Mono and dinuclear bis(ortho-tolyl)platinum(II) compounds containing diethyl sulfide ligands: Synthesis, DFT studies and use as precursors in cycloplatination reactions

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ABSTRACT:

The synthesis of bis(ortho-tolyl)platinum(II) compounds containing diethyl sulfide ligands from [PtCl2(SEt2)2] and ortho-tolyl-lithium is presented. Formation of a dimer [Pt(4-MeC6H4)2(m-SEt2)]2 is evidenced by 1H NMR and HR-MS-ESI(þ) spectra and the monomer trans-anti-[Pt(2-MeC6H4)2(SEt2)2] is characterized by X-ray diffraction analyses. Theoretical studies indicate that dimerization of the most stable form of the monomer (cis-syn) to the most stable conformer of the dinuclear species (abba) is favored (DE ¼ 10.1 kJ/mol). The reactions of the dimer [Pt(4-MeC6H4)2(m-SEt2)] with imine ligands 4-ClC6H4CH ¼ NCH2CH2NMe2 and 2-Br,6-FC6H3CH ¼ NCH2Ph gave a tridentate [C, N, N'] five-memberedand a bidentate [C, N] seven-membered platinacycles, respectively.

1. INTRODUCTION

Cyclometalated platinum compounds containing N-donor ligands have attracted a great deal of interest due to their applications in several areas [1]. In recent years we have been involved in the use of diarylplatinum(II) complexes as precursors in the synthesis of a novel class of five- or seven-membered platinacycles in a process involving the formation of biaryl linkages [2e4]. These reactions involve an oxidative addition/reductive elimination/ oxidative addition sequence and thus their study is of relevance in relation to both stoichiometric and catalytic processes that often include these fundamental steps. Moreover, we have reported that this class of metalacycles display a remarkable antiproliferative activity, even greater than cisplatin, in several human cancer cell lines [4,5]. In order to analyze the influence of the electronic effects of the para substituent of the diarylplatinum precursors, compounds containing bis(para-tolyl)platinum and bis(para-fluorophenyl) platinum moieties have been compared [6]. Kineticomechanistic studies carried out for these systems [6e9] have allowed to establish the sequence of fundamental steps and the importance of the nature of the substituents. As part of this project aimed at analyzing the scope of the process, the present work focuses on the synthesis of di(ortho-tolyl)platinum(II) compounds containing labile diethyl sulfide ligands and its evaluation as precursors for cyclometalated compounds in order to ascertain the influence of an ortho substituent in the aryl ligand.

2. RESULTS AND DISCUSSION

2.1. Synthesis of di(ortho-tolyl)platinum(II) compounds

The synthetic procedure previously reported for dinuclear compounds [Pt(4-MeC6H4)2(m-SEt2)]2 [10] or [Pt(4-FC6H4)2(m- SEt2)]2 [4], both of which had been obtained in good yields and characterized crystallographically, was tested from cis-[PtCl2(SEt2)2] and Li(2-MeC6H4) with the aim of preparing the analogous dinuclear species [Pt(2-MeC6H4)2(m-SEt2)]2 (see reaction 1): 2 cis-[PtCl2(SEt2)2] þ 4 LiAr/[PtAr2(m-SEt2)]2 þ 4LiCl þ 2 SEt2(1) Ar ¼ 4-MeC6H4; 4-FC6H4; 2-MeC6H4

The product was characterized by 1H NMR and HR-MS spectra and elemental analyses. The HR-MS and the elemental analyses of the product were consistent with formation of the dimer [Pt(4-MeC6H4)2(m-SEt2)]2 (D). The 1H NMR spectrum of the product at room temperature shows the presence of two set of signals in contrast to the results reported for Ar ¼ 4-MeC6H4 [10] or 4-FC6H4 [4] for which a single isomer was observed. In this case, the presence of an ortho-methyl substituent in the aryl rings might give rise to several atropisomers of the dinuclear compound, as described for compounds [Pt(Hbph)2(m-SEt2)]2 (Hbph ¼ biphenyl monoanion) [11] and we might assume that the observed signals should correspond to two of these isomers. The 1H NMR spectra were also taken at low temperature (see supplementary data) and an increased complexity of the NMR spectra is observed suggesting restricted rotation of the ortho-tolyl groups. In particular, at 223 K resonances corresponding to four distinct isomers were clearly observed in the range 1.00e1.30 ppm (see supplementary material). Atropisomers are stereoisomers that can be interconverted by rotation about single bonds but for which the barrier to rotation is large enough so that the stereoisomers do not interconvert readily. The term atropisomers originally referred to biaryl compounds which display axial chirality along a C-C single bond and are defined by the chirality rule (R and S nomenclature) or the helicity rule (P and M nomenclature). However, the term atropisomer is now expanded to other systems in which stereoisomerism is caused by restricted rotation of a single bond. Examples include diarylpalladium compounds with restricted rotation around the MC bond [12,13] and “Picket-fence” porphyrins [14] which exist as a mixture of four atropisomers. For the latter, the descriptors aaaa, abab, aabb and aaab in which a and b indicate the orientation of the ortho substituents in relation to the plane of the porphyrin have been used. These descriptors were also used for dinuclear compounds containing four Pt-C bonds with restricted rotation [11] and will be used along this work. For compound [Pt(4-MeC6H4)2(m-SEt2)]2 (D), the four ortho-methyl substituents (one in each platinum) might be oriented up or down the Pt2S2 plane, thus leading to the five possible atropisomers (abba, abab, abbb, bba, aaaa) depicted in Scheme 1.

Surprisingly, the crystals obtained from recrystallization of compound D in dichloromethane-methanol correspond, according to the X-ray diffraction analyses, to a monomer [Pt(2-MeC6H4)2(SEt2)2] (M) possibly present in a small amount in the reaction mixture. Two geometrical isomers (cis and trans) are possible for the monomer [Pt(2-MeC6H4)2(SEt2)2] (M) and the presence of an ortho-methyl substituent

in both aryl rings give rise to two atropisomers; as depicted in Scheme 2, the descriptors syn/ anti commonly used for bis(aryl) complexes [12,13] are used in this case.

The structure determination revealed that the crystals correspond to trans-anti-[Pt(2-MeC6H4)2(SEt2)2] (M1). The asymmetric unit contains two independent molecules that differ in the arrangement of the ethyl substituents of the sulfide ligands and in each molecule, the two half molecules are related by a symmetry center. The molecular structure (see Fig. 1) consists of a mononuclear compound with a square planar geometry around the platinum and a mutual trans arrangement of both the two h1-aryl and the two diethyl sulfide ligands. As expected for arylplatinum(II) compounds, the aryl groups are tilted (78.5(2)° for molecule 1 and 80.9(2)° for molecule 2) from the coordination plane. The methyl substituents in the two ortho-tolyl groups display a mutually anti orientation, leading to the geometry with least steric crowding. Bond lengths and angles are well within the range observed for analogous compounds [4,10,15,16].

