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DFT Thermochemical Investigation of Rearrangement for 3-Hydroxy Analogs of 2,3-Dihydrobenzothiophen-2- and -3-ones

Deniz Hür
Anadolu University, Faculty of Science, Department of Chemistry, Eskişehir, Turkey

Abstract

Thermodynamic and kinetic controlled reaction coordinate for the rearrangement of 2-benzotriazol-1-yl-2-alkyl-3-phenyl-2,3-dihydro-benzo[b]thiophen-3-ol derivatives have been predicted by using DFT calculated thermodynamic properties and comparing DFT calculated NMR and IR spectroscopic properties with experimental ones.

Key Words: DFT, thermodynamic, kinetic control, benzotriazole.

INTRODUCTION

2,3-Dihydrobenzothiophene-3-ones have been used for the preparation of tetrahydro-1,2-benzothiazepin-5-ones and 3-vinyl-1,2-benzoisothiazoles [1]. Several methods have been developed for the synthesis of 2,3-dihydrobenzothiophene-3-ones 2a-c in literature [2-6]. Recently, in Katritzky group, we have prepared and described details for preparation of 2-alkyl-2-aryl-substituted 2,3-dihydrobenzothiophen-3-ones 2a-c and 3-alkyl-3-aryl-substituted 2,3-dihydrobenzothiophene-2-ones 3a-c starting from 3-hydroxy analogs 1a-c [7]. During the experimental works, it was found that different reaction conditions leads reaction to different products. In experimental works, X-ray spectroscopy was used for the description of structures. It is also possible to do this by using computational approaches by comparing calculated NMR and IR properties with experimental ones. Over the decades, chemists have used computational approaches to predict reaction mechanisms and termodynamic properties of compounds involved in reactionsn [8-14]. Now, we disclose a computational work to describe thermodynamic behaviour of rearrangement reaction described in Scheme 1 below.

MATERIALS AND METHODS

Detailed preparation and characterisation data for compounds 2a-c and 3a-c have been given in our previously published work [7]. The experimental procedure for the synthesis method and structure of compounds are given in Scheme 1 and the selected experimental NMR and IR data can be seen in Table 1 for selected carbonyl group on compounds. In conclusion; at early stages of experimental work, rearrangement reactions of 1a-c carried out refluxing starting material at 100°C in open vessel in presence of $ZnBr_2$ (method A). Under this condition only 2a-b has been obtained as products. Then, during the optimization of synthetic method, compounds 1a-c were treated with $ZnBr_2$ in sealed tube in THF at 90 to 100°C (method B). These rearrangement reactions were resulted to give mixture of both 2a-c and 3a-c as products.

