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Diels−Alder Cycloadducts of [60]Fullerene with Pyrimidine *o*-Quinodimethanes

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Novel organofullerenes bearing a pyrimidine nucleus covalently attached to the C_{60} cage have been prepared by [4 + 2] cycloaddition reactions of C_{60} and pyrimidine *o*-quinodimethanes generated "in situ" from the readily available cyclobutapyrimidines which are prepared in a one-pot procedure from cyclobutanone and alkyl or aryl nitriles. The reaction mechanism involves formation of a nitrilium cation with participation of two molecules of the respective nitrile. A side-product (**16**) formed from two cyclobutanone molecules is obtained together with the target cyclobutapyrimidines **4a**−**d**. Compounds **4a**−**d** are appropriate precursors for the generation of substituted pyrimidine *o*-quinodimethanes **5a**−**d** which are efficiently trapped by the C_{60} molecule in a cycloaddition reaction which according to theoretical calculations is controlled by the HOMO of the diene. ^{1}H NMR spectra indicate the presence of a dynamic process attributed to the boat-to-boat interconversion of the cyclohexene ring. The activation free energy has been measured by dynamic NMR experiments showing values $\Delta G^{\ddagger} \approx 16-17$ kcal/mol for both methylene groups, depending upon the substituents on the pyrimidine unit. Theoretical calculations at the semiempirical PM3 level confirm the presence of a boat conformation for the cyclohexene ring which undergoes a rapid flipping motion resulting in an average C_s symmetry as it is observed in the ^{1}H NMR spectra. The cyclic voltammetry measurements show the presence of reduction waves cathodically shifted, related to C_{60}, due to the saturation of a double bond of the C_{60} cage. A weak electronic interaction is observed between the pyrimidine moiety and the C_{60} core.

Introduction

The synthesis of novel chemically modified fullerenes is mainly directed to the search of other features to add to the already known unique properties of fullerenes. Among the different chemical procedures available for such modifications of C_{60}, cycloaddition reactions have proved to be one of the most important methods for the preparation of novel organofullerenes, and a wide variety of cycloadducts have been reported.[1] Addition of *o*-quinodimethanes[2] to C_{60} affords to a set of particularly stable cycloadducts as a consequence of the aromatization process which takes place during product formation. Much less is known, however, on the reaction of heterocyclic analogues of *o*-quinodimethane[3] despite the interest they have in the preparation of organofullerenes with potential biological[4] or materials science[5] applications.

Recently, the first cycloadducts formed from C_{60} and heteroaromatic *o*-quinodimethanes have been described by Eguchi[6] et al. and us.[7] Only a limited number of five-membered ring heterocycle-containing organofullerenes (**1**) are known so far.[6] Furthermore, we have recently reported the [4 + 2] cycloaddition reactions of six-membered heterocyclic *o*-quinodimethanes, generated in situ from 2,3-bis(bromomethyl)pyrazine derivatives to [60]fullerene yielding cycloadducts **2**.[8]

In this work we describe the synthesis of novel pyrimidine-containing organofullerenes **17a**−**d** prepared by Diels−Alder cycloaddition of C_{60} and pyrimidine *o*-quinodimethanes **5** which are in turn generated in situ from readily available cyclobutapyrimidine derivatives **4a**−**d**. As it is well-known, the pyrimidine ring occurs

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(3) Ando, K.; Takayama, H. *Heterocycles* **1994**, *37*, 1417. Chou, T.-S. *Rev. Heteroat. Chem.* **1993**, *8*, 65. Chou, T.-S.; Chang, R.-C. *J. Org. Chem.* **1993**, *58*, 493. Chaloner, M. L.; Crew, A. P. A.; O'Neill, P. M.; Storr, R. C.; Yelland, M. *Tetrahedron* **1992**, *48*, 8101.

(4) Sijbesma, R. P.; Srdanov, G.; Wudl, F.; Castoro, J. C.; Wilkins, Ch.; Friedman, S. H.; DeCamp, D. L.; Kenyon, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 6510. Friedman, S. H.; DeCamp, D. L.; Sijbesma, R. P.; Srdanov, G.; Wudl, F.; Kenyon, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 6506. Tokuyama, H.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 7918. Toniolo, C.; Bianco, A.; Maggini, M.; Scorrano, G.; Prato, M.; Marastoni, M.; Tomatis, R.; Spisani, S.; Palù, G.; Blair, E. D. *J. Med. Chem.* **1994**, *37*, 4558. da Ros, T.; Prato, M.; Novello, F.; Maggini, M.; Banfi, E. *J. Org. Chem.* **1996**, *61*, 9070. Zan, Y.-Z.; Chen, C.-H.; Anderson, J. L.; Sigman, D. S.; Foote, C. S.; Rubin, Y. *Tetrahedron* **1996**, *52*, 5179. For a recent review, see: Jensen, A. W.; Wilson, S. R.; Schuster, D. L. *Bioorg. Med. Chem.* **1996**, *4*, 767.

(5) Prato, M. *J. Mater. Chem.* **1997**, *7*, 1097.

(6) For a recent review on the synthesis of heterocycle-containing [60]fullerenes, see: Eguchi, S.; Ohno, M.; Kojima, S.; Koide, N.; Yashiro, A.; Shirakawa, Y.; Ishida, H. *Fullerene Sci. Technol.* **1996**, *4*, 303.

(7) Fernández-Paniagua, U. M.; Illescas, B. M.; Martín, N.; Seoane, C. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1077.

(8) (a) Fernández-Paniagua, U. M.; Illescas, B. M.; Martín, N.; Seoane, C.; de la Cruz, P.; de la Hoz, A.; Langa, F. *J. Org. Chem.* **1997**, *62*, 3705. An alternative synthetic procedure was simultaneously reported from 2-hydroxycyclohexanone-fused [60]fullerene. See: (b) Torres-García G.; Luftmann, H.; Wolff, Ch.; Mattay, J. *J. Org. Chem.* **1997**, *62*, 2752. (c) Ohno, M.; Koide, N.; Sato, H.; Eguchi, S. *Tetrahedron* **1997**, *53*, 9075.

