Functionalized Pyrazoles as Agents in C–C Cross-Coupling Reactions

Marijana Pejic, Sebastian Popp, Michael Bolte, Matthias Wagner, and Hans-Wolfram Lerner

Institut für Anorganische Chemie, Goethe-Universität Frankfurt am Main, Max-von-Laue-Straße 7, 60438 Frankfurt am Main, Germany

Reprint requests to Dr. Hans-Wolfram Lerner. Fax: ++49-69-79829260. E-mail: lerner@chemie.uni-frankfurt.de

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The 1-tetrahydropyranyl-(THP)-protected pyrazoles 4-R-pz(THP) (R = pinacolatoboryl = Bpin (3a(THP)), Me₂Si(4a(THP)), Me₂Sn (5a(THP))), and 4-R-3,5-Ph₂pz (R = Bpin (3b(THP)), Me₂Si (4b(THP)), Me₂Sn (5b(THP))) were obtained by the following syntheses: i) In a first step, 4-X-pz (X = Br (1a), I (2a), and 4-X-3,5-Ph₂pz (X = Br (1b), I (2b)) were reacted with 3,4-dihydro-2H-pyran (DHP) to give the related THP-protected bromo- or iodopyrazole derivatives. ii) In a second step these THP derivatives were metalated by treatment with nBuLi or iPrMgCl. Subsequent reactions of the THP-protected metallopyrazoles 4-M-pz(THP) and 4-M-3,5-Ph₂pz(THP) (M = Li, MgBr) with Bpin(OiPr), Me₂SiCl, and Me₂SnCl yielded the pyrazole derivatives 3a(THP), 3b(THP), 4a(THP), 4b(THP), 5a(THP), and 5b(THP). In contrast to the stannylated pyrazoles 5a(THP) and 5b(THP), the corresponding borylated and silylated derivatives could be easily deprotected: treatment of 3a(THP), 3b(THP), and 4a(THP) with HCl yielded the parent pyrazoles 3a, 3b, and 4a. The microwave-assisted C–C cross-coupling reactions of these pyrazoles with aryl halides were examined. e. g. Suzuki reactions of 3a with p-pentylphenylbromide, p-hexylphenylbromide, and p-(2-ethylhexyl)phenylbromide. Similar reactions were also performed with 1a, 1b, 2a, and 2b and aryl-substituted pinacolatoboranes or boronic acids. Crystals of 5b(THP) suitable for X-ray diffraction were grown (monoclinic P2₁/c) and their structure determined. The crystal structures of 1a·HBr (monoclinic P2₁/n), 1b (triclinic P1), (1c)·HBr (monoclinic P2/c), 1c·HBr (Br₂) (triclinic P1), 2a·H₂SO₄ (triclinic P1), 3a (orthorhombic P2₁2₁2₁), (3a)·H₂O (trigonal R3c), 3b (orthorhombic Pna2₁), and 4a (monoclinic Pc) reveal interesting hydrogen bonding networks.

Key words: Pyrazoles, C–C Cross-Coupling, Luminescence, X-Ray Structure Analysis, Hydrogen Bonding Networks

Introduction

Multidentate ligand systems have attracted considerable interest in the last decades. Prominent examples of this class of ligands are the (pyrazol-1-yl)borates (scorpionates) [R₄Bpz₄₋ₙ₋₁] (R = H, alkyl, aryl; n = 2, 1, 0; pz = pyrazol-1-yl) [1 – 8]. Scorpionates have found applications in a wide range of chemistry, from modelling the active site of metalloenzymes, through analytical chemistry and organic synthesis to catalysis and materials science [9].

However, degradation reactions of these scorpionate ligands were often observed in the presence of transition metal salts MX₃ [10 – 12]. We found that deboronation of scorpionates easily takes place if the metal center in MX₃ is more Lewis acidic than the boron center in the corresponding borane of the pyrazolyl borate (Fig. 1). In these cases there is competition between the reactions of metal cations and the pyrazolide anion and the BN adduct formation (Fig. 1). Another important factor which influences the stability of scorpionates is the degree of steric crowding. Several studies have shown that the scorpionates of the type R(B(3-R’pz)₃)₃ decompose in the presence of transition metal salts MX₃ much more easily when R and R’ are bulky (Fig. 1) [10]. Especially scorpionates with pyrazoles which bear bulky substituents in 3- and 5-position tend to degradation. Therefore it is unfavorable to tune the properties of scorpionate ligands by introducing solubility-mediating or functionalized groups in their 3- or 5-position. Since our group has a long-standing interest in the development of new
ligand systems based on pyrazole, both for use in homogeneous catalysis and in the assembly of coordination polymers and networks, we decided to work out a new strategy to introduce functional groups on pyrazoles. In the course of this study we found that pyrazole derivatives could conveniently be borated, silylated or stannylated in the 4-position. Moreover, coupling protocols allow further functionalization of these pyrazoles.

The purpose of this paper is to describe the synthesis and properties of pyrazoles which bear functional groups in the 4-position. To this end we examined microwave-assisted C–C cross-coupling reactions of these pyrazoles with aryl halides. Finally the THP derivatives 4-boryl- or iodopyrazoles were reacted with 3,4-dihydro-2H-pyran to give the related THP-protected bromo- or iodopyrazole derivatives 1a(THP), 1b(THP), 2a(THP), and 2b(THP). In a second step these THP derivatives were metalated by treatment with nBuLi or iPrMgCl. Subsequent reactions of the THP-protected metallopyrazoles 4-M-pz(THP) and 4-M-3,5-Ph2pz(THP) (M = Li, MgBr) with Bpin(OiPr), Me3SiCl, and Me3SnCl yielded 3a(THP), 3b(THP), 4a(THP), 4b(THP), 5a(THP), and 5b(THP) whose boryl and silyl substituents are inert against protic agents could be easily transformed into their parent pyrazoles 3a, 3b, and 4a (Scheme 1). However, stannyl group elimination took place when the THP derivatives 5a(THP) and 5b(THP) were treated with HCl. Therefore we were not able to synthesize the deprotected pyrazoles 5a and 5b.

