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# The Suzuki–Miyaura reaction as a tool for modification of phenoxy-nitroxyl radicals of the 4*H*-imidazole *N*-oxide series†

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2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-5-(4-iodophenyl)-4,4-dimethyl-4*H*-imidazole 3-oxide reacts with phenylboronic acid and its substituted derivatives in a cross-coupling reaction of the Suzuki–Miyaura type to form 5-biphenyl derivatives of 4*H*-imidazole-*N*-oxide. Interaction of the same compound with B<sub>2</sub>(pin)<sub>2</sub> in the presence of PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub> proceeds through the formation of intermediate 1,3,2-dioxaborolane and leads to the product of homocoupling: biphenyl-bis(imidazole). Oxidation of the resultant imidazoles with lead dioxide quantitatively yields stable conjugated phenoxy-nitroxyl mono- and diradicals, which are of interest as electroactive paramagnetic materials. The crystal structure of the monoradical, 2,6-di-*tert*-butyl-4-[1-oxido-4-(biphenyl-4-yl)-5,5-dimethyl-1*H*-imidazole-2(5*H*)-ylidene]cyclohex-2,5-dienone, its magnetic susceptibility, EPR spectra of the obtained hybrid radicals in solution, and cyclic voltammetry characteristics of 4*H*-imidazoles were studied.

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## Introduction

The cross-coupling reaction of the Suzuki–Miyaura type<sup>1</sup> can be undoubtedly considered as one of the fundamental methods for constructing aromatic and heteroaromatic ensembles in the synthesis of biologically active compounds for pharmaceutical chemistry<sup>2</sup> as well as in the chemistry of new materials (preparation of components of optoelectronic devices<sup>3</sup> and liquid-crystalline semiconducting oligomers<sup>4</sup>) and in organic photovoltaics.<sup>5</sup> Recent research on the Suzuki–Miyaura reaction includes extensive studies of various substrates involved in this process (for example, low-reactive aryl chlorides, aryl fluorides, or tosylates),<sup>6</sup> a wide range of reagents (boronic acids and their derivatives),<sup>7</sup> and several generations of palladium catalysts with different ligand environments.<sup>8</sup>

Continuing the research on the reactivity of new stable radicals, *i.e.*, hybrid phenoxy-nitroxides of the 4*H*-imidazole *N*-

oxide series (Chart 1),<sup>9</sup> we turned our attention to the possibility of modifying the *para*-haloaryl group at the 5th position of the heterocycle using Pd-catalyzed cross-coupling reactions, in particular, the Suzuki–Miyaura process.

On the one hand, the introduction of an electron-withdrawing type of substituent possessing an –M-effect into the *para*-position of the 5-aryl moiety should lead to the additional stabilization of the radical center owing to further distribution of the electron density of an unpaired electron over the conjugated system. On the other hand, further functionalization of hybrid radicals means developing their practical

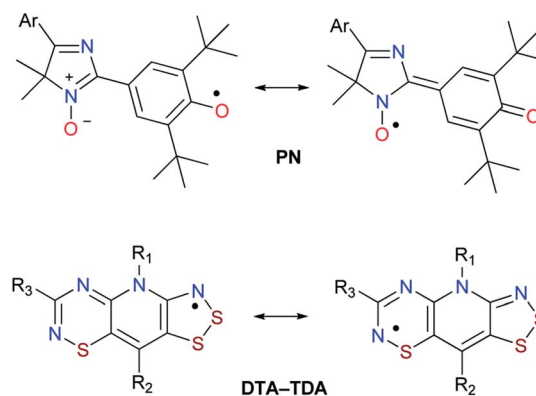


Chart 1 Examples of stable hybrid radicals: 4*H*-imidazole *N*-oxide based phenoxy-nitroxides (PN); 1,2,3-dithiazolo-1,2,4-thiadiazinyls (DTA-TDA).

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applicability because of creation of new promising dyadic and triadic molecular systems.

While developing fundamentally new smart devices based on fully organic materials, researchers have become more interested in the design and construction of dyads and triads of DA (donor–acceptor) or ADA (acceptor–donor–acceptor) types, where the group containing a stable radical moiety plays the role of the acceptor.<sup>10</sup> These systems can be considered molecular switches (transforming from a neutral state to a zwitterionic or diradical form in solution under the influence of external stimuli, *i.e.*, temperature, pressure, or light), and some of them can have properties of conductors in a solid form.<sup>11</sup> Typical examples of such dyads and triads are shown in Chart 2.

As for stable hybrid radicals, only a few representatives of this type of paramagnetics were synthesized by scientists in the last decade. For instance, resonance-stabilized planar 1,2,3-dithiazolo-1,2,4-thiadiazinyl<sup>12a</sup> (Chart 1) and related radicals<sup>12b</sup> possess highly delocalized and easily tuned spin distributions. Therefore, the wide range of physical and chemical properties of thiazyl-based radicals make them useful building blocks for magnetic and conductive materials as well as coordinating ligands.

Depending on the kinetic stability of radical types, there are two fundamentally different methods for their functionalization. The first method represents the interaction of their diamagnetic precursors directly along a reactive group with various nucleophilic or electrophilic reagents, and the radical center is generated at the final stage, when the product is treated with an oxidizing agent (or an excess of an electrophilic reagent). The second method consists of treating the stable

radical with a mild selective reagent whose redox potential cannot change the paramagnetic status of the substrate. In this respect, a study on Pd-catalyzed C–C cross-coupling reactions (particularly, the Suzuki–Miyaura process) involving various types of persistent radicals was carried out here under the conditions of both methods.

For example, thermally unstable nitroxyl radicals stabilized by nitroxyl group conjugation with the benzene nucleus (*t*-butylaryl, tetrahydroquinolinyl, [3,1]-benzoxazinyl, and dihydroacridinyl type) were introduced into the Suzuki–Miyaura reaction in the form of their stable precursors, namely, secondary amines. After formation of the cross-coupling products, the latter were transformed into target nitroxides with *m*-CPBA in a yield of 37–70%.<sup>13</sup> At the same time, more robust iodoarene derivatives of the benzotriazinyl radical (Blatter's radical),<sup>14a–c</sup> verdazyl radical,<sup>14d</sup> and iso-indolinoyls<sup>14e</sup> readily reacted in cross-coupling with either arylboronic acids or aryltriolborate salts, which in contrast to parent acids possess greater reactivity. Depending on the number of iodoarene groups in these radicals, mono-, bis-, and tris-cross-coupling products were obtained without losing a radical center. The yields ranged from 97% for the mono-cross-coupling product to 67% for bis- and 52% for the tris-phenyl-substituted compound. As to the cyclic nitroxide based on an imidazole nucleus, to the best of our knowledge, there is only one report about the Suzuki–Miyaura reaction involving nitronyl nitroxyl radicals containing an *ortho*(*meta*)-iodophenyl group at the C-2 atom of the heterocycle. The authors explained a rather low yield of cross-coupling products in this reaction (40–43% for the *ortho*-iodophenyl derivative and 44% for the *meta*-iodophenyl derivative) by competitive destruction of a nitronyl nitroxide occurring at the elevated temperature under typical conditions of the Suzuki process (80 °C, 2 h).<sup>15</sup>

Accordingly, it was interesting to find out how hybrid phenoxyl-nitroxide radicals would behave under the conditions of the Suzuki–Miyaura reaction and whether they would be sufficiently stable to retain the paramagnetic center. Besides, Pd-catalyzed cross-coupling reactions involving 5-(haloaryl)-4*H*-imidazole derivatives and their *N*-oxides are not mentioned in any databases.