While most reactions of cis-[PtCl2(SEt2)2] with methyl or aryl lithium reagents have been reported to produce dimers, the reaction with LiC6F5 produces the monomer cis-[Pt(C6F5)2(SEt2)2] in high yield [17,18]. On the other hand, equilibria monomer-dimer have been reported for both methyl [19,20] and aryl [15,21] platinum complexes containing sulfide ligands (see Scheme 3), and it has been shown that the presence of an excess of sulfide ligand might drive the equilibrium towards the monomer. Interestingly, platinum monomers containing two aryl ligands, including those containing ortho-tolyl groups generally display a cis arrangement of both aryl groups, as described for compounds cis-[Pt(2-MeC6H4)2(SMe2)2] [22,23] and cis-[Pt(2-MeC6H4)2(dmso)2] [24]. For the latter both cis-anti and cis-syn isomers have been structurally characterized [24]. However, compounds containing the bulkier mesityl groups such as [Pt(2,4,6-Me3C6H2)2(SMe2)2] [25] and [Pt(2,4,6-Me3C6H2)2(dmso)2] [24] display a trans arrangement. Cis-trans isomerization has been described for square-planar bis(diethyl sulfide)platinum(II) complexes [18]. Since a facile dissociation of SR2 ligands due to the strong s-donor power of the aryl group which weakens the Pt-S bond has been reported for cis-[PtAr2(SR2)2] compounds [15,21] a dissociative pathway via an unsaturated 14-electron [PtAr2(SR2)] species is assumed for the cistrans isomerization.

In an attempt to ensure formation of monomer species, compound D was treated with an excess of SEt2. The HR-MS of the resulting product was consistent with monomer formation. However, the 1H NMR spectrum in CDCl3 shows the presence of four distinct species, along with other minor resonances. Two sets of signals are identical to those obtained for the dimer at room temperature and their intensities maintain the approximate ratio observed in the 1H NMR spectrum of the dimer described above. The two additional set of signals that altogether amount to 55% of the mixture are assigned to two distinct isomers of the monomer compound [Pt(2-MeC6H4)2(SEt2)2] (M) (see Scheme 2). These results are consistent with the equilibria shown in Scheme 3 although the presence of free SEt2 could not be unambiguously assigned due to the complexity of the spectrum

149 2.2. Theoretical studies
150 In order to study the behavior of these complexes in solution we studied the relative stability of the
151 monomer and dimer atropisomers. In a first step, we performed a systematic search of conformers of the
152 monomeric complexes using molecular mechanics, for both the cis- and trans-isomers. The different
153 conformers have been recalculated using the PM6 semi-empirical method, and the three most stable
154 conformations of each of the trans-anti, trans-syn, cis-syn and cis-anti isomers were reoptimized at the
155 DFT level (see Computational Details, section 4.3). Table 1 shows the relative DFT energies while Fig.
156 2 shows the optimized geometries corresponding to the most stable conformation of eac isomer. The cis
157 isomer is about 40 kJ/mol more stable than the trans, while for each one the anti atropisomer is slightly
158 less stable than the syn. This difference between atropisomers is more accentuated in the trans isomr,
159 probably due to interactions with the SEt2 groups. These trends are maintained upon including the
160 solvent used in the synthesis (diethyl ether) and vibrational effects. The same procedure esystematic
161 search of conformers using molecular mechanics, refining the energies at the semi-empirical level and
162 final reoptimizations using DFTe was performed for the dimers but, due to the greater complexity of the
163 calculations, we have reoptimized at the DFT level only the most stable conformation of each
164 atropisomer as found using PM6. Table 1 shows the energies corresponding to each atropisomer while
165 the molecular geometries are depicted in Fig. 3. The relative energies in gas phase increase in the order
166 abba < abab < abbb < aaaa < aabb, but if we add the solvent (diethyl ether) and vibrational effects, the
167 gradation in free energies in solution varies slightly: the abbb atropisomer becomes more stable than
168 abab. As in the case of the monomeric complexes, the interactions between the methyl and the SEt2
169 groups can be important in the energy differences.
170 In general the interconversion of atropisomers by bond rotation is a plausible process. The energy
171 required for such rotation is influenced by the steric hindrance and electronics of each system and
172 depends also on the solvent and temperature. The rotation barrier corresponding to the aromatic ring for
173 the cis and trans isomers of the monomer and for the dimer was calculated using PM6 and the results are
174 shown in Fig. 4. The barrier is slightly lower for the dimer than for the monomers and in all cases the
175 height of the barrier suggests that the rotation is restricted, leading to atropisomers. Recalculation of the
176 energies at the DFT level is in agreement with the PM6 results, with the energy barrier for the dimer
177 being 29 kJ/mol smaller than for the monomers.
178 After calculating all the species at the DFT level, we have computed the energy corresponding to the
179 dimerization reaction. We have considered only the most stable form of the monomer (cissyn) and the
180 dimer (abba). Thus the reaction studied is shown in Scheme 4. The reaction is exoergic both in gas
181 phase (DE¼ 4.8 kJ/mol) and in solution (DE¼ 10.1 kJ/mol). The inclusion of enthalpic and entropic
182 effects tends to favor even more the formation of dimers: DG0 is 53.1 kJ/mol in gas phase and 55.7
183 kJ/mol in solution. The increment of entropy corresponding to the formation of two molecules of SEt2
184 can be an important factor to make the reaction spontaneous.
185

2.3. Synthesis of cycloplatinated compounds from di(ortho-tolyl) platinum(II) precursors

In order to assess whether the obtained compounds are adequate precursors for preparing new cycloplatinated compounds, the reactions of imine ligands with the dimer [Pt(4-MeC6H4)2(m-SEt2)]2 (D) were tested under analogous conditions to those reported for similar systems [3,4,7,8]. It is worth noting that both mono- and dinuclear diarylplatinum(II) compounds containing labile ligands such as dialkyl sulfides or dimethylsulfoxide (dmso), including monomers with a trans arrangement of the aryl ligands, have been employed as metalating agents [2,26]. Imines 4-ClC6H4CH¼NCH2CH2NMe2 (1) and 2-Br,6-FC6H3CH¼NCH2Ph (2) were selected for this study in order to explore both potentially tridentate (1) and bidentate (2) ligands, and both formation of five or seven-membered platinacycles. The reaction involving imine 4-ClC6H4CH¼NCH2CH2NMe2 (1) was carried out in toluene at 90□ for six hours and gave an orange solid which was characterized by 1H and 13C NMR spectra, elemental analyses and crystal structure as the cycloplatinated compound [Pt(2-MeC6H4) {C6H3ClCH¼NCH2CH2NMe2}] (3) depicted in Scheme 5. According to previous findings [3,7,8], the process consists on [N, N'] coordination of the imine to platinum either through bridge-splitting or substitution of labile ligands reactions (step A in Scheme 5) followed by intramolecular C-H bond activation and release of a toluene molecule (step B). The molecular structure of compound 3 (see Fig. 5) was confirmed by monocrystal X-ray diffraction analysis. The square-planar geometry around the platinum (II) is completed with tridentate [C, N, N'] and an ortho-tolyl ligand which is tilted 88.34□ from the mean coordination plane. Both the fivemembered metalacycle and the [N, N'] chelate are nearly coplanar with the coordination plane, the dihedral angles being 1.37□ and 7.17□ , respectively. Bond lengths and angles are well within the range observed for analogous compounds. The Pt-N(amine) bond is longer than Pt-N(imine) bond in agreement with the weaker ligating ability of amines for platinum. The bond angles at platinum are close to 90□ , and the smallest angles correspond to the chelate N(1)-Pt(1)-N(2) (82.2□) and the metalacycle C(1)-Pt(1)-N(2) (80.8□). In the 1H NMR spectrum, due to the presence of the ortho-tolyl ligand nearly orthogonal to the coordination plane, the methyl substituents of the dimethylamino group, both coupled to 195Pt, are non-equivalent. The imino and the ortho aromatic protons of both the ortho-tolyl and the metalated aryl are also coupled to 195Pt. The 13C NMR spectrum shows seven C-H resonances in the aromatic region thus confirming the cyclometallation process.

