

Synthesis and Characterization of Natural Abundance and Isotopically Labeled 1,4-Bis(3,3,3-triphenylpropynyl)-2,3-difluorobenzene. A Molecular Gyroscope with a Polar Rotator

Rosa Santillán,^{1*} Steven D. Karlen,² Hung Dang,² and Miguel A. Garcia-Garibay^{2*}

¹ Departamento de Química, Centro de Investigación y Estudios Avanzados del Instituto Politécnico Nacional, A.P. 14-740, 07000 México D.F., México. E-mail: rsantill@cinvestav.mx

² Department of Chemistry and Biochemistry, University of California, Los Angeles, CA 90095-1569, USA. E-mail: mgg@chem.ucla.edu

Recibido el 4 de diciembre de 2007; aceptado el 13 de mayo de 2008

Abstract. Sonogashira coupling of natural abundance and d_2 -deuterated 1,4-bis(trifluoromethanesulfonate)-2,3-difluorobenzene provides access to 1,4-bis(3,3,3-triphenylpropynyl)-2,3-difluorobenzene, a structure that emulates a molecular gyroscope with a dipolar rotator. Two crystal forms of this compound are of interest for the construction of ferroelectric materials.

Key words: Molecular machines, molecular rotors, isotopic substitution, X-ray structure.

Resumen. Con un acoplamiento de tipo Sonogashira usando muestras de 2,3-difluorobenzeno-1,4-bis(trifluorometanosulfonato) en sus formas isotópicas de abundancia natural y deuterada, se prepararon muestras de 1,4-bis(3,3,3-trifenilpropinil)-2,3-difluorobenzeno. Este compuesto posee características similares a las de un giroscopio con un rotor dipolar. Las dos estructuras cristalinas obtenidas son de interés para preparar materiales ferroeléctricos.

Palabras clave: Máquinas moleculares, rotores moleculares, sustitución isotópica, estructura de rayos X.

Introduction

Recent interest in the development of molecular machinery has led to the design of compounds that emulate the structure and dynamics of macroscopic objects [1]. Among those, we have been interested in the design and synthesis of molecular gyroscopes to study their rotary dynamics in the crystalline state [2]. A relatively simple but highly versatile structural motif consists of a central aromatic group, which is axially linked by triple bonds to two relatively bulky triphenylmethyl substituents (Scheme 1) [3]. Following the terminology suggested by Michl *et al.*, [4] the entire molecule may be referred to as a *molecular rotor*, the moving element can be named a *molecular rotator*, and the static components that provides a frame of reference to describe the motion of the rotator is referred to as the *molecular stator*. When equipped with a polar rotator, molecular rotors such as that in Figure 1 are able to interact with external fields and possess some properties akin to those of a macroscopic compass [5]. Using dielectric spectroscopy, we recently showed that introduction of a 2,3-difluorophenylene as a rotator in 1,4-bis(3,3,3-triphenylpropynyl)-2,3-difluorobenzene (**1**) allows for the relatively simple interfacing of its rotary dynamics with external AC fields [6]. After having reported the physicochemical and materials characterization of compound **1**, we wish to report here the synthesis of its natural abundance and d_2 -deuterated forms as well as its structural characterization in solution and in the solid state.