## Results and discussion

To conduct cross-coupling experiments, the *para*-iodoarene substituted derivative of 4*H*-imidazole *N*-oxide was chosen as a model substrate because solely iodo derivatives show the greatest reactivity among other haloaryl compounds and produce quantitative yields of biphenyls under the classical Suzuki reaction conditions.

A diamagnetic precursor of the hybrid radical, key 5-(*p*-iodophenyl)substituted 4*H*-imidazole 3-oxide **1**, was synthesized in 6 stages based on Friedel–Crafts acylation of an iodo-benzene excess with iso-butyric acid chloride followed by bromination of 4-iodo-iso-butyrophenone **2**, treatment of bromo compound **3** with hydroxylamine, and hydrolysis of the formed 2-hydroxylamine oxime **4** by boiling with concentrated hydrobromic acid. Condensation of the obtained salt of 2-

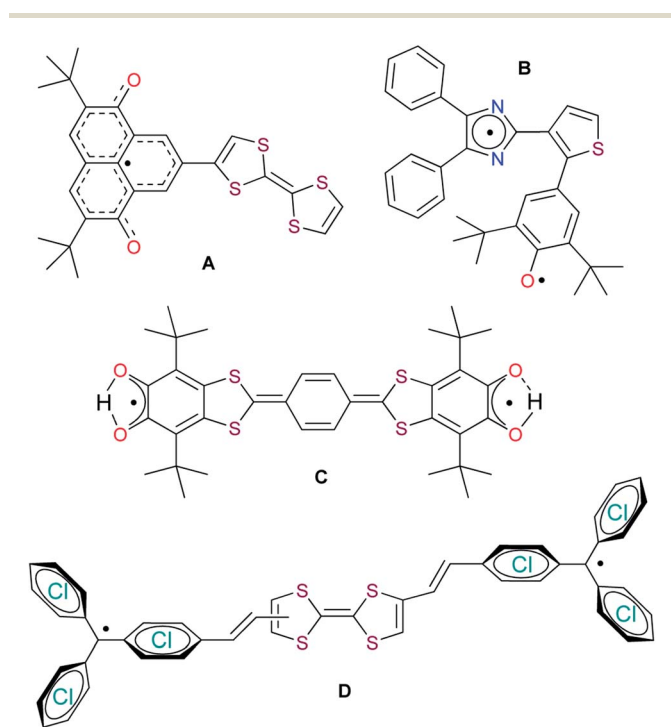
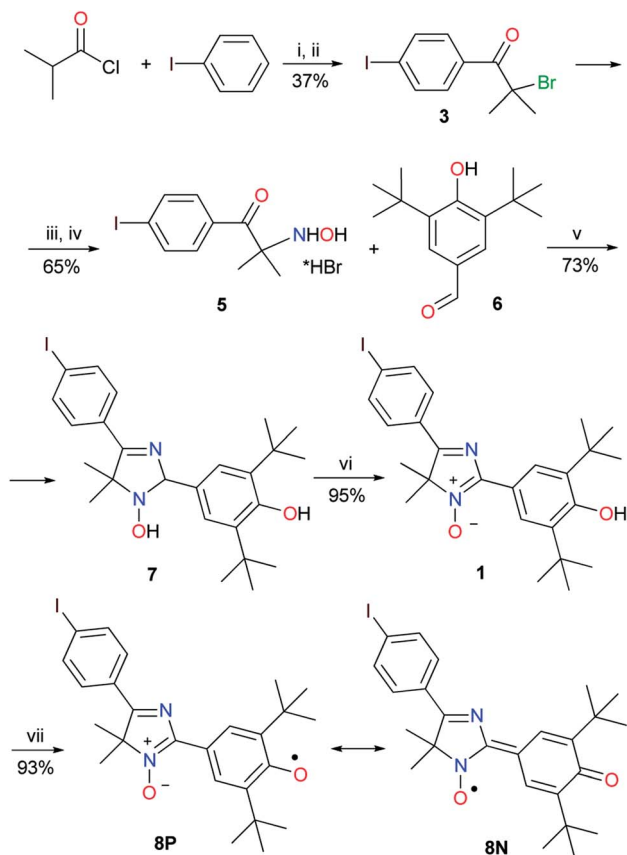


Chart 2 Some electroactive and photoactive dyads and triads based on stable radicals: oxophenalyloxyl (A),<sup>10i</sup> phenoxyl-imidazolyl (B),<sup>10d,f</sup> di-*tert*-butyl-*ortho*-semiquinonyl (C),<sup>10e,g</sup> and trityl (D).<sup>10b</sup>





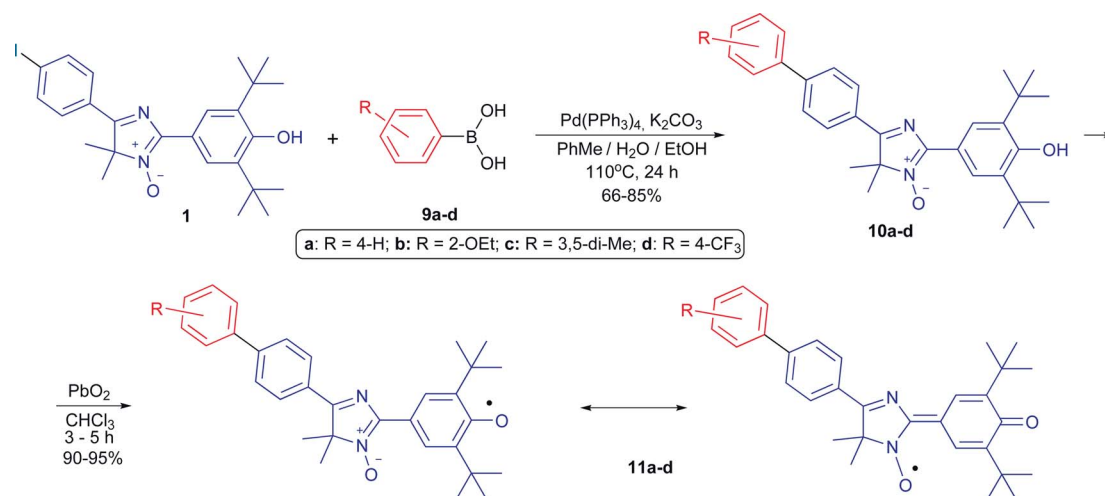
**Scheme 1** Reagents and conditions: (i)  $\text{AlCl}_3$ , 45 °C, 15 h; (ii)  $\text{Br}_2$ ,  $\text{Et}_2\text{O}$ /dioxane, room temperature (rt), 2 h; (iii)  $\text{NH}_2\text{OH} \times \text{HCl}$ ,  $\text{NaOH}$ ,  $\text{MeOH}/\text{H}_2\text{O}$ , 65 °C, 7 h; (iv) 48%  $\text{HBr}$ ,  $\Delta$ , 2 h; (v)  $\text{NH}_4\text{OAc}$ ,  $\text{MeOH}$ , rt, 6 h; (vi)  $\text{MnO}_2$ ,  $\text{CHCl}_3$ , rt, 7 h; and (vii)  $\text{PbO}_2$ ,  $\text{CHCl}_3$ , rt, 2 h.

hydroxylamino ketone **5** with 4-hydroxy-3,5-di-*tert*-butylbenzaldehyde **6** in the presence of ammonium acetate led to 2,4-diaryl-2,5-dihydroimidazole **7** with a good yield, and oxidation of **7** with air oxygen in the presence of  $\text{Cu}(\text{OAc})_2$  or a manganese

dioxide excess (the second method is preferable because the yield of 4*H*-imidazole *N*-oxide is quantitative in this case) gave compound **1** (Scheme 1). Hybrid phenoxyl nitroxyl radical **8** was formed with a yield of more than 90% when imidazole **1** was treated with a threefold excess of  $\text{PbO}_2$ .

