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Thermal [2 + 2] Cycloaddition of Morpholinoenamines with C_{60} via a Single Electron Transfer

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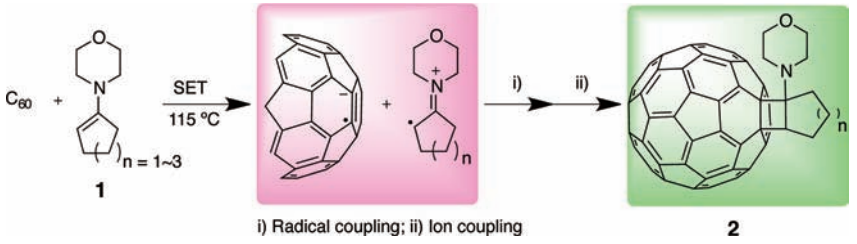
ABSTRACT



The thermal reaction of C_{60} with five- and six-membered morpholinocycloalkenes in refluxing toluene exclusively gave the [2 + 2] cycloadducts in high yields. However, a seven-membered homologue sluggishly reacted with C_{60} because of the increasing steric hindrance. This cycloaddition reaction is likely to proceed via a single electron transfer (SET), a radical-coupling, and subsequent ion cyclization rather than the prior proton transfer between the radical ions.

Cycloaddition reactions of fullerenes at the [6,6] conjunct double bond are valuable methods for chemical modification and have attracted continuous attention in view of the synthesis of fullerene derivatives and new materials.[1] Especially, a vast amount of study has been made of the thermally allowed [2 + 4] and [2 + 3] concerted reactions such as Diels–Alder[2] and 1,3-dipolar cycloadditions.[3] In these reactions, fullerenes behave as electron-poor 2π components due to the highly conjugated low lying LUMO. In contrast to the photochemical [2 + 2] cycloadditions,[4] however, the thermal [2 + 2] cycloaddition of fullerenes is very scarcely known in fullerene chemistry as found in some extreme cases such as the

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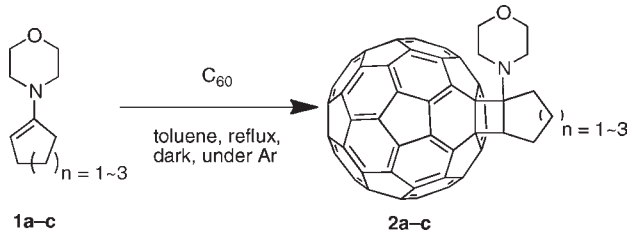
reactions with tetraalkoxyethylenes,[5] 1,2-dicarbomethoxycyclobutadiene,[6] and allenamides.[7] In this paper, we report that morpholinocycloalkenes (enamines) react with C_{60} to give exclusively [2 + 2] monoadducts in high yields in refluxing toluene. We also proposed a possible mechanism of this cyclobutanation of C_{60} in view of a single electron transfer (SET).

The reaction of a 50 equiv excess of five- to seven-membered morpholinocycloalkenes **1a**–**c** (7 mmol) with C_{60} (100 mg, 0.14 mmol) was carried out in the dark under an Ar atmosphere in dry toluene (50 mL) at the refluxing temperature to afford exclusively the 1:1 adducts **2** in excellent (for **1a**–**b**) but very low (for **1c**) yields (Table 1). The products **2a,b** were isolated by silica gel column chromatography, eluted with toluene, and purified by recrystallization by a vapor diffusion method using CS_2 and hexane. Unfortunately, the product **2c** could not be isolated probably because of very low yield (Figure S1, Supporting Information) and/or a possible lability on column chromatographic treatment.

Table 1. Reaction of Enamines **1a**–**c** with C_{60}



1a–c **2a–c**

run	enamine	temp (°C)	time (h)	yield of **2** (%)[a]
1	**1a**	115	3	97 (77)
2	**1b**	115	46	92 (64)
3	**1c**	115	72	6 (–)[b]

[a] Determined by HPLC area ratio. Values in parentheses are isolated yields by column chromatography on silica gel. [b] Not isolated.

