Synthesis of Pinacol Esters of 1-Alkyl-1*H*-pyrazol-5-yl- and 1-Alkyl-1*H*-pyrazol-4-ylboronic Acids

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Starting from 1*H*-pyrazol, a wide number of 1-alkyl-1*H*-pyrazol-4-yl and 1-alkyl-1*H*-pyrazol-5-ylboronic acids and their pinacol esters were synthesized and characterized. The key step in the described methodology is the regioselective lithiation of the pyrazole ring. The synthesized pinacolates are stable under prolonged storage and can be used as convenient reagents in organic synthesis.

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Introduction.

Reaction of cross-coupling of organoboron compounds discovered by A. Suzuki [1] is important to various fields of organic synthesis and combinatorial chemistry. Among a relatively wide assortment of available aryl- and heteroarylboronic acids used for the Suzuki reaction, the derivatives of pyrazole are still rare species [2], despite the fact that the first representatives of this class were described in the middle of the 20th century [3]. In addition, the pyrazole fragment is present in a large number of natural and synthetic small molecule ligands that interact with various enzymes and receptors of pharmacological significance [4].

In this paper, we describe a convenient method for the synthesis of novel 1-alkylpyrazolboronic acids that can be used as building blocks for the synthesis of biologically active compounds. The scope and limitations of the involved chemistry are discussed.

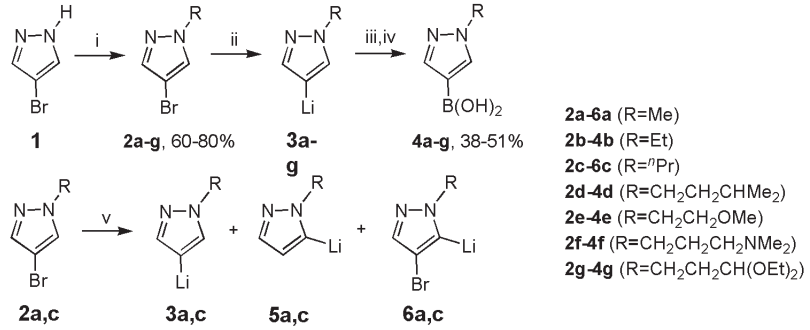
Results and Discussion.

The general synthetic approach to 1*H*-pyrazol-4-ylboronic acids is depicted in Scheme 1. The initial 4-bromo-1*H*-pyrazole **1** was alkylated upon treatment with the appropriate alkyl halide in ethanol in the presence of KOH. Subsequent reaction of 4-bromo-1-alkyl-1*H*-pyrazoles **2a-g** with BuLi [5] in THF led to lithium derivatives **3a-g**, which were successfully converted into boronic acids **4a-g** upon the reaction with $B(OMe)_3$ in THF followed by treatment with a solution of aqueous ammonium chloride.

We have found that for the smooth formation of lithium derivatives **3a-g**, the temperature of the reaction mixture should be kept below -80 °C. Under increased temperatures, two side reactions become possible which lead to complex mixtures of products (Scheme 1). Both reactions are well documented in the literature. The first reaction is the rearrangement of 1*H*-pyrazol-4-yllithium derivatives **3** into the more stable 5-lithium structures **5**, which proceeds at temperatures 0 – -10 °C [5a,c]. The second possible side reaction is the concurrent direct lithiation of 4-bromo-1*H*-pyrazole **1** leading to 4-bromo-1*H*-pyrazol-5-yllithium derivatives **6** [5a,6]. Based on ^{1}H NMR spectral analysis of pyrazolylboronic acids from the reaction mixtures, we have determined the following ratio between different products of reaction of 4-bromo-1-alkyl-1*H*-pyrazoles **2a,c** with BuLi at -40 – -50 °C: **3a,c**:**5a,c**:**6a,c** ≈ 1.5:1.5:1.

Interestingly, for some particular initial reactants the second reaction can be the predominant conversion route [6].

