Palladium-Catalyzed Cross-Coupling Reactions of Paramagnetic Vinyl Bromides and Paramagnetic Boronic Acids

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Dedicated to Prof. Ernõ Brücher on the occasion of his 70th birthday

Abstract: Suzuki reactions are utilized for the synthesis of heterobifunctional cross-linking reagents (thiol- or aminospecific and photoactivatable), polyaromatics (such as phenanthrene) and heterocycles (such as coumarin and quinoline), anellated nitroxides and paramagnetic, biologically active molecules (such as *cis*-stilbene and nicotinamide). Furthermore, the synthesis of new vinyl and allyl boronic acid esters is also reported.

Key words: boron, cross-coupling, free radicals, heterocycles, palladium

A variety of applications of stable nitroxide free radicals has been described to date. The most important ones are spin-labelling,[1] utilization as a co-oxidant,[2] as double (fluorescent and spin) sensor reagent,[3] as building blocks of organic magnets[4] and oxymmetry reagents,[5] just to mention a few.

Today, most of these applications require properly designed stable nitroxide free radicals; however, the formation of the carbon–carbon bond is often a troublesome reaction in the presence of a nitroxide free radical moiety. Several methods have been reported from our and other laboratories, such as Grignard reaction,[6] Wittig reaction,[7] aldol condensation,[8] Michael addition[9] and Diels–Alder reaction.[10] Recently, we have found that the palladium-catalyzed cross-coupling reactions[11] can be accomplished under mild conditions and tolerate a wide variety of functional groups including the nitroxide moiety. This observation was important because the application of palladium-catalyzed cross-coupling reactions increases exponentially. We were able to underline this tendency[12] also in nitroxide chemistry by showing the possibility of synthesizing a variety polysubstituted nitroxides. The only prerequisite of this cross-coupling reaction is the synthesis of paramagnetic vinyl halogenides available from the Favorskii reaction[13] or from the oxidation of hydrazones.[14] The other challenge in this field was the synthesis of a paramagnetic boronic acid[15] in order to couple the paramagnetic boronic acid with any aryl, vinyl, or hetaryl halogenides. In this paper we extend the utilization of cross-coupling reactions to paramagnetic vinyl halogenides to obtain new spin labels, double (spin and fluorescence) sensor molecules with a polyaromatic fluorophore, paramagnetically modified bioactive molecules, and new paramagnetic boronic acid esters.

In the cross-coupling spin-label reagent synthesis β-bromo-α,β-unsaturated ester **1**[13] reacted with 4-benzoylphenylboronic acid under N_2 in aqueous dioxane in the presence of Na_2CO_3 base and $Pd(PPh_3)_4$ as catalyst to give compound **2a**. The introduction of the benzophenone group makes this reagent photoactivatable at 350 nm. Ester **2a** was hydrolyzed to acid **2b**, which was converted into succinate **2c** with DCC and *N*-hydroxysuccinimide. This means that **2c** is a cross-linking reagent with an amino-specific and with a photoactivatable arm. Reaction of compound **1** with 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol under the above conditions directly gave paramagnetic coumarin **3** as a result of the Suzuki cross-coupling reaction followed by a base-catalyzed transesterification reaction. The Suzuki reaction of alcohol **4** with 4-benzoylphenylboronic acid gave compound **5a** in which the alcohol substituent was converted into bromide **5b** via its mesylate. This bromide was replaced with SSO_2CH_3, which is a thiol-specific arm, forming a cleavable S–S bond with a cysteine side-chain,[16] meaning that compound **5c** can be regarded as a thiolspecific and photoactivatable cross-linking spin-label reagent. It can be utilized in a similar way as the earlier published cross-linking reagent with an aromatic azide (photoactivatable arm) and with a methanethiosulfonate (thiolspecific arm)[17] (Scheme 1).

Continuing our earlier work on heterocycle-anellated nitroxides, aldehyde **6** was treated with 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline in the presence of an aqueous Na_2CO_3/dioxane solution and $Pd(PPh_3)_4$ as catalyst, giving quinoline derivative **7** in a one-pot procedure with an imine formation and Suzuki cross-coupling reaction.[18] It is interesting to note that heating aniline with compound **6** in DMF gave isoquinoline **8** which is an isomer of compound **7**.[19] Reaction of β-bromo-α,β-unsaturated nitrile **9** with 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline in the presence of Cs_2CO_3, aminoadamantane bases and $Pd(OAc)_2$ as catalyst gave the paramagnetic 2-aminoquinoline[20] derivative **10** (Scheme 2).

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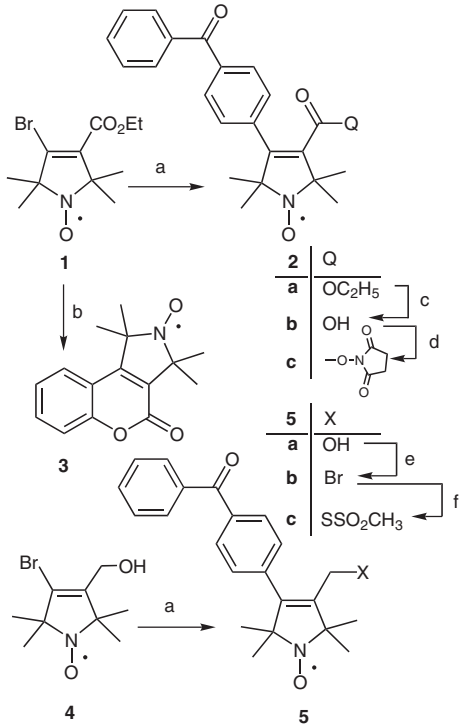
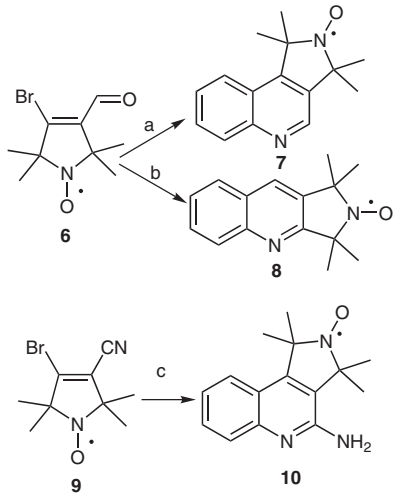
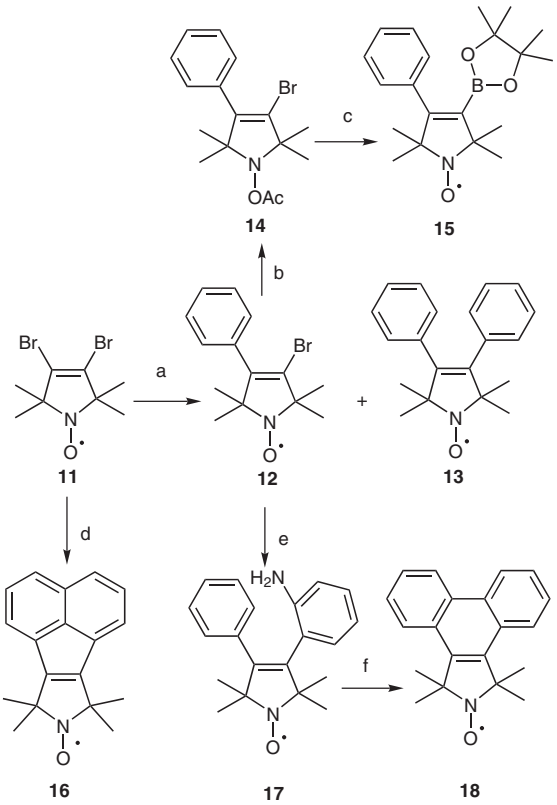


