ORGANIC LETTERS

2007
Vol. 9, No. 10
1851−1854

How Accurate Are DFT Treatments of Organic Energies?

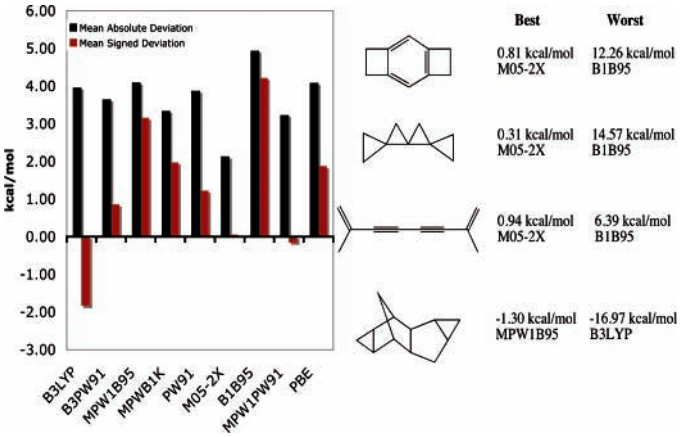
Matthew D. Wodrich,[§] Clémence Corminboeuf,[§] Peter R. Schreiner,[‡] Andrey A. Fokin,[‡] and Paul von Ragué Schleyer*,[§]

Department of Chemistry and Center for Computational Chemistry, University of Georgia, Athens, Georgia 30602, and Institute of Organic Chemistry, Justus-Liebig University Giessen, Heinrich-Buff-Ring 58, 35392 Giessen, Germany

schleyer@chem.uga.edu

Received February 10, 2007

ABSTRACT



Increasing awareness that popular functionals fail to describe many energies accurately has ended expectations of black-box DFT usage. The performance of nine density functionals, compared by computing the bond separation energies of 72 illustrative hydrocarbons with available experimental data, reveals that only Zhao and Truhlar's recently proposed M05-2X functional, with a 2.13 kcal/mol average deviation from experiment, performs satisfactorily. B3LYP and other functionals show larger deviations.

Several papers pointing out failures of density functional theory and highlighting shortcomings regarding energetic descriptions of organic systems are disturbing.[1] The poor performance of B3LYP is particularly alarming because many organic chemists use it as a "black-box" computational tool. Inaccurate predictions of alkane heats of formation,[2] bond energies,[1a−c,3] relative energies,[1d−f,k−m] and molecular geometries[1i,j] are only a few examples of systematic deficiencies. The inability of several DFT functionals to reproduce accurately energy differences of isomeric hydrocarbons with multiple structural features also is troublesome.[1f] Schreiner et al.[1f] noted failures for saturated and small-ring systems and increasing errors with larger molecules. The B3PW91 hybrid functional was claimed to be better than other tested functionals. Nevertheless, the computation of post Hartree−Fock single-point energies on DFT-optimized geometries was

[§] University of Georgia.
[‡] Justus-Liebig University Giessen.

(1) (a) Check, C. E.; Gilbert, T. M. *J. Org. Chem.* **2005**, *70*, 9828. (b) Yao, X.-Q.; Hou, X.-J.; Jiao, H.; Xiang, H.-W.; Li, Y.-W. *J. Phys. Chem. A* **2003**, *107*, 9991. (c) Izgorodina, E. I.; Coote, M. L.; Radom, L. *J. Phys. Chem. A* **2005**, *109*, 7558. (d) Grimme, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 4460. (e) Wodrich, M. D.; Corminboeuf, C.; Schleyer, P. v. R. *Org. Lett.* **2006**, *8*, 3631. (f) Schreiner, P. R.; Fokin, A. A.; Pascal, R. A., Jr.; de Meijere, A. *Org. Lett.* **2006**, *8*, 3635. (g) Zhao, Y.; Truhlar, D. G. *Org. Lett.* **2006**, *8*, 5753. (h) Grimme, S.; Steinmetz, M.; Korth, M. *J. Chem. Theory Comput.* **2007**, *3*, 42. (i) Carlier, P. R.; Deora, N.; Crawford, T. D. *J. Org. Chem.* **2006**, *71*, 1592. (j) Zhao, Y.; Truhlar, D. G. *J. Org. Chem.* **2007**, *72*, 295. (k) Kafafi, S. A. *J. Phys. Chem. A* **1998**, *102*, 10404. (l) Woodcock, H. L.; Schaefer, H. F., III; Schreiner, P. R. *J. Phys. Chem. A* **2002**, *106*, 11923. (m) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2006**, *110*, 10478. (n) Grimme, S.; Steinmetz, M.; Korth, M. *J. Org. Chem.* **2007**, *72*, 2118. (o) Riley, K.; Op't Holt, B. T.; Merz, K. M., Jr. *J. Chem. Theory Comput.* **2007**, *3*, 407.