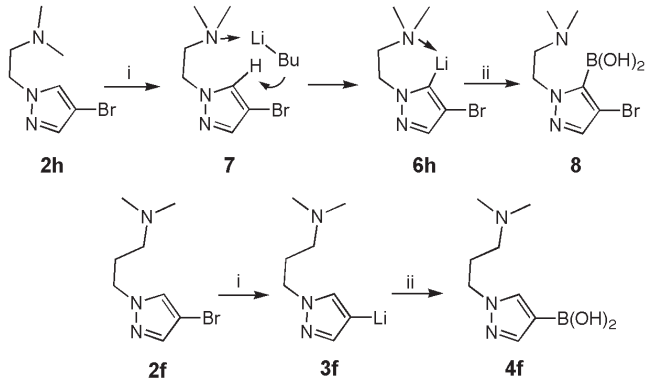
Scheme 1



Reagents and conditions: (i) RHal, KOH, EtOH, 78 °C; (ii) *n*-BuLi, THF, -90 °C – -80 °C; (iii) $B(OMe)_3$, THF, -75 °C – -70 °C; (iv) NH_4Cl/H_2O; (v) *n*-BuLi, THF, -50 °C – -45 °C.

Thus, we have observed that the reaction of **2h** with *n*-butyllithium exclusively leads to 5-lithium derivative **6h** (Scheme 2). The explanation for the observed phenomenon is the strong coordination of a lone pair of electrons of the dimethylamino group and lithium atom in intermediate **7**. This intermediate is easily converted into structure **6h**, which contains a stable 6-membered intermolecular complex.

Scheme 2



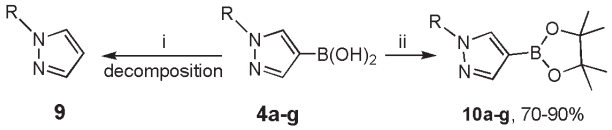
Reagents and conditions: (i) *n*-BuLi; (ii) 1. $B(OMe)_3$, 2. NH_4Cl/H_2O.

Structure **6h** can be readily converted into pyrazolylboronic acid **8**. However, the steric hindrances within the reaction center prevent further formation of the corresponding pinacol ester from **8**. For comparison, the lithiation of **2f**, in which the dimethylamino group and N-1 atom of the pyrazole ring are divided by three methylene fragments proceeds *via* the common halogen-lithium exchange route (Scheme 2).

We have observed that 1-alkyl-1*H*-pyrazol-4-ylboronic acids **4** are unstable and are easily decomposed in the presence of water yielding 1-alkyl-1*H*-pyrazoles **9** (Scheme 3). ^{1}H NMR spectroscopic analysis of the solutions of **4a-g** in DMSO-d_6/$D_2$0 (4:1) mixtures has shown that approximately 50% of the initial acids are decomposed within 24 h. The slow deboration also occurs in the absence of moisture in an atmosphere of dry argon, probably, due to hydroxyls at the boron atom.

The problem of instability can be addressed using the conversion of acids **4** into their more stable derivatives. We have found that 1-alkyl-1*H*-pyrazol-4-ylboronic acids **4** can be effectively converted into the corresponding pinacol esters **10a-g** (yield 70-90%) upon treatment with pinacol in the presence of water-absorbing agents, such as molecular sieves (Scheme 3). The pinacol esters are also useful reagents for the Suzuki cross-coupling reaction [2]. In addition, they have some beneficial features over the initial boronic acids **4a-g**. Thus, they do not form the cyclic trimeric anhydrides (boroxines), which often complicate the analysis of arylboronic acids [7]. In addition, they are much more stable. For example, we could not even detect traces of the deboration products after 6 months storage of the pinacol esters **10a-g** at 5-10 °C.

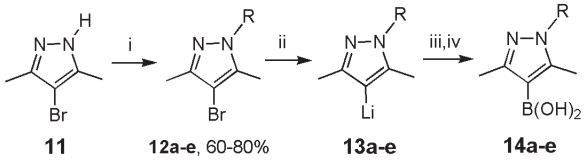
Scheme 3



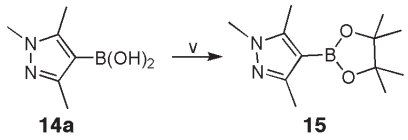
Reagents and conditions: (i) H_2O; (ii) pinacol, molecular sieves 4Å.

In this work, we also attempted to synthesize 1-alkyl-3,5-dimethyl-1*H*-pyrazol-4-ylboronic acids **14a-e** starting from the corresponding 4-bromo-1-alkyl-3,5-dimethyl-1*H*-pyrazoles **12a-e** (Scheme 4). Acids **14a-e** are prone to deboration even to a greater extent than 1-alkyl-1*H*-pyrazol-4-ylboronic acids **4**: in all the cases studied they rapidly decomposed immediately after synthesis. Such instability can be explained by strong steric interactions between the hydroxyls at boron atom and the adjacent methyl groups. As a result, all our attempts to obtain the corresponding stable pinacol esters were unsuccessful, with only one exception: 1-methyl derivative **14a** has been converted in low yield (10% from **11**) into the pinacolate **15**.