Scheme 1 *Reagents and conditions*: (a) 4-Benzoylphenylboronic acid (1 equiv), $Pd(PPh_3)_4$ (0.05 equiv), dioxane/aq Na_2CO_3, under N_2, 4 h, 53–68%; (b) 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)phenol (1.1 equiv), $Pd(PPh_3)_4$ (0.05 equiv), dioxane/aq Na_2CO_3, under N_2, 2 h, 76%; (c) NaOH/MeOH, reflux, 1 h, then r.t., 12 h, H^+, 78%; (d) *N*-Hydroxysuccinimide (1 equiv), DCC (1 equiv), EtOAc, r.t., 3 h, 55%; (e) MsCl (1.1 equiv), Et_3N (1.1 equiv), CH_2Cl_2, 0 °C → r.t., 1 h, then LiBr, acetone, reflux, 30 min, 49%; (f) $NaSSO_2CH_3$ (2.0 equiv), acetone–H_2O, reflux, 45 min, 62%



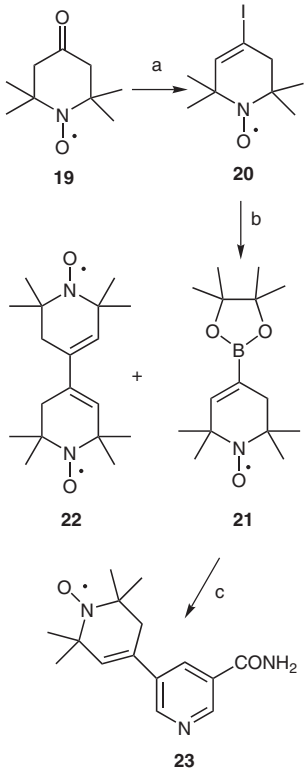
Scheme 2 *Reagents and conditions*: (a) 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2yl)aniline (1.1 equiv), $Pd(PPh_3)_4$ (0.05 equiv), dioxane/aq Na_2CO_3, under N_2, 2 h, 38%; (b) Aniline (1.1 equiv), DMF, 80 °C, 3 h, 56%; (c) 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.1 equiv), $Pd(OAc)_2$ (0.05 equiv), 1-adamantaneamine (0.4 equiv), Cs_2CO_3 (2.2 equiv), dioxane, 16 h, 45%

Reaction of dibromide **11** with one equivalent of phenylboronic acid gave a mixture of compounds **12** and **13** (2:3 ratio). Vinyl bromide **12** was converted into *O*-acetyl-protected (to avoid O-butylation) derivative **14**.[21] Treatment of compound **14** with *n*-BuLi[22] at –78 °C afforded the 3-lithiopyrroline whose reaction with trimethylborate gave the corresponding boronic acid. After the oxidation of the nitroxide, the formed boronic acid was not purified, but after isolation it was converted into its pinacolate ester **15** with pinacol alcohol in the presence of $MgSO_4$ in MeOH.[23] Suzuki reaction of dibromide **11** and 1-naphthylboronic acid in a sealed tube in the presence of DBU as base and $Pd_2(dba)_3$ as catalyst furnished paramagnetic cyclopent[a]acenaphthylene **16**.[24] Our next polyaromatic target was phenanthrene. The Suzuki cross-coupling of bromide **12** and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline in the presence of $Pd(PPh_3)_4$ as catalyst provided amine **17**. Diazotation of the aromatic amide and heating of an aqueous solution of the diazonium salt in the presence of Cu powder gave phenanthrene-anellated nitroxide **18** in a Pschorr reaction (Scheme 3).[18]



Scheme 3 *Reagents and conditions*: (a) Phenylboronic acid (1 equiv), $PdCl_2(PPh_3)_2$, (0.05 equiv), $Ba(OH)_2 \cdot 9H_2O$ (1 equiv), dioxane–H_2O, reflux, 2 h, under N_2, 24% for **12** and 20% for **13**; (b) Ascorbic acid (10 equiv), dioxane–H_2O, then extraction, AcCl (1.1 equiv), Et_3N (1.1 equiv), 0 °C → r.t., 1 h, 55%; (c) *n*-BuLi (2 equiv), THF, –78 °C, then $B(OMe)_3$ (1.1 equiv), –78 °C → r.t., 2 h, then MeOH, H_2O, r.t., 12 h, extraction, MnO_2 (0.1 equiv), 15 min, then azeotropic dry pinacol, (1.2 equiv), $MgSO_4$, MeOH, 12 h, 33%; (d) 1-Naphthylboronic acid (1.1 equiv), DBU (1.0 equiv), $Pd_2(dba)_3$ (0.25 equiv), $P(Cy)_3$ (0.6 equiv), DMF, sealed tube, 48 h, 150 °C, 29%; (e) 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (1.1 equiv), $Pd(PPh_3)_4$ (0.05 equiv), dioxane/aq Na_2CO_3, under N_2, 2 h, 61%; (f) $NaNO_2$ (1.1 equiv), aq 1 M HCl, 0 °C, 30 min, then Cu powder/H_2O, 60 °C, 40 min, 27%

Starting from 4-oxo-TEMPO (**19**) we synthesized its 4-iodo-1,2,3,6-tetrahydropyridine derivative.[25] Treatment of the starting ketone with hydrazine hydrate followed by oxidation with iodine in diethyl ether in the presence of tetramethyl guanidine (TMG) yielded compound **20**. Unfortunately, our attempt to obtain the six-membered paramagnetic boronic acid failed when the *O*-acetyl-protected derivative of **20** was treated with *n*-BuLi followed by $B(OMe)_3$. Therefore, compound **21** could be produced only in a reaction of compound **20** with bis(pinacolato)diboron and $PdCl_2$(dppf) as catalyst and KOAc as base in DMSO,[26] but only in low (28%) because of the formation of biradical **22**. Compound **21** was used for paramagnetic modification of 5-bromo-nicotinamide in a Suzuki reaction under the conditions used above, i.e. refluxing boronic acid **21** with 5-bromo nicotinamide in an aqueous Na_2CO_3/dioxane solution in the presence of $Pd(PPh_3)_4$ as catalyst (Scheme 4).