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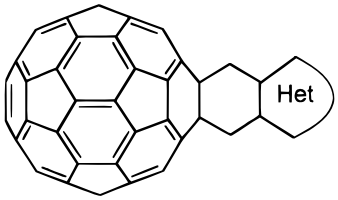
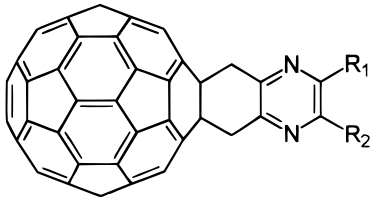
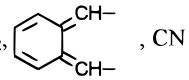
Chart 1



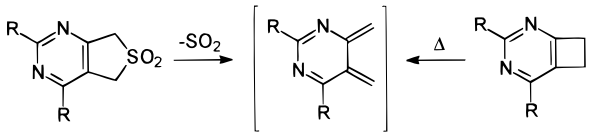
1: Het = thiophene, furan, thiazole, oxazole, indole





2: R_1, R_2 = $(CH{=}CH)_2$, , CN

Scheme 1



3 **5** **4**

widely in compounds with biological and pharmaceutical activity and, therefore, pyrimidine-containing organofullerenes are of particular interest in the search of novel properties.

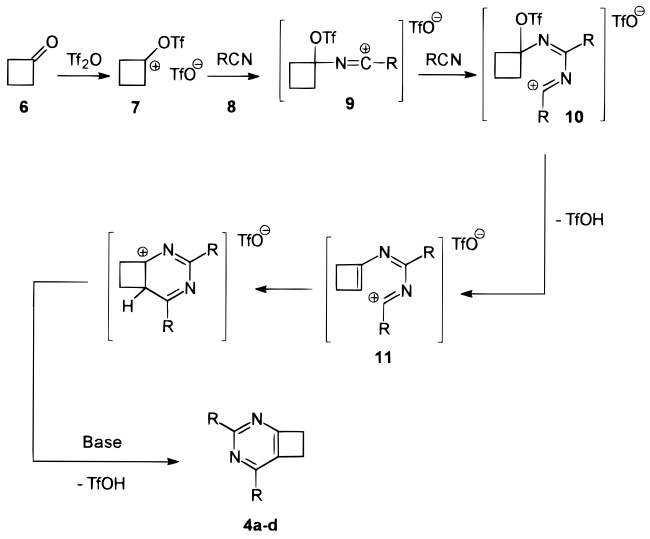
Pyrimidine *o*-quinodimethane (**5**) has been generated very recently by two different procedures (Scheme 1): (a) from pyrimidine-fused-3-sulfolenes **3** by thermal extrusion of sulfur dioxide in a multistep synthetic procedure in which the starting sulfolenes **3** were prepared in a synthesis involving four steps.[9] (b) A straightforward route from substituted cyclobutapyrimidines **4** which are in turn prepared in a one-step procedure from commercially available nitriles and cyclobutanone, according to the procedure that we have recently reported.[10] By following this approach, we have prepared a series of novel organofullerenes **17a**−**d** bearing alkyl- or aryl-substituted pyrimidines from the readily available substituted cyclobutapyrimidines **4**.

Dynamic behavior of the cycloadducts **17** has been investigated by using variable-temperature ^{1}H NMR measurements. The redox properties of the different organofullerenes have been measured by cyclic voltammetry (CV) in solution in order to determine the influence that the substituted pyrimidine ring has on the reduction potentials of the [60]fullerene moiety. Finally, theoretical calculations at the semiempirical PM3 level were also performed in order to predict the geometry of the obtained cycloadducts and to gain some understanding of the experimental findings.

Results and Discussion

The target pyrimidine-containing cycloadducts **17a**−**d** were prepared by [4 + 2] cycloaddition of the respective pyrimidinoquinodimethanes (**5**) to [60]fullerene. The reactive intermediate **5** is generated "in situ" by thermally allowed conrotatory [σ2 + π2] electrocyclic ring opening of cyclobutapyrimidines **4** in *o*-dichlorobenzene (ODCB) at 180 °C. The starting cyclobutapyrimidines **4** are readily prepared in an expeditious one-step procedure by reaction of aliphatic or aromatic nitriles **8** with cyclobutanone **6** and triflic anhydride (Tf_2O) according to the method previously reported for other related aliphatic or alicyclic ketones leading to differently substituted pyrimidines.[11]

Scheme 2



The mechanism proposed for the formation of the novel cyclobutapyrimidines is analogous to that previously reported for the reaction of nitriles with highly enolizable ketones in the presence of trifluoromethanesulfonic anhydride (Tf_2O).[11] This mechanism starts with an electrophilic attack of triflic anhydride to cyclobutanone **6** leading to the formation of a (triflyloxy)carbenium ion **7** followed by nucleophilic attack of the nitrile to form a resonance-stabilized nitrilum cation (**9**). This cation is subsequently attacked by a second molecule of nitrile to yield the cationic intermediate **10** which undergoes elimination of triflic acid to afford **11**. A further intramolecular cyclization and loss of a proton yields the target cyclobutapyrimidines **4** (Scheme 2).

