Competitive Retro-Cycloaddition Reaction in Fullerene Dimers Connected through Pyrrolidinopyrazolino Rings

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Competitive retro-cycloaddition in [60] and [70] fullerene homodimers (1a, 1c) as well as [60]/[70] heterodimer (1b), linked through 2-pyrazolinopyrrolidino bridges, has been studied by means of HPLC, mass spectrometry, and theoretical calculations at the density functional theory (DFT) level by using the two-layered ONIOM approach. The results of these investigations indicate that the retro-cycloaddition reaction of pyrrolidinofullerenes is favored compared to the retro-cycloaddition reaction of 2-pyrazolinofullerenes in compounds 1a–c. Evidence of the occurrence of this process have been observed both by HPLC and MS-MALDI, these findings being in good agreement with those predicted by theoretical calculations.

Introduction

Since fullerenes1 and other molecular carbon nanostructures2 were discovered, a remarkable effort has been devoted to their chemical modification.3 Moreover, owing to their exceptional electronic and geometrical characteristics, fullerenes represent an exceptional scenario for testing a wide variety of new reactions.4 Some of us have previously reported the thermally induced transition metal catalyzed

quantitative retro-cycloaddition reaction of pyrrolidino-
[3,4:1,2]fullerenes as well as isoxazolino[3,4:1,2]fullerenes, and
proved its convenience as a new and useful protection–deprotection protocol. Recently, this methodology also has been applied to induce the retro-cycloaddition process in 2-pyrazolino[3,4:1,2]fullerenes. The results of that study clearly indicated that C-substitution on the pyrazole ring plays an important role on the course of the reaction, as 1,3-diaryl-2-pyrazolino[60]fullerenes are thermally stable under these conditions and form C60 in very low yields. In contrast, 1-aryl-3-alkyl-2-pyrazolino derivatives are more vulnerable to these experimental conditions, undergoing an efficient thermally induced transition metal catalyzed retro-cycloaddition reaction. In a previous paper, we have reported the preparation and photovoltaic applications of a new family of fullerene-based compounds, namely, soluble [60]- and [70]fullerene homodimers (1a, 1c) and the [60]/[70]heterodimer (1b), linked through 2-pyrazolinopyrroldino bridges (Figure 1). These dimers represent the first example of covalently bonded pyrrolidinopyrazolinofullerene dimers, despite the fact that pyrrolidinofullerenes and pyrazolinofullerenes are well-known in fullerene chemistry and have been extensively studied. In the present paper we report on the competitive retro-cycloaddition reaction that takes place in these dimers (1a–e), by means of thermally induced treatment in the presence of an excess of dipolarophile (maleic anhydride), as well as copper triflate (CuOTf2). The competitive retro-cycloaddition process that takes place on these dimers has also been studied by mass spectrometry and the experimental findings are underpinned by theoretical calculations at the density functional theory (DFT) level, using the two-layered ONIOM approach.

Analysis of the experimental and theoretical results obtained by these three different approaches reveals that the retro-cycloaddition occurs preferentially on the pyrrolidinofullerene moiety, due to the lower activation barrier and the slightly more favorable reaction energy for the entire process.

**Results and Discussion**

**Thermal Treatment.** To investigate the thermal stability of these dimers, compound 1a has been submitted to the same experimental conditions previously reported for other fullerene-fused pentagonal heterocyclic rings. Compound 1a was first heated at reflux in o-DCB for 24 h (Figure 2), and then a small amount (0.5 mL) of the reaction mixture was collected, diluted, and submitted to HPLC analysis (Table 1, 0-DCB-24 h). The results of this experiment showed that pristine C60 was obtained in moderate yield (50%) under thermal treatment. Then, we carried out the same experiment by adding a large excess (30 equiv) of maleic anhydride as an efficient dipolarophile in order to trap the in situ generated dipole (Table 1, MA-24 h). Analysis of this experiment by HPLC showed that pristine C60 was obtained in a better yield (66%) together with a new peak located at 11.25 min (toluene 1 mL/min), which was identified by the detector of the HPLC as a fullerene-based compound.

