# $^{225}$Ac Metallofullerene: Toward $^{225}$Ac Nanogenerator in Fullerene

Kazuhiko Akiyama,*[1] Hiromitsu Haba,[2] Keisuke Sueki,[3] Kazuaki Tsukada,[4] Masato Asai,[4]
Atsushi Toyoshima,[4] Yuichiro Nagame,[4] and Motomi Katada[1]
[1]*Graduate School of Science and Engineering, Tokyo Metropolitan University, Hachioji 192-0397*
[2]*Nishina Center for Accelerator-Based Science, RIKEN, Wako 351-0198*
[3]*Graduate School of Pure and Applied Sciences, University of Tsukuba, Tsukuba 305-8577*
[4]*Advanced Science Research Center, Japan Atomic Energy Agency, Tokai, Naka-gun, Ibaraki 319-1195*

(Received August 7, 2009; CL-090737; E-mail: kakiyama@tmu.ac.jp)

We report on the successful production of a metallofullerene encapsulating the radioactive tracer $^{225}$Ac and on its electronic properties studied by radiochromatography. Considering the number of $\pi$ electrons on the fullerene cage estimated from the HPLC retention time on the 5PBB column and the general oxidation state of Ac(III), the chemical species of the dominant chromatographic peak is suggested to be Ac@$C_{82}$.

Metallofullerenes are extremely interesting and fascinating materials due to their characteristic structures and electronic properties. One of their most attractive characteristics is the ability to encapsulate various species, such as rare earth elements, metal and metal carbide clusters, and noble gas atoms.[1] Recently, fullerenes encapsulating specific radioisotopes have been found to be promising materials for nuclear medical applications. An in vivo experiment with mice using a poly(vinylpyrrolidine) (PVP) emulsion of the radioactive metallofullerenes, $^{140}$La@$C_{82}$ and $^{140}$La$_2$@$C_{80}$, was conducted by Kobayashi et al.[2] in 1995. The radioactivity of $^{140}$La was primarily observed in the liver and blood. Wilson et al.[3] reported the synthesis of metallofullerenols encapsulating $^{166}$Ho generated in a nuclear reactor and investigated their biodistribution and metabolism properties. They found that the $^{166}$Ho metallofullerenol is localized in the liver. These reports illustrate the possibility using chemically modified metallofullerenes as potential carriers of radioisotopes to targeted organs.

Additionally, $\alpha$-emitting isotopes with successive cascade decays are anticipated to serve as nanosized radiation generators in the medical and pharmaceutical fields.[4] In 2001, McDevitt et al. reported that the radioisotope $^{225}$Ac coupled to internalizing monoclonal antibodies specifically killed leukemia, lymphoma, breast, ovarian, neuroblastoma, and prostate cancer cells at becquerel (Bq) levels.[5] Actinium-225 decays with a half life of 10 d and becomes $^{209}$Bi after four $\alpha$ decays and two $\beta$ decays in succession. An $\alpha$ particle has high linear energy transfer (LET) radiation, and its range in the tissue is about 50 to 80 μm. The exposure of the normal tissue is suppressed low so that $^{225}$Ac is considered to be a promising nuclide for radioimmunotherapy. For further application of $^{225}$Ac in nuclear medicine, development of more efficient delivery systems is required. As a potential candidate for carriers, a metallofullerene encapsulating $^{225}$Ac is one of the most preferable materials. So far, we have successfully produced some metallofullerenes encapsulating lanthanide and actinide elements and studied their electronic properties using radiochromatographic techniques[6–8] which are very sensitive methods and extremely powerful tools for studying the properties of tracer amounts of materials. In this paper, we report the successful production of an $^{225}$Ac metallofullerene and on its electronic properties studied by radiochromatography.

The radioactive tracer $^{225}$Ac was prepared as an $\alpha$ decay product of $^{229}$Th. It was chemically separated by cation exchange from the $^{229}$Th and was stored in $HNO_3$ solution.[9] $La(NO_3)_3$ was added to the solution as a carrier. Next, the solution containing $^{225}$Ac and La was adsorbed on a porous carbon rod (10 mm$\phi$ × 60 mm) and was sintered at 800 °C under He atmosphere. The $^{225}$Ac metallofullerene was generated by arc discharge using the sintered carbon rod. The products were extracted by $CS_2$ from the generated soot. The $CS_2$ solution was filtered to remove the insoluble substance and the filtrate was evaporated to dryness. The dried sample was dissolved in toluene for injection onto a HPLC column of 5PBB (10 mm$\phi$ × 250 mm). The effluent was monitored on-line by a UV absorption detector and was collected on stainless steel disks every 2 min. The HPLC elution behavior of the Ac metallofullerene was determined by $\alpha$-particle measurements on each fraction. The HPLC chromatogram of the La metallofullerene was also measured by monitoring $^{140}$La $\gamma$ radiation in the eluate with a NaI(Tl) scintillation counter. The radioactive $^{140}$La metallofullerene was produced via the thermal neutron irradiation of the separately synthesized crude extract of the La metallofullerene at the JRR3M nuclear reactor at Japan Atomic Energy Agency (JAEA). The sample in toluene was injected onto the 5PBB column under the same developing conditions used for $^{225}$Ac.

