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Efficient One-Flask Synthesis of Water-Soluble [60]Fullerenols

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Abstract: C_{60} molecule exhibited high reactivity towards the addition reaction of nitrogen dioxide radicals ($\cdot NO_2$), which were generated by reaction of sodium nitrite with conc. HNO_3. This chemical functionalization of C_{60} resulted in polynitro fullerenes, $C_{60}(NO_2)_n$. Hydrolysis of polynitro fullerenes in aqueous NaOH gave the corresponding polyhydroxylated fullerene derivatives (fullerenols) in moderate overall yields. Results from mass spectra (FAB, negative ion) of fullerenols indicated their structure as C_{60} derivatives with at least 16 hydroxy groups.

INTRODUCTION

Functionalization of C_{60} molecule with multiple polar hydroxy groups leads to fullerenolic materials with high solubility in water. Several synthetic methods have been developed recently for the preparation of polyhydroxylated fullerene derivatives (fullerenols).[1-5] The chemical composition and the structure of fullerenol deviate slightly from each other upon the variation of reagents and condition used in the reaction. Owing to the nature of multiple additions of hydroxy on C_{60} molecules, there is often a distribution of the number of hydroxy groups per C_{60} unit in their structure. These variations result in difference of their solubility in water and polar, water-compatible organic solvents. In general, the solubility of fullerenols in water increases significantly when the number of hydroxy groups per C_{60} cage reaches 15 or higher. It has been demonstrated that combination of polyol functions and the ball-shaped C_{60} cage in fullerenols enriches their utilization as a spherical molecular core in the design of dendritic, star-shaped polymers.[6,7] Synthesis of C_{60}-derived star-shaped polymers was performed on the basis of high nucleophilic reactivity of fullerenolic hydroxy groups with isocyanate functions in the presence of tin catalyst. In this case, structural distribution of fullerenols was found to cause no disadvantage in the synthesis of C_{60}-derived dendritic polymers. These dendritic polymers were characterized to consist of a narrow distribution of the number of urethanic polyether arms per polymer molecule with a polydispersity index of 1.45 only. Given a polydispersity index of 2.11 for each urethanic polyether arms into account, the observed polydispersity index value of synthesized dendritic polymers fits closely with the theoretically calculated value of 1.37 which was obtained on the assumption of mono-dispersed polymer arms in dendritic polymer.[8] These observations encourage future applications of polyhydroxylated fullerenes and their derivatives in the design of advanced polymeric materials.

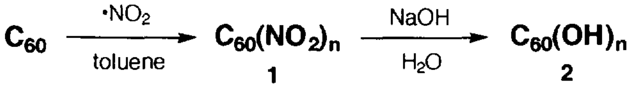
One of methods for the synthesis of water-soluble fullerenols was demonstrated by the nitronium ion (NO_2^+)-activated reaction of [60]fullerene either with a mixture of H_2SO_4 and KNO_3 at 95 °C[1] or with nitronium tetrafluoroborate in the presence of alkyl or aryl carboxylic acid in methylene chloride at ambient temperature under an atmospheric pressure of N_2.[2] In the latter reaction, the instantaneous formation of a nitronium alkyl or aryl carboxylate salt was observed upon treatment of nitronium tetrafluoroborate with the corresponding organocarboxylic acid. The initial electrophilic attack of nitronium ion on fullerenes may give reactive carbocationic intermediates of $C_{60}(NO_2^+)_x$ adducts. The subsequent nucleophilic 1,3- or 1,5-substitution of nitro groups on these adducts by alkyl or aryl carboxylates, followed by treatment of resulting products with water, afforded the corresponding poly(hydroxyorganocarboxylate) derivatives of fullerenes. Fullerenols were then prepared by hydrolysis of poly(hydroxyorganocarboxylate) fullerenes with aqueous NaOH at 70 °C. These results reveal that the fullerenic nitro function may behave as an excellent leaving group and be substituted easily by various nucleophiles.