The reaction of 2-Br,6-FC6H3CH ¼ NCH2Ph (2) with dimer D was also tested with the aim of obtaining a seven-membered platinacycle. The presence of a methyl substituent in the ortho position of the aryl ligand might hinder the formation of the non-planar seven-membered platinacycle, or, alternatively, might lead to formation of an eight-membered platinacycle through Caliphatic-H bond activation at the methyl group. The reactionwas carried out in toluene at 90□ for six hours and gave a yellow solid which was characterized by 1H, 19F and 13C NMR spectra and elemental analyses as the cycloplatinated compound [PtBr{C6H3Me(C6H3F) CH¼NCH2Ph}(SEt2)] (4) depicted in Scheme 5. 1H NMR data are similar to those reported for analogous seven-membered platinacycles [3,6], in

particular the imine and the ortho aromatic protons are coupled to 195Pt. Both the methyl and the methylene resonances of the SEt2 ligand appear as broad signals in the NMR spectrum taken at 400 MHz at room temperature. However at 223 K and 600 MHz a better resolution was obtained for this region and two triplets and four multiplets corresponding respectively to non-equivalent methyl and methylene protons were observed. In the 13C NMR spectrum, the imine and aromatic carbon atoms C4, C5 and C6 appear as doublets due to coupling with 19F and the JC-F values agree with those reported for analogous compounds [3,4]. The mechanism of formation of such complexes has been thoroughly studied for analogous systems [7,8] and there is evidence that a cyclometalated platinum(IV) compound is initially formed via intramolecular C-Br bond activation (step C in Scheme 5), followed by reductive elimination to yield a non-cyclometalated compound containing a dangling biphenyl (step D), which finally produces the seven-membered platinacycle (step E). The obtained result indicates that the presence of a methyl substituent in the aryl ring does not prevent the reductive elimination from the cyclometalated platinum(IV) compound which involves the metalated carbon and one ortho-tolyl ligand. The final step consisted on selective activation of a Caromatic-H bond (position a in Scheme 5) to produce a seven-membered platinacycle. There was no evidence of other reaction pathways such as Caliphatic-H bond activation at the methyl (position b), Caromatic-F bond activation (position c), or aromatic- H bond at the benzyl group (position d) taking place. This result is a further example of the high stability of endo (containing the imine moiety) seven-membered platinacycles [6,7].

As a whole, the obtained results indicate that the presence of an sterically significant ortho-tolyl ligand is not a limitation to follow the reactivity patterns previously reported for substrates such as [Pt(4-MeC6H4)2(m-SEt2)]2 [3] or [Pt(4-FC6H4)2(m-SEt2)]2 [4] and therefore the dimer containing bis(ortho-tolyl)platinum moieties is an adequate precursor for the synthesis of either five- or sevenmembered platinacycles containing bidentate [C, N] or tridentate [C, N, N’] ligands.

3. **CONCLUSIONS**

A dinuclear bis(ortho-tolyl)platinum(II) compound containing bridging diethyl sulfide ligands was prepared from [PtCl2(SEt2)2] and ortho-tolyl-lithium. Recrystallization of this compound gave crystals of the monomer trans-anti-[Pt(2-MeC6H4)2(SEt2)2] that was characterized by X-ray analysis of. A detailed computational analyses of the monomer species reveals that the cis-syn isomer is in fact the most stable conformer in solution. Calculations carried out for the dinuclear compound indicate that abba is the most stable of the five possible conformations arising from the presence of an ortho-methyl substituent in each of the four aryl rings. It is interesting to point out that the calculated energy corresponding to dimerization reveals that this process is spontaneous in solution. The dinuclear compound was sucessfully tested as metalating agent since the reactions of imines 4-ClC6H4CH¼NCH2CH2NMe2 and 2-Br-6-FC6H3CH¼NCH2Ph with this new precursor lead to successful formation of a five- and a seven-membered platinacycles containing tridentate [C, N, N’] or bidentate [C, N] ligands, respectively.

4. EXPERIMENTAL SECTION

4.1. General

Microanalyses were performed at the Centres Científics i Tecnol ogics (Universitat de Barcelona). Mass spectra were performed at the Unitat d'Espectrometria de Masses (Universitat de Barcelona) in a LC/MSD-TOF spectrometer using H2O-CH3CN 1:1 to introduce the sample. NMR spectra were performed at the Unitat de RMN d'Alt Camp de la Universitat de Barcelona using a Mercury-400 (1H, 400 MHz; 13C, 100.6 MHz; 19F, 376.5 MHz) or a Bruker Digital Avance (1H, 600 MHz) and referenced to SiMe4 (1H and 13C) or CFCl3 (19F). d Values are given in ppm and J values in Hz. Abbreviations used: s ¼ singlet; d ¼ doublet; t ¼ triplet; m ¼ multiplet; br ¼ broad. 4.2. X-ray diffraction Suitable crystals of compounds M1 and 3 were grown at room temperature in dichloromethane-methanol or methanol, respectively. X-ray diffraction data were collected for prism-like specimens on a D8 VENTURE system equipped with a multilayer monochromator and a Mo high brilliance Incoatec Microfocus Source (l ¼ 0.71073 Å) at 100 K. The structures were solved and refined using the Bruker SHELXTL Software package [27]. Crystallographic details are given in Table S1.

4.3. Computational details

Molecular mechanics conformers calculations have been performed using the MMFF force field [28], and energies have been refined using the PM6 semi empirical method [29], both implemented in the Spartan 14 software [30]. The geometries for the most stable atropisomers (three for the monomers and one for the dimers) have been reoptimized using Gaussian 03 [31] at the DFT level using the B3LYP functional [32,33]. The basis set has been chosen as follows: LANL2DZ [34,35] for platinum and 6-31G* (including polarization functions for the non-hydrogen atoms) [36] for the remaining atoms. Geometries have been optimized without imposing any symmetry restriction. using the standard convergence criteria supplied by the software, and have been confirmed to be true minima by vibrational analysis. A xyz file included the optimized coordinates of the systems studied has been included as supplementary material. Solvent effects have been included using the CPCM method [37] using the geometries optimized in vacuum. The rotation barriers have been calculated at the PM6 level, performing a relaxed scan of the rotation of the aromatic rings, varying the dihedral angle with a 10 step size, fixing the bond angles of the atoms coordinated to the metal and allowing the remaining geometric parameters to relax. In order to have a better estimation of the barrier energy, single point calculations have been performed at the DFT level using the geometries corresponding to the maximum and minimum of the barrier.

