. Paneth[3*]

[1]*FQS-Poland, Cracow, Poland*
[2]*Department of Chemistry, University of Minnesota, 207 Pleasant, Minneapolis, MN 55414, USA*
[3]*Institute of Applied Radiation Chemistry, Zeromskiego 116,
Technical University of Lodz, 90-924 Lodz, Poland*

Organometallic systems provide an exceptional tool in the stereoselective synthesis. The source of this selectivity, however, frequently remains a challenging question. In recent years, theoretical studies of mechanisms of organometallic and metalloprotein catalysis have received considerable attention. The density functional theory (DFT) methods have been shown to be very successful in these studies. Their application, however, is still limited by the performance of the present computers. As the result, a new class of methods, which employ quantum mechanical calculations combined with either semiempirical and/or molecular mechanics levels (QM/MM), has been developed. This stimulated development of a number of new semiempirical methods, which can handle metals. We present a comparison of a few of these new methods with the DFT level on the example of the acetyliron. In addition, the DFT calculations are used to shed some light on the mechanism of the stereospecific catalysis by acetyliron.

Key words: theoretical calculations, DFT, semiempirical

Recent advances in computational chemistry increased our ability to study mechanisms of biochemical reactions. Part of this effort is directed [1] toward proteins containing metal atoms in the active site, usually coming from a coenzyme such as cytochrome P450, chlorophylls, or vitamin B$_{12}$ to name a few. Density functional theory (DFT) methods have been found to give satisfactory description [2] of such metal centers but their use is limited, by the performance of the present computers, to models comprising less than 50–60 atoms. Notably, the DFT optimization of the whole vitamin B$_{12}$ has been reported [3] recently. In order to address computationally larger systems several approaches, such as divide-and-concur and MOZYME [4], have been developed. The most promising approach of recent years seems to be the treatment of different parts of a system at a different theory level, generally referred to as QM/MM (quantum mechanics/molecular mechanics) methods. Among these methods several schemes, such as ONIOM [5], take advantage of the speed of the

---

*Author for correspondence.

semiempirical calculations by using them in the high (QM/MM), middle (QM/QM/MM) or lower (QM/QM) levels. Because of the success of the QM/MM approach there is a growing demand for semiempirical methods reliably describing organometallic compounds. In this study we have carried out calculations using three available methods, namely PM3(tm) [6], AM1/d [7], and SAM1 [8] and compared them to the DFT results.

Acetyliron, $(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)(C(O)Et)$, is an important catalyst in organic synthesis. Deprotonation of the acetyl ligand with butyllithium opens the possibility of high-yield reactions with alkylating and arylating agents [9], carbonyl compounds [10], epoxides [11], sugar epoxides [12], sugar aldehydes [13], nitrones and imines [14]. Substantial stereoselectivity of this reactant has been reported [15]. Based on the crystal structure of the neutral form, it has been postulated [16] that the source of this specificity comes from stacking of the enolate over one of the phenyl rings as illustrated in Figure 1. This stacking prevents an attack from underneath of the enolate.
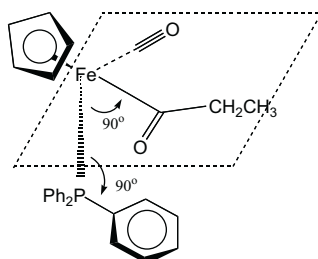

Figure 1. Proposed stacking of the phenyl ring with the acetyl ligand in the $(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)(C(O)Et)$ complex.

In quest for finding semiempirical methodology adequate for the treatment of organometallics we have studied geometry of the title complex, acetyliron, using several methods capable of treating metals. The anion of this complex has been chosen for several reasons. Firstly, each ligand on iron belongs to a different class of organic molecules what puts the theoretical methods to a severe test. Secondly, the moiety in question being an anion makes computational effort even more demanding and because it is short-lived intermediate, not amenable to direct experimental scrutiny. Thus, our results provide new insight into metallorganic catalysis. Thirdly, the structure of stable analogs has been published [17,18], which allows for comparison of semiempirical results not only to DFT calculations but, indirectly, to experimental results as well. Finally, the title anion is a precursor in the stereoselective synthesis. The theory for its stereoselectivity has been postulated [16]. Thus, the calculations presented here can be use to test this theory.