Other method reported for the synthesis of fullerenols involved a cyclosulfation reaction of fullerenes leading to products of polycyclosulfated fullerenes.[3] Cyclosulfation reaction of C_{60} molecule and its analogs was performed in neat fuming sulfuric acid at 55 °C under an atmospheric pressure of N_2. Hydrolysis of polycyclosulfated fullerenes in aqueous NaOH solution at ambient temperature gave polyhydroxylated fullerenes in a quantitative yield. The functional characteristics and the quantity of sulfate moieties per C_{60} cage in polycyclosulfated fullerenes and the chemical composition of fullerenols were determined on the basis of data analyses from the TGA–mass spectrum and the XPS spectrum. The curve-fitting analysis of absorption bands corresponding to the binding energy of sulfur (S_{2p}) and carbon (C_{1s}) in the XPS spectrum allows estimation of the atomic percentage of tetraoxygenated sulfurs (sulfate) and monooxygenated carbons in the molecule. As a result, an average of 10 to 12 hydroxy addends in this type of fullerenols was resolved, which can be correlated to a composition of polycyclosulfated C_{60} precursors containing 5 to 6 cyclosulfate units.

Unlike unsaturated hydrocarbons, the attack of sulfur trioxide (SO_3) on C_{60} molecules gave no 1,2 (α)- or 1,4 (δ)-sultone or related fullerene adducts as reaction intermediates.[3] The primary function of sulfur trioxide in this reaction was to promote the one-electron oxidation of fullerene molecules and form the cationic C_{60} radical intermediates. Subsequent trapping of the C_{60} cation by HSO_4^- or $HS_2O_7^-$ (a combination of HSO_4^- and SO_3) anionic species afforded the corresponding hydrogensulfated C_{60} radicals. Further electronic oxidation of hydrogensulfated C_{60} radicals to the corresponding cations followed by the intramolecular cyclization of their hydrogensulfate moieties produced 1,2 or 1,4-cyclosulfated fullerenes. Repetition of these reaction steps resulted in polycyclosulfated fullerenes.

Fullerenols were also synthesized by reaction of hydroborated fullerene derivatives with a mixture of H_2O_2 and NaOH.[4] Infrared spectrum of the resultant polyhydroxylated C_{60} products showed the characteristic fullerenolic IR bands, corresponding to absorptions of O–H, C–O, and C=C functions, which are in close resemblance to those of fullerenols synthesized by reaction of C_{60} with nitronium ion. Finally, fullerenes were hydroxylated rapidly by NaOH/O_2 in a two-phase (toluene–H_2O) solution, using tetra(*n*-butyl)ammonium hydroxide as a phase-transfer catalyst, to give brown products of water-soluble C_{60} derivatives.[5] The presence of air, perhaps O_2, is necessary during the reaction to ensure high reaction efficiency. The reaction mechanism of this synthetic pathway is not fully understood.

Herein we describe a novel, one-flask synthesis of polyhydroxylated fullerenes by a sequence of reactions shown in Scheme 1. The approach involves utilization of the fast chemical response of fullerene molecules towards nitrogen dioxide radicals ($\cdot NO_2$) in solution. Multiple addition of nitrogen dioxide radicals on C_{60} molecules led to isolable solids of polynitro fullerenes **1**. Hydrolysis of polynitro fullerenes afforded fullerenols **2** in moderate yields.



$$C_{60} \xrightarrow[\text{toluene}]{\cdot NO_2} \underset{\mathbf{1}}{C_{60}(NO_2)_n} \xrightarrow[H_2O]{NaOH} \underset{\mathbf{2}}{C_{60}(OH)_n}$$

