

## Highlight Review

Chemistry in Calixarenes and Radicals:  
Inclusion, Spin Label, Reaction, and ESR Studies

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**Abstract**

Due to inclusion function and easy chemical modification of calixarenes, they should be able to form inclusion complexes with free radicals, spin labeled calixarenes, and polyradicals based on calixarene skeletons. It is therefore important not only to utilize radicals as spin probes to investigate inclusion function and conformational changes of calixarenes, but also to develop potentially new molecular magnetic devices and materials. Recent research advances, especially using ESR technique, in interdisciplinary of calixarene and radical, are briefly reviewed.

**◆ Introduction**

Since the early work of Gutsche,<sup>1</sup> calixarenes, as complexing agents, biomimetics, physiological compounds, and catalysts, have been attracting more and more attention in host-guest supramolecular chemistry and other fields because of their structural features. Among all studies associated with calixarenes, a large part focus on chemical modification, conformational change, inclusion and complexation of small neutral molecules, anions, or metal cations.<sup>2</sup>

A new branch of calixarene chemistry associated with free radicals has been developing over the past decade. Studies on the chemistry of calixarenes and free radicals are mainly focused on spin probes and magnetic interaction. Free radicals captured in cavities of calixarenes can be stabilized and used to investigate inclusion. A variety of spin-labeled calixarenes have been synthesized and have been used as spin probe to investigate and modulate spin-spin exchange interaction (SSEI) and conformational changes. Multispin-labeled calixarenes or polyradicals based on calixarene skeletons prepared by means of molecularly functionalized designs are also expected to be used to explore potentially new molecular magnetic devices and materials originating from molecular magnetism of calixarene radicals. Scheme 1 shows structures of calixarenes mentioned in the present paper.

**◆ Inclusion of Free Radicals**

In comparison to the numerous studies of inclusion and complexation of small neutral molecules, anions, and cations in calixarenes as an important class of macrocyclic host molecules, inclusion of free radicals in calixarenes has been less studied. We found that inclusion effects of calixarenes can stabilize some