297 4.4. Preparation of the complexes

298 Ligands 1 [38] and 2 [39] and compound cis-[PtCl2(SEt2)2] [40] were prepared as reported elsewhere.

299

300 4.4.1. Compound [Pt(2-MeC6H4)2(m-SEt2)]2 (D)

301 Compound D was prepared using the following procedure: 3.5 mL (37.15 mmol) of n-butyl-lithium in
302 hexane were added under N2 to 30 mL of diethyl ether and the solution was cooled to 0 C. 2-
303 iodotoluene (1.204 g; 5.52 mmol) was slowly added and the mixture was stirred for 30 min at 0 C
304 After this time, [PtCl2(SEt2)2] (0.502 g; 1.23 mmol) was added and the mixture was stirred for 2 h at
305 room temperature. After cooling to 0 C, water (5 mL) was added, the aqueous layer was extracted with
306 dichloromethane (3 15 mL) and the combined organic layers were dried over magnesium sulfate,
307 filtered, and evaporated to give an oily residue. The solid obtained upon addition of hexane was filtered
308 and dried in vacuum. Yield: 0.446 g (88.0%). 1H NMR (400 MHz, CDCl3), major isomer (66%) d ¼
309 7.48 (dd, 3JH-H ¼ 8.0, 4JH-H ¼ 2.0 3JH-Pt ¼ 24.0, 4H, Hortho), 6.97e6.81 (m, aromatics), 2.64 (s,
310 12H, Me), 2.30 (q, 3JH-Pt ¼ 22.0, 3JH-H ¼ 7.2, 8H, SCH2CH3), 1.15 (t, 3JH-H ¼ 7.2, 12H,
311 SCH2CH3); minor isomer (33%) d ¼ 7.52 (dd, 3JH-H ¼ 8.0, 4JH-H ¼ 2.0 4H, Hortho), 6.97e6.81 (m,
312 12H, aromatics), 2.63 (s,12H, Me), 2.23 (q, 3JH-H ¼ 7.2, 8H, SCH2CH3), 1.13 (t, 3JH-H ¼ 7.2, 12H,
313 SCH2CH3). 13C NMR (100.6 MHz, CDCl3), major isomer d ¼ 161.06, 145.47, 138.63, 128.01, 124.22,
314 122.63, 28.27 (SCH2CH3), 25.53 (Me), 12.63 (SCH2CH3); minor isomer (33%) d ¼ 144.57, 145.60,
315 138.55, 127.91, 124.04, 122.20, 28.14 (SCH2CH3), 26.09 (Me), 12.59 (SCH2CH3). HRMS-ESI-(þ)
316 {H2O:CH3CN (1:1)}, m/z: 952.2816 (calc. for C36H52NPt2S2 952.2831) [MþNH4]þ, 1886.5258 (calc.
317 for C72H100NPt4S4 1886.5324) [2MþNH4]þ. EA calc. for C36H48Pt2S2, C 46.24%; H 5.17%; S
318 6.86%; found, C 46.14%; H 5.47%; S 6.64%.

319

320 4.4.2. Compound [Pt(2-MeC6H4)2(SEt2)2] (M)

321 CompoundMwas prepared following the same procedure as for compound D followed by reaction of the
322 crude product with 1 mL of SEt2 in 20 mL of dichloromethane for 2 h. The mixture was evaporated to
323 dryness and the residue was washed with small amounts of diethyl ether. Yield 0.273 g (43.5%).
324 HRMS-ESI-(þ) {H2O:CH3CN (1:1)}, m/z: 575.2092 (calc. for C22H38NPtS2 575.2088) [MþNH4]þ,
325 1132.3828 (calc. for C44H72NPt4S4 1132.3837) [2MþNH4]þ. 1H NMR (400 MHz, CDCl3), in
326 addition to resonances assigned to compound D (see above) the following resonances were observed:
327 isomer 1 (35.7%) d ¼ 7.48 (dd, 3JH-H ¼ 8.0, 4JH-H ¼ 2.0, 2H, Hortho), 2.69 (s, 6H, Me), 2.47 (q, 3JH-
328 H ¼ 8.0, 8H, SCH2CH3), 1.32 (t, 3JH-H ¼ 8.0, 12H, SCH2CH3); isomer 2 (19.1%) d ¼ 7.44 (dd, 3JHH

¼ 8.0, 4JH-H ¼ 2.0, 2H, Hortho), 2.59 (s, 6H, Me), 2.45 (q, 3JH-H ¼ 8.0, 8H, SCH2CH3), 1.30 (t, 3JH-H ¼ 8.0, 12H, SCH2CH3).

4.4.3. Compound [Pt{C6H3ClCH¼NCH2CH2NMe2}(2-MeC6H4)] (3)

Compound 3 was obtained after stirring for 6 h at 90 C a solution containing 0.042 g (0.045 mmol) of compound D and 0.023 g (0.090 mmol) of compound 1 in toluene. The solvent was evaporated and the residue was treated with a minimum amount of methanol (ca. 1 mL). Orange crystals are formed at room temperature. Yield: 25 mg (56.2%). 1H NMR (400 MHz, CDCl3), d ¼ 8.42 (t, 4JH-H ¼ 1.2, 3JH-Pt ¼ 56.4, 1H, CHN), 7.37 (dd, 3JH-H ¼ 6.4, 4JH-H ¼ 2.4, 3JH-Pt ¼ 57.1, 1H, H4), 7.09 (d, 3JH-H ¼ 8.0, 1H, H7), 7.00 (dd, 3JHH ¼ 6.0, 4JH-H ¼ 2.8, 1H, H1), 6.84 (m, 3H, H2, H3, H6), 6.74 (d, 4JHH ¼ 2.0, 3JH-Pt ¼ 72.0, 1H, H5), 3.99 (t, 3JH-H ¼ 5.8, 2H, CH2), 3.12 (td, 3JH-H ¼ 6.0, 4JH-H ¼ 1.4, 2H, CH2), 2.71 (s, 3JH-Pt ¼ 21.2, 3H, NCH3), 2.62 (s, 3JH-Pt ¼ 22.4, 3H, NCH3), 2.41 (s, 3H, CCH3). 13C NMR (100.6 MHz, CDCl3), d ¼ 168.21 (CHN), {136.39, 135.89, 128.87, 128.04, 123.91, 122.45, 121.61, aromatic C-H}, {67.58, 52.69, CH2}, {50.01, 48.76, NMe2}, 28.07 (Me). EA calc. for C18H21ClN2Pt, C 43.60%; H 4.27%; N 5.65%; found, C 43.65%; H 4.45%; N 5.47%.

