An unexpected Diels–Alder reaction on the fullerene core rather than an expected 1,3-dipolar cycloaddition

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Fullerene derivatives resulting from an unexpected Diels–Alder cycloaddition have been obtained by reaction of *trans*-2-stilbenecarboxaldehyde derivatives with *N*-methylglycine and C_{60} .

The 1,3-dipolar cycloaddition of azomethine ylides generated *in situ* from aldehydes and *N*-methylglycine has proven to be a very powerful procedure for the functionalization of C_{60} due to its versatility and the ready availability of the starting materials.¹ The reaction is fast, clean and fulleropyrrolidines are obtained in fair to good yields. As part of our research program on the synthesis and the study of fullerene-donor systems,² we became interested in the preparation of new fulleropyrrolidines by reaction of *trans*-2-stilbenecarboxaldehyde derivatives with *N*-methylglycine and C₆₀. Surprisingly, the expected 1,3-dipolar cycloaddition on the fullerene core does not take place and fullerene derivatives resulting from an unexpected Diels–Alder reaction have been obtained instead. This new reaction and the characterization of the resulting fullerene adducts are now reported.

The synthetic approach to prepare the *trans*-2-stilbenecarboxaldehyde derivatives **3a–c** used in this study relies upon the Heck cross-coupling reaction³ of 2-bromobenzaldehyde (2) with the styrene derivatives **1a–c** (Scheme 1).

Treatment of 2 and 1a-c with a catalytic amount of Pd(OAc)₂ in the presence of tri-o-tolylphosphine (POT) afforded the corresponding *trans*-stilbene derivatives 3a-c in 70 to 80% yield. All of the spectroscopic studies were consistent with the proposed molecular structures. In particular, the Econfiguration of the double bond in **3a-c** was confirmed by a coupling constant of ca. 17 Hz for the AB system corresponding to the vinylic protons in their 1H-NMR spectra. The reaction of aldehydes 3a-c with C_{60} was performed under the conditions used for the preparation of fulleropyrrolidines.¹ However, rather than the expected products 4a-c, the fullerene derivatives 5a-c were obtained in 40 to 42% yield. In a typical procedure, a solution of 3a (194 mg, 0.69 mmol), C₆₀ (1 equiv.) and Nmethylglycine (10 equiv.) in toluene (500 ml) was refluxed for 36 h under argon. The reaction mixture was then filtered over celite and the solvent evaporated. Two successive chromatographic separations (SiO₂, toluene-hexane 6:4 then Al₂O₃, CH₂Cl₂-hexane 3:7) yielded pure **5a** (284 mg, 40%).

As shown in Fig. 1, this compound must be the product of the Diels–Alder reaction of C_{60} with diene (±)-7 which itself results from a cyclisation of the intermediate azomethine ylide **6** initially formed by reaction of **3** with *N*-methylglycine.

In principle, the reaction of C_{60} with diene (±)-7 should lead to two diastereoisomeric pairs of enantiomers [(±)-5 and (±)-8] depending on which face of (±)-7 the Diels–Alder [4 + 2]-cycloaddition takes place. Surprisingly, this reaction is highly diastereoselective and only compound (±)-5 was obtained. Molecular modeling studies have not revealed any particular steric hindrance to explain the preferential approach of the C_{60} on one face of (±)-7. Actually, it might be possible that π - π interactions of the fullerene sphere with the phenyl group in (±)-7 are able to assist the approach of the C_{60} , thus allowing a regioselective attack and the formation of (±)-5 only.

The structure of 5a-c were deduced from their ¹H-NMR spectra with the help of 2D-COSY and 2D-NOESY experiments. The typical pattern seen in the ¹H-NMR spectra for the bicyclic structure is shown for compound 5a in Fig. 2. It must be noted that the experimental vicinal coupling constants ${}^{3}J$ observed in the ¹H-NMR spectrum of **5a** are in perfect agreement with the theoretical ones given by the Karplus-*Conroy* curve⁴ based on the dihedral angles deduced from the calculated structure of 5a.† In addition, the 2D-NOESY spectrum of 5a provided further support for the stereochemistry of the C atom bearing the tert-butyloxyphenyl group. Effectively, NOE cross-peaks have been observed for the following pairs of protons: H₀-H_A, H₀-H_C and H_B-H_D. The ¹³C-NMR spectra of 5a-c are also in full agreement with the proposed structures. For example, in addition to the resonances corresponding to the sp² carbons, the ¹³C-NMR spectrum recorded for 5a in CD₂Cl₂ is characterized by nine signals: $\delta = 29.10$ and 78.62 for the *t*-Bu group, $\delta = 49.27$ for the N-CH₃, $\delta = 70.69$ and 72.32 for the fullerene sp³ carbons, $\delta = 47.96$ (CH), 55.71 (CH₂), 60.26 (CH) and 78.03 (CH) for the sp³ C atoms of the cycle. Finally, it can also be pointed out that the UV-Vis spectra of 5a-c show all the characteristic features described in the literature for C60 Diels-Alder adducts.5



Scheme 1 Reagents and conditions: i, Pd(OAc)₂, POT, Et₃N, toluene, Δ (70 to 80%); ii, C₆₀, *N*-methylglycine, toluene, Δ (40 to 42%).