To shed some light on the nature of this new fullerene-based compound, we isolated a small amount of this new derivative by semipreparative HPLC chromatography and submitted this sample to MALDI MS analysis. The recorded mass spectra, both in positive and in negative modes of detection, do not exhibit the corresponding molecular ion proposed for the trapping of the thermally generated azomethyne ylide by the maleic anhydride (compound 2, molecular weight 1134 Da). In contrast, a peak at m/z 1104 (M – 30 Da) and a fragment at m/z 1060 (1104 – 44 Da) were observed both in the negative and in the positive modes of detection. The structure of the proposed new derivative with a cyclic anhydride moiety supports the formation of both fragments. Thus, an elimination of 30 Da (formaldehyde) and a subsequent loss of 44 Da (carbon dioxide) explain the formation of these ions, thus indicating that the retro-cycloaddition of 1a takes place with trapping of the intermediate dipole (see the SI). It is important to note that the mass spectra of cyclic anhydrides are known to give small or negligible molecular ion peaks but produce abundant peaks due to CO2 elimination. The fragmentation pattern of this new derivative therefore can be considered as a proof of the proposed structure. This conclusion is, indeed, well supported by our previous research findings: when performing the retro-cycloaddition study with different 2-pyrazolinofullerenes, we were not able to observe the trapped nitrile-imine species in any case. On the contrary, dealing with fulleropyrrolidines, the retro-cycloaddition process is more favored, and efficient trapping of the thermally generated azomethyne ylide has recently been described.

Then, we performed the same experiment but adding copper triflate, a metal Lewis acid, in order to find out if a possible coordination with the nitrogen atoms could activate the retro-cycloaddition reaction (Table 1, entry 3). The results of this experiment showed that pristine C60 was obtained in 58% yield, a value that resembles that obtained with simple thermal treatment, being therefore, the influence of copper triflate, scarce or negligible on the retro-cycloaddition process. When the experiment was performed in the presence of maleic anhydride, the new compound 1a was not observed. The appearance of the new peak at 11.25
min was also detected, thus confirming the formation of the trapped azomethine ylide in the presence of maleic anhydride.

The experiments performed on derivative 1a suggest that the best condition to trap the dipole and induce thermal retro-cycloaddition of fulleropyrrolidines is to add a large excess of dipolarophile. Therefore, we carried out analogous experiments with derivatives 1b and 1c. Derivative 1b is especially important in order to determine which retro-process is favored, since both fullerene units (C60 and C70) are present in this compound. Interestingly when compound 1b was heated at reflux in the presence of maleic anhydride (30 equiv), C70 was obtained in a larger amount (60%) than that observed for C60 (11%), providing strong evidence that the retro-cycloaddition of fulleropyrrolidines is more favored compared to the retro-cycloaddition of 2-pyrazolinopyrrolidino-fullerenes. Moreover, we also observed the appearance of the peak located at 11.25 min (toluene 1 mL/min.), confirming the formation of the trapped azomethine ylide in the presence of maleic anhydride. The same experiment carried out with derivative 1c showed that C70 was generated in good yield (84%) together with other peaks that display UV–vis spectra typical for a C70-based compound, most likely due to the trapping of the generated azomethine ylide.

**Mass Spectrometry.** The mass spectrum of an organic compound provides two types of complementary information: one is the knowledge of the molecular weight and formula based on the molecular ion, and the second one is the determination of the structure on the grounds of the fragmentation pattern. Since fragmentation is a chemical process resulting in bond breaking, the spectrometric fragmentation is sometimes closely related to chemical degradation processes.13 Cycloadditions and their corresponding retro-processes are one of the most classical reactions which can be investigated either chemically or under the mass spectrometric point of view. The well-known retro-Diels–Alder (RDA) reaction originating in the mass spectrometer was first recognized by Biemann14 and is actually one of the most investigated spectrometric reactions.15 Ionization methods such as electron-impact-ionization (EI) are hardly

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**FIGURE 1.** [60]- and [70]fullerene homodimers (1a, 1c) and the [60][70]heterodimer (1b), linked through 2-pyrazolinopyrrolidino bridges. Thermally generated azomethine ylide trapped by the maleic anhydride (2).

**FIGURE 2.** Chromatogram of the thermal retro-cycloaddition of 1a in the presence of maleic anhydride (24 h); the inset shows the UV–vis absorption spectrum of the new compound observed at 11.25 min.

