SUPPLEMENTARY INFORMATION

Selective Catechol-Triggered Supramolecular Gel Disassembly

José A. Sáez, Beatriu Escuder, Juan F. Miravet

Departament de Química Inorgànica i Orgànica, Universitat Jaume I, Avda. Sos Baynat s/n, 12071 Castelló, Spain.

Synthesis

The preparation of compound **1** has been described elsewhere.[1]

Compound **2.** Isonicotinic acid (1.66 g, 13.5 mmol) and triethylamine (1.87 mL, 13.5 mmol) were dissolved in THF (120mL) and cooled to 0ºC (ice-bath) under N_2 atmosphere. Then a solution of ethyl chloroformate (1.29 mL, 13.5 mmol) in THF (10mL) was added dropwise with vigorous stirring. After 30 minutes a solution of N-L-valinyl-propylamine[2] (1.78 g, 11.2 mmol) in THF (50mL) was added dropwise. The resulting reaction mixture was stirred at 0ºC for 1 hour and allowed to warm up to room temperature overnight. THF was evaporated under reduced pressure. The resulting yellowish solid was washed sequentially with 1 M aqueous sodium hydroxide and cold water. Then after drying overnight under vacuum at 60ºC pure compound **2** was obtained as a white solid (2.37 g, 9.0 mmol, 80%).

[1] J. F. Miravet, B. Escuder, *Chem. Commun.*, 2005, 5796.
[2] a) M. I. Burguete, F. Galindo, M. A. Izquierdo, S. V. Luis, L. Vigara, *Tetrahedron*, **63**, 2007, 9493.

^{1}H NMR (DMSO-d_6): 8.70 (dd, J1=4.5 Hz, J2=1.5 Hz, 2H), 8.56 (d, J=8.6 Hz, 1H), 8.04 (t, J=5.5 Hz, 1H), 7.77 (dd, J1=4.5 Hz, J2=1.5 Hz, 2H), 4.24 (t, J=8.4 Hz, 1H), 3.09-2.97 (m, 2H), 2.10 (m, 1H), 1.40 (m, 2H), 0.90 (dd, J1=6.7 Hz, J2=4.4 Hz, 6H), 0.83 (t, J=7.4 Hz, 3H)

^{13}C NMR (DMSO-d_6): 170.90, 165.39, 150.52, 141.70, 122.00, 59.71, 40.75, 30.45, 22.70, 19.72, 19.30, 11.84.

HRMS (ESITOF+): Calcd. for $C_{14}H_{21}N_3NaO_2^+$ [M + Na^+] 286.1531; found 286.1535.

Gel disassembly studies.

Gels of compound **1** in toluene were prepared by cooling at room temperature a hot dissolution of this compound in 1 mL of hot toluene prepared in a screw-capped vial (6.0 mg, 12 mM). Thermal stability and electron microscopy study of these gels has been reported elsewhere.[3]

For the gel disassembly studies gels were prepared from a 1 mL of a hot solution of the gelator (12 mM) and the corresponding hydroxyaromatic compound (24 mM) in a screw-capped vial. After resting for 10 minutes at room temperature, gel formation was observed in all the cases. Gel stability with time was tested by vial inversion.

Alternatively, 1 mL of a 24 mM solution of the hydroxyaromatic compounds was added on the top of the preformed gels of **1** in toluene. Gel stability with time was tested by vial inversion.

[3] D. S. Tsekova, J. A. Sáez, B. Escuder, J. F. Miravet, *Soft Matter*, 2009, **5**, 3727.

NMR studies.

NMR studies were carried out with a spectrometer operating at 300 MHz for ^{1}H.

To monitor gel disassembly in the presence of resorcinol a gel containing gelator **1** (12 mM), catechol (24 mM) and tetrachloroethane (12 mM) as internal standard was prepared in 0.6 mL of toluene-d_8. The integration of the signals was monitored every 15 minutes for 12 hours. The NMR spectra recorded for the fresh sample and for the sample after 12 hours (the gel was disassembled) are shown in Fig. S1.