4.4.4. Compound [Pt{C6H3Me(C6H3F)CH¼NCH2Ph}Br(SEt2)] (4)

Compound 4 was obtained after stirring for 6 h at 90 C a solution containing 0.084 g (0.090 mmol) of compound D and 0.050 g (0.180 mmol) of compound 2 in toluene. The solvent was evaporated and the residue was treated with diethyl ether. The yellow residue was recrystallized in dichloromethane-methanol and dried in vacuum. Yield: 75 mg (62.7%). 1H NMR (400 MHz, CDCl3), d ¼ 8.55 (s, 3JH-Pt ¼ 116.0, 1H, CHN), 7.33 (td, 3JH-H ¼ 8.0, 4JH-F ¼ 6.0, 1H, H5), 7.21 (m, 1H, aromatic), 7.16 (t, 3JH-H ¼ 8.0, 2H, aromatic), 7.06 (d, 3JH-H ¼ 8.0, 2H, aromatic), 6.99 (t, 3JH-H ¼ 8.0, 2H, aromatic), 6.70 (d, 3JH-H ¼ 8.0, 1H, H3), 6.60 (t, 3JH-H ¼ 8.0, 1H, H2), 6.31 (d, 3JHH ¼ 8.0, 3JH-Pt ¼ 52.0, 1H, H1), 5.48 (dd, 2JH-H ¼ 13.0, 4JH-H ¼ 2.0, 1H, CH2Ph), 5.00 (d, 3JH-H ¼ 13.0, 3JH-Pt ¼ 48.0, 1H, CH2Ph), 3.02 (s, br, 1H, SCH2), 2.64 (s, br, 2H, SCH2), 2.35 (s, br, 1H, SCH2), 1.96 (s, 3H, Me), 1.19 (s, br, 3H, SCH2CH3), 0.87 (s, br, 3H, SCH2CH3). 1H NMR (600 MHz, 223 K, CDCl3), SEt2 resonances: 3.12 [m, 1H], 2.79 [m, 1H], 2.63 [m,1H], 2.46 [m, 1H], 1.27 [t, 3JH-H ¼ 6.0, 3H], 0.90 [t, 3JHH ¼ 6.0, 3H]. 13C NMR (100.6 MHz, CDCl3), d ¼ 160.95 (d, 3JC-F ¼ 6.0, CHN), 159.43, 143.85, 140.19, 137.38, 134.99, 134.07, 133.74 (C1), 130.86 (d, 3JC-F ¼ 9.0, C5), 130.06 (2C, Ph), 128.44 (2C, Ph), 128.02 (1C, Ph), 127.37 (C2), 127.20 (d, 4JC-F ¼ 3.1, C4), 125.91 (C3), 113.32 (d, 2JC-F ¼ 20.1, C6), 68.78 (CH2Ph), 31.80 (br, SCH2), 21.71 (Me), 12.73 (SCH2CH3). 19F NMR (376.5 MHz,

CDCl3), d ¼ 115.6 (ddd, 3JFH ¼ 11.2, 4JF-H ¼ 7.5, 5JF-H ¼ 4.0). EA calc. for C25H27BrFNPtS, C 44.98%; H 4.08%; N 2.10%; S 4.80%; found, C 45.21%; H 4.38%; N 2.32%; S 4.69%.

ACKNOWLEDGEMENTS

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Legends to figures

Scheme 1. The five possible isomers for compound [Pt(4-MeC6H4)2(m-SEt2)]2 (D).

Scheme 2. The four possible isomers for compound [Pt(4-MeC6H4)2(m-SEt2)2] (M).

Figure. 1 Molecular structure of compound M1. Selected bond lengths (Å) and angles (deg.) with estimated standard deviations: molecule 1, Pt(1)-C(6): 2.098(5); Pt(1)-S(1): 2.2777(11); C(6a)-Pt(1)-S(1): 86.19(13); C(6)-Pt(1)-S(1): 93.81(13). molecule 2, Pt(2)-C(12): 2.095(4); Pt(2)-S(2): 2.2765(11); C(12)-Pt(2)-S(2): 86.83(12); C(12a)-Pt(2)-S(2): 93.17(12).

Scheme 3. Equilibria dimer-monomer and cis-trans observed for diarylplatinum compounds

Figure. 2 DFT optimized geometries corresponding to the most stable conformation of each isomer of the monomer.

Figure. 3 Optimized geometries corresponding to the most stable conformation of each isomer of the dimer.

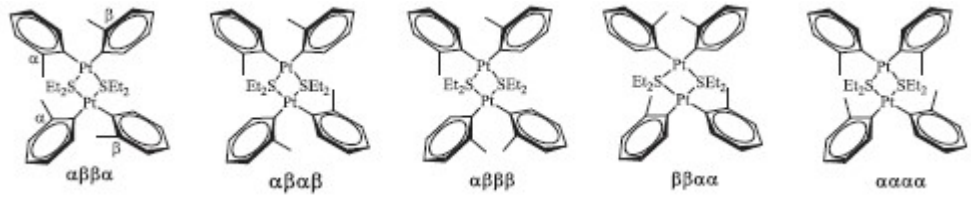
Figure. 4. Rotation barrier for the ortho-tolyl group in mononuclear and dinuclear compounds.

Scheme 4. Dimerization reaction from the more stable monomer to the more stable dimer conformations.

Scheme 5. Synthesis of platinacycles 3 and 4 from bis(ortho-tolyl)platinum(II) precursors.

Figure. 5. Molecular structure of compound 3. Selected bond lengths (Å) and angles (deg.) with estimated standard deviations: Pt(1)-C(12): 1.977(10); Pt(1)-C(1): 1.886(8); Pt(1)-N(2): 2.020(8); Pt(1)-N(1): 2.170(5); C(12)-Pt(1)-C(1): 98.8(3); C(1)-Pt(1)-N(2): 80.8(3); C(12)-Pt(1)-N(1): 98.2(3); N(2)-Pt(1)-N(1): 82.2(3).