As shown in Scheme 2, Suzuki-type coupling protocols allow the further functionalization of the pyrazoles 1a–3b (Fig. 2). We examined the following microwave-assisted C–C cross-coupling reactions in detail: Suzuki reactions of 3a with p-
Scheme 2. Substituted pyrazoles 1–3 in C–C cross-coupling reactions. (i) e.g. 1b(THP) (R = Ph), p-R’PhBpin (R’ = H) [9]; (ii) e.g. 2b(THP) (R = Ph), p-R’PhBpin (R’ = Me) [13]; (iii) e.g. 3a(THP) (R = H), p-R’PhBpin (R’ = pentyl): +Pd(PPh3)4, K3PO4, H2O/DMF, 110 °C.

Fig. 4. Structure of 1a·HBr in the solid state (ORTEP, displacement ellipsoids are drawn at the 50% probability level). Selected bond lengths (Å), atom···atom distances (Å), and bond angles (deg): Br(1)–C(1) 1.854(6), C(1)–C(2) 1.381(9), C(1)–C(5) 1.383(9), C(2)–N(3) 1.321(9), N(3)–N(4) 1.320(10), N(3)–H(3) 0.89(1), N(4)–H(4) 0.89(1), N(4)–C(5) 1.305(10), N(3)···Br(2) 3.213(6), N(4)···Br(2) 3.258(6); N(3)–H(3)–Br(2) 131(7), N(4)–H(4)–Br(2) 147(7).

The molecular structures of the compounds 1a·HBr, 1b, (1c)2·HBr, 1e·HBr·(Br2)0.5, (2a)3·H2SO4, 3a, 3a·H2O, 3b, 4a, and 5b are shown in Figs. 4–15. Selected bond lengths and angles are listed in the corresponding figure captions, details of the crystal structure analyses are summarized in Table 1.

The 1 : 1 addition product of 1a and HBr crystallizes in the monoclinic space group P21/n with Z = 4 (Fig. 4). The coordinates of the H atoms bonded to N were refined with a bond length restraint of 0.89(1) Å. The packing in the crystal shows layers of pyrazolium cations [1aH]+ parallel to the (1 0 4) plane and bromide anions. The bromide anion connects three cations by N–H···Br hydrogen bonds (N(3)–H(3) = 0.89(1) Å, N(3)···Br(2) = 3.213(6) Å, N(3)–H(3)···Br(2) = 131(7)°, N(4)–H(4) = 0.89(1) Å, N(4)···Br(2) = 3.258(6) Å, N(4)–H(4)···Br(2) = 147(7)°, N(3)–H(3) = 0.89(1) Å,
Fig. 5. Molecular structure of 1b in the solid state (ORTEP, displacement ellipsoids are drawn at the 50% probability level). Selected bond lengths (Å), atom···atom distances (Å), bond angles (deg), and torsion angles (deg): Br(1)–C(2) 1.878(3), C(1)–N(5) 1.340(4), C(1)–C(2) 1.395(4), C(1)–C(11) 1.476(4), C(2)–C(3) 1.401(4), C(3)–C(4) 1.346(4), C(3)–N(21) 1.476(4), N(5)–H(5) 0.875(10), N(5A)–H(5A) 0.875(10), N(4)–N(5A) 2.827(4), N(5)–N(4A) 2.814(4); N(5)–H(5)–N(4A) 142(3), N(5A)–H(5A)–N(4) 142(3); pz(N(4))//Ph(C(11)) 35.25(12), pz(N(4))//Ph(C(21)) 31.09(13), pz(N(4A))//Ph(C(11A)) 31.90(12), pz(N(4A))/Pb(C(21A)) 27.80(15).

N(3)···Br(2) = 3.449(7) Å, N(3)–H(3)–Br(2) = 124(6)°; Fig. 4). Thus, one of the H atoms (H(3)) forms two hydrogen bonds, whereas the other one forms just one.

The molecular structure of the pyrazole derivative 1b (triclinic space group P1 with Z = 4) is shown in Fig. 5. The coordinates of the H atoms bonded to N were refined with a bond length restraint of 0.88(1) Å. There are two molecules in the asymmetric unit differing in the dihedral angles between the central pyrazol ring and the attached phenyl rings. In the first molecule, the dihedral angles are 35.25(12)° and 31.09(13)° for the rings containing C(11) and C(21), respectively. In the second molecule, the dihedral angles are 31.90(12)° and 27.80(15)° for the rings containing C(11A) and C(21A), respectively. The two molecules in the asymmetric unit are connected by N–H···N hydrogen bonds to form dimers.

Two different addition products of 3,4,5-tribromopyrazole (1c) are shown in Figs. 6 and 7. The first one is composed of two molecules of 1c and one of Br ((1c)2·HBr) and the second one of one molecule each of 1c and HBr, and a half molecule of Br2 [1c·HBr·(Br2)0.5]. The H atoms in (1c)2·HBr bonded to the N atoms were geometrically positioned and refined using a riding model. The position of the H atom bonded to the N(1) atom is only half-occupied. The asymmetric unit is composed of protonated pyrazole dimers [(1c)2·H]+ and a bromide anion located on a two-fold axis. In the crystal, cations and bromide anions are connected via N···H···N and N···H···Br hydrogen bonds (N(1)–H(1) = 0.88 Å, N(1)···N(1) = 2.610(10) Å, N(1)–H(1)···N(1) = 175.8°, N(2)–H(2) = 0.88 Å, N(2)···Br(1) = 3.186(6) Å, N(2)–H(2)···Br(1) 166.1°; Fig. 7) forming zigzag chains running along the a axis.
The H atoms in 1c·HBr·(Br2)0.5 bonded to the N atoms were geometrically positioned and refined using a riding model. The asymmetric unit is composed of one cation, one anion and half a Br2 molecule which is located on a centre of inversion. In the crystal, two cations are connected to each other mediated by two bromide anions forming centrosymmetric dimers via N–H···Br hydrogen bonds (N(2)–H(2) = 0.88 Å, N(2)···Br(1) 3.180(6) Å, N(2)–H(2)···Br(1) = 161.8°, N(1)–H(1) = 0.88 Å, N(1)···Br(1) = 3.174(6) Å, N(1)–H(1)···Br(1) = 167.0°; Fig. 7). Anions and cations form layers in the (1 2 0) plane. The Br2 molecules are located between the dimers. The shortest contact of a Br2 molecule is to a bromide anion (3.0906(13) Å).

