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Highly efficient Pauson–Khand reaction with C_{60}: regioselective synthesis of unprecedented *cis-1* biscycloadducts†

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Fullerenes undergo regioselectively and highly efficiently the intramolecular Pauson–Khand reaction to afford a new type of unprecedented structure with three fused pentagonal rings on the same fullerene six-membered ring.

The chemistry of fullerenes has undergone a rapid development due to the pioneering work of several synthetic groups during the last decade.[1] However, sizeable challenging synthetic work remains to be done. Thus, a variety of important modern organic reactions, available in the arsenal of alkenes chemistry involving transition metal catalysts, have never been explored in the related fullerenes.

Among the most significant reactions involving an alkene in organic synthesis, the Pauson–Khand (PK) reaction plays an important role. This formal [2+2+1] metal (mostly cobalt) mediated carbonylative cycloaddition of an alkene and an alkyne represents the most versatile method for the preparation of cyclopentenones, including the asymmetric version leading to enantiopure substituted cyclopentenones and fulfilling the principle of atom economy.[2]

Alkenes bearing electron-withdrawing groups are not appropriate substrates in PK reactions due to their low reactivity and high tendency to afford 1,3-dienes by a competitive elimination reaction. However, during recent years a wide variety of examples of inter- and intramolecular PK reactions involving electron-withdrawing substituted alkenes have been reported.[3]

In this communication we describe the first PK reaction on the C_{60} molecule affording regioselectively unprecedented *cis-1* biscycloadducts. Our first attempts of intermolecular PK reaction with the parent [60]fullerene and different alkynes in the presence of $Co_2(CO)_8$ were unsuccessful. Therefore, we carried out the design of novel fullerene derivatives (**3a–d**, **6**) endowed with a 1,6-enyne moiety involving a fullerene double bond as suitable candidates to undergo the PK reaction. A further advantage of the fullerene core is the absence of hydrogen atoms on the C_{60} surface, thus preventing the competitive β-hydride elimination process.

The synthesis of the C_{60}-based enyne **2** was carried out by 1,3-cycloaddition reaction of the azomethyne ylide, generated *in situ* from DL-propargylglycine **1** and formaldehyde, to C_{60} in refluxing *o*-dichlorobenzene by following Prato's procedure (Scheme 1).[4] Compound **2** is endowed with a pyrrolidine amino group able to undergo acylation reactions with acyl chlorides to form more soluble *N*-acylfulleropyrrolidines (**3a–d**) which were obtained in excellent yields (90–95%, see supplementary information).

Compounds **2** and **3a–d** showed in the ^1H NMR spectra the expected alkynyl protons at around 2.2 and 2.4 ppm, respectively. However, while fulleropyrrolidine **2** showed a well-resolved set of signals for the pyrrolidine protons, non-resolved broad signals were observed for *N*-acylfulleropyrrolidines **3a–d** at room temperature. ^1H NMR experiments at different temperatures showed that a good resolution of **3a** was observed when increasing the temperature at 323 K (see supporting information). This dynamic behaviour can be accounted for by the rotational barrier of the acyl group linked to the nitrogen atom.[5] Furthermore, the presence of the acyl group has a strong impact on the δ values of the pyrrolidine hydrogen atoms which are significantly shifted to a lower field [**3a** (323 K): δ_{CH} = 6.4 (br t, 1H); δ_{CH_2} = 5.71 (d, ^2J = 12 Hz, 1H); δ_{CH_2} = 5.55 (d, ^2J = 12 Hz, 1H)] in comparison with fulleropyrrolidine **2** [δ_{CH} = 4.87 (dd, ^3J = 7.8, ^3J = 4.8 Hz, 1H); δ_{CH_2} = 4.99 (d, ^2J = 11.3 Hz, 1H); δ_{CH_2} = 4.77 (d, ^2J = 11.3 Hz, 1H)].

