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The first example of the configurational assignment at the C=N bond of allenylthioimidates

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Dedicated to Professor Dr. L. Brandsma (Utrecht University, The Netherlands) on the occasion of his 70th birthday

Abstract—Configurational assignment of methyl 2-methoxy-*N*-methyl-2,3-butadienimidothioate, a representative member of a new prospective allenylthioimidates series has been performed by means of low-temperature natural-abundance *J*(C,C) measurements in combination with the high-level ab initio SOPPA calculations. Electronic structure and predominant conformations of the isomers of the title allenylthioimidate are discussed based on the DFT-B3LYP calculations.

1. Introduction

Allenylthioimidates, $R^1R^2C{=}C{=}C(R^3){-}C(SR^4){=}NR^5$, have recently become available through the reaction of the allenic carbanions (easily generated in situ from the corresponding allenes or alkynes and *n*-BuLi)[1] with isothiocyanates.[2–4] These highly unsaturated and highly reactive species are unique intermediates for the novel syntheses of a variety of rare functionalised fundamental carbo- and heterocycles, such as iminocyclobutenes (via an intramolecular [1,3]-transfer of the alkylsulfanyl group, followed by intramolecular [2+2]-cycloaddition, when $R^3 = Ar$),[4a] 2-(alkylsulfanyl)pyrroles (via [1,5]-nucleophilic intramolecular cyclisation),[4b–f] quinolines (via tandem electrocyclisation and aromatisation, when $R^5 = Ar$),[4e–k] as well as the completely conjugated azatrienic systems (via [1,5]-H shift, when $R^5 \neq Ar$)[2,3] which are of considerable theoretical and synthetic interest (as precursors of still rare 2,3-dihydropyridines—via 6π-electrocyclisation;[4b–d,k–p] pyridines—via aromatisation of 2,3-dihydropyridines;[4o,p] 1-cyclohexyl-5-methyl-2(1*H*)-thione—via spontaneous tandem [1,7]-sigmatropic proton migration, electrocyclisation into 1,2-dihydropyridine and elimination of methane,[4q] and cyclobuta[1,2-*b*]pyrroles—via a series of so far unclear intramolecular rearrangements[4k,q–t]).

Methyl 2-methoxy-*N*-methyl-2,3-butadienimidothioate **1**—the parent member of a 2-methoxy-2,3-butadienimidothioate series—was obtained in almost quantitative yield by a one-pot synthesis (three reactions) starting from the accessible methoxyallene, involving: lithiation, addition to methyl isothiocyanate and finally *S*-methylation (Scheme 1).[3c]

The structure of **1**, isolated, as a mixture of *E* and *Z* isomers, was confirmed by means of the spectroscopic data (NMR and IR). However, the usual NMR methods failed to allow configurational assignment of the individual isomers of **1**.

The present study was undertaken to establish the stereochemistry of the thioimidate **1**. In order to assign the carbon signals to *E* and *Z* isomers, we tried to measure the one-bond carbon–carbon coupling constants, ^1J(C,C), used previously with great success for configurational assignments in related systems.[5] However, the main problem was the easy transformation[4c,u,v] of allenylthioimidate **1** into pyrrole **2** and 2,3-dihydropyridine **3** taking place even at ambient temperature (Scheme 2). The above-mentioned heterocycles were detected in the NMR spectra of allenylthioimidate **1** even after storage in a refrigerator.

Keywords: NMR; SOPPA; DFT-B3LYP; Carbon–carbon spin–spin coupling constants; Allenylthioimidates; *E*–*Z* Isomers; Conformational analysis.
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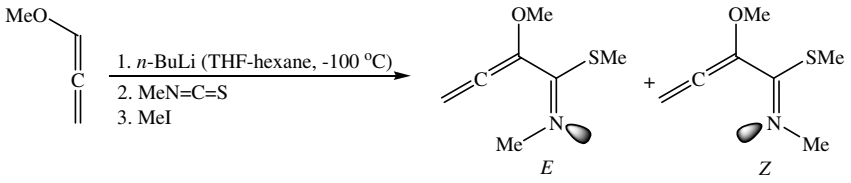
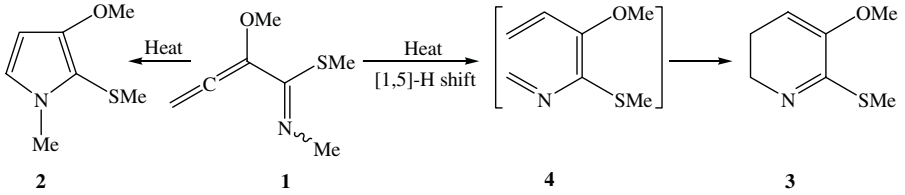


Scheme 1.