The H atoms bonded to the N atoms in (2a)3·H2SO4 were freely refined with a bond length restraint of 0.88(1) Å for the bond N(2A)–H(2A). The asymmetric unit is composed of two protonated 4-iodopyrazolium cations [2aH]+, one 4-iodopyrazole molecule, and one sulfate anion. The neutral iodopyrazole molecule donates a hydrogen bond to a sulfate anion (N(1)–H(1) = 0.97(8) Å, N(1)···O(2) = 2.787(5) Å, N(1)–H(1)···O(2) = 158 (7)°) and accepts one hydrogen bond from a iodopyrazolium cation (N(2B)–H(2B) = 0.86(7) Å, N(2B)···N(2) = 2.678(6) Å, N(2B)–H(2B)···N(2) = 166(6)°). The other N–H group of this iodopyrazolium cation donates a hydrogen bond to a sulfate anion (N(1B)–H(1B) = 0.84(6) Å, N(1B)···O1 = 2.599(5) Å, N(1B)–H(1B)···O(1) = 172(6)°). The second iodopyrazolium cation connects two sulfate anions via N–H···O hydrogen bonds (N(1A)–H(1A) = 0.88(5) Å, N(1A)···O(4) = 2.631(5) Å, N(1A)–H(1A)···O(4) = 175(5)°, N(2A)–H(2A) = 0.88(2) Å, N(2A)···O(2) = 2.723(4) Å, N(2A)–H(2A)···O2 = 166(5)°). As a result, only three of the four sulfate O atoms act as hydrogen bond acceptors, whereas the N atom of the iodopyra-
The molecular structure of the pyrazole 3a (orthorhombic, space group $P_{2_1}2_12_1$ with $Z = 4$) is shown in Figs. 9 and 10. The H atom bonded to N was freely refined. The planar five-membered 1,3,2-dioxaborolane ring (r. m. s. deviation = 0.118 Å) is almost coplanar with the pyrazole ring (dihedral angle 8.98(13)°). In the crystal, the molecules are connected via N–H···N hydrogen bonds (N(2)–H(2) = 0.81(3) Å, N(2)···N(1) = 2.935(3) Å, N(2)–H(2)–N(1) = 166(3)°) to zigzag chains running along the $a$ axis (Fig. 10). The molecules in this chain are coplanar and form ribbons in the (0 1 3) and (0 1 $\bar{3}$) planes.

The water O atom in 3a·H$_2$O is located on a threefold rotation axis. The water H atoms are thus disordered over three positions with a site occupation factor of 1/3 and 2/3 in accord with the disorder of the water H atoms. Due to the absence of anomalous scatterers, the absolute structure could not be determined. The planar five-membered 1,3,2-dioxaborolane ring (r. m. s. deviation = 0.124 Å) is almost coplanar with the pyrazole ring (dihedral angle = 8.06(6)°). In the crystal, three molecules are arranged about a threefold rotation axis surrounding the water molecule which is located on the threefold axis. The water molecule donates two hydrogen bonds to the N atoms of two pyrazole rings (O(1W)–H(1W) = 0.842(14) Å, O(1W)···N(4) = 2.885(3) Å, O(1W)–H(1W)–N(4) = 160(6)°), and the latter two donate an N–H bond to the N atom of the third molecule (N(3)–H(3) = 0.908(15) Å, N(3)···N(3) = 3.140(5) Å, N(3)–H(3)–N(3) = 142(7)°). This molecule donates an N–H bond to the water molecule (N(4)–H(4) = 0.909(15) Å, N(4)···O(1W) = 2.885(3) Å, N(4)–H(4)–O(1W) = 144(9)°) completing a tripodal arrangement of three molecules of pyrazole 3a and a water molecule (Fig. 11). These complexes are not further connected via hydrogen bonds to symmetry-equivalent complexes.

The borylated pyrazole 3b crystallizes with two molecules in the asymmetric unit in the orthorhombic space group $Pna2_1$ with $Z = 8$, as shown in Fig. 12. In one molecule, the dioxaborolane ring is disordered over two positions with a site occupation factor of 0.695(7) for the site of major occupancy. The disordered atoms were refined isotropically, while
Fig. 9. Molecular structure of 3a in the solid state (ORTEP, displacement ellipsoids are drawn at the 50% probability level). Selected bond lengths (Å), atom–atom distances (Å), bond angles (deg), and torsion angles (deg): B(1)–C(4) 1.542(3), N(1)–C(5) 1.321(3), N(1)–N(2) 1.351(3), C(3)–C(4) 1.337(3), C(3)–C(5) 1.376(4), C(4)–C(5) 1.407(3), N(2)–H(2) 0.81(3), C(4)–N(2) 2.935(3); N(2)–H(2)–N1 166(3), pz(N(1))//Bpin(B(1)) 8.98(13).