10.1021/ol070354w CCC: $37.00
Published on Web 04/07/2007

recommended as a reliability check. Responding to the calls for better-performing functionals, Zhao and Truhlar parametrized the exchange and correlation hybrid meta-GGA M05-2X functionals,[4] which reduce the errors in energies of organic systems.[1g] The M05-2X functional has an improved dependence on spin kinetic energy density. This results in a better description of medium-range correlation, a source of error in alkanes identified by Grimme.[1d] DFT failures may also arise from attractive long-range van der Waals (vdW) interaction and self-interaction errors. Grimme et al. recently demonstrated that SCS-MP2[5] (a spin scaled variant of MP2) and the pertubatively corrected density functional, X2-PLYP[6] (X = B or mPW), were very successful in reproducing 34 experimental isomerization energies.[1n] They also called for performance tests of highly parametrized meta-hybrid functionals, such as M05-2X, in general practice. We provide this information here.

Pople's isodesmic bond separation energy (BSE) reactions[7,8] can be used to calculate molecular heats of formation easily. Additionally, BSEs provide a simple way to quantify the performance of the nine density functionals examined here.[9] We chose 72 hydrocarbons (Figure 1) having experimental data (NIST 298K)[10] for this purpose. The Figure 1 set includes diverse structural features, benzene moieties, three-membered rings (3MRs), conjugated or isolated double and triple bonds, cumulenes, and saturated hydrocarbons. The functionals tested are the popular B3LYP,[11] the hybrid B3PW91,[11a,12] Becke's first hybrid meta-GGA (B1B95),[13] two nonempirical GGAs (PBE[14] and PW91[12]), MPW1PW91,[15] as well as Truhlar's recent hybrid meta-GGAs MPW1B95,[13a,16]

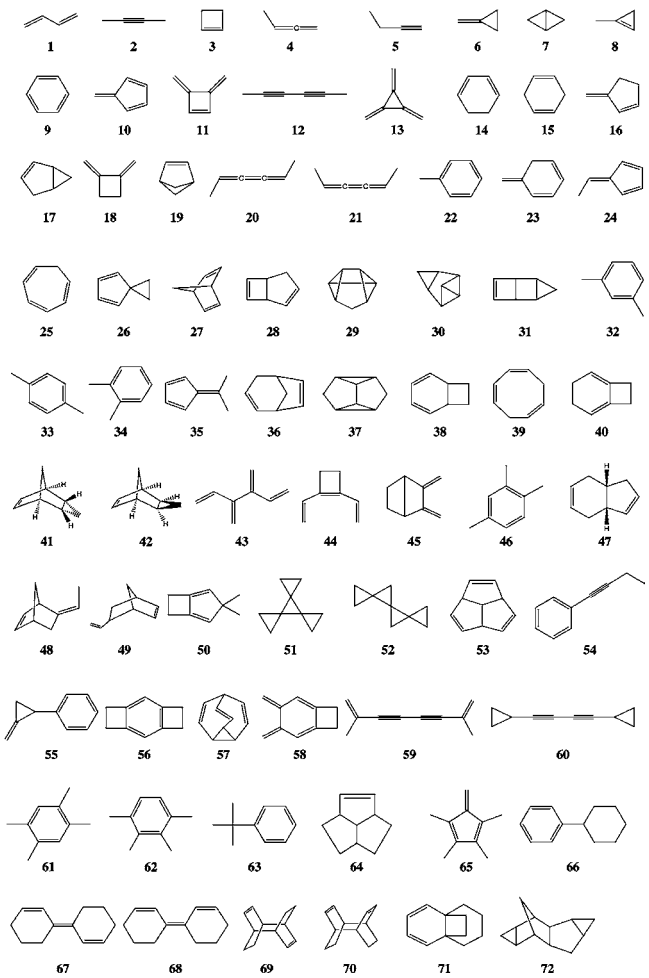


Figure 1. Schematic representation of the 72 hydrocarbons used for density functional testing. An enlargement of this figure is given in the Supporting Information.

MPWB1K,[16] and M05-2X functionals as implemented in the Gaussian 03[17,18] and NWChem 5.0[19] program packages. All calculations employed the 6-311+G(d,p) basis set and include unscaled zero-point energy corrections (see Supporting Information).