The lower yields obtained for 5,6-dihydrocyclobuta[*d*]-pyrimidines (**4**) in comparison to other aliphatic or alicyclic ketones[11] can be explained by considering the difficulty of elimination of triflic acid which leads, in this case, to a highly strained cyclobutenyl intermediate (**11**). This result is in agreement with the higher difficulties found in the formation of the cyclobutene ring in comparison to other related larger systems.[12]

Compounds **4** are thus obtained in moderate yields due to the competitive formation of *N*-[1-(2′-oxocyclobutyl)]-cyclobutylamide (**16**) as side-products which are isolated in 20−30% yields. The formation of such unexpected products could be explained from dimer **12** resulting from an aldol condensation of cyclobutanone. Reaction of **12** with Tf_2O followed by easy nucleophilic substitution by

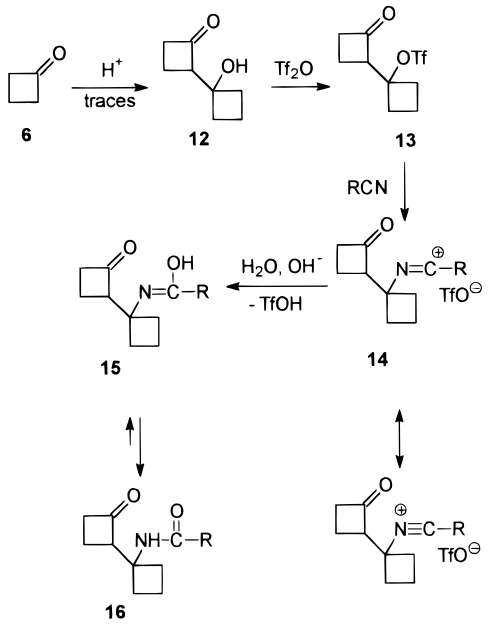
(9) (a) Tomé, A. C.; Cavaleiro, J. A. S.; Storr, R. C. *Tetrahedron* **1996**, *52*, 1735. (b) Tomé, A. C.; Cavaleiro, J. A. S.; Storr, R. C., *Tetrahedron* **1996**, *52*, 1723.

(10) Herrera, A.; Martínez, R.; González, B.; Illescas, B.; Martín, N.; Seoane, C. *Tetrahedron Lett.* **1997**, *38*, 4873.

(11) García Martínez, A.; Herrera Fernández, A.; Moreno Jiménez, F.; García Fraile, A.; Subramanian, L. R.; Hanack, M. *J. Org. Chem.* **1992**, *57*, 1627.

(12) Schlosser, M. *Houben-Weyl "Methoden der Organishen Chemie"*; Georg Thieme: Stuttgart, 1972; Vol V/1b, p 201.

Scheme 3



a molecule of nitrile leads to the stabilized nitrilium cation **14** which undergoes basic hydrolysis (**15**) and a further isomerization to yield amides **16** (Scheme 3). ^{1}H NMR spectra of **16a**−**c** show the same characteristic pattern for the aliphatic framework corresponding to the two directly attached rings. ^{13}C NMR spectra, H,C-COSY experiments and selective 1D INEPT spectrum are in full agreement with the structure of **16a**−**c**. Since the molecular ion is not observed in the mass spectra recorded with ionization by electronic impact (70 eV), we have registered the spectra obtained with chemical ionization using methane as reagent gas. This method of shoft ionization yields the molecular ion and a small extent of cleavage. The mass spectra of the three compounds are in total agreement with the proposed structures.

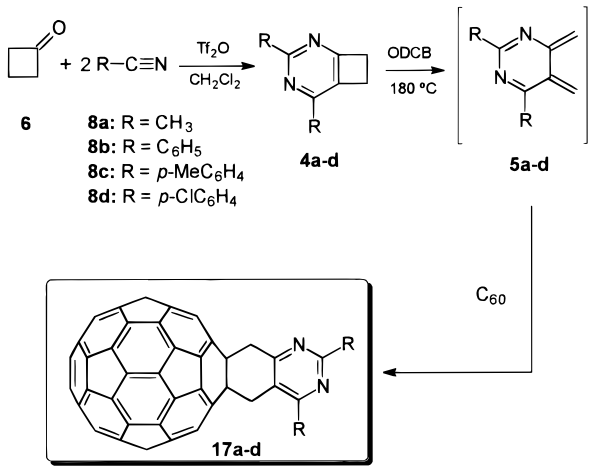
5,6-Dihydrocyclobuta[*d*]pyrimidines (**4**) are versatile precursors for the generation of the highly reactive pyrimidinoquinodimethanes (**5**) which are efficiently trapped by C_{60} or by other dienophiles such as *N*-phenylmaleinimide (NPM) or *p*-benzoquinone derivatives.[10] This result offers an elegant and straightforward procedure for the "in situ" generation of pyrimidinoquinodimethanes from readily available cyclobutapyrimidines **4** in comparison to the alternative multistep procedure from substituted sulfolenes **3**. By following the sulfolene approach, the synthesis of pyrimidine and pyrimidone derivatives of [60]fullerene has been very recently reported from the respective heterocyclic *o*-quinodimethanes.[13]

According to theoretical calculations, carried out at a semiempirical level (PM3 and AM1) (Hyperchem 3.0), the cycloaddition to form the novel organofullerenes **17a**−**d** is controlled by the HOMO of the pyrimidine *o*-quinodimethanes. The HOMO(diene)−LUMO(C_{60}) energy differences are clearly in the range of energetically favored cycloadditions (5.4−5.6 eV).

The structure of organofullerenes **17a**−**d** was established on the basis of their spectroscopic data. The UV−vis spectra of compounds **17a**−**d** show a typical weak

(13) Tomé, A. C.; Enes, R. F.; Cavaleiro, J. A. S.; Elguero, J. *Tetrahedron Lett.* **1997**, *38*, 2557.

Scheme 4



absorption band at around 430 and 700 nm.[14] The ^{13}C NMR spectra clearly indicate that the molecule has an average C_s symmetry resulting from the fast flipping motion of the cyclohexene ring linking the pyrimidine ring to the C_{60} cage. The methylene groups appear at around δ 40 and 47 ppm, and the quaternary sp^3-hybridized carbon atoms of attachment to the organic addend appear at δ 67.7 and 68.1 ppm for **17a**, δ 64.8 and 65.3 ppm for **17b**, and δ 64.7 and 65.2 ppm for **17d**, thus confirming the 6,6-ring junction on the C_{60} cage. The lower solubility of cycloadduct **17c** prevented the recording of its ^{13}C NMR spectrum.