COMPUTATIONAL METHODS

All DFT calculations were performed using the Becke B88 exchange functional [19] combined with the Perdew and Wang PW91 correlation functional [20] (BPW91) functional and the DZVP2 basis set of Salahub and Andzelm [21] optimized for the DFT calculations, as implemented in Dgauss [22] program of the the Cache packet [23]. AM1/d calculations were performed using the WinMopac program [24]. For iron the newly developed AM1/d set of parameters was used [25] with standard AM1 parameters [26] for all other atoms. SAM1 Hamiltonian implemented in the Ampac package [27] was used. The original PM3(tm) Hamiltonian includes not only d-orbitals for metal atoms but also additional energy term, which prevents hydrogen atoms from coming too close together. This Hamiltonian is implemented in the Spartan program [6]. The additional energy term may be revoked, in which case calculations are similar to those described above for AM1/d, *e.g.*, PM3(tm) parameters are used for iron and standard PM3 parameters [28] for all other atoms as implemented in Hyperchem [29]. Both implementations of the PM3(tm) method have been tested. In order to distinguish between them we call the latter PM3tm-HCH. All calculations used default convergence criteria, with gradient being about 0.1 kcal/mol/Å. Fitting analysis was performed using Hyperchem.

RESULTS AND DISCUSSION

We have addressed the question of stereospecificity of the acetyliron using the computational approach. The calculations have been performed in the gas phase, which usually give satisfactory results for nonpolar solvents (THF in the present case). First, we have optimized the geometry of the neutral acetyliron using the DFT-BPW91 functional and the DZVP2 basis. In Table 1 geometrical parameters obtained in our calculations are compared with the reported crystallographic and molecular modeling (MM) results [30]. As can be seen, the computational results are in agreement with the experimental data for the bond lengths and the valence angles. Also the torsional angles are in very good agreement with the experiment although data for only three torsional angles was available. The structure of the DFT-optimized neutral acetyliron is illustrated in Figure 1, in which hydrogen atoms have been omitted for clarity. These results indicate that there is no stacking of a phenyl ring with the acetyl substituent. Stacking requires two valence angles C_{ac}–Fe–P and C_{Ph}–P–Fe to be close to 90 degrees as indicated in Figure 1. We have found the C_{ac}–Fe–P angle to be 91 degrees but the particular C_{Ph}–P–Fe angle, to phenyl ring, which can be involved in stacking [31], is much larger, 118 degrees. It seems possible, that the stacking is enforced by the packing in the crystalline form but is not present in the solution.

There are numerous examples in literature of the successful modeling of organometallic compounds using the DFT methods [32]. The excellent agreement between the theoretical and experimental geometrical parameters for the neutral compound (Figure 2) confirms that the BPW91 functional is very useful in such studies. We have, therefore, used the same theory level (BPW91/DZVP2) in calculations of the structure of (η⁵-C₅H₅)Fe(CO)(PPh₃)(C(O)CHMe) anion, which is short-lived intermediate in synthesis, not amenable to direct structural analysis. The results are listed in the first column of Table 2. Structures of the anion and the neutral molecule do not differ significantly.

Table 1. Comparison of the basic geometric parameters of the (η^5-C$_5$H$_5$-R,R′)Fe(CO)(PPh$_3$)(C(O)R″) complex obtained from the X-ray, MM, and DFT calculations.

