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Isomerization barriers in bis(4*H*-thiopyran) and in bithioxanthenes

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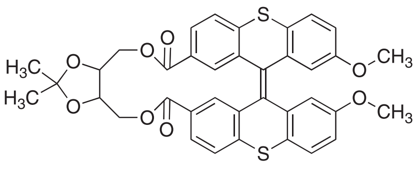
The inversion and rotation mechanisms for the isomerization of Feringa's bithioxanthenes existing in two conformations, up/up and up/down, have been calculated at the B3LYP/6-31G(d) and B3LYP/6-311++G(d,p) levels. The inversion mechanism that maintains the double bond nature of the central bond is a classical one but the rotation mechanisms that break the double bond to form a biradical needs to explore the singlet and triplet states. To do this we have removed the four fused phenyl rings of bithioxanthene and calculated at the CASSCF and CASPT2 levels bis(4*H*-thiopyran) proving that B3LYP calculations yield reasonable results for the rotation barriers.

1. Introduction

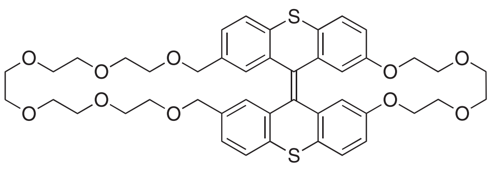
In the field of molecular nanotechnology and supramolecular chemistry, control of dynamics, i.e., translational and rotational motions, is one of the most challenging goals toward future nanoscale machines and molecular electronics. In 1991, Feringa reported the first optical molecular switches in which chirality is controlled by light.[1] This system also allowed for the first time unidirectional control of rotary motion in a molecule. The design and synthesis of the first light-driven unidirectional rotary motor are arguably the most spectacular achievement from this research group, which resulted in world-wide media attention.[2–5] Major advances have been published on molecular motors in recent years including chemically driven translational and unidirectional rotary motors, light-driven motors bound to surfaces, dramatic speed enhancement of molecular motors, and the discovery of rotation of microscale objects using nanoscale motors.[6–10] Recently, Dutch scientists have succeeded in a long term goal to reverse the direction of their molecular motor with some simple chemistry.[11]

The molecular motor used by Feringa group is formed by a rotor, usually a benzopyran (chromane) or a benzothiopyran (thiochromane or thioxanthene), the rotor being connected to the stator via an alkene bond that acts as an axle. In Scheme 1 are represented some of the reported structures. Structures **1** and **2** are bithioxanthenes, an original class of organic compounds, that are the object of the present work.[12,13]

We have carried out a search in the Cambridge Structural Database[14] and we have found only two structures, both reported by Feringa. Bithioxanthene itself (**3**) is reported (ZZZUGM), but without coordinates.



CUKYUC



LETLAY

The geometries of the central bithioxanthene rings (Fig. 1) could be characterized by the torsion angles ϕ ($C_{8a}{-}C_9{=}C_{9'}{-}C_{8a'}$ and $C_{9a}{-}C_9{=}C_{9'}{-}C_{9a'}$) and the $S_{10}\cdots S_{10'}$ distance.