The ^{1}H NMR spectra of cycloadducts **17a**−**d** show the methylene protons as two broad singlets at δ 4.7−5.0 at room temperature. The singlets become sharp at higher temperatures which indicate a dynamic process due to the boat-to-boat interconversion of the cyclohexene ring. This behavior has already been reported for other related organofullerenes.[8,14b,15,16] The activation free energy for the boat-to-boat inversion has been determined for the new cycloadducts **17a**−**d** by dynamic NMR experiments, and the experimental data are collected in Table 1.

We have shown that the coalescence temperature and $\Delta G^{\ddagger}$ values depend on the pentagonal or hexagonal nature of the heterocyclic system covalently attached to the C_{60} core.[8] In fact, a good linear correlation between the activation energies $\Delta G^{\ddagger}$, measured experimentally for a series of C_{60}-*o*-quinodimethane adducts, and the bond lengths calculated for the fused double bond between the cyclohexene and the aromatic ring was found.[16] The coalescence temperature and $\Delta G^{\ddagger}$ values show a remarkable dependence on the alkyl or aryl substitution on the pyrimidine ring in cycloadducts **17a**−**d** (Table 1).

The ^{1}H NMR spectrum of **17a** at 293 K in $CDCl_3$ solution displays two broad signals centered at δ 4.72 for CH_2(a) and δ 4.66 ppm for CH_2(b) respectively, which become sharp with increasing temperature. At 214 K two AB systems are observed [δ_B = 4.86, δ_A = 4.54, J_{AB} = 14.15 Hz for CH_2(a); δ_B = 4.66, δ_A = 4.63, J_{AB} = 14.65

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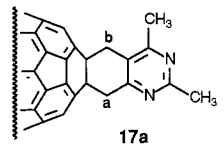
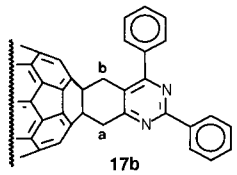
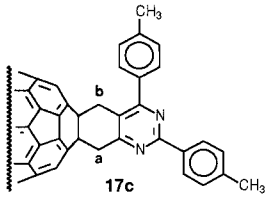
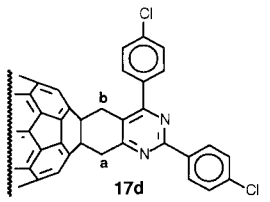
(15) (a) Zhang, X.; Foote, C. S. *J. Org. Chem.* **1994**, *59*, 5235. (b) Tago, T.; Minowa, T.; Okada, Y.; Nishimura, J. *Tetrahedron Lett.* **1993**, *34*, 8461. (c) Nakamura, Y.; Minowa, T.; Shizuka, H.; Nishima, J. *J. Chem. Soc., Perkin Trans. 2* **1995**, 2351.

(16) Illescas, B. M.; Martín, N.; Seoane, C.; Ortí, E.; Viruela, P. M.; Viruela, R.; de la Hoz, A. *J. Org. Chem.* **1997**, *62*, 7585.

Table 1. Activation Free Energies Determined for Cycloadducts 17a−d

Compound	T_c (K)	Δν	$\Delta G^{\neq}$ [a, b]	$\Delta G^{\neq}$ [b, c]	J_{AB} (Hz)	$\Delta G^{\neq}$ [a, d]	$\Delta G^{\neq}$ [c, d]	δ (ppm)	T[e]
 **17a**			**a**	**a**		**a**	**a**	214 **a**$_1$ 4.86 **a**$_2$ 4.54	313 4.72
	270	96	64.8±0.4	15.5	14.15 (214)	64.7±0.4	15.5±0.1		
			b	**b**		**b**	**b**	214 **b**$_1$ 4.66 **b**$_2$ 4.63	4.66
	263	9	62.6±0.4	15.0	14.65 (214)	62.4±0.4	14.9±0.4		
 **17b**			**a**	**a**		**a**	**a**	258 **a**$_1$ 5.04 **a**$_2$ 4.86	323 4.96
	296	54	70.9	17.0	14.03 (258)	70.9	17.0		
			b	**b**		**b**	**b**	258 **b**$_1$ 4.96 **b**$_2$ 4.84	4.89
	293	36	70.14	16.8	14.65 (258)	70.0	16.8		
 **17c**			**a**	**a**		**a**	**a**	243 **a**$_1$ 5.00 **a**$_2$ 4.80	338 4.93
	296-8	60	71.0-71.5	17.0-17.1	13.92 (243)	70.9-71.4	17.0-17.1		
			b	**b**		**b**	**b**	243 **b**$_1$ 4.85 **b**$_2$ 4.72	4.86
	296	39	71.8	17.2	14.65 (243)	70.8	16.9		
 **17d**			**a**	**a**		**a**	**a**	193 **a**$_1$ 5.04 **a**$_2$ 4.81	333 4.94
	300	69	72.0	17.2	13.67 (193)	71.9	17.2		
			b	**b**		**b**	**b**	243 **b** 4.89	4.84
	293	0	69.7	16.7	—	69.7	16.7		

[a] In KJ/mol; [b] Activation free energies at the coalescence temperatures according to $\Delta G^{\neq} = aT[9.972 + \log(T+\Delta\nu)]$. a = 1.914 x 10^{-2} kJ mol^{-1} (Ref. 17); [c] In Kcal/mol ; [d] Activation free energies at the coalescence temperatures according to $\Delta G^{\neq} = aT[9.972 + \log(T+ (\delta\nu^2+6J^2_{AB})^{1/2}]$. a = 1.914 x 10^{-2} kJ mol^{-1} (Ref.17); [e] Temperature at which sharp singlets are observed.