Scheme 1

RESULTS AND DISCUSSION

High electronegativity of fullerene molecules enhances their reactivity towards the nucleophilic attack of electron-rich organic carbanions.[9] Decrease of the electron density at the reactive site of reagents does not reduce the reaction kinetics significantly. Examples were given by electron-deficient organic radicals generated photochemically. These radicals exhibited excellent chemical reactivities with olefinic moieties of fullerenes, including C_{60}[10] and C_{70} molecules.[11] That resulted in rapid formation of fullerene derivatives with multiple addends. The total number of attached radical addends in each C_{60} derivatives can be more than 15 and 34 for the application of benzyl and methyl radicals, respectively. Short-lived carbo-radicals have higher tendency to perform the addition reaction on fullerenes than hindered *tert*-butoxy radical, which gave no *tert*-butoxy adducts of fullerene if active hydrogen-containing reagents were present. In this case, *tert*-butoxy radical executed the proton extraction than the addition reaction on C_{60} molecule. Nitrogen dioxide is the solely reported heteroatom-containing radical and shows respectable reactivity with fullerenes. Quick reaction of $\cdot NO_2$ with fullerenes in solution[12] or with anionic fullerenes in gas phase under mass spectrometric conditions[13] gave the corresponding poly(nitrohydroxy) fullerenes or mononitro fullerides ($C_{60}NO_2^{-\bullet}$ and $C_{70}NO_2^{-\bullet}$), respectively.

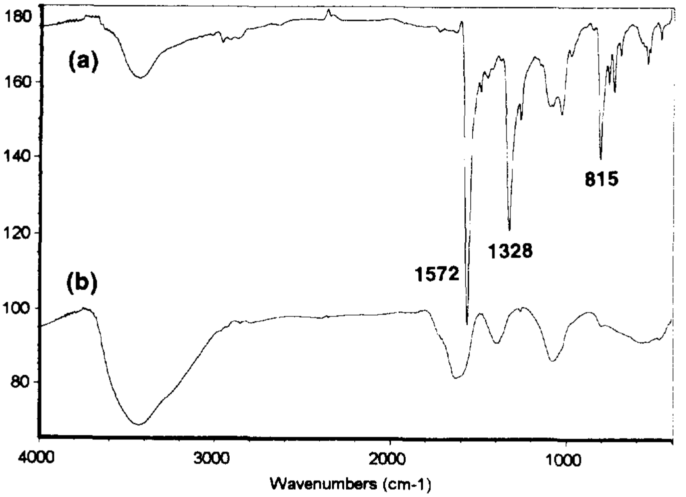


Figure 1: Infrared spectrum (KBr pellet) of (a) polynitro fullerenes **1** showing sharp absorptions at 1572, 1328, and 815 cm^{-1}, corresponding to the asymmetric (ν_{as}) N–O stretching, the symmetric (ν_{s}) N–O stretching, and the N–O bending (δ), respectively, and (b) polyhydroxylated fullerenes **2** (fullerenols).

Direct conversion of fullerenic nitro functions into hydroxy groups with aqueous NaOH may allow us to develop an efficient route for the synthesis of fullerenols. We found that reaction of [60]fullerene with an excess of nitrogen dioxide, which was generated by reaction of sodium nitrite with conc. HNO_3, in benzene gave orange–brown solids within 30 min. During this reaction, the instantaneous production of $\cdot NO_2$ gas upon the treatment of $NaNO_2$ with HNO_3 was noticed by its red–brown color. The color was used to distinguish NO_2 itself from other colorless NO_x species including NO and N_2O_4. Initial proceeding of the reaction was monitored by disappearance of purple solution of C_{60} in a progressive color change to orange–red. To minimize the undesirable hydrolysis of nitro functions by moisture, we isolated and purified the reaction products, polynitro fullerenes **1**, under an atmospheric pressure of N_2. Compounds **1** exhibit high solubility in common organic solvents in the relative order of DMF > THF ≈ CH_3OH > CH_2Cl_2 > toluene. Infrared spectrum of **1** showed two strong, sharp peaks at 1572 and 1328 cm^{-1}, corresponding to absorptions of the asymmetric (ν_{as}) and the symmetric (ν_s) N–O stretching of NO_2 functions, respectively, as shown in Fig. 1a. It also showed a sharp absorption in medium intensity at 815 cm^{-1} corresponding to the N–O bending (δ) of NO_2 functions, indicating the predominate presence of nitro groups on C_{60} cage. The lack of IR absorptions at 1600–1630 cm^{-1} excludes the possibility of the presence of nitrite function (–ONO) in **1**.