Scheme 4 *Reagents and conditions*: (a) $N_2H_4{\cdot}H_2O$ (6 equiv), EtOH, r.t., 3 h, then reflux, 1 h, H_2O–$CHCl_3$ extraction, PbO_2 (0.1 equiv), O_2, 30 min, then TMG (3.5 equiv), I_2 (2.2 equiv), Et_2O, 1 h, r.t., 59%; (b) Bis(pinacolato)diboron (1.1 equiv), $PdCl_2$(dppf) (0.05 equiv), KOAc (3 equiv), DMSO, 80 °C, 3 h, under N_2, 28% for **21** and 65% for **22**; (c) 5-Bromonicotinamide, $Pd(PPh_3)_4$ (0.05 equiv), dioxane/aq Na_2CO_3, under N_2, 2 h, 39%

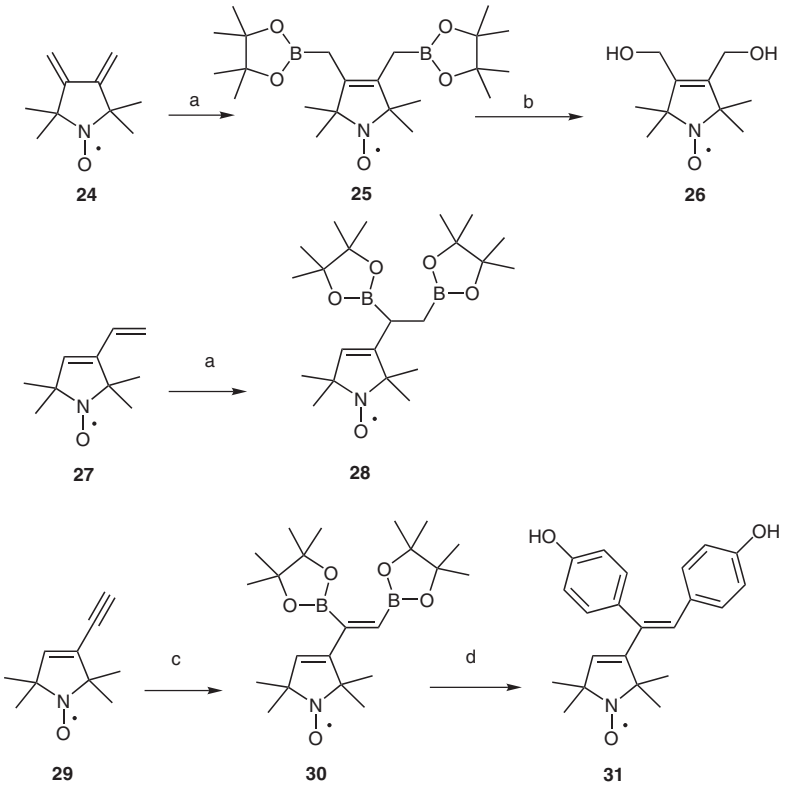
An interesting approach for allyl boronic acid is the addition reaction of bis(pinacolato)diboron to alkenes in toluene in the presence of $Pt(PPh_3)_4$ as catalyst.[27] In a 1,4-addition reaction symmetrical paramagnetic diene **24** gave bis(boronic acid ester) **25**. Our attempts to use the allyl boronic ester compound for a C–C bond formation[28] failed; however, oxidation with H_2O_2 in the presence of NaOH[29] yielded alcohol **26**,[10] which we prepared more economically earlier. The addition of bis(pinacolato)diboron to asymmetric diene **27**[30] afforded pinacolate ester **28**. This 1,2-addition was proven by ^{1}H NMR spectroscopy studies on the *O*-acetyl derivative of **28**. The assumed arrangement of protons was confirmed by mononuclear decoupling experiments: selective irradiation of the CH triplet (δ = 1.79 ppm) only resulted in the change of the CH_2 multiplet (δ = 1.03 ppm). This proton arrangement is true only for the 1,2-addition product. The addition of bis(pinacolato)diboron to paramagnetic terminal acetylene **29** in DMF catalyzed by $Pt(PPh_3)_4$ afforded compound **30**.[31] A Suzuki reaction of this bis(vinylboronic acid) and 4-bromophenol provided paramagnetic *Z*-hydroxystilbene compound **31** (Scheme 5). The importance of this type of compound is well supported by the fact that several hydroxylated stilbenes exhibit important biological properties.[32]

In conclusion, Suzuki reactions can be accomplished with paramagnetic vinyl halogenides in synthetic target-oriented syntheses to create heterocycles, carbocycles, anellated nitroxides as well as cross-linking spin-label reagents. Paramagnetic boronic acids can be applied in C–C bond forming reactions in the presence of a great variety of functional groups which are retained to obtain bioactive paramagnetic molecules.

Melting points were determined with a Boetius micro melting point apparatus and are uncorrected. Elemental analyses (C, H, N, S) were performed on Fisons EA 1110 CHNS elemental analyzer. The IR (Specord 85) spectra were in each case consistent with the assigned structure. Mass spectra were recorded on Thermoquest Automass Multi and VG TRIO-2 instruments in EI mode. ^{1}H NMR spectra were recorded on a Varian ^{UNITY}*INOVA* 400 WB spectrometer. Chemical shifts are referenced to Me_4Si. Measurements were run at 298K-probe temperature in $CDCl_3$ solution. To obtain high-resolution NMR spectra of the radicals those compounds were reduced by co-dissolved PhNHNHPh additive. ESR spectra were taken on a Miniscope MS 200 in 10^{-4} M $CHCl_3$ solution. All monoradicals gave triplet lines between a_N = 14.7–15.1 G whereas biradical **22** gave a quintet line at a_{N1} = 15.2 G, a_{N2} = 7.4 G. Flash column chromatography was performed on Merck Kieselgel 60 (0.040–0.063 mm). Qualitative TLC was carried out on commercially prepared plates (20 × 20 × 0.02 cm) coated with Merck Kieselgel GF_{254}. 4-Benzoylphenylboronic acid, 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline, 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol, 1-naphthyl boronic acid, compound **19** as well as palladium and platinum catalysts were purchased from Aldrich. Compounds **1**, **4**, **6**, **9**,[33] **11**, **13**,[11] **24**, **26**, **29**[10] and **27**[30] were prepared according to published procedures.