Table 2. Redox Potentials of Novel Organofullerenes[a]

compound	E^1_{red}	E^2_{red}	E^3_{red}	E^4_{red}
C_{60}	−0.60	−1.00	−1.52	−2.04
17a	−0.66	−1.05	−1.64	−
17b	−0.65	−1.03	−1.61	−
17c	−0.66	−1.04	−1.65	−
17d	−0.64	−1.03	−1.64	−

[a] V *vs* SCE; GCE as working electrode; 0.1 mmol/dm^3 $NBu_4^+ClO_4^-$; toluene:MeCN (5:1); 200 mV/s.

Hz for CH_2(b)]. These quartets coalesce at temperature of 270 and 263 K, respectively. A similar behavior is observed in the ^{1}H NMR spectra of compounds **17b−d** (see Table 1).

The closer proximity of the heterocyclic nitrogen to the methylene hydrogens (a) could be responsible for the observed slight shift of the CH_2(a) signals to lower field in the ^{1}H NMR spectra.

It is interesting to note that cycloadduct **17a**, bearing methyl substituents on the pyrimidine ring, presents a lower activation free energy for both methylene groups (a and b) than those determined for cycloadducts bearing aryl groups (**17b−d**) on the pyrimidine moiety (Table 1). The experimental values obtained are in the range of those previously measured for other carbocyclic (14.6−16.6 kcal/mol)[14b,15] analogues or six-membered heterocyclic (15.4−15.8 kcal/mol)[8a] analogues, being much higher than those determined for pentagonal heterocycles (11−12 kcal/mol).[8a] The experimental values now reported are the highest observed so far for these type of organofullerenes (~17 kcal/mol) and could be due to the high torsional and angular constraints of these structures because of the rigidity of the C_{60} cage,[14b,15a] which now is reinforced by the presence of the aryl groups on the pyrimidine ring.

To rationalize the above experimental findings, we have optimized the molecular structure of the parent organofullerenes **17a** and **17b** bearing methyl and phenyl groups as substituents on the pyrimidine moiety at the semiempirical PM3 level.[18] Figure 2 displays the optimized structure of **17b** together with the bond lengths and bond angles obtained for the organic addend.

The PM3 method predicts a geometry with the cyclohexene ring adopting a boat conformation as the minimum energy structure. The cycloadducts present, however, a C_s symmetry in the ^{1}H NMR spectra as a result of the rapid flipping motion of the cyclohexene moiety. The C1−C2 bond, to which the organic addend is fused in a 6/6 junction, has a bond length of 1.586 Å which is quite similar to that calculated for other organofullerenes in which the pyrimidine ring is substituted by an unsubstituted benzene ring (1.586 Å)[16] or a pyrazine ring (1.583 Å).[8a] These bond lengths are very close to those observed by X-ray analysis for other related 1,2-dihydrofullerenes.[14b,19]

(17) Sandström, J. *Dynamic NMR Spectroscopy*; Academic Press: London, 1982; p 96.

(18) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209; **1989**, *10*, 221. The calculations were carried out using the Hyperchem 3.0 program.

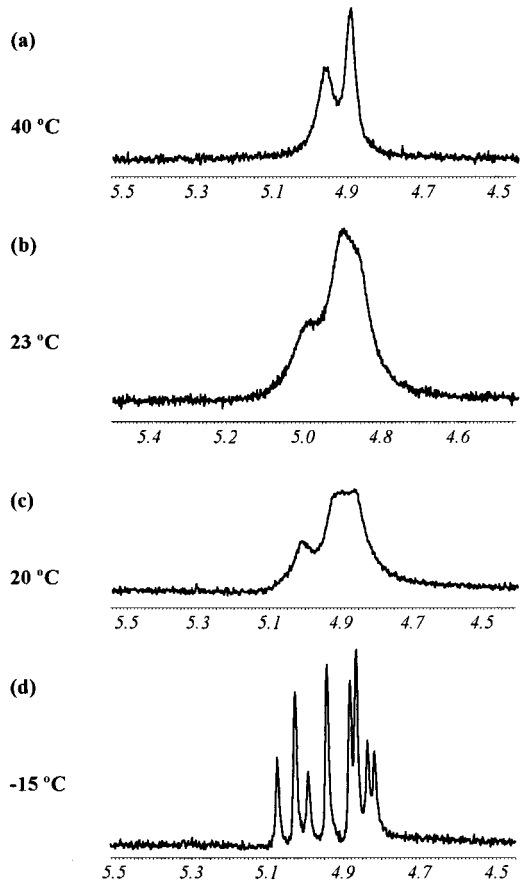


Figure 1. Temperature-dependent ^{1}H NMR spectra of compound **17b**.

The remaining bond lengths and bond angles are similar to those found for the benzene- or pyrazine-containing analogues and are in good agreement with the reported X-ray data.[14b,19] The bond length between C4−C9 (1.408 Å) (see Figure 2) is slightly larger than that found when the pyrimidine unit is substituted by a benzene ring (1.400 Å).[16] Taking into account the linear correlation found between the activation energies, $\Delta G^{\ddagger}$, measured experimentally for this type of organofullerenes, and the lengths calculated for the respective C4−C9 bond,[16] a value of ∼16 kcal/mol should be expected. These values confirm that for these organofullerenes reasonably good predictions for activation barriers can be obtained from readily performed theoretical calculations.

The redox properties of the novel cycloadducts **17a**−**d** were studied by cyclic voltammetry (CV) measurements at room temperature in toluene/acetonitrile (5/1) as solvent. The reduction potential peaks are shown in Table 2 together with those of the parent [60]fullerene measured under the same experimental conditions for comparison purposes.