The structures of **2a** and **2b** were fully characterized by LCMS, ^{1}H NMR, ^{13}C NMR, HSQC, HMBC, ^{1}H–^{1}H COSY, and UV–vis spectroscopic techniques. The HSQC and ^{1}H–^{1}H COSY spectra of **2a** revealed the presence of a methine proton (3.67 ppm, C^3–H proton) linked with three methylene segments (C^4–H_2, C^5–H_2, and C^6–H_2) and the adjacent C^7-substituted morpholino group (Figure 1). The absence of the methine peak at around 6 ppm unequivocally denied the presence of the proton directly bound to the fullerene cage as depicted in the hypothetical compound **A** (Scheme 1). Moreover, cyclobutane fusion was proven by the HMBC spectrum in which C^3–H showed no crosspeak with C^1 and C^5 but a clear two-bond crosspeak with C^2 and C^7.

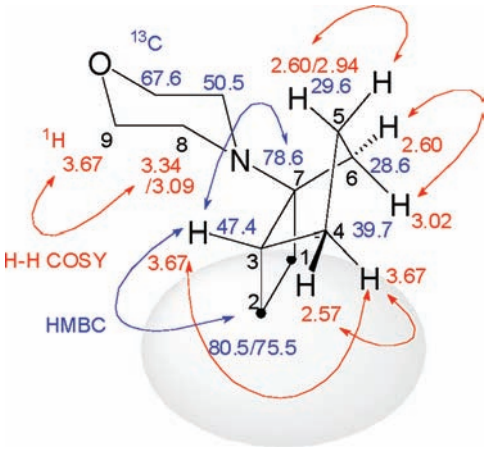
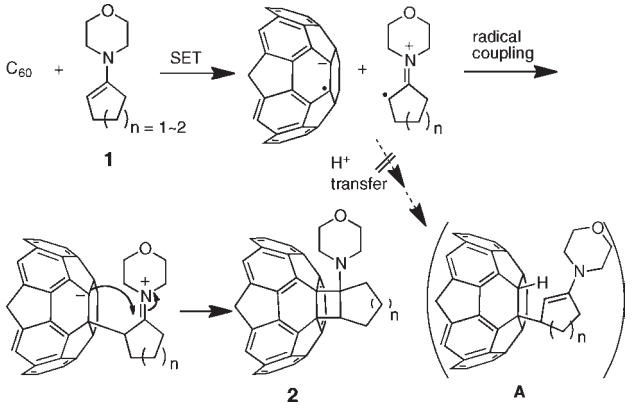


Figure 1. ^{1}H and ^{13}C NMR chemical shifts (δ) and ^{1}H–^{1}H COSY (red) and selected HMBC (blue) correlations.

Scheme 1. A Suggested Pathway of Thermal [2 + 2] Addition of Morpholinoenamines **1** to C_{60}



The reactivity of morpholinocycloalkenes **1a**–**c** decreases with increasing cycloalkene ring size as seen in Table 1. This trend in reactivity reduction is probably because of the increasing steric hindrance of enaminocycloalkenes in going from almost planar cyclopentene to the chair-formed cycloheptene.[8] Such a steric problem will significantly disturb the approach of **1** to the fullerene surface regardless of the mechanistic features and also enhance the lability of possible product **2c**. Another noticeable point of this thermal [2 + 2] addition is the high yield of monoadducts even in the presence of a large excess of enamine addend (50 equiv) as shown in time-course HPLC measurements (Figure 2a). An attempt to follow the disappearance of C_{60} provided the pseudo-first-order plots of $-\ln([C_{60}]/[C_{60}]^0)$ vs time (Figure 2b),[9] and thus the second-order rate constants were obtained for both of the enamines at 115 °C in toluene, i.e., 3.45×10^{-4} for **1a** and

