Synergic Para-Directed Monometalation of Bis(toluene)chromium by Alkali-Metal-Mediated Magnesiation

Prokopis C. Andrikopoulos, David R. Armstrong, Eva Hevia,* Alan R. Kennedy, and Robert E. Mulvey*

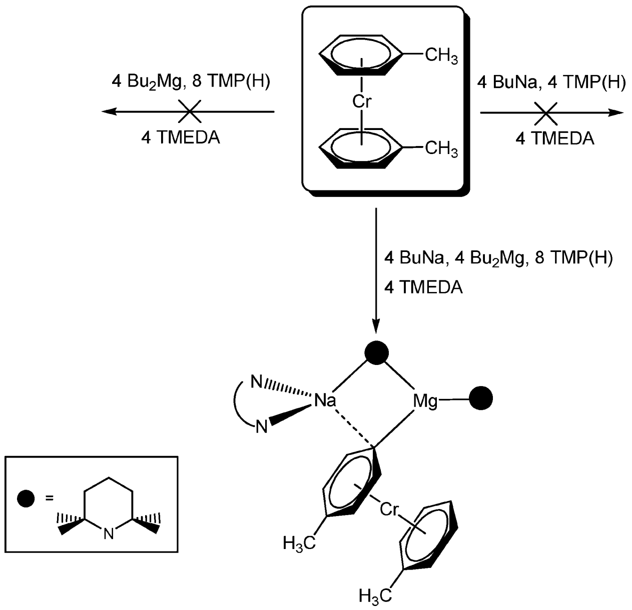
WestCHEM, Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, U.K.

Received March 7, 2006

Summary: Bis(toluene)chromium is regioselectively deprotonated at the para position on one ring only by a mixed sodium−magnesium alkyl bis(amide) TMEDA activated synergic base in a reaction influenced by the Na⋯π-arene contacts present in the crystalline trimetallic product.

Metalation is one of the most important synthetic tools used for the functionalization of metallocenes.[1] Therefore, the efficiency and selectivity of metalation procedures have played a crucial role in the development of metallocene chemistry. As an example, dimetalation of ferrocene is easily achieved by reaction with butyllithium in the presence of the diamine TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine),[2] and subsequent treatment with the desired electrophile constitutes a standard approach to preparing the large family of disubstituted ferrocenyl compounds. When more than one hydrogen needs to be removed from the metallocene (or when a ring-substituted metallocene is employed), regioselectivity is an important requirement. Thus, we have recently demonstrated that ferrocene can be readily tetradeprotonated in the 1,1′,3,3′-positions by the mixed-metal tris(diisopropylamide) base $NaMg(N^iPr_2)_3$.[3] The special selectivities attainable with these mixed-metal reagents have also been revealed in the synergic metalation of organic molecules, such as toluene, which can be regioselectively deprotonated in the meta position by the base [(TMEDA)Na(μ-Bu)(μ-TMP)Mg(TMP)] (**1**; TMP = 2,2,6,6-tetramethylpiperidide), leaving the methyl site (the most acidic position in pK_a terms) intact.[4] The same reagent accomplishes the synergic monometalation of the classical organometallic molecule [$Cr(C_6H_6)_2$][5,6] to give [(TMEDA)Na(μ-TMP){μ-C_6H_5)Cr(C_6H_6)}Mg(TMP)], opening up a new route to synthesize heteroleptic bis(arene)chromium complexes. To date, the standard way to metalate this sandwich complex, developed by Elschenbroich, has been lithiation by BuLi in the presence of TMEDA, which affords mainly the dilithio species [$Cr(C_6H_5Li)_2$] and the monolithio species [$Cr(C_6H_5Li)(C_6H_6)$], formed only as a minor product (5−20%).[7] Using a similar approach, but employing the more reactive branched alkyllithium reagent ^{t}BuLi, Braunschweig reported in 2005 the selective metalation of [$(C_5H_5)Cr(C_7H_7)$] in both rings of the molecule in yields of up to 80%.[8] The metalation of other bis(arene)chromium complexes remains largely unexplored. This communication reports the regioselective para monodeprotonation of bis(toluene)chromium manifested in the mixed-metal sodium−magnesium amido complex [(TMEDA)Na(μ-TMP){μ-(p-C_6H_4Me)Cr(C_6H_5Me)}Mg(TMP)] (**2**).[9] We describe the synthesis and characterization of **2** and present the results of a theoretical study which shed light on the reasons for the para selectivity of the synergic metalation.