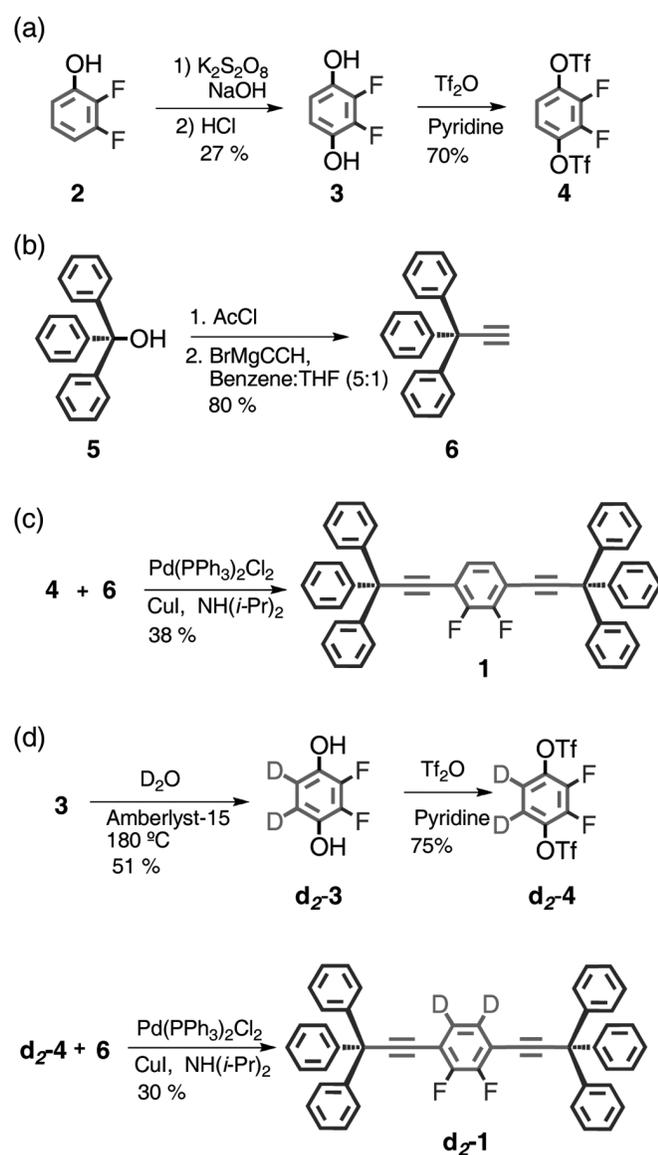
Results and Discussion

Synthesis. As illustrated in Scheme 1a-c, the preparation compound **1** followed a convergent strategy with the prepara-



Fig. 1. Structural analogy between a macroscopic gyroscope and a simple 1,4-bis(3,3,3-triphenylpropynyl)-2,3-difluorobenzene. The central phenylene in the molecular analog rotates in the kHz regime at ambient temperature in the solid state [6].

tion of the two components followed by their coupling with a Pd(0)-catalyzed Sonogashira reaction. Samples of 2,3-difluorophenol (**2**) were converted to 2,3-difluorohydroquinone (**3**) by oxidation with basic potassium persulfate. Hydroquinone **3** was converted to the corresponding ditriflate (**4**) in 70% yield by reaction with triflic anhydride in pyridine. Trityl acetylene **6** was prepared as previously reported [3], by reaction of trityl alcohol **5** with acetyl chloride followed by reaction with ethynyl magnesium bromide. A double Sonogashira coupling was used to link ditriflate **4** to terminal acetylene (**6**) to give compound **1** in 38% yield. The selective deuteration of the central phenylene of **1** was accomplished by double deuterium exchange in hydroquinone **3** by heating in a pressure tube with D_2O in the presence of Amberlyst-15. Hydroquinone d_2 -**3** was then converted to the corresponding ditriflate d_2 -**4** and then the difluoro rotor d_2 -**1** by using the procedures utilized for the compounds with natural isotopic abundance.



Scheme 1

Structural Analysis. Spectral analysis of compound **1** by ^1H and ^{13}C NMR agreed with expectations from its average molecular symmetry. A singlet corresponding to the ^1H hydrogens of the central phenylene at 7.25 ppm can be identified by comparing the spectra from natural abundance and d_2 -deuterated samples. The ^{13}C NMR consists of the expected 7 aromatic signals, the two alkynes with carbons at 77.5 and 96.1 ppm, and the quaternary trityl carbons at 56.0 ppm. A signal for the fluorinated carbons appears at 151.36 ppm as doublet of doublets with $^1J_{\text{C-F}}$ and $^2J_{\text{C-F}}$ of 254.8 and 14.6 Hz. Long range $J_{\text{C-F}}$ coupling is also observed for the central phenylene *ipso* and protonated carbons, as well as for the benzylic alkyne carbons.