Suzuki Coupling Reaction (2a, 3, 5a, 7, 17, 23, 31); General Procedure

A solution of vinylic bromide (**1**, **4**, **6**, **12**, 5-bromonicotinamide, or 4-bromophenol) (2.0 mmol) and $Pd(PPh_3)_4$ (100 mg, 0.1 mmol) in dioxane (10 mL) was purged with N_2 for 5 min. Then boronic acid or boronic acid ester (2.0 mmol, for **31** only 1.0 mmol diester) was added followed by aq Na_2CO_3 (10%, 10 mL). The mixture was stirred and heated to reflux under N_2 until the consumption of the starting halogen compound (2–8 h, followed by TLC). After cooling, the dark-yellow or brown solution was evaporated in vacuo, brine (10 mL) was added and the aqueous phase was washed with $CHCl_3$ (2 × 20 mL). The organic phase was dried ($MgSO_4$), filtered



Scheme 5 *Reagents and conditions*: (a) Bis(pinacolato)diboron (1 equiv), $Pt(PPh_3)_4$ (0.05 equiv), toluene, reflux, 5 h, under N_2, 38–63%; (b) 30% H_2O_2, aq NaOH, MeOH, reflux 2 h, 67%; (c) Bis(pinacolato)diboron (1 equiv), $Pt(PPh_3)_4$ (0.05 equiv), DMF, 80 °C, 24 h, under N_2, 42%; (d) 4-Bromophenol (2.0 equiv), $Pd(PPh_3)_4$ (0.1 equiv), dioxane/aq Na_2CO_3, under N_2, 8 h, 40%

and evaporated. The residue was purified by flash column chromatography (hexane–EtOAc or $CHCl_3$–Et_2O) to give the compounds in 38–76% yield.

4-(4-Benzoylphenyl)-3-carbethoxy-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (2a)
From compound **1** and 4-benzoylphenylboronic acid with 4 h heating.

Yellow solid; yield: 533 mg (68%); mp 100–101 °C; R_f = 0.44 (hexane–EtOAc, 2:1).

IR (nujol): 1710, 1660 (C=O), 1590 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 392 (M^+, 13), 377 (2), 105 (100), 77 (53).

Anal. Calcd for $C_{24}H_{26}NO_4$: C, 73.45; H, 6.68; N, 3.57. Found: C, 73.39; H, 6.62; N, 3.41.

1,1,3,3-Tetramethyl-2,3-dihydrochromeno[3,4-*c*]pyrrol-4(1*H*)-4-one-2-yloxyl Radical (3)
From compound **1** and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenol with 2 h heating.

Yellow solid; yield: 392 mg (76%); mp 205–206 °C; R_f = 0.4 (hexane–EtOAc, 2:1).

IR (nujol): 1720 (C=O), 1600, 1570 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 258 (M^+, 59), 243 (100), 228 (59), 213 (67), 115 (33).

Anal. Calcd for $C_{15}H_{16}NO_3$: C, 69.75; H, 6.24; N, 5.42. Found: C, 69.80; H, 6.22; N, 5.24.

4-(4-Benzoylphenyl)-3-hydroxymethyl-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (5a)
From compound **4** and 4-benzoylphenylboronic acid with 4 h heating.

Yellow solid; yield: 413 mg (53%); mp 134–136 °C; R_f = 0.23 ($CHCl_3$–Et_2O, 2:1).

IR (nujol): 3400 (OH), 1660 (C=O), 1560 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 350 (M^+, 4), 335 (3), 128 (15), 105 (100), 77 (79).

Anal. Calcd for $C_{22}H_{24}NO_3$: C, 75.40; H, 6.90; N, 4.00. Found: C, 75.36; H, 6.88; N, 3.89.

1,1,3,3-Tetramethyl-1,3-dihydro-2*H*-pyrrolo[3,4-*c*]quinolin-2-yloxyl Radical (7)
From compound **6** and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline with 2 h heating.

Yellow solid; yield: 183 mg (38%); mp 157–159 °C; R_f = 0.25 (hexane–EtOAc, 2:1).

IR (nujol): 1650 (C=N), 1570 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 241 (M^+, 91), 226 (95), 211 (100), 196 (62).

Anal. Calcd for $C_{15}H_{17}N_2O$: C, 74.66; H, 7.10; N, 11.61. Found: C, 74.52; H, 7.06; N, 11.57.

3-(2-Aminophenyl)- 2,2,5,5-tetramethyl-4-phenyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (17)
From compound **12** and 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline with 2 h heating.

Yellow solid; yield: 374 mg (61%); mp 160–163 °C; R_f = 0.29 (hexane–EtOAc, 2:1).

IR (nujol): 3440, 3300 (NH_2), 1610, 1565 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 307 (M^+, 39), 292 (7), 277 (44), 262 (27), 234 (100).

Anal. Calcd for $C_{20}H_{23}N_2O$: C, 78.14; H, 7.54; N, 9.11. Found: C, 78.02; H, 7.48; N, 9.00.

1′-Oxyl-2′,2′,6′,6′-tetramethyl-1′,2′,3′,6′-tetrahydro-[3,4′]-bipyridyl-5-carboxylic Acid (23)

From 5-bromonicotinamide and compound **21** with 2 h heating.

Yellow solid; yield: 213 mg (39%); mp 145–147 °C; R_f = 0.18 ($CHCl_3$–MeOH, 9:1).

IR (nujol): 3360, 3160 (NH_2), 1640 (C=O), 1605 (N–C=O) cm^{-1}.

MS (EI): *m*/*z* (%) = 274 (M^+, 50), 244 (15), 229 (100).

Anal. Calcd for $C_{15}H_{20}N_3O_2$: C, 65.67; H, 7.35; N, 15.32. Found: C, 65.61; H, 7.29; N, 15.30.

3-[(*E*)-1,2-Bis(4-hydroxyphenyl)vinyl]-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (31)

From 4-bromophenol (2 equiv) and diboronic acid ester **30** with 8 h heating.

Yellow solid; yield: 140 mg (40%); mp 228–230 °C; R_f = 0.25 ($CHCl_3$–MeOH, 9:1).

IR (nujol): 3300 (OH), 1610, 1560 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 350 (M^+, 21), 336 (23), 320 (100), 305 (48).

Anal. Calcd for $C_{22}H_{24}NO_3$: C, 75.40; H, 6.90; N, 4.00. Found: C, 75.25; H, 6.86; N, 3.83.

4-(4-Benzoylphenyl)-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl-3-carboxylic Acid Radical (2b)

To a solution of compound **2a** (392 mg, 1.00 mmol) in MeOH (10 mL), 10% aq NaOH (5 mL) was added and the mixture was boiled under gentle reflux for 1 h and then allowed to stay at r.t. overnight. After evaporating the alcohol, the mixture was acidified with 5% aq H_2SO_4. The precipitated solid was dried on air and it was pure enough for the next reaction step. 50 mg of the compound were purified by chromatography ($CHCl_3$–MeOH, 9:1) for analysis.

Yield: 284 mg (78%); mp 224–226 °C; R_f = 0.44 ($CHCl_3$–MeOH, 9:1).

IR (nujol): 3400 (OH), 1690, 1660 (C=O), 1590 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 364 (M^+, 2), 349 (1), 319 (4), 105 (100), 77 (53).

Anal. Calcd for $C_{22}H_{22}NO_4$: C, 72.51; H, 6.08; N, 3.84. Found: C, 72.55; H, 6.00; N, 3.79.