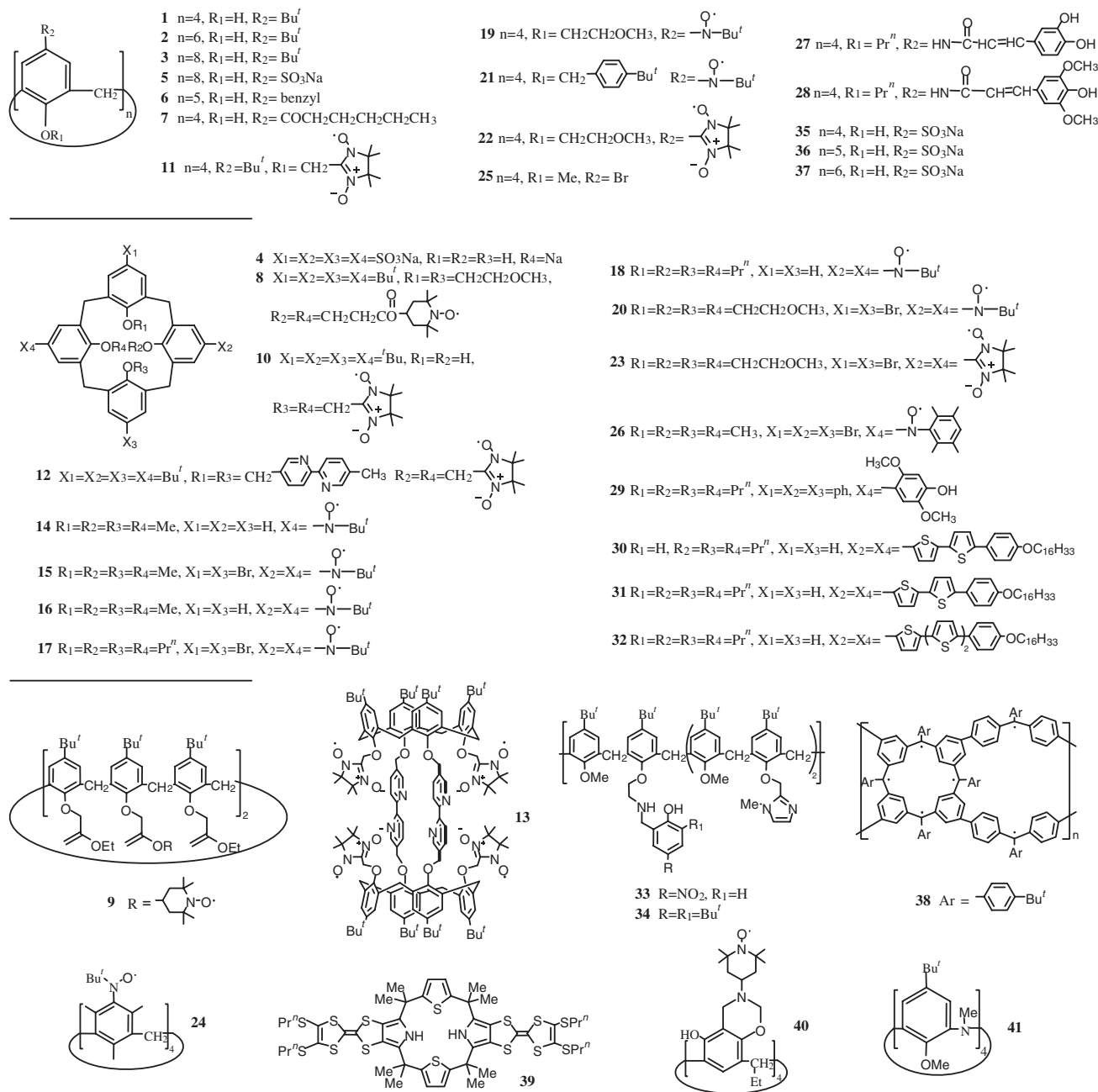
short-lived free radicals.<sup>3</sup> 2,2-Azobisisobutyronitrile (AIBN) easily generates carbon centered free radicals by UV light irradiation. Its lifetime is too short to directly detect an ESR signal of the radical. However, when calixarene **1** was added to an AIBN solution, a weak ESR signal was observed. The radicals generated from AIBN can be trapped by nitrosodurene (ND) to form a stable spin adduct. One can find that the ESR signals of the spin adduct appeared faster in the presence of **1** and its intensity became much stronger than that observed in the absence of **1**. This suggests that inclusion of the radical in **1** occurred and decreased the reactive probability of the radical quenched by each other or by other species. Therefore, **1** plays a marked role to stabilize the short lifetime radical and to prolong the lifetime, so that it is advantageous for ND to trap the radical. Similar experiments were carried out for **2** and **3**, however, no similar effects were observed.

On the basis of changes in ESR parameters between free and included radicals, one can monitor inclusion processes and obtain information on structures and effects of inclusions.<sup>3,4</sup> We found that the nitrogen hyperfine coupling constant (hfcc) of di-*t*-butyl nitroxide (di-*t*-butylaminoxyl) generated by self-trapping of 2-methyl-2-nitrosopropane (MNP) under irradiation became smaller in the presence of **1** than that in the absence of **1**.<sup>3</sup> It is well-known that the hfcc is sensitive to the surroundings and will become smaller in more hydrophobic environments. Therefore a possible inclusion form is believed to be that the N–O group of the radical is immersed inside the cavity and surrounded by the *t*-butyl groups of **1**, which is a more hydrophobic environment, and two *t*-butyl groups of the radical are directed outside.