	X-ray		MM	BPW91/DZVP2
	R=R″=Me, R′=Ph[17]	R=R′=H, R″=CH$_2$Sme[18]		R=R′=H, R″=Et
bond lengths[a]				
Fe–P	2.216	2.199	2.20	2.220
Fe–C$_{CO}$	1.700	1.733	1.85	1.731
Fe–C$_{acyl}$	1.964	1.964	2.05	1.970
av. Fe–C$_{Cp}$[b]	2.136	2.118		2.135
av. P–C$_{Ph}$	1.844	1.839		1.858
C≡O$_{CO}$		1.167		1.189
valence angles				
C$_{CO}$–Fe–C$_{acyl}$	92.4	93.4	100.5	95.2
C$_{CO}$–Fe–P	94.6	92.4	88.6	93.3
C$_{acyl}$–Fe–P	90.6	91.1	92.8	90.7
O≡C–Fe	178.1	177.5		174.9
O=C$_{acyl}$–Fe	122.0	124.8		122.4
av. C$_{Ph}$–P–Fe	115.8	115.8		115.9
torsional angles				
Fe–P–(C–C)$_{Ph1}$		−56.2	−55.7	−59.6
Fe–P–(C–C)$_{Ph2}$		−53.1	−67.4	−59.4
Fe–P–(C–C)$_{Ph3}$		−23.0	−35.1	−15.5

[a]Bond lengths in Å, valence and torsional angles in degrees.
[b]C$_p$ denotes the cyclopentadienyl ring.
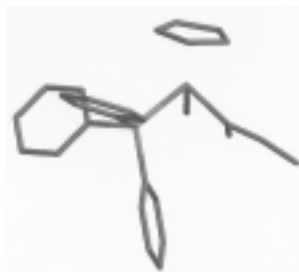
Figure 2. Geometry of the (η^5-C$_5$H$_5$)Fe(CO)(PPh$_3$)(C(O)CHMe) from the BPW91/DZVP2 calculations.

The main changes occur in acetyl ligand as the result of the deprotonation and include elongation of the C–O bond from 1.240 Å typical for the double bond to 1.283 Å and shortening of the C–C bond from 1.541 Å typical for the single bond to 1.387 Å. These changes are consistent with the formation of an enolate. As the result the distance between phosphorus atom and acetyl oxygen changes from 3.293 Å to 2.986 Å and is consistent with the significant negative charge build-up on the oxygen atom. In addition to these changes, cyclopentadienyl ring moves toward the acetyl ligand by about 0.2 Å, and the phenyl ring, which could be involved in the putative stacking, is

rotated out of the plane parallel to the acetyl plane by about 30 degrees. The C_{ac}–Fe–P angle is 88 degrees but the C_{Ph}–P–Fe angle increases to 122 degrees. Thus, stacking in the anion is even less probable than in the neutral compound and thus, stereo-selectivity must originate in some other geometrical feature. Upon deprotonation the C_p ring shifts toward the enolate moiety and one of the hydrogens of this ring is in the same distance from the enolate carbon as one of the hydrogen atoms of the phenyl rings. From the inspection of the optimized structure of the anion it is not obvious what causes the observed stereospecificity. It may be caused by the phenyl ring acting as a bulky substituent. If this was the case, however, a substantial specificity should not be expected. It should be noted that we have performed gas-phase calculations. Specific interactions with solvent molecules in the liquid phase may play a role in the stereospecificity of acetyliron. Much more computationally intense studies would be required to address this question, and they are beyond the scope of the present study.

Table 2. Comparison of calculated basic geometric parameters of the (η⁵-C₅H₅)Fe(CO)(PPh₃)(C(O)CHMe) anion.

