Preparation and characterization of a highly water-soluble pendant fullerene polymer

Ya-Ping Sun,* Bing Liu and Dwella K. Moton

Laboratory of Medicinal Chemistry, Department of Chemistry, Howard L. Hunter Chemistry Laboratory, Clemson University, Clemson, South Carolina 29634-1905, USA

A highly water-soluble pendant [60]fullerene–poly-(propionylethylenimine-*co*-ethylenimine) polymer is prepared and characterized, with the equivalent aqueous solubility of the polymer-bound [60]fullerene units (> 10 mg ml^{-1}) being much higher than that of monomeric [60]fullerene in toluene (2.9 mg ml^{-1}).

Since the discovery and large-scale production of [60]fullerene (C_{60}) and [70]fullerene (C_{70}), there has been great scientific interest in the potential biological applications of these fascinating molecules.[1] Great effort has been devoted to the introduction of fullerene species into an aqueous environment.[2–10] While a number of fullerene derivatives have been prepared for such a purpose, most have only poor aqueous solubility. Here, we report a somewhat different approach in which fullerene species are solubilized by being covalently attached to a hydrophilic linear polymer. The pendant C_{60}–aminopolymer thus prepared is highly water soluble, with the equivalent aqueous solubility of the polymer-bound C_{60} units being much higher than the solubility of monomeric C_{60} in a fullerene solvent such as toluene.

Poly(propionylethylenimine) (PPEI)[11,12] was partially hydrolysed under acidic conditions to yield the copolymer poly(propionylethylenimine-*co*-ethylenimine) (PPEI–EI). According to GPC analysis (Me$_2$SO with 0.2% LiBr as mobile phase), the copolymer has an average molecular mass M_w of 54 000 and polydispersity index of 1.7 by reference to linear poly(2-vinylpyridine) standards. The proton NMR spectrum of the copolymer in deuteriated chloroform shows a broad peak at δ 2.8 (CH_2NH) in addition to broad peaks at δ 3.6 (CH_2NCOC$_2$H$_5$), 2.5 (NCOCH_2CH$_3$) and 1.2 (–CH$_2$CH_3) observed in the spectrum of PPEI. The degree of hydrolysis (population of NH units in PPEI–EI) of *ca.* 13% was estimated on the basis of proton NMR signal integration.

Diethyl methano[60]fullerene dicarboxylate (DMFC) was prepared following a procedure reported in the literature,[13] except that a lower molar ratio of bromomalonate to [60]fullerene (1.2 : 1) was used to promote the formation of the mono-adduct. In the reaction, nucleophilic addition of a bromomalonate carbanion from the deprotonation of bromomalonate with sodium hydride was followed by an intramolecular substitution. The reaction mixture consists of mono- and multi-adducts. The mono-adduct was separated from the mixture in 55% yield by silica gel column chromatography using toluene as eluent, and was positively identified in MALDI-TOF MS, ^{1}H and ^{13}C NMR, and FTIR characterization. The mono-DMFC was then converted to methano[60]fullerene dicarboxylic acid (MFDA) by hydrogenolysis.[14,15] MFDA is a brown solid which is slightly soluble in alkaline water and more soluble in acetone, THF and methanol. Proton NMR spectra of MFDA in both D$_2$O with added K$_2$CO$_3$ and in (CD$_3$)$_2$CO show no signals due to ethyl or methoxy groups, indicating that the hydrolysis was complete and that no nucleophilic addition reaction of methoxy anion to MFDA took place in the reaction.

The pendant MFDA–PPEI–EI polymer was prepared through the condensation of the carboxylic acid groups in MFDA and the secondary amine units in PPEI–EI using 1-ethyl-3-(di-

methylaminopropyl)carbodiimide (EDAC) as a coupling agent (Scheme 1).[16,17] In a typical reaction, 30 mg of EDAC were added to a solution of 20 mg of MFDA in 20 ml of chloroform–THF (1 : 1) and stirred for 30 min at 0 °C. Then, 80 mg of PPEI–EI in 50 ml of chloroform was added to the solution and the coupling reaction proceeded over 12 h at 0 °C. After evaporating the solvent, the reaction mixture was dissolved in water, the brown aqueous solution centrifuged to remove unreacted MFDA, and dialysed against fresh water for three days to remove any small molecules (primarily water-soluble amide from the coupling reaction). After dialysis, the water was removed on a rotary evaporator and the resulting dark brown pendant polymer sample was dried overnight in a vacuum oven at 40 °C. Based on the recovered amount of unreacted MFDA, the MFDA loading in the pendant polymer was estimated to be *ca.* 15%.