4-(4-Benzoylphenyl)-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl-3-carboxylic Acid *N*-Succinimide Ester Radical (2c)

To a mixture of compound **2b** (182 mg, 0.5 mmol) and *N*-hydroxysuccinimide (58 mg, 0.5 mmol) in anhyd EtOAc (10 mL), DCC (103 mg, 0.5 mmol) dissolved in anhyd EtOAc (5 mL) was added dropwise at r.t. After stirring at r.t. for 3 h the precipitated dicyclohexyl urea was filtered off, the filtrate was evaporated and the residue was purified by flash column chromatography ($CHCl_3$–Et_2O, 2:1) to yield compound **2c**.

Yellow solid; yield: 127 mg (55%); mp 71–73 °C, R_f = 0.6 ($CHCl_3$–Et_2O, 2:1).

IR (nujol): 1780, 1730, 1660 (C=O), 1590 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 461 (M^+, 9), 446 (1), 347 (3), 105 (100), 77 (64).

Anal. Calcd for $C_{26}H_{25}N_2O_6$: C, 67.67; H, 5.46; N, 6.07. Found: C, 67.58; H, 5.44; N, 6.03.

4-(4-Benzoylphenyl)-3-bromomethyl-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (5b)

To a solution of alcohol **5a** (700 mg, 2.0 mmol) and Et_3N (2.2 mmol) in CH_2Cl_2 (20 mL), methanesulfonylchloride (252 mg, 2.2 mmol) dissolved in CH_2Cl_2 (5 mL) was added dropwise at 0 °C. The mixture was stirred at r.t. for 1 h, then the reaction mixture was washed with H_2O (10 mL), the organic phase was separated, dried ($MgSO_4$), filtered off and evaporated. The residue was dissolved in anhyd acetone (20 mL), then LiBr (348 mg, 4.0 mmol) was added and the reaction mixture was stirred and boiled at gentle reflux for 30 min. After cooling, the acetone was evaporated, the residue was partitioned between H_2O (10 mL) and EtOAc (20 mL). The phases were then separated and the aqueous phase was washed again with EtOAc (10 mL). The combined organic phase was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash column chromatography (hexane–EtOAc, 2:1) to give compound **5b**.

Yellow solid; yield: 404 mg (49%); mp 112–113 °C; R_f = 0.42 (hexane–EtOAc, 2:1).

IR (nujol): 1660 (C=O), 1560 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 414/412 (M^+, 10/10), 399/397 (1/1), 318 (8), 105 (100), 77 (48).

Anal. Calcd for $C_{22}H_{23}BrNO_2$: C, 63.93; H, 5.61; N, 3.39. Found: C, 64.03; H, 5.53; N, 3.32.

4-(4-Benzoylphenyl)-3-methanethiosulfonylmethyl-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (5c)

A solution of bromide **5b** (413 mg, 1.0 mmol) and $NaSSO_2CH_3$ (268 mg, 2.0 mmol) in acetone (15 mL) and H_2O (5 mL) was boiled at gentle reflux for 45 min. After cooling, the acetone was evaporated in vacuo, H_2O (10 mL) and $CHCl_3$ (15 mL) were added and the methanethiosulfonate was extracted into the organic phase. After separation, the organic phase was dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash column chromatography (hexane–EtOAc, 1:1, then $CHCl_3$–Et_2O, 2:1) to give compound **5c**.

Yellow solid; yield: 275 mg (62%); mp 136–138 °C; R_f = 0.54 ($CHCl_3$–Et_2O, 2:1).

IR (nujol): 1660 (C=O), 1560 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 444 (M^+, 12), 414 (12), 105 (100), 77 (60).

Anal. Calcd for $C_{23}H_{26}NO_4S_2$: C, 62.14; H, 5.89; N, 3.15; S, 14.42. Found: C, 62.07; H, 5.85; N, 3.29; S, 14.25.

1,1,3,3-Tetramethyl-1,3-dihydro-2*H*-pyrrolo[3,4-*b*]quinolin-2-yloxyl Radical (8)

A solution of aniline (511 mg, 5.5 mmol) and aldehyde **6** (1.23 g, 5.0 mmol) in DMF (15 mL) was stirred at 80 °C for the consumption of aldehyde **6** (3 h). DMF was removed under reduced pressure, the residue was dissolved in CH_2Cl_2 (20 mL) and washed with H_2O (10 mL). The organic phase was separated, dried ($MgSO_4$), filtered and evaporated. Compound **8** was obtained after flash chromatography (hexane–EtOAc, 2:1).

Yellow solid; yield: 675 mg (56%); mp 156–158 °C; R_f = 0.54 (hexane–EtOAc, 2:1).

IR (nujol): 1640 (C=N), 1570 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 241 (M^+, 49), 226 (26), 211 (100), 196 (80).

Anal. Calcd for $C_{15}H_{17}N_2O$: C, 74.66; H, 7.10; N, 11.61. Found: C, 74.58; H, 7.03; N, 11.55.

4-Amino-1,1,3,3-tetramethyl-1,3-dihydro-2*H*-pyrrolo[3,4-*c*]quinolin-2-yloxyl Radical (10)

A mixture of compound **9** (244 mg, 1.0 mmol) and $Pd(OAc)_2$ (12 mg, 0.05 mmol) in dioxane (15 mL) was purged with N_2 for 10 min. Adamantylamine hydrochloride (76 mg, 0.4 mmol), 2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (241 mg, 1.1 mmol) and

Cs_2CO_3 (715 mg, 2.2 mmol) were added and the mixture was stirred under reflux for 16 h under N_2. After cooling to r.t. the mixture was concentrated in vacuo to a quarter of its initial volume and partitioned between H_2O (10 mL) and $CHCl_3$ (20 mL). The organic phase was separated, the aqueous phase was washed with $CHCl_3$ (10 mL) and the combined organic phases were dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash column chromatography ($CHCl_3$–MeOH) to give compound **10**.

Beige solid; yield: 115 mg (45%); mp 188–190 °C; R_f = 0.30 ($CHCl_3$–MeOH, 9:1).

IR (nujol): 3430, 3300 (NH_2), 1640 (C=N), 1625 (C=C) cm^{-1}.

MS (EI): *m/z* (%) = 256 (M^+, 93), 241 (100), 226 (82), 211 (47).

Anal. Calcd for $C_{15}H_{18}N_3O$: C, 70.29; H, 7.08; N, 16.39. Found: C, 70.21; H, 7.00; N, 16.28.