	BPW91/DZVP2	AM1/d	SAM1	PM3(tm)	PM3tm-HCH
bond lengths and interatomic distances[a]					
Fe–P	2.262	2.116	2.451	2.217	2.217
Fe–C_{CO}	1.723	2.740	1.721	1.675	1.676
Fe–C_{acyl}	2.005	1.960	2.009	1.934	1.934
av. Fe–C_{Cp}[b]	2.160	2.342	2.326	2.212	2.214
av. P–C_{Ph}	1.888	1.700	1.903	1.913	1.912
C≡O_{CO}	1.193	1.209	1.209	1.185	1.184
O–C_{acyl}	1.283	1.361	1.428	1.340	1.340
C–C_{acyl}	1.387	1.351	1.370	1.346	1.345
O···Fe	2.979	1.814	1.686	1.875	1.876
valence angles					
C_{CO}–Fe–C_{acyl}	95.9	90.2	88.4	95.7	96.0
C_{CO}–Fe–P	97.0	87.1	90.4	101.2	101.3
C_{acyl}–Fe–P	78.9	73.7	68.1	71.3	71.1
O≡C–Fe	174.0	170.8	175.3	167.1	167.4
O=C_{acyl}–Fe	106.6	102.9	103.7	108.3	108.3
av. C_{Ph}–P–Fe	117.3	113.8	117.3	115.6	115.5
torsional angles					
Fe–P–(C–C)$_{Ph1}$	−164.4	−155.9	−156.2	−156.2	−167.2
Fe–P–(C–C)$_{Ph2}$	−99.0	−141.5	−104.1	−142.9	−133.4
Fe–P–(C–C)$_{Ph3}$	−12.2	−102.2	−14.3	24.2	7.0
RMS fitting					
partial RMS fit[c]	–	0.53	0.48	0.36	0.35
RMS fit	–	1.72	1.35	1.32	1.13

[a]Bond lengths, interatomic distances (marked as ···), and RMS fit in Å, valence and torsional angles in degrees.
[b]Cp denotes the cyclopentadienyl ring.
[c]Partial fitting, see text for details.

Comparison of the semiempirical calculations with the DFT results indicates two major flaws of the semiempirical methods. Firstly, in the acetyl ligand, all semiempirical methods find methyl in *trans* position to oxygen favorable by a few kcal/mol, while the BPW91/DZVP2 calculations indicate that the *cis* isomer is more stable. Secondly, all semiempirical methods significantly overestimate electrostatic interactions between the phosphorus atom and the acetyl oxygen. Consequently, the P–O distance, which is about 3.0 Å in the DFT-optimized structure, is only about 1.8 Å for AM1/d, PM3(tm), and PM3tm-HCH, and even less for SAM1. AM1/d exhibits also problems with phenyl rings planes as indicated by the Fe–P–(C–C)$_{Ph}$ torsional angle of the phenyl closest to acetyl ligand. From Table 2 it is not apparent, which semiempirical method gives geometry closest to this obtained from the DFT calculations. We have quantified this by performing a root mean squared (RMS) fit of the Cartesians coordinates of the semiempirically obtained structures to those obtained by the DFT method. The results for the whole molecule are given in the last line of Table 2. Since torsional position of phenyl rings projects significantly on this fit, we have performed a partial fit listed in Table 2 one row above. In this fit all hydrogen atoms, methyl carbon, and PPh$_3$ were neglected. Thus, the partial fit addresses more directly the quality of this part of the geometry that is close to the iron atom. As can be seen, the trends of both fits are the same and indicate that the PM3(tm) Hamiltonian without the extra H-H energy correction term performs the best for the system studied here. This supports earlier observations that PM3(tm) can frequently provide reliable geometries of organometallic compounds [33], and can be used in QM/MM schemes [34].

CONCLUSIONS

Several conclusions can be drawn from our results. Firstly, the excellent agreement between the theoretical and experimental geometrical parameters for the neutral compound confirms, that the DTF methods, and the BPW91 functional in particular, are very successful in modeling organometallic compounds. Secondly, the origin of the stereospecificity of the (η^5-C$_5$H$_5$)Fe(CO)(PPh$_3$)(C(O)CHMe) anion is not obvious since the proposed stacking with the phenyl ring is not shown by the calculations. Thirdly, comparison of the semiempirical calculations with the results of the DFT calculations indicates that the PM3tm Hamiltonian without an extra H-H energy correction term performs the best for the system studied here.

