




Article

Tethered Blatter Radical for Molecular Grafting: Synthesis of 6-Hydroxyhexyloxy, Hydroxymethyl, and Bis(hydroxymethyl) Derivatives and Their Functionalization †

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† Dedicated to Professor Mieczysław Mąkosza.

Abstract: Synthetic access to 7-CF₃-1,4-dihydrobenzo[*e*][1,2,4]triazin-4-yl radicals containing 4-(6-hydroxyhexyloxy)phenyl, 4-hydroxymethylphenyl or 3,5-bis(hydroxymethyl)phenyl groups at the C(3) position and their conversion to tosylates and phosphates are described. The tosylates were used to obtain disulfides and an azide with good yields. The Blatter radical containing the azido group underwent a copper(I)-catalyzed azide–alkyne cycloaddition with phenylacetylene under mild conditions, giving the [1,2,3]triazole product in 84% yield. This indicates the suitability of the azido derivative for grafting Blatter radical onto other molecular objects via the CuAAC “click” reaction. The presented derivatives are promising for accessing surfaces and macromolecules spin-labeled with the Blatter radical.

Keywords: heterocycles; stable radicals; functional group transformation; azide–alkyne “click” reaction



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1. Introduction

Functionalization of flat surfaces [1–9], polymers [10–14], well-defined macromolecules (dendrimers [15–18], cyclodextrins [19–22], fullerene [23], and nanotubes [24]), and nanoparticles [25–30] with stable radicals is becoming an important avenue for obtaining materials [31,32] for advanced technologies [33], which include organic electronics [11,34], spintronics [1,3,6], contrast agents in bioimaging [15,35,36], and energy storage [12,37–39]. This effort has concentrated mainly on the traditional stable radicals, such as nitroxides [6,14–19,32], tris(2,4,6-trichlorophenyl)methyl (TTM) [7,9], and verdazyl [40], while the exploration of 1,4-dihydrobenzo[*e*][1,2,4]triazin-4-yls (so-called Blatter radicals) as active components of these materials began only recently and is rapidly intensifying.

Radicals have been chemisorbed onto an Au surface using the SR [1,2,6,26,41] and C≡CH [7,42] groups, and the latter was used to graft radicals onto reduced Si surfaces [42]. Chemisorption of radicals and typical organic molecules onto other surfaces has been accomplished using PO(OR)₂ groups (metal oxide substrates, e.g., Fe₃O₄ [25] and LSMO [6]), COOH group (GaAs) [43] and siloxanes (for SiO_x and indium tin oxide–ITO–substrates) [44]. Grafting of radicals onto macromolecules has been achieved using a variety of acylation and condensation reactions [15–18,35,45,46]. One of the most efficient grafting methods involves the Cu(I)-catalyzed [3+2] cycloaddition (“click”) reaction between an azide and a terminal alkyne, leading to the formation of the [1,2,3]triazole ring with the 1,4-substitution pattern [47–49]. This approach has been applied to grafting ethynyl-containing radicals into systems with pending azido groups [24,25,29,50]. It should be added that radical polymers

have also been obtained by polymerization of monomers containing stable radicals using, e.g., Rh catalysts, ring opening metathesis polymerization (ROMP), and electropolymerization methods [13,14,40].

The 1,4-dihydrobenzo[e][1,2,4]triazin-4-yls [33,51], formal derivatives of the prototypical 1,3-diphenyl derivative known as the Blatter radical [52] **A** (Figure 1), are exceptionally stable, π -delocalized radicals characterized by favorable redox behavior with a narrow electrochemical window (~ 1.2 V) [37,38] and a broad absorption in the visible range [53]. The stability of Blatter radical **A** is further enhanced by placing the CF_3 group in the C(7) position leading to derivative **B**, the so-called “super stable” radical [54]. For these reasons, 1,4-dihydrobenzo[e][1,2,4]triazin-4-yls are promising paramagnetic structural elements of functional materials [33], and have been explored as photoconductive liquid crystals [55–57], sensors [58], photodetectors [59], and also in spintronics [41,60,61].

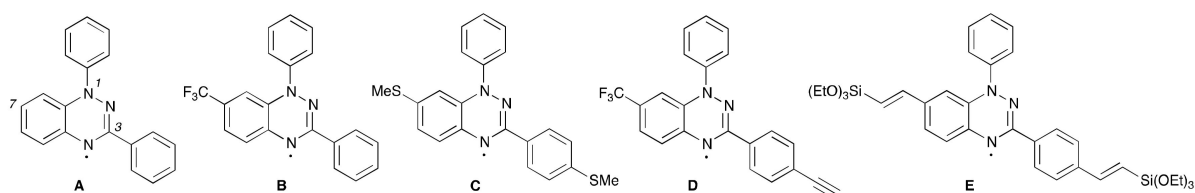


Figure 1. The structure of the prototypical Blatter radical (**A**), the “super stable” derivative (**B**), and functional derivatives (**C–E**).

There are still relatively few studies on Blatter radicals chemisorbed on surfaces or grafted on macromolecules, mainly due to insufficiently developed access to derivatives with appropriate functional groups. For instance, Blatter radical containing two Au-anchoring SMe groups (**C**, Figure 1) was chemisorbed on the Au(111) surface and the interactions of the resulting molecular films with the surface were investigated in detail [41]. Acetylene derivative **D** was prepared and reacted with an azidonorborene derivative under the “click” reaction conditions to give a norbornene-containing monomer, which was polymerized using the ROMP method. The acetylene derivative **D** could also be used for chemisorption onto the Au surface. Finally, bis(triethoxysilyl) derivative **E** was used for grafting the Blatter radical onto mesoporous silica [62] and could also be used for the functionalization of Si and metal surfaces with native oxides.

Despite progress in functional derivatives of the Blatter radical, there is a need to broaden the range of intermediates containing active functionalities for grafting onto diverse types of surfaces and macromolecules.

Herein we describe three derivatives of the “super stable” Blatter radical containing the 6-hydroxyhexyloxy (**Ia**, Figure 2) or hydroxymethyl (**IIa** and **IIIa**) substituents on the C(3)–Ph ring as key intermediates to functional derivatives suitable for grafting onto low dimensional systems. We report a conversion of the alcohols **Ia–IIIa** to the corresponding tosylates **Ib–IIIb** and phosphates **Ic** and **IId**, and transformations of the tosylates to disulfides **Id** and **IIId**, and azide **Ie**. As a proof of concept, we demonstrate the “click” reaction of azide **Ie** with an alkyne.

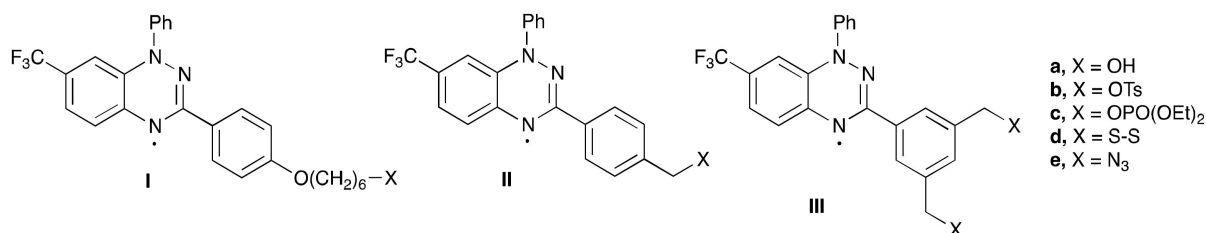
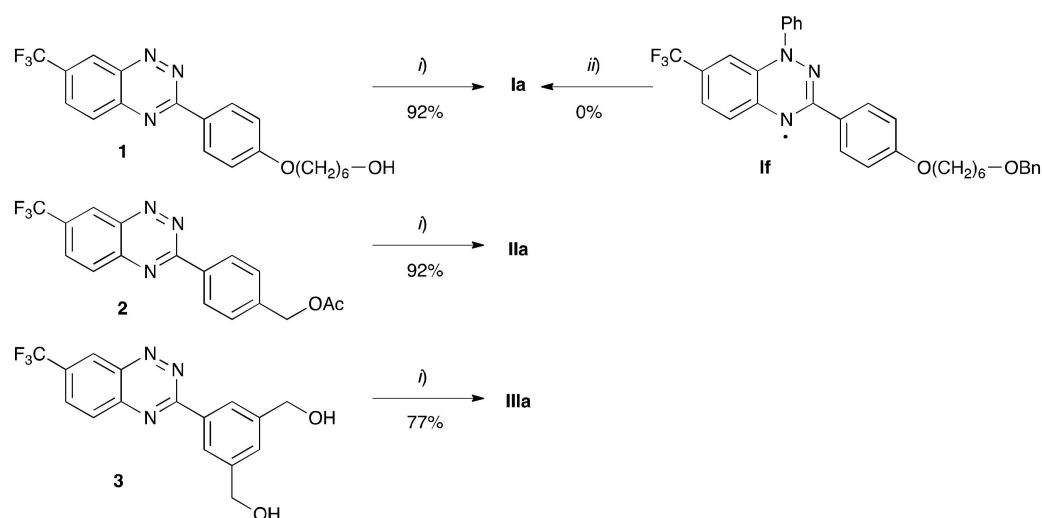


Figure 2. The structure of three types of radicals (**I–III**) for molecular grafting. Reported compounds: **Ia–Ie**, **IIa–IIId**, **IIIa** and **IIIb**.