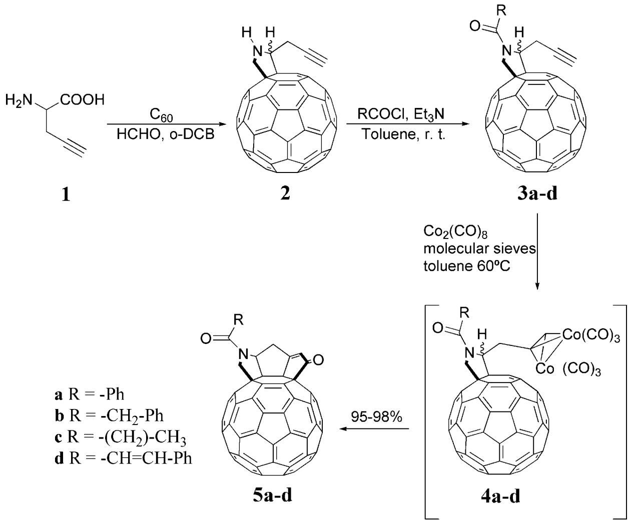
Compounds **3a–d** were further reacted with $Co_2(CO)_8$ using stoichiometric amounts in toluene at 60 °C and in the presence of molecular sieves (4 Å) previously activated.[6] The reaction leads directly to the formation of the PK products (**5a–d**) as stable brown solids in excellent yields (95–98%) without isolation of the intermediate dicobalt carbonyl clusters (**4a–d**).[7] Further purification of compounds **5a–d** was accomplished by flash chromatography in neutral alumina or neutral silica-gel in order to prevent the hydrolysis of the amido group.

The intramolecular PK reaction from **3a–d** leads regioselectively to the formation of the respective *cis-1* biscycloadducts (**5a–d**), thus affording a highly rigid system containing three fused pentagonal rings.

The structure of the novel compounds was unambiguously established by spectroscopic techniques (UV-vis, FTIR, ^1H, ^{13}C NMR, MS). Thus, as a diagnostic signal, the ^1H NMR spectra of compounds **5a–d** show a proton corresponding to the enone moiety at $\delta \sim 6.8$ ppm. The ^{13}C NMR spectra of compounds **5a–d** showed their lack of symmetry as well as the presence of the carbonyl group at around 202 ppm. The structure of compounds **5a–d** was further and unambiguously confirmed as the *cis-1* biscycloadduct, based on the above spectroscopic data, as well as by HMQC and HMBC experiments, comparison with UV-vis spectra[8] and high resolution mass spectroscopy (see supporting information).

Formation of compounds **5a–d** reveals that fullerene double bonds are reactive enough to undergo the highly versatile PK reaction.

In order to compare the reactivity of the fullerene moiety with that of an olefinic double bond, we have carried out the synthesis of compound **6** endowed simultaneously with reactive alkynyl and



Scheme 1

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† Electronic supplementary information (ESI) available: experimental section. See http://www.rsc.org/suppdata/cc/b4/b402616k/

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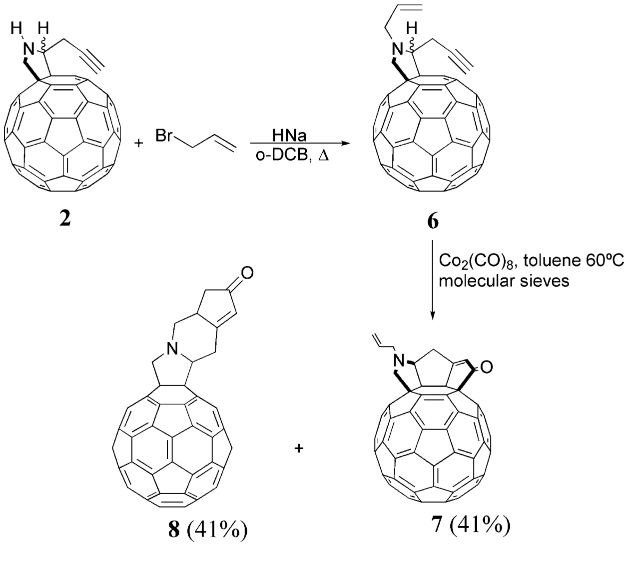
allyl systems. The synthesis of **6** was carried out in moderate yield from fulleropyrrolidine **2** by alkylation reaction with allyl bromide under basic conditions (Scheme 2).