Fig. 10. Packing of borylated pyrazole molecules in crystals of 3a, viewed in the ab plane. Hydrogen atoms except those on nitrogen atoms have been omitted for clarity. The H atoms bonded to N were freely refined. Due to the absence of anomalous scatterers, the absolute structure could not be determined. The pyrazole ring containing N(1) forms dihedral angles of 39.39(10)° and 36.64(8)° with the phenyl ring containing C(21) and C(31), respectively. The pyrazole ring containing N(1A) forms dihedral angles of 38.85(11)° and 41.40(6)° with the phenyl rings containing C(21A) and C(31A), respectively. The two molecules in the asymmetric unit form dimers connected by

Fig. 11. Connectivity of (3a)2·H2O in the solid state. Hydrogen atoms except those on nitrogen and oxygen atoms have been omitted for clarity.
Fig. 12. Molecular structure of 3b (ORTEP, displacement ellipsoids are drawn at the 50% probability level). Selected bond lengths (Å), atom···atom distances (Å), bond angles (deg), and torsion angles (deg): B(1)–C(4) 1.549(5), N(1)–C(5) 1.353(4), N(1)–N(2) 1.364(4), N(2)–C(3) 1.341(4), C(3)–C(4) 1.414(5), C(3)–C(21) 1.477(5), C(4)–C(5) 1.386(5), C(5)–C(31) 1.480(5), N(1)–H(1) 0.91(4), N(1A)–H(1A) 0.89(5), N(1)···N(2A) 2.926(4), N(2)···N(1A) 2.830(4), N(1)–H(1)–N(2A) 138(3), N(1A)–H(1A)–N(2A) 147(4); pz(N(1))//Ph(C(21)) 39.39(10), pz(N(1))//Ph(C(31)) 36.64(8), pz(N(1A))//Ph(C(21A)) 38.85(11), pz(N(1A))//Ph(C(31A)) 41.40(6), pz(N(1))//pz(N(1A)) 34.43(10).

N–H···N hydrogen bonds (N(1)–H(1) = 0.91(3) Å, N(1)···N(1) = 2.926(4) Å, N(1)–H(1)–N(2A) = 138(3)°, N(1A)–H(1A) = 0.89(3) Å, N(1)···N(1A) = 2.830(4) Å, N(1)–H(1)–N(2A) = 147(3)°). The two hydrogen-bonded pyrazole rings are not coplanar but inclined at an angle of 34.43(10)°.

The molecular structure of the silylated pyrazole 4a (monoclinic, space group Pc with Z = 8) is shown in Figs. 13 and 14. The three methyl groups in two molecules are disordered over two positions with site occupation factors of 0.55(6) and 0.78(2) for the site of major occupancy. Si–C and C–C bond lengths in the disordered parts were restrained to be equal to those in a non-disordered SiMe3 group. One methyl C atom (C(6C)) was restrained to an isotropic behavior. The H atoms could not be located and were geometrically positioned. The absolute structure could not be reliably determined (Flack (ξ) parameter 0.8(5)). There are four molecules in the asymmetric unit, which are connected by N–H···N hydrogen bonds to zigzag chains running along the b axis (N(3)–H(3) = 0.88 Å, N(3)···N(4A) = 2.951(14) Å, N(3)–H(3)–N(4A) = 152, N(3A)–H(3A) = 0.88 Å, N(3A)···N(4B) = 2.850(15) Å, N(3A)–H(3A)–N(4B) = 148, N(3C)–H(3C)–N(4) 165.)

Fig. 13. Molecular structure of 4a (ORTEP, displacement ellipsoids are drawn at the 50% probability level). Selected bond lengths (Å), atom···atom distances (Å), and bond angles (deg): C(1)–C(2) 1.395(18), A(1)–C(1)–C(5) 1.348(18), C(1)–Si(1) 1.860(12), C(2)–N(3) 1.316(18), N(3)–N(4) 1.379(19), N(4)–C(5) 1.377(16), N(3)–H(3) 0.88, N(3A)–H(3A) 0.88, N(3B)–H(3B) 0.88, N(3C)–H(3C) 0.88, N(3)–N(4A) 2.95(14), N(3A)–N(4B) 2.850(15), N(3B)–N(4C) 2.932(15), N(3C)–N(4) 2.828(17), N(3)–H(3)–N(4A) 152, N(3A)–H(3A)–N(4B) 169, N(3B)–H(3B)–N(4C) 148, N(3C)–H(3C)–N(4) 165.
Fig. 14. Packing diagram for 4a, viewed along the \( ab \) plane. Hydrogen atoms except those on nitrogen atoms have been omitted for clarity.

\[
= 169^\circ, \ N(3B)\text{--}H(3B) = 0.88 \text{ Å}, \ N(3B)\text{--}N(4C) = 2.932(15) \text{ Å}, \ N(3B)\text{--}H(3B)\text{--}N(4C) = 148^\circ, \ N(3C)\text{--}H(3C) = 0.88 \text{ Å}, \ N(3C)\text{--}N(4) = 2.828(17) \text{ Å}, \ N(3C)\text{--}H(3C)\text{--}N(4) = 165^\circ; \text{ Fig. 14.}
\]

The stannylated pyrazole 5b(THP) crystallizes in the monoclinic space group \( P2_1/\text{c} \) with two almost identical molecules in the asymmetric unit (Fig. 15). A least-squares fit of all non-H atoms gives an r.m.s. deviation of 0.104 Å. Thus, only one molecule is discussed here. The pyrazole ring forms dihedral angles of 40.1(2)° and 45.0(2)° with the phenyl ring containing C(21) and C(31), respectively. The tetrahydropyranyl ring adopts a chair conformation. The Sn atom deviates by 0.381(9) Å from the plane of the pyrazole ring. The Sn–C bonds adopt typical values (Sn(1)–C(4) = 2.137(5) Å, Sn(1)–C(6) = 2.122(7) Å, Sn(1)–C(7) = 2.145(7) Å, Sn(1)–C(8) = 2.161(6) Å, Sn(1)–C(9) = 2.158(6) Å, Sn(1)–C(10) = 2.146(8) Å, Sn(1)–C(12) = 2.161(6) Å).

In summary, it was found that the crystal structures of herein described pyrazoles reveal two different types of hydrogen bonding networks in the solid state: infinite hydrogen-bridged zigzag chains of pyrazoles for small substituents in the 3- and 5-position (e.g. Fig. 2, \( R = \text{H} \)) and hydrogen-bridged dimers for bulky groups in these positions (e.g. Fig. 2, \( R = \text{Ph} \)). Also, it was found that proton-active compounds could easily be intercalated in this network. The pyrazole derivatives which are shown in Fig. 3 are excellent fluorophores and emit in the near ultraviolet to blue regime [13]. Moreover most of these compounds feature remarkable high solid-state quantum yields [13]. It is our current working hypothesis that the rigid framework of these pyrazoles, due to the hydrogen bonding networks in the solid state, prevents self-quenching. In contrast to these pyrazoles, despite of their strong fluorescence in dilute solutions, many related arenes, e.g.
### Crystal Data and Refinement

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### Table 1

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M. Pejic et al. - Functionalized Pyrazoles as Agents in C–C Cross-Coupling Reactions
the pyridyl indols 8(3) and 8(6) (Fig. 16) [14], tend to show a poor performance in the solid state, mainly due to π stacking.