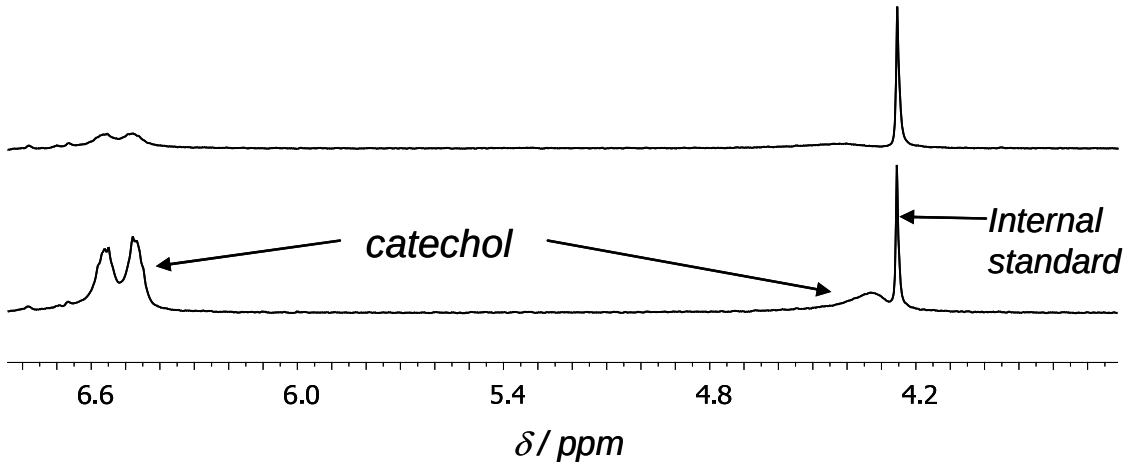

Fig. S1. Fragment of the NMR spectra in toluene-d_8 of a sample containing **1** (12 mM), catechol (24 mM) and tetrachloroethane as internal standard. Bottom: fresh gel sample; top: Disassembled gel after 12 hours.

UV-VIS release studies

Gels of **1** in toluene (12 mM, 2 mL) were prepared in the presence of tetrakisphenilporphyrin (0.2 mg, 3.25 mmol). To these gels solutions of hydroxyaromatic compounds were added on top (1 mL, 0.1 M). Aliquots of the overnatant solution (100 μL) were taken every 15 minutes and diluted to 0.4 mL. The absorbance of these solutions at 420 nm was monitored by UV-VIS spectroscopy in a cell with a 0.1 cm path.

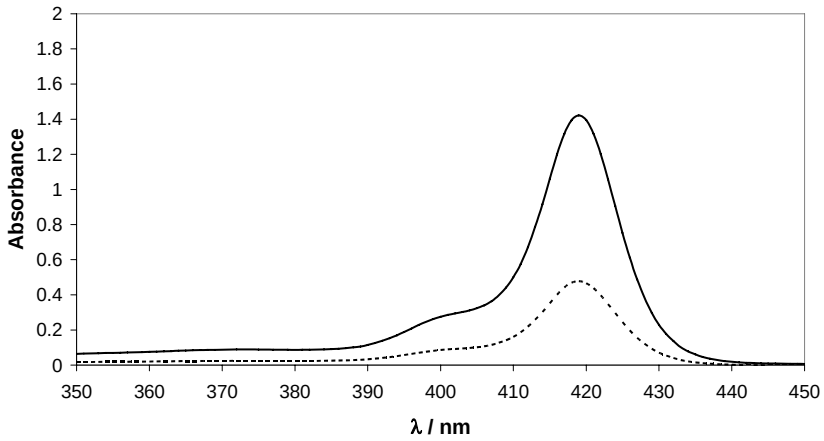

Fig. S2. UV-VIS detection of tetrakisphenylporphyrin liberated after 30 min from 2 mL of a 12 mM gel of **1** in toluene after addition of an overnanant solution (1 mL, 0.1 M) of resorcinol (dotted line) and catechol (solid line).

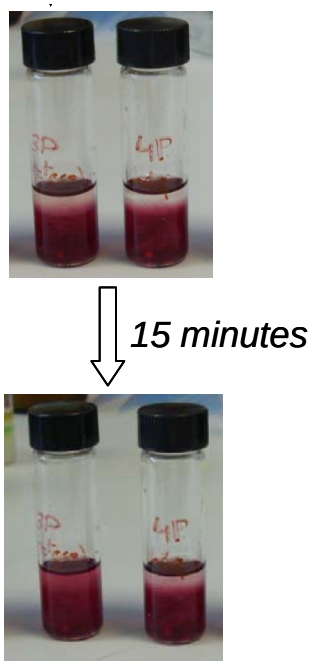

Fig. S3. Pictures of the dye release form vials containing supramolecular gels and solutions with catechol (left) and hydroquinone (right).