Mean absolute deviations (MADs) and mean signed deviations (MSDs) for pertinent sets of molecules help evaluate the functionals. The MAD gives the average unsigned deviation from the experimental BSE for a particular set of compounds, and the MSD assesses systematic errors (i.e., consistent over- or underestimation of the BSE). Deficiencies in the DFT descriptions of particular molecular features identify strengths and weaknesses of each functional. Further improvements in functional performance should re-

(2) (a) Raghavachari, K.; Stefanov, B. B.; Curtiss, L. A. *Mol. Phys.* **1997**, *91*, 555. (b) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **1997**, *106*, 1063. (c) Curtiss, L. A.; Raghavachari, K.; Redfern, P. C.; Pople, J. A. *J. Chem. Phys.* **2000**, *112*, 7374. (d) Saeys, M.; Reyniers, M.-F.; Marin, G. B.; van Speybroeck, V.; Waroquier, J. *J. Phys. Chem. A* **2003**, *107*, 9147.

(3) (a) Feng, Y.; Liu, L.; Wang, J.-T.; Huang, H.; Guo, Q.-X. *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 2005. (b) Fu, Y.; Dong, X. Y.; Wang, Y. M.; Liu, L.; Guo, Q.-X. *Chin. J. Chem.* **2005**, *23*, 474. (c) Coote, M. L.; Pross, A.; Radom, L. In *Fundamental World of Quantum Chemistry*; Brandas, E. J., Kryachko, E. S., Eds.; Kluwer Academic Publishers: The Netherlands, 2004; Vol. III, p 563.

(4) Zhao, Y.; Schultz, N. E.; Truhlar, D. G. *J. Chem. Theory Comput.* **2006**, *2*, 364.

(5) Grimme, S. *J. Chem. Phys.* **2003**, *118*, 9095.

(6) Grimme, S. *J. Chem. Phys.* **2006**, *124*, 034108.

(7) (a) Hehre, W. J.; Ditchfield, R.; Radom, L.; Pople, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 4796. (b) Radom, L.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1971**, *93*, 289. (c) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; John Wiley & Sons: New York, 1986; p 300.

(8) The BSE reactions for all 72 compounds evaluated are given in the Supporting Information.

(9) Small errors in the experimental heats of formation of methane, ethane, ethylene, and acetylene may accumulate and decrease the accuracy of the reference bond separation energies of larger molecules.

(10) Afeefy, H. Y.; Liebman, J. F.; Stein, S. E. Neutral Thermochemical Data. In *NIST Chemistry Webbook, NIST Standard Reference Database Number 69*; Linstrom, P. J., Mallard, W. G., Eds.; National Institute of Standards and Technology: Gaithersburg, MD (http://webbook.nist.gov).

(11) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(12) Perdew, J. P. In *Electronic Structure of Solids '91*; Ziesche, P., Eschig, H., Eds.; Akademie Verlag: Berlin, 1991; p 11.

(13) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098. (b) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040.

(14) Perdew, J. P.; Burke, K.; Ernzerhof, M. *Phys. Rev. Lett.* **1996**, *77*, 3865.

(15) Adamo, C.; Barone, V. *J. Chem. Phys.* **1998**, *108*, 664.

(16) Zhao, Y.; Truhlar, D. G. *J. Phys. Chem. A* **2004**, *108*, 6908.

(17) Frisch, M. J. et al. *Gaussian 03*, revision C.02; Gaussian, Inc.: Wallingford, CT, 2004. Full reference given in Supporting Information.

(18) All computations have made use of the Gaussian 03 program with the exception of the M05-2X functional, which made use of NWChem 5.0.

(19) Bylaska, E. J. et al. *NWChem, A Computational Chemistry Package for Parallel Computers*, version 5.0; Pacific Northwest National Laboratory: Richland, Washington, 2006. Full reference given in Supporting Information.