### Experimental Section

The solvents THF, pentane, toluene, and C<sub>6</sub>D<sub>6</sub> were stirred over sodium/benzophenone and distilled prior to use. 1a [16], 1a(THP) [17], 1b [18], 1c [19], 2a [20], 2a(THP) [21], 2b [20], 3a [22], 3a(THP) [23], and 4a [24] were prepared according to published procedures. All other starting materials were purchased from commercial sources and used without further purification. The NMR spectra were recorded on Bruker AM 250, DPX 250, Avance 400, and Avance 500 spectrometers. NMR chemical shifts are reported in ppm. Abbreviations: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; m = multiplet; br = broad; n. o. = not observed. Mass spectrometry was performed with a Fisons VG Platform II instrument and microwave irradiation was generated with a Biotage Initiator<sup>+</sup> System. Elemental analyses were carried out by the Microanalytical Laboratory of the Goethe University Frankfurt.

Crystals of 4-bromo-1H-pyrazole and HBr (1a-HBr)

The bromopyrazole 1a was prepared according to the published procedure [16]. By slow evaporation of the solvent water crystals of 1a and HBr were grown from the reaction mixture at r.t.

### Single crystals of 4-bromo-3,5-diphenyl-1H-pyrazole (1b)

The bromopyrazole 1b was prepared according to the published procedure [18]. Single crystals of 1b were grown from a CH<sub>2</sub>C<sub>2</sub> solution by slow evaporation of the solvent at r.t.

### 4-Bromo-3,5-diphenyl-1-THP-pyrazole (1b(THP))

3,4-Dihydro-2H-pyran (DHP) (0.62 g, 7.35 mmol) was added dropwise at 85 °C to a mixture of 1b (2.00 g, 6.69 mmol) and a catalytic amount of trifluoroacetic acid (TFA) (0.04 g, 0.33 mmol) in 20 mL toluene. The solution was warmed up to 95 °C and kept stirring for further 1 h. After removing all volatiles in vacuo, 1b(THP) remained as a pale-yellow oil that was suitable for direct conversion (yield: 2.54 g, 99%). - 1H NMR (400 MHz, CDCl<sub>3</sub>): δ = 7.98 – 7.95 (m, 2H, oPh-H), 7.60 – 7.57 (m, 2H, oPh-H), 7.55 – 7.50 (m, 3H, Ph-H), 7.46 – 7.42 (m, 2H, mPh-H),

### Table 1. (Continued.)

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<td>0.999</td>
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<td>0.51/−0.27</td>
<td>1.66/−0.48</td>
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<sup>a</sup> R(F) = Σ||F<sub>obs</sub>||−|F<sub>calc</sub>|/Σ||F<sub>obs</sub>|; |wR<sup>2</sup>| = Σ(|F<sub>o</sub>|<sup>2</sup>−|F<sub>c</sub>|<sup>2</sup>)<sup>2</sup>/Σ|F<sub>o</sub>|<sup>2</sup>;<sup>2</sup>/; GoF<sup>2</sup> = Σ(|F<sub>o</sub>|<sup>2</sup>−|F<sub>c</sub>|<sup>2</sup>)<sup>2</sup>/Σ(w<sub>o</sub>−w<sub>calc</sub>)<sup>2</sup>/; w = (σ<sup>2</sup>|F<sub>c</sub>|<sup>2</sup> + (aP<sup>2</sup> + bP))<sup>−1</sup>, where P = (Max(|F<sub>c</sub>|<sup>2</sup>, 0) + 2|F<sub>c</sub>|<sup>2</sup>)/3.
7.39–7.35 (m, 1H, pPh-H), 5.14 (dd, J = 2.5, 10.1 Hz, 1H, THP-H), 4.14–4.10 (m, 1H, THP-H), 3.56–3.50 (m, 1H, THP-H), 2.65–2.55 (m, 1H, THP-H), 2.10–2.06 (m, 1H, THP-H), 1.79–1.69 (m, 1H, THP-H). – 13C NMR (100 MHz, CDCl3): δ = 149.0 (pz-C-3,5), 143.4 (pz-C-3,5), 132.5 (PhC), 130.4 (PhCh), 129.5 (PhCh), 128.7 (PhCh), 128.4 (PhCH), 128.3 (PhCH), 93.6 (pz-C-4), 85.2 (THP), 67.9 (THP), 29.5 (THP), 24.9 (THP), 22.9 (THP), n. o. (PhC).

Single crystals of (1c)2-HBr and 1c-HBr·(Br2)0.5

The bromopyrazole 1c was prepared according to the published procedure [19]. Single crystals of (1c)2-HBr were grown from the reaction mixture at r. t. In a second crop crystals containing 1c, HBr, and Br2 in the ratio of 1:1:0.5 were obtained from this solution at r. t.

Crystals of 4-iodo-1H-pyrazole and H2SO4 ((2a)2·H2SO4)

The iodopyrazole 2a was prepared according to the published procedure [20]. By slow evaporation of the solvent crystals of (2a)2·H2SO4 were grown from a chloroform solution at r. t.

Single crystals of 4-iodo-3,5-diphenyl-1H-pyrazole (2b)

The iodopyrazole 2b was prepared according to the published procedure [20]. Single crystals of 2b were grown from a CHCl3 solution by slow evaporation of the solvent at r. t.