**TABLE 1.** Experimental Conditions Used for the Retro-Cycloaddition Reaction Undergone by the 2-Pyrazolinopyrrolidino[60]fullerenes and Formation of Pristine C60 (%) Determined by HPLC

<table>
<thead>
<tr>
<th>entry</th>
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<th>C70 (%)</th>
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<td>o-DCB-24 h</td>
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<tr>
<td>2</td>
<td>1a</td>
<td>MA-24 h</td>
<td>66</td>
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<tr>
<td>5</td>
<td>1b</td>
<td>MA-24 h</td>
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<td>60</td>
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<td>6</td>
<td>1c</td>
<td>MA-24 h</td>
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*All the reactions were performed in o-DCB at reflux. MA = 30 equiv of maleic anhydride; Cu(OTf2) = 1 equiv of copper triflate.*

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used in the fullerene mass spectrometry field. In contrast, soft ionization methods, especially matrix-assisted laser desorption/ionization (MALDI) and electrospray ionization (ESI), are widely used, even overcoming problems like insolvency and/or degradation of the sample.

In a previous study by some of us, we reported that the thermally induced retro-cycloaddition reaction in isoxazolino[60]- and [70]-fullerene derivatives can also be observed from the molecular ions generated by ESI-MS. On the other hand, N-methyl-substituted and N-unsaturated pyrrolidinofullerenes undergo the thermal retro-cycloaddition affording pristine fullerene. In contrast, N-benzoyl pyrrolidinofullerenes do not give this reaction. The study of the collision-induced dissociation (CID) mass spectra of the molecular ions generated from these molecules under ESI conditions also supports these findings. 2-Pyrazolinofullerenes also undergo a thermal retro-cycloaddition, and evidence of this process can be obtained from the CID-ESI mass spectra of these compounds, which form C60 in the main fragmentation pathway of the corresponding molecular ions.

We have investigated the HRMS MALDI mass spectra of compounds 1–3 in order to verify if the observed thermal retro-cycloadditions also take place when these reactions are induced in the mass spectrometer. Thus, the homodimer 1a exhibits a molecular ion [M + H]+ at m/z 1757.1972, which eliminates 720 Da (C70) to form a fragment at m/z 1037.204 ([60]3a) as the main fragmentation through a retro-cycloaddition process. However, the existence of an open 1,3-dipole instead of an aziridine ring cannot be ruled out. A second observed fragment at m/z 874.153 ([60]3b), which corresponds to the formula C59H30N, clearly indicates a cleavage of the heterocycle bridge with charge retention on the pyrrolidinofullerene moiety (Scheme 1).

Thus, the question is to know in which heterocycle the retro-cycloaddition takes place. The mass spectrum of heterodimer 1b shows a molecular ion [M + H]+ at m/z 1877.1972, which undergoes a retro-cycloaddition reaction with loss of 840 Da (C70) leading to the formation of a fragment at m/z 1037.307 ([60]3a), identical with the fragment obtained from 1a. This result can only be explained assuming that the retro-cycloaddition takes place more easily on the pyrrolidinofullerene moiety. The cleavage of the heterocycle bridge is also observed in this case provoking the formation of a fragment at m/z 994.160 ([70]3b) with the formula C69H30N, which indicates that the charge retention occurs in the pyrrolidinofullerene moiety. The mass spectrum of 1c confirms these facts. The molecular ion [M + H]+ at m/z 1997.1972 (C157H25N4O2) eliminates C70 to form a fragment at m/z 1157.205 ([70]3a) resulting from the retro-cycloaddition on the pyrrolidinofullerene substructure with elimination of C70. Moreover, the cleavage of the heterocycle bridge yields a fragment at m/z 994.160 ([70]3b) identical with the ion found for the cleavage of 1b.