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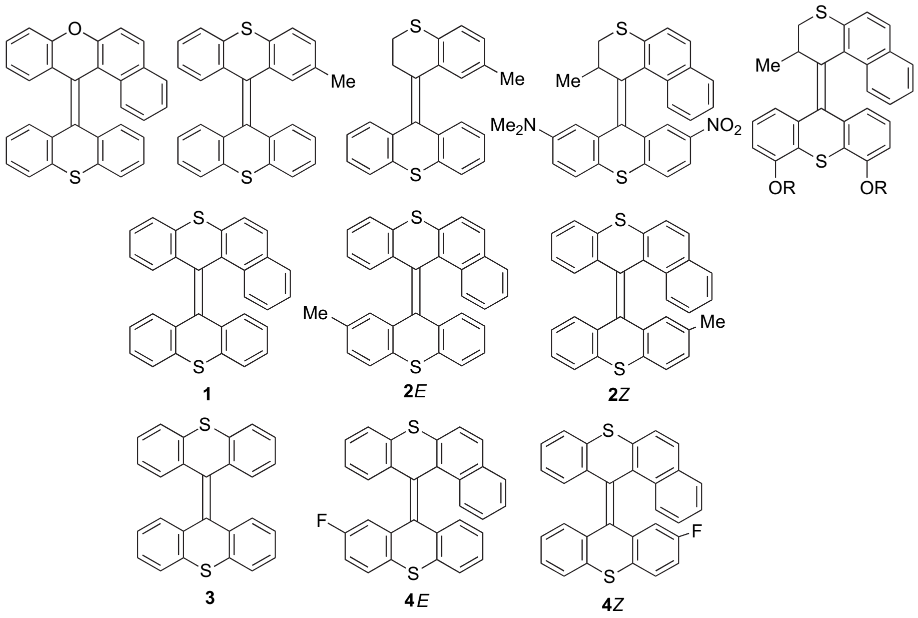
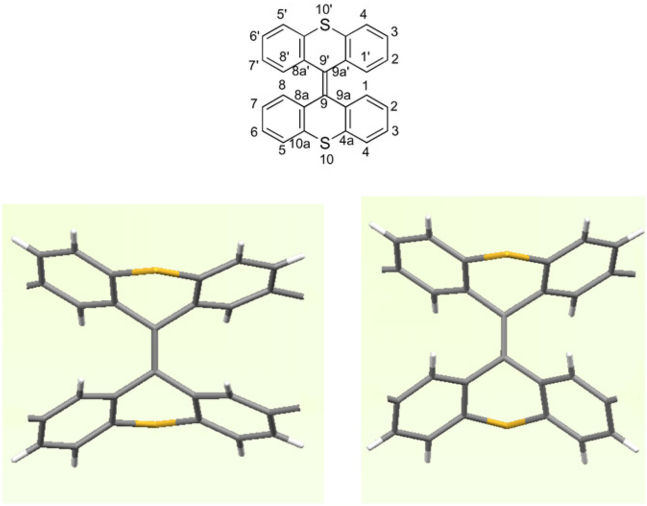


Scheme 1. Feringa's molecular rotors.



CUKYUC LETLAY

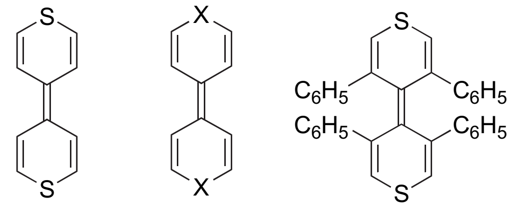
Fig. 1. The central core of CUKYUC (average ϕ=3.72°, S···S=7.12 Å) and LETLAY (average ϕ=3.80°, S···S=7.105 Å).

2. Results and discussion

To explore the conformational behavior of Feringa's molecular rotors we decided to study theoretically the four numbered compounds of Scheme 1. The calculations were carried out at the B3LYP/6-31G(d) and B3LYP/6-311++G(d,p) levels (see Computational details). Note that there are two isomers, one *E* and one *Z*, for **2** and **4**.

2.1. Study of the model compound 5 [4,4′-bis(4*H*-thiopyran)-4-ylidene]

In order to ascertain the rotational mechanism of Feringa's compounds we decided to previously study the simplified model **5** at a higher level to see if our B3LYP/6-31G(d) and B3LYP/6-311++G(d,p) calculations yielded acceptable results (Scheme 2). This compound is planar in its ground state and therefore it has not an inversion mechanism. Compound **5** is a particular case of compounds **6** (X=O, S, Se, Te) whose electrical properties are similar to TTF.[15] The electrochemical properties and electrical conductivity of bis(4*H*-thiopyrans) with four phenyl groups at positions 2,2′,6,6′ **7** have been reported by Reynolds et al.,[16] and related compounds with several double bonds between the thiopyran rings have also been described.[17]



Scheme 2. Model compounds.