4-Iodo-3,5-diphenyl-1-THP-pyrazole (2b(THP))

2b(THP) was synthesized following the same procedure as described for 1b(THP) from DHP (0.13 g, 1.59 mmol), 2b (0.50 g, 1.44 mmol), TFA (0.01 g, 0.07 mmol) and 10 mL toluene. Pale-yellow oil (yield: 0.61 g, 98%)

1H NMR (400 MHz, CDCl3): δ = 7.92–7.90 (m, 2H, oPh-H), 7.60–7.50 (m, 5H, Ph-H), 7.47–7.40 (m, 2H, mPh-H), 7.40–7.38 (m, 1H, pPh-H), 5.12 (dd, J = 2.5, 10.1 Hz, 1H, THP-H), 4.12–4.08 (m, 1H, THP-H), 3.53–3.47 (m, 1H, THP-H), 2.65–2.51 (m, 1H, THP-H), 2.08–2.04 (m, 1H, THP-H), 1.87–1.83 (m, 1H, THP-H), 1.79–1.68 (m, 1H, THP-H), 1.60–1.49 (m, 2H, THP-H). – 13C NMR (100 MHz, CDCl3): δ = 152.3 (pz-C-3,5), 146.8 (pz-C-3,5), 133.2 (PhC), 130.7 (PhCh), 129.9 (PhCh), 129.5 (PhCh), 128.8 (PhCH), 128.7 (PhCH), 128.3 (PhCH), 128.2 (PhCH), 85.4 (THP), 67.9 (THP), 62.3 (pz-C-4), 29.6 (THP), 24.9 (THP), 22.9 (THP).

Single crystals of 4-pinacolatoboryl-1H-pyrazole (3a)

The pyrazole 3a was prepared according to the published procedure [22]. Single crystals of 3a were grown from an ethyl acetate solution by slow evaporation of the solvent at r. t.

Crystals of 4-pinacolatoboryl-1H-pyrazole and H2O ((3a)2·H2O)

The pyrazole 3a was prepared according to the published procedure [22]. By slow evaporation of the solvent crystals of (3a)2·H2O were grown from the reaction solution at r. t.

4-Pinacolatoboryl-3,5-diphenyl-1H-pyrazole (3b)

A 2 M solution of iPdMeCl (0.31 g, 3.03 mmol) was added dropwise to a cooled (−4 °C) solution of 2b(THP) (0.87 g, 2.02 mmol) in THF (10 mL). After 15 min (Bpin)OPr (1.13 g, 6.07 mmol) was added dropwise to −4 °C to the suspension. The resulting mixture was stirred for further 1.5 h and slowly warmed up to r. t. overnight. After the addition of saturated aqueous NH4Cl solution, the slurry was diluted with toluene (25 mL) and washed with brine (3 × 20 mL). The organic layer was dried over anhydrous MgSO4. After removal of all volatile compounds in vacuo, a yellow oil was obtained. 3b(THP) was treated with 20 mL of a methanolic HCl solution (AcCl in MeOH) and stirred for 30 min. After the addition of NEt3 (2 mL), the solution was stirred for further 30 min, diluted with Et2O (50 mL), and dried over anhydrous MgSO4. Evaporation of the solvents gave a yellow oil, which was purified by column chromatography (hexane/ethyl acetate 3:1). Single crystals were grown by gas-phase diffusion of cyclohexane into a solution of 3b in benzene. Colorless solid (yield: 0.52 g, 60%). – 1H NMR (500 MHz, CDCl3): δ = 7.73–7.71 (m, 4H, oPh-H), 7.43–7.36 (m, 6H, Ph-H), 1.26 (s, 12H, CH2), n. o. (N-H). – 13C NMR (126 MHz, CDCl3): δ = 154.6 (pz-C-3,5), 132.5 (PhC), 128.6 (PhCH), 128.5 (PhCH), 83.8 (CCH3), 24.9 (CH3). – 11B[1H] NMR (160 MHz, CDCl3): δ = 31.3 (b1/2 = 350 Hz). – MS (+)-ESI: m/z (%): 347.6 (100) [M+H]+. – C21H23BN2O2 (342.2): calcld. C 72.85, H 6.81, N 8.20; found C 73.41, H 6.68, N 8.09.

4-Trimethylsilyl-1H-pyrazole (4a)

The pyrazole 4a was synthesized from 4a(THP) following the same procedure as described for 3a and 3b. The THP-protected iodopyrazole 2a(THP) [21] (0.20 g, 0.72 mmol), nBuLi (0.12 g, 1.80 mmol), and Me3SiCl (0.23 g, 2.16 mmol) were used as starting materials. – 1H NMR (250 MHz, C6D6): δ = 7.81 (s, 1H, pz-H-3,5), 7.28 (s, 1H, pz-H-3,5), 5.68 (dd, J = 3.2, 9.1 Hz, 1H, THP-H), 4.10–4.04 (m, 1H, THP-H), 3.84–3.67 (m, 1H, THP-H), 2.63–2.51 (m, 1H, THP-H), 2.08–2.04 (m, 1H, THP-H), 1.87–1.83 (m, 1H, THP-H), 1.79–1.68 (m, 1H, THP-H), 1.60–1.49 (m, 2H, THP-H), 0.15 (s, 9H, CH3).
ment of 4a(THP) with 20 mL of a methanolic HCl solution (AcCl in MeOH) 4a was obtained. Spectroscopic data see ref. [24].

An alternative and more convenient synthesis of 4a: 4-Bromo-1H-pyrazole (6.69 g, 45.52 mmol) was dissolved in 50 mL THF and the solution was cooled to −78 °C. This solution was treated dropwise with a 1 M BuLi solution in hexane (5.83 g, 91.04 mmol). The reaction mixture was subsequently stirred for 1 h at 0 °C. Me3SiCl (14.02 g, 129.05 mmol) was added dropwise at −78 °C. The reaction mixture was warmed up to r.t. overnight. Then it was quenched with an aqueous NaOH solution, diluted with ethyl acetate 2:1 to yield colorless crystals (yield: 2.19 g, 60%). Spectroscopic data see ref. [24].