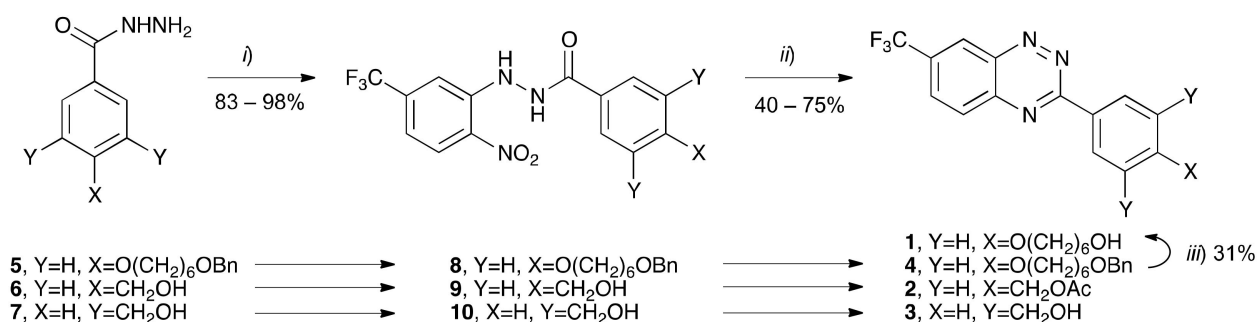
2. Results and Discussion

2.1. Synthesis of Hydroxyl Derivatives Ia–IIIa

Radicals **Ia–IIIa** containing versatile hydroxyl groups were prepared using the recently discovered regioselective azaphilic addition of aryllithium to benzo[*e*][1,2,4]triazines [63]. Thus, phenyllithium was reacted with benzo[*e*][1,2,4]triazines **1–3**, and the resulting anions were oxidized with air to the corresponding radicals **Ia–IIIa**, which were conveniently isolated by column chromatography (SiO₂ support) in yields up to 92% (Scheme 1). It should be noted that both hydroxy (**1** and **3**) and acetoxy (**2**) derivatives were suitable starting materials for this reaction affording the corresponding radicals in comparable yields. The route to **Ia** involving addition of phenyllithium to compound **4**, the *O*-benzyl protected alcohol **1** (Scheme 2), followed by Pd-catalyzed reductive debenzylolation of the resulting radical **If** (Scheme 1) turned out to be inefficient. While the PhLi addition and formation of **If** worked well (yield up to 64%, Scheme 2), debenzylation of **If** gave only decomposition products. This presumably resulted from the more vigorous conditions needed for the removal of the *O*-benzyl group in the alkyl benzyl ethers than in the aryl analogues.



Scheme 1. Synthesis of radicals (**Ia–IIIa**). Reagents and conditions: (i) 1. PhLi, THF, Ar, $-5\text{ }^{\circ}\text{C}$, 1 h; 2. Air, 0.5 h, 77–92% yield; (ii) 1. Pd/C, H₂, 50 psi, THF/EtOH, 2 days, 2. Air, 0% yield.



Scheme 2. Preparation of benzo[*e*][1,2,4]triazines **1–3**. Reagents and conditions: (i) 1-fluoro-2-nitro-5-trifluoromethylbenzene, DMSO, $70\text{ }^{\circ}\text{C}$, 7 h; (ii) 1. Sn, glacial AcOH, rt for 2 h, then $115\text{ }^{\circ}\text{C}$ for 0.5 h; 2. NaIO₄; (iii) 1. Pd/C, H₂, THF/EtOH, 2 days; 2. Air.

The requisite alcohols **1** and **3** and acetate **2** were obtained in two steps following an established general procedure [57,63,64], as shown in Scheme 2. Thus, the readily available benzhydrazides **5–7** were N-arylated with 1-fluoro-2-nitro-5-trifluoromethylbenzene. The resulting hydrazides **8–10** were subsequently cyclized under reductive conditions (Sn powder/AcOH) followed by oxidation of the dihydro products with Ag₂O or NaIO₄ giving

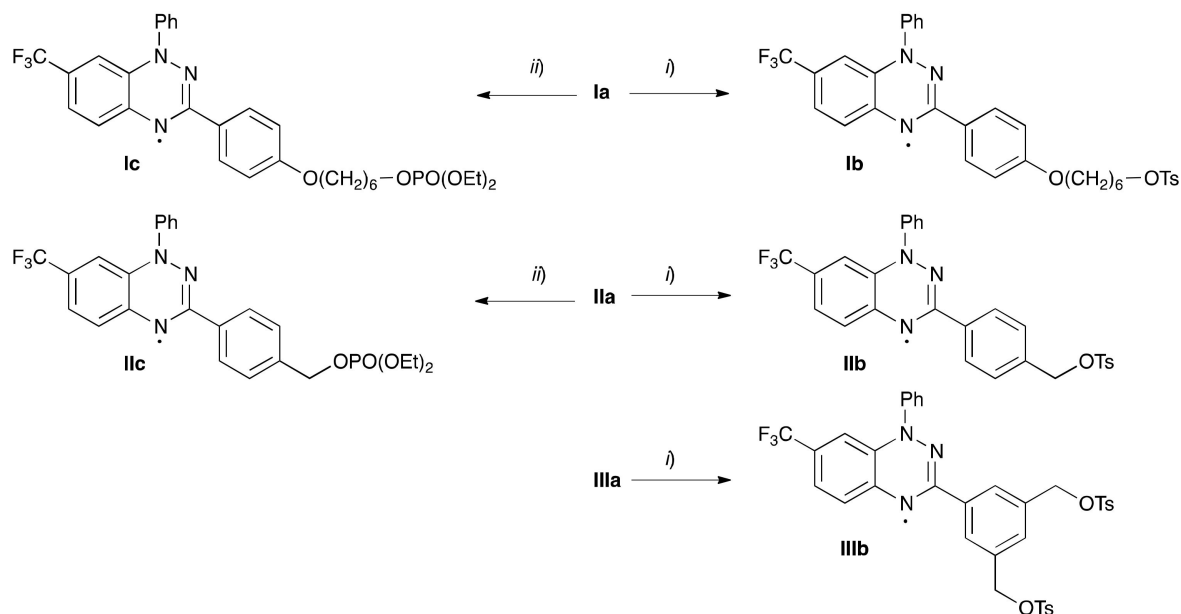
benzo[*e*][1,2,4]triazines **2–4** in good overall yields (40–75%). Interestingly, during reductive cyclization of **9** at temperatures above 100 °C, the hydroxymethyl group underwent esterification with AcOH, used as the solvent and reagent in this reaction, and acetate **2** was isolated in 45% yield. The analogous acetate was not observed in the case of cyclization of hydrazide **10** conducted at ambient temperatures.

The hydroxyhexyloxy derivative **1** was obtained in 31% overall yield by Pd-catalyzed debenzoylation of **4**, followed by aerial oxidation of the dihydro form. As noted above, debenzoylation of **4** required longer-than-typical reaction times. The obtained hydroxy derivative **1** turned out to be sensitive to elevated temperatures: concentration of solutions of purified **1** on a rotavap at 40 °C resulted in its decomposition and formation of a foul-smelling orange oil. Handling of **1** at lower temperatures avoided this problem, and pure product was obtained.

Benzhydrazides **5–7** were obtained by hydrazinolysis of the corresponding methyl benzoates with hydrazine hydrate.

2.2. Synthesis of Tosylates and Phosphates

Reactions of alcohols **Ia–IIIa** with tosyl chloride gave the desired tosylates **Ib–IIIb** in 82–96% yield (Scheme 3). The relatively high stability of **Ib** allowed for isolation of the pure compound using standard silica gel chromatography. In contrast, tosylates **IIb** and **IIIb** were sensitive to chromatography conditions and were used for the next step as crude materials.

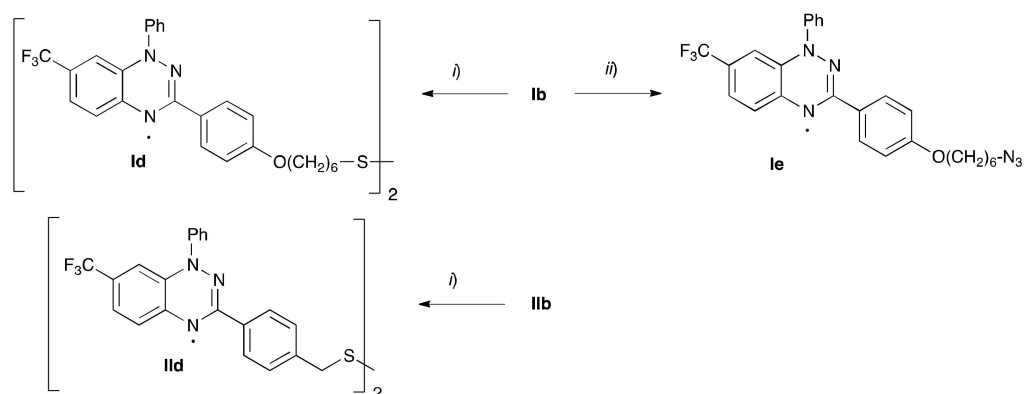


Scheme 3. Synthesis of tosylates **Ib–IIIb** and phosphates **Ic** and **IIc**. Reagents and conditions: (i) TsCl, pyridine, CH₂Cl₂, rt, Ar, overnight, 82–96% yield; (ii) (EtO)₂POCl, DMAP, Et₃N, THF, rt, 1 h, Ar, 83–86% yield.

Phosphorylation of alcohols **Ia** and **IIa** with diethyl chlorophosphate in the presence of DMAP and Et₃N gave the phosphates **Ic** and **IIc**, respectively, isolated in about 85% yield (Scheme 3).

2.3. Transformation of Tosylates: Preparation of Disulfides and Azide

Disulfides **Id** and **IId** were obtained in 18% yield from tosylates **Ib** and **IIb** using a general procedure [65] involving reactions with the thiosulfate (S₂O₃^{2−}) nucleophile in DMSO, followed by oxidation of the resulting mercaptan with I₂ (Scheme 4).

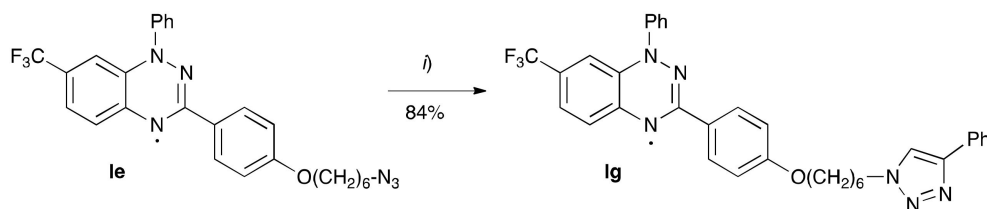


Scheme 4. Synthesis of disulfides **Id** and **IId**, and azide **Ie**. Reagents and conditions: (i) 1. $\text{Na}_2\text{S}_2\text{O}_3$, DMSO, 60°C , overnight, 2. I_2 , CH_2Cl_2 , rt, 10 min, 18% yield; (ii) NaN_3 , DMF, 50°C , Ar, 5 h, 42–73% yield.