We carried out CASSCF and in a subsequent step CASPT2 calculations on **5** (see Computational details). The results obtained at CASPT2 level show that the difference between singlet-90° and triplet-90° is very small, 4.0 kJ mol^{-1}, while the energy barriers respect to the ground state are 92.6 and 96.6 kJ mol^{-1}, respectively. The MS-CASPT2 calculations on the singlet-90° and triplet-90° reveal that the first singlet excited state is 188.0 kJ mol^{-1} above the singlet-90°, whereas the first triplet excited state is 185.2 kJ mol^{-1} above the triplet-90°. Thus, the excited states do not affect the energy barrier at low temperatures. Furthermore, the comparison of the HOMO orbital of the singlet and triplet electronic configurations in the TS has shown that they are almost identical (Fig. 1 of the Supplementary data).

The rotational barriers calculated at the B3LYP/6-31G(d) and B3LYP/6-311++G(d,p) levels are: singlet-open shell, 105.2 and 106.2 kJ mol^{-1}, respectively, and triplet, 106.0 [B3LYP/6-311++G(d,p)]. These values compare well (they are about 12 kJ mol^{-1} higher) than those calculated at the CASPT2 level, thus giving confidence to the following calculations.

2.2. Conformational analysis of bithioxanthenes 1–4

These compounds present two conformations, the **uu** (up/up) and the **ud** (up/down) that we have illustrated in Fig. 1 for compound **7**. Note the almost identity of the geometries of the **ud** conformations (Fig. 2) with the experimental data of Fig. 1.

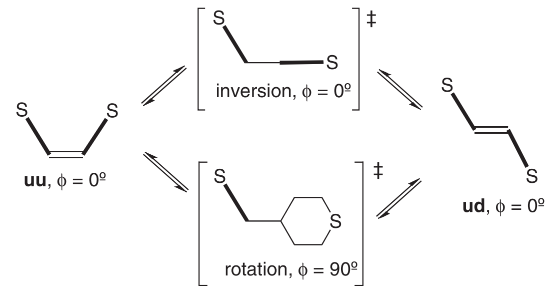
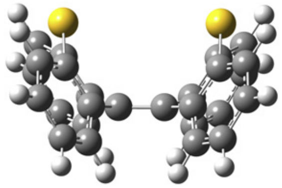
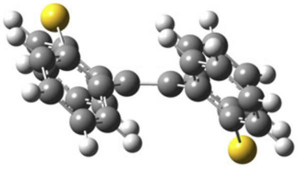


Fig. 2. The inversion and rotation mechanisms. The **uu** (left, symmetry C_s) and **ud** (right, symmetry C_2) conformations of **3** both having ϕ C–C=C–C angles of 0° and S⋯S distances of 4.66 Å (**uu**) and 7.14 Å (**ud**).





Bithioxanthenes can use two mechanisms for the **uu**/**dd** interconversion, similar to what happens for olefins[18] and imines (aldimines, oximes, hydrazones, and azines):[19] inversion and rotation (Fig. 2).

It should be noted that the situation is more complex in the case of compounds lacking any element of symmetry, **2** and **4** (Scheme 1).

We have gathered in Table 1 the energies calculated at the B3LYP/6-31G(d) (all of them) and B3LYP/6-311++G(d,p) levels (only minima). It must be taken into account that the *E*/*Z* isomerism of compounds **2** and **4** implies two inversion barriers but only one rotation barrier (either singlet or triplet).

As expected the transition state geometries (ϕ average) are close to 0° for inversion process (5.2° on average) and close to 90° for the rotation processes (94.5° for the singlet and 96.5° for the triplet on average). The fact that geometries of the transition states $\text{TS}_{\text{rotation}}$(singlet) and $\text{TS}_{\text{rotation}}$(triplet) are very similar indicates that both TSs belong to the same electronic configuration. We have represented in Fig. 3 the ground states of **3** and **1** and in Fig. 4 the inversion and rotation (singlet) TSs of **3** and **1**; those of **3** and **4** are similar to those of **1**.

The **uu** minima, both calculated at the B3LYP/6-31G(d) and B3LYP/6-311++G(d,p) levels, are about 34 kJ mol^{-1} less stable than the **ud** ones in agreement with the X-ray structures reported in Fig. 1. Concerning the *E*/*Z* isomerism of compounds **2** and **4**, the *Z* isomers are slightly more stable than the *E* ones but the difference (0.2–0.3 kJ mol^{-1}) is too small to affect the barriers.

