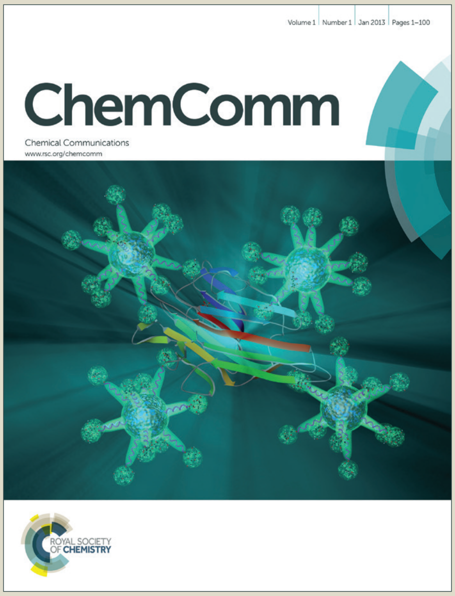
ChemComm

Accepted Manuscript



ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/chemcomm

Journal Name

ARTICLE TYPE

Cite this: DOI: 10.1039/xxxxxxxxxx

External Electric Field Reverses Helical Handedness of a Supramolecular Columnar Stack†

Karteek K. Bejagam,[a] Chidambar Kulkarni,[a,b] Subi J. George*[b] and Sundaram Balasubramanian*[a]

Received Date
Accepted Date

DOI: 10.1039/xxxxxxxxxx

www.rsc.org/journalname

Benzene-1,3,5-tricarboxamide (BTA) molecules self-assembles into one-dimensional columnar structures that possesses a macrodipole moment along the stacking direction. Application of an external electric field on its liquid crystalline (LC) phase consisting of aligned stacks leads to a net polarization whose sign can be reversed by changing the direction of the field. Atomistic molecular dynamics simulations predict that such an experiment must be associated with a reversal of helical handedness of the stacks as well. An experiment to demonstrate this prediction in a chiral supramolecular assembly is proposed.

Chiral amplification is the process by which a racemic mixture is preferentially enriched towards an enantiopure system. Molecular crystals[1], covalent[2,3] and supramolecular polymers [4] have often served as models for biological systems to understand homochirality in the latter. Circularly polarized light[5], external fields[6,7], stirring[8–10] and electrochemical treatment[11] have been used to break the chiral symmetry.

Supramolecular polymers not only serve as an ideal platform to understand chiral enrichment, but they are intensely studied for applications as smart functional materials[12]. Within the realm of supramolecular polymers, benzene-1,3,5-tricarboxamides (BTA) are a class of extensively studied molecules[13]. Each molecule of BTA can form three intermolecular hydrogen bonds, through which self-assembly proceeds in a cooperative manner leading to the formation of one-dimensional columnar stacks[14]. The triple hydrogen bonded network is helical and the dipole moment of the individual hydrogen bonds sum up to yield a macrodipole along the stacking direction (Fig. 1). Although the formation of such stacks require longer alkyl tails, the generation of a macrodipole can be illustrated with molecules containing a methyl group which reduces the computational cost considerably.

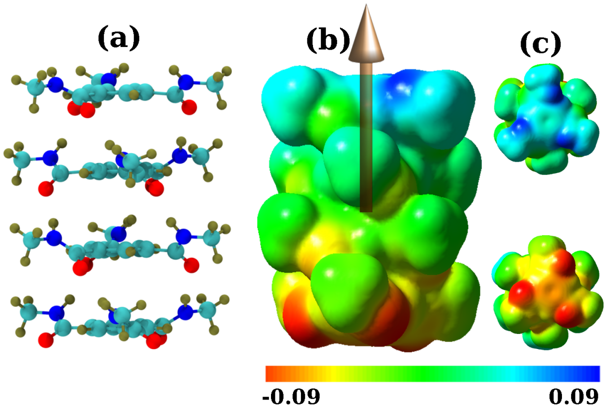


Fig. 1 (a) Optimized geometry of tetramer of *N,N',N''*-tris(methyl)benzene-1,3,5-tricarboxamide at B3LYP/6-311+g(d,p)//B3LYP/cc-pVTZ level of theory. Side chains are methyl groups. Color: C-cyan; O-red; N-blue; H-tan. (b) Isosurface of electrostatic potential at 0.004 e bohr^{-3}. Arrow indicates macrodipole. (c) Top and bottom views of a tetrameric stack.