In contrast, the preparation of azide **Ie** was straightforward and more efficient. Thus, reaction of tosylate **Ib** with NaN_3 in DMF gave azide **Ie** isolated in yields up to 73% yield (Scheme 4).

2.4. Copper(I)-Catalyzed Azide-Alkyne Cycloaddition of Azide **Ie**

Compound **Ie** represents the first azido derivative of the Blatter radical, and its suitability for the Cu(I)-catalyzed cycloaddition reaction (“click”) with alkynes, the CuAAC reaction, required experimental verification. Thus, the azide **Ie** was reacted with phenylacetylene in the presence of Cu(I), generated in situ from CuSO_4 and sodium ascorbate, according to a general literature method [66]. The “click” product, [1,2,3]triazole **Ig**, was isolated in a high yield of 84% (Scheme 5). This result compares to 53% yield of [1,2,3]triazole formation in an analogous CuAAC reaction of acetylene-substituted Blatter radical **D** (Figure 1) with an azido derivative of norbornene [13].



Scheme 5. Synthesis of **Ig** via azide-alkyne “click” reaction. Reagents and conditions: (i) Phenylacetylene, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, sodium *L*-ascorbate, benzoic acid, *t*-BuOH/ H_2O 1:2, rt, 5 h, 84% yield.

Pure **Ig** showed no decomposition during storage for 4 years under ambient conditions, according to thin-layer chromatography analysis.

2.5. Spectroscopic Characterization of Radicals

All radicals **I–III** exhibit low-intensity broad absorption in the entire visible range, as shown for **Ia** in Figure 3. Consequently, the compounds appear dark brown in solutions and nearly black in the solid state. EPR analysis of the radicals conducted in benzene solutions revealed seven principal lines resulting from hyperfine splitting with three ^{14}N nuclei modulated with additional smaller splitting by ^{19}F and ^1H nuclei, as shown for derivative **Ia** in Figure 3. For some radicals, the principal lines are less resolved, presumably due to aggregation in benzene solutions (see the Supplementary Materials). Analysis demonstrated that the a_{N} *hfcc* values for radicals **I–III** are consistent with those for other Blatter radical derivatives, and are about 7.6 G for $a_{\text{N}(1)}$ and about 4.5–4.9 G for $a_{\text{N}(2)}$ and $a_{\text{N}(4)}$. Simulation of the experimental spectra indicates that the a_{F} *hfcc* value is in a range of 3.2–3.6 G.

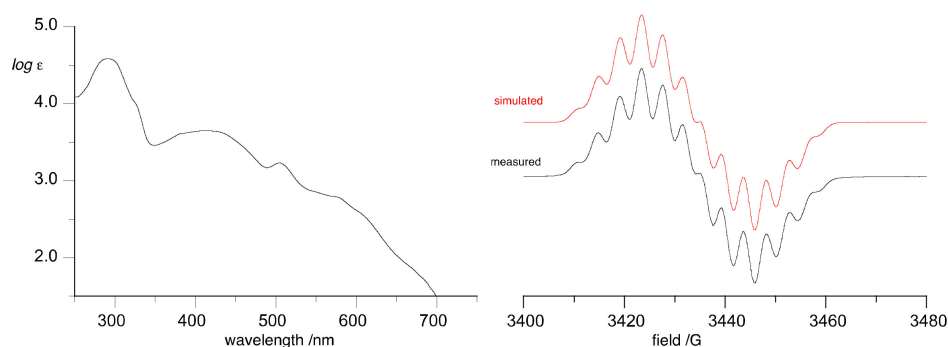


Figure 3. Electronic absorption spectrum in CH_2Cl_2 (left) and ERP spectrum in benzene (right) for **Ia**.

3. Conclusions

The “super stable” Blatter radical **B** was substituted at the C(3) phenyl ring with a long tether ($\text{O}(\text{CH}_2)_6\text{-X}$, **I**), a short tether ($\text{CH}_2\text{-X}$, **II**) or two anchoring groups ($2 \times \text{CH}_2\text{-X}$, **III**). The key intermediates contain the hydroxyl group ($\text{X} = \text{OH}$, **a**), which could be used for grafting in condensation (acylation) and addition (e.g., carbamination) reactions. The hydroxyl derivatives **Ia–IIIa** are efficiently converted to tosylates **Ib–IIIb**, which served as electrophilic intermediates to disulfides **Id** and **IId** (for chemisorption onto Au surfaces) and azide **Ie** (for the CuAAC reaction). Tosylates **Ib** and **IIIb** can additionally be exploited to attach the Blatter radical to hydroxyl-functionalized partners through the formation of benzyl-type ether linkages. Following prior work on the synthesis and supramolecular properties of cyclodextrin–xylylene hybrids [67–70], we have conducted preliminary experiments supporting the viability of such an approach, and the results will be published in due course.

The demonstration of efficient “click” reaction of azide **Ie** with $\text{PhC}\equiv\text{CH}$ paves the way to grafting radical **B** onto surfaces and macromolecules functionalized with terminal ethynyl groups. This method represents a more versatile approach to paramagnetic materials, since many macromolecules substituted with the propargyl group are available.

The presented results constitute a promising approach to novel paramagnetic polymers with high radical density, e.g., for polymer electrodes with high charge storage capacity and for high-density paramagnetic surfaces for spintronic applications. This work is continued in our laboratory.

4. Materials and Methods

General. Reagents and solvents were purchased and used as received. THF was dried over Na metal in the presence of benzophenone and distilled before use. Column chromatography was performed on silica gel. For separation of radicals silica gel was passivated by mixing with CH_2Cl_2 containing 2% of Et_3N and removal of the solvent to dryness (rotovap). Reported yields refer to analytically pure samples. NMR spectra were recorded with a Bruker AVIII 500 or 600 instrument. Chemical shifts are reported relative to solvent (CDCl_3) residual peaks (^1H NMR: $\delta = 7.26$ ppm and ^{13}C NMR: $\delta = 77.16$ ppm) [71]. All ^{13}C NMR spectra are proton-decoupled. IR spectra were measured in KBr pellets with a FTIR NEXUS spectrometer. High-resolution mass spectrometry (HRMS) measurements were performed using SYNAPT G2-Si High-Definition Mass Spectrometry equipped with an ESI or APCI source and Quantitative Time-of-Flight (QuanTof) mass analyzer. Melting points were determined in capillaries with a MEL-TEMP II apparatus and are uncorrected. If not stated otherwise, reactions were carried out under argon atmosphere in flame-dried flasks with addition of the reactants via syringe. Subsequent manipulations were conducted in air.

EPR spectra of radicals **I–III** were recorded on an X-band EMX-Nano EPR spectrometer at ambient temperature using dilute and degassed solutions in distilled benzene in a concentration range of $2\text{--}5 \times 10^{-4}$ M. Additional details are shown in the SI.

Preparation of radicals Ia–IIIa via PhLi addition to benzo[e][1,2,4]triazines 1–3. A general method. To a solution of the appropriate benzo[e][1,2,4]triazine derivative **1**, **2**, or **3** (0.792 mmol) in dry THF (10 mL), PhLi (1.9 M in dibutyl ether, 1.24 mL, 2.360 mmol) was added dropwise at $-5\text{ }^{\circ}\text{C}$ under argon and the reaction mixture was stirred at this temperature for 1 h, then for 1 h at rt under air. Water was added and the product was extracted with CH_2Cl_2 ($3\times$). The combined organic extracts were dried (Na_2SO_4), and volatiles were removed on a rotavap. Pure product was isolated by column chromatography followed by recrystallization (MeCN).

1-Phenyl-3-[4-(6-hydroxyhexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e]-[1,2,4]triazin-4-yl (Ia). Starting from triazine **1**. Yield: 322 mg (87–94% range yield) of pure **Ia** as a brown solid: mp 145–146 $^{\circ}\text{C}$; IR (KBr) ν 3400, 2932, 2854, 1607, 1514, 1393, 1356, 1314, 1246, 1118, 1063, 841 cm^{-1} ; UV (CH_2Cl_2) λ_{max} (log ϵ) 291 (4.58), 413 (3.65), 504 (3.20) nm; EPR (benzene) a_{N} 7.57, 4.54, 4.87, a_{F} 3.51 G, $g = 2.0048$; HRMS (ESI-TOF) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{26}\text{H}_{26}\text{F}_3\text{N}_3\text{O}_2$: 469.1977; found: 469.1984. Anal. Calcd for $\text{C}_{26}\text{H}_{25}\text{F}_3\text{N}_3\text{O}_2$: C, 66.66; H, 5.38; N, 8.97. Found: C, 66.46; H, 5.45; N, 8.77.

1-Phenyl-3-(4-hydroxymethylphenyl)-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (IIa). Starting from triazine **2**. The crude product was passed through a passivated silica gel plug (pet. ether/AcOEt 1:1) and recrystallized (MeCN) to give 279 mg (92% yield) of pure **IIa** as an olive solid: mp 204–205 $^{\circ}\text{C}$; IR (KBr) ν 3366, 3275, 3054, 1592, 1489, 1397, 1355, 1315, 1265, 1166, 1117, 1062, 1013, 905 cm^{-1} ; EPR (benzene) a_{N} 7.40, 4.59, 4.90, a_{F} 3.24 G, $g = 2.0034$; HRMS (ESI-TOF) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{16}\text{F}_3\text{N}_3\text{O}$: 383.1245; found: 383.1233. Anal. Calcd for $\text{C}_{21}\text{H}_{15}\text{F}_3\text{N}_3\text{O}$: C, 65.97; H, 3.95; N, 10.99. Found: C, 66.10; H, 4.06; N, 11.25.