On the other hand, inclusion of nitroxide free radicals in water-soluble calixarenes usually orients N–O groups toward outside. Pedulli and his co-workers reported using benzyl *t*-butyl nitroxide (BBN) to probe its inclusion in a water-soluble calixarene **4**.<sup>5</sup> In the presence of **4**, additional ESR signals assigned to BBN included in the cavity of **4**, which is in equilibrium with the free nitroxide, were observed. When the absolute concentration of **4** was increased, the ratio between included ( $a(\text{N}) = 1.686 \text{ mT}$ ,  $a(2\text{H}) = 1.211 \text{ mT}$ , and  $g = 2.0056$ ) and free ( $a(\text{N}) = 1.669 \text{ mT}$ ,  $a(2\text{H}) = 1.064 \text{ mT}$ , and  $g = 2.0056$ ) species varied linearly, and the spectrum of the included BBN became dominant. The ESR spectra were consistent with the formation of 1:1 inclusion complexes of BBN with **4**. The similarity of the  $a(\text{N})$  values for free and included BBN indicates that the N–O group in the included BBN is exposed to bulk water; it is therefore conceivable that the phenyl moiety is

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**Scheme 1.** Structures of calixarenes mentioned in the present paper.

instead selectively bound to the calixarene cavity. On the other hand, the increased splitting of the benzylic proton signals suggests that inclusion into the calix[4]arene cavity is accompanied by a change either of the preferred conformation adopted by the radical or of the height of the barrier to the internal rotation of the phenyl group. The kinetics of the inclusion of BBN in **4** in water was also studied by analyzing variations in the ESR line shape. The reaction enthalpy for the inclusion process is negative, suggesting that the driving force to inclusion is the  $\pi$ - $\pi$  stabilizing interaction between the phenyl ring of BBN and the aromatic system of **4** or a hydrophobic effect or both. From the large enthalpy of activation, it may be inferred

that the phenyl ring of BBN is not yet deep enough inside the calixarene cavity to provide the stabilizing interaction between the guest and host  $\pi$  systems.

Sueishi et al. first reported interesting bidirectional inclusion of nitroxide free radicals in water-soluble calixarene.<sup>6,7</sup> They utilized a unique nitroxide free radical probe, *t*-butyl  $\alpha$ -(2,4,6-trimethoxyphenyl)benzyl nitroxide, as the guest molecule for **5**, and detected two isomeric inclusion complexes with **5** in aqueous media by ESR spectrometry.<sup>6</sup> The ESR spectra were assignable to *t*-butyl-in and phenyl-in complexes. The association constants at room temperature were estimated based on the ESR experiments for *t*-butyl-in and phenyl-in complexes,

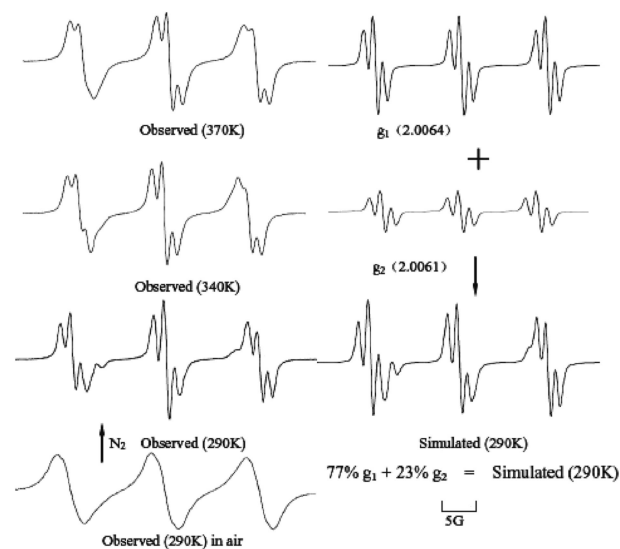
respectively. **5** favors the inclusion from the *t*-butyl side over the phenyl side probably because the N–O group is located closer to the sulfonato groups than in the case of phenyl-side inclusion and is easily able to interact with polar calixarene walls. Second, the diameter of the trimethoxyphenyl group is slightly smaller than the calixarene opening, it may form a shallowly inserted complex. Furthermore, Sueishi et al. investigate the analog of a probe with a cyclohexyl group instead of a phenyl group, *t*-butyl ( $\alpha$ -cyclohexyl-2,4,6-trimethoxybenzyl) nitroxide in a similar system and found that the ESR spectra of two group-in complexes were not separated from each other. However, they found that the addition of alkali salts significantly increased the binding between **5** and a guest group.<sup>7</sup> In the present case, the ESR peaks for two independent group-in complexes became visible and were assigned to cyclohexyl-in and *t*-butyl-in complexes. The magnitude of separation was dependent on the salt concentration. Inclusion from the *t*-butyl side was also favored over the cyclohexyl side.