Scheme 2.

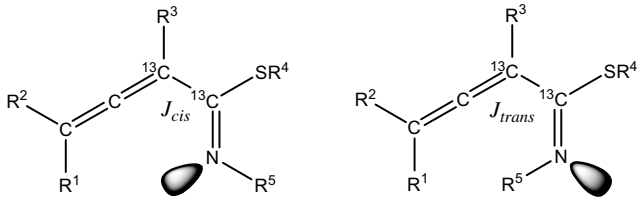
For this reason, all our attempts to measure carbon–carbon coupling constants at ambient temperature proved to be unsuccessful. Therefore, to exclude the pyrrole cyclisation or sigmatropic rearrangement, followed by the electrocyclisation of **4** (Scheme 2), we performed natural-abundance measurements of ^{1}J(C,C) at low temperature (−10 °C) by means of INADEQUATE accumulation overnight.

2. Results and discussion

It is well known that in imines, ^{1}J(C,C) involving the α-imino carbon demonstrate a profound stereochemical dependence on the orientation of the nitrogen lone pair. Indeed, the difference between J_{cis} and J_{trans} (see notations below) amounts to 20% of their total values and provides an unambiguous guide to the configurational assignment of the C=N bond in oximes and their derivatives.[5]

Theoretical studies[6] of this interesting effect revealed that the difference between J_{cis} and J_{trans} could be accounted for by three different contributions, namely those of (i) the nitrogen lone pair, (ii) the carbon–carbon bonds containing coupled carbons and (iii) the carbon inner core orbitals. The first one relates to direct nitrogen lone pair participation in the transmission of ^{13}C–^{13}C spin–spin coupling giving a positive contribution to J_{cis} and a negative one to J_{trans} (primary lone pair effect). On the other hand, the second and the third contributions originate mainly in charge transfer from the nitrogen lone pair to the antibonding orbital of the adjacent carbon–carbon bond oriented trans to the nitrogen lone pair. This charge transfer interaction, very similar to the anomeric effect, results in a substantial lengthening of the *transoid* carbon–carbon bond and hence in the negative contribution to J_{trans} (secondary lone pair effect).

In much the same way, we expected the manifestation of this lone pair effect upon ^{1}J(C,C) in the series of allenylthioimidates to enable us to perform the configurational assignment of these species.



R^1, R^2 = H, Alk; R^3 = H, Alk, OAlk, SAlk, Ar, HetAr; R^4 = Alk; R^5 = Alk, *c*-Alk, Ar

Predominant conformations of *E* and *Z* isomers of **1** located at the B3LYP/6-311G** level are shown in Figure 1, and in the further calculations of ^{1}J(C,C) it was assumed that both isomers adopt their predominant conformations. It follows from these calculations that the *E* isomer is more stable by 2.0 kcal/mol. Indeed, *E* and *Z* isomers were isolated from the reaction mixture (Scheme 1) in a ratio of ca. 65:35 (C_6D_6), which means that this process is under thermodynamic control.

It is noteworthy that in the predominant conformation of the *E* isomer, the orientation of the C=N double bond and the allenyl moiety, C=C=C, is *skew s-trans* (dihedral angle $\varphi_{C=N-C=C}$ is 122.0°) while that of the *Z* isomer is *skew s-cis* (dihedral angle $\varphi_{C=N-C=C}$ is 59.5°), which implies considerable steric inhibition of π,π conjugation in both isomers.

The methoxy group is essentially *s-cis* with respect to the allenyl moiety in *E* and *Z* isomers; in contrast, the methylthio group is *s-cis* towards the C=N bond in the *E* iso-