In a sample where the supramolecular stacks and fibers are aligned, a macroscopic polarization ensues, whose direction can be switched by an external electric field. Exploiting this aspect, Fitié et al.[15,16] studied the ferroelectric behavior of the liquid crystalline (LC) phase of BTA. Ferroelectricity was demonstrated through a hysteresis loop for systems of achiral BTA molecules. Reorientation of amide bonds was suggested to be responsible for the polar switching.[16] The current manuscript explores the microscopic details of these experiments through atomistic molecular dynamics (MD) simulations. Serendipitously, we observe the reversal of the handedness of the molecular assembly on the ap-

---

[a] *Chemistry and Physics of Materials Unit, Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bangalore 560 064, India. Tel: +91 (80) 2208 2808; E-mail: bala@jncasr.ac.in*

[b] *New Chemistry Unit, JNCASR, Bangalore 560 064, India. E-mail: george@jncasr.ac.in*

† Electronic Supplementary Information (ESI) available: [Relaxation mechanism in the solution phase is described in Fig. S1. Dihedral definition to identify the handedness of a molecule is given in Fig. S3. Additional figures are shown.]. See DOI: 10.1039/b000000x/

plication of electric field, which on hindsight, is to be expected based on electrostatic grounds. Thus, an electric field can reorient not only the direction of polarization (the macrodipole vector of a stack), but also the handedness of a supramolecular assembly. In the following, we examine the effects of an external electric field for the cases of chiral and achiral molecular systems in the LC phase using atomistic MD simulations.

A hydrogen-bonded dimer of BTA can exist in two configurations - symmetric (3:0) and asymmetric (2:1)[14], where the symbols in paranthesis denote the number of pairs of hydrogen bond dipole vectors which are parallel:antiparallel to each other. In symmetric stacking, all the oxygens of a molecule are oriented in the same direction with respect to the benzene plane. However, in asymmetric stacking, two oxygens are on one side and the third is on the other side of the benzene plane. Since a stack of BTA molecules consists of three hydrogen-bonded helical networks, the direction of the macrodipole moment of one helix in an asymmetric stack is opposite to those of the other two helices. In our earlier work[14], asymmetric stacking was argued and shown to be a thermodynamically favoured state over the symmetric one.

Nine pre-formed decamers (2:1 kind) of BTA with decyl substituents on the amide hydrogen were taken in a non-orthogonal box, an arrangement which closely resembles the extended LC phase[17,18], via periodic boundary conditions. The stacks were aligned along the z-direction. An initial inter-stack spacing of 30 Å was chosen to avoid hard contacts between alkyl tails.

MD simulations were performed using LAMMPS[19] program. As earlier[14], BTA molecules were modelled using the DREIDING force field[20]. Gasteiger charges[21] were adopted as partial charges on the atoms. Other details are provided in ESI. The MD simulation was carried out in the constant temperature-constant stress ensemble[22] at 400 K, at which temperature the LC phase is stable[16]. The system was equilibrated for 2 ns during which time the distance between the stacks converged to around 22 Å. Snapshots were visualized using VMD[23]. Cross-sectional and side views of the equilibrated system are displayed in Fig. 2.

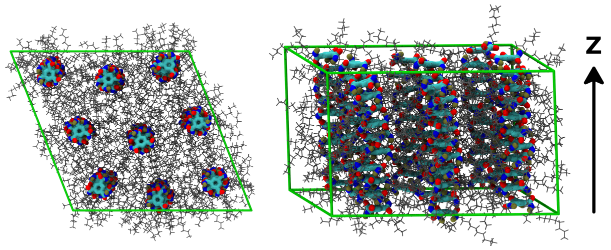


Fig. 2 Top (left) and side (right) views of the liquid crystalline phase of BTA at 400 K obtained from MD simulations.