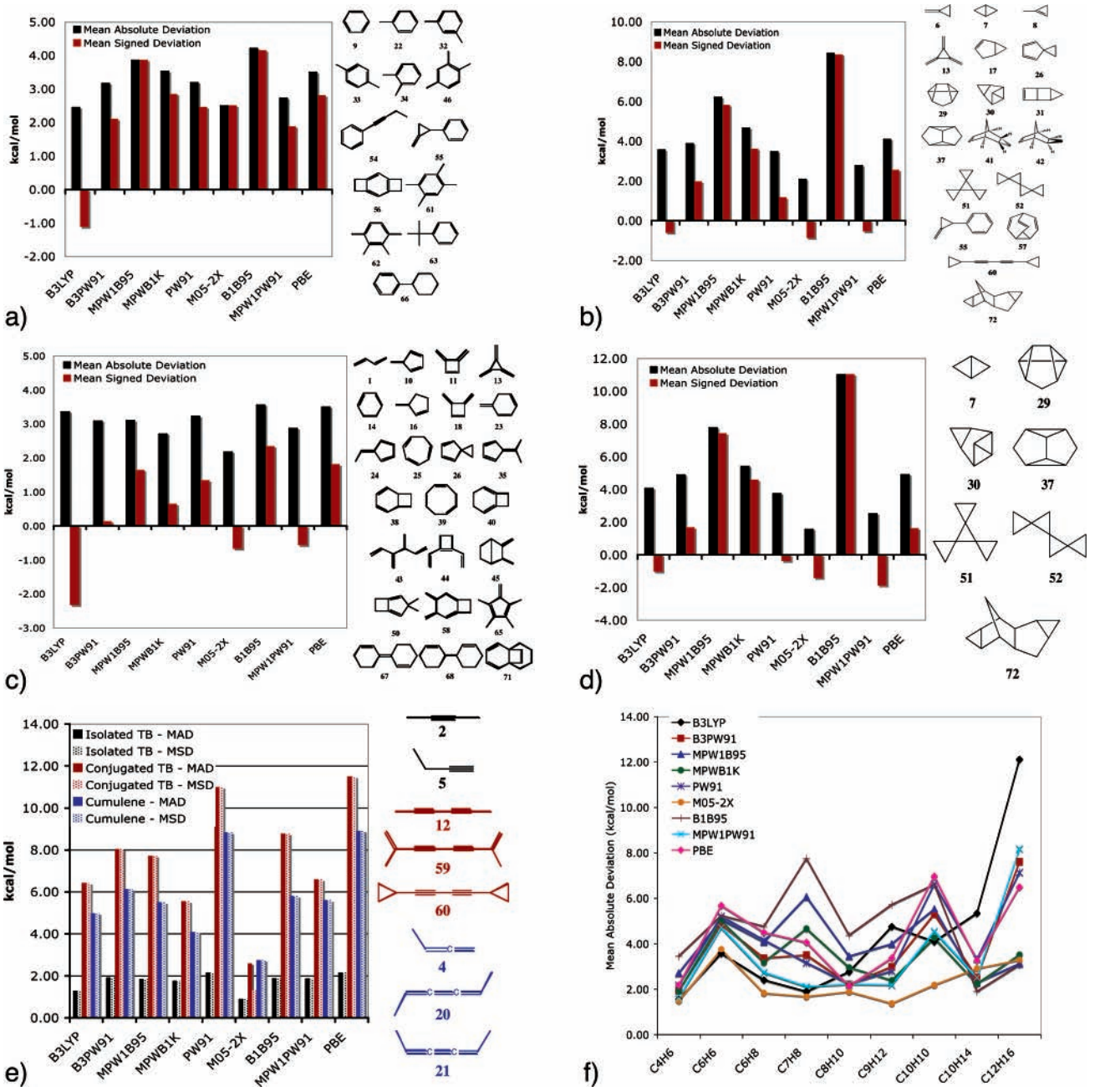


Figure 2. (a−f) Mean absolute and mean signed deviations (in kcal/mol) of compounds containing: a benzene moiety (a), one or more three-membered rings (b), one or more conjugated double bonds (c), complete saturation (d), isolated triple bonds (black), conjugated triple bonds (red), and cumulenes (blue) (e). Mean absolute deviation (in kcal/mol) of increasingly larger molecular systems. Nearly constant errors of most functionals indicate the average deviation does not increase with increasing system size (f).

establish the confidence of chemists toward the use of computational methods to describe the energies of hydrocarbons and other larger organic molecules.[1n]

Benzene Moiety. Thirteen compounds in the Figure 1 set incorporate a benzene ring. Although this aromatic feature is generally well described, substituents can introduce significant errors. For instance, deviations from experiment for the MPW1PW91 functional are 3.9 kcal/mol for an acetylene substituent (**54**), 4.0 kcal/mol for a 2-methylenecyclopropyl (**55**), and 5.6 kcal/mol for fused four-membered rings (**56**); all are significantly higher than the MAD, which is 2.75 kcal/mol for the entire set of 13 compounds. Despite its difficulties describing unsaturated alkyl substituents, B3LYP has the lowest MAD (2.47 kcal/mol, Figure 2a and Supporting Information Table 22). M05-2X and MPW1PW91 also perform satisfactorily. All other tested functionals systematically overestimate the BSEs of molecules containing benzene moieties, judging from their MSDs.