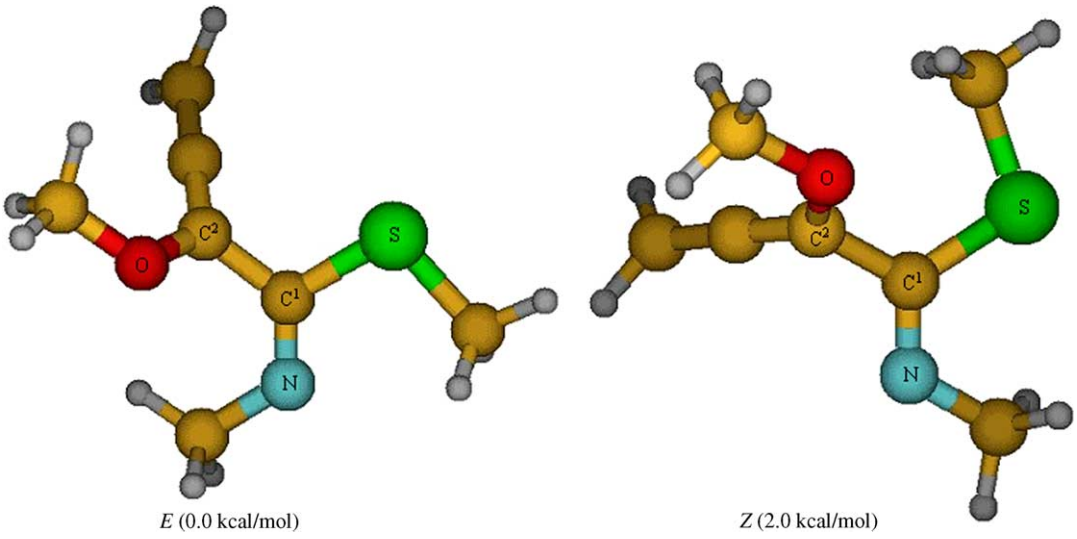


Figure 1. B3LYP/6-311G** optimised structures and relative energies of *E* and *Z* isomers of methyl 2-methoxy-*N*-methyl-2,3-butadienimidothioate **1**.

mer while it is *s-trans* in the *Z* isomer. There are two possible explanations of this conformational effect. On the one hand, the *s-cis* conformation of the methylthio group in the *Z* isomer of **1** should be dramatically destabilised by the strong steric repulsion between the protons of two methyl groups on sulfur and nitrogen. On the other hand, the *s-trans* conformation of the methylthio group in the *Z* isomer is stabilised by the attractive intramolecular interactions between the protons of the NCH_3 group and sulfur (interatomic distance is 2.9 Å) and between those of the SCH_3 group and oxygen (interatomic distance is 2.4 Å). Accordingly, the *s-cis* conformation of the methylthio group in the *E* isomer of **1** is stabilised by the attractive intramolecular interactions between the protons of the NCH_3 group and oxygen (interatomic distance is 2.5 Å) and between those of the SCH_3 group and nitrogen (interatomic distance is 2.6 Å) (see Fig. 1).

The ^1J(C,C) calculated at the SOPPA (second order polarisation propagator approach)[7] level in the diverse isomers of allenylthioimidate **1** are shown in Table 1, showing them to be in good agreement with experiment. In a number of our recent publications,[8] the SOPPA method was successfully used for the calculation of *J*(C,C) and other coupling constants and this laid the foundation for the utilisation of this method in the present study. All four coupling contributions, namely Fermi contact, J_{FC}, spin–dipolar, J_{SD}, diamagnetic spin–orbital, J_{DSO} and paramagnetic spin–orbital, J_{PSO}, have been taken into account in the calculation of ^1J(C,C).

Table 1. Spin–spin coupling constants ^1J(C,C) of methyl 2-methoxy-*N*-methyl-2,3-butadienimidothioate **1** calculated at the SOPPA level in comparison with experiment[a]

Isomer	J_{DSO}	J_{PSO}	J_{SD}	J_{FC}	J	Experiment
E	0.40	−0.99	0.69	66.85	66.95	68.4
Z	0.40	−1.22	0.59	90.59	90.36	86.1

[a] All couplings and their contributions are in hertz.

However, it follows from the data in Table 1 that total values of ^1J(C,C) and accordingly the orientational nitrogen lone pair effect resulting in a dramatic difference between J_{cis} and J_{trans} are almost solely governed by the dominant Fermi contact contribution while the non-contact contributions are essentially negligible in both isomers, in line with our previous results for oximes.[5d] Thus, the net lone pair effect upon the values of ^1J(C,C) in **1** totals to ca. 20 Hz (!), which allows the unambiguous configurational assignment of its *E* and *Z* isomers.

The most encouraging result of the present study is that the experimental difference between J_{cis} and J_{trans} induced by the nitrogen lone pair effect in allenylthioimidates is very well reproduced in the SOPPA calculations and this provides an additional tool in the configurational assignment at the C=N bond in related systems when the experimental measurement of ^1J(C,C) is restricted to only one isomer.

