

## Reply to "Comments on a Comparison of AM1 with the Recently Developed PM3 Method"

James J. P. Stewart

*The Frank J. Seiler Research Laboratory, U. S. Air Force Academy, Colorado 80840*

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In the previous comment, Dewar et al. raise objections to my two articles<sup>1,2</sup> on the optimization of parameters for semiempirical methods. As might be expected, I do not agree with some inferences that might reasonably be made from their remarks.

The applications article<sup>2</sup> states explicitly, both in the abstract and in the text, that mixed parameter sets were used for aluminum, phosphorus, and sulfur. The statistical summary gives average values for  $\Delta H_f$  differences for PM3, AM1, (including MNDO/AM1 calculations) and MNDO for all compounds reported, as well as for the same set less all compounds which would have required mixed parameters. Using these data, the accuracy of prediction of  $\Delta H_f$  of "pure" AM1 as well as mixed MNDO/AM1 can be compared with MNDO and to PM3.

From its release in 1985, AMPAC<sup>3</sup> has been maintained and developed<sup>4</sup> by the Dewar research group. AMPAC was the first program containing the AM1 method to be put into the public domain. Until the time PM3 was in press, AMPAC has allowed mixed AM1/MNDO calculations to be done. I regret any misconceptions which may arise from my use of mixed parameter sets. A possible benefit from these two letters is that users of AMPAC and MOPAC will now be more aware of the mixed parameter sets, and the pitfalls involved in their use. Now that Dewar has made available real AM1 phosphorus parameters, and has recently developed AM1 parameters for sulfur, we have recalculated the tables from reference 2. The "correct" AM1 results for phosphorus have been submitted for publication as part of the reference work "MOPAC—A Semiempirical Molecular Orbital Program," by J. J. P. Stewart, ESCOM Science Publishers, Holland, which is expected to be in print in early 1990.

A statistical summary of the results obtained using the new parameters is given in Table I. This is an exact equivalent to the original Table III, except that results for aluminum are not given, and for phosphorus, only 70 of 71 original molecules are represented.

In their letter, Dewar et al. have concentrated on heats of formation as the measure of the value of a method. We can use this quantity to estimate the worth of PM3 relative to AM1. Consider the change in average errors in heats of formation between AM1 and MNDO, and between PM3 and AM1. From the bottom line of Table I, we see that average  $\Delta H_f$  AM1 error is 38.7% less than the equivalent MNDO error, and that the average  $\Delta H_f$  PM3 error is 40.5% less than the equivalent AM1 error. According to this criterion, if PM3 is "only marginally better than AM1," then it follows that AM1 is only marginally better than MNDO. Of course, this is not the case. Heats of formation are a very crude guide to the value of a method. AM1 was intended to correct various errors in MNDO, most specifically the lack of a hydrogen bond. In like manner, PM3 was intended to be a more accurate version of AM1. As is pointed out in the above letter, errors in AM1 heats of formation can amount to hundreds of kcal/mol, in, e.g.,  $\text{FCIO}_3$ ,  $\text{ClF}_5$ ,  $\text{BrF}_5$ , and  $\text{IF}_5$ .

PM3, like AM1, MNDO, and MINDO/3, has good and bad features. The most efficient way to determine the accuracy and applicability of these methods is by reporting the comparison of experimental results, high level ab initio results, or molecular mechanics methods of known high accuracy results, with calculated semiempirical results. Not until a significant number of results have been reported<sup>5</sup> on the application of PM3 to systems which were not used in the parameterization can the usefulness of PM3 as a method be determined. Hopefully, PM3 will be used by researchers who have faith that it will work as well for molecules not reported in reference 2. I will welcome PM3 being subjected to the same extensive, critical evaluation that MINDO/3, MNDO, and AM1 have received.

Other points raised, such as the definition of *major* advance and *marginal* improvement, and the notion that AM1 is in an evolutionary dead-end, are presented from a personal point of view. While I may differ in opinion on these points, I will address only one other fundamental differ-

**Table I.** Statistical analysis of difference between experimental and calculated  $\Delta H_f$ .

Type of compounds	Number of compounds	Averages (unsigned)			Averages (signed)			Root mean square		
		PM3	MNDO	AM1	PM3	MNDO	AM1	PM3	MNDO	AM1
Hydrogen	456	6.2	12.8	7.3	1.5	4.9	-0.1	8.3	24.2	10.4
Carbon	459	6.2	12.8	7.9	1.2	3.5	-0.3	8.7	23.1	11.5
Nitrogen	117	6.5	18.8	9.6	0.6	10.0	13.3	8.3	27.0	12.5
Oxygen	234	9.0	32.4	14.4	-0.1	26.8	4.5	12.9	56.4	25.2
Fluorine	133	8.6	44.4	22.7	0.7	37.4	6.2	11.2	84.2	49.5
Silicon	78	10.1	22.4	14.5	1.9	13.0	3.6	14.2	32.9	20.8
Phosphorus	70	12.4	37.7	19.5	-0.8	25.0	6.4	16.1	55.6	29.1
Sulfur	101	12.0	50.3	23.4	-1.4	36.9	-10.4	16.2	79.8	34.0
Chlorine	93	9.6	24.6	18.8	-0.1	15.1	2.6	13.4	54.1	37.8
Bromine	67	11.4	27.8	23.4	1.5	16.4	6.2	15.5	46.5	39.9
Iodine	73	10.7	29.2	25.7	-0.3	10.9	4.2	15.8	60.7	53.5
Set of Compounds used in references 3 and 4	138	4.4	6.2	5.5	0.0	-1.4	0.7	6.3	9.1	7.3
Compounds of C, H, N, and O, only	276	5.5	11.2	7.5	0.4	3.8	1.4	7.9	18.5	10.5
Nitro compounds	29	5.2	39.6	15.7	2.5	38.1	14.5	6.2	44.1	18.5
Organophosphorus-V compounds	15	10.9	53.9	15.5	3.6	50.2	-4.7	14.3	56.7	17.3
Normal valent compounds	607	7.3	13.1	9.6	0.5	3.1	-0.2	11.2	24.3	14.8
Hypervalent	106	13.6	75.8	37.7	-0.8	67.2	8.9	17.3	104.5	62.3
All compounds	713	8.2	22.5	13.8	0.3	13.8	1.2	11.6	46.2	27.6

ence of opinion. Professor Dewar maintains that "The development of effective models of this kind therefore requires an extensive search of the potential hypersurface, guided by previous experience and chemical intuition."<sup>6</sup> On the other hand, I maintain that, with the completion of the parameter optimization program, "the rate-determining step for parameterizing elements changes from the mechanics of parameterization to the assembling of experimental reference data."<sup>1</sup> While we have these two very different philosophies, Dewar relying on chemical intuition and my relying on mathematics, we have a common goal: to produce improved methods for common application by chemists in support of experimen-

tal research. A healthy competition between the two groups benefits everyone.

## References

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5. See, for example, H. S. Rzepa, M. Yin Yi, *J. Chem. Soc., Chem. Commun.*, 1502 (1989) and P. A. Hunt and H. S. Rzepa, *J. Chem. Soc., Chem. Commun.*, 623 (1989).
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