Webster and his co-workers conducted ESR experiments on  $C_{60}^{\bullet-}$  in the presence of **6**.<sup>8</sup> The intensity of ESR signals decreased when  $C_{60}^{\bullet-}$  was electrochemically generated in the presence of **6**, indicating that the inclusion and host–guest  $\pi$ – $\pi$  interactions were sufficiently strong to alter the EPR signals of  $C_{60}^{\bullet-}$ .

Ananchenko et al. successfully isolated and characterized the first solid inclusion complexes of **7** with stable nitroxyl radicals, *N*-(2-methylpropyl)-*N*-(1-diethylphosphono-2,2-dimethylpropyl)aminoxyl (DEPN) and 4-methoxy-2,2,6,6-tetramethylpiperidine-*N*-oxyl (MT).<sup>9,10</sup> The single-crystal X-ray diffraction experiments revealed that one DEPN or MT is entrapped in a capsule of two calixarene molecules. Multi-frequency (X-, W-band and 360 GHz) cw and pulse ESR were also employed to study the mobility of the nitroxides in capsules of **7** in the solid state to extract the canonical values of the hyperfine and *g*-tensors of the encapsulated radicals as well as information on restricted orientational dynamics of the caged spin probes.<sup>10</sup> Echo-detected ESR spectra revealed that the main type of motion of encapsulated MT in the temperature range 90–200 K is vibrations. At higher temperatures,  $T > 250$  K, the fast restricted rotation of radicals becomes the main type of motion for both radicals. The rotation is found to be more isotropic for DEPN than for MT, but still definite restrictions for mobility prevail inside the capsule similar to what happens for MT.

## ◆ Spin-labeled Calixarenes

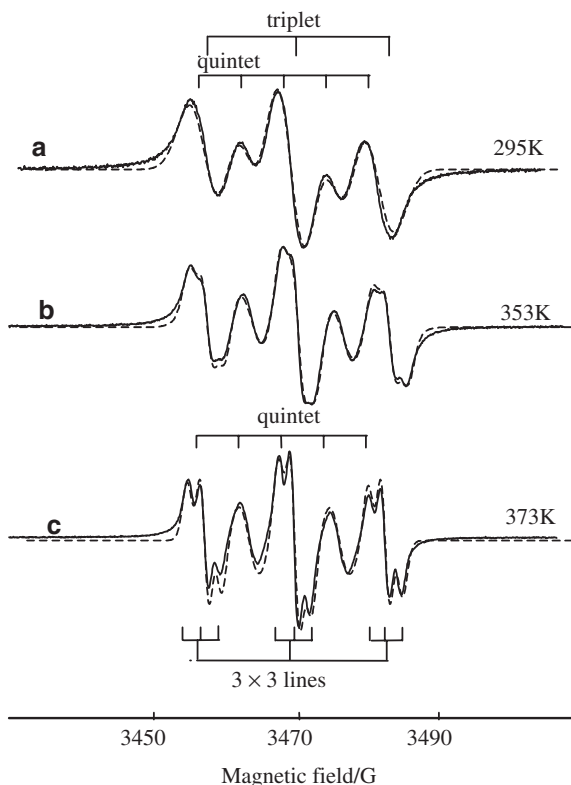
The covalent attachment of stable nitroxide radicals to specific sites on calixarenes could provide valuable information describing local molecular environments. In particular, the intramolecular SSEI and dipolar interaction between different radicals usually are sensitive to dynamic conformational changes and could show unique magnetic behavior. Shinkai et al. synthesized calix[*n*]aryl ester bearing two stable nitroxide radicals **8** and **9** on the low rim.<sup>11</sup> According to NMR and ESR investigations, they found that intramolecular SSEI can be controlled by the alkali metal-binding event occurring on the calixarene platform. In **9** the SSEI changes in response to a metal-induced 1,2,3-alternate-to-cone conformational change, but in **8** only the metal-induced rotation of the carbonyl groups take places and is not enough to change the SSEI.



