COMMUNICATION

New one-pot method for the synthesis of pyrrolidinofullerenes†

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The reaction of fullerene C_{60} with isocyanoacetates and EtMgBr in the presence of stoichiometric amounts of $Ti(Oi\text{-}Pr)_4$ was studied for the first time. Unlike esters and nitriles of carboxylic acids and isonitriles, isocyanoacetates were found to react with C_{60} under the developed conditions to give N-unsubstituted pyrrolidinofullerenes. The electrochemical reduction of the C_{60} derivatives we synthesized was found to proceed less easily than that of C_{60} but more easily than that of unsubstituted pyrrolidinofullerenes.

Introduction

The interest in pyrrolidinofullerenes is caused by their potential applications in medicine,[1] in electronics and non-linear optics[2] and as organic ferromagnets,[3] photosensitizers in the generation of singlet oxygen,[4] molecular switches,[5] and photoconverters of solar energy.[6]

The key method for the synthesis of pyrrolidinofullerenes is 1,3-dipolar cycloaddition of azomethine ylides generated *in situ* to fullerenes (Prato reaction), which gives the target fulleroheterocycles in preparative yields.[7] Alternative methods include photochemical[8] and catalytic[9] cycloaddition of tertiary amines to C_{60}, but these methods have not received wide use in fullerene chemistry because of low yields of the target adducts or the necessity to use starting amines of a particular structure.
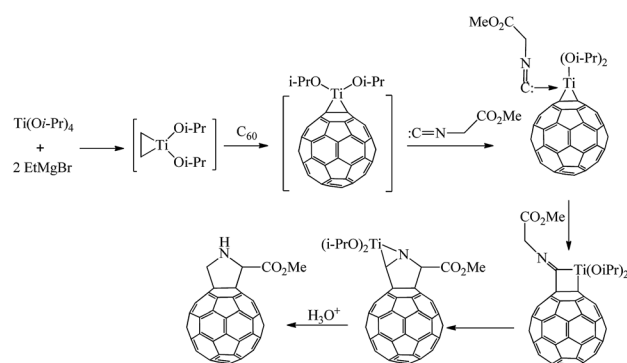
Recently,[10] we developed a novel original method for functionalization of fullerene C_{60} with various functional compounds and EtMgBr in the presence of $Ti(Oi\text{-}Pr)_4$, which gave, depending on the reactant structure, various acyclic or cyclic C_{60} derivatives difficult to prepare by other methods. For example, esters of aromatic carboxylic acids give fullerenyl ketones in this reaction,[10a] nitriles afford previously unknown

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fullerotetrahydropyridines,[10b] and cyanoacrylates and isonitriles are converted to aminomethanofullerenes previously difficult to obtain.[10c,d]

As a continuation of this study, we investigated the reaction of C_{60} with isocyanoacetates under the previously developed conditions.[10]

Result and discussion

Resorting to published data,[10–12] we assumed that isocyanoacetates containing divalent carbon in the carbene canonical form and an active methylene group between the isonitrile and ester groups would react with fullerene C_{60} and EtMgBr in the presence of the $Ti(Oi\text{-}Pr)_4$ catalyst to give pyrrolidinofullerenes, which are difficult to obtain by other methods, according to the following chart:
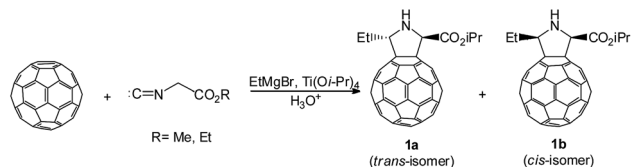

We found that the reaction of model methyl isocyanoacetate with fullerene C_{60} and EtMgBr proceeds under argon in the presence of $Ti(Oi\text{-}Pr)_4$ in chlorobenzene at 80 °C at the C_{60} : isocyanoacetate : [Mg] : [Ti] ratio of 1 : 4 : 8 : 3 and gives, after hydrolysis of the reaction mixture with 5% aqueous HCl, a mixture of pyrrolidinofullerene stereoisomers **1a** and **1b** in a ~65% total yield (in relation to taken C_{60}) and in 1 : 2 ratio, respectively (Scheme 1). A change in the ratio of the reactant and catalyst components and a decrease in the reaction

Scheme 1 The reaction of methyl or ethyl isocyanoacetates with fullerene C_{60} and EtMgBr in the presence of $Ti(Oi-Pr)_4$.