Computational details.

The geometry of the the compound **2** and the complex between compound **2** and catechol **6** was firstly modeled and minimized with AMBER* force field (Macromodel v. 9.5)[1] and then optimized using B3LYP[2] exchange-correlation functionals together with the standard 6-31G(d) basis set[3]. Solvent effects of toluene were considered at the optimization and NMR (see later) calculations using a self-consistent reaction field (SCRF)[4] based on the polarizable continuum model (PCM) of the Tomasi's group[5]. To ensure that the proposed structures were a minima, a frequency analysis was done, verifying that all imaginary frequencies had dissappeared. NMR properties in toluene of **2** and its complex were computed using the GIAO method[6] obtaining ^{1}HNMR chemical shifts subtracting the isotropic magnetic shielding value of the selected ^{1}H nuclei to that obtained for the ^{1}H of TMS (in ppm). All these calculations were carried out with Gaussian03 (rev. C02)[7] suite of programs.

The geometry of the optimized complex between compound **2** and catechol **6** is shown in Figure S2. The distances of the hydrogen bonding between catechol (hydrogen acceptor) and **2** (hydrogen donor) are of 2.087 and 2.16 Å, respectively, and the distances between the centers of the diphenolic and pyridine rings are of 4.30 Å, being 4.51 Å the maximum distance and 3.65 Å the minimum one, since both rings are not arranged in a parallel manner, but in a skew one. The geometries in XYZ coordinates, together with the first vibrational frequency, for the optimized geometries of the compound **2** and its complex with **6** may be found below.

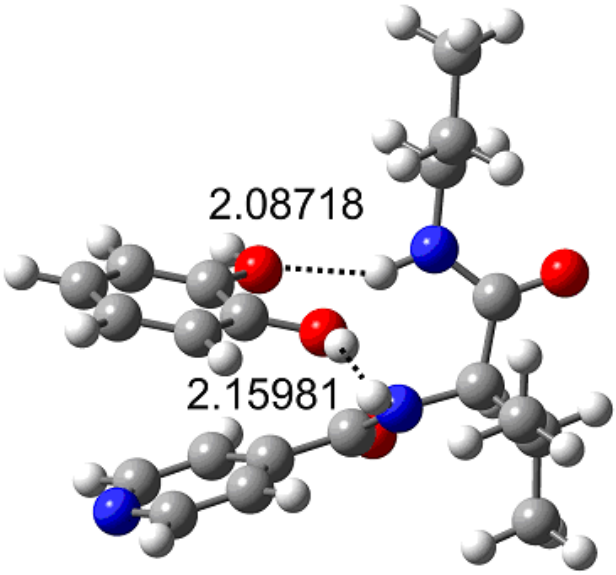

Fig. S2. B3LYP/6-31G(d) geometry in toluene (PCM method) of the complex between compound **2** and catechol **6**. The lenghts are given in Angstroms.

In the Table S1, the chemical shifts for selected ^{1}H nuclei have been depicted. In the first column, the computed ^{1}H shifts for the B3LYP/6-31G(d)/toluene(PCM) geometry of compound **2** are depicted. These values are in reasonable agreement with that estimated from a ChemDraw ^{1}H spectra simulation at the second column in Table S1 (except on H24 and H33, the relatively acidic amidic hydrogens implied in the H-bonding of catechol) and are almost equal to those computed for the compound **2** with the same geometry as in **2**-**6** complex (third column), fact that discards the influence of the geometrical parameters over the ^{1}H computed shifts for **2**-**6** complex and points out the influence of the catechol molecule in the magnetic shielding and deshielding of the ^{1}H nuclei of the pyridine ring experimentally observed.