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Fig. 1 Proposed mechanism for the formation of the diene intermediate and representation of the two possible diastereoisomers resulting from its reaction with C_{60} .



Fig. 2 ¹H-NMR spectrum of 5a (CD₂Cl₂, 200 MHz).

The reaction conditions developed for the preparation of 5a-c were also used for the synthesis of 12 (Scheme 2). The aldehyde precursor 11 was obtained in five steps from 2-bromo-p-xylene (9). Treatment with CuCN under Rosenmund-von Braun conditions led to the corresponding benzonitrile derivative. Benzylic halogenation with NBS followed by treatment with triethylphosphite then gave bisphosphonate 10. Reaction of 10 with 3,4,5-tridodecyloxybenzaldehyde under Wadsworth-Emmons conditions and subsequent reduction of the resulting nitrile with DIBAL-H afforded 11. The E configuration of both double bonds in 11 was confirmed by coupling constants of ca. 16.5 Hz for the two AB systems corresponding to the two sets of vinylic protons in its ¹H-NMR spectrum. As observed for 3ac, treatment of 11 with an excess of N-methylglycine in the presence of C_{60} gave the fullerene derivative 12 resulting from a Diels-Alder cycloaddition and the expected fulleropyrrolidine derivative could not be detected. All of the spectroscopic studies were consistent with the proposed molecular structure.† In particular, the ¹H-NMR spectrum of **12** shows the characteristic features of the bicyclic structure discussed for 5a-c. It is also interesting to note that the diagnostic absorption band of the extended conjugated π -system observed at 375 nm in the UV-Vis spectrum of 11 is shifted to 326 nm in 12. The latter observation is in perfect agreement with the reduced conjugation length resulting from the loss of a double bond during the transformation of 11 into 12.



Scheme 2 Reagents and conditions: i, CuCN, NaI, DMF, Δ (89%); ii, NBS, AIBN, CCl₄, Δ (40%); iii, P(OEt)₃, Δ (80%); iv, 3,4,5-tridodecyl-oxybenzaldehyde, *t*-BuOK, THF, 0 to 25 °C (74%), v, DIBAL-H, CH₂Cl₂, Δ (54%); vi, C₆₀, *N*-methylglycine, toluene, Δ (34%).

In conclusion, a new reaction for the functionalization of C_{60} has been discovered and new covalent fullerene derivatives for materials science or biological applications should become available by this facile new methodology.

Notes and references

[†] Selected analytical data. For **5a**: ¹H-NMR (200 MHz, CD₂Cl₂): 7.66 (m, 3 H), 7.56 (m, 1 H), 7.23 (d, J = 8.5 Hz, 2 H), 6.95 (d, J = 8.5 Hz, 2H), 5.37 (s, 1 H), 4.82 (dd, $J_{BC} = 11.5$ Hz, $J_{BD} = 4.5$ Hz, 1 H), 4.64 (s, 1 H, it can be noted that $J_{AB} = 0$), 3.04 (dd, $J_{CD} = 11.5$ Hz, $J_{BD} = 4.5$ Hz, 1 H), 4.64 (s, 1 H, 1), 2.87 (s, 3 H), 2.40 (t, $J_{CD} = J_{BC} = 11.5$ Hz, 1 H), 1.34 (s, 9 H). ¹³C-NMR (100 MHz, CD₂Cl₂): 158.74, 157.96, 157.95, 156.04, 154.81, 148.03, 146.82, 146.57, 146.53, 146.51, 145.95, 145.93, 145.91, 145.80, 145.75, 145.68, 145.20, 142.99, 142.98, 142.84, 142.67, 142.62, 142.36, 142.34, 142.32, 141.95, 141.88, 140.29, 139.37, 138.20, 137.95, 136.15, 135.76, 134.54, 129.83, 129.77, 129.47, 128.67, 128.35, 124.64, 78.62, 78.03, 72.32, 70.69, 60.26, 55.71, 49.27, 47.96, 29.10. FAB-MS: *m/z* (%): 1028.1 (55, *M*++), 719.9 (100, C₆₀+). UV-Vis (CH₂Cl₂): 256 (96000), 308 (32100), 433 (2700), 706 (310).

For **12**: ¹H-NMR (400 MHz, CD₂Cl₄): 7.83 (s, 1 H), 7.78 (d, J = 1.5 Hz, 1 H), 7.60 (d, J = 1.5 Hz, 1 H), 7.24 (AB, J = 16 Hz, 2 H), 6.89 (s, 2 H), 6.61 (s, 2 H), 5.42 (s, 1 H), 4.84 (dd, J = 11.5 Hz, J = 4.5 Hz, 1 H), 4.70 (s, 1 H), 4.06 (m, 12 H), 3.20 (dd, J = 11.5 Hz, J = 4.5 Hz, 1 H), 3.01 (s, 3 H), 2.59 (t, ² $J = ^{3}J = 11.5$ Hz, 1 H), 1.90 (m, 12 H), 1.82 (m, 108 H), 0.96 (m, 18 H). ES-MS: 2164.8 (MH⁺). UV-Vis (CH₂Cl₂): 254 (110000), 326 (63200), 431 (3400), 706 (300).

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