In addition to the expected FTIR signals (2228 cm^{-1} for the di-substituted alkyne) and parent ion (HRMS, $m/e = 646.2461$, MALDI-TOF), the structure of **1** was confirmed by X-ray diffraction with single crystals obtained by slow

evaporation of a saturated acetone solution. Notably, in a crystallization behavior reminiscent of previously reported analogous structures, colorless prisms from hot saturated benzene solutions slowly allowed to cool down were found to change from translucent to opaque after several days, suggesting the loss of solvent of crystallization [5]. Single crystal X-ray diffraction confirmed a clathrate structure [7] with two benzene molecules per unit cell (Figure 2). The loss of benzene from the crystal was accelerated by suspending the clathrate in mineral oil or by heating the sample up to 77 $^\circ\text{C}$, when desolvation occurred as a first order phase transition [5]. The main crystallographic parameters of the solvent free (form A) and benzene clathrate (form B) structures are listed in Table 1.

The solvent-free structure **1A** was solved in the triclinic space group $P\bar{1}$ with an asymmetric unit that consists of half a molecule of **1** as a result of coincident molecular and crystallographic inversion centers (Figure 3, top). The discrepancy between molecular and crystallography symmetries is the result of the positional disorder of the fluorine atoms,

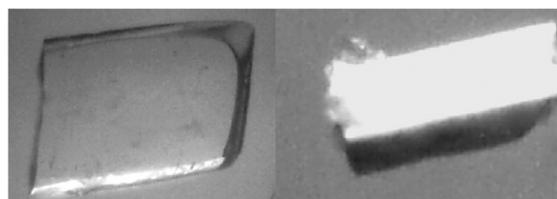


Fig. 2. Left: solvent-free crystal of **1** grown from Acetone. Right, partially desolvated benzene-clathrate of **1**.

Table 1. Main crystallographic parameters for the crystal forms of **1**.

	Form A	Form B
Empirical formula	$\text{C}_{48}\text{H}_{32}\text{F}_2$	$\text{C}_{48}\text{H}_{32}\text{F}_2 \cdot 2\text{C}_6\text{H}_6$
Formula weight	646.74	802.95
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
Z	1	1
Size, mm^3	$0.4 \times 0.4 \times 0.1$	$0.8 \times 0.5 \times 0.3$
Color, morphology	colorless prisms	colorless prisms
Temperature, K	102(2)	104(2)
Unit cell dimensions		
<i>a</i> , Å	9.1776(7)	8.511(3)
<i>b</i> , Å	10.5350(8)	9.532(3)
<i>c</i> , Å	10.5458(8)	14.630(5)
α , deg	62.7430(10)	77.451(5)
β , deg	70.8950(10)	76.548(5)
γ , deg	85.3720(10)	74.715(5)
<i>V</i> , Å ³	853.58(11)	1098.0(6)
<i>D_c</i> , Mg/m^3	1.258	1.214
Total reflections	7704	9805
Independent reflections	3998	5141
	$[R(\text{int}) = 0.0133]$	$[R(\text{int}) = 0.0172]$
<i>R</i> 1 [<i>I</i> > 2σ(<i>I</i>)]	0.0393	0.0492
<i>wR</i> 2 (all data)	0.1042	0.1287

which occur with equal probability on either side of the central phenylene (Figure 3, top). It is interesting to point out that the structure of compound **1** is isomorphous with that of the previously reported unsubstituted system, as expected for the nearly isosteric nature of hydrogen and fluorine. A visible deviation from linearity of the two alkynes is shown in the ORTEP diagram of compound **1**, which is drawn with thermal ellipsoids at 50% probability level. The elongation of the thermal ellipsoids of the carbon atoms of the central phenylene is consistent with the oscillatory and rotary motion previously described by ^2H NMR and dielectric spectroscopy [6].

The packing diagram for molecular rotor **1** is illustrated at the bottom of Figure 3. As in previous examples, and in agreement with the low crystallographic symmetry, molecules pack with their long axes along a parallel direction. Translation along the long molecular axis is characterized by a six fold phenyl embrace, consisting of complementary edge-to-face interactions [8]. Close contacts between aromatic C—H—F—C groups, illustrated by dotted lines in the figure, may or may not play a significant role in the packing structure of **1**.