Scheme 4



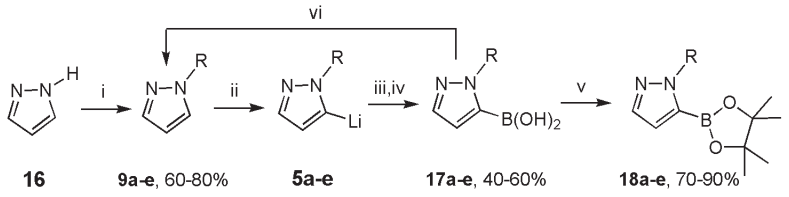
R = Me (a), Et(b), ^{n}Pr (c), $CH_2CH_2CH_2NMe_2$ (d), $CH_2CH_2CH(OEt)_2$ (e)



Reagents and conditions: (i) RHal, KOH, EtOH, 78 °C; (ii) *n*-BuLi, THF, -90 °C – -80 °C; (iii) $B(OMe)_3$, THF, -75 °C – -70 °C; (iv) NH_4Cl/H_2O; (v) pinacol, molecular sieves 4 Å.

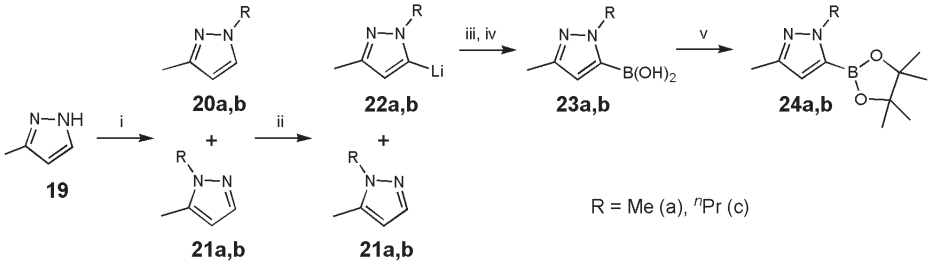
In this work, we also synthesized 1-alkylpyrazol-5-ylboronic acids using the direct lithiation of 1-alkylpyrazoles. This process has been extensively studied in literature [5a,c,6,8]. The reaction of 1-alkylpyrazoles with *n*-BuLi in THF proceeded smoothly at 0-20 °C leading to 5-lithium derivatives **5a-e** (Scheme 5). The further synthetic route to boronic acids **17a-e** and their pinacol esters **18a-e** is similar to the synthesis of 1-alkyl-1*H*-pyrazol-4-ylboronic acids.

Scheme 5



Reagents and conditions: (i) Me_2SO_4, NaOH (a), RBr, KOH, EtOH, 78 °C (b-e); (ii) *n*-BuLi, THF, 0 – 20 °C; (iii) $B(OMe)_3$, THF, -75 °C – -70 °C; (iv) NH_4Cl/H_2O; (v) pinacol, molecular sieves 4 Å; (vi) H_2O.

Scheme 6



Reagents and conditions: (i) Me_2SO_4, NaOH (a); PrBr, KOH, EtOH, 78 °C (b); (ii) *n*-BuLi, THF, 0-20 °C; (iii) $B(OMe)_3$, -75 °C – -75 °C; (iv) NH_4Cl, H_2O; (v) pinacol, molecular sieves 4 Å.

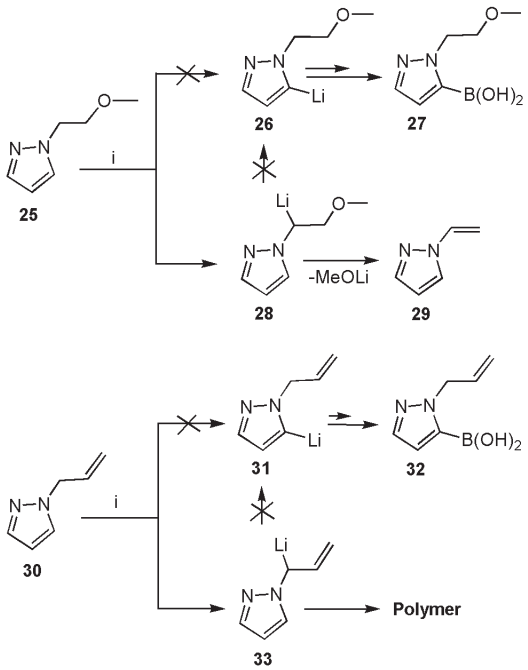
1*H*-Pyrazol-5-ylboronic acids **17a-e** are less prone to decomposition than their 1*H*-pyrazol-4-ylboronic analogs **4**. However, we were able to detect the deboration products, 1-alkyl-1*H*-pyrazoles **9a-e**, after 10-15 days of storage. To prevent the decomposition, we converted acids **17a-e** into the corresponding pinacol esters **18a-e** (Scheme 5).