^{1}H nuclei	Computed ^{1}H shifts for compound **2** (ppm)	ChemDraw estimated ^{1}H shifts for compound **2** (ppm)	Computed ^{1}H shifts for compound **2*** (ppm)	Computed ^{1}H shifts for **2** - **6** complex (ppm)
H20	9,2	8,8	9,1	8,8
H21	9,1	8,8	9,1	8,5
H22	7,5	7,7	7,5	7,4
H23	8,2	7,7	8,2	7,9
H24	5,9	8,9	5,8	7,6
H25	5,0	4,5	5,1	5,0
H33	6,0	8,0	5,9	8,0
H38	1,1	1,0	1,2	1,0
H39	0,9	1,0	0,9	0,9

Table S1. ^{1}H chemical shifts (in ppm) for selected ^{1}H nuclei of compound **2** and complex **2** - **6** (see Figure S3). * ^{1}H shifts computed for the **2** compound with the same geometry as in **2** - **6** complex (see text).

The presence of the diphenol moiety of the catechol hydrogen-bonded near the pyridine of **2** pushes the shift of the ^{1}H nuclei of the pyridine (H20 to H23) *ca.* 0.3 ppm upfield, leaving unmodified the shift of valine stereogenic hydrogen H25 and the shifts of the C3 lateral chain of **2**. The shifts of the amidic hydrogens are the most disturbed ones, being displaced downfield 1.8 (H24) and 2.1 (H33) ppm with the formation of the complex.

Although the modification extent of pyridine ^{1}H shifts is reasonably well predicted (*ca*. 0.3 ppm theoretically predicted *versus ca*. 0.2 ppm experimentally observed), the direction is not since all the ^{1}H shifts are predicted to be pushed upfield and experimentally the aromatic pyridine doublets get closer. Anyway, an interaction between catechol and **2** beyond hydrogen-bonding is predicted to take place.