**Figure 1.** ESR spectra of **14** in toluene under nitrogen protection at different temperatures and the simulated 290 K ESR spectrum.<sup>14</sup>

Ziessel et al. synthesized a family of spin-labeled calixarenes with two or four nitronyl–nitroxide radicals **10**–**13**.<sup>12</sup> ESR studies revealed that for **12** a marked decrease in the extent of through-space SSEI between the two nitroso subunits result from increased spatial separation of the radicals because of coordination of  $Zn^{2+}$  at the bipyridine sites, whereas the ESR spectrum of **11** exhibited obvious spin coupling between the four nitroso radicals but unlike **12** is not perturbed by the presence of cation. ESR spectra recorded for **10** with or without added cation show no pronounced SSEI between the radicals because of restricted conformational mobility. The ESR spectrum of **13** resembles that recorded for **12** in the presence of  $Zn^{2+}$  because the rigid and enlarged structure of **13** prevents close contact between the nitroso radicals, thereby restricting SSEI to a low level. As expected for this compound, addition of  $Zn^{2+}$  has no effect on the observed EPR spectrum.

In contrast to the previous work which introduced nitroxide radicals at the lower rim of calixarenes, we are interested in what would happen if multiple radicals were introduced directly on the phenyl rings, such as in *N*-*t*-butyl phenyl nitroxides, which have been developed as good coupler units of various magnetic compounds. Therefore we have synthesized a series of stable spin labeled calix[4]arenes with *N*-*t*-butyl nitroxide on the upper rim.<sup>13–15</sup> In order to remove the influence of intramolecular SSEI between different spin centers, a paramagnetic calix[4]arene with an N–O monoradical on the upper rim was prepared.<sup>14</sup> Its ESR behaviors were mainly induced by its intrinsic conformational flexibility. Combining with NMR spectra, it could be deduced that the observed ESR spectra are mainly superposed by the ESR spectra of two different monoradicals of **14** which may takes cone or partial cone conformations. When a solution of **14** was heated, the ESR signals of two monoradicals were enhanced and began to close up. As the temperature was raised to 370 K, the two ESR signals coalesced gradually (Figure 1). This suggested that conformational transitions among the different conformational isomers of **14** were accelerated upon heating.



**Figure 2.** ESR spectra of **15** in toluene at different temperatures (solid line: experimental spectra, dashed line: the best fits of simulation).<sup>13</sup>

The complexation of  $\text{Ag}^+$  with **14** caused marked changes in ESR spectra, whereas  $\text{Zn}^{2+}$  almost gave no effect. This means that **14** selectively complexes  $\text{Ag}^+$ , and suggests that the complexation of  $\text{Ag}^+$  modulates the conformation of **14** and changes the ratio of the two different monoradicals causing the ESR spectra to change.

Four spin-labeled calixarenes **15–18** with two opposite nitroxide radicals on the upper rims were also synthesized, and their SSEI, which were found to be affected by many factors such as conformational flexibility, steric hindrance, temperature, solvent effect, and complexation of  $\text{Ag}^+$ , were studied.<sup>13,15</sup> Based on the ESR line shapes, all the ESR spectra of **15–18** can be regarded as two sets of overlapping signals: a broad triplet is caused by nitrogen hyperfine coupling as two nitrogen nuclei are separated, and a quintet arises from SSEI of two equivalent nitrogen nuclei when they placed in proximity in cone conformation. The quintet ESR peaks are clear indication of strong through-space SSEI. Due to the peculiar conformational flexibility of calixarenes, interesting conformational transitions are induced upon heating and give rise to temperature-sensitive ESR observations in which reversible changes in ESR spectra were observed for **15** with decreasing and increasing temperature (Graphical abstract and Figure 2).<sup>13</sup>