3. Experimental

Methyl 2-methoxy-*N*-methyl-2,3-butadienimidothioate **1** was prepared according to the reported procedure starting from 1-lithio-1-methoxyallene and methyl isothiocyanate.[2] ^{13}C NMR (100.69 MHz, C_6D_6): δ values in ppm (relative to HMDS) at −10 °C of **1** (*E*) and **1** (*Z*): two groups of signals corresponding to the ca. 65:35-mixture of *E* and *Z* isomers of **1**. Isomer *E*: 199.60 (=C=), 155.72 (N=C), 129.14 (2-C=), 94.52 (H_2C=), 56.37 (OMe), 41.97 (NMe), 13.48 (SMe). Isomer *Z*: 200.27 (=C=), 161.66 (N=C), 132.27 (2-C=), 93.56 (H_2C=), 56.50 (OMe), 40.77 (NMe), 14.96 (SMe).

Carbon–carbon coupling constants were measured at −10 °C using the INADEQUATE pulse sequence adjusted for $J = 75$ Hz. Settings for the INADEQUATE experiments were as follows: 90° pulse length, 12–

14 μs; spectral width, 10–15 kHz; acquisition time, 4–6 s; relaxation delay, 6–10 s; characteristic delay $\tau = 1/4\,J$, 5.6 ms; digital resolution 0.05–0.1 Hz/pt; accumulation time, 12 h.

Geometrical optimisations were performed with the GAMESS code,[9] at the DFT-B3LYP level (Becke's three-parameter hybrid functional[10] where nonlocal correlation is provided by Lee et al. correlation functional[11]) with the 6-311G** basis set of Pople and co-workers.[12] Calculations of spin–spin coupling constants have been carried out using the DALTON package[13] at the SOPPA level[7] with the correlation-consistent basis set cc-pVTZ of Dunning and co-workers,[14] augmented with the core *s*-functions of Woon and Dunning[15] on coupled carbons as described elsewhere.[8] In all calculations, no symmetry constraints were applied assuming the C_1 symmetry point group throughout.