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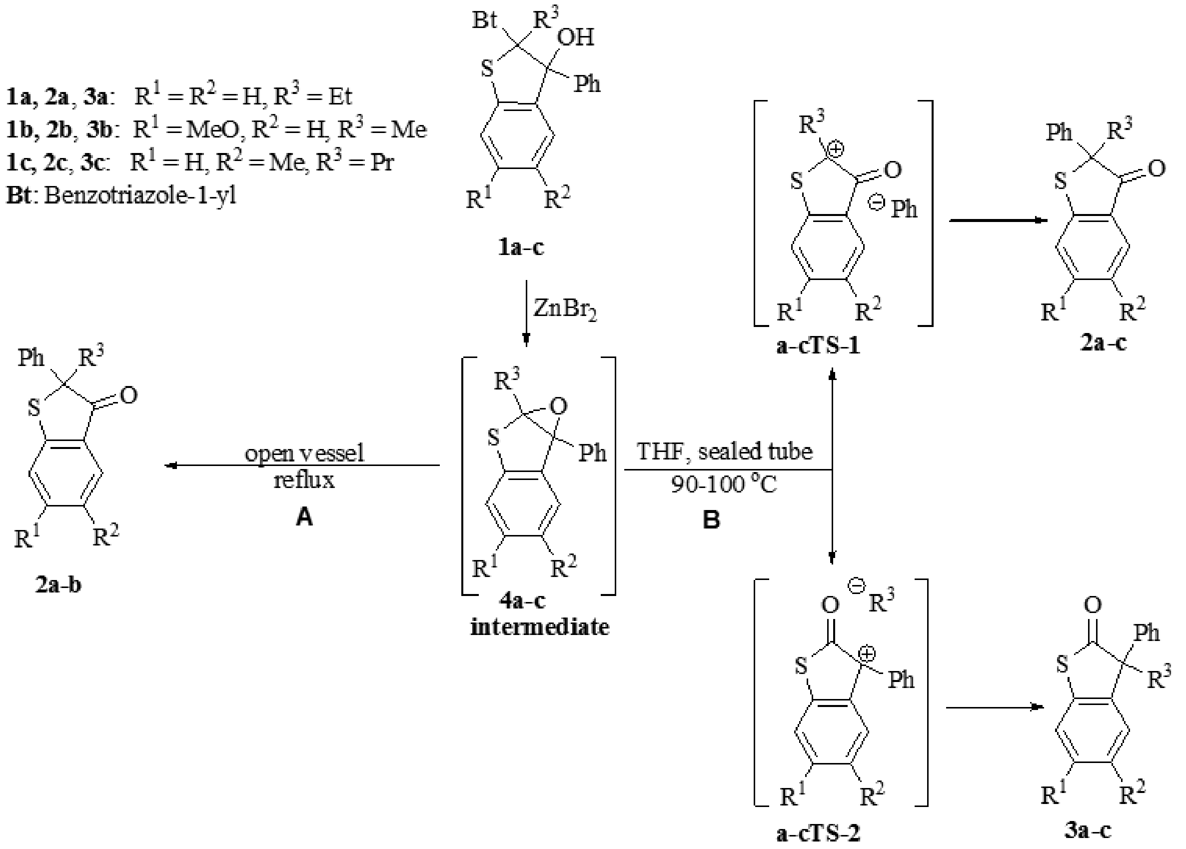
* Correspondence to: Deniz Hür

Anadolu University, Faculty of Science, Department of Chemistry 26470, Eskişehir, Turkey

Tel: +90 222 335 05 80 Fax: +90 222 320 49 10
E-mail: address.dhur@anadolu.edu.tr



Scheme 1. Rearrangement reaction of 3-hydroxy analogs of 2,3-dihydrobenzothiophen-2- and 3-ones.

Because previously published similar work [15]. supported epoxide mechanism by successful isolation of intermediate alkoxyoxiranes, it is suggested that, in our experimental works, after the addition of zinc bromide, compounds 1a-c were also converted to oxiran intermediate 4a-c (Scheme 1).

Computational

Calculations were done using Gaussian03 program package [16] implemented in Pentium 4, 3.20 GHz computer. B3LYP exchange functional hybrid DFT method [17] was used to describe the systems by using the 6-31G(d) [18] basis set. The B3LYP method employs the Becke's three-parameter (B3) gradient-corrected exchange functional along with the gradient-corrected correlation functional of Lee, Yang and Parr (LYP). Global minima and transition structures (TS) in the optimizations were confirmed via frequency calculations. Thermodynamic properties and IR frequencies were calculated using ReadIsotope keyword in Frequency calculations specifying a different temperature and pressure for the reactions. Pressure for the reaction carried out in sealed tube was estimated as 2.8 atm using the Clausius-Clapeyron equation. Solvation was calculated on the optimized geometries utilizing two SCRF models, Onsager [19] method and isodensity polarized continuum model (IPCM) [20] at the B3LYP/6-31G(d) level. In Onsager method, it is assumed that the solute occupies a fixed cavity of radius within the solvent field. The IPCM model, on the other hand, defines the cavity as an isodensity surface of the molecule [21]. The Onsager solvation results were used as a starting point to make convergence faster for the IPCM calculations.

RESULTS AND DISCUSSION

The calculated and experimental NMR and IR data for carbonyl group of 2-ones and 3-ones are given in Table 1. The relative deviation for calculated NMR and IR results from experimental ones are around

7.45% and 4.76%, respectively. These relative deviations show that calculated NMR and IR results are in consistent with experimental ones (Table 1, Figure 1-2). It is expected that NMR shift for carbonyl carbon of compounds 3a-c (2-ones) should be in lower frequencies (higher ppm values) than compounds 2a-c (3-ones) because of thioester carbonyl group in 2-ones. All calculated NMR chemical shifts supported this idea (Table 1, Figure 1). On the other hand, as expected, IR frequencies of carbonyl carbon for 2a-c are lower in frequency than that of 3a-c in both calculated and experimental results (Table 1, Figure 2). All calculated thermo dynamic Gibbs free energies for compounds and transition states, relative activation energies were given below in Table 2.