3-Bromo-2,2,5,5-tetramethyl-4-phenyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (12)

A solution of compound **11** (2.98 g, 10.0 mmol), phenylboronic acid (1.21 g, 10.0 mmol), $PdCl_2(PPh_3)_2$ (350 mg, 0.5 mmol) and $Ba(OH)_2{\cdot}8H_2O$ (3.15 g, 10.0 mmol) in dioxane (32 mL) and H_2O (8 mL) was stirred and heated to reflux for 2 h under N_2. After cooling, the brownish-black mixture was filtered through celite and the celite pad was washed with MeOH (20 mL). The filtrate was evaporated in vacuo and the residue was partitioned between EtOAc (30 mL) and H_2O (15 mL). The organic phase was separated, dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash column chromatography (hexane–Et_2O, 2:1) to give a first colorless band (diffuse spot on TLC) as biphenyl, followed by the starting compound **11** as the second band. The third band contained compound **12** and the fourth contained compound **13** [yield: 584 mg (20%); R_f = 0.37 (hexane–Et_2O, 2:1)].

Compound 12

Yield: 708 mg (24%); mp 88–90 °C; R_f = 0.60 (hexane–Et_2O, 2:1).

IR (nujol): 1600, 1550 (C=C) cm^{-1}.

MS (EI): *m/z* (%) = 296/294 (M^+, 26/26), 266/264 (11), 200 (15), 185 (100).

Anal. Calcd for $C_{14}H_{17}BrNO$: C, 56.96; H, 5.80; N, 4.74. Found: C, 56.88; H, 5.76; N, 4.78.

1-(Acetyloxy)-3-bromo-2,2,5,5-tetramethyl-4-phenyl-2,5-dihydro-1*H*-pyrrole (14)

To a solution of radical **12** (1.47 g, 5.0 mmol) in dioxane (30 mL), a solution of ascorbic acid (8.8 g, 50 mmol) in H_2O (10 mL) was added and the mixture was stirred at 40 °C for 15 min under N_2. The pale yellow or colorless solution was extracted with $CHCl_3$ (2 × 20 mL) and dried ($MgSO_4$) under N_2. First acetyl chloride (430 mg, 5.5 mmol) was added followed by Et_3N (slowly, 555 mg, 5.5 mmol) while the temperature was kept below 10 °C. Stirring was continued for 1 h at r.t., the mixture was filtered and the filtrate was evaporated in vacuo. The residue was partitioned between brine (10 mL) and EtOAc (15 mL). The aqueous phase was washed with EtOAc (2 × 10 mL), the combined organic phase was dried ($MgSO_4$), filtered, evaporated and after flash chromatography (hexane–Et_2O, 2:1) the *O*-acetyl derivative was obtained.

White solid; yield: 930 mg (55%); mp 75–76 °C; R_f = 0.50 (hexane–Et_2O, 2:1).

IR (nujol): 1750 (C=O), 1590 (C=C) cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.20 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.38 (s, 6 H, CH_3), 2.16 (s, 3 H, CH_3CO), 7.17–7.37 (m, 5 H, Ar).

MS (EI): *m/z* (%) = 339/337 (M^+, 1/1), 324/322 (22/22), 297/295 (16/16), 282/280 (100/100).

Anal. Calcd for $C_{16}H_{20}BrNO_2$: C, 56.82; H, 5.96; N, 4.14. Found: C, 56.69; H, 5.91; N, 4.05.

2,2,5,5-Tetramethyl-3-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (15)

To a stirred solution of compound **14** (1.35 g, 4.0 mmol) in anhyd THF (15 mL), BuLi (3.2 mL, 8.0 mmol in 2.5 M hexane solution) was added dropwise under N_2 at –78 °C. The reaction mixture was stirred at this temperature for 60 min, then trimethyl borate (520 mg, 5.0 mmol) in THF (5 mL) was added dropwise over 30 min and the mixture was stirred for another 2 h at –78 °C. After warming the solution to 0 °C MeOH (1 mL) was added followed by H_2O (10 mL) and the mixture was stirred overnight on air at r.t. Then the mixture was diluted with Et_2O (15 mL), the organic phase was separated and the aqueous phase was acidified with AcOH and extracted again with Et_2O (10 mL). The combined organic phase was dried ($MgSO_4$), activated MnO_2 (5.0 mmol, 430 mg) was added and O_2 was bubbled through for 15 min. The mixture was filtered, evaporated and the residue was suspended in toluene (50 mL) and heated under reflux for 1 h in a Dean–Stark apparatus to remove water. The toluene was evaporated and the residue was dissolved in anhyd MeOH (20 mL). $MgSO_4$ (4.8 g, 40 mmol) and anhyd pinacol (472 mg, 4.0 mmol) were added and the mixture was stirred overnight at r.t. Then the $MgSO_4$ was filtered off, the filtrate was evaporated and the residue was partitioned between H_2O (10 mL) and EtOAc (20 mL). The organic phase was dried ($MgSO_4$), filtered and evaporated and the residue was purified by flash column chromatography (hexane–EtOAc, 2:1) to yield compound **15**.

Yellow solid; yield: 452 mg (33%); mp 148–150 °C; R_f = 0.71 (hexane–EtOAc, 2:1).

IR (nujol): 1600, 1560 (C=C) cm^{-1}.

MS (EI): *m/z* (%) = 342 (M^+, 28), 327 (52), 312 (100).

Anal. Calcd for $C_{20}H_{29}BNO_3$: C, 70.19; H, 8.54; N, 4.09. Found: C, 70.12; H, 8.39; N, 4.18.

7,7,9,9-Tetramethyl-7,9-dihydro-8*H*-acenaphtho[1,2-*c*]pyrrol-8-yloxyl Radical (16)

A 50 mL pressure tube equipped with stirring bar was filled with $Pd_2(dba)_3$ (258 mg, 0,25 mmol), compound **11** (298 mg, 1.0 mmol), 1-naphthaleneboronic acid (189 mg, 1.1 mmol), tricyclohexyl phosphine (168 mg, 0.6 mmol), DBU (1 mL) and DMF (10 mL) and the mixture was purged with N_2 for 10 min. Then the tube was closed, immersed in an oil bath and the solution was stirred at 150 °C for 48 h. After cooling, the mixture was diluted with CH_2Cl_2 (30 mL) and filtered through celite. Then solvents were evaporated under reduced pressure and the residue was partitioned between Et_2O (20 mL) and H_2O (10 mL). The organic phase was separated, dried ($MgSO_4$), filtered and evaporated. The residue was purified by flash column chromatography (hexane–EtOAc, 2:1) to give compound **16**.

Yellow solid; yield: 76 mg (29%); mp 111–113 °C; R_f = 0.36 (hexane–EtOAc, 2:1).

IR (nujol): 1560, 1540, 1510 (C=C) cm^{-1}.

MS (EI): *m/z* (%) = 264 (M^+, 9), 249 (12), 234 (100), 219 (74).

Anal. Calcd for $C_{18}H_{18}NO$: C, 81.79; H, 6.86; N, 5.30. Found: C, 81.72; H, 6.81; N, 5.14.