Furthermore, the increasing sequence of the proportions of the quintet in four ESR spectra is: **15** < **16** < **17** < **18**.<sup>15</sup> When the calixarene is immobilized in cone conformation, the two opposite nitroxide radicals have larger propensity toward SSEI, whereas conformational flexibilities of **15** and **16** give two

radicals a chance to adopt an *anti*-position, resulting in long distance between two radicals and restricting SSEI to somewhat lower level. As for **17** and **18**, although the conformations are fixed in cone conformation, the phenyl rings also can make little angle rotation, leading to conformational interconversions between the pinched and flatten cones or between two  $C_{2v}$  cones.<sup>16</sup> The ESR spectra of **17** and **18** show not only one kind of pure biradical pattern, but show superposition of different biradical ESR signals. On the other hand, half-field forbidden transitions  $\Delta M_S = \pm 2$ , which are shown by a triplet, were detected in 77 K ESR spectra of **15–18**. The spin multiplicity of **15** was also identified using pulsed ESR 2D-electron spin transient nutation (ESTN) spectroscopy.<sup>17</sup> Cw and pulsed ESR studies show that the triplet state of **15** is in a thermally accessible excited state, revealing that the two nitroxide radicals antiferromagnetically interact with each other. The average distance between two nitroxide radicals of **15** estimated from zero-field splitting parameter  $D$  based on the point dipole approximation, is about 0.53 nm,<sup>17,18</sup> which is slightly longer than that between the two hydroxy groups of the hydroxyamino precursor of **15** determined by X-ray crystal structure analysis.<sup>13,18</sup>

Rajca et al. reported pioneering work on calix[4]arene derivatives having four and two *tert*-butyl nitroxide radicals **19–21** in the upper rim of the calixarene skeleton and characterized them by X-ray crystallography, ESR and  $^1\text{H}$ NMR spectroscopy, and magnetic susceptibility measurements.<sup>19,20</sup> Through-bond and through-space SSEI in the calix[4]arene scaffolds functionalized on the upper rim with nitroxide radicals were studied. The through-bond SSEI between the adjacent nitroxide radicals is controlled by the conformation of the nitroxide-*m*-phenylene- $\text{CH}_2$ -*m*-phenylene-nitroxide coupling pathway. In the 1,3-alternate calixarene scaffold **19**, the SSEI is antiferromagnetic, whereas in the cone calixarene scaffold **21**, the SSEI is ferromagnetic. The through-space SSEI between the diagonal nitroxides at the N...N distance of 5–6 Å in the 1,3-alternate and cone calixarene scaffolds **19–21** is antiferromagnetic. The X-ray crystal structure of **21** revealed that the two diagonally arranged radical sites formed an intramolecular dimeric structure then undergoing a strong antiferromagnetic interaction. Similar studies were also carried out for nitronyl nitroxide tetradical **22** and diradical **23** in the fixed 1,3-alternate calix[4]arene conformations.<sup>21</sup>

Takui et al. showed for the first time that nitroxide tetradical **24** with four nitroxide radical sites in the upper rim of the calixarene skeleton is in a quintet state.<sup>22</sup> The X-ray crystal structure of **24** has a 1,3-alternate conformation. The results of the 2D-ESTN spectroscopy demonstrated that the nutation signals arising from the quintet state are observed at 3.8 K, showing the quintet state is in the ground state or nearly degenerate with singlet ground states. It was indicated that the steric hindrance introduced by mesityl groups yields a relatively rigid macrocyclic molecule with four nitroxide radicals, generating the high-spin quintet state.

## ◆ Free Radical-Related Reactions

Free radical-related reactions are another important field of chemistry in calixarenes and free radicals. We investigated the reaction between **25** and ND under UV irradiation using ESR

methods.<sup>4</sup> In the presence of the optimum amount of ND, a typical hyperfine splitting was observed for the spin adduct of ND **26** which was due to cleavage of one C–Br bond at a *para*-position of **25** under irradiation.