Table 1. IR and NMR spectroscopic data for compounds 2a-c and 3a-c.

Compound	IR(exp.)[a]	IR(calc.)[b]	NMR(exp.)[c]	NMR(cal.)[d]	IR (RD%)[e]	NMR (RD%)[f]
2a	1701	1773.32	202.7	186.98	4.19	7.75
3a	1712	1802.33	207.4	192.73	5.27	7.07
2b	1694	1767.34	201.2	184.9	4.3	8.1
3b	1707	1800.65	207.4	193.29	5.48	6.8
2c	1696	1764.02	202.7	188.25	4.02	7.12
3c	1711	1801.99	208	191.61	5.3	7.87

[a] Experimental IR frequencies (cm^{-1})

[b] DFT calculated IR frequencies (cm^{-1})

[c] Experimental NMR chemical shifts (ppm)

[d] DFT calculated NMR chemical shifts (ppm)

[e] Relative IR frequency deviation, RD% = [IR(calc.)-IR(exp.)/IR(exp.)].100

[f] Relative NMR shift deviation, RD% = [NMR(calc.)-NMR(exp.)/NMR(exp.)].100

Since $ZnBr_2$ was used as a catalyst for formation of oxiran ring 4a-c and thermodynamic activation energies were calculated between oxiran intermediate and transition structures, we did not take $ZnBr_2$ into account during the calculations. Thus, all calculated activation energies for investigated reactions are described as the energy gap between intermediates 4a-c and transition structures a-cTS-1 and a-cTS-2 which are the transition structure for aryl migration and the transition structure for alkyl migration, respectively.

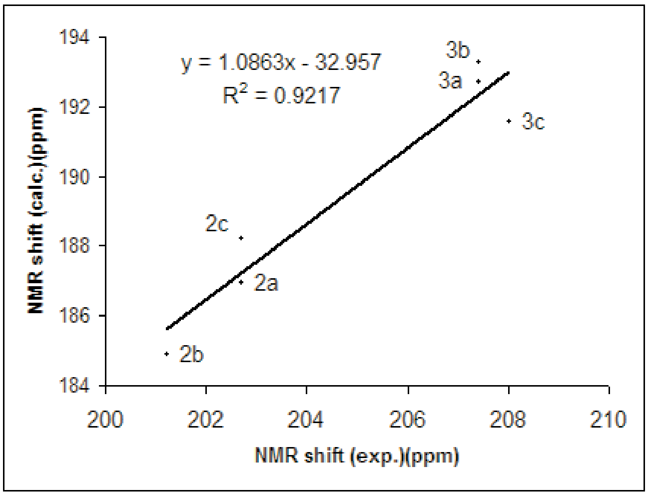


Figure 1. Correlation graph of the experimental versus calculated NMR chemical shifts for the investigated compounds.

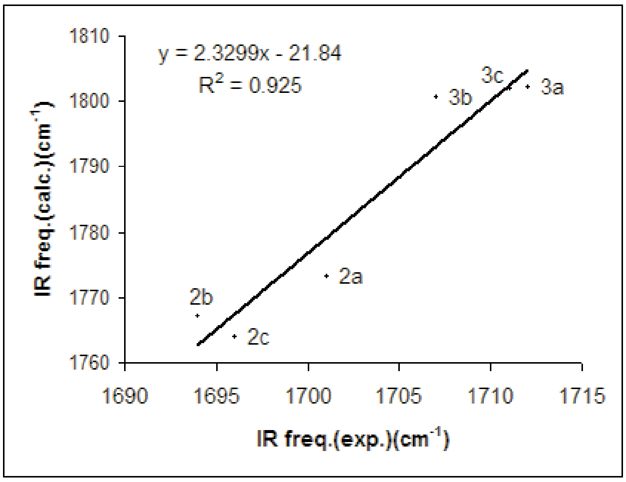


Figure 2. Correlation graph of the experimental versus calculated IR frequencies for the investigated compounds.