temperature result in a sharp decrease of the total yield of target pyrrolidinofullerenes **1a,b** (8–15%) and in the formation of side products *via* C_{60} carbomagnesiation and hydrogenation.
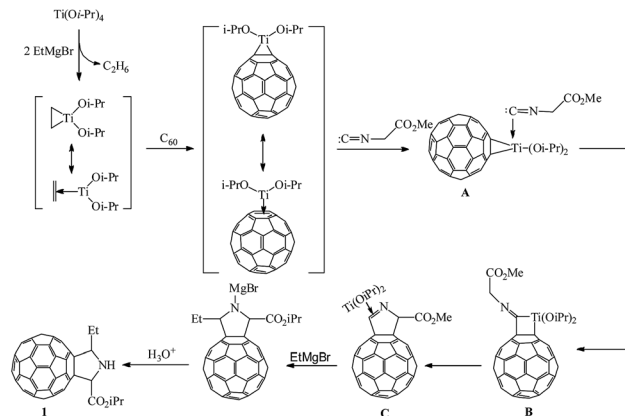
The results obtained using ethyl isocyanoacetate rather than methyl isocyanoacetate were similar.

Pyrrolidinofullerenes **1a,b** were isolated from the reaction mixture by means of preparative HPLC. According to 1D (^{1}H and ^{13}C) and 2D (HHCOSY, HSQC, HMBC) NMR experiments and IR and MALDI TOF MS data, the reaction under conditions we developed affords a mixture of stereoisomeric cycloadducts **a** and **b**.

Indeed, the ^{13}C NMR spectrum of a mixture of stereoisomers **1a,b** shows a doubled set of signals with 1 : 2 intensity ratio both for carbon atoms of the fullerene cage and for the attached addend. The intense signals at δ_C 79.38 and 78.34 ppm correspond to the sp^3 hybridized atoms of the fullerene cage of *cis*-isomer **1b**, while the methine carbon atoms of the pyrrolidine ring are responsible for higher-field signals at δ_C 74.20 and 75.24 ppm, correlated with the nitrogen signal in the HMBC (NH) experiment, δ_N 60.96 ppm. For *trans*-isomer **1a**, the spectrum exhibits a set of similar signals of low intensity, belonging to the sp^3 hybridized carbon atoms of C_{60} (δ_C 76.77 and 77.58 ppm), methine carbon atoms of the heterocycle (δ_C 72.32 and 74.03 ppm), and the nitrogen atom (δ_N 55.17 ppm). The $C(3')$ methine carbon signals of *cis*-(δ_C 75.24 ppm) and *trans*-(δ_C 74.03 ppm) isomers also show cross-peaks with the signals of the ethyl-group methylene protons (δ_H 2.20 and 2.32 ppm, respectively) in the HMBC spectra. The *cis*-configuration of the 1′,3′ substituents in **1b** was unambiguously proved by the cross-peaks in the NOESY experiment between the methine proton signals at δ_H (1′) 5.43 ppm and (3′) 4.68 ppm, whereas *trans*-isomer **1a** does not show this cross-peak.

The formation of stereoisomeric pyrrolidine cycloadducts **1a,b** of the composition $C_{68}H_{15}NO_2$ was confirmed by the MALDI TOF mass spectrometry. The experiments were performed in the linear (TOF) and reflection (TOF/TOF) modes and in both positive and negative ion modes using elemental sulfur as the matrix and showed the molecular ion $[M + H]$ peak, m/z 878.044 ($M_{calcd} = 877.110$).

According to the published[11,12] and our[10] experimental data, we assumed a probable pathway for the formation of pyrrolidinofullerene **1** in the reaction in question (Scheme 2). In the first step, $Ti(Oi-Pr)_4$ reacts with EtMgBr to give dialkoxy-titanocyclopropane occurring in equilibrium with the ethylene complex. Fullerene present in the reaction mixture displaces the ethylene molecule from the complex to afford the key reaction intermediate, namely, fullerotitanacyclopropane **A**.
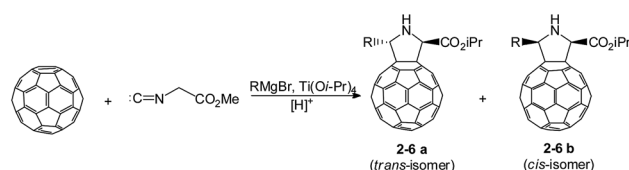

Scheme 2 Probable pathway for the formation of pyrrolidinofullerenes in the reaction of isocyanoacetates with fullerene C_{60} and EtMgBr in the presence of $Ti(Oi-Pr)_4$.

