Fullerene Spin Label. Synthesis and Characterization of the [60]Fullerene-substituted TEMPO Radical

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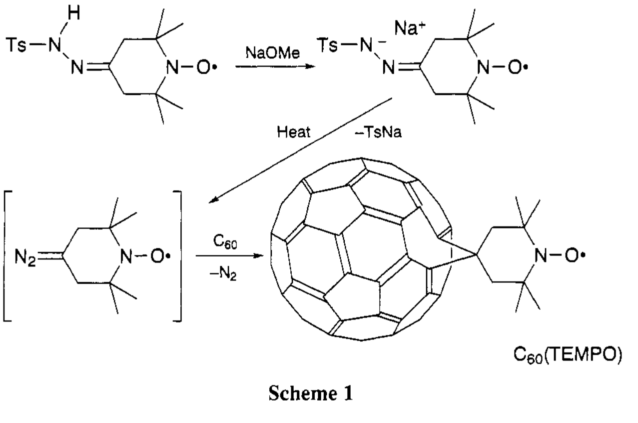
A spin-labelled reagent C_{60}(TEMPO) (TEMPO = 2,2,6,6-tetramethylpiperidin-1-oxyl) is synthesized, purified by LC, and characterized by spectroscopic, magnetic and electrochemical measurements.

In the course of extensive studies on fullerene chemistry,[1] there have been studies of its inhibition of HIV-1 protease[2] and DNA cleavage.[3] A variety of labels[4,5] designed to be observed by ESR, for instance, are known for probing local environment, molecular rotational motion, and bioorganic structure.

Wudl *et al.* reported that the reactions of diazomethane derivatives and [60]fullerene gave the corresponding open [5,6] adducts 'fulleroids'.[6,7] We adopted this reaction for the introduction of TEMPO (2,2,6,6-tetramethylpiperidin-1-oxyl) moiety to [60]fullerene by use of 4-diazo-TEMPO. A part of the Bamford–Stevens reaction was applied and the pyrolysis of the sodium salt was conducted in the presence of [60]fullerene as an *in situ* trapping method in order to avoid isolation of the hazardous diazo compound (Scheme 1).

To a suspension of TEMPON tosylhydrazone (663 mg)† in MeOH (3 ml) was added NaOMe/MeOH (28%; 0.4 ml) at room temp. under Ar (TEMPON = 4-oxo-TEMPO). The solvent of the resulting orange solution was removed under reduced pressure to give the sodium salt (676 mg) of TEMPON tosylhydrazone (96%) as an orange hygroscopic solid. The IR spectrum had no absorption due to N–H stretching. The solid was thoroughly washed (benzene, hexane), and dried under vacuum.

A mixture of the sodium salt (51.7 mg), [60]fullerene (53.2 mg) and chlorobenzene (10 ml) was stirred at 132 °C under Ar for 30 min. The mixture was filtered on a silica-gel short column; a hexane–toluene–EtOH mixed solvent was used for the eluent with a gradual increase of the content of polar solvents. The coloured elution was concentrated under reduced pressure below 45 °C, and addition of MeOH resulted in the precipitation of a brown powder. The powder was collected, dissolved in a small amount of CS_2, and reprecipitated with hexane to give 67.4 mg of brown powder. The solid (61.9 mg) was applied on a gel permeation chromatography (Jaigel 1H + 1H, toluene) to yield the following products in the order of retention times: 7.5 mg (9%) of [60]fullerene(TEMPO)$_3$, 16.6 mg (22%) of [60]fullerene (TEMPO)$_2$, 16.5 mg (26%) of [60]fullerene(TEMPO),‡ and 6.4 mg (12%) of recovered [60]fullerene. Fractions containing a slight amount of tetra- or more-addition products were obtained in some cases. These formulae were determined by MS. All products are dark-brown powders (mp > 350 °C) and more soluble in ordinary organic solvents than [60]fullerene. The mono- and di-adducts are purple and other adducts brown in solution. In order to prevent destruction of radical sites, the reaction temperature must be as low as possible. However, practically no reaction occurred < 120 °C.



Scheme 1

The electron-spray-ionization mass spectrum (ESI MS) of the mono-adduct [60]fullerene(TEMPO) showed only one signal at *m/z* 874 asscribable to the molecular ion. The ESR spectrum of [60]fullerene(TEMPO) exhibited a triplet centred at g = 2.006 with a_N = 1.49 mT in toluene (Fig. 1). These values are characteristic to TEMPO-based radicals.[5] The IR spectrum of [60]fullerene(TEMPO) showed the bands ascribable to the TEMPO moiety and [60]fullerene skeleton without any band due to a pyrazoline or N=N group. This finding indicates the complete elimination of N_2 under these reaction conditions. The UV–VIS absorption spectrum of [60]fullerene(TEMPO) is shown in Fig. 2, which is very similar to that of [60]fullerene. The electronic structure of the [60]fullerene moiety is only slightly perturbed, strongly suggesting that [60]fullerene-(TEMPO) has an open [5,6] structure with [60]fullerene conjugation retained.