Subsequently, a constant external electric field ($\vec{E}$) was applied along the z-direction. From classical theory, a dipole placed in an electric field experiences a torque $\vec{\tau}=\vec{p}$ x $\vec{E}$ with potential energy as U= -$\vec{p}.\vec{E}$, where $\vec{p}$ is the dipole moment vector. In the presence of the field, the dipole direction of either one or two helices is opposite to that of $\vec{E}$. The hydrogen bonds constituting the helix which are anti-aligned with the field become unstable (*vide infra*) and the individual H-bond dipoles flip so as to align with the field. The sequence of events is: hydrogen bond breakage, bond rotation, followed by the formation of a new hydrogen bond. This process, in effect, transforms the 2:1 type oligomer into a 0:3 one wherein all the helix dipole vectors are oriented parallel to the field. Snapshots of one of the stacks from the MD simulation of the LC phase, before and after the application of the external field are shown in Fig. 3. Since a 2:1 stack transforms to a 0:3 one due to the external electric field, we shall consider the effect of E-field on 3:0 stacks themselves in the rest of the discussion.

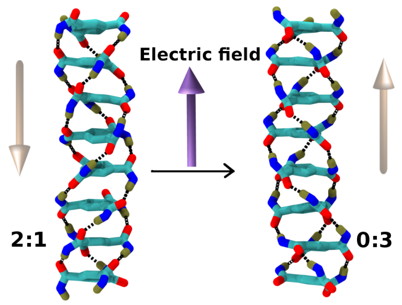


Fig. 3 Snapshot of one stack from MD simulations of the LC phase at 400 K. The change from an asymmetric (2:1) dipole configuration to a symmetric (0:3) one, upon application of the electric field ($\vec{E}$=0.2 V/Å) is seen. The macrodipole moment is indicated by the brown arrow.

With the same protocols as before, we proceed to examine the effect of electric field on the LC phase constituted by stacks of 3:0 type. The field was applied in directions either parallel or antiparallel to the macrodipole vector. Expectedly, the former does not disturb the structure. In contrast, when the field is applied in a direction opposite to the macrodipole, the stack relaxes by aligning its macrodipole with the field and the same is observed as a ferroelectric hysteresis loop (P-E loop)[15,16]. In order to unravel the mechanism of polarization switching, MD simulation of the LC phase (wherein the macrodipoles of all the stacks were parallel to each other) was carried out at 400 K in the NPT ensemble by applying a field of 0.2 V/Å [24] antiparallel to the direction of the macrodipoles. Although the torque ($\vec{\tau}$) on the H-bond dipoles is zero, the potential energy (U) of the system is highly positive which destablizes the dipole forcing the macrodipole to align with $\vec{E}$. As the overall rotation of the stacks is infeasible, intermolecular hydrogen bonds within a stack break, so that the amide groups become free to rotate. Since the barrier for the bond rotation is around 1.5 kcal/mol[14], the amide group of each molecule can flip about the benzene plane such that H-bond dipole moment vector ($\vec{p}$) of amide is inverted. Post rotation, they reform the hydrogen bond with a neighboring molecule (different from the one it was initially hydrogen bonded to). In this manner, the triply hydrogen bonded network is regained. *However, in this process, the handedness of each hydrogen bonded helix is reversed.* A snapshot of an arbitrarily chosen octamer (part of the LC phase) from the MD trajectory demonstrates the switching mechanism (Fig. 4).

In Fig. 4, each H-bonded helical network is colored differently so as to clearly distinguish left- and right- handed systems. In the initial geometry, the helices are twisted in clockwise (left-handed) direction, and the electric field makes the helices turn counterclockwise (right-handed). The dihedral angle between the amide

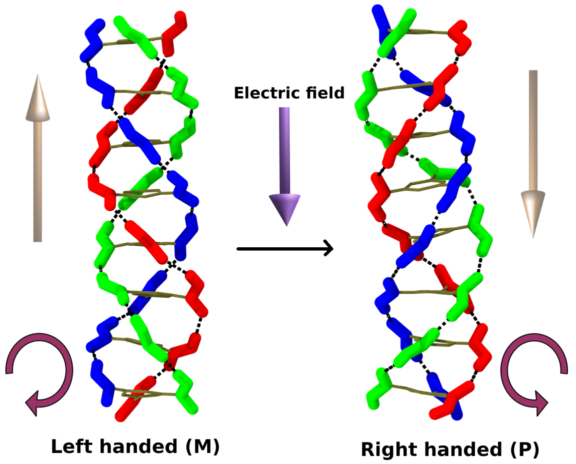


Fig. 4 Snapshot of a stack from MD simulations of the LC phase illustrates the reversal of chirality on application of electric field. In the initial geometry (left), H-bonded helices are twisted in clockwise direction and the macrodipole points up. Amides present in each H-bonded helix are colored differently. Application of an electric field in the direction opposite to that of the macrodipole reverses the handedness i.e., the helical twist turns counter-clockwise.