The subsequent reaction of intermediate **A** with the isocyanoacetate at the metal–carbon bond yields titanacyclobutane **B**. Demetallation of **B** under the reaction conditions and subsequent transformations involving the reactive methylene group of the starting isonitrile result in the formation of pyrrolinofullerene **C**. In view of the excess of EtMgBr and $Ti(Oi-Pr)_4$ in the reaction mixture, the intermediate **C** undergoes carbomagnesiation of the heterocyclic moiety at the $C=N$ bond with simultaneous transesterification of the ester group, being thus converted to complex **D**, which is hydrolyzed to furnish the target pyrrolidinofullerene **1**.

In view of the fact that the structure of substituents in the pyrrolidine ring of the C_{60} derivative depends on the structure of the Mg organic compound, we carried out this reaction under the developed conditions using a variety of alkyl- and arylmagnesium bromides (Scheme 3, Table 1). More bulky structure of substituent in the initial organomagnesium compound was found to lead to higher proportions of *trans*-fulleropyrrolidines, up to the selective formation of the *trans*-isomers in the case of PhMgBr. The introduction of a substituent into the aromatic ring of the organomagnesium compound reduced the selectivity, and the reaction gave a mixture of stereoisomeric pyrrolidinofullerenes **6** with a *cis* to *trans* ratio of 1 : 2, indicating that the electronic effects as well as the steric effects influence on selectivity of formation of the *cis*,*trans* isomers.

As model compounds, we chose phenyl-substituted fulleropyrrolidine **5** and study the electrochemical reduction.

Fulleropyrrolidine **5** can reversibly add four electrons in four steps (Fig. 1) to give stable multianions:
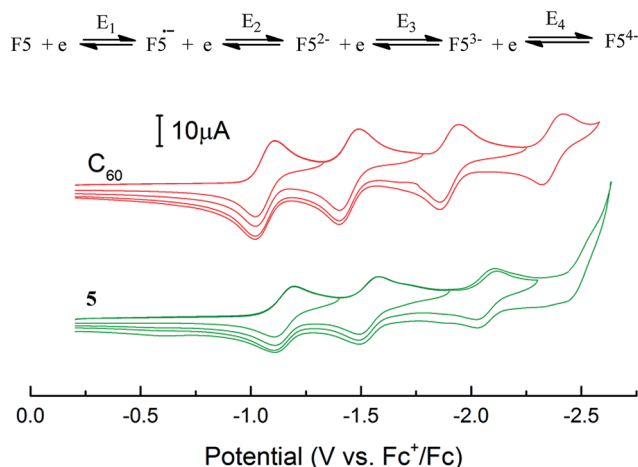

Scheme 3 Variation of alkyl- and arylmagnesium bromides in the reaction of C_{60} with methyl isocyanoacetate.

Table 1 Effect of the structure of substituent in RMgX on the selectivity of formation of pyrrolidinofullerenes **2–6**

Entry	R	Product	Yield, %	Ratio a	b
1	Bu	2	50	2	3
2	i-Pr	3	55	1	1
3	Cy	4	51	8	10
4	Ph	5	45	1	0
5	o-MePh	6	43	2	1

$$F5 + e \underset{}{\overset{E_1}{\rightleftarrows}} F5^{\cdot-} + e \underset{}{\overset{E_2}{\rightleftarrows}} F5^{2-} + e \underset{}{\overset{E_3}{\rightleftarrows}} F5^{3-} + e \underset{}{\overset{E_4}{\rightleftarrows}} F5^{4-}$$

Fig. 1 Cyclic voltammograms of C_{60} and its novel derivative **5** (10^{-3} M in 1,2-dichlorobenene, Bu_4NBF_4).

The first reduction potentials of functionally substituted fullerene **5** are somewhat more negative than that of fullerene C_{60}, which is caused by the effect of substituents (Table 2). The fourth reduction peak is is nearly merged with the background. The stability of the electrochemically reduced fullerene species (radical anion formed in the first step and polyanions formed in the subsequent steps) can be evaluated from the ratio of anodic and cathodic currents in the i_{pa}/i_{pc} peak (Table 2).