The oxiran ring 4a-c disclosed to give two different results in two different conditions: in method A, aryl migration occurred and only compounds 2a-c (3-ones) were observed. On the other hand, in method B, not only aryl migration but also alkyl migration took placed on intermediate 4a-c, thus together with aryl migrated products 2a-c (3-ones), alkyl migrated products 3a-c (2-ones) were also observed. This means that, under harsher conditions (high pressure, sealed tube) the rearrangement reaction has been pushed to alkyl migration. It is well known that aryl migration is much more favorable than alkyl migration.

In our calculations given in Table 2, calculated free energy of a-cTS-1 is lower than a-cTS-2 and activation energy for the formation of 2a-c (aryl migration, 3-ones) is lower than that of 3a-c (alkyl migration, 2-ones). Thus, it is suggested that 2a-c is kinetic controlled and 3a-c is thermodynamic controlled products. Additionally, compared free energy level of products 2a-c and 3a-c has supported this idea (Figure 3).

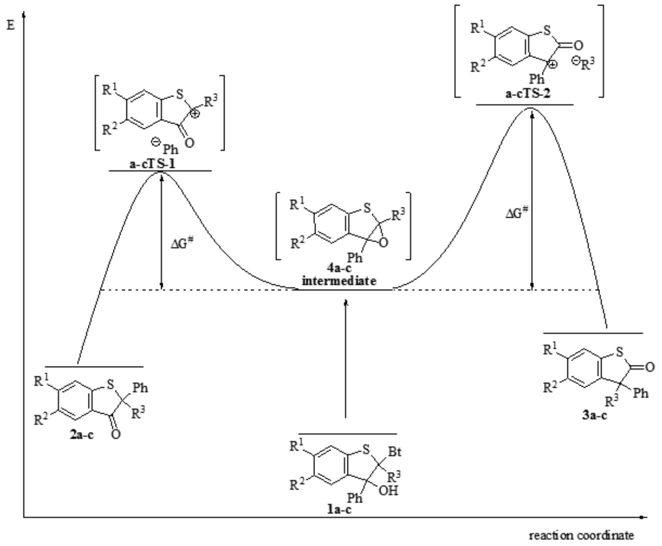


Figure 3. Energy diagram for rearrangement reaction in method B.

CONCLUSION

Kinetic and thermodynamic controlled products of rearrangement for 3-Hydroxy analogs of 2,3-dihydrobenzothiophene-2- and 3-ones were investigated using computational thermodynamic properties. Calculated results showed that refluxing compounds 1a-c at 90 to 100 $^{238}_{92}$C in open vessel gave only kinetic controlled products 2a-c (3-ones), and rearrangement reaction in sealed tube, in THF under 2.8 atm pressure at 90 to 100 $^{238}_{92}$C gives both kinetic controlled 2a-c and thermodynamic controlled 3a-c.

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REFERENCES

1. Tamura Y., Bayomi, S. M., Mukai, C., Ikeda, M.Murase, M., Kise, M. Sulfilimines in organic syntheses: new entries into tetrahydro-1,2-benzothiazepine and 1,2-benzisothiazole systems. Tetrahedron Lett. 21, 533,1980. (b) Tamura, Y., Bayomi, S. M., Mukai, C., Ikeda, M., Kise, M. Novel Conversion of Benzo[b]thiophen-3(2H)-ones into 1,2-Benzisothiazole and Tetrahydro-1,2-benzothiazepin-5-one Systems via Sulphimide Intermediates. J. Chem. Soc., Perkin Trans. 1 (1980) 2830.

2. Beck, J. R. Facile Synthesis of 2-Phenyl benzo[b]thiophene-3-amin and corresponding S-oxides. J. Heterocycl. Chem. 15 (1978) 513 .

3. Cabiddu, M. G., Cabiddu, S., Fattuoni, C., Floris, C., Gelli, G., Melis, S. Metalation Reactions.19. One-step Synthesis of 5-Membered Heterocyclic-Compounds Involving The Dilithiated Species 2-Lithio [(1-Lithio-1-Methyl ethyl) sulfonyl] benzene. Synthesis, 41(1993).

4. Regitz, M. Reaktionen Aktiver Methylen verbindungen mit aziden. V. Uber ein alpha-Diazo-Beta-Keto-Sulfon. Chem. Ber. 98 (1965) 36 .

5. Shenoy, V.U., Patel, V. P., Seshadri, S. Disperse Dyes Derived From 3-Oxo-2,3-Dihydrobenzo[b] Thiophene-1,1-dioxide and 3-Dicyanomethylene-2,3-dihydrobenzo [b] thiophene-1,1-dioxide. Dyes and Pigments, 11 (1989) 37.