1-Phenyl-3-[3,5-bis(hydroxymethyl)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e]-[1,2,4]triazin-4-yl (IIIa). Starting from triazine **3**. The crude product was passed through a passivated silica gel plug (pet. ether/AcOEt 1:1) and recrystallized (MeCN) to give **IIIa** as an olive solid (251 mg, 77% yield): mp 180–181 $^{\circ}\text{C}$; IR (KBr) ν 3394, 3219, 3066, 2858, 1709, 1592, 1490, 1427, 1396, 1322, 1278, 1130, 1070, 875, 841, 765, 692 cm^{-1} ; EPR (benzene) a_{N} 7.64, 4.60, 4.79, a_{F} 3.49 G, $g = 2.0038$; HRMS (ESI-TOF) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{22}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_2$: 413.1351; found: 413.1355.

Preparation of 1-phenyl-3-[4-(6-tosyloxyhexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (Ib). To a solution of alcohol **Ia** (500 mg, 1.07 mmol) in dry CH_2Cl_2 (6 mL), pyridine (0.25 mL, 3.10 mmol) and tosyl chloride (305 mg, 1.60 mmol) were added and the reaction mixture was stirred at rt overnight under argon. The reaction mixture was washed with H_2O , brine and dried (Na_2SO_4). Organic solvents were removed on a rotavap and the residue was passed through a silica gel plug ($\text{CH}_2\text{Cl}_2/\text{EtOAc}$ 19:1) to give 637 mg (96% yield) of pure tosylate **Ib** as a brown solid: mp 120–121 $^{\circ}\text{C}$; IR (KBr) ν 2940, 2864, 1605, 1390, 1355, 1316, 1244, 1172, 1119, 960, 842 cm^{-1} ; HRMS (ESI-TOF) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{33}\text{H}_{32}\text{F}_3\text{N}_3\text{O}_4\text{S}$: 623.2066; found: 623.2062. Anal. Calcd for $\text{C}_{33}\text{H}_{31}\text{F}_3\text{N}_3\text{O}_4\text{S}$: C, 63.65; H, 5.02; N, 6.75; S, 5.15. Found: C, 63.65; H, 5.16; N, 6.63; S, 5.03.

Preparation of tosylates IIb and IIIb. A general method. To a solution of alcohol **IIa** or **IIIa** (0.79 mmol) and tosyl chloride (300 mg, 1.57 mmol) in dry THF (10 mL), 60% NaH in mineral oil (475 mg, 11.85 mmol) was added in portions over 30 min. The suspension was stirred at rt for another 30 min, and water was added dropwise to neutralize the unreacted NaH. The reaction mixture was extracted with CH_2Cl_2 ($3\times$). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude product was passed through a silica gel plug passivated with Et_3N (pet ether/AcOEt 4:1) to give **IIb** or **IIIb** as green-brown solid. The product was immediately used for the next step without further purification.

1-Phenyl-3-[4-(tosyloxymethyl)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (IIb). Starting from **IIa**. Yield: 413 mg (98% yield) of **IIb** as a brown solid; HRMS (ESI-TOF) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{28}\text{H}_{22}\text{F}_3\text{N}_3\text{O}_3\text{S}$: 537.1334; found: 537.1330.

1-Phenyl-3-[3,5-bis(tosyloxymethyl)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e]-[1,2,4]triazin-4-yl (IIIb). Starting from **IIIa**. Yield: 558 mg (98% yield) of **IIIb** as a

brown solid; HRMS (ESI-TOF) $[M+H]^+$ HRMS, m/z calcd for $C_{36}H_{30}F_3N_3O_6S_2$: 721,1528; found: 721.1536.

Preparation of phosphates Ic and IIc. A general method. To a solution of alcohol **Ia** or **IIa** (0.2 mmol, 1.0 equiv.), DMAP (0.02 mmol, 0.1 equiv.) and Et_3N (1.0 mmol, 5 equiv.) dissolved in THF (2 mL) diethyl chlorophosphate (1.0 mmol, 5 equiv.) was added slowly via syringe. During the addition, a white precipitate formed. The reaction mixture was stirred at rt for 1 h until substrate was no longer present in the reaction mixture (TLC control). The reaction was quenched with sat. NH_4Cl solution, extracted with CH_2Cl_2 , and the product was purified by column chromatography (pet. ether/AcOEt 3:2).

1-Phenyl-3-[4-(6-diethoxyphosphoryloxyhexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (Ic). Starting from **Ia**. Yield: 103.9 mg (86% yield) of phosphate **Ic** as a soft waxy material; IR (KBr) ν 2925, 2854, 1607, 1490, 1399, 1318, 1248, 1165, 1108, 1027, 829, 698 cm^{-1} ; EPR (benzene) a_N 7.56, 4.78, 4.53, a_F 3.56 G, $g = 2.0037$; HRMS (ESI-TOF) $[M+H]^+$ m/z calcd for $C_{30}H_{35}N_3O_5F_3P$: 605.2266; found: 605.2273.

1-Phenyl-3-[4-(diethoxyphosphoryloxymethyl)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (IIc). Starting from **IIa**. Yield: 86.1 mg (83% yield) of phosphate **IIc** as a soft waxy material; IR (KBr) ν 2925, 2854, 1593, 1492, 1422, 1323, 1265, 1166, 1120, 1036, 824, 698 cm^{-1} ; EPR (benzene) a_N 7.59, 4.63, 4.72, a_F 3.56 G $g = 2.0046$; HRMS (ESI-TOF) $[M+H]^+$ m/z calcd for $C_{25}H_{25}N_3O_4F_3P$: 519.1535; found: 519.1529.

Preparation of disulfides Id and IId. A general method. A mixture of tosylate **Ib** or **IIb** (0.64 mmol) and solid $Na_2S_2O_3$ (102 mg, 0.64 mmol) in DMSO (15 mL) was stirred at 60 °C overnight. The reaction mixture was cooled to rt and extracted with AcOEt (3 \times). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The residue was dissolved in CH_2Cl_2 (10 mL) and solid I_2 (49 mg, 0.19 mmol) was added and stirred at rt for 10 min, filtered, the solid was washed with CH_2Cl_2 and the filtrate was evaporated. The crude product was passed through a passivated silica gel plug (pet. ether/AcOEt 5:1) and recrystallized (MeCN) to give pure product **Id** or **IId** as brown solids.

Disulfide Id. Starting from **Ib**. Yield: 55.0 mg (18% yield); mp 73 °C; IR (KBr) ν 2936, 2855, 1605, 1512, 1487, 1426, 1398, 1319, 1251, 1170, 1115, 1060, 840, 695 cm^{-1} ; UV (CH_2Cl_2) λ_{max} (log ϵ) 292 (4.82), 384 (4.01), 503 (3.34) nm; EPR (benzene) a_N 7.32, 4.66, 4.55, a_F 3.32 G, $g = 2.0038$; HRMS (ESI-TOF) $[M]^+$ m/z calcd for $C_{52}H_{48}F_6N_6O_2S_2$: 966.3184; found: 966.3218. Anal. Calcd for $C_{52}H_{48}F_6N_6O_2S_2$: C, 64.58; H, 5.00; N, 8.69; S, 6.63. Found: C, 64.30; H, 5.10; N, 8.63; S, 6.84.

Disulfide IId. Starting from **IIb**. Yield: 45.8 mg (18% yield); mp 170 °C; IR (KBr) ν 3073, 1592, 1488, 1397, 1316, 1264, 1116, 1062, 905, 844, 763, 693 cm^{-1} ; UV (CH_2Cl_2) λ_{max} (log ϵ) 284 (4.89), 374 (4.04), 430 (3.78), 498 (3.42) nm; HRMS (ESI-TOF) $[M]^+$ m/z calcd for $C_{42}H_{28}F_6N_6S_2$: 794.1721; found: 794.1726. Anal. Calcd for $C_{42}H_{28}F_6N_6S_2$: C, 63.47; H, 3.55; N, 10.57; S, 8.07. Found: C, 63.45; H, 3.61; N, 10.46; S, 8.05.

Preparation of 1-phenyl-3-[4-(6-azidohexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (Ie). To a solution of tosylate **Ib** (750 mg, 1.204 mmol) in dry DMF (18 mL) sodium azide (391 mg, 6.02 mmol) was added in one portion and the reaction mixture was stirred for 5 h at 50 °C under argon. After the reaction is completed (no starting material detected by TLC), H_2O and brine were added, and the product was extracted with CH_2Cl_2 (3 \times). The organic layer was washed with H_2O (3 \times), then with brine, and dried (Na_2SO_4). Solvents were removed and the residue was purified by column chromatography (SiO_2 , CH_2Cl_2 100%) to give 432 mg (73% yield) of pure azide **Ie** as brown solid: mp 88–90 °C; IR (KBr) ν 2939, 2857, 2098 (N_3), 1606, 1397, 1354, 1317, 1247, 1113 cm^{-1} ; EPR (benzene) a_N 7.57, 4.82, 4.98, a_F 3.33 G, $g = 2.0049$; HRMS (ESI-TOF) $[M+H]^+$ m/z calcd for $C_{26}H_{25}F_3N_6O$: 494.2042; found: 494.2031.

Preparation of 1-phenyl-3-[4-(6-benzyloxyhexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[e][1,2,4]triazin-4-yl (If). Radical **If** was obtained in 44–64% yield by addition of PhLi to triazine **4** according to the general procedure for preparation of alcohol **Ia–IIIa**. The crude product was passed through a silica gel plug (pet. ether/ Et_2O 3:2) and recrystallized ($EtOH$) to give pure **If** as a brown solid: mp 98–100 °C; HRMS (ESI-TOF) $[M]^+$

m/z calcd for $C_{33}H_{31}F_3N_3O_2$: 558.2368; found: 558.2363. Anal. Calcd for $C_{33}H_{31}F_3N_3O_2$: C, 70.95; H, 5.59; N, 7.52. Found: C, 70.95; H, 5.56; N, 7.62.