The ORTEP diagram of the benzene-clathrate **1B**, with thermal ellipsoids drawn at the 50% probability level is illustrated in Figure 4. The benzene-clathrate is closely related to the solvent free structure with the same space group ($P\bar{1}$) and similar packing arrangements. The asymmetric unit is also composed of half a molecule of **1** but with an additional molecule of benzene sitting near the middle of the structure (Figure 4). As in the solvent-free structure, the fluorine atoms occupy the two positions of the central phenylene to satisfy, on average, the symmetry of the double trityl framework. Not surprisingly, there are no close C—H—F—C interactions in the clathrate as the benzene molecules adopt a parallel displaced dimeric

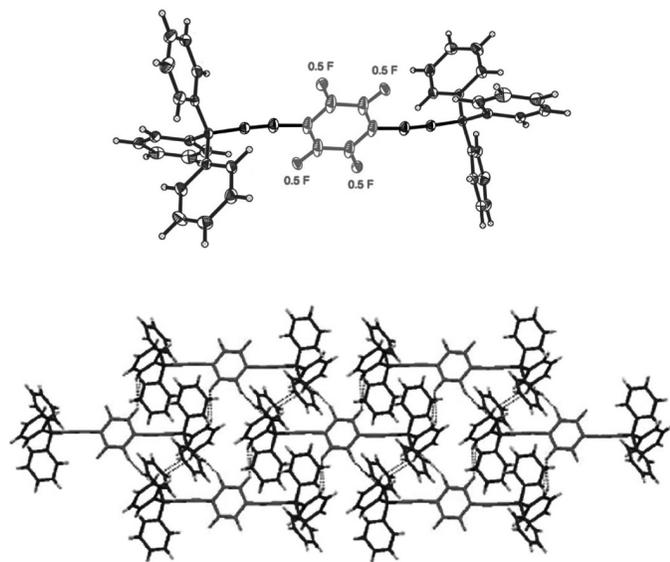


Fig. 3. Top: ORTEP structure of molecular rotor with thermal ellipsoids drawn at the 50% probability level. The occupancy of the fluorine atoms is also indicated as 0.5. Bottom: Packing arrangement of the solvent-free structure of **1**. X-Ray data were acquired at 102 K from colorless prisms grown from acetone at room temperature.

structure (not shown) that occupies much of the space at the center of structure. Also in agreement with the previously measured rotary dynamics of the central phenylene rotator, the thermal ellipsoids for carbon and fluorine atoms are elongated along the direction of rotation. Notably, the thermal ellipsoids for the benzene solvent molecules are extended along the plane of the ring, suggesting rapid rotation about the six-fold axis. As in the solvent-free structure, the long molecular axes are all aligned in infinite chains of trityl group experiencing edge-to-face interactions characteristic of “6-fold phenyl embrace” [8].

Conclusions. The synthesis and characterization of compound **1**, the intermediate 2,3-difluoro-1,4-trifluoromethanesulfonate **4**, and their deuterated analogs should be very valuable for the preparation of molecular gyroscopes with polar rotators. These compounds may lead to the preparation of new rotary dielectrics and novel molecular compasses.

Experimental

Materials

All reagents and solvents were purchased from Aldrich, Alfa Aesar, and Fisher and used as received, unless otherwise indicated. Difluorophenol (**2**) was purchased from Matrix Scientific.