4-Trimethylsilyl-3,5-diphenyl-1-THP-pyrazole (4b(THP))

The pyrazole 4b(THP) was synthesized following the same procedure as described for 3a(THP), 3a(THP), and 4a(THP). The THP-protected iodopyrazole 2b(THP) [21] (0.20 g, 0.52 mmol), nBuLi (0.08 g, 1.30 mmol), and Me3SiCl (0.17 g, 1.57 mmol) were used as starting materials. −1H NMR (250 MHz, CD2D2): δ = 7.86–7.82 (m, 2H, oPh-H), 7.30–7.10 (m, 8H, Ph-H), 5.04 (dd, J = 3.2, 9.6 Hz, 1H, THP-H), 3.88–3.84 (m, 1H, THP-H), 3.10–3.06 (m, 1H, THP-H), 2.87–2.68 (m, 1H, THP-H), 1.74–1.61 (m, 2H, THP-H), 1.37–1.26 (m, 1H, THP-H), 1.07–0.88 (m, 2H, THP-H). −0.01 (s, 9H, CH3).

4-Trimethylsilyl-3,5-diphenyl-1-TMS-pyrazole (4b(TMS))

4-Bromo-3,5-diphenyl-1H-pyrazole (0.40 g, 1.34 mmol) was dissolved in 10 mL THF, and the solution was cooled to −78 °C. This solution was treated dropwise with a 1.52 M nBuLi solution in hexane (0.21 g, 3.34 mmol). The reaction mixture was subsequently stirred for 1 h at 0 °C. Me3SiCl (0.43 g, 4.01 mmol) was added dropwise at −78 °C. The reaction mixture was warmed up to r.t. overnight. NMR data were collected without further purification. Colorless solid (yield: 0.95 g, 72%). −1H NMR (500 MHz, CD2D2): δ = 7.85–7.83 (m, 2H, oPh-H), 7.29–7.27 (m, 2H, oPh-H), 7.24–7.21 (m, 2H, mPh-H), 7.18–7.14 (m, 1H, mPh-H), 7.10–7.03 (m, 3H, Ph-H), 0.19 (s, 9H, N(SiCH3)2). 0.00 (s, 9H, CSSiCH3). −13C NMR (125 MHz, CD2D2): δ = 161.3 (pzC-3,5), 156.9 (pzC-3,5), 137.7 (PhC), 135.3 (PhC), 131.2 (PhC), 130.1 (PhC), 128.9 (PhC), 128.4 (PhC), 128.2 (PhC), 128.0 (PhC), 113.8 (pzC-4), 1.2 (CSSiCH3), 0.9 (NSiCH3). −29Si NMR (99 MHz, CD2D2): δ = 15.4, −10.9.

4-Trimethylstannyl-1-THP-pyrazole (5a(THP))

A 1.52 M nBuLi solution in hexane (0.14 g, 2.20 mmol) was added dropwise (−78 °C) to a stirred solution of 1a(THP) (0.39 g, 1.70 mmol) in THF (6 mL). After stirring at −78 °C for 2 h, a solution of Me3SnCl (0.50 g, 2.53 mmol) in THF (5 mL) was added dropwise to the cooled reaction mixture (−78 °C). The suspension was warmed to r.t. overnight, then diluted with Et2O (60 mL) and treated with water (60 mL). The organic layer was dried over anhydrous MgSO4 and evaporated to dryness in vacuo. However, the synthesis of 5a(THP) was not quantitative. Beside the main product 5a(THP) we observed two other stannylated and THP-protected pyrazole derivatives, namely 3-Me3Sn-pz(THP) and 5-Me3Sn-pz(THP) (ratio in the 1H NMR spectrum: ~65% for 5a(THP), ~25% for 3-Me3Sn-pz(THP), ~10% for 5-Me3Sn-pz(THP)). Spectroscopic data for 5a(THP): −1H NMR (500 MHz, CDCl3): δ = 7.53 (s, 1H, pzH-3,5), 7.51 (s, 1H, pzH-3,5), 5.42 (dd, J = 2.3, 10.0 Hz, 1H, THP-H), 4.09–4.06 (m, 1H, THP-H), 3.73–3.68 (m, 1H, THP-H), 2.21–2.13 (m, 1H, THP-H), 2.09–2.04 (m, 2H, THP-H), 1.74–1.66 (m, 3H, THP-H), −0.19 (s, 9H, CH3). −13C NMR (125 MHz, CDCl3): δ = 145.6 (pzC-3,5), 132.8 (pzC-3,5), 111.7 (pzC-4), 87.5 (THP), 68.1 (THP), 30.8 (THP), 25.2 (THP), 22.8 (THP), −9.1 (CH3).

4-Trimethylstannyl-3,5-diphenyl-1-THP-pyrazole (5b)