group and benzene plane was used as a parameter to identify the type of handedness (ESI Section 3). The progress of the change in handedness over time is shown in Fig. 5. The fraction of dihedrals which are left-handed exhibits step-wise changes. The same quantity for individual stacks is shown in Fig. S4a. The time taken for any stack to reverse its macrodipole is rather short (Inset to Fig. 5). Thus, the reversal of handedness proceeds in a sequential manner – one stack completely switches its direction, followed by the next and so on, i.e., *each oligomer switches its handedness independent of the others*. The effect of temperature and field strength on the switching mechanism was examined by carrying out additional simulations at different conditions: (i) 370 K & 0.2 V/Å (Fig. S4b) and (ii) 400 K & 0.1 V/Å (Fig. S5). Reversal of handedness was observed in these two simulations as well but the rate of switching was considerably slower than at 400 K & 0.2 V/Å[25]. Our simulations thus strongly suggest that a handedness reversal should have been concomitant with ferroelectric switching in the experiments of Sijbesma and co-workers[15,16].

The identification of handedness in a MD simulation is rather straightforward. Yet, in order to substantiate our conclusions, we calculated the circular dichroism (CD) spectrum using the semi-empirical ZINDO/s method within Gaussian-09[26]. The initial and final coordinates of eight molecules (the core region of an arbitrarily chosen stack) obtained from the MD simulations were used as input for the ZINDO/s calculations. The CD spectra too reveal the reversal of handedness as can be seen from Fig. S6.

We now examine the prospects of investigating the reversal of handedness experimentally. The LC phase of achiral molecules is racemic whose nature remains unchanged in the presence of an electric field. An achiral supramolecular system will consist of an equal proportion of stacks which are left- or right-handed. Furthermore, equal fraction of stacks can have their macrodipole moments either aligned or anti-aligned with the electric-field.

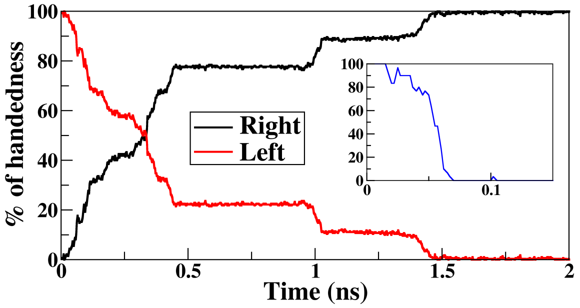


Fig. 5 Change of handedness of BTA stacks in the LC phase with time. The ordinate is the fraction of dihedrals ($C_{Ar}-C_{Ar}-C-O$) that are left-handed. See Fig. S3 for dihedral definition. An electric field of magnitude 0.2 V/Å was applied at a temperature of 400 K at t=0. Inset shows the same for an arbitrarily chosen stack. Results for all stacks are shown in Fig. S4a.

Accordingly, a LC phase of achiral molecules, with equal number of right- and left- handed stacks was constructed as a model for the racemic mixture. The stacks can be of four types: PU, PD, MU and MD, where ‘P’ and ‘M’ stand for right- and left-handed stacks respectively, while ‘U’ and ‘D’ denote the direction of the macrodipole moment. The racemic mixture consisted of four stacks of each kind. All the 16 stacks were arranged in a hexagonal packing. MD simulation was carried out in the constant temperature-constant stress ensemble (fully flexible simulation cell) at a temperature of 400 K and the final snapshot is shown in Fig. S7. After equilibration (over a duration of 2 ns), an external electric field $\vec{E}$ of 0.2 V/Å was applied in the positive Z direction (upwards) on the racemic mixture. Stacks whose macrodipole were aligned with the field remained unaltered. However, intermolecular hydrogen bonds in stacks whose macrodipoles were anti-parallel to the field reoriented so that the resultant macrodipole vector was aligned with the field. As a result, PD stacks converted to MU and MD ones converted to PU. Thus, the mixture remained racemic even after the application of electric field. This process is schematically shown in Fig. S8a and demonstrated in Fig. S8b. Even after the application of electric field, an equal number of right- and left- handed stacks prevail, keeping the mixture chiro-optically inactive.