SCHEME 1



476 **SCHEME 2**

477

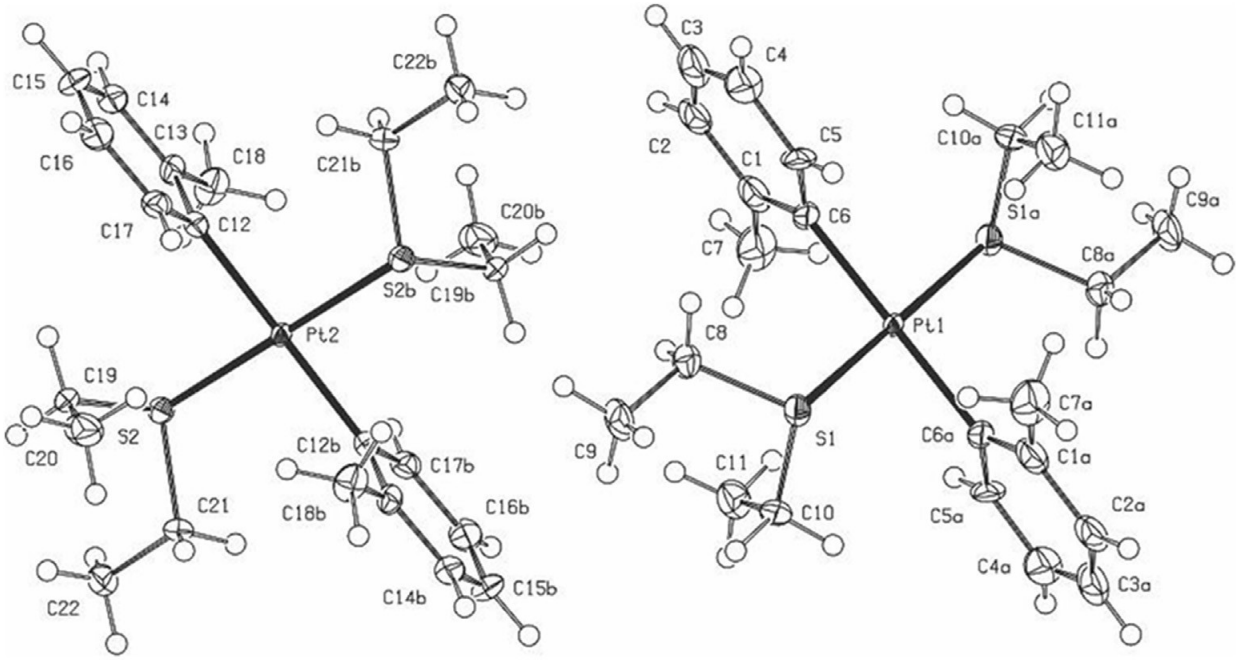
478

trans-anti **(M1)** ***trans-syn*** ***cis-syn*** ***cis-anti***

479

480

FIGURE 1



molecule 2 molecule 1

SCHEME 3

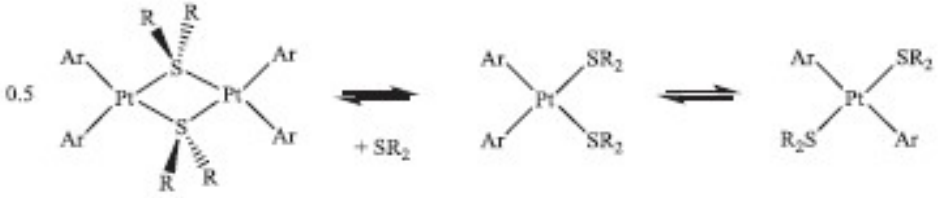
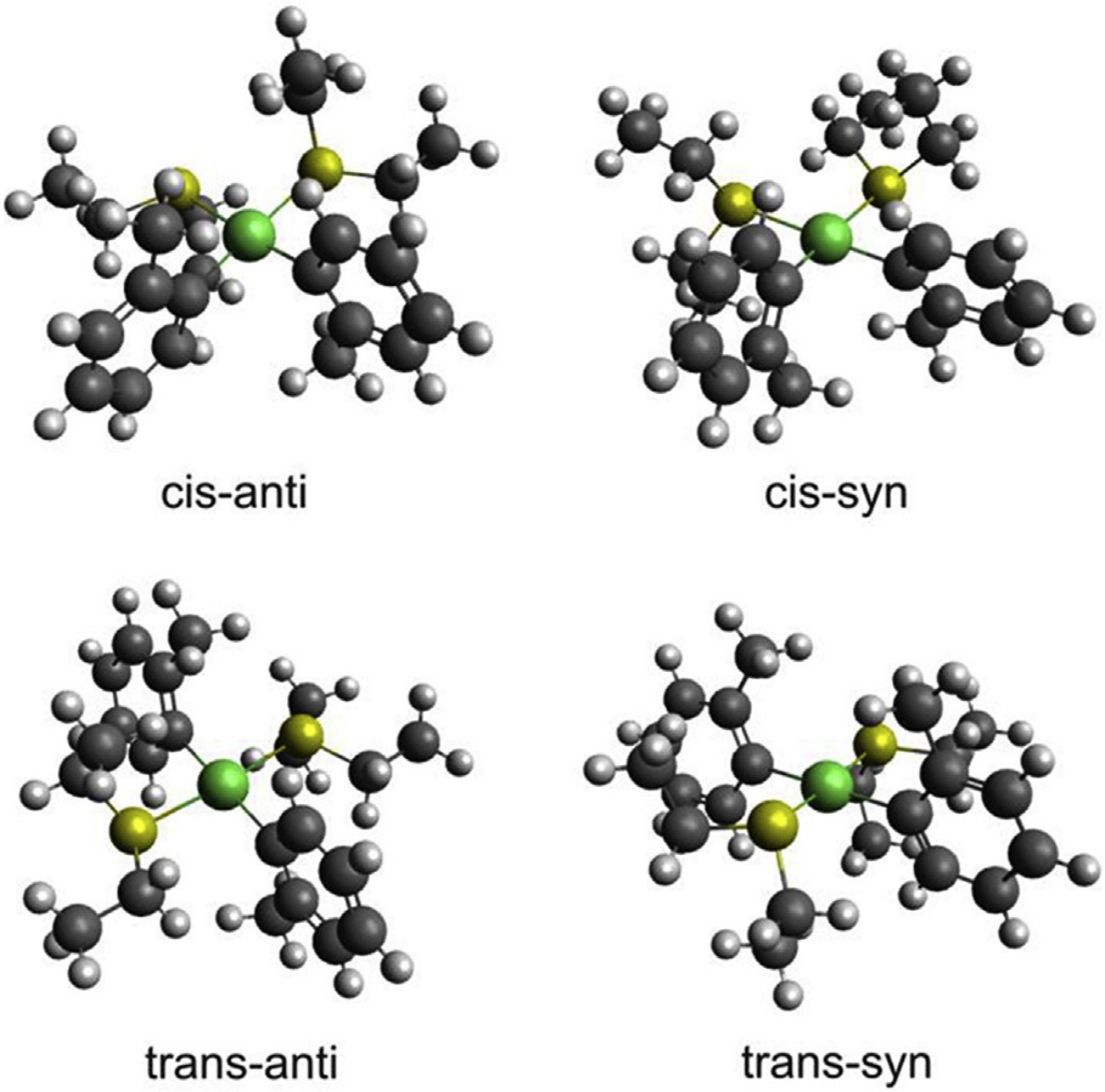