The described approach was used for the synthesis of 5-boronic acid derivatives of 3-methyl-1*H*-pyrazole (Scheme 6). The principal difficulty with this product series is the formation of two isomers, 1-alkyl-3-methyl-1*H*-pyrazole **20a,b** and 1-alkyl-5-methyl-1*H*-pyrazole **21a,b**, upon the alkylation of 3-methyl-1*H*-pyrazole **19**. It should be noted that the isomerically pure 1-alkyl-3-methyl-1*H*-pyrazoles are more difficult to obtain synthetically [8e]. However, it is known from literature that the lithiation of pyrazoles selectively proceeds into position 5 [5a,8d-h]. Therefore, upon the treatment of the mixture of **20a,b** and **21a,b** with *n*-BuLi, only 5-lithium derivatives of 1-alkyl-3-methyl-1*H*-pyrazoles **22a,b** were obtained.

The latters were readily converted into the corresponding boronic acids **23a,b** and then to stable pinacolates **24a,b**. The unreacted 1-alkyl-5-methyl-1*H*-pyrazole **21a,b** were easily separated from the arylboranes **23a,b** using extraction with ether or vacuum distillation (0.01 mm Hg).

Unexpectedly, when we attempted to obtain 1-(2-methoxyethyl)-1*H*-pyrazol-5-ylboronic acid **27** from 1-(2-methoxyethyl)-1*H*-pyrazole **25**, only 1-vinyl-1*H*-pyrazole

Scheme 7



Reagents and conditions: (i) *n*-BuLi, 20 °C

29 could be isolated from the reaction mixture (Scheme 7). It can be suggested that the intermediate **28** is initially formed, which then undergoes rapid β-elimination yielding 1-vinyl-1*H*-pyrazole **29**. This mechanism is consistent with the experimental data on alternative metallation of 1-alkyl-1*H*-pyrazoles [5c,8e-g]. Moreover, Katrizky *et al*. [8f] suggested that the generation of α-lithiated intermediates such as **28** represents the first step in the lithiation of the most of 1-alkylpyrazoles, while the 5-lithium derivatives are formed upon the rearrangement of such initial intermediates. Thus, we observed that the lithiation of 1-allyl-1*H*-pyrazole **30** leads to a mixture of polymeric products instead of the desired 5-lithium derivative **31** and the corresponding boronic acid **32**. Probably, this fact can be explained by the suggested α-lithiation of 1-allyl-1*H*-pyrazole **30** leading to structure **33** prone to rapid polymerization.

Conclusion.

In summary, we have obtained and characterized a number of 1-alkylpyrazolylboronic acids **4a-g**, **14a**, **17a-e** and **23a,b**. We have observed that these acids are unstable and undergo rapid deboration. The stability of the studied 1-alkyl-1*H*-pyrazolylboronic acids increases in an order shown in Figure 1.

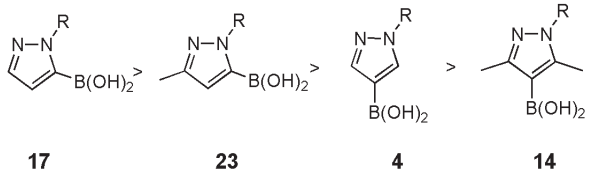


Figure. 1

In order to prevent the degradation process, we have converted 1-alkyl-1*H*-pyrazolylboronic acids into the corresponding pinacol esters **10a-g**, **15**, **18a-e** and **24a,b**. These esters are viscous oils or low melting point solids practically insensitive to air and moisture. ^{11}B NMR spectra of these compounds contain signals at 27.5-29.5 ppm characteristic of arylboronic acids and their esters [9]. These data indicate the absence of a substantial B-N coordination in the solutions of the obtained dioxaborolanes, which usually accompanies the formation of donor-acceptor complexes consisting of two or more molecules.