Scheme 1



The synergic base **1** (which was previously introduced by our research group in a recent communication)[10] can be readily prepared in situ by reaction of the individual alkyl reagents butylsodium and dibutylmagnesium with 2 molar equiv of the cyclic amine TMP(H) and 1 molar equiv of the chelating diamine ligand TMEDA. The addition of freshly prepared [$Cr(C_6H_5$-$Me)_2$][11] to a solution of **1** in hexane initially afforded a brown solution. However, after only a few minutes of heating under reflux, a distinct color change to deep red occurred, similar to the change that accompanies the metalation of [$Cr(C_6H_6)_2$]. In view of the results previously found for the latter metallocene, **1** was used in a 4 molar equiv excess with respect to bis(toluene)chromium (see Scheme 1). This afforded [(TMEDA)Na(μ-TMP){μ-(p-C_6H_4Me)Cr(C_6H_5Me)}Mg(TMP)] (**2**) as a red crystalline solid in isolated yields exceeding 60%. As

---

(1) Long, N. J. *Metallocenes: An Introduction to Sandwich Chemistry*, 1st ed.; Blackwell Science: Oxford, U.K., 1998.

(2) (a) Rausch, M.; Ciappenelli, D. *J. Organomet. Chem.* **1967**, *10*, 127. (b) Butler, I. R.; Cullen, W. R.; Ni, J.; Retting, S. J. *Organometallics* **1985**, *4*, 2196.

(3) Andrikopoulos, P. C.; Armstrong, D. R.; Clegg, W.; Gilfillan, C. J.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Parkinson, J. A.; Tooke, D. M. *J. Am. Chem. Soc.* **2004**, *126*, 11612.

(4) Andrikopoulos, P. C.; Armstrong, D. R.; Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 3459.

(5) Hevia, E.; Honeyman, G.; Kennedy, A. R.; Mulvey, R. E.; Sherrington, D. C. *Angew. Chem., Int. Ed.* **2005**, *44*, 68.

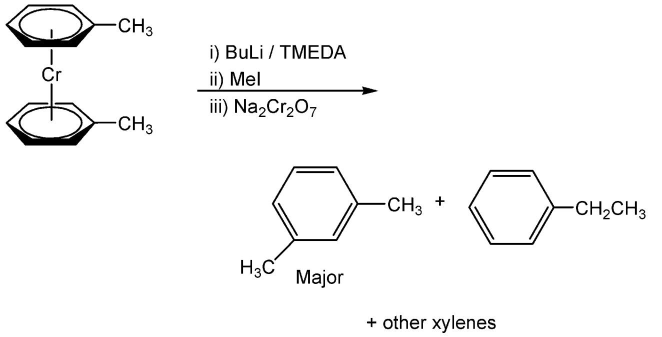
(6) For a historical review see also: (a) Seyferth, D. *Organometallics* **2002**, *21*, 1520. (b) Seyferth, D. *Organometallics* **2002**, *21*, 2800.

(7) Elschenbroich, C. *J. Organomet. Chem.* **1968,** *14*, 157.

(8) Braunschweig, H.; Lutz, M.; Radacki, K. *Angew. Chem., Int. Ed.* **2005**, *44*, 5647.

10.1021/om060216v CCC: $33.50

Scheme 2



discussed below, the selective monomagnesiation of [Cr(C_6H_5-Me)$_2$] in the para position of one of the rings has occurred, leaving the second ring untouched (even when a 4 molar equiv excess of **1** is employed) and, more surprisingly, the methyl position of the metalated ring remains intact. This is in contrast with previous experiments treating the metallocene with ^{n}BuLi/TMEDA followed by treatment of the metalated product with MeI and subsequent oxidation with $Na_2Cr_2O_7$, which show that the methyl groups are meta-directing in the metalation process and that lithiation of the methyl substituents also occurred, affording a mixture of products (Scheme 2).[12]

In our case the presence of TMEDA in the reaction is required to successfully accomplish the deprotonation of bis(toluene)-chromium. When the same reaction is attempted in the absence of TMEDA, that is, using a BuNa/Bu$_2$Mg/2 TMP(H) mixture, no color change indicating metalation is observed. Thus, the diamine plays a pivotal role in this reaction. It not only aids in the crystallization of **2** but also activates the mixed-metal reagent in its metalating ability. However, strictly, what is required to effect metalation is the presence of a donor ligand (as even an excess of TMP(H) in the absence of TMEDA will suffice).