To understand the applicability of reversal of handedness for chiral molecules (Fig. S9), MD simulation of a chiral system in its LC phase (consisting of 9 decamers) was performed. The same mechanism as described earlier was found to hold good for these as well (Fig. S10). The macrodipole vectors of a given stack has equal probability to be pointing either up or down. As the chiral center is of ‘S’ type, the assembly prefers left-handedness[27]. Thus, we constructed a LC phase of the chiral compound out of 8 MU and 8 MD stacks. MD simulation of a LC system consisting of only one enantiomer was carried out with protocols same as those described earlier. This mixture is chiro-optically active. On the application of an electric field in the positive ‘Z’ direction, a MU stack remains aligned with $\vec{E}$ while MD transforms into PU. Thus, while the original system was optically active (all left handed stacks), application of the electric field nullifies optical activity by changing the handedness of one set of stacks. A schematic representation of this process is depicted in Fig. 6 and the conversion of a chiro-optically active mixture into a chiro-optically inactive one is displayed in Fig. 7. Since stacks can neither exhibit overall rotation nor can disaggregate in the LC phase, the quenching of optical activity upon application of the field will be permanent. The system will be optically inactive even after the removal of the E-field.

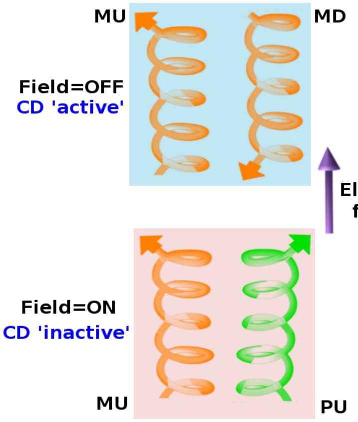


Fig. 6 Schematic representation of the effect of electric field on a left-handed chiral system. At equilibrium, an equal proportion of stacks with macrodipoles pointing either up or down can exist. Upon application of an external electric field, a stack whose macrodipole is opposite to the field relaxes by changing its handedness. Thus, the chiro-optical activity of the compound is quenched.

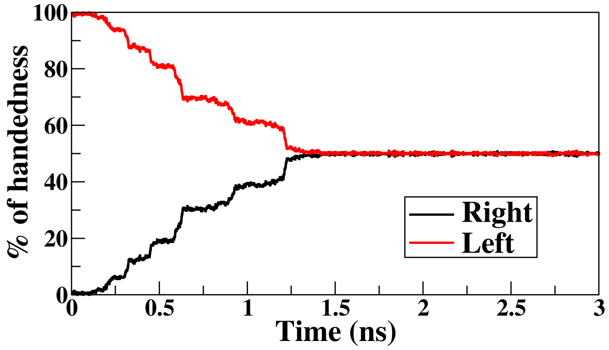


Fig. 7 Transformation of a enantiomerically pure (left-handed) system into a racemic mixture upon the application of electric field. At t=0, all the stacks are left-handed (100%) which yield equal amounts of left- (50%) and right- (50%) handed stacks on the application of electric field.

In conclusion, we have elucidated the mechanism involved in ferroelectric switching[15,16] of columnar stacks of BTA in its liquid crystalline phase using MD simulations. When an external field is applied in a direction opposite to that of the macrodipole, intermolecular hydrogen bonds break, and are re-formed in the opposite direction by virtue of amide bond rotation. This process leads to a reversal of handedness of the stack. *Experimental measurements of the P-E hysteresis loop in hydrogen bonded supramolecular polymers must be associated with such a handedness switch as well, which to our knowledge, has not been recognized yet.* Although the fields employed in the current work are 25 to 50 times larger than experimental values, the mechanism is independent of the field magnitude, and thus should be observable under experimental conditions. It is hoped that the current work will spur experimental efforts in this direction. Within a computational paradigm, it will be interesting to study the effect of an external electric field applied during the process of self-assembly itself. We plan to pursue such aspects in future.

K.K.B. thanks CSIR, India for a senior research fellowship. S.J.G and S.B. thanks Sheikh Saqr Laboratory, JNCASR for a senior fellowship. We are thankful to A.V. Raagesh and Prof. K.S. Narayan, JNCASR for fruitful discussions.