REFERENCES

1. a) Bersuker I.B., Leong M.K., Boggs J.E. and Pearlman R.S., in Gao J. and Thompson M.A. (Eds.), Combined Quantum Mechanical and Molecular Mechanical Methods, ACS Symp. Ser. 712; ACS; Washington, DC, p. 66; b) Röthlisberger U., in Gao J. and Thompson M.A. (Eds.), Combined Quantum Mechanical and Molecular Mechanical Methods, ACS Symp. Ser. 712; ACS; Washington, DC, p. 264; c) Andruniow T., Zgierski M.Z. and Kozlowski P.M., *Chem. Phys. Lett.,* **331**, 509 (2000); d) Higgins L.A., Korzekwa K.R., Rao S., Shou M. and Jones J.P., *Arch. Biochem. Biophys*., **385**, 220 (2001); e) Dunietz B.D., Beachy M.D., Cao Y., Whittington D.A., Lippard S.J. and Friesner R.A., *J. Am. Chem. Soc.,* **122**, 2828 (2000).
2. a) Hong G., Strajbl M., Wesolowski T.A. and Warshel A., *J. Comput. Chem.*, **21**, 1554 (2000); b) Ogliaro F., Cohen S., Filatov M., Harris N. and Shaik S., *Angew. Chem., Int. Ed.,* **39**, 3851 (2000); c) Dudev T. and Lim C., *J. Am. Chem. Soc.,* **122**, 11146 (2000).
3. Jensen K.P., Sauer S.P.A., Liljefors T. and Norrby P.-O., *Organomet.,* **20**, 550 (2001).
4. a) Stewart J.J.P., *Int. J. Quantum Chem.,* **58**, 133 (1996); b) Daniels A.D., Milliam J.M. and Scuseria G.E., *J. Chem. Phys.,* **107**, 425 (1997); c) Dixon S.L. and Merz K.M., *J. Chem. Phys.,* **107**, 879 (1997).
5. Maseras F. and Morokuma K.J., *Comp. Chem.*, **16**, 1170 (1995).
6. PC Spartan Pro Version 1.0.5, Wavefunction, Inc., Irvine, CA, USA, 2000.
7. Voityuk A.A. and Rosch N., *J . Phys. Chem. A*, **104**, 4089 (2000).
8. a) Dewar M.J.S., Jie C. and Yu G., *Tetrahedron*, **23**, 5003 (1993); b) Holder A.J., Dennington R.D., Jie C. and Yu G., *Tetrahedron*, **50**, 627 (1994).
9. a) Aktogu N., Felkin H., Baird G.J., Davies S.G. and Watts O., *J. Organomet. Chem.,* **262**, 49 (1984); b) Bartnicka E. and Zamojski A., *Polish J. Chem.,* **71**, 1108 (1997); c) Wiśniewski K., Zamojski A. and Rogers R.D., *Tetrahedron*, **54**, 14201 (1998).
10. a) Davies S.G., Dordor-Hedgecock I.M., Warner P., Jones R.H. and Prout K., *J. Organomet. Chem.,* **285**, 213 (1985); b) Liebeskind L.S., Welker M.E. and Fengl R.W., *J. Am. Chem. Soc.,* **108**, 6328 (1986); c) Wiśniewski K. and Zamojski A., *Polish J. Chem.,* **72**, 1937 (1998).
11. Brown S.L., Davies S.G., Warner P., Jones R.H. and Prout K., *J. Chem. Soc., Chem. Commun.,* 1446 (1985).
12. Davies S.G., Kellie H.M. and Polywka R., *Tetrahedron: Asymmetry,* **5**, 2563 (1994).
13. a) Krajewski J.W., Gluziński P., Pakulski Z., Zamojski A., Mishnev A. and Kemme A., *Carbohydr. Res*., **252**, 97 (1994); b) Pakulski Z. and Zamojski A., *Tetrahedron*, **51**, 871 (1995); c) Bartnicka E. and Zamojski A., *Polish J. Chem.,* **72**, 688 (1998).
14. Davies S.G., *Aldrichimica Acta*, **23**, 37 (1990).
15. Brunner H., *Angew. Chem. Int. Ed.,* **38**, 1194 (1999) and references therein.
16. Davis S.G. and Seeman J.I., *Tetrahedron Lett.,* **25**, 1845 (1984).
17. Attig T.G., Teller R.G., Wu S.-M., Bau R. and Wójcicki A., *J. Am. Chem. Soc.,* **101**, 619 (1979).
18. Wiśniewski K., Pakulski Z., Zamojski A. and Sheldrick W.S., *J. Organomet. Chem.,* **523**, 1 (1996).
19. Becke A.D., *Phys. Rev. A,* **38**, 3098 (1988).
20. Perdew J.P, in: Ziesche P. P and Eschrig H. (Eds.), Electronic Structure of Solids '91, Akademie Verlag; Berlin, 1991, page 11.
21. Godbout N., Salahub D.R., Andzelm J. and Wimmer E., *Can. J. Chem*., **70**, 560 (1992).
22. Andzelm J. and Wimmer E., *J. Chem. Phys*., **96**, 1280 (1992).
23. CAChe v4.4, CAChe Group, Fujitsu, Beaverton, OR 97006, USA, 2000.
24. WinMOPAC Version 3.0, Fujitsu Ltd, Tokyo, Japan, 2000.
25. Stewart J.J.P., MOPAC2000, Fujitsu Limited, Tokyo; Japan, 2000.
26. Dewar M. and Thiel W., *J. Am. Chem. Soc*., **99**, 4499 (1997).
27. AMPAC Version 6.55, Semichem, Inc., Shawnee, KS, USA, 1999.
28. Stewart J.J.P., *J. Comp. Chem*., **10**, 209 (1989).
29. HyperChem Release 6.02, Hypercube, Inc., Gainsville, FL, USA, 2000.
30. PC Model 4, Serena Software, Bloomington, IN, USA, 1995.
31. Since only an average value of the three C$_{Ph}$–P–Fe valence angles has been reported in litrerature, we were unable to compare the calculated value to the experimental one.
32. a) Wondimagegn T. and Ghosh A., *J. Phys. Chem. B*, **104**, 10858 (2000); b) Havlin R.H., Godbout N., Salzmann R., Wojdelski M., Arnold W., Schulz C.E. and Oldfield E., *J. Am. Chem. Soc*., **120**, 3144