As proof of this concept, homometallic control reactions which combine TMP(H) and TMEDA with one of the corresponding alkyl monometallic reagents (BuNa and Bu$_2$Mg) were carried out, but these failed to achieve the deprotonation of the metallocene. This confirms that the selective metalation of [Cr-(C_6H_5-Me)$_2$] by the mixed-metal reagent **1** is genuinely synergic in origin and constitutes a new example of the emerging concept of alkali-metal-mediated magnesiation.[13]

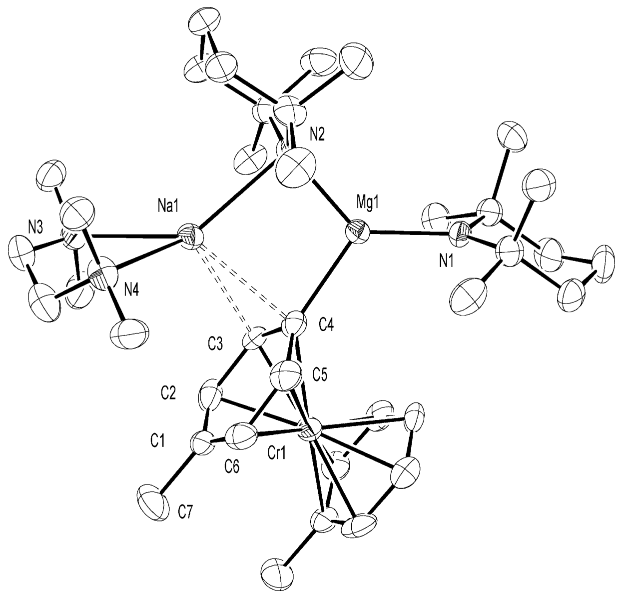


Figure 1. Molecular structure of **2**, with hydrogens atoms omitted for clarity and 50% probability displacement ellipsoids. Selected distances (Å) and angles (deg): Mg(1)−C(4) = 2.185(6), Mg(1)−N(2) = 2.085(4), Mg(1)−N(1) = 2.004(5), Na(1)−C(4) = 2.662(6), Na(1)−C(5) = 2.847(6), Na(1)−N(2) = 2.503(4), Na(1)−N(3) = 2.562(5), Na(1)−N(4) = 2.494(5); N(2)−Mg(1)−C(4) = 104.37(19), N(2)−Na(1)−C(4) = 81.50(16), Mg(1)−C(4)−Na(1) = 83.90(19), Mg(1)−N(2)−Na(1) = 90.05(16).

The molecular structure of **2** has been determined by X-ray crystallography (Figure 1).[14] A four-membered NaNMgC ring constitutes the central feature of the structure, with two bridging ligands connecting the two metals, a TMP anion, and a molecule of bis(toluene)chromium selectively monodeprotonated in the para position (this molecule can be considered as a ligand that coordinates through a single C atom). The remainder of the metal coordination is completed by a terminal TMP ligand attached to Mg and the chelating diamine TMEDA bonded in a bidentate mode to the Na atom. The central NaNMgC ring is essentially planar (sum of the endocyclic angles 359.82°). This four-membered-ring motif is also present in other related mixed-metal Na/Mg compounds such as the base **1** itself or in [(TMEDA)Na(μ-TMP)(μ-C_6H_5)Mg(TMP)][10] and [(TMEDA)-Na(μ-TMP){(μ-C_6H_5)Cr(C_6H_6)}Mg(TMP)],[5] the products resulting from the synergic metalation of benzene and bis(benzene)-chromium respectively by **1**.