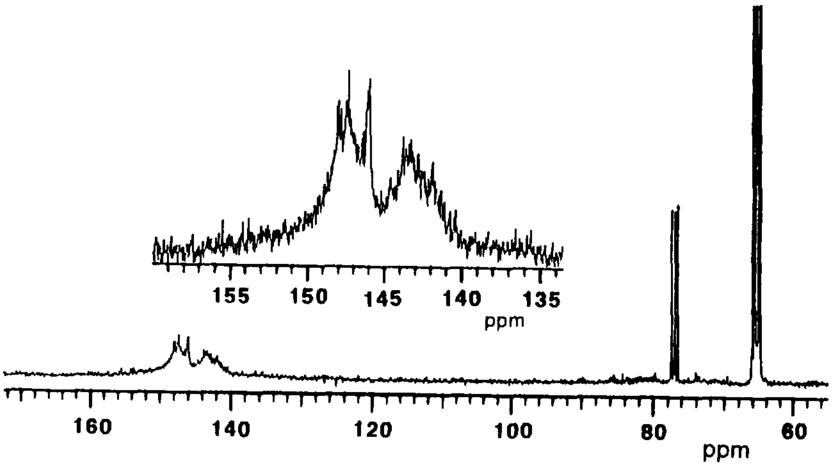


Figure 2. ^{13}C NMR spectrum of polyhydroxylated fullerenes **2** in THF-d_8.

Hydrolysis reaction of polynitro fullerenes **1** was carried out in aqueous solution of NaOH at 40 °C for 4 h to afford, after workup, dark brown solids of polyhydroxylated fullerenes **2** in moderate yields. Direct synthesis of fullerenols from C_{60} and analog fullerenes in one-flask without isolation of intermediates **1** gave slightly improved yields (roughly 10% higher than that from the two-step reaction) of **2**. Infrared spectrum (Fig. 1b) of fullerenols **2** showed a strong, broad band at 3434 cm^{-1} corresponding to the absorption of hydroxy groups ν(OH). It also showed four broad bands centered at 1631, 1387, 1065, and 472 cm^{-1}, which are in close resemblance to the characteristic IR absorptions of fullerenols synthesized by the reaction of C_{60} and analog molecules with nitronium tetrafluoroborate in the presence of organic carboxylic acid.[2] Owing to the lack of hydrogens on fullerene carbons and a great number of regioisomers present in the mixtures of **2**, the acquisition of ^{13}C NMR spectroscopic data required a long relaxation time and accompanied with the problematic low intensity of each individual carbon peak, which reduced the resolution of the overall spectrum. Nevertheless, two broad bands between 140 and 152 ppm, corresponding to the chemical shift of conjugated olefinic carbons in fullerenols **2**, were detected as shown in Fig. 2. The broad carbon bands reveal existence of many non-equivalent fullerenic carbons in **2**. Intensity of the hydroxylated carbon peaks centered at roughly 80 ppm is rather weak that provides no clear NMR information on hydroxylated carbons.

A mass spectrum of fullerenols **2** was obtained in fairly good resolution by the utilization of the negative ion fast atom bombardment (FAB) technique as illustrated in Figure 3. It shows a most abundant ion fragmentation peak centered at *m/z* 720 corresponding to the mass of C_{60} fragmented ion. Many ion clusters above *m/z* 720 clearly separated by multiples of 17 (OH) mass unit provides strong evidence on the presence of hydroxy entities in fullerenols. The highest mass peak of these ion clusters at *m/z* 736 (n = 1), 753 (n = 2), 770 (n = 3), 787 (n = 4), 804 (n = 5), 821 (n = 6), 838 (n = 7), 855 (n = 8), 872 (n = 9), 889 (n = 10), 906 (n = 11), 923 (n = 12), 940 (n = 13), 957 (n = 14), 974 (n = 15), and 991 (n = 16) consists with the mass of ion fragmentations of fullerene derivatives with a structural formula of $C_{60}(OH)_n$.