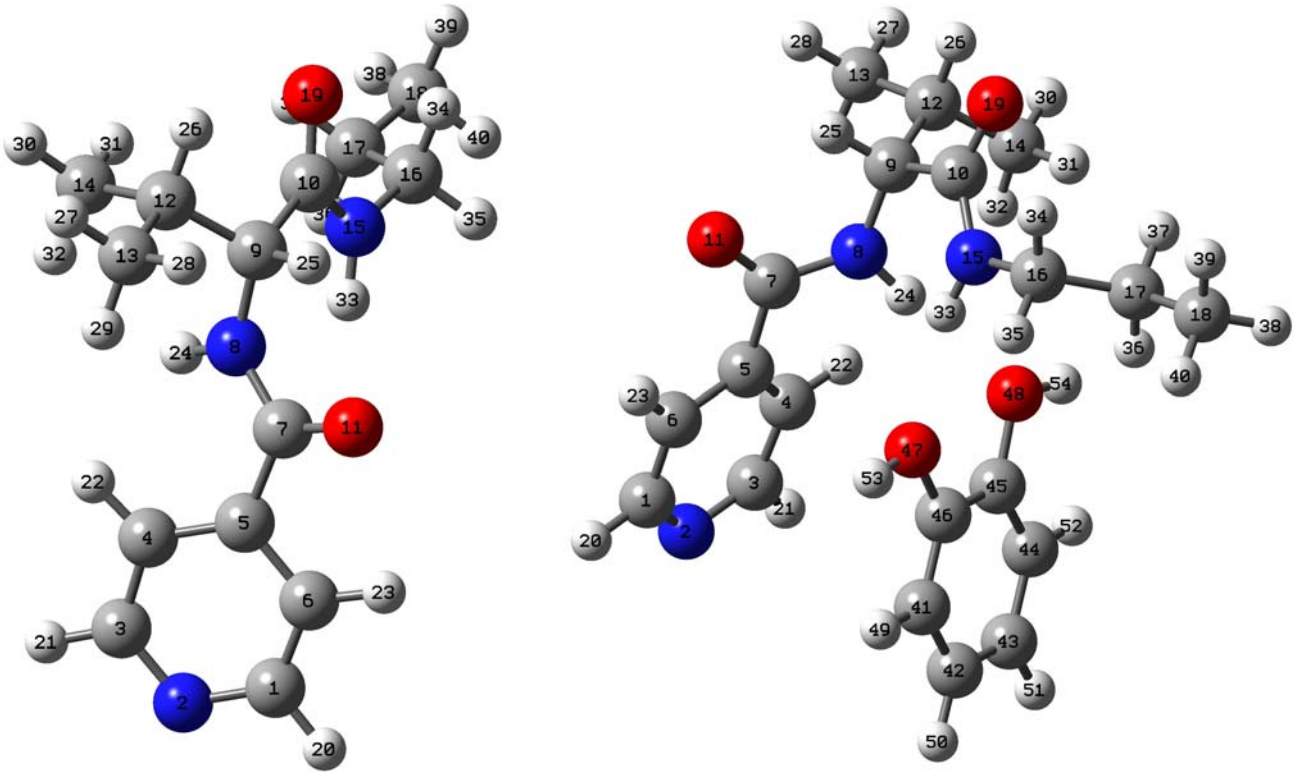

Fig. S3. B3LYP/6-31G(d) geometry in toluene (PCM method) of the compound **2** (left) and **2-6** complex (right) together with the atom numbering used in **Table S1**.

Geometries of selected stationary points.

Compound **2**

Charge: 0; multiplicity: 1; 1st freq: 32.7564

C	4.39956500	-1.90757200	-0.39562800
N	4.80214700	-1.65081200	0.85795900
C	4.09286900	-0.75363300	1.55366100
C	2.96455600	-0.10082800	1.05454100
C	2.54510400	-0.38658700	-0.25005700
C	3.29676500	-1.30122100	-0.99384900
C	1.35198200	0.25492000	-0.91117500
N	0.34340500	0.65036700	-0.07221200
C	-0.82442500	1.40261700	-0.52478600
C	-2.13564800	0.57723900	-0.51857600
O	1.29362000	0.38036900	-2.13188800

C	-1.00090200	2.73868800	0.23726900
C	0.15690300	3.70119600	-0.05335100
C	-1.20422000	2.54018500	1.74712800
N	-1.99100800	-0.77196200	-0.50643400
C	-3.12434600	-1.68834100	-0.57135400
C	-3.60559400	-2.16567400	0.80514600
C	-4.78542100	-3.13638900	0.69640300
O	-3.22689100	1.14040200	-0.58169700
H	4.98957000	-2.63492300	-0.94925600
H	4.44342200	-0.53983600	2.56188900
H	2.45822900	0.63370100	1.67354100
H	3.01582400	-1.52748700	-2.01665900
H	0.43260600	0.46089700	0.91686100
H	-0.62706100	1.62650700	-1.57938100
H	-1.92470700	3.16578600	-0.16591400
H	-0.01654200	4.66694900	0.43454200
H	0.26758600	3.88182800	-1.12872600
H	1.11082400	3.30824400	0.31916700
H	-1.41056700	3.50141200	2.23036100
H	-2.05021800	1.87663300	1.95510500
H	-0.30909900	2.12866000	2.23402800
H	-1.05659900	-1.15185800	-0.44063600
H	-3.93212400	-1.16228400	-1.08759600
H	-2.83274300	-2.54490800	-1.19032500
H	-2.77181700	-2.64718100	1.33463700
H	-3.89144500	-1.28702500	1.39619900
H	-5.12563000	-3.45740800	1.68624200
H	-5.63600800	-2.66895400	0.18657700
H	-4.51226500	-4.03566200	0.13059600

2 - **6** complex

Charge: 0; multiplicity: 1; 1st freq: 21.4608

C	0.00000000	0.00000000	0.00000000
N	1.34142663	0.00000000	0.00000000
C	1.95237080	1.18995192	0.00000000
C	1.27159490	2.40920820	0.00634433
C	-0.12718490	2.40205385	0.00530679
C	-0.77119097	1.16005252	-0.01055888
C	-0.98057526	3.64637127	-0.04738787
N	-0.41883466	4.78683386	0.45150387
C	-1.09549848	6.07832073	0.39057734
C	-1.62441576	6.59815787	1.74792008
O	-2.10808879	3.60474830	-0.53877610
C	-0.23215071	7.16738257	-0.29905960