At first, this radical **8** was introduced into the typical Suzuki cross-coupling reaction under standard classical conditions (arylboronic acid **9d**,  $\text{Pd}[(\text{PPh}_3)_4]$  (5 mol%),  $\text{K}_2\text{CO}_3$ , a two-phase system (toluene–water), 110 °C, argon atmosphere). Heating the mixture for 24 h caused the solution to lose its dark brown color typical for the conjugated radical, then disappearance of the EPR signal and formation of a single product, bright yellow diamagnetic 5-biphenyl-4*H*-imidazole *N*-oxide **10d**, in a quantitative yield. Oxidation of the obtained compound with lead dioxide in chloroform smoothly led to corresponding stable phenoxyl-nitroxyl radical **11d**. Thereafter, its immediate precursor, phenolic imidazole **1**, was introduced into the cross-coupling reaction to reduce the total number of steps necessary to synthesize new biphenyl derivatives of the hybrid radical. Thus, compound **1** was involved in the Suzuki–Miyaura reaction with various arylboronic acids possessing both donor and acceptor groups (Scheme 2). Regardless of the nature of substituents in the reagent and its steric features, conversion of imidazole **1** was complete, and cross-coupling products **10a–d** were obtained in good yields (66–85%). Apparently, the presence of a sterically hindered phenolic group in the substrate did not inhibit the cross-coupling process, nor did it have a significant effect on the reaction yields. It should be noted that transformation of biphenyl derivatives of **10a–d** into phenoxyl-nitroxide radicals starts even when their solutions are kept in ambient air, whereas oxidation of 4*H*-imidazoles **10a–d** with lead dioxide ends within a few hours, and hybrid radicals **11a–d** form quantitatively (Scheme 2).

Cyclic voltammograms of the 4*H*-imidazoles **10a–d** are presented in Fig. 1. All the compounds show similar redox behavior consisting of irreversible oxidation and reduction features. Apparently, oxidation of starting phenol-imidazole **10** proceeds



**Scheme 2** The Suzuki cross-coupling reaction of 4*H*-imidazole *N*-oxide **1** with substituted arylboronic acids and the synthesis of biphenyl derivatives of hybrid phenoxyl-nitroxide.



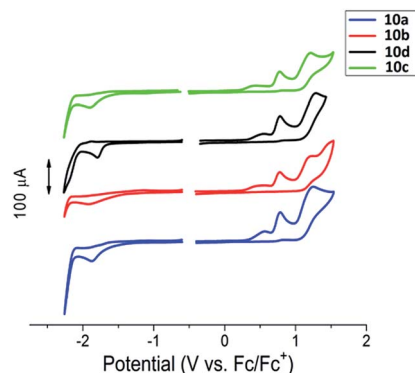


Fig. 1 Cyclic voltammograms for cross-coupling products, 4*H*-imidazoles **10a–d** in a CH<sub>3</sub>CN solution. Potentials calibrated vs. Fc/Fc<sup>+</sup>.

via irreversible step-by-step formation of galvinoxyl radical **I**, quinoid cation **II**, and dication radical **III**, respectively (Scheme S1 in ESI<sup>†</sup>). The reduction step consists only of an irreversible peak, which corresponds to the formation of anion-radical **IV**. Oxidation and reduction peaks are listed in Table S1, ESI<sup>†</sup>.

EPR spectra of all the obtained hybrid radicals contain a set of 21 lines, characterized by a triplet form consisting of 7 lines in each segment due to the interaction of the unpaired electron with two nonequivalent nitrogen nuclei (with the isotropic hyperfine splitting (hfs) constants  $A_{N1} = 0.541$  mT and  $A_{N2} = 0.061$  mT, respectively) and with two nonequivalent protons in the molecular quinone fragment (hfs constants  $A_{H1} = 0.161$  mT,  $A_{H2} = 0.149$  mT) (Fig. 2 and S2–S4 in ESI<sup>†</sup>). The hfs constants for “distant” protons of the biphenyl moiety are negligible, indicating the absence of noticeable spin density delocalization on the aryl substituent at the C-4 position of the heterocycle.

We succeeded in growing suitable single crystals of unsubstituted biphenyl derivative **11a** for X-ray crystallographic

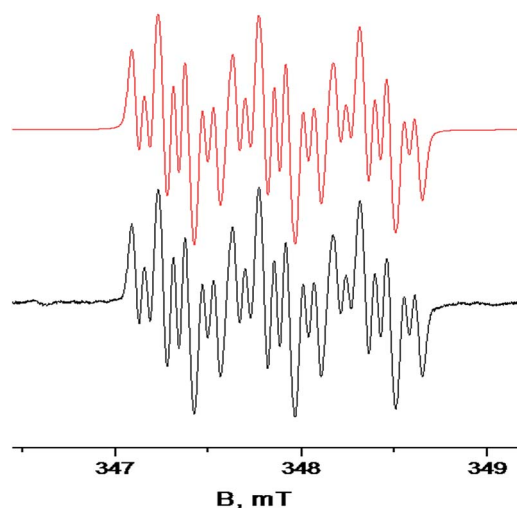


Fig. 2 An ESR spectrum of 4-biphenyl-substituted hybrid radical **11a**, recorded at 20 °C in a degassed toluene solution; the black curve is the experimental spectrum, the red curve is its mathematical reconstruction;  $g_{iso} = 2.0059$ ,  $A_{N1} = 0.541$  mT,  $A_{N2} = 0.061$  mT,  $A_{H1} = 0.161$  mT,  $A_{H2} = 0.149$  mT.

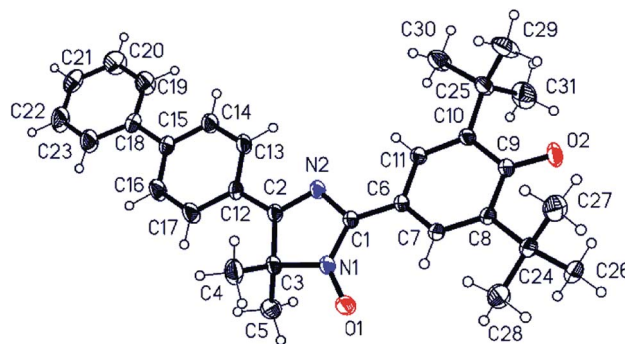


Fig. 3 Molecular structure (an ORTEP diagram with 30% ellipsoid probability) and atom numbering of hybrid phenoxyl-nitroxide **11a**. Selected bond lengths (Å): N1–O1 1.270(3), N1–C1 1.354(3), N2–C1 1.395(3), N2–C2 1.296(3), C2–C3 1.511(4), N1–C3 1.502(3), C1–C6 1.409(3), C6–C7 1.420(3), C7–C8 1.357(3), C8–C9 1.477(4), C9–O2 1.246(3), C2–C12 1.464(3), and C15–C18 1.489(4). Valence angles (°): N1–C1–N2 109.6(2), C1–N1–C3 110.2(2), C1–N2–C2 109.3(2), and C2–C3–N1 98.1(2). Torsion angles (°): N1–C1–C6–C7  $-6.6(4)$ , N2–C2–C12–C13  $-1.5(4)$ , and C14–C15–C18–C19  $8.0(5)$ .

analysis (Fig. 3). The best solvent for these hybrid radicals seemed to be dipolar aprotic acetonitrile having a high dielectric constant. It should be noted that if solutions of radicals are kept long in a nonpolar solvent at room temperature, then these radicals partially decompose.