Finally, we demonstrate the use of polynitro fullerenes **1** as the versatile precursors for the synthesis of water-soluble fullerenols. The allylic *tert*-nitro or double allylic *tert*-nitro functions in structure of **1** are apparently excellent leaving groups for 1,3- or 1,5-nucleophilic substitutions by hydroxide ion. Our observations contradict the previous report[12] on the rearrangement of nitro functions in **1** to its nitrite analog before hydrolysis. Results from mass spectra of fullerenols indicated their structure as C_{60} derivatives with at least 16 hydroxy groups.

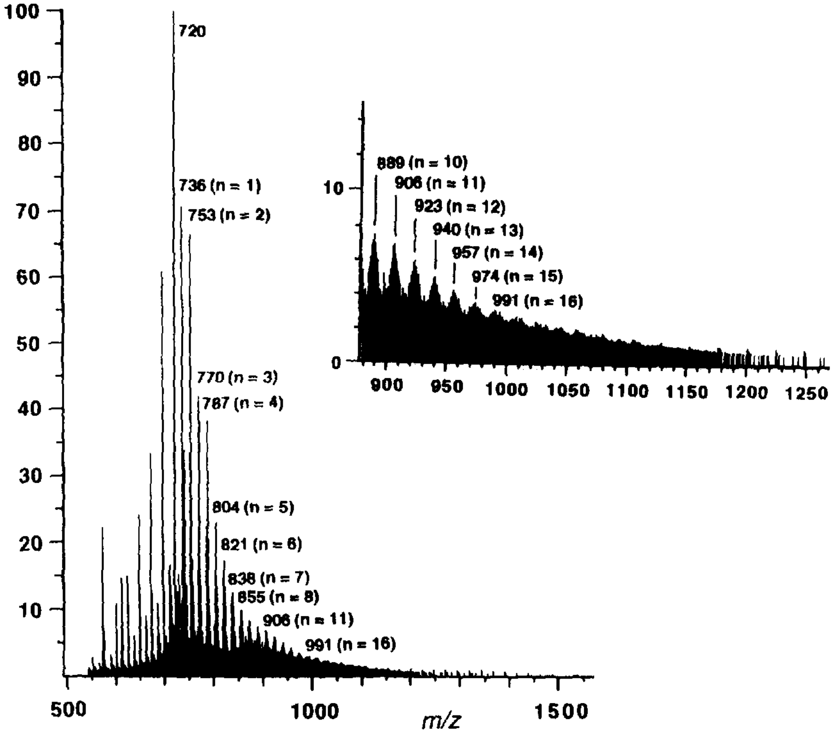


Figure 3: Mass spectrum (FAB, negative ion) of fullerenols **2**, $C_{60}(OH)_n$, showing ion fragmentations with mass of a consecutive increase of the number of hydroxy groups per C_{60} cage.

EXPERIMENTAL

General. Infrared spectra were recorded as KBr pellets on a Nicolet 750 series FT-IR spectrometer or a JASCO FT-IR-300E spectrometer. ^{13}C NMR spectra were recorded on a Varian Gemini-300 spectrometer. Mass spectroscopic studies of fullerenols were performed by use of the fast atom bombardment (FAB) technique on a SX102/SX102CBU mass spectrometer at National Chung-Hsing University, Taiwan. Benzene was dried and distilled over Na. Both sodium nitrite and nitric acid were purchased from Merck Inc. Elemental analyses of fullerenols were carried out at National Cheng Kung University, Taiwan.