Concerning the transition states calculated at the B3LYP/6-31G(d) level and defined from the most stable conformation, the **ud**, we observe:

(i) $\text{TS}_{\text{rotation}}$(triplet) is actually a minimum (compounds **2**, **3**, and **4**) lying only 0.2 kJ mol^{-1} of the triplet minimum in the case of **1**.

(ii) Both rotation processes, the singlet and the triplet, have very similar energies so we can discuss them together as rotation mechanism.

(iii) The rotation process is always preferred to the inversion one but the differences (or the ratios) are very dependent on the structure of the bithioxanthene. In the case of the less hindered compound, **3**, the difference is large, 46.8 kJ mol^{-1} (ratio 1.60). For the series of benzo-fused derivatives, the values are R^7=H, **1**, 8.25 kJ mol^{-1} (ratio 1.08), R^7=CH$_3$, **2**, 10.40 kJ mol^{-1} (ratio

Table 1
Geometries (°, Å) and relative energies involved in the isomerization processes of bithioxanthenes. In bold the energy of the minima

Compd	Conf.	ϕ	ϕ average	S⋯S	E_{rel} (kJ mol^{-1}) 6-31G(d)	E_{rel} (kJ mol^{-1}) 6-311++G(d,p)
3	**uu**	0.0	0.0	4.66	34.8	32.6
	ud	0.0	0.0	7.14	**0.0**	**0.0**
	$\text{TS}_{\text{inversion}}$	5.8/−5.8	0.0	7.90	124.7	—
	$\text{TS}_{\text{rotation}}$(s)	90.0	90.0	7.88	77.4	—
	$\text{TS}_{\text{rotation}}$(t)	90.0	90.0	7.88	78.3	—
1 H	**uu**	4.2/10.4	7.3	4.58	33.6	32.7
	ud	1.7/2.4	2.0	7.06	**0.0**	**0.0**
	$\text{TS}_{\text{inversion}}$	2.3/10.3	6.3	6.42	115.2	—
	$\text{TS}_{\text{rotation}}$(s)	87.2/92.8	90.0	7.85	106.5	—
	$\text{TS}_{\text{rotation}}$(t)	87.2/92.8	90.0	7.86	107.4	—
2*E* CH$_3$	**uu**	3.6/9.9	6.8	4.54	33.9	33.3
	ud	1.9/2.1	2.0	7.07	0.2	0.4
	$\text{TS}_{\text{inversion}}$	1.0/11.7	6.4	6.42	115.3	—
2*Z* CH$_3$	**uu**	3.6/9.9	6.8	4.54	33.3	33.2
	ud	1.9/2.1	2.0	7.07	**0.0**	**0.0**
	$\text{TS}_{\text{inversion}}$	1.0/11.7	6.4	6.42	115.2	—
	$\text{TS}_{\text{rotation}}$(s)	103.5/112.9	108.2	7.87	103.5	—
	$\text{TS}_{\text{rotation}}$(t)	103.5/112.9	108.2	7.87	106.1	—
4*E* F	**uu**	4.3/10.2	7.2	4.58	33.4	32.4
	ud	1.8/2.2	2.0	7.06	0.3	0.4
	$\text{TS}_{\text{inversion}}$	2.6/9.9	6.2	6.41	113.8	—
4*Z* F	**uu**	4.3/10.2	7.2	4.58	33.0	32.5
	ud	1.8/2.2	2.0	7.06	**0.0**	**0.0**
	$\text{TS}_{\text{inversion}}$	2.6/9.9	6.2	6.41	114.2	—
	$\text{TS}_{\text{rotation}}$(s)	92.7/87.0	89.9	7.86	106.1	—
	$\text{TS}_{\text{rotation}}$(t)	91.8/103.7	97.8		105.9	—