Compounds **17a**−**d** show the presence of three reduction waves at potential values shifted to more negative values, related to the parent C_{60}, as expected for most dihydrofullerenes[20] due to the saturation of a double bond in the C_{60} cage which raises the LUMO energy of these organofullerenes (**17a**−**d**). Substitution on the phenyl groups linked to the pyrimidine ring has a very slight influence on the first reduction potential values since the presence of the most electronegative chlorine atoms anodically shift the E^1_{red} value (Table 2). Although the presence of a pyrimidine unit shifts the first reduction potential of the C_{60} unit to more positive values in comparison to a benzene ring,[21] the effect of the nitrogen atoms in the pyrimidine ring is smaller than in the pyrazine ring[8a] due, probably, to the longer bond connectivity of the second nitrogen atom to the C_{60} core. Thus, the pyrimidine nucleus does not significatively alter the redox properties of the parent [60]fullerene.

Summary and Conclusions

The synthesis of novel pyrimidine-containing organofullerenes **17a**−**d** has been carried out by Diels−Alder reaction of C_{60} and pyrimidine *o*-quinodimethanes which are, in turn, generated in situ from novel cyclobutapyrimidines **4a**−**d**. These compounds (**4a**−**d**) are easily prepared in a one-pot procedure through a mechanism involving the formation of a nitrilium cation. Cyclobutapyrimidines open up an elegant and convenient route for the generation of the highly reactive pyrimidine *o*-quinodimethanes. Theoretical calculations confirm that cycloaddition to form **17a**−**d** are controlled by the HOMO of the pyrimidine *o*-quinodimethanes, being energetically favored reactions.

The energy barriers for the boat-to-boat inversion of the cyclohexene ring have been determined by dynamic NMR experiments, and the $\Delta G^{\ddagger}$ values show a significant dependence of the alkyl or aryl substitution on the pyrimidine unit. The molecular geometry of cycloadducts **17a** and **17b** have been optimized at the semiempirical PM3 level and predict a structure in which the cyclohexene ring adopts a boat conformation, thus confirming the C_s symmetry observed in the ^{1}H NMR spectra. The redox properties of the novel organofullerenes determined by cyclic voltammetry indicate a certain interaction between the organic addend and the C_{60} moiety.

This methodology for the preparation of cyclobutapyrimidines paves the way to the generation of elusive pyrimidine *o*-quinodimethanes with other substituents and functional groups on the pyrimidine nucleus from the appropriately substituted nitriles. These modified fullerenes bearing a pyrimidine nucleus offer a prospect for biological probes based on the possibilities that the pyrimidine ring presents for further functionalization and the unique properties of [60]fullerene.

Experimental Section

Synthesis of 5,6-Dihydrocyclobuta[*d*]pyrimidines. General Procedure. To a well stirred solution of triflic anhydride (2.70 g, 9.6 mmol) and the corresponding nitrile (16.8 mmol) in anhydrous CH_2Cl_2 was added slowly a solution of cyclobutanone (0.56 g, 8 mmol) in 10 mL of CH_2Cl_2. The brown mixture was stirred under reflux for the appropriate time. Saturated $NaHCO_3$ solution (50 mL) was carefully added, and the organic layer was washed with brine (2 × 50 mL) and dried over $MgSO_4$. The solvent was removed under

(19) Iyoda, M.; Sasaki, S.; Sultana, F.; Yoshida, M.; Kuwatani, Y.; Nagase, S. *Tetrahedron Lett.* **1996**, *37*, 7987.

(20) (a) Chlistunoff, J.; Cliffel, D.; Bard, A. J. *Handbook of Organic Conductive Molecules and Polymers*; Nalwa, H. S., Ed., John Wiley & Sons Ltd.: New York, 1997; Ch. 7, Vol. 1. (b) Suzuki, T.; Maruyama, Y.; Akasaba, T.; Ando, W.; Kobayashi, K.; Nagase, S. *J. Am. Chem. Soc.* **1994**, *116*, 1359.

(21) Illescas, B.; Martín, N.; Seoane, C.; de la Cruz, P.; Langa, F.; Wudl, F. *Tetrahedron Lett.* **1995**, *36*, 8307.

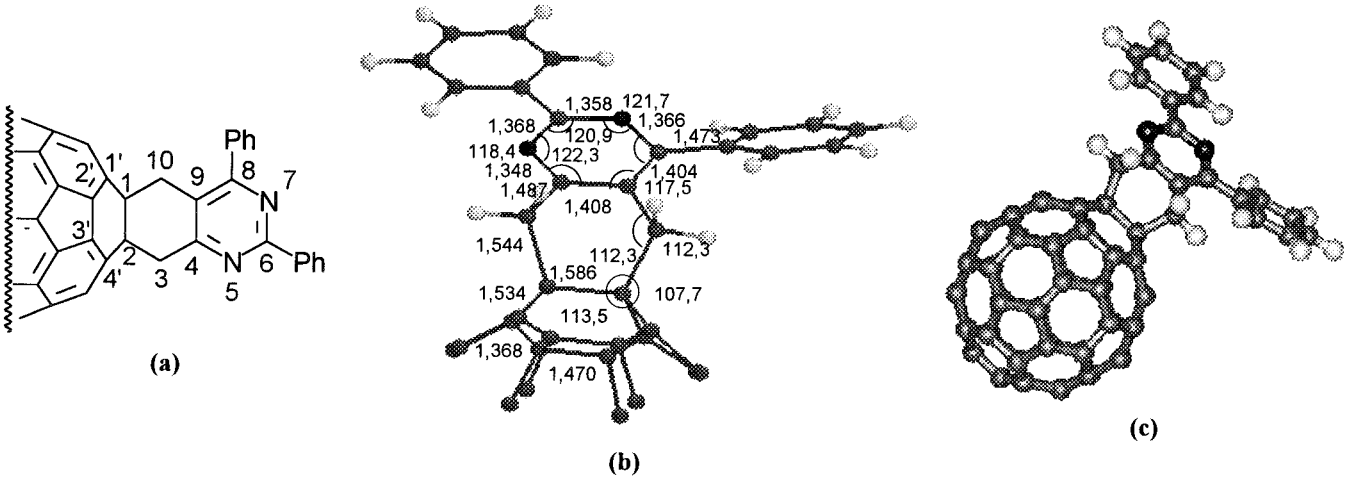


Figure 2. Detail of the PM3-optimized molecular structure of **17b**. (a) Cyclohexene aleatory numbering used in the text. (b) Geometry of the organic addend for **17b**. (c) Minimum energy conformation of **17b**. Bond lengths are in angstroms and bond angles in degrees.

vacuum, and the crude product was column chromatographed over silica gel 60 (Merck) using hexane/ethyl acetate as the eluent, allowing the isolation of pure 5,6-dihydrocyclobuta[*d*]-pyrimidines **4a**−**d** and *N*-[1-(2′-oxocyclobutyl)]cyclobutylamides **16a**−**c** as byproducts.