Three-Membered Rings. This structural feature is poorly described overall (Figure 2b and Supporting Information

Table 23). Figure 2b shows the B1B95 and MPW1B95 performance to be the worst; both have large overall and systematic errors. M05-2X matches the experimental BSEs most accurately. However, deviations from experiment for [3]-radialene (M05-2X = −8.76 kcal/mol, B1B95 = −0.72 kcal/mol) and the multistructural compound **72** (M05-2X = −6.52 kcal/mol, B1B95 = 1.77 kcal/mol) are both smaller for the B95 correlation functional and larger for the M05-2X functional.

Double-Bond Conjugation. The 24 conjugated structures include syn and anti configurations as well as cyclic and acyclic units. These features can challenge their theoretical description. The conjugation of double bonds in linear chains (i.e., **1** and **43**) and in monocycles (i.e., **14** and **25**) does not present major difficulties for DFT (the deviations are less than 2 kcal/mol). However, other structural patterns, such as fused cycloalkane rings (**26** and **71**), worsen agreement with the experimental BSE. The overall performance of each functional is still good; M05-2X is best (Figure 2c and Supporting Information Table 24). Note that the M05-2X functional shows a particularly large deviation for **44**, −6.76 kcal/mol, the worst description by any functional.

Saturated Compounds. The failure of density functionals to evaluate the energies of saturated hydrocarbons is now well documented and accepted.[1a,c−g] The BSE performance of most functionals is unsatisfactory (Figure 2d and Supporting Information Table 25). Truhlar's M05-2X is an exception and provides an excellent energetic description for such systems. The MPW1PW91 functional also performs well.

Miscellaneous Structural Features. Whereas isolated triple bonds and hyperconjugation in alkynes are generally described well by DFT, conjugation in cumulenes and polyenes is overestimated strongly (Figure 2e and Supporting Information Tables 26−28). M05-2X overestimates the stabilization in these compounds but still perfoms best. The errors of other functionals are nearly twice as large. Surprisingly, the M05-2X errors for **59** (0.94 kcal/mol) and **60** (−1.94 kcal/mol) are smaller than that for the simplest analogue **12** (4.9 kcal/mol). We attribute this to the cancellation of errors due the overestimation of the conjugation of the triple bonds in **12** and to the underestimation of the other structural patterns present in **59** and **60**.

System Size Effects. Figure 2f illustrates the effect of molecular size on the functional performance. With the exception of B3LYP, which shows a much greater mean absolute deviation for the $C_{12}H_{16}$ stoichiometric group, there is little or no increase in error with increasing system size, unlike the saturated hydrocarbons.[1a,e] Indeed, the C_6H_6 set has the largest MAD for the M05-2X functional. Several functionals show an alternating "zigzag"-like error trend as the system size increases. However, the performance of functionals for systems containing 20 or more carbon atoms has yet to be tested and may potentially show larger deficiencies than the set of small hydrocarbons tested here.

General Performance. The M05-2X functional has the lowest MAD and is nearly free from systematic deviations over the test set of 72 hydrocarbons (TOC Figure). Truhlar's recent hybrid meta-GGA shows large deviations only for specific cases such as [3]-radialene (**13**, −8.8 kcal/mol), 1,2-divinylcyclobutene (**44**, −6.8 kcal/mol), and triquinacene (**53**, −6.0 kcal/mol). However, it should be noted that M05-2X is a highly parametrized functional, resulting in unexpected failures for some hydrocarbons. The B1B95 and MPW1B95 functionals err in describing 3MRs, and the pure GGAs (PBE and PW91) give poor results for cumulenes. B3LYP and B3PW91 compute the largest deviations for saturated structural units. Benzene moieties and, more generally, conjugation in linear chains or monocycles are reproduced well by DFT. However, conjugated triple bonds are problematic. In agreement with a previous report,[1f] we find B3PW91 to be more accurate than B3LYP, albeit marginally for the set of molecules and functionals compared in the present paper.

Finally, it is important to emphasize that the increase in error with increased system size, noted earlier for hydrocarbons using B3LYP,[1f] is *not* found for other functionals (Figure 2f). Instead, their large errors depend on the presence of particular structural and stereoelectronic features. We strongly discourage the uncritical black-box use of older density functionals for computing the energies of organic molecules. The success of the new generation of functionals and the possibility of further improvement in computational methods engender optimism.[1n,4]

Acknowledgment. We acknowledge the Computer Resource Center at the University of Georgia for providing computer time. NSF Grant CHE-0209857 supported this work. C.C. acknowledges the support of the Swiss NSF Grant PA002−115322/1.

Supporting Information Available: Calculated energies, equations, and tabular data evaluating the 72 compounds tested are available. This material is available free of charge via the Internet at http://pubs.acs.org.

OL070354W