The other carboxylic acid group can either couple with another NH unit, most likely on the same polymer chain to form an additional amide linkage, or undergo intrapolymer protonation. GPC analysis of the pendant MFDA–PPEI–EI polymer in Me$_2$SO with 0.2% LiBr shows only a single peak corresponding to an average molecular mass M_w of 49 000 and polydispersity index of 2.67 by reference to linear poly(2-vinylpyridine) standards. The GPC peaks of the pendant polymer and the parent PPEI–EI are very similar, which indicates the absence of significant amounts of higher molecular mass species in the pendant polymer sample arising from crosslinking of two PPEI–EI chains through coupling with the two carboxylic acid groups in an MFDA molecule. The smaller observed M_w for the
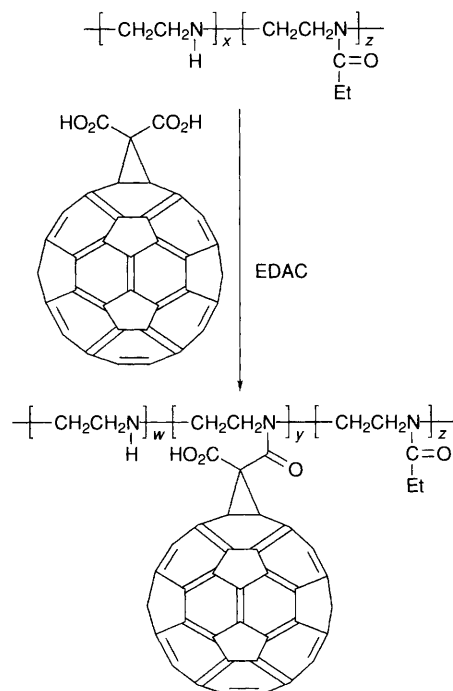
Scheme 1

pendant polymer as a result of smaller hydrodynamic volume in the GPC analysis might be due to conformational changes upon incorporation of MFDA into the copolymer or intrapolymer coupling of two NH units with two germinal carboxylic acid groups in an MFDA molecule.

The proton NMR spectrum of the pendant polymer is similar to that of the parent PPEI–EI, but the relative intensity of the peak at δ 2.8 is lower, which is attributed to the coupling of MFDA with the secondary amine units in PPEI–EI to form N–C=O linkages. The ^{13}C NMR spectrum of the pendant polymer, which is compared with the spectrum of DMFC in Fig. 1, exhibits structured peaks in the fullerene region. This is different from the spectra of other polymers in which the fullerene signals show up as an extremely broad peak.[18–21] It seems that in the pendant polymer the environment surrounding MFDA units is relatively homogeneous.

The FTIR spectrum of the pendant MFDA–PPEI–EI polymer is essentially the same as that of the parent PPEI–EI, except for an additional weak absorption peak at 527 cm^{-1} due to the functionalized C_{60} cage in the polymer-bound MFDA.

The UV–VIS spectrum of the pendant MFDA–PPEI–EI polymer is similar to that of MFDA, with a characteristic
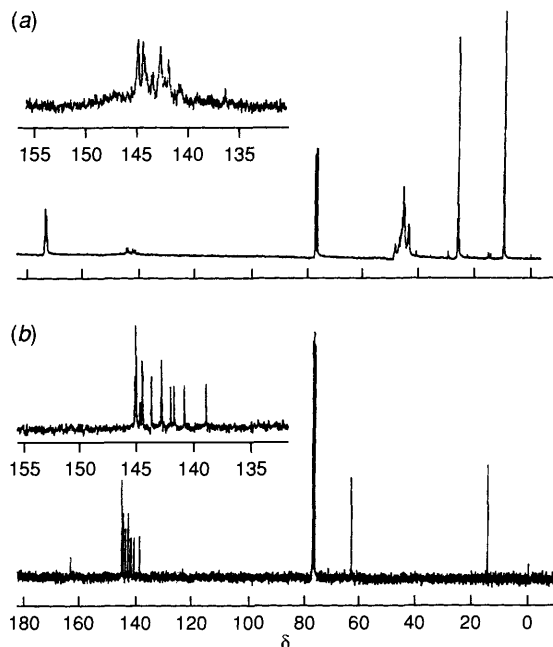

Fig. 1 ^{13}C NMR spectra (75 MHz) of the pendant MFDA–PPEI–EI polymer (a) and mono-DMFC (b) in deuteriated chloroform with TMS as an internal standard
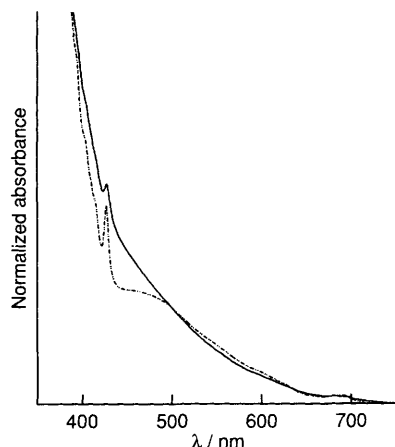

Fig. 2 UV–VIS spectra of the pendant MFDA–PPEI–EI polymer in aqueous solution (—) and MFDA in THF (------)

absorption peak at *ca.* 430 nm and a weak band at *ca.* 700 nm (Fig. 2).

The pendant MFDA–PPEI–EI polymer is highly water-soluble, forming a viscous deep dark brown solution. With an MFDA content of 15% (or 12% C_{60} cages), the polymer aqueous solubility of >90 mg ml^{-1} corresponds to an equivalent aqueous solubility of >10 mg of C_{60} cages (ml water)$^{-1}$. This is much higher than the solubility of monomeric C_{60} in a fullerene solvent such as toluene (2.9 mg ml^{-1}).[22,23] The high aqueous solubility of the pendant polymer is due to the presence of N,N-diethylenepropionamide units in the polymer chain, which are structurally similar to water-miscible N,N-dimethylformamide and N,N-dimethylacetamide.

The preparation of pendant fullerene polymers represents an efficient approach for the introduction of fullerene species into an aqueous environment. The high water solubility of the pendant fullerene-aminopolymer renders it amenable to studies of fullerene biological properties.[1] Investigations of photodynamic activities of the pendant C_{60}–PPEI–EI polymer are in progress.

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