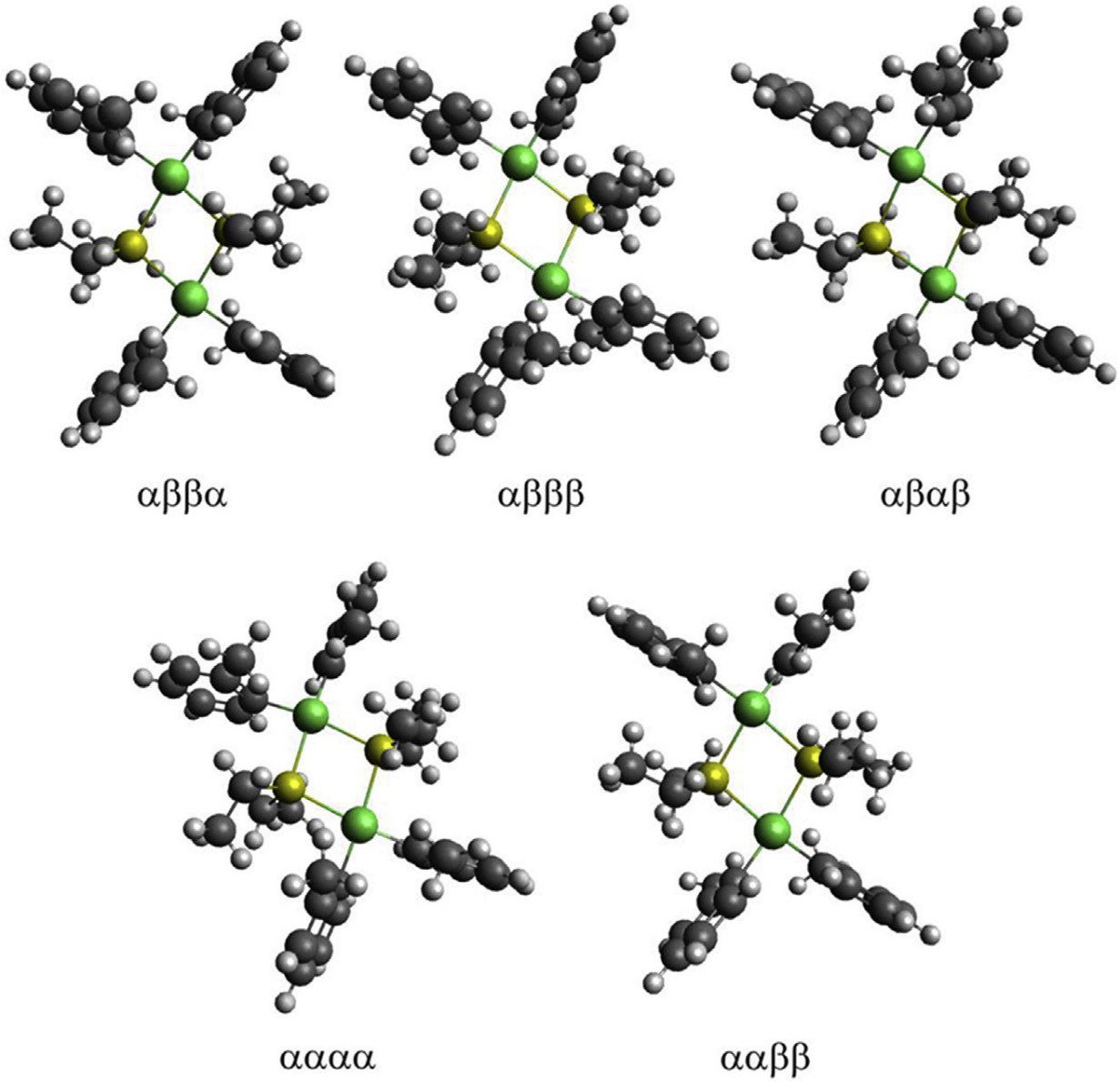
FIGURE 2



501 **FIGURE 3**

502

503



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506 **FIGURE 4**

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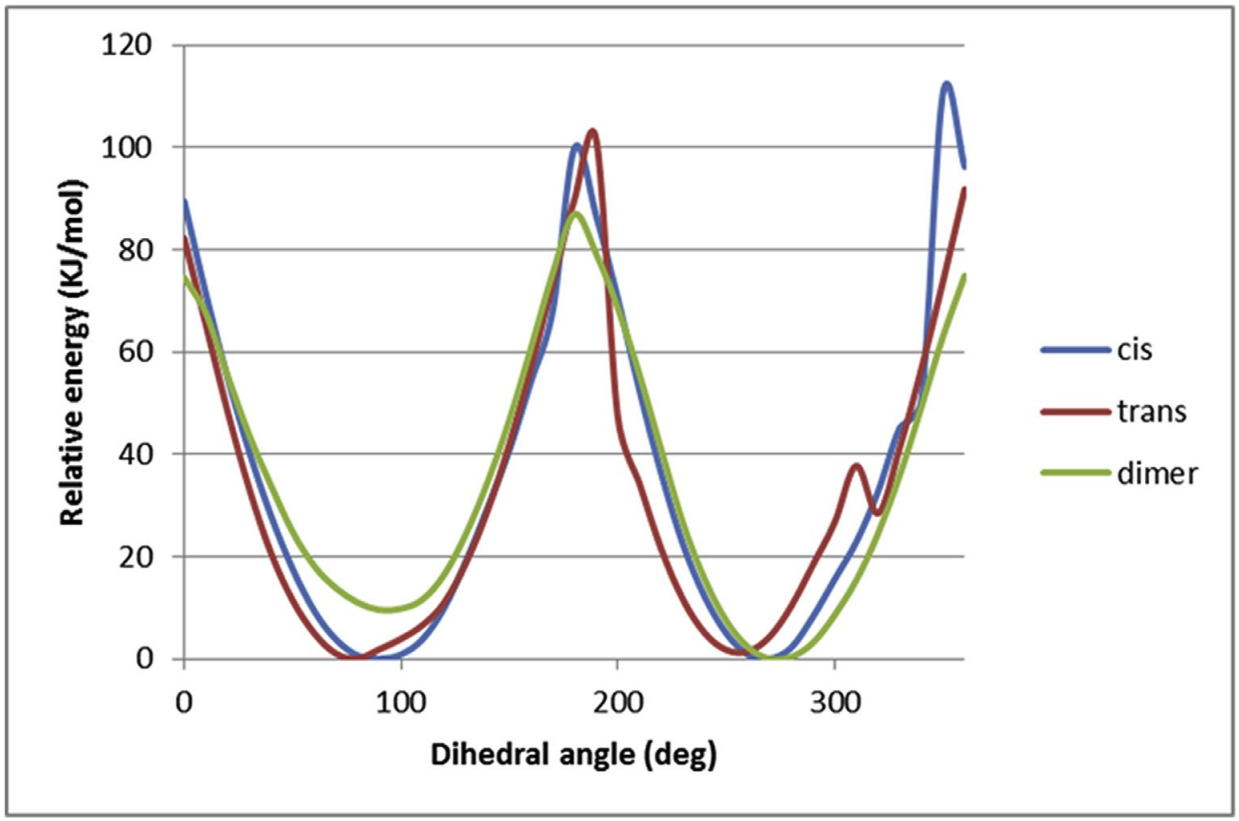
508



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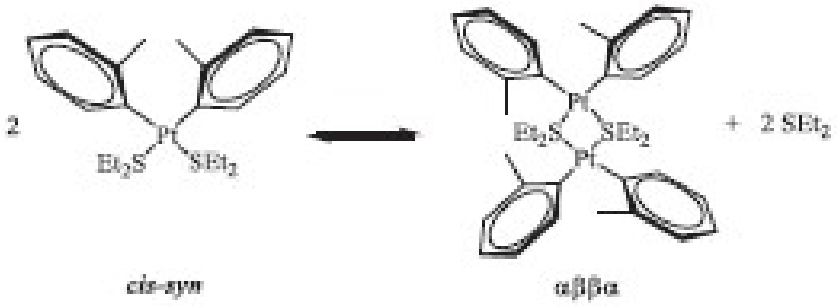
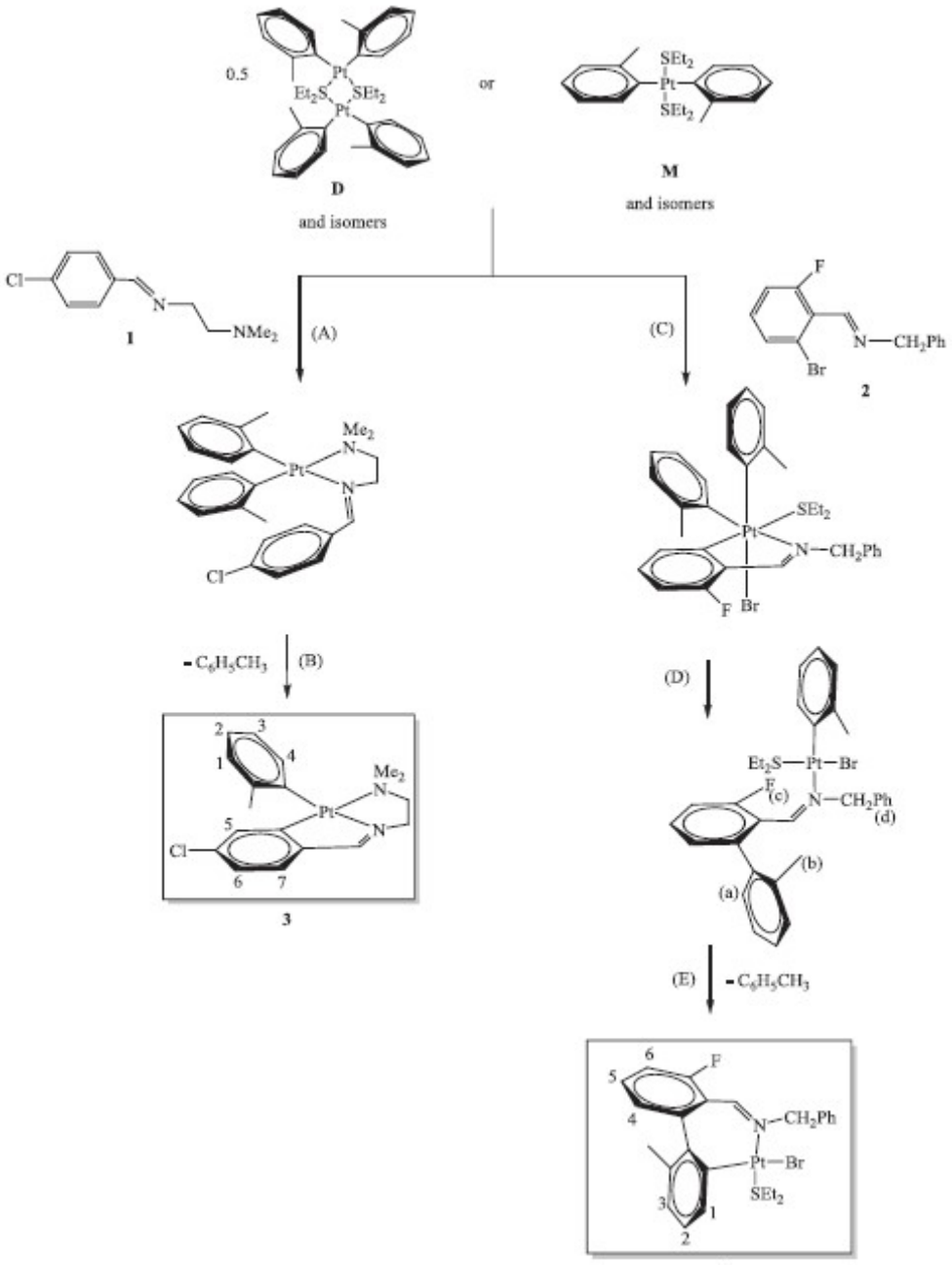
SCHEME 4