2,4-Dimethyl-5,6-dihydrocyclobuta[*d*]pyrimidine (4a): 20% yield; bp 25 °C/2 mbar (bulb to bulb); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.33 (s, 3H), 2.66 (s, 3H), 3.13 (dist. t, 2H), 3.36 (t, J = 4.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.1, 26.5, 26.6, 35.0, 133.7, 157.9, 167.4, 173.0; MS *m*/*z* 174 (M^+, 49), 93 (29), 66 (44), 52 (100), 42 (94).

***N*-[1-(2′-Oxocyclobutyl)cyclobutyl]acetamide (16a):** 20% yield; mp: 107−108 °C (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (m, 11H), 2.90 (m, 2H), 4.15 (m, 1H), 5.56 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.2, 15.2, 27.8, 30.3, 31.0, 44.5, 56.5, 65.4, 169.3, 210.0; IR (KBr) 3250, 3050, 2990, 2950, 1775, 1630 cm^{-1}; MS (CI, CH_4) *m*/*z* (%): 182 (M + H, 30), 123 (81), 95 (100), 87 (71). Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.08; H, 7.77; N, 8.15

2,4-Diphenyl-5,6-dihydrocyclobuta[*d*]pyrimidine (4b): 27% yield; mp: 118−119 °C (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.53−3.61 (4H, AA'BB'), 7.51 (m, 5H), 8.25 (m, 3H), 8.54 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.2, 36.3, 127.9, 128.2, 128.6, 129.0, 130.4, 131.1, 132.2, 135.9, 138.8, 155.0, 164.4, 174.4; IR (KBr) 3050, 1600, 1580, 1560, 1500, 760, 700 cm^{-1}; MS *m*/*z* 258 (M^+, 62), 155 (13), 104 (19), 77 (19), 52 (100).

***N*-[1-(2′-Oxocyclobutyl)cyclobutyl]benzamide (16b):** 23% yield; mp: 129−130 °C (hexane); IR (KBr) 3310, 1775, 1640, 730, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05 (m, 8H), 2.95 (m, 2H), 4.25 (m, 1H), 6.40 (bs, 1H), 7.60 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 15.5, 30.7, 31.5, 44.9, 57.0, 65.8, 127.0, 128.7, 131.6, 134.9, 166.9, 210.2; MS (CI, CH_4) *m*/*z* (%): 244 (M + H, 22), 122 (65), 105 (100), 95 (23), 81 (16). Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.83; H, 6.74; N, 5.75

2,4-Bis(4-methylphenyl)-5,6-dihydrocyclobuta[*d*]pyrimidine (4c): 30% yield; mp: 162−163 °C (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 6H), 3.40, 3.50 (4H, AA′BB′), 7.30 (m, 4H), 8.10, 8.45 (4H, AA′XX′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 21.7, 29.1, 36.2, 127.9, 128.1, 129.3, 129.7, 131.5, 133.2, 136.2, 140.4, 141.4, 154.7, 164.4, 174.0; IR (KBr) 1610, 1580, 1520, 795 cm^{-1}; MS *m*/*z* 286 (M^+, 66), 154 (23), 118 (33), 91 (16), 52 (100).

***N*-[1-(2′-Oxocyclobutyl)cyclobutyl]-4-methylbenzamide (16c):** 26% yield; mp: 121−122 °C (hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.95 (m, 2H), 2.30 (m, 6H), 2.40 (s, 3H), 2.95 (m, 2H), 4.25 (m, 1H), 6.40 (br s, 1H), 7.40 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.5, 15.5, 21.5, 30.8, 31.4, 44.8, 57.0, 67.8, 127.0, 129.3, 132.1, 142.0, 166.8, 210.3; IR (KBr) 3300, 1785, 1640 cm^{-1}; MS (CI, CH_4) *m*/*z* (%): 258 (M + H, 36), 136 (82), 123 (8), 119 (100), 95 (16), 81 (9). Anal. Calcd for $C_{16}H_{19}NO_2$: C, 74.68; H, 7.44; N, 5.44. Found: C, 74.13; H, 7.19; N, 5.41.

2,4-Bis(4-chlorophenyl)-5,6-dihydrocyclobuta[*d*]pyrimidine (4d): 25% yield; mp 157−158 (MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.50, 3.62 (4H, dist. AA'BB'), 7.50, 7.63 (4H, AA′BB′), 8.10, 8.50 (4H, AA′XX′); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.0, 36.2, 128.6, 129.0, 129.2, 132.0, 134.0, 136.5, 136.9, 137.2, 153.5, 163.4, 174.5; IR (KBr) 1600, 1580, 1500, 1100, 800 cm^{-1}; MS *m*/*z* 326 (M^+, 100), 291 (82), 154 (38), 52 (92).

Synthesis of Organofullerenes 17a−d. General Procedure. A solution of the corresponding dihydrocyclobutapyrimidine **4a**−**d** and [60]fullerene in 10−20 mL of *o*-dichlorobenzene was heated under reflux for a variable period of time. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel. Further purification of the solid was accomplished by washing and centrifuging three times with methanol.