Among notable features of the molecular structure of radical **11a** are characteristic lengths of the C–O bond (1.246(3) Å) and C–C bond connecting imidazole and quinoid rings (1.409(3) Å). The first one is equal to the same C–O bond of 2,4,6-tri-*tert*-butylphenoxy radical<sup>16</sup> and very slightly differs from that of the C–O bond in related biradicaloids (1.252 Å (ref. 17*a*) and 1.241 Å,<sup>17*c*</sup> respectively) but significantly differs from C=O bond length in diamagnetic 3,5,3',5'-tetra-*tert*-butyl-4,4'-diphenoquinone (1.228 Å).<sup>18</sup> The second one is the typical “one-and-half” bond with the length close to that of the “bridge bond” C=C (1.408 Å) of conjugated phenoxy radical galvinoxyl<sup>19</sup> and the C=C bond (1.403 Å) between phenoxy and heterocyclic moieties in biradicaloid QBT.<sup>17*c*</sup> The data above suggest that a radical molecule should exist mostly in the phenoxy form in a solid state. Although the imidazole and both biphenyl rings are plane within the margin of experimental error, the quinoid ring is slightly distorted [ $\pm 0.040(3)$  Å], with C9 and O2 atoms deviating from the quinoid ring plane by 0.051(3) and 0.186(2) Å, respectively. The tetracyclic frame of **11a** is virtually flat; for example, dihedral angles between imidazole and adjacent rings are 5.8° for the phenoxy ring and 1.2° for an aryl unit of biphenyl. The torsion angle between ring planes in the biphenyl moiety is 7.2°. Such planarity of the tetracyclic moiety is appropriate for formation of 0D supramolecular unity, namely a dimer of molecules, via an interaction of plane  $\pi$ -systems (Fig. 4 and Table S2 in ESI<sup>†</sup>) through “head-to-head” stacking. The molecular dimers in turn interact with the nearest ones via weak C17–H $\cdots$ O2 hydrogen bonds (Table S2 in ESI<sup>†</sup>) binding them along two directions into layers parallel to plane (1, 0,  $-2$ ). There are no short interatomic distances between the layers.



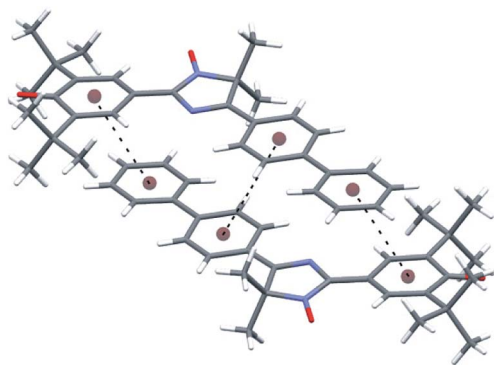


Fig. 4 The pair of molecules of compound **11a** associated by  $\pi$ - $\pi$  interactions.

Assessment of magnetic features of biphenyl radical **11a** showed that at 300 K,  $\mu_{\text{eff}}$  was  $1.73 \mu_{\text{B}}$ , in good agreement with the theoretical spin value  $\mu_{\text{B}}$  (Fig. 5) for one paramagnetic center with spin  $S = 1/2$  for a  $g$ -factor equal to 2. Intermolecular exchange interactions are weak.

Having such a reactive substrate as imidazole **1**, we were tempted to try it in the self-coupling reaction to obtain a symmetric biphenyl compound bearing *4H*-imidazole moieties at positions C-4 and C-4', *i.e.*, to carry out a reaction of the following type:  $2\text{Ar-I} + \{\text{M}\} \rightarrow \text{Ar-Ar} + \text{MI}_2$ . This approach would allow us to synthesize another interesting type of a paramagnetic substance, namely, a symmetrical hybrid diradical, which has not been known previously. Similar compounds, for example, molecules formed by quinonoidal residues conjugated with donor bridging fragments, switch to the biradicaloid state under the influence of external stimuli (*e.g.*, temperature).<sup>17</sup> As reported recently, they could substantially increase the power conversion efficiency of organic photovoltaic systems if used in small quantities (0.3–0.6 wt%) as additives.<sup>20</sup> There is another class of stable diradicals, bis(nitronyl nitroxides), and their paramagnetic nuclei interact with each other through a rigid  $\pi$ -

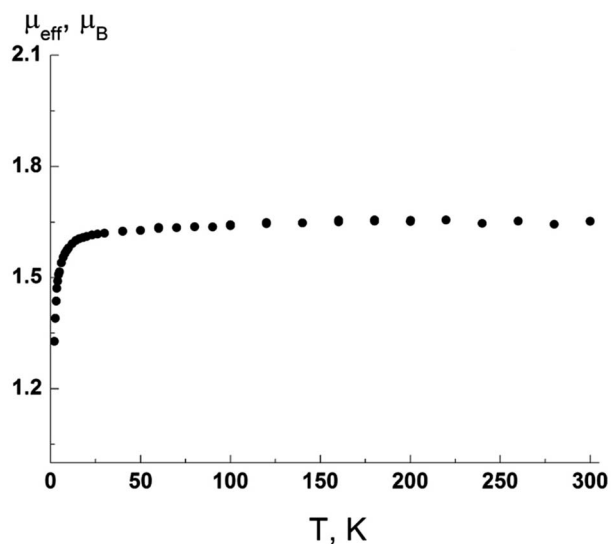


Fig. 5 Experimental  $\mu_{\text{eff}}$  ( $T$ ) dependence for radical **11a**.

linker; they are of interest as weakly antiferromagnetically coupled spin-dimers with a singlet ground state that can be turned into a triplet state in a magnetic field.<sup>21</sup>