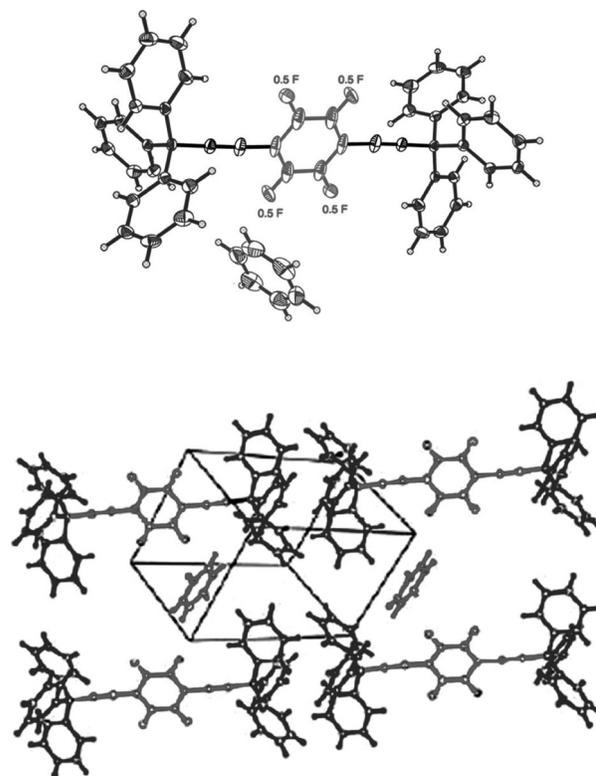


Fig. 4. (Top): ORTEP and (Bottom) packing arrangement of the benzene-clathrate of molecular rotor **1**. Thermal ellipsoids are drawn at the 50% probability level. X-Ray data were acquired at 104 K from colorless prisms grown by slowly cooling a hot benzene solution.

2,3-Difluoro-1,4-hydroquinone (3) [9]. 2,3-Difluorophenol (**2**) (2g, 15.3 mmol) was dissolved in 80 ml of a 6% w/w NaOH aqueous solution. Potassium persulfate (4.0 g, 15.3 mmol) was dissolved in the minimum amount of water and added drop wise to the solution of difluorophenol (20-30 min) using an addition funnel. The reaction was stirred for 2 days at room temperature, neutralized with concentrated HCl, concentrated to 1/2 the volume by rotary evaporation, and extracted with ethyl ether. The organic phase was dried over MgSO₄ or Na₂SO₄ and evaporated to recover starting material. The aqueous phase was acidified with concentrated HCl to pH 2, boiled for 1 h, concentrated to half its volume and extracted with diethyl ether. The second organic extract was dried over MgSO₄ and evaporated under vacuum. The procedure was repeated, the organic fractions combined, and the product chromatographed over silica gel using increasing hexane-ethyl ether in increasing solvent polarities. The product eluted with 8-2 and 7-3 hexane-ethyl ether and was collected as a crystalline solid with a m.p. = 124-26 °C in 27 % yield. ¹H NMR (500 MHz, acetone-d₆) δ 6.38 (m, 2H), 8.37 (s, 2H); ¹³C NMR (125 MHz, acetone-d₆) δ 112.3 (t, J_{C-F} = 3.1 Hz, CH), 139.60 (dd, J_{C-F} = 7.9, 3.4 Hz, CO), 142.10 (dd, J_{C-F} = 242.5, 13.6 Hz, CF); ¹⁹F NMR (470.39 MHz, acetone-d₆) δ -160.3 (s). FTIR (Powder, cm⁻¹): 3255 (b), 1621.5 (m), 1500.5 (s), 1385.1 (m), 1317.3 (m), 1258.4 (m), 1196.4 (m), 1165.5 (w), 1044.2 (m), 983.7 (s), 676.5 (b).

2,3-Difluoro-(1,4-ditriflate)hydroquinone (4). 2,3-Difluoro-hydroquinone (**4**) (256 mg, 1.7 mmol) was dissolved in 5 ml dry pyridine and cooled to -20 °C. Triflic anhydride (0.7 ml, 3.5 mmol) was added drop wise, the solution was allowed to warm to 0 °C and maintained at this temperature for 48 h by using an ice bath. The reaction mixture was poured into ethyl ether, the organic phase was washed several times with water, dried with MgSO₄ and evaporated to dryness under vacuum with a crude yield of 70%. This compound was used without further purification. ¹H NMR (500 MHz, acetone-d₆) δ 7.27 for a complex AA'BB' system, ¹³C NMR (125 MHz, acetone-d₆) δ 118.4 (s, CH), 118.6 (q, J = 318 Hz, CF₃), 137.2 (m, C), 144.27 (dd, J = 14 Hz, 160 Hz, CF) [10].