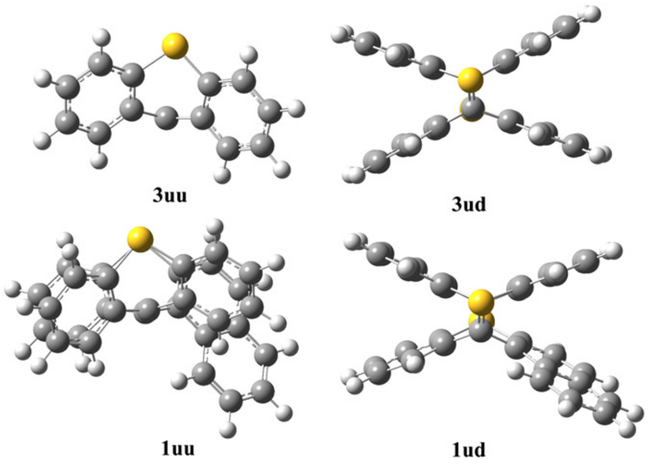


Fig. 3. A view of the **uu** and **ud** minima of **3** and **1** calculated at the B3LYP/6-31G(d) level.

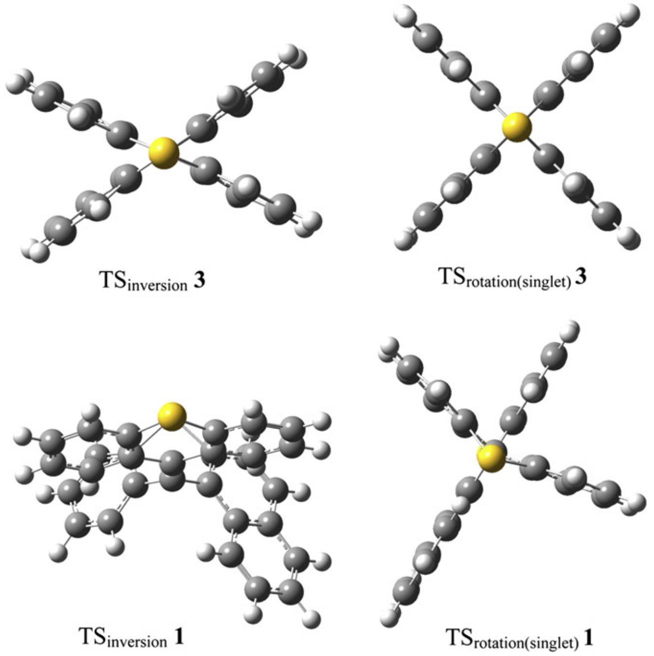


Fig. 4. A view of the TSs (inversion and rotation-singlet) of **3** and **1** calculated at the B3LYP/6-31G(d) level.

1.10), and R^7=F, **4**, 8.2 kJ mol^{-1} (ratio 1.08). For the three benzo-fused derivatives, TS$_{\text{inversion}}$=114.9 kJ mol^{-1} on average and TS$_{\text{rotation}}$=105.9 kJ mol^{-1} on average. Thus, the substituent CH$_3$ or F has almost no effect on the barriers. On the contrary the benzo-fusion (compare **3** and **1**) increases the inversion barrier by 9.5 and considerably decreases the rotation barrier by 29.1 kJ mol^{-1}. These effects are due to strong deformations in TSs due to the benzo annelation (Fig. 4).

3. Conclusions

The calculations carried out on the ground states of bis(4*H*-thiopyran) and four bithioxanthenes, two of them existing in two *E*/*Z* isomers (that calculations show to be of very similar energies), have shed light on the thermal molecular motions of these compounds. For bithioxanthenes, the **ud** minima are more stable than the **uu** ones by about 34 kJ mol^{-1}, this being consistent with the two reported structures of bithioxanthenes. Two **ud**/**uu** isomerization mechanisms have been explored, the inversion and the rotation, this last being in turn splits into singlet and triplet. The rotation mechanism is always preferred, the singlet and triplet are almost identical in energy, a result that was not known nor expected.