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References and notes

1. (a) Brandsma, L.; Verkruijsse, H., *Preparative Polar Organometallic Chemistry*; Springer: Berlin, Heidelberg, N.Y., London, Paris, Tokyo, 1987; Vol. 1, 240p; (b) Brandsma, L., *Best Synthetic Methods; Synthesis of Acetylenes, Allenes and Cumulenes: Methods and Techniques*; Elsevier, Academic Press: Amsterdam, Boston, Heidelberg, London, N.Y., Oxford, Paris, San Diego, San Francisco, Sydney, Tokyo, 2004; 469p.
2. Nedolya, N. A. Novel Chemistry Based on Isothiocyanates and Polar Organometallics. Ph.D. Thesis, Utrecht University, The Netherlands; 1999; 144p.
3. For recent reviews, see: (a) Brandsma, L.; Nedolya, N. A.; Tarasova, O. A.; Trofimov, B. A. *Chem. Heterocycl. Compd. (N.Y.)* **2000**, *36*, 1241–1260; (b) Brandsma, L. *Eur. J. Org. Chem.* **2001**, 4569–4581; (c) Brandsma, L.; Nedolya, N. A. *Synthesis* **2004**, 735–745.
4. (a) Tarasova, O. A.; Nedolya, N. A.; Brandsma, L.; Albanov, A. I. *Tetrahedron Lett.* **2004**, *45*, 5881–5883; (b) Nedolya, N. A.; Brandsma, L.; Trofimov, B. A. *Khim. Geterotsikl. Soedin.* **1996**, 917–918; (c) Nedolya, N. A.; de Lang, R.-J.; Brandsma, L.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1997**, *33*, 76–79; (d) Nedolya, N. A.; Brandsma, L.; Zinov'eva, V. P.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1997**, *33*, 80–85; (e) Brandsma, L.; Nedolya, N. A.; Tarasova, O. A.; Klyba, L. V.; Sinegovskaya, L. M.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1999**, *35*, 928–932; (f) Nedolya, N. A.; Brandsma, L. *Russ. J. Org. Chem.* **2003**, *39*, 609–610; (g) Brandsma, L.; Nedolya, N. A.; de Lang, R.-J.; Trofimov, B. A. *Russ. Chem. Bull. (Engl. Transl.)*. **1996**, *45*, 2873–2874; (h) Taherirastgar, F.; Nedolya, N. A.; Brandsma, L.; de Lang, R.-J.; Trofimov, B. A. *Dokl. Chem. (Engl. Transl.)*. **1997**, *353*, 39–40; (i) Brandsma, L.; Nedolya, N. A.; de Lang, R.-J.; Trofimov, B. A. *Chem. Heterocycl. Compd. (N.Y.). (Engl. Transl.)*. **1997**, *33*, 491–492; (j) Nedolya, N. A.; Brandsma, L.; de Lang, R.-J.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1997**, *33*, 1361–1362; (k) Brandsma, L.; Nedolya, N. A.; Verkruijsse, H. D.; Owen, N. L.; Li, Du; Trofimov, B. A. *Tetrahedron Lett.* **1997**, *38*, 6905–6908; (l) Nedolya, N. A.; Brandsma, L.; Trofimov, B. A. *Russ. Chem. Bull. (Engl. Transl.)*. **1996**, *45*, 2670–2671; (m) Nedolya, N. A.; Brandsma, L.; Trofimov, B. A. *Dokl. Chem. (Engl. Transl.)*. **1996**, *350*, 210–211; (n) Nedolya, N. A.; Brandsma, L.; Zinov'eva, V. P.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1998**, *34*, 1494–1499; (o) Nedolya, N. A.; Brandsma, L.; de Lang, R.-J.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1997**, *33*, 580–581; (p) Nedolya, N. A.; Schlyakhtina, N. I.; Klyba, L. V.; Ushakov, I. A.; Fedorov, S. V.; Brandsma, L. *Tetrahedron Lett.* **2002**, *43*, 9679–9681; (q) Nedolya, N. A.; Brandsma, L.; Trofimov, B. A. *Khim. Geterotsikl. Soedin.* **2002**, 1396–1398; (r) Brandsma, L.; Nedolya, N. A.; van der Kerk, A. C. H. T. M.; Heerma, V.; Lutz, E. T. H. G.; de Lang, R.-J.; Afonin, A. V.; Trofimov, B. A. *Russ. Chem. Bull. (Engl. Transl.)*. **1997**, *46*, 832–833; (s) Brandsma, L.; Nedolya, N. A.; Heerma, V.; van der Kerk, A. C. H. T. M.; Lutz, E. T. H. G.; de Lang, R.-J.; Afonin, A. V.; Trofimov, B. A. *Chem. Heterocycl. Compd. (N.Y.). (Engl. Transl.)*. **1997**, *33*, 493–495; (t) Nedolya, N. A.; Brandsma, L.; van der Kerk, A. C. H. T. M.; Heerma, V.; Lutz, E. T. H. G.; Afonin, A. V.; de Lang, R.-J.; Trofimov, B. A. *Russ. J. Org. Chem. (Engl. Transl.)*. **1997**, *33*, 1359–1360; (u) Nedolya, N. A.; Brandsma, L.; Tarasova, O. A.; Verkruijsse, H. D.; Trofimov, B. A. *Tetrahedron Lett.* **1998**, *39*, 2409–2410; (v) Shagun, V. A.; Toryashinova, D.-S. D.; Nedolya, N. A.; Tarasova, O. A.; Brandsma, L. *Russ. J. Org. Chem.* **2004**, *40*, 775–789; (w) Brandsma, L.; Nedolya, N. A.; Trofimov, B. A. *Eur. J. Org. Chem.* **1999**, 2663–2664.
5. (a) Krivdin, L. B.; Kalabin, G. A.; Nesterenko, R. N.; Trofimov, B. A. *Tetrahedron Lett.* **1984**, *25*, 4817–4820; (b) Kalabin, G. A.; Krivdin, L. B.; Shcherbakov, V. V.; Trofimov, B. A. *J. Mol. Struct.* **1986**, *143*, 569–572; (c) Krivdin, L. B.; Shcherbakov, V. V.; Kalabin, G. A. *Russ. J. Org. Chem. (Engl. Transl.)* **1986**, *22*, 300–305; (d) Krivdin, L. B.; Scherbina, N. A.; Istomina, N. V. *Magn. Reson. Chem.* **2005**, *43*, 435–443.
6. (a) Barone, V.; Peralta, J. E.; Contreras, R. H.; Sosnin, A. V.; Krivdin, L. B. *Magn. Reson. Chem.* **2001**, *39*, 600–606; (b) Krivdin, L. B.; Zinchenko, S. V.; Shcherbakov, V. V.; Kalabin, G. A.; Contreras, R. H.; Tufro, M. F.; Ruiz de Azua, M. C.; Giribet, C. G. *J. Magn. Reson.* **1989**, *84*, 1–8; (c) Contreras, R. H.; Giribet, C. G.; Ruiz de Azua, M. C.; Cavasotto, C. N.; Krivdin, L. B. *J. Mol. Struct. (Theochem)* **1990**, *210*, 175–186; (d) Krivdin, L. B.; Zinchenko, S. V.; Kalabin, G. A.; Tufro, M. F.; Contreras, R. H.; Denisov, A. Yu.; Gavrilyuk, O. A.; Mamatyuk, V. I. *J. Chem. Soc., Faraday Trans.* **1992**, *88*, 2459–2463.
7. (a) Nielsen, E. S.; Jørgensen, P.; Oddershede, J. *J. Chem. Phys.* **1980**, *73*, 6238–6246; (b) Packer, M. J.; Dalskov, E. K.; Enevoldsen, T.; Jensen, H. J. A.; Oddershede, J. *J. Chem. Phys.* **1996**, *105*, 5886–5900; (c) Enevoldsen, T.; Oddershede, J.; Sauer, S. P. A. *Theor. Chem. Acc.* **1998**, *100*, 275–284; (d) Bak, K. L.; Koch, H.; Oddershede, J.; Christiansen, O.; Sauer, S. P. A. *J. Chem. Phys.* **2000**, *112*, 4173–4185.
8. (a) Krivdin, L. B.; Sauer, S. P. A.; Peralta, J. E.; Contreras, R. H. *Magn. Reson. Chem.* **2002**, *40*, 187–194; (b) Krivdin, L. B. *Magn. Reson. Chem.* **2003**, *41*, 91–101; (c) Krivdin, L. B. *Magn. Reson. Chem.* **2003**, *41*, 157–168; (d) Krivdin, L. B. *Magn. Reson. Chem.* **2003**, *41*, 417–430; (e) Krivdin, L. B. *Magn. Reson. Chem.* **2003**, *41*, 885–901; (f) Krivdin, L. B. *Magn. Reson. Chem.* **2004**, *42*, 1–13;