Preparation of 1-phenyl-3-[4-(6-[1,2,3]triazolylhexyloxy)phenyl]-7-trifluoromethyl-1,4-dihydrobenzo[*e*][1,2,4]triazin-4-yl (Ig). To a solution of $CuSO_4 \times 5H_2O$ (~3 mg), sodium ascorbate (~3 mg) and benzoic acid (~3 mg) in *t*-BuOH/ H_2O 1:2 (4 mL) a mixture of phenylacetylene (20.0 mg, 0.196 mmol) and azide **Ie** (95.0 mg, 0.192 mmol) was added at rt. The resulting mixture was stirred for 5 h (TLC monitoring, CH_2Cl_2 , $R_f = 0.08$ and 0.45 for product **Ig** and azide **Ie**, respectively). CH_2Cl_2 was added and the organic phase was washed with H_2O and brine and dried (Na_2SO_4). Solvents were removed in vacuum and the product was purified by column chromatography (SiO_2 , CH_2Cl_2 100% gradient to CH_2Cl_2 /EtOAc 4:1) to give 97 mg (84% yield) of pure triazole **Ig** as a brown solid: mp 160 °C dec.; IR (KBr) ν 2943, 1607, 1400, 1357, 1319, 1246, 1121, 837, cm^{-1} ; UV (CH_2Cl_2) λ_{max} (log ϵ) 290 (4.58), 411 (3.62), 504 (3.20) nm; EPR (benzene) a_N 7.59, 4.73, 4.87, a_F 3.50 G, $g = 2.0054$; HRMS (ESI-TOF) $[M+H]^+$ m/z calcd for $C_{34}H_{31}F_3N_6O$: 596.2511; found: 596.2506. Anal. Calcd for $C_{34}H_{30}F_3N_6O$: C, 68.56; H, 5.08; N, 14.11. Found: C, 68.59; H, 5.00; N, 13.97.

Preparation of 3-[4-(6-hydroxyhexyloxy)phenyl]-7-trifluoromethylbenzo[*e*][1,2,4] triazine (1). A solution of benzyloxy derivative **4** (3.00 g 6.23 mmol) in THF (35 mL) was added to a suspension of 5% Pd/C (2.60 g) in EtOH (35 mL), and the resulting mixture was hydrogenated (50 psi) overnight. The reaction mixture was passed through a Celite pad and oxidized by exposure to air (TLC monitoring) and the solvents were removed under reduced pressure (cold bath!). Crude product was purified by column chromatography (SiO_2 , CH_2Cl_2 /EtOAc 4:1) to give 0.76 g (31% yield) of pure product **1** as a yellow solid: mp 144–145 °C; 1H NMR (600 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.74 (d, $J = 8.9$ Hz, 2H), 8.16 (d, $J = 8.8$ Hz, 1H), 8.08 (dd, $J_1 = 8.9$ Hz, $J_2 = 1.9$ Hz, 1H), 7.10 (d, $J = 8.9$ Hz, 2H), 4.11 (t, $J = 6.5$ Hz, 2H), 3.69 (t, $J = 6.5$ Hz, 2H), 1.87 (quint, $J = 7.0$ Hz, 2H), 1.64 (quint, $J = 7.1$ Hz, 2H), 1.56 (quint, $J = 7.5$ Hz, 2H), 1.48 (quint, $J = 7.4$ Hz, 2H), 1.25 (s, 1H); $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ 162.8, 160.9, 144.9, 142.3, 131.2 (q, $J = 34$ Hz), 131.1, 130.9 (q, $J = 3$ Hz), 130.7, 127.9 (q, $J = 4$ Hz), 127.3, 123.3 (q, $J = 273$ Hz), 115.1, 68.2, 63.0, 32.8, 29.3, 26.0, 25.7; IR (KBr) ν 3297, 2938, 2863, 1605, 1510, 1487, 1427, 1337, 1252, 1173, 1134, 1059, 1003, 908, 842, 699, 638 cm^{-1} ; HRMS (ESI-TOF) $[M+H]^+$ m/z calcd for $C_{20}H_{21}F_3N_3O_2$: 392.1586; found: 392.1590. Anal. Calcd for $C_{20}H_{20}F_3N_3O_2$: C, 61.38; H, 5.15; N, 10.74. Found: C, 61.57; H, 5.12; N, 10.74.

Preparation of triazines 2–4. A general method. To a solution of hydrazide **8**, **9** or **10** (6.96 mmol) in glacial AcOH (100 mL), Sn powder (4.54 g, 38.3 mmol) was added and stirred at rt for 2 h, and then at 115 °C for 30 min. After cooling, EtOAc and H_2O were added, and the mixture was filtered through a Celite pad. The solution was extracted with two portions of EtOAc, and the combined organic extracts were washed with saturated aq. $NaHCO_3$ (3 \times) and dried (Na_2SO_4). Solvents were removed on a rotavap, and the residue was dissolved in a CH_2Cl_2 /MeOH mixture (1:1) and solid $NaIO_4$ (2.23 g, 10.44 mmol) or Ag_2O (354 mg, 1.52 mmol) was added. The mixture was stirred at rt until complete consumption of the dihydro form. The solution was filtered, and the solvents were removed under reduced pressure. The crude product was purified on silica gel and recrystallized to give pure triazines 2–4.

3-(4-Acetoxyphenyl)-7-trifluoromethylbenzo[*e*][1,2,4]triazine (2). Starting from hydrazide **9** using modified method. The suspension was stirred at 70 °C overnight and at 120 °C for 1 h. Solid Ag_2O was used for oxidation. The crude product was purified by column chromatography (SiO_2 , pet. ether/AcOEt 4:1) and further by recrystallization (CH_2Cl_2 /EtOH) to give 967 mg (40% yield) of triazine **2** as yellow crystals: mp 136–137 °C; 1H NMR (500 MHz, $CDCl_3$) 8.84 (s, 1H), 8.76 (d, $J = 8.3$ Hz, 2H), 8.21 (d, $J = 8.9$ Hz, 1H), 8.11 (dd, $J_1 = 8.9$ Hz, $J_2 = 1.9$ Hz, 1H), 7.58 (d, $J = 8.4$ Hz, 2H), 5.23 (s, 2H), 2.16 (s, 3H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.9, 160.6, 145.3, 142.1, 140.4, 134.8, 132.0 (q, $J = 34$ Hz), 131.1 (q, $J = 3$ Hz), 131.0, 129.5, 128.7, 128.0 (q, $J = 4$ Hz), 123.2 (q, $J = 273$ Hz), 65.8, 21.1; IR (KBr) ν 3070, 1744, 1630, 1508, 1425, 1328, 1257, 1173, 1131, 1056, 1012, 901, 842, 641 cm^{-1} ; HRMS (AP-TOF) $[M+H]^+$ m/z calcd for $C_{17}H_{13}F_3N_3O_2$: 348.0960; found: 348.0961. Anal. Calcd for $C_{17}H_{12}F_3N_3O_2$: C, 58.79; H, 3.48; N, 12.10. Found: C, 58.83; H, 3.45; N, 12.25.

3-[3,5-Bis(hydroxymethyl)phenyl]-7-trifluoromethylbenzo[e][1,2,4]triazine (3). Starting from hydrazide **10** using modified method. The suspension was stirred at rt overnight without further heating. Solid Ag₂O was used for oxidation. The resulting crude product was purified by chromatography (SiO₂, pet. ether/AcOEt 1:1) and further by recrystallization (AcOEt) to give 1.28 g (40–55% yield) of triazine **3** as yellow crystals: mp 174–175 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.02 (s, 1H), 8.52 (s, 2H), 8.37 (s, 2H), 7.54 (s, 1H), 5.43 (t, *J* = 5.7 Hz, 2H), 4.66 (d, *J* = 5.6 Hz, 4H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 160.1, 145.0, 143.6, 141.7, 134.3, 131.4, 131.2, 130.3 (q, *J* = 33 Hz), 128.3, 127.8, 125.1, 123.3 (q, *J* = 273 Hz), 63.2; IR (KBr) *v* 3270, 3180, 2945, 2884, 1627, 1509, 1421, 1330, 1236, 1214, 1167, 1121, 1055, 1021, 846, 664 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₁₆H₁₃F₃N₃O₂: 336.0960; found: 336.0964. Anal. Calcd for C₁₆H₁₂F₃N₃O₂: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.39; H, 3.58; N, 12.62.

Preparation of 3-[4-(6-benzyloxyhexyloxy)phenyl]-7-trifluoromethylbenzo[e][1,2,4] triazine (4). Starting from **8** using general method. The crude product was purified on column chromatography (SiO₂, CH₂Cl₂ 100%) to give 2.50 g (75% yield) of pure triazine **4** as an orange solid: mp 109–110 °C; ¹H NMR (500 MHz, CDCl₃) δ 8.80 (s, 1H), 8.71 (d, *J* = 8.9 Hz, 2H), 8.14 (d, *J* = 8.9 Hz, 1H), 8.06 (dd, *J*₁ = 8.9 Hz, *J*₂ = 1.7 Hz, 1H), 7.35 (d, *J* = 4.4 Hz, 4H), 7.30–7.27 (m, 1H), 7.07 (d, *J* = 8.9 Hz, 2H), 4.52 (s, 2H), 4.08 (t, *J* = 6.5 Hz, 2H), 3.51 (t, *J* = 6.5 Hz, 2H), 1.86 (quint, *J* = 6.9 Hz, 2H), 1.68 (quint, *J* = 7.0 Hz, 2H), 1.53–1.49 (m, 4H); ¹³C{¹H} NMR (126 MHz, CDCl₃) δ 162.8, 160.9, 144.8, 142.3, 138.7, 131.2 (q, *J* = 34 Hz), 131.1, 130.8 (q, *J* = 2 Hz), 130.7, 128.5, 127.9 (q, *J* = 3 Hz), 127.8, 127.6, 127.2, 123.3 (q, *J* = 273), 115.1, 73.0, 70.4, 68.3, 29.8, 29.3, 26.1, 26.0; IR (KBr) *v* 2939, 2849, 1603, 1509, 1426, 1322, 1258, 1178, 1128, 1089, 1055, 977, 842 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₂₇H₂₇F₃N₃O₂: 482.2055; found: 482.2050. Anal. Calcd for C₂₇H₂₆F₃N₃O₂: C, 67.35; H, 5.44; N, 8.73. Found: C, 67.32; H, 5.56; N, 8.50.

Preparation of hydrazides 5–7. A general method. The solution of methyl benzoate derivative (4.00 g, 24.0 mmol) and hydrazine monohydrate (8.0 mL) in EtOH (100 mL) was refluxed for 48 h. The reaction mixture was cooled and concentrated in vacuo. Crude hydrazides **6** and **7** were recrystallized from hot EtOH to give pure products as white crystals. The crude hydrazide **5** was dissolved in EtOAc, washed with H₂O and dried (Na₂SO₄). Solvents were removed on rotavap, and the product was purified by column chromatography (SiO₂, CH₂Cl₂/EtOAc 4:1 gradient to 1:3).