Taking into account that calixarenes have free-radical scavenging and antioxidative phenolic units, Feng et al. investigated the effect of  $\gamma$ -radiation on polypropylene (PP) in the presence of **1–3** as additives in air or in vacuum at ambient temperature.<sup>23,24</sup> The influence of radiation dose and storage time upon the mechanical properties of the irradiated PP sheets were measured. By means of ESR spectra and other spectra the formation of the stable calixarene radicals was confirmed, and the results showed that PP is stabilized more efficiently in the presence of the calixarene at higher dose and the radiation stabilization was reduced with the increase of the ring size of calixarene. Consoli et al. also reported free radical scavenging and antioxidative activities of calixarene derivatives **27** and **28** exposing four units of hydroxycinnamic acid in *all-syn* orientation, which were determined by using 2,2-diphenyl-1-picrylhydrazyl radical (DPPH $\cdot$ ) and AIBN $\cdot$ -induced linoleic acid peroxidation, respectively.<sup>25</sup> Ananchenko et al. showed that the nitroxyl radical TEMPO abstracts a hydrogen atom from a phenolic OH group of amphiphilic calixarene **7**, and the hydroxylamine TEMPOH formed yields a stable inclusion complex with another molecule of **7**.<sup>26</sup>

Rathore et al. synthesized and characterized a modified 1,3-alternate calixarene derivative **29** that allows the preparation of a stable cation radical of **29** via chemical or an equivalent electrochemical oxidation, and for the first time the isolation of a stable cation radical that binds a single molecule of nitric oxide deep within its cavity with remarkable efficiency for use as a colorimetric sensor of nitric oxide.<sup>27</sup> Swager et al. demonstrated that stable  $\pi$ -dimers are formed upon oxidation of calixarenes **31** and **32** converted to radical cations.<sup>28</sup> As expected, bis(radical cation) **30**<sup>2(+)</sup> was ESR-active because **30**<sup>2(+)</sup> consists of two independent radical cations. In contrast, **31**<sup>2(+)</sup> was almost ESR-silent, which indicates that the two radical cations are bound to form a  $\pi$ -dimer which is dependent upon the conformational flexibility of the calixarene hinge. Reinaud et al. designed novel calixarenes **33** and **34**.<sup>29</sup> An X-ray structure along with the electrochemical, ESR and UV–vis spectroscopic studies revealed that **33** or **34** allows the formation of a calixarene system in that it associates a metal ion (Cu<sup>2+</sup> or Zn<sup>2+</sup>), an aryloxy radical and a hydrophobic cavity leading to a supramolecular redox active assembly. The oxidative activity appears highly controlled by the supramolecular system hence providing a good model for radical enzymes such as Galactose oxidase. Liu et al. investigated the binding behaviors and thermodynamic origins of **35** and **36** with methyl viologen (MV<sup>2+</sup>) by isothermal titration calorimetry, NMR, and cyclic voltammetry, showing that the binding abilities of **35** and **36** and their host selectivity are dramatically pH-controlled.<sup>30</sup> Moreover, the radical form of MV<sup>+</sup> upon one-electron reduction can also be effectively included by **35** and **36**.

Intramolecular electron-transfer processes of calixarene derivatives have been studied in recent research. Ikeda et al. investigated a photoinduced electron transfer between C<sub>60</sub> connected with homooxa[3]calixarene and a molecule obtained by the protonation of *N*-(3-aminopropyl)-*N*-methylaniline (ammonium aniline), in which the ammonium moiety is included in

the calixarene.<sup>31</sup> By connecting it with calixarene, C<sub>60</sub> is given the ability to interact with the primary alkylammonium. When a selective pulse laser irradiates the C<sub>60</sub> moiety of the calixarene/ammonium aniline system, formation of C<sub>60</sub><sup>•–</sup> was observed in high quantum yield. Biczók et al. studied the interaction of triplet excited C<sub>60</sub> with **1–3** and with their 2,4,6-trimethylpyridine and pyridine complexes with laser flash photolysis experiments.<sup>32</sup> It has been found that in polar solvents triplet C<sub>60</sub> is only quenched by **2** via electron transfer, producing C<sub>60</sub><sup>•–</sup> radical anion. Recently, the photochemical reactions of methylene blue (MB) included in water soluble calixarenes **5**, **35**, and **37** have been studied by Murai et al. using time-resolved ESR.<sup>33</sup> The chemically induced dynamic electron polarization (CIDEP) spectra showed the formation of a complex radical pair composed of the MB monocation radical and calixarene (phenoxy) radical. The lifetime and broadened spectral shape are dependent on the size of the calixarene and are due to the longitudinal and transverse relaxation mainly induced by the tumbling motion of the radical pair with spin dipole–dipole interaction.