**Theoretical Calculations**

Under thermal treatment and in the presence of reagent excess of some dipolarophile such as maleic anhydride, pyrrolidino[3,4,1.2]60fullerenes can efficiently revert back to [60]fullerene and azomethine ylide in what is called the retro-Prato reaction. Experimentally, pyrrolidinofullerenes revert to [60]fullerene and azomethine ylide by reducing the barrier of the retro-cycloaddition reaction. Theoretical Calculations were assessed in the presence of maleic anhydride as a dipolarophile. Figure 3 shows the relative energies and Gibbs free energies of the transition states (TSs) and products for the most favorable mechanism. Calculations showed that the presence of maleic anhydride did not improve the efficiency of the reaction by reducing the barrier of the retro-cycloaddition reaction. However, the retro-Prato reaction was clearly favored as the final 1,3-dipole generated was stabilized through reaction with maleic anhydride, converting the overall reaction from highly endothermic (the reaction energy for the retro-Prato reaction was 53.2 kcal mol−1) to substantially exothermic (in the presence of maleic anhydride, the reaction energy became −16.4 kcal mol−1) (see Figure 3). Therefore, the most favorable mechanism was obtained when the assistance of the dipolarophile was not produced along the whole reaction path, but only at the final stage of the reaction. The retro-cycloaddition
presented a high-energy barrier of 45.4 kcal mol\(^{-1}\) (\(\Delta G^\ddagger = 39.2\) kcal mol\(^{-1}\)), which was smaller than the reaction energy found (53.1 kcal mol\(^{-1}\), \(\Delta G_r = 34.0\) kcal mol\(^{-1}\)). However, no minimum structure was located indicating the existence of a very shallow minimum close to the TS. Once the retro-cycloaddition was produced (4a + 5 \(\rightarrow\) C\(_{60}\) + 6a + 5), the formed azomethine ylide reacted immediately with maleic anhydride generating the final product 7a (C\(_{60}\) + 6a + 5 \(\rightarrow\) C\(_{60}\) + 7a, see Figure 3). The latter process was barrierless as neither a TS nor an intermediate could be located during the approach of 6a and 5.
The same mechanism has been explored for the nitrile imine case. Figure 4 contains the relative energies and the Gibbs free energies of the TSs and products of each step of the reaction. The retro-cycloaddition reaction (4b + 5 → C60 + 6b + 5) is also highly endothermic with a reaction energy of 45.4 kcal mol⁻¹ and an activation barrier of 46.7 kcal mol⁻¹. Gibbs free energies are somewhat smaller, 28.1 and 41.7 kcal mol⁻¹, as expected from the fact that there is an increase in the entropy along the reaction coordinate. The reaction energy obtained in the first step of the reaction is more favorable (less endothermic) for the nitrile imine dipole (45.4 and 53.2 kcal mol⁻¹ for nitrile imine and azomethine ylide, respectively). This lower reaction energy found is basically attributed to the highest stability of nitrile imine as compared to the reactive azomethine ylide. The much lower HOMO - LUMO gap for the azomethine ylide (3.62 eV) than for the nitrile imine (5.85 eV) provides evidence for the higher stability of the nitrile imine. Although the reaction energy found for the first step of the reaction (4b + 5 → C60 + 6b + 5) is more favorable for the case of the nitrile imine, the activation barrier is 1.5 kcal mol⁻¹ (or 2.5 kcal mol⁻¹ in terms of Gibbs free energies) higher than that for the azomethine ylide. The latter difference computed from single point energy calculations at the B3LYP/6-31G(d) level by using the optimized ONIOM geometries (i.e., B3LYP/6-31G(d)/ONIOM(B3LYP/6-31G(d); SVWN/STO-3G)) is 0.9 kcal mol⁻¹. Although the energy differences found are very low, there is a slight preference for the retro-cycloaddition for the azomethine ylide case, which is indeed in accordance with experimental findings. Figure 5 shows the optimized structures for the TSs corresponding to the retro-cycloaddition reaction in the case of the azomethine ylide (TS1a) and the nitrile imine (TS1b). In both cases the TSs structures are concerted. However, TS1a is almost synchronous whereas TS1b is clearly asynchronous as expected from symmetry considerations. The C–C bond distances of those bonds being broken are longer in TS1a (2.71 Å) than in TS1b (2.59/2.20 Å) as could be anticipated from Hammonds postulate.19

Finally, nitrile imine reacts with maleic anhydride giving the cycloaddition product 7b (C60 + 6b + 5 → C60 + 7b). The TS involving the formation of this product has a relative energy of 44.1 kcal mol⁻¹, which is lower in energy than the previous intermediates (C60 + 6b + 5) (45.4 kcal mol⁻¹). Although a minimum structure should be found between these two stationary points, we were unable to locate any intermediate in this extremely flat region of the potential energy surface. The intrinsic reaction coordinate (IRC) has been performed to ensure that the TS2b found connects with the expected product (7b).