cis-syn αββα

517 **SCHEME** 5

518



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520

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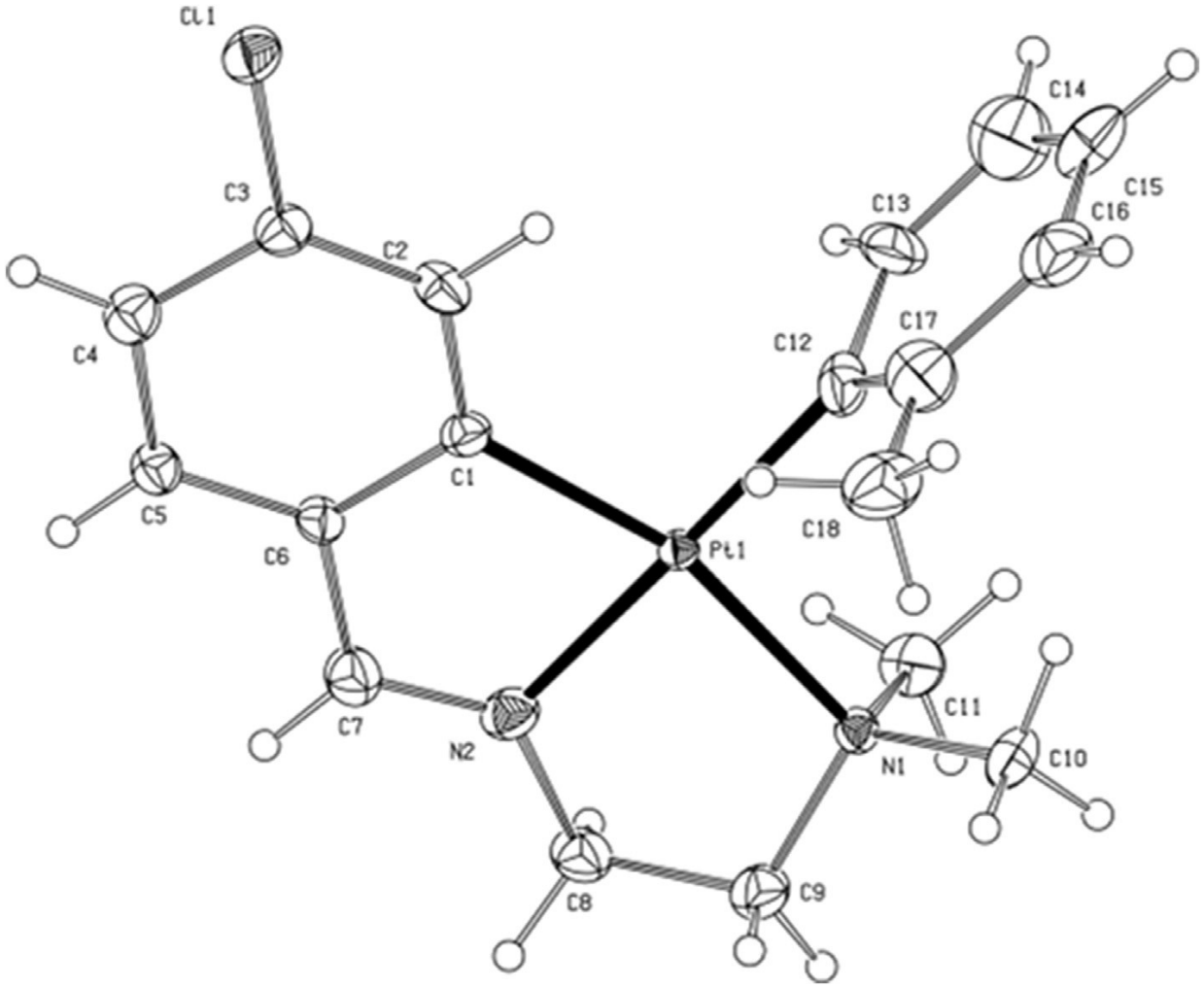
FIGURE 5


CL1
C3
C2
C4
C5
C6
C1
Pt1
C7
N2
C8
C9
N1
C11
C10
C12
C13
C14
C15
C16
C17
C18

527 **Table 1**.. Relative DFT energies and free energies (in KJ/mol) in vacuum and in diethyl ether solution
528 calculated for the monomeric and dimeric complexes studied in this work. The cis-syn and abba
529 atropisomers has been selected as reference for the monomers and dimers, respectively.
530

	Rel E. (vacuum)	Rel. E (ether)	Rel. G (vacuum)	Rel. G (ether)
Monomers				
cis-syn[a]	0.0	0.0	0.0	0.0
cis-anti	0.3	0.3	0.2	1.9
trans-syn	39.3	42.8	40.5	45.6
trans-anti	44.2	47.8	45.1	50.4
Dimers				
αβ/αβ[a]	0.0	0.0	0.0	0.0
αβ/αβ	6.6	7.0	9.4	9.8
αβ/βα	8.3	7.1	4.0	2.8
αααα	15.7	14.1	13.2	11.6
ααββ	16.6	14.0	15.2	12.6

[a] Values taken as reference.

531