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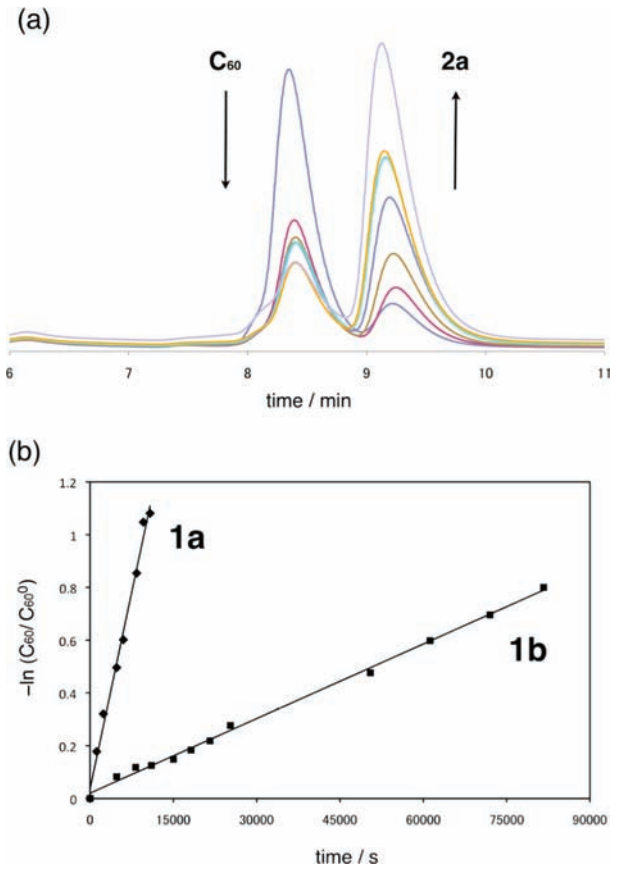
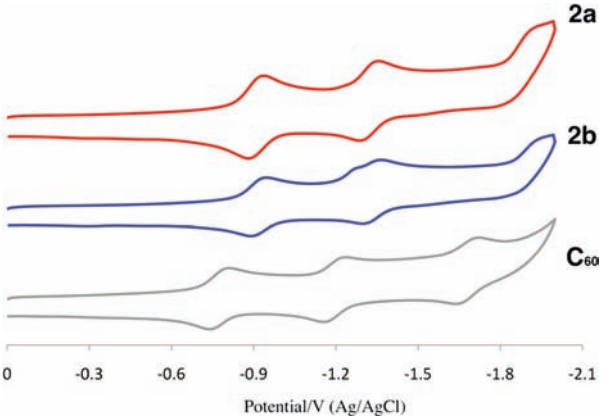


Figure 2. (a) Time-dependent HPLC charts for the reaction of **1a** with C_{60}. Column: Buckeyprep; eluent: toluene (1 mL/min). (b) Pseudo-first-order plot of $-\ln[C_{60}]/[C_{60}]^0$ vs time for the reaction of C_{60} with **1a** and **1b**.

$3.50 \times 10^{-5}\,M^{-1}\,s^{-1}$ for **1b**, respectively. It was found that **1a** is 10 times more reactive than the more sterically hindered **1b**.

Considering that multiaddition usually takes place in the chemical modification of fullerenes, the present reaction is very profitable for the selective formation of monofunctionalized fullerenes.[10] To explore the reason for the high selectivity, we carried out cyclic voltammetry analysis since the electronic nature of fullerenes and their derivatives play a decisive role in the fullerene chemistry. The obtained first to third one-electron reduction potentials (E_{1red}, E_{2red}, and E_{3red}) of **2a**, **2b**, and pristine C_{60} are collected along with the estimated LUMO level of these compounds in Table 2. In light of the oxidation potentials (E_{ox}) of **1a,b** (+0.19 V, +0.18 V vs Ag/Ag^+),[11] the ~0.96 V of potential difference ($E_{ox(\mathbf{1a,b})} - E_{red(C60)}$) is likely to cause such an electron transfer.[12]

Table 2. Cyclic Voltammograms and Reduction Potentials of **2a**, **2b**, and C_{60} in PhCN[a]



	$E^{1/2}$V vs Fc/Fc^+		
compd	E_{1red} (LUMO level/eV)[b]	E_{2red}	E_{3red}
2a	−1.06 (−3.74)	−1.45	
2b	−1.07 (−3.73)	−1.46	
C_{60}	−0.92 (−3.88)	−1.35	−1.83

[a] Electrolyte 0.1 M TBAP; scan rate 100 mV s^{-1}; potentials measured vs Ag/Ag^+ reference electrode and standardized to Fc/Fc^+ couple [$E_{Fc/Fc+}$ = +0.15 V vs Ag/Ag^+ (PhCN)]. [b] Values from the vacuum level were estimated using the following equation; LUMO level = $-(E_{1red}{}^{1/2} + 4.8)$.[13]

The LUMO levels of compounds **2a** and **2b** are found to be considerably raised by ca. 0.1 eV as compared with that of C_{60}, thus suppressing the secondary SET necessary for the [2 + 2] cycloaddition (*vide infra*).