The overall reaction (4b + 5 → C60 + 7b) is exothermic by -15.6 kcal mol⁻¹ (or by -14.4 kcal mol⁻¹ in terms of Gibbs free energies). However, the final reaction energy found for azomethine ylide was slightly more favorable (-16.4 kcal mol⁻¹). The reaction energies computed with single point energy calculations at the B3LYP/6-31G(d) level with use of the optimized ONIOM geometries (i.e., B3LYP/6-31G(d)/ONIOM(B3LYP/6-31G(d); SVWN/STO-3G)) are -20.6 and -21.3 kcal mol⁻¹ for the nitrile imine and the azomethine ylide, respectively. B3LYP results do also support that the retro-Prato reaction is slightly more favored than the nitrile imine retro-cycloaddition reaction.

These results show that the retro-cycloaddition reaction for nitrile imine is slightly less favorable than that for azomethine ylide. The difference in reactivity observed experimentally is basically attributed to the highest (Gibbs free) energy required to surmount the TS that involves the formation of the dipole (first step of the reaction). The retro-cycloaddition of azomethine ylide presents not only a lower activation barier, but also a slightly more favorable reaction energy for the whole process.

**Summary and Conclusions**

In summary, we have studied the retro-cycloaddition process in a new family of fullerene dimers linked through 2-pyrazolinopyrrolidino bridges (1a–e). According to the experimental findings, dimers 1a–e undergo an efficient retro-Prato (retro-cycloaddition on the pyrrolidine ring) reaction under the experimental conditions of this study. In contrast, the retro-cycloaddition reaction of 2-pyrazolino-fullerenes is less favored under these conditions. We have observed experimental evidence that support these conclusions, which are also in good agreement with the theoretical predictions.

These studies on the retro-cycloaddition processes are of interest since the thermal and chemical stability of fullerene derivatives is a critical issue for their applications in molecular electronics and, in particular, in the development of photovoltaic devices where fullerene cycloadducts are the materials of choice as electron acceptors in the construction of bulk heterojunction solar cells.20 Since light and heat are key parameters in photovoltaic cells, a better knowledge of their influence in the stability of modified fullerenes can help in achieving a better understanding of aspects such as morphology, charge transport, and efficiency in these devices.

**Experimental Section**

**General procedure for the retro-cycloaddition experiments:** All the reactions were monitored by HPLC (Cosmosil Buckyprep column, 4.6 mm (i.d.) F 250 mm; toluene, flow rate: 1 mL min⁻¹). Retention times: 13.2 min for C70, 8.5 min for C60.


Experiment o-DCB-24 h: In a typical experiment, compound 1a (0.005 mol) was heated at reflux in o-DCB (5 mL).

Experiment MA-24 h: Compound 1a–c (0.005 mol) and maleic anhydride (0.016 mmol) were heated at reflux in o-DCB (5 mL).

Experiment Cu(OTf)2-24 h: Compound 1a (0.005 mol) and copper(II) triflate (0.005 mmol) were heated at reflux in o-DCB (5 mL).

Experiment MA-Cu(OTf)2-24 h: 1a (0.005 mol), maleic anhydride (0.016 mmol), and copper(II) triflate (0.005 mmol) were heated at reflux in o-DCB (5 mL).

Computational Details

Full geometry optimizations have been carried out with the two-layered ONIOM approach with the Gaussian 03 program. The density functional theory (DFT) SVWN method together with the standard STO-3G basis set was used for the low-level calculations, and the hybrid density functional B3LYP method with the standard 6-31G(d) basis set was employed for the high-level system. The latter ONIOM methodology was recently shown to give accurate results close to the full B3LYP (high level method) calculations for studying cycladdition reactions in fullerene derivatives. All systems were treated with the spin-restricted formalism. The choice of DFT methods was based on previous studies which showed that DFT (and in particular B3LYP together with 6-31G(d) basis set) gives accurate descriptions of the reaction mechanism of pericyclic reactions. Hessians were computed to determine the nature of stationary points (one or zero imaginary frequencies for transition states and minima, respectively) and to calculate unscaled zero-point energies (ZPEs) as well as thermal corrections and entropy effects, using the standard statistical-mechanics relationships for an ideal gas from which Gibbs free energies have been calculated at 298 K and 1 atm.

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Supporting Information Available: (ONIOM2/UB3LYP/6-31G(d):SVWN/STO-3G) optimized Cartesian XYZ coordinates of all analyzed species and MS-MALDI spectra of the three dimers. This material is available free of charge via the Internet at http://pubs.acs.org.