Further reaction of **6** under the same conditions [$Co_2(CO)_8$, molecular sieves, toluene, 60 °C] afforded a mixture of compounds (**7** and **8**) resulting from the PK reaction on the fullerene double bond and the allyl group, respectively. The reaction was highly efficient, leading to compounds **7** and **8** with the same yield (41%), thus revealing the high reactivity of the fullerene core in the intramolecular PK reaction.

Compound **7** showed in the ^{1}H NMR spectrum the vinyl proton of the cyclopentenone ring at δ 6.81 ppm. This proton was coupled with the Csp^2 at 126.5 ppm in the HMQC experiment, and with the Csp^2 at 184.1 ppm, the carbonyl carbon at 202.2 ppm and a fullerene Csp^3 at ~ 70 ppm in the HMBC experiments. As expected, the signals of the olefinic protons of the unreacted allyl moiety are observed at δ 6.15 (m, –CH=), 5.48 (m, =CH_2) and 5.36 (m, =CH_2). In contrast, these allyl protons are not present in the ^{1}H NMR spectrum of **8** which shows the vinyl proton of the cyclopentenone ring as a singlet at δ 6.19 ppm. HMQC and HMBC experiments unambiguously confirmed the proposed structures (see supporting information).

It is worth mentioning that the competitive PK reaction to form the analogue to **8** from **3d** was not observed. In this case, the presence of the carbonyl and phenyl groups linked to the double bond strongly prevent this reaction, thus accounting for the sole formation of compound **5d**.

Cis-1 biscycloadducts **5a–d** and **7** are, to the best of our knowledge, the first example of three fused pentagonal rings on the same hexagonal ring of the fullerene core. These compounds are obtained as a mixture of enantiomers provided that the PK cyclization yields, in addition to the chiral center on the fulleropyrrolidine ring, four new chiral carbons on the fullerene surface with a well-defined stereochemistry.



Scheme 2

In summary, we report for the first time a new [2+2+1] cycloaddition reaction on the fullerene core which regioselectively affords a new type of *cis-1* biscycloadducts with three fused pentagonal rings. This new reaction opens the way for compounds bearing a larger number of fused rings on the fullerene surface with interest in fields such as materials science or biological applications. In addition, this new reactivity of fullerenes should promote research with other transition metal catalysts affording a new avenue in the chemistry of fullerenes. This study is currently under investigation in our laboratory.

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Notes and references

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5 A. Bagno, S. Claeson, M. Maggini, M. L. Martini, M. Prato and G. Scorrano, *Chem. Eur. J.*, 2002, **8**, 1015–1023.

6 (*a*) L. Pérez-Serrano, L. Casarrubios, G. Domínguez and J. Pérez-Castells, *Org. Lett.*, 1999, **8**, 1187–1188; (*b*) J. Blanco-Urgoiti, L. Casarrubios, G. Domínguez and J. Pérez-Castells, *Tetrahedron Lett.*, 2002, **43**, 5763–5765. It is worth mentioning that the PK reaction also proceeds in the absence of molecular sieves although in a lower yield.

7 Acetylene-linked di-cobalt and tetra-cobalt carbonyl clusters covalently connected to the C_{60} have also been reported by S. M. Draper, M. Delamesiere, E. Champeil, B. Twamley, J. J. Byrne and C. J. Long, *J. Organomet. Chem.*, 1999, **589**, 157–167. It is important to note that isolation of the intermediate dicobalt carbonyl complexes can be achieved by carrying out the reaction at room temperature. Thus, intermediate **4a** (FTIR (KBr): ν = 2922, 2050, 2017, 1647, 518 cm^{-1}) was isolated in 75% yield after flash chromatography.

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