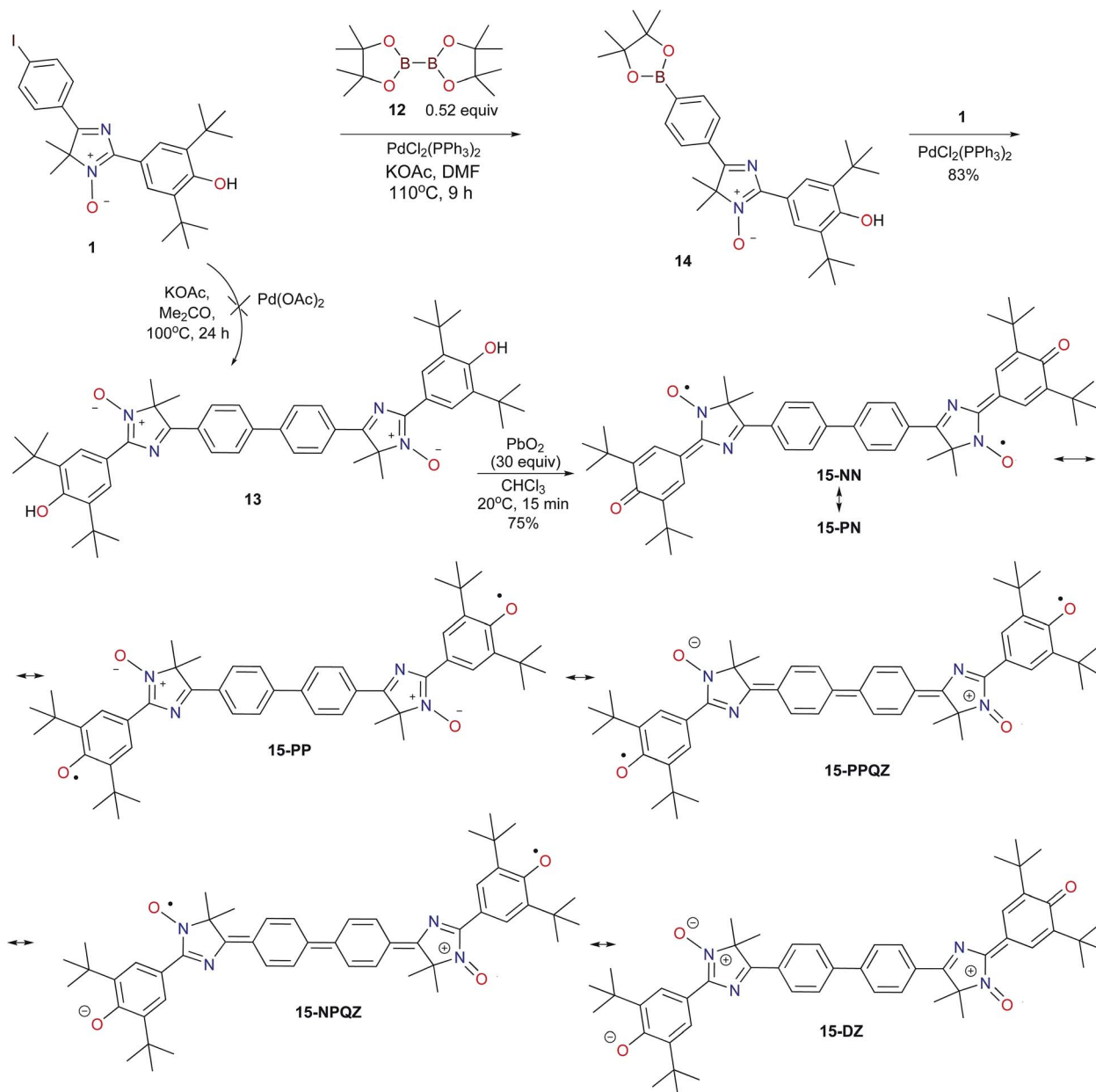
To obtain the desired diradical based on imidazole **1**, we tried to employ the recently developed palladium-catalyzed version of the Ullmann-type reaction, which proceeds with iodoarene derivatives without phosphine ligands in the presence of palladium and potassium acetates under aerobic conditions.<sup>22</sup> Nevertheless, under reductive coupling conditions described by those authors (10 mol%  $\text{Pd}(\text{OAc})_2$ , 5 equiv. of  $\text{AcOK}$ ,  $\text{Me}_2\text{CO}$ , 100 °C), imidazole **1** remained unchanged even after 24 h heating in a sealed ampoule.

Earlier, Higuchi and Kurth proposed practical one-pot synthesis of dimeric polyheterocycles, bis(terpyridines), which involves forming the corresponding boronic ester from 4'-(*para*-bromophenyl) terpyridine *via* the Miyaura reaction, followed by the Suzuki reaction of the appropriate bromo derivative under specially selected and controlled conditions (temperature, the solvent, base, quantity of the boron reagent, and Pd catalyst).<sup>23</sup> We tested a similar tandem process involving tricyclic iodo derivative **1** under conditions that allowed us to avoid the use of strong bases. Indeed, the interaction of two equivalents of *4H*-imidazole **1** with bis(pinacolato)diboron **12** and potassium acetate as a base in the presence of dichlorobis(triphenylphosphine)palladium in dimethylformamide (DMF) with heating to 110–115 °C resulted in formation of a dark orange precipitate of homocoupling product **13** (Scheme 3). This reaction is likely to proceed with the formation of an intermediate (2-aryldioxaborolane **14**) which then reacts with an excess of substrate **1**, leading to biphenyl derivative **13**. Indeed, 1,3,2-dioxaborolane **14** was isolated as the dominant product in the temperature-controlled process *via* the interaction of *4H*-imidazole **1** with a slight excess of  $\text{B}_2(\text{pin})_2$ . Its structure was proved unambiguously by a combination of elemental analysis data and  $^1\text{H}$ ,  $^{13}\text{C}$ , and  $^{11}\text{B}$  NMR spectra.

Obtained biphenyl bis(imidazole) **13** was poorly soluble in conventional organic solvents (alcohols, halocarbons, DMF, or DMSO); therefore, it can be isolated from the reaction mixture quantitatively. To separate the precipitated product from palladium compounds and inorganic impurities, we performed the Soxhlet hot extraction by boiling the precipitate with chloroform. Again, heating compound **13** in an oxygen atmosphere resulted in staining the solution with a dark orange color, as was the case for biphenyl imidazole derivatives **10**. Evidently, the staining was due to the formation and accumulation of stable phenoxyl-nitroxyl radicals (TLC control). To prove the dimeric structure of the obtained product, we used NMR spectroscopy along with elemental analysis data.

Thus, signals typical for a symmetrical structure were observed in the spectra of bis(imidazole) **13** in a trifluoroacetic acid solution. For example, singlets of *gem*-methyl and *t*-butyl groups shifted downfield to 2.06 and 1.57 ppm, respectively, in the proton spectrum of compound **13**. Protons of the biphenyl part represent the AA'BB' system with doublets at 8.05 and 8.51 ppm. The  $^{13}\text{C}$  NMR spectrum of **13** is even more remarkable in this respect (downfield shifting of several signals). Thus, low-field signals at 166.0 and 194.3 ppm were attributed to





Scheme 3 The Suzuki–Miyaura homocoupling reaction involving 4*H*-imidazole *N*-oxide **1** and preparation of symmetrical hybrid diradical **15**.

carbon atoms respectively associated with nitrogen atoms of nitron and imino groups of the heterocycle (which corresponds to the downfield shifting of these signals by 18–19 ppm). Apparently, the covalent interaction of bis(imidazole) **13** with trifluoroacetic acid contributes to the downfield shifting of signals of the  $^1\text{H}$  and  $^{13}\text{C}$  nuclei.  $\text{CF}_3\text{COOH}$  is known to be capable of protonating a number of organic compounds, for instance, ketones, various imino derivatives, and cyclic nitrones, by shifting an appropriate carbon signal of the double  $\text{C}=\text{X}$  bond in the  $^{13}\text{C}$  NMR spectrum into a low field from 1.5 to 27.5 ppm.<sup>24</sup>

