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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 C_{60}. 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.

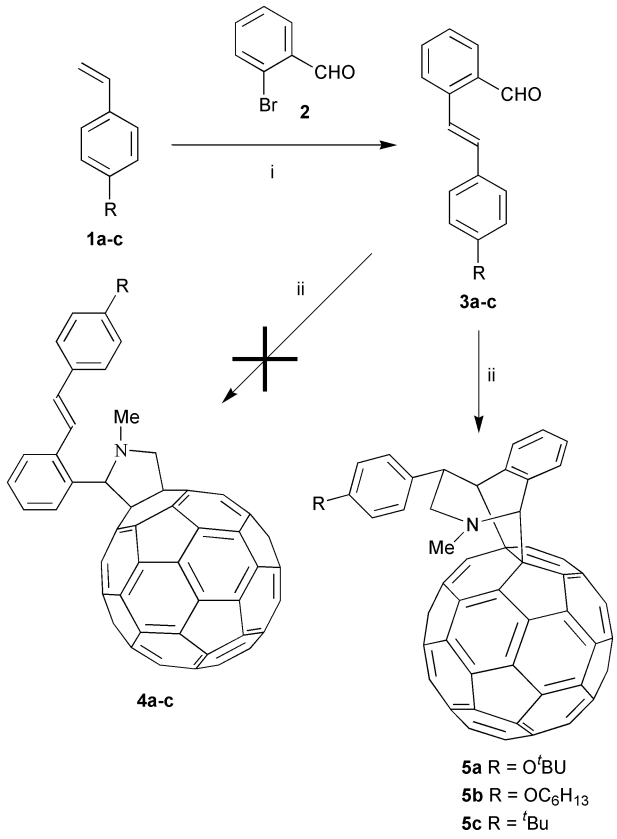
The synthetic approach to prepare the *trans*-2-stilbenecarboxaldehyde derivatives **3a–c** used in this study relies upon the Heck cross-coupling reaction[3] of 2-bromobenzaldehyde (**2**) with the styrene derivatives **1a–c** (Scheme 1).

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 *E* configuration 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 ^{1}H-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), C_{60} (1 equiv.) and *N*-methylglycine (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 (SiO_2, toluene–hexane 6:4 then Al_2O_3, CH_2Cl_2–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 ^{1}H-NMR spectra with the help of 2D-COSY and 2D-NOESY experiments. The typical pattern seen in the ^{1}H-NMR spectra for the bicyclic structure is shown for compound **5a** in Fig. 2. It must be noted that the experimental vicinal coupling constants ^3J observed in the ^{1}H-NMR spectrum of **5a** are in perfect agreement with the theoretical ones given by the *Karplus–Conroy* curve[4] 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: H_o–H_A, H_o–H_C and H_B–H_D. The ^{13}C-NMR spectra of **5a–c** are also in full agreement with the proposed structures. For example, in addition to the resonances corresponding to the sp^2 carbons, the ^{13}C-NMR spectrum recorded for **5a** in CD_2Cl_2 is characterized by nine signals: δ = 29.10 and 78.62 for the *t*-Bu group, δ = 49.27 for the N-CH_3, δ = 70.69 and 72.32 for the fullerene sp^3 carbons, δ = 47.96 (CH), 55.71 (CH_2), 60.26 (CH) and 78.03 (CH) for the sp^3 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 C_{60} Diels–Alder adducts.[5]



Scheme 1 *Reagents and conditions*: i, $Pd(OAc)_2$, POT, Et_3N, toluene, Δ (70 to 80%); ii, C_{60}, *N*-methylglycine, toluene, Δ (40 to 42%).

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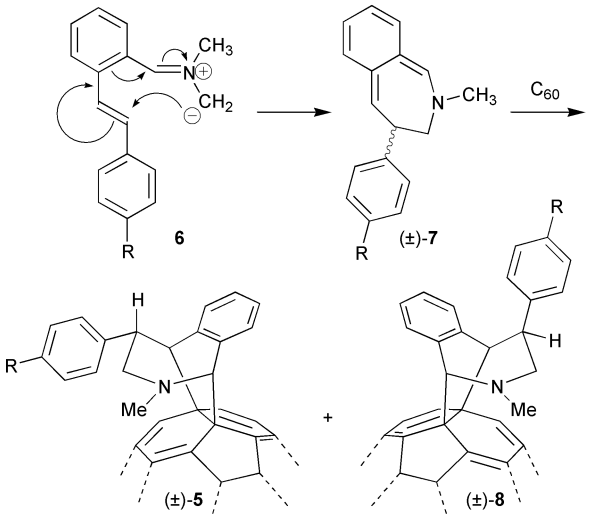


Fig. 1 Proposed mechanism for the formation of the diene intermediate and representation of the two possible diastereoisomers resulting from its reaction with C_{60}.