(g) Krivdin, L. B. *Magn. Reson. Chem.* **2004**, *42*, 500–511; (h) Sauer, S. P. A.; Krivdin, L. B. *Magn. Reson. Chem.* **2004**, *42*, 671–686; (i) Krivdin, L. B. *Magn. Reson. Chem.* **2004**, *42*, S168–S179; (j) Krivdin, L. B. *Magn. Reson. Chem.* **2004**, *42*, 919–930; (k) Krivdin, L. B. *Magn. Reson. Chem.* **2005**, *43*, 101–116.

9. Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S. J.; Windus, T. L.; Dupuis, M.; Montgomery, J. A. *J. Comp. Chem.* **1993**, *14*, 1347–1363.
10. Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648–5652.
11. Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B.* **1988**, *37*, 785–789.
12. Krisnan, R.; Binkley, J. S.; Seeger, R.; Pople, J. A. *J. Chem. Phys.* **1980**, *72*, 650–654.
13. Agren, H.; Angeli, C.; Bak, K. L.; Bakken, V.; Christiansen, O.; Cimiraglia, R.; Coriani, S.; Dahle, P.; Dalskov, E. K.; Enevoldsen, T.; Fernandez, B.; Haettig, C.; Hald, K.; Halkier, A.; Heiberg, H.; Helgaker, T.; Hettema, H.; Jensen, H. J. A.; Jonsson, D.; Joergensen, P.; Kirpekar, S.; Klopper, W.; Kobayashi, R.; Koch, H.; Ligabue, A.; Lutnaes, O. B.; Mikkelsen, K. V.; Norman, P.; Olsen, J.; Packer, M. J.; Pedersen, T. B.; Rinkevicius, Z.; Rudberg, E.; Ruden, T. A.; Ruud, K.; Salek, P.; Sanchez de Meras, A.; Saue, T.; Sauer, S. P. A.; Schimmelpfennig, B.; Sylvester-Hvid, K. O.; Taylor, P. R.; Vahtras, O.; Wilson, D. J. Dalton, A Molecular Electronic Structure Program, Release 2.0, 2005, see, http://www.kjemi.uio.no/software/dalton/dalton.html.
14. (a) Dunning, T. H., Jr. *J. Chem. Phys.* **1989**, *90*, 1007–1023; (b) Kendall, R. A.; Dunning, T. H., Jr.; Harrison, R. J. *J. Chem. Phys.* **1992**, *96*, 6796–6806; (c) Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1993**, *98*, 1358–1371.
15. Woon, D. E.; Dunning, T. H., Jr. *J. Chem. Phys.* **1995**, *103*, 4572–4585.