4-(6-Benzyloxyhexyloxy)benzhydrazide (5). Yield: 5.43 g (70% yield) of pure product **5** as a colorless solid: mp 88–89 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.61 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 2H), 7.35–7.30 (m, 4H), 7.27 (t, *J* = 6.9 Hz, 1H), 6.95 (d, *J* = 8.8 Hz, 2H), 4.44 (s, 4H), 3.99 (t, *J* = 6.5 Hz, 2H), 3.42 (t, *J* = 6.5 Hz, 2H), 1.70 (quint, *J* = 6.8 Hz, 2H), 1.55 (quint, *J* = 6.8 Hz, 2H), 1.44–1.34 (m, 4H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 165.6, 160.9, 138.7, 128.7, 128.2, 127.4, 127.3, 125.3, 114.0, 71.8, 69.5, 67.6, 29.2, 28.6, 25.5, 25.3; IR (KBr) *v* 3321, 2940, 2852, 2796, 1618, 1605, 1536, 1500, 1455, 1341, 1258, 1175, 1127, 1105, 1026, 942, 846, 740 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₂₀H₂₇N₂O₃: 343.2022; found: 343.2027. Anal. Calcd for C₂₀H₂₆N₂O₃: C, 70.15; H, 7.65; N, 8.18. Found: C, 70.10; H, 7.60; N, 8.36.

4-Hydroxymethylbenzhydrazide (6). Yield: 3.80 g (95% yield) of **6** as colorless crystals: ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.73 (s, 1H), 7.78 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 5.30 (t, *J* = 5.7 Hz, 1H), 4.54 (d, *J* = 5.2 Hz, 2H), 4.48 (s, 2H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 166.0, 145.8, 131.7, 126.9, 126.1, 62.5; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₈H₁₁N₂O₂: 167.0821; found: 167.0821. Anal. Calcd for C₈H₁₀N₂O₂: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.84; H, 6.04; N, 16.89.

3,5-Bis(hydroxymethyl)benzhydrazide (7). Yield: 4.24 g (90% yield) of **7** as colorless crystals: mp 173–174 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 9.72 (s, 1H), 7.63 (s, 2H), 7.42 (s, 1H), 5.28 (t, *J* = 5.7 Hz, 2H), 4.52 (d, *J* = 5.4 Hz, 4H), 4.48 (s, 2H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 166.2, 142.5, 133.1, 127.2, 123.6, 62.8; IR (KBr) *v* 3263, 3149, 3051, 2929, 2872, 2783, 2664, 1638, 1536, 1460, 1355, 1260, 1156, 1045, 874, 704 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₉H₁₃N₂O₃: 197.0926; found: 197.0930. Anal. Calcd for C₉H₁₂N₂O₃: C, 55.09; H, 6.16; N, 14.28. Found: C, 55.08; H, 6.11; N, 14.03.

Preparation of hydrazides 8–10. A general method. To a solution of substituted benzhydrazide 5–7 (8.76 mmol) in dry DMSO (20 mL), 1-fluoro-2-nitro-5-trifluoromethylbenzene (1.83 g, 8.76 mmol) was added, and the reaction mixture was stirred at 70 °C overnight. The solution was cooled to rt and poured into a large amount of H₂O and extracted with EtOAc. The organic layer was separated, washed with H₂O (3x), then with brine, and dried (Na₂SO₄). Solvents were removed under vacuum and the crude product was recrystallized twice from EtOH to give corresponding pure hydrazide 5–7 as an orange solid.

***N*-(2-nitro-5-trifluoromethylbenzene)-4-(6-benzyloxyhexyloxy) benzhydrazide (8).** From hydrazide 5. Yield: 3.85 g (83% yield) of 8 as an orange solid: mp 115–116 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.74 (s, 1H), 9.69 (s, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.34–7.30 (m, 5H), 7.27 (t, *J* = 6.8 Hz, 1H), 7.17 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.6 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 2H), 4.44 (s, 2H), 4.04 (t, *J* = 6.4 Hz, 2H), 3.43 (t, *J* = 6.4 Hz, 2H), 1.74 (quint, *J* = 6.8 Hz, 2H), 1.57 (quint, *J* = 6.8 Hz, 2H), 1.46–1.36 (m, 4H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 165.7, 161.9, 145.3, 138.8, 135.2 (q, *J* = 32 Hz), 133.5, 129.5, 128.2, 127.9, 127.4, 127.3, 123.9, 123.1 (q, *J* = 274 Hz), 114.4, 113.4, 111.8, 71.8, 69.6, 67.8, 29.2, 28.5, 25.5, 25.3; IR (KBr) *v* 3319, 3253, 2933, 2854, 1642, 1607, 1540, 1493, 1436, 1339, 1297, 1256, 1227, 1174, 1128, 937, 892, 844, 765, 731, 697 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₂₇H₂₉F₃N₃O₅: 532.2059; found: 532.2062. Anal. Calcd for C₂₇H₂₈F₃N₃O₅: C, 61.01; H, 5.31; N, 7.91. Found: C, 61.01; H, 5.36; N, 8.14.

***N*'-(4-(hydroxymethyl)phenyl)-2-nitro-5-(trifluoromethyl) benzhydrazide (9).** From hydrazide 6. Yield: 3.05 g (98% yield) of 9 as yellow crystals: mp 189–190 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.86 (s, 1H), 9.72 (s, 1H), 8.32 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.3 Hz, 2H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 1.2 Hz, 1H), 7.18 (dd, *J*₁ = 8.8 Hz, *J*₂ = 1.8 Hz, 1H), 5.37 (t, *J* = 5.7 Hz, 1H), 4.59 (d, *J* = 5.7 Hz, 2H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 166.2, 147.2, 145.2, 135.2 (q, *J* = 32 Hz), 133.6, 130.3, 127.9, 127.4, 126.4, 123.1 (q, *J* = 273 Hz), 113.4, 111.8, 62.4; IR (KBr) *v* 3325, 3256, 1648, 1594, 1536, 1492, 1339, 1263, 1228, 1190, 1127, 1056, 935, 831, 763 cm⁻¹; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₁₅H₁₃F₃N₃O₄: 356.0858; found: 356.0849. Anal. Calcd for C₁₅H₁₂F₃N₃O₄: C, 50.71; H, 3.40; N, 11.83. Found: C, 50.78; H, 3.39; N, 12.00.

***N*'-(3,5-bis(hydroxymethyl)phenyl)-2-nitro-5-(trifluoromethyl)benzohydrazide (10).** From hydrazide 7. Yield: 3.04 g (90% yield) of 10 as yellow crystals: mp 195–196 °C; ¹H NMR (500 MHz, DMSO-*d*₆) δ 10.89 (s, 1H), 9.73 (s, 1H), 8.33 (d, *J* = 8.6 Hz, 1H), 7.79 (s, 2H), 7.53 (s, 1H), 7.33 (d, *J* = 1.1 Hz, 1H), 7.17 (dd, *J*₁ = 8.9 Hz, *J*₂ = 1.7 Hz, 1H), 5.37 (t, *J* = 5.7 Hz, 2H), 4.59 (d, *J* = 5.6 Hz, 4H); ¹³C{¹H} NMR (126 MHz, DMSO-*d*₆) δ 166.5, 145.2, 143.0, 135.2 (q, *J* = 32 Hz), 133.6, 131.8, 128.2, 128.0, 123.9, 123.2 (q, *J* = 273 Hz), 113.4, 111.7, 62.6; IR (KBr) *v* 3260, 2952, 1648, 1590, 1489, 1339, 1263, 1182, 1130, 1057, 987, 882; HRMS (ESI-TOF) [M+H]⁺ *m/z* calcd for C₁₆H₁₅F₃N₃O₅: 386.0964; found: 386.0962. Anal. Calcd for C₁₆H₁₄F₃N₃O₅: C, 49.88; H, 3.66; N, 10.91. Found: C, 49.90; H, 3.47; N, 11.04.

Supplementary Materials: The following are available online: NMR (¹H and ¹³C{¹H}); Figures S1–S18), UV (Figures S19–S22) and EPR spectra (Figures S23–S30). The supporting information can be downloaded.