C	0.02555136	6.82621972	-1.77184948
C	1.07968705	7.44600766	0.44958510
N	-1.51956137	5.76617555	2.80781808
C	-1.92836701	6.15544010	4.15113398
C	-0.81105204	6.85198998	4.94100205
C	-1.23548605	7.19666672	6.37152785
O	-2.13217007	7.72010929	1.81093697
H	-0.47958858	-0.97727008	-0.00285576
H	3.04045307	1.17317320	-0.02078527
H	1.83449816	3.33665528	-0.01673431
H	-1.85452391	1.11668817	-0.04080953
H	0.42450313	4.70891059	1.01139197
H	-1.98518903	5.90967048	-0.22396980
H	-0.84325910	8.07498888	-0.24996321
H	0.57632690	7.63635257	-2.26378445
H	-0.91325232	6.67774994	-2.31775990
H	0.61952049	5.90986930	-1.87280297
H	1.61686121	8.27852033	-0.01824101
H	0.89770212	7.71450290	1.49637821
H	1.75082698	6.57679243	0.42617216
H	-1.04458337	4.87711546	2.70835570
H	-2.79393988	6.81812336	4.05932529
H	-2.25113487	5.24865614	4.67598075
H	0.07060599	6.19791828	4.95415735
H	-0.52353803	7.76283465	4.40158129
H	-0.42728612	7.69873975	6.91474837
H	-2.10571748	7.86421910	6.37761397
H	-1.50439273	6.29429686	6.93542712
C	1.10877939	1.28763265	4.21524647
C	2.41013211	0.86327831	4.49924899
C	3.49060379	1.69444618	4.21411593
C	3.26855342	2.94781553	3.63541508
C	1.97424450	3.37037827	3.34421900
C	0.88409726	2.53456001	3.63804373
O	-0.36909635	3.00174022	3.32724129
O	1.69535378	4.58527964	2.75335090
H	0.25913587	0.64916894	4.44833758
H	2.56808029	-0.11236396	4.94851183
H	4.50484276	1.37613455	4.43468146
H	4.10573295	3.60281124	3.40177588
H	-1.02702715	2.31609155	3.52907718
H	2.50109047	5.12866806	2.75237369

Computational details references:

[1] (a) F. Mohamadi, N.G.J. Richards, W.C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson and W.C. Still, J. Comput. Chem. 11 (1990), pp. 440–467. (b) Schrodinger, L. L. C. New York, NY, 2005.

[2] (a) Becke, A. D. J. Chem. Phys. 1993, 98, 5648-5652. (b) Lee, C.; Yang, W.; Parr, R. G. Phys. Rev. B 1988, 37, 785-789.

[3] Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. Ab initio Molecular Orbital Theory; Wiley: New York, 1986.

[4] (a) Tomasi, J.; Persico, M. Chem.Rev. 1994, 94, 2027–2094. (b) Simkin, B.Y.; Sheikhet, I. Quantum Chemical and Statistical Theory of Solutions-A Computational Approach; Ellis Harwood: London, 1995.

[5] (a) Cances, E.; Mennucci, B.; Tomasi, J. J. Chem. Phys. 1997, 107, 3032–3041.(b) Cossi, M.; Barone, V.; Cammi, R.; Tomasi, J.Chem. Phys. Lett. 1996, 255, 327–335. (c) Barone, V.; Cossi, M.; Tomasi, J. J.Comput.Chem. 1998, 19, 404–417.

[6] (a) F. London, “The quantic theory of inter-atomic currents in aromatic combinations,” J. Phys. Radium, 8 (1937) 397-409. (b) R. McWeeny, “Perturbation Theory for Fock-Dirac Density Matrix,” Phys. Rev., 126 (1962) 1028. (c) R. Ditchfield, “Self-consistent perturbation theory of diamagnetism. 1. Gauge-invariant LCAO method for N.M.R. chemical shifts,” Mol. Phys., 27 (1974) 789-807. (d) K. Wolinski, J. F. Hilton, and P. Pulay, “Efficient Implementation of the Gauge-Independent Atomic Orbital Method for NMR Chemical Shift Calculations,” J. Am. Chem. Soc., 112 (1990) 8251-60. (e) J. R. Cheeseman, G. W. Trucks, T. A. Keith, and M. J. Frisch, “A Comparison of Models for Calculating Nuclear Magnetic Resonance Shielding Tensors,” J. Chem. Phys., 104 (1996)

5497-509.

[7] 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.