The two tolyl rings of the metallocene in **2** adopt an almost eclipsed disposition (torsion angle C14−C8−C1−C7 = 9.1-(6)°). On the other hand, the metalation of a single ring of the sandwich compound does not seem to affect the values of the C−C and C−Cr distances in the metalated ring (average C−C bond length, 1.420 Å; average Cr−C bond length, 2.151 Å) compared with those in the nonmetalated ring (average C−C bond length, 1.404 Å; average Cr−C bond length, 2.135 Å).

---

(9) Preparation of **2**: n/sBu$_2$Mg (5 mL of a 1 M solution in heptane, 5 mmol) was added to a suspension of nBuNa (0.40 g, 5 mmol) in hexane (10 mL). TMP(H) (1.7 mL, 10 mmol) was then introduced, and the mixture was stirred for 15 min, affording a slightly cloudy pale yellow solution. At this stage TMEDA (0.75 mL, 5 mmol) and Cr(Tol)$_2$ (0.30 g, 1.25 mmol) were introduced and the resulting brown solution was heated at reflux for 30 min; a dramatic color change from brown to deep red was observed. Half of the solvent was removed under vacuum, and the resulting bright red solution was placed in the freezer (at −20 °C), producing a crop of red crystals (0.58 g, 66%). ^{1}H NMR (400 MHz, 25 °C, C_6D_6): δ 4.91 (m, 1H, H_{para}, C_6H_5Me), 4.85 (m, 2H, H_{meta}, C_6H_5Me), 4.48 (m, 2H, H_{ortho}, C_6H_5Me), 4.16 (d, 2H, H_{meta}, C_6H_4Me), 4.09 (d, 2H, H_{ortho}, C_6H_4Me), 2.20, 2.02 (s, 3H each, CH_3, C_6H_5Me and C_6H_4Me), 1.95 (m, 4H, H_γ, TMP), 1.63 (m, broad, 40H, 12 H, CH_3 of TMEDA, 4H, CH_2 of TMEDA, 24H, CH_3 of TMP), 1.36 (m, 8H, H_β, TMP). $^{13}C\{^1H\}$ NMR (100.63 MHz, 25 °C, C_6D_6): δ 88.24, 86.95 (C_{ipso}, C_6H_4Me and C_{ipso}, C_6H_5Me), 82.94 (C_{meta}, C_6H_4Me), 81.43 (C_{ortho}, C_6H_4Me), 78.36 (C_{ortho}, C_6H_5Me), 75.46 (C_{meta}, C_6H_5Me), 74.86 (C_{meta}, C_6H_5Me), 52.73 (CH_2, TMEDA), 49.68 (C_α, TMP), 42.65 (CH_3, TMEDA), 40.76 (C_β, TMP), 32.23 (CH_3, TMP), 21.75, 21.09 (CH_3, C_6H_4Me, CH_3, C_6H_5Me) 20.64 (C_γ, TMP).

(10) Hevia, E.: Gallagher, D. J.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Chem. Commun.* **2004**, 2422.

(11) Calderazzo, F.; Invernizzi, R.; Marchetti, F.; Masi, F.; Moalli, A.; Pampaloni, G.; Rocchi, L. *Gazz. Chim. Ital*. **1993**, *123*, 53.

(12) Davis, R.; Kane-Maguire, A. P. *Comprehensive Organometallic Chemistry*; Wilkinson, G., Ed.; Pergamon: Oxford, U.K., 1982; Vol. 3, pp 995−996.

(13) Graham, D. V.; Hevia, E.; Kennedy, A. R.; Mulvey, R. E.; O'Hara, C. T.; Talmard, C. *Chem. Commun.* **2006**, 417.

(14) Crystal data for **2**: $C_{38}H_{67}CrMgN_4Na$, M_r = 679.26, triclinic, space group $P1$, a = 8.4126(5) Å, b = 11.0513(7) Å, c = 11.2962(8) Å, α = 74.006(3)°, β = 73.075(3)°, γ = 85.554(3)°, V = 965.83(11) Å^3, Z = 1, λ = 0.710 73 Å, μ = 0.354 mm^{-1}, T = 123 K, 12 496 reflections, 6233 unique reflections, R_{int} = 0.072; final refinement to convergence on F^2 gave R = 0.0640 (F, 4785 observed data only) and R_w = 0.1487 (F^2, all data), GOF = 1.088.