The oxidation of biphenyl bis(imidazole) **13** with a large excess of lead dioxide (20–30 equiv.) in a dilute chloroform solution for 15–30 min resulted in complete conversion of

bis(phenol) **13** and formation of hybrid diradical **15**, which was isolated in a high yield by gentle evaporation of the reaction solution in a solid form as a dark brown powder. We found that compound **15** could be purified by flash chromatography on silica gel without any noticeable decomposition. The diradical is highly soluble in chlorinated solvents (methylene chloride, chloroform, and  $\text{CCl}_4$ ) but is virtually insoluble in nonpolar or protic/aprotic solvents (hexane, ether, ethanol, and acetone). The use of other oxidizing systems to transform bis(phenol) **13** (for example, DDQ or an aqueous alkaline solution of potassium ferricyanide) also led to the preferential formation of compound **15**, but there was significant accumulation of impurities in this case. Isolated from chloroform, the diradical is a crystal solvate containing one molecule of the solvent. A peak at  $m/z$  782.4 with



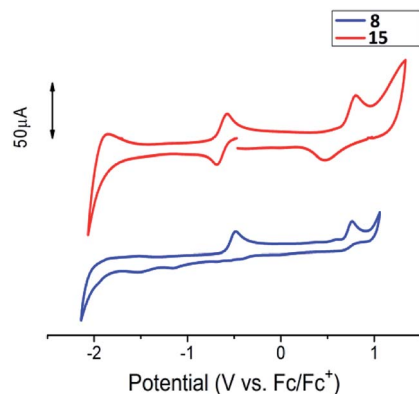


Fig. 6 Cyclic voltammograms for monoradical **8** and diradical **15** in a  $\text{CH}_3\text{CN}$  solution.

the intensity of  $\sim 4\%$  corresponding to the  $[\text{M} + 2]$  ion (Fig. S5 in ESI $^\dagger$ ) is observed in the high-resolution mass spectrum of diradical **15**. It is worth noting that all the previously obtained hybrid monoradicals in their high-resolution mass spectrum are characterized by an  $[\text{M} + 1]$  ion. Other characteristic signals in the mass spectrum of compound **15** are ions at  $m/z$  766 (12%) and 750 (18%), corresponding to a sequential loss of one and two oxygen atoms by the diradical molecule.

It should be noted that this is the first example of formation of a stable dimeric phenoxyl-nitroxide that can apparently exist in various hybrid forms (**15-NN**, **15-NP**, and **15-PP**), including exotic biradical species with a zwitterionic structure whose charged parts are separated by the diphenoquinone linker (**15-PPQZ** and **15-NPQZ**) as well as diamagnetic zwitterionic structure **15-DZ** (Scheme 3).

Comparative cyclic voltammograms of radicals **8** and **15** are presented in Fig. 6. Iodine-substituted radical **8** yields two irreversible one-electron oxidation peaks at  $-0.48$  and  $0.76$  V, which correspond to formation of the oxoammonium cation and radical dicationic species. Nonetheless, diradical **15** undergoes reversible two-electron oxidation at  $E_{1/2} = -0.63$  V forming a dioxammonium feature (Scheme S2 in ESI $^\dagger$ ). Further oxidation of dioxammonium dication proceeds quasi-reversibly at  $0.80$  V.

The EPR spectral and structural characteristics of this unusual diradical and its magnetic analysis will be the subject of our future study and deserve a separate publication.

## Conclusions

Thus, we showed that 5-(*para*-iodophenyl)-4,4-dimethyl-2-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-4*H*-imidazole 3-oxide possessing high reactivity in Pd-catalyzed processes can readily react with various arylboronic acids as well as bis(pinacolato)diboron in one-pot tandem synthesis with formation of the corresponding biphenyl derivatives in high yields. The products can be easily oxidized to stable hybrid mono- and diradicals of the phenoxyl-nitroxyl series. We are planning to extend this approach to other types of cross-coupling (*e.g.*, the Stille reaction<sup>25</sup> and direct arylation of donor heterocycles<sup>26</sup>) to synthesize new dimeric

conjugated diradicals, corresponding to A–D–A triads in which the ter(quarter)phenyl or ter(quarter)thiophene core will be the donor linker. Obviously, the 1,3,2-dioxaborolane derivative of 4*H*-imidazole 3-oxide synthesized here can be applied to obtain asymmetric hetero diradicals bearing different types of a paramagnetic nucleus,<sup>27</sup> which are appealing as building blocks for functional materials, particularly, for creation of components of a quantum computer.

## Experimental

### General

Analytical-grade reagents and solvents were used, and reactions were monitored by TLC. Column chromatography and TLC were performed using Acros silica gel 60A (0.035–0.070 mm) and Sorbfil PTLC-AF-UV 254 (Russia), respectively. Mass spectra were registered on a DFS high-resolution mass spectrometer.  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were recorded on Bruker AV-300, AV-400, DRX-500 spectrometers at 300/400/500 and 75/100/125 MHz, respectively, for 1–5% solutions of compounds in  $\text{CDCl}_3$ ,  $\text{DMSO}-d_6$ , or  $\text{CF}_3\text{COOH}$  (for bis(imidazole) **13**). Residual proton signals from the deuterated solvents served as references [ $\text{DMSO}-d_6$  (2.50 ppm),  $\text{CDCl}_3$  (7.24 ppm), for  $^1\text{H}$  spectra].  $^{13}\text{C}$  NMR chemical shifts are reported in reference to an undeuterated residual solvent [ $\text{CDCl}_3$  (76.9 ppm) or  $\text{DMSO}-d_6$  (39.4 ppm)]. The assignment of signals of carbon atoms in  $^{13}\text{C}$  NMR spectra of 4*H*-imidazole derivatives **1** and **10a–d** was carried out on the basis of an earlier spectral study on the spectra of cyclic nitrones.<sup>28</sup> Fourier transform infrared (FT-IR) spectra were acquired in KBr pellets on a Bruker Vector-22. The UV-Vis spectra were obtained for EtOH solutions using a Hewlett-Packard HP 8453 spectrophotometer. Raman spectrum of diradical **15** was recorded with a Bruker Optics SENTERRA microscope spectrometer equipped with a 785 nm direct diode laser with  $1\text{ cm}^{-1}$  resolution and 25 mW laser power. The Raman shift range considered was between 170 and  $3000\text{ cm}^{-1}$ . Elemental analyses were performed on an automatic CNS analyzer Euro EA 3000. The melting points were determined on an FP 81 HT instrument, Mettler Toledo.

Cyclic voltammetry measurements were conducted in a  $\text{CH}_3\text{CN}$  solution on a computer-controlled P-8nano potentiostat/galvanostat (Elins, Russia) in combination with a three-electrode cell (Gamry);  $0.1\text{ M } n\text{-Bu}_4\text{NPF}_6$  was applied as a supporting electrolyte. Pt, a Pt wire, and Ag/AgCl served as a working, counter, and reference electrode, respectively. The reference electrode was calibrated by measurement of the redox potentials of ferrocene.

Arylboronic acids **9a–d**,  $\text{B}_2(\text{pin})_2$  (bis(pinacolato)diboron) **12**, and palladium catalysts were obtained from commercial sources (Acros Organics); 3,5-di-*t*-butyl-4-hydroxy-benzaldehyde **6** was synthesized according to a procedure described in the literature.<sup>29</sup> All the other reagents were purchased from Acros Organics or Alfa-Aesar.