4. Computational details

4.1. Model compound 6

Due to the high values in the $\langle S^2 \rangle$ on the DFT calculations a multireference wavefunction-based method was used. Complete Active Space Self-Consistent Field calculations were carried out in order to describe the multiconfigurational nature of singlet-90 and triplet-90. For the treatment of the dynamic correlation, second-order perturbation theory calculations were carried out using the previous CASSCF/6-31G(d,p)[20] wave function as reference. First, a study of the active space was performed including HOMO and LUMO molecular orbitals up to eight active electrons within 14 active molecular orbitals. These calculations will be named CASSCF (8,14). Once the active space was obtained, the CASPT2/6-31G(d,p)[21,22] calculations were carried out in which all the electrons from the active space were correlated.

In order to verify the energy separation between the singlet-90 and the triplet-90 and their excited states, a State Average-Complete Active Space Self-Consistent Field (SA-CASSCF)[20] and in a subsequent step a Multi State CASPT2 (MS-CASPT2)[23,24] with the same characteristics described above were performed. All the wavefunction-based calculations have been carried about using MOLCAS 7.4 program.[25]

4.2. Feringa's compounds

All the molecules were optimized at the B3LYP/6-31G(d) level[26,27] where frequencies[28] were calculated to verify that all of them were minima (number of imaginary frequencies=0) or transition states (number of imaginary frequencies=1). These optimized geometries were further optimized at the B3LYP/6-311++G(d,p) level.[29] These calculations were carried using the facilities of the Gaussian 09 software.[30] The electron density of the systems has been analyzed with the Atoms in Molecules (AIM) methodology[31,32] and the MORPHY program.[33,34]

Acknowledgements

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Supplementary data

Optimized geometries of all studied compounds and figure of the HOMO orbitals of the singlet and triplet configuration of **5**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.07.042.

References and notes

1. Feringa, B. L.; Jager, W. F.; de Lange, B.; Meijer, E. W. *J. Am. Chem. Soc.* **1991**, *113*, 5468.
2. Feringa, B. L.; van Delden, R. A.; Koumura, N.; Geertsema, E. M. *Chem. Rev.* **2000**, *100*, 1789.
3. Feringa, B. L. *Acc. Chem. Res.* **2001**, *34*, 504.