The thermal reaction of amines with C_{60} is well recognized to start with a single electron transfer (SET).[14] Thus, primary and secondary aliphatic amines give rise to hydroaminofullerenes via the first radical ion pair formation, radical recombination, and final proton transfer. However, usual tertiary amines do not add to C_{60} because of the fast back electron transfer as well as the absence of a labile proton. The present reaction is also markedly in contrast to the thermal reaction of morpholine itself because the cyclic secondary amines are reported to bring about the tetraamination of C_{60} via oxygen-mediated ground state SET in DMSO.[15]

Since morpholinoenamines **1a,b** are classified as tertiary amines having a cycloalkenyl substituent, the double bond

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(12) For example, electron + hydrogen transfer reaction from 1-benzyl-1,4-dihydronicotinamide to chloro-*p*-benzoquinone with 0.91 V of ($E_{ox} - E_{red}$) showed high reactivity ($k = 7.6\,M^{-1}\,s^{-1}$, at 298 K), while the reaction of *p*-benzoquinone with more gap (1.07 V) showed far reduced reactivity ($k = 1.3 \times 10^{-2}$). See: Fukuzumi, S.; Nishizawa, N.; Tanaka, T. *J. Chem. Soc., Perkin Trans. 2* **1985**, 371–378.

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is expected to behave as a 2π component. Although the concerted [2 + 2] cycloaddition is a symmetry forbidden process,[16] the stepwise one via a biradical/zwitterion intermediate is thermally allowed. Mechanistically, we therefore suggest that the first SET generates a radical ion pair which performs the radical collapse to give the zwitterion intermediate which then cyclizes to the [2 + 2] adduct (Scheme 1). As far as we know, this is the first example of the [2 + 2] cycloaddition of enamine to C_{60}.

If the proton transfer precedes the radical-coupling process, the possible product would be **A**. Over ten years ago, Wu et al. proposed the formation of type **A** adduct in a similar SET reaction of C_{60} with enamines such as pyrrolidino- and piperidinocyclopentene.[17] They have only isolated the compound **3a** on acid-catalyzed hydrolysis of the reaction products. This observation prompted us to investigate the acid-catalyzed hydrolysis of the [2 + 2] adduct **2a** and compare the reactivity with that of the type **A** product. Interestingly, we have obtained the same product **3a** and considered a plausible mechanism as shown in Scheme 2. The hydrolysis reaction seems to proceed through a sequential process involving acid-catalyzed demorpholination to bicyclo[3.2.0]hept-1-ene fused C_{60}, the heterolytic bond cleavage assisted by water, the formation of hydrofullerene-substituted cyclopentenol via proton transfer, and tautomerization to ketone **3a**.

In summary, we first obtained the thermal [2 + 2] cycloadducts in good yields in the reaction of enamines **1a,b** with C_{60}. This reaction seems to proceed via a mechanism involving initial ground state single electron transfer (SET), radical collapse of the generated radical ion pair, and final cyclization of the zwitterion intermediate. The cycloadduct **2a** underwent acid-catalyzed hydrolysis to afford the 3-cycloalkanone substituted hydrofullerene **3a** in fair yields. The present facile [2 + 2] additions will add to the methods of preparation of new functionalized fullerene derivatives.

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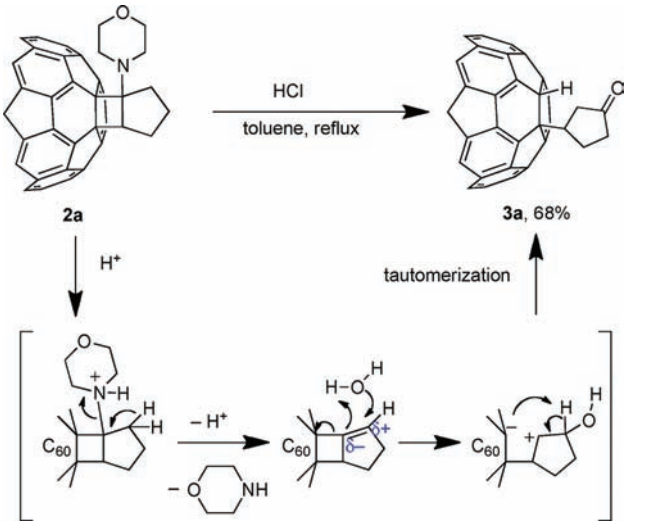
Scheme 2. A Plausible Mechanism for Hydrolysis of **2a**



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Supporting Information Available. General procedure for the reaction of **1a**–**c** with C_{60} and for the acid-catalyzed hydrolysis of the [2 + 2] adducts **2a,b**; the HPLC chart for the reaction of **1c** with C_{60}; ^{1}H, ^{13}C NMR spectra; the H–H COSY and HMBC correlations and FAB/MALDI-MS of **2a,b** and hydrolysis products **3a**. This material is available free of charge via the Internet at http://pubs.acs.org.