1,4-Bis(3,3,3-triphenylpropynyl)-2,3-difluorobenzene (1). The triflate derivative **4** (0.2 g, 0.5 mmol) was dissolved in 15 ml degassed THF, Pd(PPh₃)₂Cl₂ (35 mg, 0.05 mmol), CuI (19.0 mg, 0.1 mmol), alkyne **6** (268 mg, 1.0 mmol) and degassed iPr₂NH (2 ml) were added under argon and the solution was refluxed 2.5 h with stirring. After cooling to room temperature the reaction was quenched with saturated NH₄Cl and the organic phase separated, the aqueous phase was extracted twice with CH₂Cl₂. The combined organic phases were dried over Na₂SO₄, evaporated to dryness under vacuum. The compound crystallized from benzene to yield colorless crystals (125 mg, 38% yield), m.p. = 233-235 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.34 - 7.45 (m, 30H, Ar-H), 7.25 (s, 2H,

central phenylene); ¹³C NMR (125 MHz, CDCl₃) δ 56.5, 77.5 (t, J_{C-F} = 2.2 Hz), 103.6, 114.0 (dd, J_{C-F} = 9.5, 5.0 Hz), 127.0, 127.3 (t, J_{C-F} = 2.4 Hz), 128.1, 129.1, 144.6, 151.36 (dd, J_{C-F} = 254.8, 14.6 Hz); FTIR (powder, cm⁻¹): 3059.6 (w), 2919.3 (w), 2231.9 (w), 1597.8 (w), 1491.0 (m), 1470.7 (m), 1447.0 (m), 1230.7 (w), 1186.0 (w), 1060.1 (w), 1032.6 (w), 909.0 (w), 820.4 (w), 757.1 (m), 728.2 (m), 697.6 (s), 639.3 (m). HRMS (MALDI, TOF) m/z calculated for C₄₈H₃₂F₂ (M⁺) 646.2467, found 646.2461.

5,6-d₂-2,3-Difluorohydroquinone (d₂-3). 2,3-Difluorohydroquinone (**3**) (200 mg, 1.4 mmol) was placed in a pressure tube, to which a small amount of amberlyst-15 and 10-15 ml D₂O was added. The reaction mixture was heated at 180 °C for 24 h. The solution was allowed to cool and extracted with ethyl ether. The organic phase was washed with water, dried with MgSO₄ and evaporated under vacuum. The sample was chromatographed over silica gel using increasing solvent polarities and eluted with hexane - ethyl ether 8:2 and 7:3. The resulting product was isolated as a crystalline solid with a m.p. = 124-126 °C in 51% yield. ¹H NMR (500 MHz, acetone-d₆) δ 6.63 (s, 0.14H, residual), 8.37 (s, 2H); ¹³C NMR (125 MHz, acetone-d₆) δ 112.23 (dt, J_{C-D} = 24.8, J_{C-F} = 3.0 Hz, CD), 139.5 ppm (dd, J_{C-F} = 7.5, 3.4 Hz, CO), 142.0 (dd, J_{C-F} = 242.5, 13.6 Hz, CF); FTIR (powder, cm⁻¹): 3245 (br), 2917.9 (m), 2850.1 (m), 1686.3 (m), 1613.8 (m), 1477.7 (s), 1380.0 (m), 1293.4 (m), 1259.8 (m), 1232.2 (m), 1083.7 (m), 1048.1 (s), 990.4.7 (m), 922.9 (s), 665.6 (br).

2,3-difluoro-5,6-d₂-(1,4 ditriflate) hydroquinone. The procedure for the synthesis of **4** was followed and the resulting product used without further purification (crude yield 75%). The identity of this compound was supported by the following data: ¹³C NMR (125 MHz, acetone-d₆) δ 118.4 (t, J_{CD} = 25 Hz), 118.6 (q, J_{C-F} = 318 Hz, CF₃), 144.27 (dd, J_{C-F} = 14, 160 Hz).