The magnesium center in **2** occupies the position vacated by the para H atom in the metallocene, forming a short (2.185(2) Å), strong covalent bond with the carbon center, lying close to coplanarity with the tolyl ring (deviation of Mg from the plane 0.076(8) Å). This Mg−C distance is nearly identical with that found in the compound $[(\mathrm{TMEDA})\mathrm{Na}(\mu\text{-TMP})\{(\mu\text{-}\mathrm{C_6H_5})\mathrm{Cr}(\mathrm{C_6H_6})\}\mathrm{Mg}(\mathrm{TMP})]$ (2.197(2) Å), where the magnesium center also lies in the same plane as the phenyl ring of the metalated bis(benzene)chromium. In contrast, the sodium atom adopts a nearly perpendicular disposition to the metalated tolyl ring (lying 2.603(5) Å out of the plane). The closest Na−C contact is with the para C (Na−C4 = 2.662(6) Å), which carries most of the negative charge, but there is also another short contact with the meta C5 (2.847(6) Å). The remainder of the Na−C(tolyl) distances are too long (ranging from 3.279(6) to 4.081(6) Å) to be indicative of a significant interaction. These facts are consistent with the harder magnesium center σ-bonded to the metalated tolyl ring of the metallocene, whereas the softer sodium center engages more with the π-system of the metallocene. This σ/π distinction in the way magnesium and sodium respectively bind to the deprotonated substrate has become a signature feature of inverse crown compounds and related mixed-metal structures.[15]

Compound **2** has also been characterized in solution using NMR spectroscopy. Its ^{1}H NMR spectrum in deuterated benzene shows three multiplets (at 4.91, 4.85, and 4.48 ppm) of relative intensity 1:2:2, which can be assigned to the para, meta, and ortho hydrogen atoms, respectively, of the nonmetalated tolyl ring of the metallocene, whereas the signals of the metalated ring appear slightly upfield as two doublets at 4.16 and 4.09 ppm for the meta and ortho protons, respectively. The corresponding signals of the two methyl groups of the tolyl rings can also be observed at 2.20 and 2.02 ppm. Its ^{13}C NMR spectrum in the same deuterated solvent shows the presence of seven resonances between 88.24 and 74.86 ppm corresponding to the $\mathrm{C_{tolyl}}$ atoms. However, no signal for $\mathrm{Mg{-}}C_{\mathrm{para}}$ could be observed, as a result of the low solubility of **2** in $\mathrm{C_6D_6}$. Attempts to record a spectrum employing longer accumulation times or a more polar deuterated solvent such as THF failed, due to the partial decomposition of **2**.

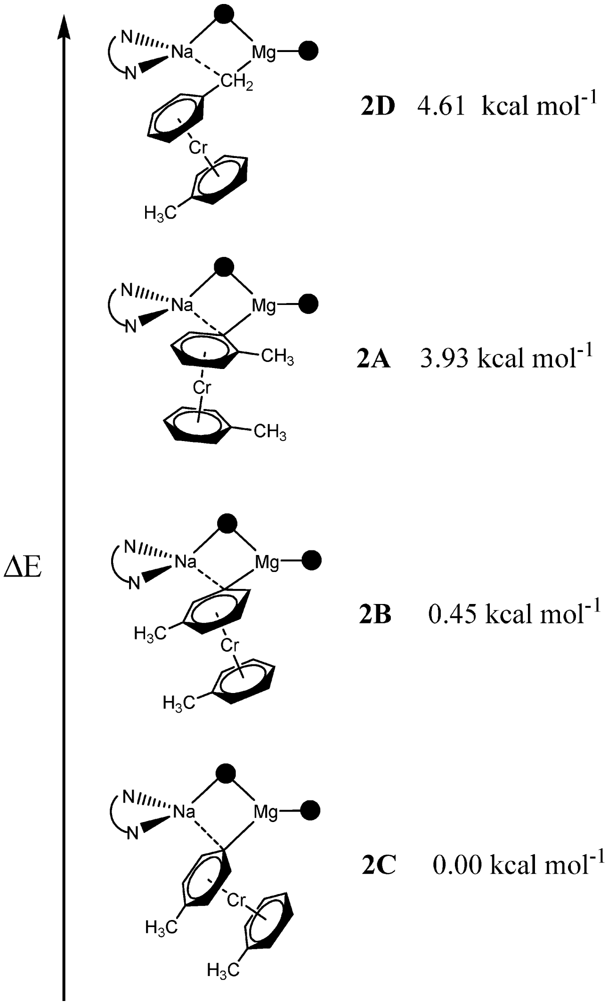


Figure 2. Theoretical structures of **2A**−**D**, in order of decreasing stability.