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References

1. Giaconi, N.; Sorrentino, A.L.L.; Poggini, L.; Lupi, M.; Polewczyk, V.; Vinai, G.; Torelli, P.; Magnani, A.; Sessoli, R.; Menichetti, S.; et al. Stabilization of an Enantiopure Sub-Monolayer of Helicene Radical Cations on a Au(111) Surface through Noncovalent Interactions. *Angew. Chem. Int. Ed.* **2021**, *60*, 15276–15280. [[CrossRef](#)] [[PubMed](#)]
2. Poggini, L.; Lunghi, A.; Collauto, A.; Barbon, A.; Armelao, L.; Magnani, A.; Caneschi, A.; Totti, F.; Sorace, L.; Mannini, M. Chemisorption of nitronyl–nitroxide radicals on gold surface: An assessment of morphology, exchange interaction and decoherence time. *Nanoscale* **2021**, *13*, 7613–7621. [[CrossRef](#)] [[PubMed](#)]
3. Mas-Torrent, M.; Crivillers, N.; Mugnaini, V.; Ratera, I.; Rovira, C.; Veciana, J. Organic radicals on surfaces: Towards molecular spintronics. *J. Mater. Chem.* **2009**, *19*, 1691–1695. [[CrossRef](#)]
4. Mas-Torrent, M.; Crivillers, N.; Rovira, C.; Veciana, J. Attaching Persistent Organic Free Radicals to Surfaces: How and Why. *Chem. Rev.* **2011**, *112*, 2506–2527. [[CrossRef](#)]
5. Casu, M.B. Nanoscale Studies of Organic Radicals: Surface, Interface, and Spinterface. *Accounts Chem. Res.* **2018**, *51*, 753–760. [[CrossRef](#)]
6. Poggini, L.; Cucinotta, G.; Sorace, L.; Caneschi, A.; Gatteschi, D.; Sessoli, R.; Mannini, M. Nitronyl nitroxide radicals at the interface: A hybrid architecture for spintronics. *Rendiconti Lince* **2018**, *29*, 623–630. [[CrossRef](#)]
7. Junghoefer, T.; Nowik-Boltyk, E.M.; de Sousa, J.A.; Giangrisostomi, E.; Ovsyannikov, R.; Chassé, T.; Veciana, J.; Mas-Torrent, M.; Rovira, C.; Crivillers, N.; et al. Stability of radical-functionalized gold surfaces by self-assembly and on-surface chemistry. *Chem. Sci.* **2020**, *11*, 9162–9172. [[CrossRef](#)]
8. Ajayakumar, M.R.; Alcón, I.; Bromley, S.T.; Veciana, J.; Rovira, C.; Mas-Torrent, M. Direct covalent grafting of an organic radical core on gold and silver. *RSC Adv.* **2017**, *7*, 20076–20083. [[CrossRef](#)]
9. Ajayakumar, M.R.; Moreno, C.; Alcón, I.; Illas, F.; Rovira, C.; Veciana, J.; Bromley, S.T.; Mugarza, A.; Mas-Torrent, M. Neutral Organic Radical Formation by Chemisorption on Metal Surfaces. *J. Phys. Chem. Lett.* **2020**, *11*, 3897–3904. [[CrossRef](#)]
10. Mukherjee, S.; Boudouris, B.W. *Organic Radical Polymers: New Avenues in Organic Electronics*; Springer: Berlin/Heidelberg, Germany, 2017.
11. Tomlinson, E.P.; Hay, M.E.; Boudouris, B.W. Radical Polymers and Their Application to Organic Electronic Devices. *Macromolecules* **2014**, *47*, 6145–6158. [[CrossRef](#)]
12. Friebe, C.; Schubert, U.S. High-Power-Density Organic Radical Batteries. *Top. Curr. Chem. Collect.* **2019**, *375*, 65–99. [[CrossRef](#)]
13. Saal, A.; Friebe, C.; Schubert, U.S. Polymeric Blatter’s radical via CuAAC and ROMP. *Macromol. Chem. Phys.* **2021**, *222*, 2100194. [[CrossRef](#)]
14. Zhang, K.; Monteiro, M.J.; Jia, Z. Stable organic radical polymers: Synthesis and applications. *Polym. Chem.* **2016**, *7*, 5589–5614. [[CrossRef](#)]
15. Pinto, L.F.; Lloveras, V.; Zhang, S.; Liko, F.; Veciana, J.; Muñoz-Gómez, J.L.; Vidal-Gancedo, J. Fully Water-Soluble Polyphosphorhydrazone-Based Radical Dendrimers Functionalized with Tyr-PROXYL Radicals as Metal-Free MRI T1 Contrast Agents. *ACS Appl. Bio. Mater.* **2020**, *3*, 369–376. [[CrossRef](#)]
16. Ali, B.M.; Velavan, B.; Sudhandiran, G.; Sridevi, J.; Nasar, A.S. Radical dendrimers: Synthesis, anti-tumor activity and enhanced cytoprotective performance of TEMPO free radical functionalized polyurethane dendrimers. *Eur. Polym. J.* **2020**, *122*, 109354. [[CrossRef](#)]
17. Badetti, E.; Lloveras, V.; Muñoz-Gómez, J.L.; Sebastián, R.M.; Caminade, A.M.; Majoral, J.P.; Veciana, J.; Vidal-Gancedo, J. Radical dendrimers: A family of five generations of phosphorus dendrimers functionalized with TEMPO radicals. *Macromolecules* **2014**, *47*, 7717–7724. [[CrossRef](#)]
18. Yordanov, A.T.; Yamada, K.-I.; Krishna, M.C.; Mitchell, J.B.; Woller, E.; Cloninger, M.; Brechbiel, M.W. Spin-Labeled Dendrimers in EPR Imaging with Low Molecular Weight Nitroxides. *Angew. Chem. Int. Ed.* **2001**, *40*, 2690–2692. [[CrossRef](#)]
19. Mezzina, E.; Manoni, R.; Romano, F.; Lucarini, M. Spin-Labeling of Host-Guest Assemblies with Nitroxide Radicals. *Asian J. Org. Chem.* **2015**, *4*, 296–310. [[CrossRef](#)]
20. Casati, C.; Franchi, P.; Pievo, R.; Mezzina, E.; Lucarini, M. Unraveling Unidirectional Threading of α -Cyclodextrin in a [2]Rotaxane through Spin Labeling Approach. *J. Am. Chem. Soc.* **2012**, *134*, 19108–19117. [[CrossRef](#)]
21. Franchi, P.; Fani, M.; Mezzina, E.; Lucarini, M. Increasing the Persistency of Stable Free-Radicals: Synthesis and Characterization of a Nitroxide Based [1]Rotaxane. *Org. Lett.* **2008**, *10*, 1901–1904. [[CrossRef](#)]
22. Chechik, V.; Ionita, G. Bis spin-labelled cyclodextrins. *New J. Chem.* **2007**, *31*, 1726–1729. [[CrossRef](#)]
23. Beejapur, H.A.; Campisciano, V.; Franchi, P.; Lucarini, M.; Giacalone, F.; Gruttadauria, M. Fullerene as a Platform for Recyclable TEMPO Organocatalysts for the Oxidation of Alcohols. *ChemCatChem* **2014**, *6*, 2419–2424. [[CrossRef](#)]
24. Yang, C.; Guenzi, M.; Cicogna, F.; Gambarotti, C.; Filippone, G.; Pinzino, C.; Passaglia, E.; Dintcheva, N.T.; Carroccio, S.; Coiai, S. Grafting of polymer chains on the surface of carbon nanotubes via nitroxide radical coupling reaction. *Polym. Int.* **2016**, *65*, 48–56. [[CrossRef](#)]

25. Tucker-Schwartz, A.K.; Garrell, R.L. Simple Preparation and Application of TEMPO-Coated Fe₃O₄ Superparamagnetic Nanoparticles for Selective Oxidation of Alcohols. *Chem. A Eur. J.* **2010**, *16*, 12718–12726. [[CrossRef](#)]
26. Zawada, K.; Tomaszewski, W.; Megiel, E. A smart synthesis of gold/polystyrene core-shell nanohybrids using TEMPO coated nanoparticles. *RSC Adv.* **2014**, *4*, 23876–23885. [[CrossRef](#)]
27. Hata, K.; Fujihara, H. Preparation and electrochemical polymerization of new multifunctional pyrrolethiolate-stabilized gold and palladium nanoparticles. *Chem. Commun.* **2002**, 2714–2715. [[CrossRef](#)]
28. Caragheorghopol, A.; Chechik, V. Mechanistic aspects of ligand exchange in Au nanoparticles. *Phys. Chem. Chem. Phys.* **2008**, *10*, 5029–5041. [[CrossRef](#)]
29. Schätz, A.; Grass, R.N.; Stark, W.J.; Reiser, O. TEMPO Supported on Magnetic C/Co-Nanoparticles: A Highly Active and Recyclable Organocatalyst. *Chem. A Eur. J.* **2008**, *14*, 8262–8266. [[CrossRef](#)]
30. Gozdziwska, M.; Cichowicz, G.; Markowska, K.; Zawada, K.; Megiel, E. Nitroxide-coated silver nanoparticles: Synthesis, surface physicochemistry and antibacterial activity. *RSC Adv.* **2015**, *5*, 58403–58415. [[CrossRef](#)]
31. Megiel, E. Surface modification using TEMPO and its derivatives. *Adv. Colloid Interface Sci.* **2017**, *250*, 158–184. [[CrossRef](#)]
32. Hansen, K.-A.; Blinco, J.P. Nitroxide radical polymers—A versatile material class for high-tech applications. *Polym. Chem.* **2018**, *9*, 1479–1516. [[CrossRef](#)]
33. Ji, Y.; Long, L.; Zheng, Y. Recent advances of stable Blatter radicals: Synthesis, properties and applications. *Mater. Chem. Front.* **2020**, *4*, 3433–3443. [[CrossRef](#)]
34. Oyaizu, K.; Nishide, H. Radical Polymers for Organic Electronic Devices: A Radical Departure from Conjugated Polymers? *Adv. Mater.* **2009**, *21*, 2339–2344. [[CrossRef](#)]
35. Rajca, A.; Wang, Y.; Boska, M.; Paletta, J.T.; Olankitwanit, A.; Swanson, M.A.; Mitchell, D.G.; Eaton, S.S.; Eaton, G.R.; Rajca, S. Organic Radical Contrast Agents for Magnetic Resonance Imaging. *J. Am. Chem. Soc.* **2012**, *134*, 15724–15727. [[CrossRef](#)] [[PubMed](#)]
36. Francese, G.; Dunand, F.A.; Loosli, C.; Decurtins, S. Functionalization of PAMAM dendrimers with nitronyl nitroxide radicals as models for the outer-sphere relaxation in dendritic potential MRI contrast agents. *Org. Magn. Reson.* **2003**, *41*, 81–83. [[CrossRef](#)]
37. Wilcox, D.A.; Agarkar, V.V.; Mukherjee, S.; Boudouris, B.W. Stable Radical Materials for Energy Applications. *Annu. Rev. Chem. Biomol. Eng.* **2018**, *9*, 83–103. [[CrossRef](#)]
38. Suga, T.; Nishide, H. *Stable Radicals: Fundamentals and Applied Aspects of Odd-Electron Compounds*; Hicks, R.G., Ed.; Wiley & Sons Ltd.: Chichester, UK, 2010; pp. 507–519.
39. Nevers, D.R.; Brushett, F.R.; Wheeler, D.R. Engineering radical polymer electrodes for electrochemical energy storage. *J. Power Sources* **2017**, *352*, 226–244. [[CrossRef](#)]
40. Almubayedh, S.; Chahma, M. Electrosynthesis and characterization of stable radical-functionalized oligo/polythiophenes. *N. J. Chem.* **2015**, *39*, 7738–7741. [[CrossRef](#)]
41. Low, J.Z.; Kladnik, G.; Patera, L.L.; Sokolov, S.; Lovat, G.; Kumarasamy, E.; Repp, J.; Campos, L.M.; Cvetko, D.; Morgante, A.; et al. The Environment-Dependent Behavior of the Blatter Radical at the Metal–Molecule Interface. *Nano Lett.* **2019**, *19*, 2543–2548. [[CrossRef](#)]
42. De Sousa, J.A.; Bejarano, F.; Gutiérrez, D.; Leroux, Y.R.; Nowik-Boltyk, E.M.; Junghoefer, T.; Giangrisostomi, E.; Ovsyannikov, R.; Casu, M.B.; Veciana, J.; et al. Exploiting the versatile alkyne-based chemistry for expanding the applications of a stable triphenylmethyl organic radical on surfaces. *Chem. Sci.* **2020**, *11*, 516–524. [[CrossRef](#)]
43. Ruthstein, S.; Artzi, R.; Goldfarb, D.; Naaman, R. EPR studies on the organization of self-assembled spin-labeled organic monolayers adsorbed on GaAs. *Phys. Chem. Chem. Phys.* **2005**, *7*, 524–529. [[CrossRef](#)]
44. Glosz, K.; Stolarczyk, A.; Jarosz, T. Siloxanes—Versatile Materials for Surface Functionalisation and Graft Copolymers. *Int. J. Mol. Sci.* **2020**, *21*, 6387. [[CrossRef](#)]
45. Fu, H.; Policarpio, D.M.; Bateas, J.D.; Bergbreiter, D.E. Redox-controlled ‘smart’ polyacrylamide solubility. *Polym. Chem.* **2010**, *1*, 631–633. [[CrossRef](#)]
46. Schattling, P.; Jochum, F.D.; Theato, P. Multi-responsive copolymers: Using thermo-, light- and redox stimuli as three independent inputs towards polymeric information processing. *Chem. Commun.* **2011**, *47*, 8859–8861. [[CrossRef](#)]
47. Binder, W.H.; Sachsenhofer, R. ‘Click’ chemistry in polymer and material science: An update. *Macromol. Rapid Commun.* **2008**, *29*, 952–981. [[CrossRef](#)]
48. Johnson, J.A.; Finn, M.G.; Koberstein, J.T.; Turro, N.J. Construction of Linear Polymers, Dendrimers, Networks, and Other Polymeric Architectures by Copper-Catalyzed Azide-Alkyne Cycloaddition “Click” Chemistry. *Macromol. Rapid Commun.* **2008**, *29*, 1421. [[CrossRef](#)]
49. Le Droumaguet, B.; Velonia, K. Click Chemistry: A Powerful Tool to Create Polymer-Based Macromolecular Chimeras. *Macromol. Rapid Commun.* **2008**, *29*, 1073–1089. [[CrossRef](#)]
50. Kunz, T.K.; Wolf, M.O. Electrodeposition and properties of TEMPO functionalized polythiophene thin films. *Polym. Chem.* **2011**, *2*, 640–644. [[CrossRef](#)]
51. Rogers, F.J.M.; Norcott, P.L.; Coote, M.L. Recent advances in the chemistry of benzo[e][1,2,4]triazinyl radicals. *Org. Biomol. Chem.* **2020**, *18*, 8255–8277. [[CrossRef](#)]
52. Blatter, H.M.; Lukaszewski, H. A new stable free radical. *Tetrahedron Lett.* **1968**, *9*, 2701–2705. [[CrossRef](#)]