Polyhydroxylated Fullerene Derivatives 2 (Fullerenols). A two-necked reaction flask A (50 mL) was equipped with a vertical dropping funnel with a stopcock on one neck and a connecting gas bubbling tube on the other. The gas-bubbling tube was attached with a drying tube ($CaCl_2$) and inserted into the second two-necked reaction flask B. The other neck of flask B was attached with a bubbling tube, which was extended into a trapping flask containing aqueous sodium hydroxide solution (2 N). For the minimization of the back-flow of moisture from alkaline solution, a drying tube ($CaCl_2$) was installed in between the flask B and the trapping flask. A steady inert gas (N_2) flow was allowed starting from the top of dropping funnel, through the reaction flasks A and B in sequence, into the alkaline solution in the trapping flask. The dropping funnel and the reaction flask A were charged with conc. HNO_3 (10 mL) and sodium nitrite ($NaNO_2$, 10 g), respectively. In the reaction flask B was placed a solution of [60]fullerene (500 mg) in dry benzene (50 mL). The inert gas bubbling through the C_{60} solution in the flask B was adjusted to a flow rate of 5 mL per min. The fullerene solution was deoxygenated for at least 5 min prior to the reaction. Concentrated HNO_3 solution was then allowed to add dropwise into sodium nitrite solids in the flask A. Brown fume was produced immediately upon the contact of conc. HNO_3 with $NaNO_2$. It was carried by the steady flow of N_2 gas and bubbled through the C_{60} solution in the flask B. Within 15 min of reaction, the purple solution of C_{60} was changed to orange–red progressively. The mixture was stirred at ambient temperature for an additional 2 h to give a dark brown–red solution with suspended solids. At the end of reaction, excessive nitrogen dioxide (NO_2) was removed by bubbling of N_2 gas and destroyed in the trapping solution. Benzene was then evaporated from the product solution at reduced pressure to give dark brown solids. The solids were suspended in anhydrous *n*-hexane, separated from *n*-hexane solution by the centrifuge technique, and dried in vacuum at 40 °C to afford brown solids of polynitro fullerenes **1** (650 mg). IR υ_{max} (KBr, Fig. 1a) 1572 [s, ν_{as}(N–O)], 1328 [s, ν_s(N–O)], 1085, 1038, 973, 815 (δ), 760, 733, 696, 545, and 466. Compounds **1** exhibited appreciable solubility in common organic solvents, including THF, DMF, CH_2Cl_2, CH_3OH, and DMSO.

Polynitro fullerenes **1** (500 mg) were added into an aqueous solution of NaOH (3 N, 25 mL). The suspension was stirred and heated at 40 °C for 4 h. It was then added slowly into MeOH (80 mL) to effect the precipitation of dark brown solids. The suspended solids were separated from solution by the centrifuge technique and washed 3 times with methanol (15 mL each time) to remove an excess of NaOH. These solid products were further purified and dissolved in a limited amount of water (10 mL), filtered through Celite, reprecipitated from methanol, and dried in vacuum at 40 °C to afford brown solids of polyhydroxylated fullerenes **2** (fullerenols, 430 mg).

One-flask synthesis of fullerenols was performed by the direct hydrolysis of polynitro fullerenes **1** without their isolation from the previous reaction with NO_2 radicals. At the end of fullerene nitration reaction described above (in the same reaction scale), residual nitrogen dioxide (NO_2) was removed by bubbling of N_2 gas and destroyed in the trapping solution. Benzene was then evaporated from the product solution at reduced pressure to give solvent-free solids. An aqueous solution of NaOH (3 N, 25 mL) was added. The suspension was stirred and heated at 40 °C for 4 h. After the reaction mixture was cooled to ambient temperature, it was poured slowly into MeOH (80 mL) to effect the precipitation of dark brown solids of **2**. The rest of workup procedure was identical to that described above for polyhydroxylated fullerenes **2**.