Synthesis of key 2-(3,5-di-*t*-butyl-4-hydroxyphenyl)-5-(4-iodophenyl)-4,4-dimethyl-4*H*-imidazole 3-oxide **1**, its subsequent cross-coupling reactions, and oxidation of products are described in ESI $^\dagger$ .



## X-Ray structural analysis

The unit cell parameters and experimental intensities of radical **11a** were measured at 296(2) K with a Bruker Kappa Apex II CCD diffractometer with Mo K $\alpha$  radiation ( $\lambda = 0.71073$  Å) and a graphite monochromator. The structure was solved by direct methods and refined in an anisotropic (isotropic for H) approximation using the SHELX-97 software suite.<sup>30</sup> Positions of the hydrogen atoms were calculated and refined by means of the riding model. Analysis of the geometry and intermolecular interactions was carried out in the PLATON software.<sup>31</sup>

Crystallographic data of **11a**: $\ddagger$  C<sub>31</sub>H<sub>35</sub>N<sub>2</sub>O<sub>2</sub>, FW = 467.61, monoclinic,  $P2_1/c$   $a$  11.5429(7),  $b$  14.3317(8),  $c$  16.995(1) Å,  $\beta$  109.552(2)°,  $V$  2649.3(3) Å<sup>3</sup>,  $D_{\text{calc}}$  1.172 g cm<sup>-3</sup>,  $\mu(\text{Mo-K}\alpha)$  0.073 mm<sup>-1</sup>,  $F(000)$  1004.0, 50 398 measured reflections  $\theta_{\text{full}}$  31.19°, completeness 99.7% ( $\theta_{\text{max}}$ ), 7602 independent ( $R_{\text{int}}$  0.0558), 324 parameters,  $R_1$  0.0954 [for 5116 observed  $I > 2\sigma(I)$ ],  $wR_2$  0.3367 (all data), GooF = 1.308, largest diff. peak and hole 0.414 and -0.728 e Å<sup>-3</sup>.

## EPR spectrometry

Continuous-wave EPR spectra were acquired on a Bruker EMX spectrometer at room temperature in dilute ( $ca. 5 \times 10^{-5}$  M) toluene solutions degassed by means of repeated freeze-pump-thaw cycles. At modulation 0.01 mT@100 KHz and MW power 2 mW, the spectra were recorded as single slow scans ( $ca. 3$  h). Isotropic  $g$  values were determined using solid DPPH (2,2-diphenyl-1-picrylhydrazyl) as a standard and were found to be typical for cyclic nitroxides. The accuracy of determining hyperfine coupling constants and  $g$  values was estimated at 0.005 mT and 0.0001, respectively.

## Magnetic measurements

Magnetic susceptibility of a polycrystalline sample of **11a** was measured with a Quantum Design MPMSXL SQUID magnetometer in the temperature range 2 to 300 K in a magnetic field of up to 5 kOe.

## Conflicts of interest

There are no conflicts of interest to declare.

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## Notes and references

- (a) I. Maluenda and O. Navarro, *Molecules*, 2015, **20**(5), 7528; (b) S. Kotha, K. Lahiri and D. Kashinath, *Tetrahedron*, 2002, **58**(48), 9633; (c) N. Miyaura and A. Suzuki, *Chem. Rev.*,

- 1995, **95**, 2457; (d) N. Miyaura, T. Yanagi and A. Suzuki, *Synth. Commun.*, 1981, **11**, 513.
- 2 D. G. Brown and J. Boström, *J. Med. Chem.*, 2016, **59**, 4443.
- 3 B. S. Nehls, F. Galbrecht, A. Bilge, D. J. Brauer, C. W. Lehmann, U. Scherf and T. Farrell, *Org. Biomol. Chem.*, 2005, **3**, 3213.
- 4 G. Hu, S. P. Kitney, S. M. Kelly, W. Harrison and M. O'Neill, *Liq. Cryst.*, 2017, **44**(11), 1632.
- 5 A. Krishna, A. V. Lunchev and A. C. Grimsdale, in *Synthetic Methods for Conjugated Polymer and Carbon Materials*, ed. M. Leclerc and J.-F. Morin, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2017, **2**, pp. 59–87.
- 6 A. Littke, in *Modern Arylation Methods*, ed. L. Ackermann, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2009, **2**, pp. 25–67.
- 7 (a) H. Doucet, *Eur. J. Org. Chem.*, 2008, (12), 2013; (b) D. G. Hall, *Boronic Acids*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2005.
- 8 (a) P. G. Gildner and T. J. Colacot, *Organometallics*, 2015, **34**, 5497; (b) G. A. Molander and B. Canturk, *Angew. Chem., Int. Ed.*, 2009, **48**(49), 9240; (c) R. Martin and S. L. Buchwald, *Acc. Chem. Res.*, 2008, **41**(11), 1461.
- 9 Y. Ten, S. Amitina, A. Bogomyakov, Y. Gatilov, A. Lomanovich, I. Grigor'ev and D. Mazhukin, *Book of Abstracts of 14-th International Conference on Molecule-based Magnets*, Saint Petersburg, Russia, 2014.
- 10 (a) M. Souto, C. Rovira, I. Ratera and J. Veciana, *CrystEngComm*, 2017, **19**, 197; (b) M. Souto, V. Lloveras, S. Vela, M. Fumanal, I. Ratera and J. Veciana, *J. Phys. Chem. Lett.*, 2016, **7**, 2234; (c) S. Vela, M. Souto, I. Ratera, C. Rovira and J. Veciana, *J. Phys. Chem. A*, 2016, **120**, 10297; (d) T. Ikezawa, K. Mutoh, Y. Kobayashi and J. Abe, *Chem. Commun.*, 2016, **52**, 2465; (e) N. O. Chalkov, V. K. Cherkasov, G. A. Abakumov, A. G. Starikov and V. A. Kuropatov, *Beilstein J. Org. Chem.*, 2016, **12**, 2450; (f) H. Yamashita, T. Ikezawa, Y. Kobayashi and J. Abe, *J. Am. Chem. Soc.*, 2015, **137**, 4952; (g) N. O. Chalkov, V. K. Cherkasov, G. A. Abakumov, G. V. Romanenko, S. Y. Ketkov, I. V. Smolyaninov, A. G. Starikov and V. A. Kuropatov, *Eur. J. Org. Chem.*, 2014, 4571; (h) J. Guasch, L. Grisanti, L. Lloveras, J. Vidal-Gancedo, M. Souto, D. C. Morales, M. Vilaseca, C. Sissa, A. Painelli, I. Ratera, C. Rovira and J. Veciana, *Angew. Chem., Int. Ed.*, 2012, **51**, 11024; (i) S. Nishida, Y. Morita, K. Fukui, K. Sato, D. Shiomi, T. Takui and K. Nakasuji, *Angew. Chem., Int. Ed.*, 2005, **44**, 7277.
- 11 M. Souto, H. Cui, M. Peña, V. G. Baonza, H. O. Jeschke, M. Tomic, R. Valentí, D. Blasi, I. Ratera, C. Rovira and J. Veciana, *J. Am. Chem. Soc.*, 2016, **138**, 11517.
- 12 (a) S. M. Winter, A. R. Baló, R. J. Roberts, K. Lekin, A. Assoud, P. A. Dube and R. T. Oakley, *Chem. Commun.*, 2013, **49**, 1603; (b) P. Vasko, J. Hurmalainen, A. Mansikkamäki, A. Peuronen, A. Mailman and H. M. Tuononen, *Dalton Trans.*, 2017, **46**, 16004.
- 13 (a) H. Oka, H. Kouno and H. Tanaka, *J. Mater. Chem.*, 2007, **17**, 1209; (b) H. Oka, T. Tamura, Y. Miura and Y. Teki, *J.*

$\ddagger$  Additional crystallographic data (CCDC 1564701) for hybrid radical **11a**.