1′,2′,3′,4′-Tetrahydro-6′,8′-dimethylquinazolino[2′,3′:1,2][60]fullerene (17a). According to the general procedure, a solution of 2,4-dimethyl-5,6-dihydrocyclobuta[*d*]pyrimidine (**4a**) (30 mg, 0.22 mmol) and [60]fullerene (161 mg, 0.22 mmol) in 10 mL of *o*-dichlorobenzene was refluxed for 24 h. The product was purified by using toluene as the eluent, yielding 27 mg (14%, 96% based on consumed C_{60}) of **17a**: ^{1}H NMR ($CDCl_3/CS_2$) δ 2.79 (s, 3H), 2.87 (s, 3H), 4.66 (s, 2H), 4.73 (bs, 2H); ^{13}C NMR ($CDCl_3$) δ 26.9, 29.9, 39.6, 46.4, 67.7, 68.1, 110.6, 114.2, 125.5, 136.0, 140.1, 141.4, 141.8, 142.4, 142.9, 144.34, 144.5, 144.8, 145.2, 145.4, 146.0, 146.3, 155.0, 155.3, 163.0, 165.5, 166.4; FTIR (KBr): 2919, 1570, 1426, 1412, 1181, 766, 697, 577, 525 cm^{-1}; MS *m*/*z*: 854 (M^+, 33), 720 (C_{60}, 100). UV−vis ($CHCl_3$), λ_{max} (nm): 254, 294, 334, 434, 700.

1′,2′,3′,4′-Tetrahydro-6′,8′-diphenylquinazolino[2′,3′:1,2][60]fullerene (17b). According to the general procedure, a solution of 2,4-diphenyl-5,6-dihydrocyclobuta[*d*]pyrimidine (**4b**) (40 mg, 0.16 mmol) and C_{60} (112 mg, 0.16 mmol) in *o*-dichlorobenzene (20 mL) was refluxed during 69 h. The product was purified by using $CHCl_3$ as the eluent, yielding 70 mg (46%, 74% based on consumed C_{60}) of **17b**: ^{1}H NMR (300 MHz, $CDCl_3/CS_2$) δ 4.90 (bs, 2H), 4.98 (bs, 2H), 7.56−7.58 (m, 6H), 7.89−7.91 (m, 2H), 8.73−8.76 (m, 2H); ^{13}C NMR ($CDCl_3/CS_2$) δ 40.7, 47.3, 64.8, 65.3, 128.6, 128.7, 128.8, 129.6, 129.8, 130.9, 137.4, 137.7, 140.3, 140.5, 141.8, 141.9, 142.0, 142.1, 142.2, 142.3, 142.7, 142.7, 143.2, 144.7, 144.8, 145.6, 145.6, 145.8, 145.8, 146.3, 146.4, 146.6, 147.7, 147.8, 155.8, 163.3, 163.7, 167.7; FTIR (KBr): 2919, 1550, 1425, 1392, 1180, 766, 748, 696, 525 cm^{-1}; MS *m*/*z*: 978 (M^+, 13), 720 (C_{60}, 27); UV−vis ($CHCl_3$), λ_{max} (nm): 256, 294, 318, 434, 702.

1′,2′,3′,4′-Tetrahydro-6′,8′-bis(*p*-methylphenyl)quinazolino[2′,3′:1,2][60]fullerene (17c). According to the general

procedure, a solution of 2,4-bis(4-methylphenyl)-5,6-dihydrocyclobuta[*d*]pyrimidine (**4c**) (40 mg, 0.14 mmol) and C_{60} (101 mg, 0.14 mmol) in 20 mL of *o*-dichlorobenzene was refluxed for 27 h. The product was purified by using cyclohexane/$CHCl_3$ 1/1 as the eluent, yielding 41 mg (29%, 54% based on consumed C_{60}) of **17c**: ^{1}H NMR ($CDCl_3/CS_2$) δ 2,50 (s, 6H); 4,75−5,07 (bm, 4H); 7,32−7,38 (m, 4H); 7,79 (d, 2H, J = 8.1 Hz); 8,60 (d, 2H, J = 8.1 Hz); FTIR (KBr): 2920, 1551, 1507, 1393, 1260, 1021, 811, 795, 573, 526 cm^{-1}; MS *m*/*z*: 1006 (M^+, 8), 720 (C_{60}, 17); UV−vis ($CHCl_3$), λ_{max} (nm): 256, 292, 434, 702.

1′,2′,3′,4′-Tetrahydro-6′,8′-bis(*p*-chlorophenyl)quinazolino[2′,3′:1,2][60]fullerene (17d). According to the general procedure, a solution of 2,4-bis(*p*-chlorophenyl)-5,6-dihydrocyclobuta[*d*]pyrimidine (**4d**) (50 mg, 0.15 mmol) and [60]-fullerene (110 mg, 0.15 mmol) in *o*-dichlorobenzene (30 mL) was refluxed for 47 h. The product was purified by using cyclohexane/$CHCl_3$ 1/1 as the eluent, yielding 43 mg (27%, 76% based on consumed C_{60}) of **17d**: ^{1}H NMR ($CDCl_3/CS_2$) δ 4.85 (bs, 2H), 4.97 (bs, 2H), 7.52−7.58 (m, 4H), 7.84 (d, 2H, J = 8.4 Hz), 8.68 (d, 2H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3/CS_2$) δ 40.6, 47.2, 64.7, 65.2, 113.8, 122.2, 123.2, 125.9, 128.9, 129.1, 129.8, 130.0, 130.9, 134.6, 135.5, 136.0, 136.4, 136.5, 140.3, 142.1, 142.8, 144.8, 146.3, 146.4, 146.6, 146.7, 147.8, 155.6; FTIR (KBr): 2922, 1576, 1550, 1392, 1259, 1092, 814, 767, 527 cm^{-1}; MS *m*/*z*: 1049 (M^+, 47), 720 (C_{60}, 100); UV−vis ($CHCl_3$), λ_{max} (nm): 254, 294, 433, 700.

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Supporting Information Available: H,C COSY and mass spectra of compounds **16a**−**c** and 1D INEPT of compound **16c** (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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