Table 2 Electrochemical characteristics of the reduction of compound

Comp.	Peak #	E_{pc}	E_{pa}	i_{pa}/i_{pc}	ΔE	$E_{1/2}$	E_{LUMO}
5	1	−1.20	−1.11	0.73	0.09	−1.16	−3.65
	2	−1.58	−1.49	1.00	0.09	−1.54	−3.27
	3	−2.12	−2.02	1.00	0.10	−2.07	−2.73
	4	−2.54	N/A	N/A	N/A	N/A	N/A
$C_{60}{}^a$	1	−1.11	−1.02	0.95	0.09	−1.07	−3.74
	2	−1.49	−1.40	1.00	0.09	−1.45	−3.36
	3	−1.95	−1.86	1.00	0.09	−1.91	−2.9
	4	−2.42	−2.32	0.76	0.1	−1.37	−2.43

^{a} The data for C_{60} are close to reported values.[13] obtained under similar conditions. Due to proximity of the fourth peak to the supporting electrolyte discharge line, the calculation of i_{pa}/i_{pc} is in some cases not appropriate (this is designated as N/A). The LUMO energy (eV) was calculated as $E_{LUMO} = -(E_{[1/2,red \; vs. \; Fc^+/Fc]} + 4.8)$ (eV).[14]
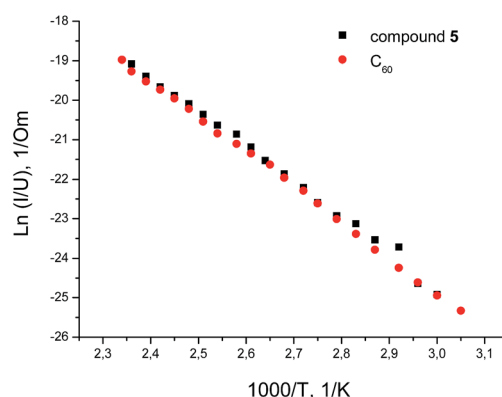
It is known that the effect of substituents present in the C_{60} molecule on the reduction potentials is composed of two effects, namely, the change in the electronic properties of the proper fullerene sphere as a result of disruption of the common π-system of conjugation and the electron-donating or -withdrawing properties of the substituents. For example, the substituents at the exo-carbon atom of C_{60} in methanofullerene **2** are not involved in the common fullerene π-system, which can be regarded as the reaction center of the electron transfer by two σ-bonds; therefore, they affect only slightly the reduction potentials of C_{60} derivatives. The potential shift reported in the literature for this class of carbon clusters is in the limits of up to 200 mV.[15] Meanwhile, strong electron-withdrawing substituents in methano-[16] or azahomofullerenes[17] can overcompensate for the loss of electron affinity as a result of disruption of π-system of conjugation. The cyclopentane and cyclohexane derivatives of C_{60} are 100 and 80 mV more difficult to reduce than parent C_{60},[18] while the presence of a nitrogen atom in fulleropyrrolidines has a slight influence on the potentials of the first two reduction steps compared with cyclopentane derivatives.[19]

The electrochemical reduction of fulleropyrrolidine **5** was found to occur at more negative potentials than that of the parent C_{60} (the difference is 60–90 mV). This distinguish compound **5** from unsubstituted pyrrolidinofullerene. This results indicate that the introduction of an aryl substituent and ester group into the heterocyclic fragment of **5** compensates, to a certain extent although not completely, for the loss of the electron affinity caused by disruption of the π-system of conjugation.

Unfortunately, we were unable to correctly calculate the E_{HOMO} and thus to determine the band gap width of the acceptor (E_g) on the basis of cyclic voltammetry data because the

Table 3 Conductivity of **5** and C_{60} at 60 °C

Compound	G, ohm^{-1} (at 60 °C)	ΔE, eV
5	1.5×10^{-11}	1.54
C_{60}	1.4×10^{-11}	1.63

Fig. 2 Temperature dependence of the conductivity of films of **5** and C_{60}.

oxidation waves of compound **5** are multielectron, which may be caused by sample polymerization under conditions of electrochemical measurements.

Nevertheless, the band gap width can be determined by electrophysical methods, in particularly, from the plot of the dependence of the film conductivity G on temperature T in the range of 300–450 K. These dependences are exponential, $G = G_0 \exp(-\Delta E/2kT)$. From the slope of the linear segments, it was possible to calculate ΔE for each sample; the result was about 1.5–1.6 eV. Meanwhile, the ΔE value can be interpreted as E_g (the gap between the LUMO and the HOMO).

It is found that the conductivity of **5** differs little from unmodified fullerene (Table 3), but is characterized by better solubility in organic solvents (Fig. 2).

Conclusions

Thus, we developed a new method for the synthesis of N-unsubstituted pyrrolidinofullerenes by the Ti(Oi-Pr)$_4$-catalyzed reaction of C$_{60}$ with isocyanoacetates and EtMgBr. The electrochemical reduction of model pyrrolidinofullerene occurs less easily than that of C$_{60}$ but more easily than that of unsubstituted pyrrolidinofullerenes, which may imply that introduction of new substituents into the heterocyclic fragment compensates somewhat for the loss of electron affinity of the fullerene cage.

Acknowledgements

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