1b(THP) (1.09 g, 2.84 mmol) in THF (15 mL) was treated dropwise with a 1.35 M nBuLi solution in hexane (0.24 g, 3.70 mmol) at −78 °C and stirred for 2 h. A solution of Me3SnCl (0.85 g, 4.27 mmol) in THF (10 mL) was added dropwise to the cooled reaction mixture (−78 °C). After warming up to r.t. overnight, the suspension was diluted with Et2O (100 mL) and treated with water (150 mL). The organic layer was dried over anhydrous MgSO4 and concentrated to a volume of 2 mL. The product precipitated after 12 h. Analytically pure 5 was obtained from the crude product by washing with hexane. Single crystals were grown by slow evaporation of a CDCl3 solution. Colorless solid (yield: 0.95 g, 72%). −1H NMR (250 MHz, CDCl3): δ = 7.64–7.59 (m, 2H, oPh-H), 7.47 (s, 5H, Ph-H), 7.42–7.33 (m, 3H, Ph-H), 5.10 (dd, J = 2.4, 10.3 Hz, 1H, THP-H), 4.14–4.08 (m, 1H, THP-H), 3.55–3.45 (m, 1H, THP-H), 2.69–2.53 (m, 1H, THP-H), 2.07–2.01 (m, 1H, THP-H), 1.90–1.85 (m, 1H, THP-H), 1.79–1.46 (m, 3H, THP-H), −0.19 (s, 9H, CH3). −13C NMR (63 MHz, CDCl3): δ = 158.7 (pzC-3,5), 151.0 (pzC-3,5), 136.2 (PhC), 132.5 (PhC), 130.4 (PhC), 128.9 (PhC), 128.8 (PhC), 128.2 (PhC), 127.7 (PhC), 112.1 (pzC-4), 84.6 (THP), 67.9 (THP), 30.0 (THP), 25.0 (THP), 23.1 (THP), −8.0 (CH3). −MS ([+]-ESI): m/z (%): 469.2 (100) [M+H]+. −C23H32NO3Sn (467.2): calcd. C 59.13, H 6.04, N 6.00; found C 58.98, H 6.12, N 5.98.
K₂PO₄ (0.33 g, 1.54 mmol) was dissolved in 5 mL dmf and 5 mL water, and the solution was saturated with argon. A mixture of Pd(PPh₃)₄ (0.06 g, 0.05 mmol), 3a(THP) (0.14 g, 0.51 mmol), and 4-pentylbromobenzene (0.12 g, 0.92 μL, 0.51 mmol) was added to the K₂PO₄ solution. The resulting suspension was treated with argon in vacuo at 120°C for 30 min. After microwave irradiation at 120°C for 20 min, the reaction mixture was treated with a saturated aqueous NaHCO₃ solution (30 mL). The product was extracted into ethyl acetate (3 × 30 mL). The combined organic layers were washed three times with 30 mL of a saturated aqueous NaCl solution and dried over anhydrous MgSO₄. After removal of the solvent in vacuo, the THP-protected product remained as a pale-yellow oil (0.12 g, 82%). Treatment with a solution of HCl in MeOH (10 mL, AcCl in MeOH) and stirring for 30 min yielded the hydrochloride of 6(pentyl) [13]. When the hydrochloride was treated with NEt₃ and 5 mL water, and the solution was saturated with argon for 30 min yielded the hydrochloride of 6(pentyl) [13].

6(pentyl) [13] was obtained quantitatively. After evaporation of the solvent, the crude product was purified by column chromatography (hexane/ethyl acetate 2:1). Colorless solid (yield: 0.07 g, 68%). - ¹H NMR (500 MHz, CDCl₃): δ = 7.90 (br, 2H), 7.46 (d, 2H, J = 8.0 Hz, Ph-H), 7.17 (d, 2H, J = 8.0 Hz, Ph-H), 2.60 (t, 2H, J = 7.6 Hz, CH₂), 1.66–1.60 (m, 2H, CH₂), 1.38–1.29 (m, 4H, 2 × CH₂), 0.91 (t, 3H, J = 7.0 Hz, CH₃), n. o. (N-H). - ¹³C NMR (126 MHz, CDCl₃): δ = 142.2 (PhC), 137.3 (pzC-3,5), 131.6 (PhC), 126.5 (PhC), 123.7 (pzC-4), 36.5 (CH₂), 32.6 (CH₂), 23.6 (CH₂), 14.4 (CH₃). - MS ((+)-ESI): m/z (%) = 319.9 (100) [M+H]+.

Crystal structure determinations

Data for (1c)·HBr and 1c·HBr·(B₃F₅O) were collected on a Stoe IPDS II two-circle diffractometer with graphite-monochromated MoKα radiation (λ = 0.71073 Å) and corrected for absorption with an empirical absorption correction using the program PLATON [25]. Data for 1a·HBr, 1b, 2a, 3a·H₂SO₄, 3a, 3a·H₂O, 3b·HBr, and 5b(THP) were collected on a Stoe IPDS II two-circle diffractometer with a Genix Microfocus tube with mirror optics using MoKα radiation (λ = 0.71073 Å) and were scaled using the frame scaling procedure in the X-AREA program system [26]. The structures were solved by Direct Methods using the program SHELXS [27] and refined against F² with full-matrix least-squares techniques using the program SHELXL-97 [27].

The H atoms bonded to the N atoms in 1a·HBr and 1c·HBr were geometrically positioned and refined using a riding model. The H atom bonded to the N(1) atom has an occupation factor of 0.5.

The coordinates of the H atoms bonded to N in 1a·HBr were refined restraining the N–H bond lengths to 0.89(1) Å. The H atoms bonded to B in 3a were isotropically refined. Due to the absence of anomalous scatterers, the absolute structure of 3a could not be determined. The coordinates of the H atoms bonded to N and O in (3a)·H₂O were refined restraining the O–H bond lengths to 0.84(1) Å and the N–H bond lengths to 0.91(1) Å. The H atoms bonded to O and N(3) have a site occupation factor of 2/3 and the H atom bonded to N(4) has a site occupation factor of 1/3. Due to the absence of anomalous scatterers, the absolute structure of (3a)·H₂O could not be determined.

In 3a the three methyl groups of two molecules are disordered over two positions with site occupation factors of 0.55(6) and 0.78(2) for the site with the major occupancy. Si–C and C–C bond lengths in the disordered parts were restrained to be equal to those in a non-disordered SiMe₃ group. The disordered atoms were refined isotropically. One methyl C atom (C(6C)) was restrained to an isotropic beha-
ior. The H atoms could not be located and were geometrically positioned. The absolute structure could not be reliably determined. Flack (s) parameter 0.8(5). Attempts to refine the structure in the space group P2₁/c failed.

The H atoms bonded to N in (1a)_3H₂SO₄ were isotropically refined restraining the N(2A)–H(2A) bond length to 0.88(1) Å.

In one molecule of 3b, the dioxaborolane ring is disordered over two positions with a factor of 0.695(7) for the site with the major occupancy. The disordered atoms were refined isotropically. The H atoms bonded to N were freely refined. Due to the absence of anomalous scatterers, the absolute structure could not be determined. The coordinates of the H atoms bonded to the N atoms in 1b were refined restraining the N–H bond lengths to 0.88(1) Å.

CCDC 954166 ((1c)₂·HBr), CCDC 954165 (1c·HBr·(Br₂)₂·SO₄), CCDC 954171 ((2a)_3H₂SO₄), CCDC 954168 (3a), CCDC 954169 ((3a)₂·H₂O), CCDC 954172 (3b), CCDC 954170 (4a), and CCDC 954173 (5b·(THP)) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.