- Mater. Chem.*, 2001, **11**, 1364; (c) H. Oka, T. Tamura, Y. Miura and Y. Teki, *J. Mater. Chem.*, 1999, **9**, 1227.
- 14 (a) A. Bodzioch, M. Zheng, P. Kaszynski and G. Utecht, *J. Org. Chem.*, 2014, **79**, 7294; (b) Y. Takahashi, Y. Miura and N. Yoshioka, *Chem. Lett.*, 2014, **43**, 1236; (c) C. P. Constantinides, P. A. Koutentis and G. Loizou, *Org. Biomol. Chem.*, 2011, **9**, 3122; (d) Y. Miura, S. Ooshima and N. Yoshioka, *Book of Abstracts of the 9-th Japanese-Russian International Workshop on Open Shell Compounds and Molecular Spin Devices*, Awaji Island, Japan, 2015; (e) K. E. Fairfull-Smith and S. E. Bottle, *Eur. J. Org. Chem.*, 2008, 5391.
- 15 C. Stroh, M. Mayor and C. Hänisch, *Eur. J. Org. Chem.*, 2005, 3697.
- 16 V. W. Manner, T. F. Markle, J. H. Freudenthal, J. P. Roth and J. M. Mayer, *Chem. Commun.*, 2008, 256.
- 17 (a) H. Wei, L. Zhang, H. Phan, X. Huang, T. S. Heng, J. Zhou, W. Zeng, J. Ding, S. Luo, J. Wu and Z. Zeng, *Chem.-Eur. J.*, 2017, **23**, 9419; (b) K. Naoda, D. Shimizu, J. O. Kim, K. Furukawa, D. Kim and A. Osuka, *Chem.-Eur. J.*, 2017, **23**, 8969; (c) F. Tampieri, L. Colella, A. Maghsoumi, J. Marti-Rujas, E. Parisini, M. Tommasini, C. Bertarelli and A. Barbon, *J. Phys. Chem. C*, 2016, **120**, 5732; (d) L. Colella, L. Brambilla, V. Nardone, E. Parisini, C. Castiglioni and C. Bertarelli, *Phys. Chem. Chem. Phys.*, 2015, **17**, 10426; (e) Z. Zeng, X. Shi, C. Chi, J. T. L. Navarrete, J. Casado and J. Wu, *Chem. Soc. Rev.*, 2015, **44**, 6578; (f) D. Fazzi, E. V. Canesi, F. Negri, C. Bertarelli and C. Castiglioni, *ChemPhysChem*, 2010, **11**, 3685.
- 18 R. Shukla and R. Rathore, *Synthesis*, 2008, 3769.
- 19 H.-S. Sheu, C.-H. Lee, Y. Wang and L. Y. Chiang, *J. Chin. Chem. Soc.*, 1994, **41**, 797.
- 20 (a) Z. Kan, L. Colella, E. V. Canesi, A. Vorobiev, V. Skrypnichuk, G. Terraneo, D. R. Barbero, C. Bertarelli, R. C. I. MacKenzie and P. E. Keivanidis, *J. Mater. Chem. A*, 2016, **4**, 1195; (b) Z. Kan, L. Colella, E. V. Canesi, G. Lerario, R. S. S. Kumar, V. Bonometti, P. R. Mussini, G. Cavallo, G. Terraneo, P. Pattanasattayavong, T. D. Anthopoulos, C. Bertarelli and P. E. Keivanidis, *Sol. Energy Mater. Sol. Cells*, 2014, **120**, 37.
- 21 (a) K. Kolanji, P. Ravat, A. S. Bogomyakov, V. I. Ovcharenko, D. Schollmeyer and M. Baumgarten, *J. Org. Chem.*, 2017, **82**, 7764; (b) Y. B. Borozdina, E. Mostovich, V. Enkelmann, B. Wolf, P. T. Cong, U. Tutsch, M. Lang and M. Baumgarten, *J. Mater. Chem. C*, 2014, **2**, 6618; (c) E. A. Mostovich, Y. Borozdina, V. Enkelmann, K. Removic-Langer, B. Wolf, M. Lang and M. Baumgarten, *Cryst. Growth Des.*, 2012, **12**, 54.
- 22 M. Yu, R.-Y. Tang and J.-H. Li, *Tetrahedron*, 2009, **65**, 3409.
- 23 F. S. Han, M. Higuchi and D. G. Kurth, *Org. Lett.*, 2007, **9**, 559.
- 24 (a) H. Günther, *NMR Spectroscopy: basic principles, concepts, and applications in chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, 2013; (b) I. A. Grigor'ev, V. I. Mamatyuk, G. I. Shchukin, V. V. Martin and L. B. Volodarskii, *Chem. Heterocycl. Compd.*, 1986, 861; *Khim. Geterotsikl. Soedin.*, 1986, 1065; (c) M. Allen and J. D. Roberts, *Can. J. Chem.*, 1981, **59**, 451.
- 25 (a) C. Cordovilla, C. Bartolome, J. M. Martínez-Irarduya and P. Espinet, *ACS Catal.*, 2015, **5**, 3040; (b) P. Espinet and A. M. Echavarren, *Angew. Chem., Int. Ed.*, 2004, **43**, 4704; (c) J. K. Stille, *Angew. Chem., Int. Ed.*, 1986, **25**, 508.
- 26 J.-R. Pouliot, F. Grenier, J. T. Blaskovits, S. Beaupre and M. Leclerc, *Chem. Rev.*, 2016, **116**, 14225.
- 27 (a) Y. Takahashi, R. Matsuhashi, Y. Miura and N. Yoshioka, *Chem.-Eur. J.*, 2018, **24**, 7939; (b) Y. Takahashi, Y. Miura and N. Yoshioka, *ChemPhysChem*, 2018, **19**, 175; (c) S. E. Tolstikov, E. V. Tretyakov, D. E. Gorbunov, I. F. Zhurko, M. V. Fedin, G. V. Romanenko, A. S. Bogomyakov, N. P. Gritsan and D. G. Mazhukin, *Chem.-Eur. J.*, 2016, **22**, 14598; (d) N. M. Gallagher, J. J. Bauer, M. Pink, S. Rajca and A. Rajca, *J. Am. Chem. Soc.*, 2016, **138**, 9377.
- 28 I. A. Grigor'ev, I. A. Kirilyuk and L. B. Volodarskii, *Chem. Heterocycl. Compd.*, 1988, 1355; *Khim. Geterotsikl. Soedin.*, 1988, 1640.
- 29 S. Rinker, P. R. James, M. Neumann, O. Erpeldinger and F. Kraushaar, *US Pat.*, 20100267992A1, 2010.
- 30 (a) G. M. Sheldrick, *SHELX-97 (Release 97-2)*, University of Göttingen, Germany, 1997; (b) G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, **64**, 112.
- 31 (a) A. L. Spek, *PLATON (Version, 10M)*, Utrecht Univ., Netherlands, 2003; (b) A. L. Spek, *J. Appl. Crystallogr.*, 2003, **36**, 7.