6. (a) Hudson, A. T., Pether, M. J. Formation of 2-Acyl benzo [b] thiophen- 3 -(2H) -ones from 2- Substitued 3-Chlorothichromen-4-ones. J.Chem. Res. (S), 56 1983. (b) Gabbutt, C. D., Hepworth, J. D., Heron, B. M., Kanjia, M. Ring contraction of sulfenamides derived from thiochroman-4-ones. Tetrahedron, 50 (1994) 827.

Table 2. Calculated thermodynamic data for investigated compounds.

	Onsager			**IPCM**		
Structure	**G (hartree)**[a]	**G (kcalmol^{-1})**	**$\Delta G^{\#}$ [b] (kcalmol^{-1})**	**G (hartree)** [a]	**G (kcalmol^{-1})**	**$\Delta G^{\#}$ [b] (kcalmol^{-1})**
1a	-1487.102741	-933171.8410		-1492.014911	-936254.2768	
2a	-1091.356393	-684837.0502		-1094.324470	-686699.5482	
3a	-1091.359285	-684838.8649		-1094.424517	-686762.3287	
4a	-1091.327776	-684819.0927		-1094.422182	-686760.8634	
aTS-1	-1091.251344	-684771.1309	47.96	-1094.297681	-686682.7379	78.12
aTS-2	-1091.231342	-684758.5794	60.51	-1094.272853	-686667.1578	93.70
1b	-1601.598522	-1005019.089		-1609.518615	-1009989.026	
2b	-1205.851167	-756683.6658		-1214.550462	-762142.5604	
3b	-1205.856337	-756686.9100		-1214.579324	-762160.6716	
4b	-1205.817176	-756662.3358		-1214.501413	-762111.7817	
bTS-1	-1205.636366	-756548.8760	113.46	-1214.315886	-761995.3616	116.42
bTS-2	-1205.631919	-756546.0855	116.25	-1214.308125	-761990.4915	121.29
1c	-1593.505332	-999940.5309		-1601.130322	-1004725.288	
2c	-1169.930264	-734142.9400		-1182.640314	-742118.6234	
3c	-1169.936432	-734146.8104		-1182.654426	-742127.4789	
4c	-1169.911335	-734131.0618		-1182.600343	-742093.5412	
cTS-1	-1169.810347	-734067.6908	63.37	-1182.512042	-742038.1315	55.41
cTS-2	-1169.797145	-734059.4065	71.65	-1182.498675	-742029.7435	63.79

[a] 1 Hartree = 627.51 kcalmol^{-1}

[b] Activation energy, $\Delta G^{\#}_{(2a\text{-}c)} = G_{(a\text{-}cTS\text{-}1)} - G_{(4a\text{-}c)}$, $\Delta G^{\#}_{(3a\text{-}c)} = G_{(a\text{-}cTS\text{-}2)} - G_{(4a\text{-}c)}$

7. Katritzky, A. R., Kirichenko, K., Hür, D., Zhao, X., Ji, Y, Steel, P.J. Synthesis of 2,3-dihydrobenzofuran-2-ones and 2,3-dihydrobenzothiophene-2- and 3-ones by rearrangements of 3-hydroxy analogs. ARKIVOC, vi, 27 (2004).

8. Hamdach, A., El Hadrami, E. M., Hajji, C., Zaballos-Garcia, E., Sepulveda-Arques, J., Zaragoza, R. J. Experimental and theoretical DFT study of the reaction of 3-amino-1,2-diols with dichloromethane and paraformaldehyde. Tetrahedron, 60 (2004) 10353.

9. Hermida-Ramon, J.M., Pena-Gallego, A., Martinez-Nunez, E., Fernandez-Ramos, A., Cabaleiro-Lago, E. M. A quantum chemical study of aniline/ammonia clusters. Thermodynamic pro-perties and frequency analysis. Journal of Molecular Structure (Theochem), 497 (2000) 105, .

10. Bazyleva, A. B., Kabo, G. J., Paulechka, Y. U., Zaitsau, D. H., Blokhin, A.V., Sevruk, V. M. The thermodynamic properties of 1-bromoadamantane in the gaseous state. Thermochimica Acta, 436 (2005) 56 .