1,1,3,3-Tetramethyl-1,3-dihydro-2*H*-dibenzo[e,g]isoindol-2-yloxyl Radical (18)

To a stirred solution of compound **17** (307 mg, 1.0 mmol) in aq 1 M HCl (10 mL), $NaNO_2$ (76 mg, 1.1 mmol) dissolved in H_2O (5 mL) was added dropwise at 0 °C and the mixture was stirred at this temperature for 30 min. The solution of the diazonium salt was poured onto a vigorously stirred suspension of Cu powder (5 g, 78.0 mmol)

in H_2O (10 mL) and the mixture was heated to 60 °C and stirred at this temperature for 40 min. After cooling, the aqueous phase was extracted with EtOAc (2 × 10 mL), the combined organic phase was dried ($MgSO_4$), filtered and evaporated. Chromatographic purification (hexane–EtOAc, 2:1) of the residue afforded the paramagnetic phenanthrene derivative **18**.

Yield: 78 mg (27%); mp 174–176 °C; R_f = 0.42 (hexane–EtOAc, 2:1).

IR (nujol): 1600, 1560 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 290 (M^+, 33), 275 (100), 260 (41).

Anal. Calcd for $C_{20}H_{20}NO$: C, 82.72; H, 6.94; N, 4.82. Found: C, 82.68; H, 6.94; N, 4.69.

4-Iodo-2,2,6,6-tetramethyl-3,6-dihydropyridin-1(2*H*)-yloxyl Radical (20)

Compound **19** (8.5 g, 50 mmol) dissolved in EtOH (30 mL) was added dropwise to hydrazine hydrate (0.3 mol, 15 mL) during 3 h. Then the mixture was boiled at gentle reflux for 1 h. After cooling, the colorless solution was evaporated to dryness, the residue was taken up in a mixture of $CHCl_3$–MeOH (9:1, 50 mL). The organic phase was washed with brine (10 mL), separated, dried ($MgSO_4$). Then PbO_2 (1.19 g, 5.0 mmol) was added and O_2 was bubbled through for 30 min. The orange solution was filtered, evaporated and the remaining orange thick oil (hydrazone) was stored in a refrigerator or used immediately. This hydrazone was dissolved in anhyd Et_2O (30 mL) and added dropwise to a stirred solution of I_2 (27.9 g, 0.11 mol) and tetramethyl guanidine (20.12 g, 0.175 mol) in Et_2O (50 mL). After addition of hydrazone, the mixture was stirred at r.t. for 60 min, diluted with Et_2O (40 mL), and washed with H_2O (30 mL) and then with 5% aq H_2SO_4 (60 mL). The organic phase was separated, dried ($MgSO_4$), filtered and evaporated. The dark brown residue was purified by flash column chromatography (hexane–Et_2O, 2:1). The first green band was discarded and the second orange-pink band contained compound **20**.

Orange solid; yield: 8.26 g (59%); mp 63–65 °C; R_f = 0.70 (hexane–Et_2O, 2:1).

IR (nujol): 1650 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 280 (M^+, 10), 250 (3), 153 (20), 81 (100).

Anal. Calcd for $C_9H_{15}INO$: C, 38.59; H, 5.40; N, 5.00. Found: C, 38.51; H, 5.39; N, 4.90.

2,2,6,6-Tetramethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridin-1(2*H*)-yloxyl Radical (21) and 2,2,6,6,2′,2′,6′,6′-Octamethyl-1,2,3,6,1′,2′,3′,6,′-octahydro-[4,4′]-bipyridin-1,1′-diyloxyl Diradical (22)

A solution of bis(pinacolato)diboron (279 mg, 1.1 mmol), $PdCl_2$(dppf) (40 mg, 0.05 mmol), KOAc 294 mg (3.0 mmol) in DMSO (6 mL) was flushed with N_2 for 10 min. Then compound **20** (280 mg, 1.0 mmol) was added and the mixture was stirred at 80 °C for 3 h. After cooling, the mixture was poured onto H_2O (20 mL) and extracted with Et_2O (2 × 15 mL). The organic phase was dried ($MgSO_4$), filtered and evaporated and the residue was purified by flash column chromatography (hexane–Et_2O, 2:1, then hexane–EtOAc, 2:1). The first band contained a small amount of starting compound **20**, the second band gave compounds **21** and the third was **22**.

Compound **21**

Yield: 78 mg (28%); mp 180 °C; R_f = 0.71 (hexane–EtOAc, 2:1).

IR (nujol): 1640 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 280 (M^+, 14), 266 (100), 250 (52), 235 (21).

Anal. Calcd for $C_{15}H_{27}BNO_3$: C, 64.30; H, 9.71; N, 5.00. Found: C, 64.27; H, 9.62; N, 4.87.

Compound **22**

Yield: 99 mg (32%); mp 222–224 °C; R_f = 0.54 (hexane–EtOAc, 2:1).

IR (nujol): 1630 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 306 (M^+, 13), 233 (58), 41 (100).

Anal. Calcd for $C_{18}H_{30}N_2O_2$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.39; H, 9.79; N, 9.00.

Addition of Bis(pinacolato)diboron to Dienes and Acetylene (25, 28, 30); General Procedure

A solution of bis(pinacolato)diboron (508 mg, 2.0 mmol) and $Pt(PPh_3)_4$ (124 mg, 0.1 mmol) in toluene (10 mL, for **25** and **28**) or in DMF (10 mL, for **30**) was purged with N_2. Then diene **24** or **27**, or acetylene **29** was added and the mixture was heated to reflux in toluene for 5 h (**25** and **28**) or heated at 80 °C for 24 h (**30**) under N_2. After cooling, the solvents were evaporated under reduced pressure, the residue was taken up in EtOAc (20 mL), and washed with H_2O (10 mL). The organic phase was separated, dried ($MgSO_4$), filtered and evaporated and the residue was purified by flash column chromatography (hexane–EtOAc, 2:1) to give the diboronic esters in 38–63%.

2,2,5,5-Tetramethyl-3,4-bis[(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)methyl]-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (25)

Yield: 529 mg (63%); mp 78–80 °C; R_f = 0.51 (hexane–EtOAc, 2:1).

IR (nujol): 1650 (C=C) cm^{-1}.

^{1}H NMR [400 MHz, $CDCl_3$ + $(PhNH)_2$]: δ = 1.25 (s, 24 H, CH_3), 1.41 (s, 12 H, CH_3), 1.66 (s, 4 H, CH_2).

MS (EI): *m*/*z* (%) = 420 (M^+, 11), 405 (10), 390 (100).

Anal. Calcd for $C_{22}H_{40}B_2NO_5$: C, 62.89; H, 9.60; N, 3.33. Found: C, 62.81; H, 9.57; N, 3.21.

3-[1,2-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)ethyl]-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (28)

Yield: 319 mg (38%); mp 71–73 °C; R_f = 0.51 (hexane–EtOAc, 2:1).

IR (nujol): 1650 (C=C) cm^{-1}.