### ◆ Polyradicals Based on Calixarene Rings and Others

Very high-spin organic molecules provide intellectual challenge and contribute to the understanding of organic magnetism. Calixarenes have been attracting much attention also in the chemistry of molecular magnetism because the 1,3-phenylene moiety acts as a ferromagnetic coupler.<sup>34</sup> Therefore a variety of calixarene polyradicals in a high-spin ground state have thus far been synthesized.<sup>35–38</sup> Rajca et al. designed polyarylmethyl high-spin polyradicals **38** with a large density of crosslinks and alternating connectivity of radical modules with unequal spin quantum numbers (*S*) between calix[4]arene macrocycles, macrocyclic *S* = 5/2 and, crosslinking *S* = 1/2 modules, which permits large net *S* values for either ferromagnetic or antiferromagnetic exchange couplings between the modules.<sup>39,40</sup> They have found an effective magnetic moment corresponding to an average *S* of about 5000 and slow reorientation of the magnetization by a small magnetic field (less than or equal to 1 Oersted) below a temperature of about 10 K. Qualitatively, this magnetic behavior is comparable to that of insulating spin glasses and blocked superparamagnets.<sup>40</sup>

Investigations of analogs of calixarenes and free radicals have been carried out. Jeppesen et al. studied complexation between bis(tetrathiafulvalene)–calix[2]pyrrole[2]thiophene **39** and 7,7,8,8-tetracyanoquinodimethane (TCNQ) in solution using absorption and ESR spectroscopy as well as in the solid state using X-ray crystallography and IR spectroscopy.<sup>41</sup> The ESR spectrum recorded on a 1:1 mixture of **39** and TCNQ showed a weak radical signal, which is in the region characteristic for both a tetrathiafulvalene (TTF) radical cation and a TCNQ radical anion. This indicated that in solution some charge transfer takes place between the TTF unit(s) and TCNQ. Rebek et al. reported the synthesis and structure of paramagnetic resorcinarene with four TEMPO units **40**.<sup>42</sup> A change in the line shape of the ESR signal of **40** compared with monomeric 4-aminoTEMPO indicates the presence of a weak exchange interaction between spins similar to that seen in nitroxides at high concentration. The average distances between the radicals of **40** are decreased by

the conformational change induced by binding of guests such as CH<sub>3</sub>CN in the cavity, the effects of exchange are further increased to significantly modulate the ESR line shape. Tsue et al. have synthesized and investigated a series of azacalixarenes.<sup>43</sup> The ESR measurements were performed on the mono-cation radical **41**<sup>+</sup> generated in situ by electrochemical oxidation and for dication radical **41**<sup>2(+)</sup> formed by chemical oxidation, then the first observation of the doublet and triplet ground state of azacalixarene cation radicals were ensured by the radical stability arising from a combination of steric protection and spin-delocalization.<sup>44</sup>

## ◆ Concluding Remarks

In the present review, recent progress in the chemistry of calixarene and free radicals, such as inclusion, spin label, reaction, and ESR studies, are described. Based on the sensitivity of radicals to conformational flexibility of calixarenes, the radicals can be considered as spin probes to provide important information on structures and conformational changes of calixarenes through inclusion complexes of radicals or spin labels. Moreover, very interesting multispin-labeled calixarenes and polyradical calixarene skeletons obtained by chemical modification should provide chances to study magnetic interaction and develop potential applications. In contrast to other fields of calixarene chemistry, however, calixarene chemistry associated with free radicals is much less explored. In the future, it is expected to be a significant frontier to design more precisely and synthesize more multispin-labeled calixarenes and polyradical calixarene skeletons, because not only it is important and useful for theoretically studying magnetic behavior, but also it should be an important field of developing and application of single-molecule magnets, molecular magnetic devices, magnetic sensors, and other organic magnetic materials. Of course, much work is still to be done requiring the imagination and ingenuity of researchers to further advance the field of calixarene chemistry associated with free radicals.

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