53. Karecla, G.; Papagiorgis, P.; Panagi, N.; Zissimou, G.A.; Constantinides, C.P.; Koutentis, P.A.; Itskos, G.; Hayes, S.C. Emission from the stable Blatter radical. *N. J. Chem.* **2017**, *41*, 8604–8613. [[CrossRef](#)]
54. Constantinides, C.P.; Koutentis, P.A.; Krassos, H.; Rawson, J.M.; Tasiopoulos, A.J. Characterization and Magnetic Properties of a “Super Stable” Radical 1,3-Diphenyl-7-trifluoromethyl-1,4-dihydro-1,2,4-benzotriazin-4-yl. *J. Org. Chem.* **2011**, *76*, 2798–2806. [[CrossRef](#)]
55. Jasiński, M.; Szczytko, J.; Pocięcha, D.; Monobe, H.; Kaszyński, P. Substituent-Dependent Magnetic Behavior of Discotic Benzo[e][1,2,4]triazinyls. *J. Am. Chem. Soc.* **2016**, *138*, 9421–9424. [[CrossRef](#)]
56. Jasiński, M.; Szymańska, K.; Gardias, A.; Pocięcha, D.; Monobe, H.; Szczytko, J.; Kaszyński, P. Tuning the Magnetic Properties of Columnar Benzo[e][1,2,4]triazin-4-yls with the Molecular Shape. *ChemPhysChem* **2019**, *20*, 636–644. [[CrossRef](#)]
57. Shivakumar, K.I.; Pocięcha, D.; Szczytko, J.; Kapuściński, S.; Monobe, H.; Kaszyński, P. Photoconductive bent-core liquid crystalline radicals with a paramagnetic polar switchable phase. *J. Mater. Chem. C* **2020**, *8*, 1083–1088. [[CrossRef](#)]
58. Zheng, Y.; Miao, M.-S.; Kemei, M.C.; Seshadri, R.; Wudl, F. The Pyreno-Triazinyl Radical—Magnetic and Sensor Properties. *Isr. J. Chem.* **2014**, *54*, 774–778. [[CrossRef](#)]
59. Zheng, Y.; Miao, M.-S.; Dantelle, G.; Eisenmenger, N.D.; Wu, G.; Yavuz, I.; Chabinyč, M.L.; Houk, K.N.; Wudl, F. A Solid-State Effect Responsible for an Organic Quintet State at Room Temperature and Ambient Pressure. *Adv. Mater.* **2015**, *27*, 1718–1723. [[CrossRef](#)]
60. Ciccullo, F.; Calzolari, A.; Bader, K.; Neugebauer, P.; Gallagher, N.M.; Rajca, A.; van Slageren, J.; Casu, M.B. Interfacing a Potential Purely Organic Molecular Quantum Bit with a Real-Life Surface. *ACS Appl. Mater. Interfaces* **2018**, *11*, 1571–1578. [[CrossRef](#)]
61. Ciccullo, F.; Gallagher, N.M.; Geladari, O.; Chasse, T.; Rajca, A.; Casu, M.B. A Derivative of the Blatter Radical as a Potential Metal-Free Magnet for Stable Thin Films and Interfaces. *ACS Appl. Mater. Interfaces* **2016**, *8*, 1805–1812. [[CrossRef](#)]
62. Poryvaev, A.S.; Gjuzi, E.; Polyukhov, D.M.; Hoffmann, F.; Fröba, M.; Fedin, M.V. Blatter radical-grafted mesoporous silica as prospective nanoplatform for spin manipulation at ambient conditions. *Angew. Chem. Int. Ed.* **2021**, *60*, 8683–8688. [[CrossRef](#)]
63. Constantinides, C.P.; Obijalska, E.; Kaszyński, P. Access to 1,4-dihydrobenzo[e][1,2,4]triazin-4-yl derivatives. *Org. Lett.* **2016**, *18*, 916–919. [[CrossRef](#)] [[PubMed](#)]
64. Kaszyński, P.; Constantinides, C.P.; Young, V.G., Jr. The Planar Blatter Radical: Structural Chemistry of 1,4-Dihydrobenzo[e][1,2,4]-triazin-4-yls. *Angew. Chem. Int. Ed.* **2016**, *55*, 11149–11152. [[CrossRef](#)] [[PubMed](#)]
65. Abbasi, M.; Mohammadzadeh, M.R.; Saeedi, N. The synthesis of symmetrical disulfides by reacting organic halides with Na₂S₂O₃·5H₂O in DMSO. *N. J. Chem.* **2016**, *40*, 89–92. [[CrossRef](#)]
66. Shao, C.; Wang, X.; Xu, J.; Zhao, J.; Zhang, Q.; Hu, Y. Carboxylic Acid-Promoted Copper(I)-Catalyzed Azide–Alkyne Cycloaddition. *J. Org. Chem.* **2010**, *75*, 7002–7005. [[CrossRef](#)]
67. Neva, T.; Carmona, T.; Benito, J.M.; Przybylski, C.; Mellet, C.O.; Mendicuti, F.; Fernández, J.M.G. Dynamic Control of the Self-Assembling Properties of Cyclodextrins by the Interplay of Aromatic and Host–Guest Interactions. *Front. Chem.* **2019**, *7*, 72. [[CrossRef](#)]
68. Neva, T.; Ortiz Mellet, C.; García Fernández, J.M.; Benito, J.M. Multiply-linked cyclodextrin–aromatic hybrids: Caps, hinges and clips. *J. Carbohydr. Chem.* **2019**, *38*, 470–493. [[CrossRef](#)]
69. Neva, T.; Carbajo-Gordillo, A.I.; Benito, J.M.; Lana, H.; Marcelo, G.; Mellet, C.O.; De Ilarduya, C.T.; Mendicuti, F.; Fernández, J.M.G. Tuning the Topological Landscape of DNA–Cyclodextrin Nanocomplexes by Molecular Design. *Chem. A Eur. J.* **2020**, *26*, 15259–15269. [[CrossRef](#)]
70. Balbuena, P.; Lesur, D.; Álvarez, M.J.G.; Mendicuti, F.; Mellet, C.O.; Fernández, J.M.G. One-pot regioselective synthesis of 2I,3I-O-(o-xyllylene)-capped cyclomaltooligosaccharides: Tailoring the topology and supramolecular properties of cyclodextrins. *Chem. Commun.* **2007**, 3270–3272. [[CrossRef](#)]
71. Fulmer, G.R.; Miller, A.J.M.; Sherden, N.H.; Gottlieb, H.E.; Nudelman, A.; Stoltz, B.M.; Bercaw, J.E.; Goldberg, K.I. NMR Chemical Shifts of Trace Impurities: Common Laboratory Solvents, Organics, and Gases in Deuterated Solvents Relevant to the Organometallic Chemist. *Organometallics* **2010**, *29*, 2176–2179. [[CrossRef](#)]