The production rate of the $^{225}$Ac metallofullerene was roughly estimated to be 0.1% from a comparison of the radioactivity in the crude extract of the metallofullerene to that in the solution adsorbed on the porous carbon rod. The rate is almost the same as that for the production of other actinide and lanthanide metallofullerenes.[6,10]

Figure 1 shows the HPLC chromatogram of the $^{225}$Ac metallofullerene on the 5PBB column. The chromatogram of the La metallofullerene monitored by NaI(Tl) and that of the hollow fullerenes monitored by UV are also depicted. The elution peak of the Ac metallofullerene is observed at a retention time of 49 ± 1 min which is in good agreement with that of La@$C_{82}$. It is known that the HPLC retention time on the 5PBB column is well correlated with the number of $\pi$ electrons on the fullerene cage.[11] Figure 2 shows the logarithm of the retention ratio $k$ of the hollow fullerenes as a function of the number of carbon atoms (the number of $\pi$ electrons). The retention ratio $k$ is defined as follows:

$$k = (t_R - t_0)/t_0 \quad (1)$$

where $t_R$ is the HPLC retention time of the fullerene, and $t_0$ is the void retention time (3.79 min) on this column. From a linear

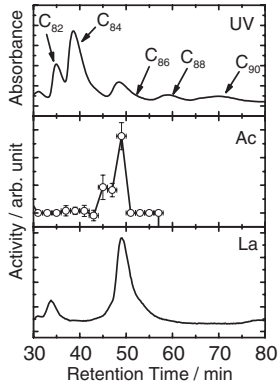


**Figure 1.** HPLC chromatogram of the Ac metallofullerene on the 5PBB column. The crude extract of the Ac metallofullerene was injected onto the 5PBB column (10 mm$\phi$ × 250 mm) at 6 mL min$^{-1}$. For comparison, the HPLC chromatogram of the La metallofullerene and that of the hollow fullerenes monitored by UV are also shown.

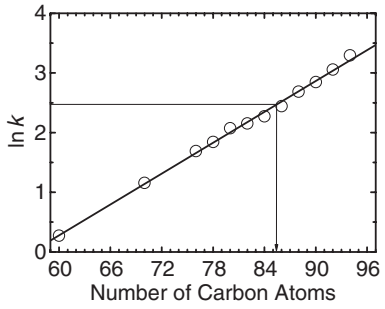


**Figure 2.** Correlation between the number of carbon atoms and the HPLC retention time of each hollow fullerene: Open circles indicate the retention time of the hollow fullerenes, and the solid line shows the result of the least-squares fit of these open circles. The fitting parameters are as follows: slope = $0.0863 \pm 0.0014$ and section = $4.90 \pm 0.11$.

least-squares fit, the number of $\pi$ electrons on the fullerene cage of the produced Ac metallofullerene is estimated to be $85.5 \pm 0.7$, which is consistent with the value of La@$C_{82}$ within the error margin.[12] As the most stable oxidation state of Ac is III, it is reasonable to consider that three electrons can transfer from the Ac atom to the fullerene cage. This means that the formal $\pi$ electrons on the fullerene cage increase by three electrons for each Ac atom.[12] Therefore, Ac@$C_{82}$ ($85\pi$ electrons) and/or $Ac_2$@$C_{80}$ ($86\pi$ electrons) are the possible candidates for the component of the HPLC elution peak. Production of the metallofullerene encapsulating two Ac atoms, however, is negligibly small because the total number of Ac atoms used for the fullerene production is low ($10^{10}$ atoms) and the possibility of the formation of diatomic metallofullerenes of Ac is also extremely low. Thus, Ac@$C_{82}$ is the most potential candidate for the component of the observed elution peak.

In conclusion, the $^{225}$Ac metallofullerene was successfully produced. The production rate of the $^{225}$Ac metallofullerene was approximately 0.1%. From the HPLC retention time, the Ac@$C_{82}$ species was suggested as the most likely candidate for the metallofullerene.

This work was supported in part by a Grant-in-Aid for JSPS Fellows (17·7096) and by the REIMEI Research Resources of the JAEA.

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Published on the web (Advance View) September 12, 2009; doi:10.1246/cl.2009.978