The physical data of compounds **2** [$C_{60}(OH)_n$] are as follow: IR υ_{max} (KBr, Fig. 1b) 3434 (br, s, OH), 1631, 1387, 1065, and 472; ^{13}C NMR (THF-d_8, the highest peak of band, Fig. 2) δ 147.4, 146.0, 143.2, 72.0–84.0 (very weak). MS (FAB, negative ion, mass of the highest ion peak in the fragmentation group, Fig. 3), *m/z* 576, 600, 624, 648, 672, 696, 720 (rel intensity 100), 736 (n = 1), 753 (n = 2), 770 (n = 3), 787 (n = 4), 804 (n = 5), 821 (n = 6), 838 (n = 7), 855 (n = 8), 872 (n = 9), 889 (n = 10), 906 (n = 11), 923 (n = 12), 940 (n = 13), 957 (n = 14), 974 (n = 15), and 991 (n = 16). Because fullerenols **2** is highly soluble in H_2O, the products often contained certain quantity of water molecules, which prohibited the accurate and reproducible measurement of carbon, oxygen, and hydrogen content in products by elemental analyses.

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References

1. Chiang, L. Y.; Swirczewski, J. W.; Hsu, C. S.; Chowdhury, S. K.; Cameron, S, Creegan, K. *J. Chem. Soc., Chem. Commun.* **1992**, 1791.
2. Chiang, L. Y.; Upasani, R. B.; Swirczewski, J. W. *J. Am. Chem. Soc.* **1992**, *114*, 10154; Chiang, L. Y.; Upasani, R. B.; Swirczewski, J. W.; Soled, S. *J. Am. Chem. Soc.* **1993**, *115*, 5453; Chiang, L. Y.; Upasani, R.; Swirczewski, J. W.; Creegan, K. *Mat. Res. Soc. Symp. Proc.* **1992**, *247*, 285; Chiang, L. Y.; Upasani, R. B.; Swirczewski, J. W. *U.S. Patent* 5,177,248, **1993**; *U.S. Patent* 5,294,732, **1994**.

3. Chiang, L. Y.; Wang, L. Y.; Swirczewski, J. W.; Soled, S.; Cameron, S. *J. Org. Chem.* **1994**, *59*, 3960.
4. Schneider, N. S.; Darwish, A. D.; Kroto, H. W.; Taylor, R.; Walton, D. R. M. *J. Chem. Soc., Chem. Commun.* **1994**, 15.
5. Li, J.; Takeuchi, A.; Ozawa, M.; Li, X.; Saigo, K.; Kitazawa, K. *J. Chem. Soc., Chem. Commun.* **1993**, 1784.
6. Chiang, L. Y.; Wang, L. Y.; Tseng, S. M.; Wu, J. S.; Hsieh, K. H. *J. Chem. Soc., Chem. Commun.* **1994**, 2675.
7. Chiang, L. Y.; Wang, L. Y.; Tseng, S. M.; Wu, J. S.; Hsieh, K. H. *Synth. Met.* **1995**, *70*, 1477.
8. Orofino, T. A. *Polymer* **1961**, *2*, 295.
9. For a review on chemical reactivity of fullerene molecules, see: Taylor, R.; Walton, D. R. M. *Nature* **1993**, *363*, 685.
10. Krusic, P. J.; Wasserman, E.; Keizer, P. N.; Morton, J. R.; Preston, K. F. *Nature* **1991**, *254*, 1183.
11. Keizer, P. N.; Morton, J. R.; Preston, K. F. *J. Chem. Soc., Chem. Commun.* **1992**, 1259.
12. Roy, S.; Sarkar, S. *J. Chem. Soc., Chem. Commun.* **1994**, 275.
13. Sunderlin, L. S.; Paulino, J. A.; Chow, J.; Kahr, B.; Ben-Amotz, D.; Squires, R. R. *J. Am. Chem. Soc.* **1991**, *113*, 5489.

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