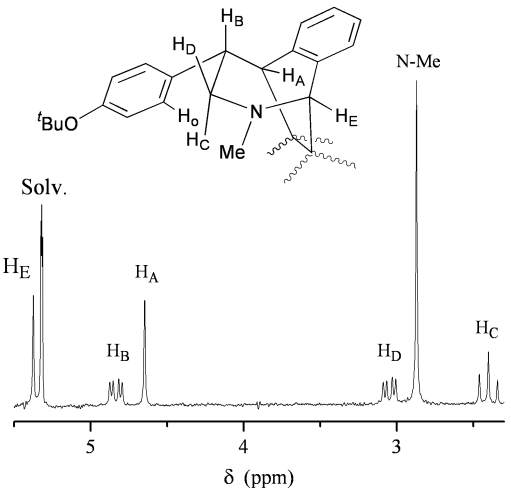
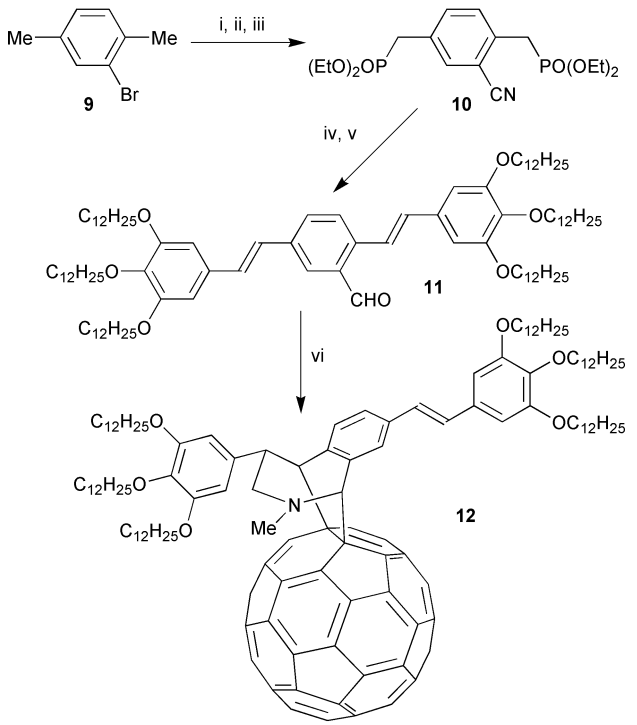


Fig. 2 ^{1}H-NMR spectrum of **5a** (CD_2Cl_2, 200 MHz).

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 ^{1}H-NMR spectrum. As observed for **3a–c**, 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 ^{1}H-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, CCl_4, Δ (40%); iii, $P(OEt)_3$, Δ (80%); iv, 3,4,5-tridodecyloxybenzaldehyde, *t*-BuOK, THF, 0 to 25 °C (74%), v, DIBAL-H, CH_2Cl_2, Δ (54%); vi, C_{60}, *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**: ^{1}H-NMR (200 MHz, CD_2Cl_2): 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), 2.87 (s, 3 H), 2.40 (t, J_{CD} = J_{BC} = 11.5 Hz, 1 H), 1.34 (s, 9 H). ^{13}C-NMR (100 MHz, CD_2Cl_2): 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*H$^+$), 719.9 (100, C_{60}^+). UV-Vis (CH_2Cl_2): 256 (96000), 308 (32100), 433 (2700), 706 (310).

For **12**: ^{1}H-NMR (400 MHz, CD_2Cl_4): 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, ^2J = ^3J = 11.5 Hz, 1 H), 1.90 (m, 12 H), 1.82 (m, 108 H), 0.96 (m, 18 H). ES-MS: 2164.8 (*M*H$^+$). UV-Vis (CH_2Cl_2): 254 (110000), 326 (63200), 431 (3400), 706 (300).

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