In order to confirm this structure, we synthesized and characterized another diamagnetic adduct suitable for NMR analysis. We obtained an adduct $C_{60}(CEt_2)$ by the same

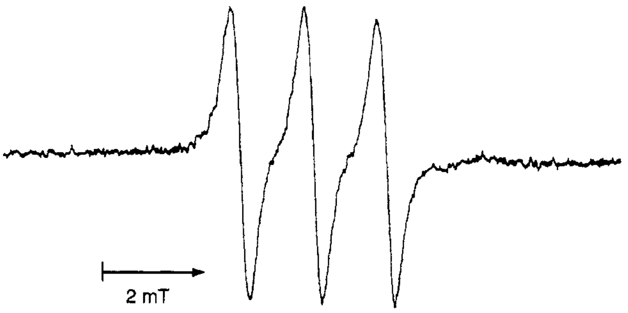


Fig. 1 X-band ESR spectrum of [60]fullerene(TEMPO) in non-degassed toluene at room temp.

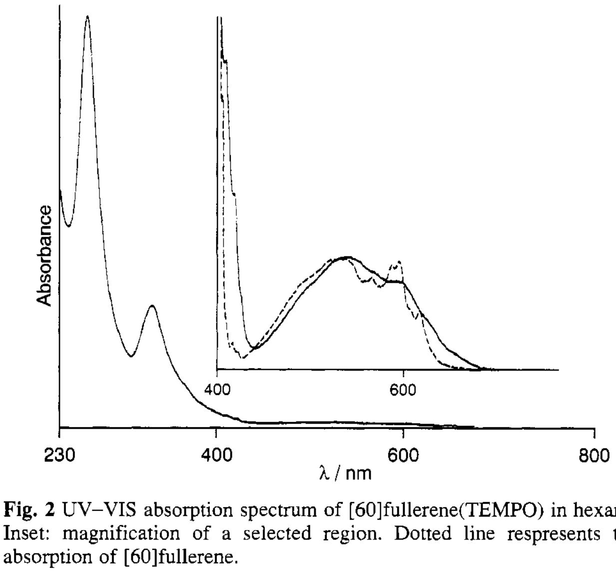


Fig. 2 UV–VIS absorption spectrum of [60]fullerene(TEMPO) in hexane. Inset: magnification of a selected region. Dotted line respresents the absorption of [60]fullerene.

procedure from diethyl ketone, instead of TEMPON, as starting material. The ^{1}H NMR analysis revealed that two ethyl groups are nonequivalent with a large difference of the chemical shifts.[8] Thus, the structure was proved to be a [5,6] adduct. It has been reported that carbenes react at [6,6] ring junctions to give closed [6,6] adducts,[1] which is incompatible with our results. The synthetic method presented here should be understood to include a 1,3-dipolar cycloaddition of diazo compounds to [60]fullerene followed by elimination of N_2, as previously clarified on the preparation of $C_{60}(CH_2)$.[7]

The elemental analysis of the samples recrystallized from CS_2 indicated the composition formula [60]fullerene(TEMPO)·$1.3CS_2$.‡ The temperature dependence of the magnetic susceptibilities on these samples obeyed the Curie–Weiss relation ($\chi = C/(T - \theta)$, where C and θ are the Curie and Weiss constants, respectively). We obtained $C = 3.53 \times 10^{-4}$ and 3.86×10^{-4} cm^3 K g^{-1} with $\theta = -0.25$ K for the samples prepared by the pyrolysis at 132 and 125 °C, respectively. From the Curie constants, the radical purities were estimated to be 92 ± 3 and 100 ± 3%, respectively, based on the above composition. The purities of the samples were proved to be very high; the introduction of the TEMPO group to [60]fullerene was accomplished without destruction of the radical sites.

The redox potentials of [60]fullerene(TEMPO) were determined by CV. This compound was proved to possess both electron-donating and -accepting sites. The halfwave redox potentials were found to be 0.62, −0.88 and −1.29 V *vs.* Ag/Ag$^+$ in *o*-dichlorobenzene. The first one can be assigned to the redox process between $>$N–O· and $>$N$^+$=O, and other to the first and second redox processes of the [60]fullerene moiety. The redox potentials of [60]fullerene were −0.84 and −1.24 V *vs.* Ag/Ag$^+$ under the same conditions.

The oxidation potentials of the nitroxide site in TEMPO derivatives are reported to be susceptible to the substituent effect.[9] The oxidation potential of [60]fullerene(TEMPO) was higher than those of TEMPO and TEMPON,[9] indicating that the [60]fullerene moiety plays the role of an electron-withdrawing group. On the other hand, slight shifts of the reduction potentials were found between [60]fullerene(TEMPO) and [60]fullerene. This finding is again in good agreement with the open [5,6] structure of [60]fullerene(TEMPO), as discussed on fulleroid derivatives.[6,7] [60]Fullerene(TEMPO) is environmentally stable, electronically unperturbed, and easily available. This labelled reagent seems to be applicable in studies on molecular systems, especially in bioorganic systems, containing fullerenes.

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Footnotes

† Prepared by condensation of TEMPON and tosylhydrazone in aqueous media. Mp 130 °C. EI MS *m/z* 338 (M$^+$, 4%), 322 (M$^+$–O, 3%), 183 (M$^+$-tosyl, 15%), 101 (100%), IR (KBr disk) 3200, 1395, 1175, 1165, 680, 540 cm^{-1}. The magnetic measurement gave $C = 0.375$ cm^3 K mol^{-1} with $\theta = -4.1$ K which ensured the radical purity.

‡ ESI MS *m/z* 874 (M$^-$). IR (KBr disk) 2960, 2910, 1240, 525, 510 cm^{-1}. UV–VIS (hexane) λ_{max} 260, 332, 540(br), 600(sh) nm. ESR (toluene) $g = 2.006$, $a_N = 1.49$ mT.

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