1,4-bis(3,3,3-triphenylpropynyl)-4,5-d₂-2,3-difluorobenzene (d₂-1). The procedure to prepare **1** was followed (40% yield, m.p.=233-235 °C). ¹H NMR (500 MHz, CDCl₃) δ 7.34 - 7.45 (m, 30H, Ar-H); ¹³C NMR (125 MHz, CDCl₃) δ 56.46, 77.47, 103.65, 113.90 (dd, J = 9.9, 5.3 Hz), 126.92 (t, J = 26.9 Hz), 127.03, 128.11, 128.32 (benzene), 129.14, 144.64, 151.34 (dd, J = 254.6, 15.2 Hz); FTIR (powder, cm⁻¹): 3057.3 (w), 2235.2 (w), 1596.5 (m), 1546.4 (w), 1489.7 (s), 1448.0 (s), 1257.9 (w), 1217.3 (w), 1185.0 (w), 119.0 (m), 1074.1 (m), 1032.0 (m), 1002.3 (w), 906.6 (m), 822.1 (w), 753.6 (s), 731.5 (s) 696.1 (s), 637.8 (s), 592.8 (m). HRMS (MALDI, TOF) m/z calculated for C₄₈H₃₀D₂F₂ (M⁺) 648.2598, found 648.2653.

CCDC 669767 and 669768 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Acknowledgments

This work was supported by the National Science Foundation through grants DMR0307028 and DGE-0114443 [NSF IGERT: Materials Creation Training Program (MCTP)]. Support for a sabbatical leave at UCLA to RS by CONACYT Mexico, and UC-MEXUS is also acknowledged.

References

1. (a) Fletcher, S. P.; Dumur, F.; Pollard, M. M.; Feringa, B. L., *Science* **2005**, *310*, 80-82. (b) Balzani, V.; Credi, A.; Venturi, M. *Molecular Devices and Machines – A Journey into the Nano World*; Wiley-VCH: Weinheim, Germany, 2003. (c) Sauvage, J.-P. *Molecular Machines and Motors*; Springer-Verlag: New York, 2001; Vol. 99. (d) Kelly, T. R.; De Silva, H.; Silva, R. A., *Nature* **1999**, *401*, 150-152. (e) Leigh, D. A.; Wong, J. K. Y.; Dehez, F.; Zerbetto, F., *Nature* **2003**, *424*, 174-179.
2. (a) Karlen, S. D.; Garcia-Garibay, M. A. *Topics Curr. Chem.* **2006**, *262*, 179-228. (b) Khuong, T.-A. V.; Nuñez, J. E.; Godinez, C. E.; Garcia-Garibay, M. A., *Acc. Chem. Res.* **2006**, *39*, 413-422.
3. (a) Dominguez, Z.; Dang, H.; Strouse, M.J.; Garcia-Garibay, M.A. *J. Am. Chem. Soc.*, **2002**, *124*, 2398-2399. (b) Dominguez, Z.; Dang, H.; Strouse, J. M.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.*, **2002**, *124*, 7719-7727.
4. Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281.
5. Dominguez, Z.; Khuong, T.A.V.; Sanrame, Dang, H.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.*, **2003** *125*, 8827-8837.
6. Horansky, R. D.; Clarke, L. I.; Winston, E. B.; Price, J. C.; Karlen, S. D.; Jarowski, P. D.; Santillan, R.; Garcia-Garibay, M.A. *Phys. Rev. B.*, **2006**, *74*, 054306.
7. A clathrate is a stoichiometric two-component crystalline structure which, unlike an inclusion compound, can only exist as such in the solid state. Compound **1** is structurally related to molecules known as wheel-and-axle clathrates. For leading references please see: McNicol, D. D.; Toda, F.; Bishop, R. *Comprehensive Supramolecular Chemistry*; Pergamon: Oxford, 1996; Vol. 6.
8. (a) Scudder, M.; Dance, I. *J. Chem. Soc., Dalton Trans.* **1998**, 329-344. (b) Scudder, M.; Dance, I. *Dalton* **2000**, 2909-2915. (c) Dance, I.; Scudder, M. *New Journal of Chemistry* **1998**, *22*, 481-492. (d) Lacour, J.; Bernardinelli, G.; Russell, V.; Dance, I. *CrystEngComm* **2002**, *4*, 165-170. (e) Karlen, S. D.; Kahn, S. I.; Garcia-Garibay, M.A. *Cryst. Growth & Design*, **2005**, *5*, 53-55.
9. Essers, M.; Haufe, G. *J. Chem. Soc., Perkin Trans. 1*, **2002**, 2719-2728.
10. Stang, Peter J.; Hanack, Michael; Subramanian, L. R. *Synthesis* **1982**, 85-126.