Notes and references

1 C. Viedma, J. E. Ortiz, T. d. Torres, T. Izumi and D. G. Blackmond, *J. Am. Chem. Soc.*, 2008, **130**, 15274–15275.

2 M. M. Green, J.-W. Park, T. Sato, A. Teramoto, S. Lifson, R. L. B. Selinger and J. V. Selinger, *Angew. Chem. Int. Ed.*, 1999, **38**, 3138–3154.

3 M. M. Green, K.-S. Cheon, S.-Y. Yang, J.-W. Park, S. Swansburg and W. Liu, *Acc. Chem. Res.*, 2001, **34**, 672–680.

4 A. R. A. Palmans and E. W. Meijer, *Angew. Chem. Int. Ed.*, 2007, **46**, 8948–8968.

5 J. Bailey, A. Chrysostomou, J. H. Hough, T. M. Gledhill, A. McCall, S. Clark, F. Ménard and M. Tamura, *Science*, 1998, **281**, 672–674.

6 D. Edwards, K. Cooper and R. C. Dougherty, *J. Am. Chem. Soc.*, 1980, **102**, 381–382.

7 N. Micali, H. Engelkamp, P. G. van Rhee, P. C. M. Christianen, L. M. Scolaro and J. C. Maan, *Nature Chem.*, 2012, **4**, 201–207.

8 J. M. Ribó, J. Crusats, F. Sagués, J. Claret and R. Rubires, *Science*, 2001, **292**, 2063–2066.

9 T. Yamaguchi, T. Kimura, H. Matsuda and T. Aida, *Angew. Chem. Int. Ed.*, 2004, **43**, 6350–6355.

10 M. Wolffs, S. J. George, Ž. Tomović S. C. J. Meskers, A. P. H. J. Schenning and E. W. Meijer, *Angew. Chem. Int. Ed.*, 2007, **46**, 8203–8205.

11 X. Yang, S. Seo, C. Park and E. Kim, *Macromolecules*, 2014, **47**, 7043–7051.

12 A. Jain and S. J. George, *Mater. Today*, 2015, **18**, 206 – 214.

13 S. Cantekin, T. F. A. de Greef and A. R. A. Palmans, *Chem. Soc. Rev.*, 2012, **41**, 6125–6137.

14 K. K. Bejagam, G. Fiorin, M. L. Klein and S. Balasubramanian, *J. Phys. Chem. B*, 2014, **118**, 5218–5228.

15 C. F. C. Fitié, W. S. C. Roelofs, M. Kemerink and R. P. Sijbesma, *J. Am. Chem. Soc.*, 2010, **132**, 6892–6893.

16 C. F. C. Fitié, W. S. C. Roelofs, P. C. M. M. Magusin, M. Wübbenhorst, M. Kemerink and R. P. Sijbesma, *J. Phys. Chem. B*, 2012, **116**, 3928–3937.

17 A. Timme, R. Kress, R. Q. Albuquerque and H.-W. Schmidt, *Chem. Eur. J.*, 2012, **18**, 8329–8339.

18 Solution phase is not suitable to study this phenomenon (Fig. S1).

19 S. Plimpton, *J. Comput. Phys.*, 1995, **117**, 1 – 19.

20 S. L. Mayo, B. D. Olafson and W. A. Goddard, *J. Phys. Chem.*, 1990, **94**, 8897–8909.

21 J. Gasteiger and M. Marsili, *Tetrahedron*, 1980, **36**, 3219 – 3228.

22 M. Parrinello and A. Rahman, *J. Appl. Phys.*, 1981, **52**, 7182–7190.

23 W. Humphrey, A. Dalke and K. Schulten, *J. Molec. Graphics*, 1996, **14**, 33–38.

24 The magnitude of the field in simulations is around fifty times larger than that in experiments.

25 Switching of the handedness of the LC phase by applying an electric field of 0.1 V/Å (twenty five times that of experimental value) takes around 100 ns (Fig. S5).

26 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *Gaussian 09 Revision D.01*, Gaussian Inc. Wallingford CT 2009.

27 L. Brunsveld, A. P. H. J. Schenning, M. A. C. Broeren, H. M. Janssen, J. A. J. M. Vekemans and E. W. Meijer, *Chem. Lett.*, 2000, **29**, 292–293.