To shed light on the para selectivity of the bis(toluene)chromium metalation a theoretical study has been carried out. Exploratory ab initio calculations at the Hartree−Fock (HF) level were performed using the 6-31G* basis set. The resultant optimized geometries were subject to a frequency analysis and then refined further by density functional theory (DFT) calculations utilizing the B3LYP functionals and the 6-311G** basis set. The reaction of **1** with bis(toluene)chromium was found to be exothermic by 7.03 kcal mol^{-1} (eq 1). Four regioisomers of

$$\underset{\mathbf{1}}{[(\mathrm{TMEDA})\mathrm{Na}(\mathrm{TMP})(\mathrm{Bu})\mathrm{Mg}(\mathrm{TMP})]} + [\mathrm{Cr}(\mathrm{C_6H_5\text{-}Me})_2] \longrightarrow \underset{\mathbf{2}}{[(\mathrm{TMEDA})\mathrm{Na}(\mathrm{TMP})\{(p\text{-}\mathrm{C_6H_4\text{-}Me})\mathrm{Cr}(\mathrm{C_6H_5\text{-}Me})\}\mathrm{Mg}(\mathrm{TMP})]} + \mathrm{Bu\text{-}H}$$

compound **2** were modeled (Figure 2), where the metallocene has been monometalated in the ortho (**2A**), meta (**2B**), para (**2C**), or methyl positions (**2D**). In agreement with the experimental results the most stable theoretical structure is found to be the para isomer **2C**, closely followed by the meta isomer **2B**, which is only 0.45 kcal mol^{-1} less stable than **2C**. The next most stable model is the ortho isomer **2A** (at 3.93 kcal mol^{-1}) and finally the least stable of all is the methyl isomer **2D** (at 4.61 kcal mol^{-1}). These results are similar to those previously obtained when the reaction of **1** with toluene was modeled theoretically. In that case toluene is exclusively deprotonated in the meta position, leaving the methyl position untouched.[4] This reversal of the normal order of thermodynamic stability when the bimetallic base **1** is employed can in part be explained in terms of the stabilizing Na−C(tolyl) π-interactions presented in the molecule. The same rationale can be applied to the selective para monometalation of bis(toluene)chromium in compound **2**. A comparison of the geometric parameters between **2C** and **2D** shows that the Mg−C distances are similar in both compounds (2.229 Å for **2C** and 2.250 Å for **2D**); however, the Na−C π-interactions (also present but to a lesser extent in the ortho and meta regioisomers) are almost nonexistent in the methyl isomer **2D** (the shortest Na−C(tolyl) distance is 3.035 Å, but the remainder of the Na−C(tolyl) contacts are in a range from 3.515 to 4.847 Å). Therefore, as in the toluene case, we can conclude that these Na−C π contacts, though individually weak, can collectively contribute to the overall stability of compound **2**.

In conclusion, we report the first example of a metallo derivative of bis(toluene)chromium, which has been isolated (in high yield) and fully characterized. This constitutes a potential new synthetic route to bis(toluene)chromium complexes regioselectively monofunctionalized in the para position.

---

(15) See review article: Mulvey, R. E. *Organometallics* **2006**, *25*, 1060.

Acknowledgment. We gratefully acknowledge the EPSRC (grant award no. GR/R81183/01), the EU (Marie Curie Fellowship to E.H.), and the Royal Society/Leverhulme Trust (Fellowship to R.E.M.) for generously sponsoring this research. Our thanks are extended to Professor F. Calderazzo and Professor G. Pampaloni from the Università di Pisa for their valuable advice in the preparation of [Cr(toluene)$_2$].

Supporting Information Available: Text, tables, and figures giving full details of the theoretical calculations and a CIF file giving X-ray crystallographic data for **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM060216V