4. Mandl, C.; König, B. *Angew. Chem., Int. Ed.* **2004**, *43*, 1622.
5. Avalos, M.; Babiano, R.; Cintas, P.; Jiménez, J. L.; Palacios, J. C. *Chem. Rev.* **1998**, *98*, 2391.
6. Feringa, B. L.; Jager, W. F.; de Lange, B. *J. Chem. Soc., Chem. Commun.* **1993**, 288.
7. Koumura, N.; Zijlstra, R. W. J.; van Delden, R. A.; Harada, N.; Feringa, B. L. *Nature* **1999**, *401*, 152.
8. van Delden, R. A.; Koumura, N.; Schoevaars, A.; Meetsma, A.; Feringa, B. L. *Org. Biomol. Chem.* **2003**, *1*, 33.
9. van Delden, R. A.; ter Wiel, M. K. J.; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. *Nature* **2005**, *437*, 1337.
10. Klok, M.; Browne, W. R.; Feringa, B. L. *Phys. Chem. Chem. Phys.* **2009**, *11*, 9124.
11. Ruangsupapichat, N.; Pollard, M. M.; Harutyunyan, S. R.; Feringa, B. L. *Nat. Chem.* **2011**, *3*, 53.
12. Korenstein, R.; Muszkat, K. A.; Fischer, E. *J. Photochem.* **1976**, *5*, 345.
13. Reynolds, G. A.; Saeva, F. D.; Doney, J. J.; Chen, C. H. *J. Org. Chem.* **1984**, *49*, 4843.
14. Cambridge Structural Database Allen, F. H. *Acta Crystallogr., Sect. B* **2002**, *58*, 380; Allen, F. H.; Motherwell, W. D. S. *Acta Crystallogr., Sect. B* **2002**, *58*, 407; http://www.ccdc.cam.ac.uk CSD version 5.31, updated Feb. 2010.
15. (a) Es-Seddiki, S.; Le Coustumer, G.; Mollier, Y.; Devaud, M. *Tetrahedron Lett.* **1981**, *22*, 2771; (b) Saeva, F. D.; Reynolds, G. A.; Kaszczuk, L. *J. Am. Chem. Soc.* **1982**, *104*, 3524; (c) Detty, M. R.; Murray, B. J.; Perlstein, J. H. *Tetrahedron Lett.* **1983**, *24*, 539.
16. (a) Reynolds, G. A.; Chen, C. H.; Van Allan, J. A. *J. Org. Chem.* **1979**, *44*, 4456; (b) Detty, M. R.; Murray, B. J. *J. Org. Chem.* **1982**, *47*, 1148; (c) Chen, C. H.; Doney, J. J.; Reynolds, G. A.; Saeva, F. D. *J. Org. Chem.* **1983**, *48*, 2757.
17. (a) Dabirian, R.; Zdravkova, A. N.; Liljeroth, P.; van Walree, C. A.; Jenneskens, L. W. *Langmuir* **2005**, *21*, 10497; (b) Faux, N.; Robin-Le Guen, F.; Le Poul, P.; Caro, B.; Le Poul, N.; Le Mest, Y.; Green, S. J.; Le Roux, S.; Kahlal, S.; Saillard, J.-Y. *Tetrahedron* **2007**, *63*, 7142.
18. Dugave, C.; Demange, L. *Chem. Rev.* **2003**, *103*, 2475.
19. Blanco, F.; Alkorta, I.; Elguero, J. *Croat. Chim. Acta* **2009**, *82*, 173.
20. (a) Roos, B. O.; Taylor, P. R.; Siegbahn, P. E. M. *Chem. Phys.* **1980**, *48*, 157; (b) Siegbahn, P. E. M.; Heiberg, A.; Almlöf, J.; Roos, B. O. *J. Chem. Phys.* **1981**, *74*, 2384; (c) Siegbahn, P.; Heiberg, A.; Roos, B.; Levy, B. *Phys. Scr.* **1980**, *21*, 323.
21. Andersson, K.; Malmqvist, P.-Å; Roos, B. O.; Sadlej, A. J.; Wolinski, K. *J. Phys. Chem.* **1990**, *94*, 5483.
22. Andersson, K.; Malmqvist, P.-Å; Roos, B. O. *J. Chem. Phys.* **1992**, *96*, 1218.
23. Finley, J.; Malmqvist, P.-Å; Roos, B. O.; Serrano-Andrés, L. *Chem. Phys. Lett.* **1998**, 288.
24. Zaitsevskii, A.; Malrieu, J. P. *Chem. Phys. Lett.* **1995**, *233*, 597.
25. Karlström, G.; Lindh, R.; Malmqvist, P.-Ǻ; Roos, B. O.; Ryde, U.; Veryazov, V.; Widmark, P.-O.; Cossi, M.; Shimmelpfennig, B.; Neogrady, P.; Seijo, L. *Comput. Mater. Sci.* **2003**, *28*, 222.
26. (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098; (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648; (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.
27. Hariharan, P. A.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.
28. McIver, J. W.; Komornicki, A. K. *J. Am. Chem. Soc.* **1972**, *94*, 2625.
29. (a) Ditchfield, R.; Hehre, W. J.; Pople, J. A. *J. Chem. Phys.* **1971**, *54*, 724; (b) Frisch, M. J.; Pople, J. A.; Binkley, J. S. *J. Chem. Phys.* **1984**, *80*, 3265.
30. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B. *Gaussian 09, Revision A.1*; Gaussian: Wallingford, CT, 2009.
31. Bader, R. F. W. In *Atoms in Molecules: A Quantum Theory; The International Series of Monographs of Chemistry*; Halpen, J., Green, M. L. H., Eds.; Clarendon: Oxford, 1990.
32. Popelier, P. L. A. *Atoms in Molecules: An Introduction*; Prentice Hall: New York, NY, 2000.
33. Popelier, P. L. A. *Chem. Phys. Lett.* **1994**, *228*, 130.
34. Rafat, M.; Devereux, M.; Popelier, P. L. A. *J. Mol. Graphics Modell.* **2005**, *24*, 111.