(1998); c) Boulet P., Buchs M., Chermette H., Daul C., Furet E., Gilardoni F., Rogemond F., Schläpfer C.W. and Weber J., *J. Phys. Chem. A*, **105**, 8999 (2001); d) Stein M., van Lenthe E., Baerends E.J. and Lubitz W., *J. Am. Chem. Soc.*, **123**, 5839 (2001); e) Maestre J.M., Lopez X., Bo C., Poblet J.M. and Casañ-Pastor N., *J. Am. Chem. Soc.*, **123**, 3749 (2001); f) Harvey J.N., *J. Am. Chem. Soc.*, **122**, 12401 (2000); g) Dudev T. and Lim C., *J. Am. Chem. Soc.*, **122,** 11146 (2000); h) Kozlowski P.M., Spiro T.G. and Zgierski M.Z., *J. Phys. Chem. B*, **104**, 10659 (2000); i) Xu X.P. and Au-Yeung S.C.F., *J. Am. Chem. Soc.*, **122**, 6468 (2000); j) Spiro T.G., *J. Phys. Chem. A*, **103**, 1357 (1999).

33. a) Borve K.J., Jensen V.R., Karlsen T., Stovneng J.A. and Swang O., *J. Mol. Model.*, **3**, 193 (1997); b) Dybała-Defratyka A. and Paneth P., *J. Inorg. Biochem.*, **86**, 681 (2001); c) Bosque R. and Maseras F., *J. Comp. Chem.*, **21**, 562 (2000); d) Ibarz A., Ruiz E. and Alvarez S., *J. Chem. Soc. Dalton Trans.*, 1463 (2000).

34. Verdaguer X., Vázquez J., Fuster G., Bernardes-Génisson V., Greene A.E., Moyano A., Perica M.A. and Riera A., *J. Org. Chem.*, **63**, 7037 (1998).