^{1}H NMR of *O*Ac derivative (400 MHz, $CDCl_3$): δ = 1.05 (m, *J* = 3.2 Hz, 2 H, CH_2) 1.21 (s, 36 H, CH_3), 1.79 (t, *J* = 1.6 Hz, 1 H, CH), 2.13 (s, 3 H, CH_3CO), 5.25 (d, *J* = 1.6 Hz, 1 H, =CH).

MS (EI): *m*/*z* (%) = 420 (M^+, 7), 406 (16), 390 (100).

Anal. Calcd for $C_{22}H_{40}B_2NO_5$: C, 62.89; H, 9.60; N, 3.33. Found: C, 62.78; H, 9.53; N, 3.19.

3-[(*E*)-1,2-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)vinyl]-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (30)

Yield: 351 mg (42%); mp 69–71 °C; R_f = 0.51 (hexane–EtOAc, 2:1).

IR (nujol): 1650 (C=C) cm^{-1}.

MS (EI): *m*/*z* (%) = 418 (M^+, 8), 403 (25), 388 (100).

Anal. Calcd for $C_{22}H_{38}B_2NO_5$: C, 63.19; H, 9.16; N, 3.35. Found: C, 63.02; H, 9.11; N, 3.26.

3,4-Bis(hydroxymethyl)-2,2,5,5-tetramethyl-2,5-dihydro-1*H*-pyrrol-1-yloxyl Radical (26)

To a stirred solution of compound **25** (420 mg, 1.0 mmol) in MeOH (10 mL), 10% aq NaOH solution (1 mL) and 30% H_2O_2 (1 mL) were added and the mixture was heated to reflux for 2 h. After cooling,

the mixture was extracted with $CHCl_3$ (2 × 10 mL), the organic phase was dried ($MgSO_4$), filtered and evaporated. Compound **26** was obtained after flash column chromatography purification ($CHCl_3$–MeOH, 9:1).

Yellow solid; yield: 134 mg (67%); mp 155–156 °C; R_f = 0.55 ($CHCl_3$–MeOH, 9:1).

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References

(1) Hubbell, W. L.; Altenbach, C.; Hubbell, C. M.; Khorana, H. G. *Adv. Protein. Chem.* **2003**, *63*, 243.
(2) Nerbouh, N.; Bobbit, J. M.; Brückner, C. *Org. Prep. Proced. Int.* **2004**, *36*, 1.
(3) Bilski, P.; Hideg, K.; Kálai, T.; Bilska, M. A.; Chignell, C. F. *Free Radical Biol. Med.* **2003**, *34*, 489.
(4) *Magnetic Properties of Organic Materials*; Lahti, M. P., Ed.; Marcell Dekker Inc.: New York, **1999**.
(5) Shen, J.; Bottle, S.; Khan, N.; Grinberg, O.; Reid, D.; Micallef, A.; Swartz, H. *Appl. Magn. Reson.* **2002**, *22*, 357.
(6) Braslau, R.; Chaplinski, V.; Goodson, P. *J. Org. Chem.* **1998**, *63*, 9857.
(7) Kálai, T.; Szabó, Z.; Jekő, J.; Hideg, K. *Org. Prep. Proced. Int.* **1996**, *28*, 289.
(8) Kálai, T.; Kulcsár, G.; Ősz, E.; Jekő, J.; Sümegi, B.; Hideg, K. *ARKIVOC* **2004**, *(vii)*, 266.
(9) Hideg, K.; Hankovszky, H. O.; Halász, H. A.; Sohár, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2905.
(10) Kálai, T.; Balog, M.; Jekő, J.; Hideg, K. *Synthesis* **1999**, 973.
(11) Kálai, T.; Balog, M.; Jekő, J.; Hubbell, W. L.; Hideg, K. *Synthesis* **2002**, 2365.
(12) Suzuki, A.; Brown, H. C. *Organic Synthesis via Boranes*, Vol. 3; Aldrich Chemical Company Inc.: Milwaukee, **2003**.
(13) Zhdanov, R. I. In *Bioactive Spin Labels*; Zhdanov, R. I., Ed.; Springer-Verlag: Berlin, **1992**, 23–82.
(14) Barton, H. R.; Bashiardes, G.; Fourrey, J.-L. *Tetrahedron* **1988**, *44*, 147.
(15) Kálai, T.; Jekő, J.; Hideg, K. *Tetrahedron Lett.* **2004**, *45*, 8395.
(16) Berliner, L. J.; Grünwald, J.; Hankovszky, H. O.; Hideg, K. *Anal. Biochem.* **1982**, *119*, 450.
(17) Lösel, R. M.; Philipp, R.; Kálai, T.; Hideg, K.; Trommer, W. E. *Bioconjugate Chem.* **1999**, *10*, 578.
(18) Mátyus, P.; Maes, B. U. W.; Riedl, Z.; Hajós, G.; Lemiére, G. L. F.; Tapolcsányi, P.; Monsieurs, K.; Éliás, O.; Dommisse, R. A.; Krajsovszky, G. *Synlett* **2004**, 1123.
(19) Sampathkumar, N. M.; Kumar, N. V.; Rajendran, S. P. *Synth. Commun.* **2004**, *34*, 2019.
(20) Gug, F.; Blondel, M.; Deaban, N.; Bouaziz, S.; Vierfond, J.-M.; Galons, H. *Tetrahedron Lett.* **2005**, *46*, 3725.
(21) Keana, J. F. W.; Hideg, K.; Birrell, G. B.; Hankovszky, H. O.; Ferguson, G.; Parvez, M. *Can. J. Chem.* **1982**, *60*, 1439.
(22) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Elsevier: Oxford, **2002**.
(23) Chaumel, H.; Le Drian, C.; Defoin, A. *Synthesis* **2002**, 757.
(24) Wegner, H. A.; Scott, T. A.; de Meijere, A. *J. Org. Chem.* **2003**, *68*, 883.
(25) Shapiro, A. B.; Dimitriev, P. I. *Bull. Acad. Sci. USSR, Div. Chemical Sci.* **1981**, 138.
(26) Ishiyama, T.; Murata, M.; Miyaura, N. *J. Org. Chem.* **1995**, *60*, 7508.
(27) Liu, X. *Synlett* **2003**, 2442.
(28) Wang, Z.; Meng, X.-J.; Kabalka, G. W. *Tetrahedron Lett.* **1991**, *32*, 1945.
(29) Barluenga, J.; Fananas, J. F.; Snaz, R.; Ignacio, J. M. *Eur. J. Org. Chem.* **2003**, 771.
(30) Hideg, K.; Csekő, J.; Hankovszky, H. O.; Sohár, P. *Can. J. Chem.* **1986**, *64*, 1482.
(31) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018.
(32) Lion, C. J.; Matthews, C. S.; Stevens, M. F. G.; Westwell, A. D. *J. Med. Chem.* **2005**, *48*, 1292.
(33) Kálai, T.; Balog, M.; Jekő, J.; Hideg, K. *Synthesis* **1998**, 1476.