11. Parker, J. K., Nelson, H. H. Kinetics and thermodynamics of the Al + trimethylaluminum reaction. Chemical Physics Letters, 360, 313, 2002.

12. Cordfunke, E. H. P., Groen, C. P. A thermodynamic study of gaseous BaSiO3. J. Chem. Thermodynamics, 32 (2000) 839.

13. Wandschneider, D., Michalik, M., Heintz, A. Spectroscopic and thermodynamic studies of liquid n-butanol + n-hexane and + cyclohexane mixtures based on quantum mechanical ab initio calculations of n-butanol clusters. Journal of Molecular Liquids, 125 (2006) 2 .

14. Wang, Z., Zhai, Z., Wang, L., Chen, J., Kikuchi, O., Watanabe, T. Prediction of gas phase thermodynamic function of polychlorinated dibenzo -p-dioxins using DFT. J. Molecular Structure (Theochem), 672 (2004) 97 .

15. Katritzky, A. R., Xie, L., Serdyuk, L. Novel and Efficient Insertions of Carbons Carrying O-, S-, and N-Linked Substituents: Synthesis of -Alkoxyalkyl, -(Alkylthio)alkyl, and -(Carbazol-9-yl)alkyl Ketones. J. Org. Chem., 61(1996) 7564, .

16. Gaussian 03, Revision C.02, Frisch, M. J., Trucks, G. W., Schlegel, H. B., Scuseria, G. E., Robb, M. A., Cheeseman, J. R., Montgomery, Jr., J. A., Vreven, T., Kudin, K. N., Burant, J. C., Millam, J. M., Iyengar, S. S., Tomasi, J., Barone, V., Mennucci, B., Cossi, M., Scalmani, G., Rega, N., Petersson, G. A., Nakatsuji, H., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Klene, M., Li, X., Knox, J. E., Hratchian, H. P., Cross, J. B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Stratmann, R. E., Yazyev, O., Austin, A. J., Cammi, R., Pomelli, C., Ochterski, J. W., Ayala, P. Y., Morokuma, K., Voth, G. A., Salvador, P., Dannenberg, J. J., Zakrzewski, V. G., Dapprich, S., Daniels, A. D., Strain, M. C., Farkas, O., Malick, D. K., Rabuck, A. D., Raghavachari, K., Foresman, J. B., Ortiz, J. V., Cui, Q., Baboul, A. G., Clifford, S., Cioslowski, J., Stefanov, B. B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Martin, R. L., Fox, D. J., Keith, T., Al-Laham, M. A., Peng, C. Y., Nanayakkara, A., Challacombe, M., Gill, P. M. W., Johnson, B., Chen, W., Wong, M. W., Gonzalez, C., and Pople, J. A., Gaussian, Inc., Wallingford CT, 2004.

17. (a) Becke, A.D. Density-functional thermochemistry. III. The role of exact exchange. J. Chem. Phys. 1993, 98, 5648. (b) Lee, C., Yang, W., Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys. Rev. B, 37 (1988) 785 .

18. (a) Muller, C., Plesset, M. S., Note on an Approximation Treatment for Many-Electron Systems. Phys. Rev., 46, 618, 1934. (b) Bartlett, R. J., Silver, D. M. Many-body perturbation theory applied to electron pair correlation energies. I. Closed-shell first-row diatomic hydrides. J. Chem.Phys., 62, 3258, 1975. (c) Lee, C., Yang, W., Parr, R. G. Development of the Colle-Salvetti correlation-energy formula into a functional of the electron density. Phys. Rev. B, 37, 785, 1988. (e) Becke, A. D. Density-functional exchange-energy approximation with correct asymptotic behavior. Phys. Rev. A , 38 (1988) 3098 .

19. Onsager, L. Electric Moments of Molecules in Liquids. J. Am. Chem. Soc., 58 (1936) 1486 .

20. Foresman, J. B., Keith, T. A., Wiberg, K. B., Snoonian, J., Frisch, M. J. Solvent Effects. 5. Influence of Cavity Shape, Truncation of Electrostatics, and Electron Correlation on ab Initio Reaction Field Calculations. J. Phys. Chem., 100 (1996) 16098.

21. Foresman, J. B., Frisch, Æ. Exploring Chemistry with Electronic Structure Methods. Gaussian Inc., Pittsburgh, PA, (1996).