Possible problems associated with incomplete reaction or deboration of pyrazolylboronic acids and their esters under the basic conditions of palladium-catalysed couplings should be stressed [10]. However, under optimal reaction conditions, such condensations can afford the desired products in quantitative yield [2b,c]. Our experiments indicate that the synthesised pinacolates **10a-g**, **15**, **18a-e** and **24a,b** are stable under storage and can be used as building blocks in organic synthesis, in particular, in Suzuki cross-coupling reaction of organoboron compounds. These data will be published in due course.

EXPERIMENTAL

Melting points were measured with a Buchi B-520 melting point apparatus and were not corrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX-500 spectrometers (500,13 MHz for ^{1}H NMR and 125,76 MHz for ^{13}C NMR) in DMSO-d_6 using TMS as an internal standard. ^{11}B NMR spectra were recorded on Bruker AC-200P (64.21 MHz) in $CDCl_3$ using $BF_3 \cdot Et_2O$ as an internal standard. Mass-spectral analyses were obtained on a Finnigan MAT INCOS 50 mass spectrometer (70 eV, electron impact). Elemental analysis were within + 0.4% of the theoretical value. Due to low stability of analytical samples, only ^{1}H NMR spectra were recorded for acids **4a-g, 8, 14a, 17a-e** and **23a,b**.

Tetrahydrofuran was dried by distillation over $LiAlH_4$ under an atmosphere of argon. All reactions with *n*-butyllithium were carried out under an atmosphere of dry argon. 1-Methyl-1*H*-pyrazole **9a** was obtained from **16** and dimethylsulfate in 60% yield as reported [5a]. 1-Allyl-1*H*-pyrazole **30** was obtained by reaction of 1*H*-pyrazole with allyl bromide as reported [11]. The mixture of 1-propyl-3-methylpyrazole **20b** and 1-propyl-5-methylpyrazole **21b** (~3:2, based on ^{1}H NMR spectral data) was obtained from 3-methylpyrazole in 64% yield as reported [8e]. This mixture was used at the next step without separation of the individual isomers. The analytical data of **20b** are reported in [8e].

General Procedure for the Synthesis of 1-Alkylpyrazoles (**2a-e**, **2g**, **9b-e**, **12a** and **25**).

Alkyl bromide (250 mmol) was added to a solution of N^1-unsubstituted pyrazole (**1, 11, 16**) (200 mmol) and KOH (14 g, 250 mmol) in 200 ml of absolute EtOH. The reaction mixture was heated at reflux for 1.5 h. The mixture was cooled to room temperature and diluted with CH_2Cl_2 (400 ml). The resulting mixture was filtered, and the solvent was evaporated. The crude product was distilled *in vacuo* to give 1-alkylpyrazole (**2a-e**, **2g**, **9b-e**, **12a** and **25**) as a liquid or low-melting point solid.

4-Bromo-1-methyl-1*H*-pyrazole (**2a**).

This compound was obtained in 72% yield as a solid; mp 77-79 °C (the analytical data of **2a** are identical to those reported in [12]).

4-Bromo-1-ethyl-1*H*-pyrazole (**2b**).

This compound was obtained in 78% yield as an oil; n^D_{20} 1.5088; bp 106-108 °C/20 mm Hg (the analytical data of **2b** are identical to those reported in [12]).

4-Bromo-1-propyl-1*H*-pyrazole (**2c**).

This compound was obtained in 75% yield as an oil; n^D_{20} 1.5076; bp 60-62 °C/1 mm Hg (the analytical data of **2c** are identical to those reported in [12]).

4-Bromo-1-(3-methylbutyl)-1*H*-pyrazole (**2d**).

This compound was obtained in 85% yield as an oil; n^D_{20} 1.4996; bp 77-79 °C/1 mm Hg; ^{1}H NMR (DMSO-d_6, ppm): δ

0.95 (d, 6H, CH_3, J = 6.6 Hz), 1.45-1.55 (m, 1H, $(CH_3)_2CH$), 1.60-1.72 (m, 2H, CH_2CH_2N), 4.10 (t, 2H, CH_2N, J = 6.2 Hz), 7.27 (s, 1H, C^3H), 7.58 (s, 1H, C^5H).

4-Bromo-1-(2-methoxyethyl)-1*H*-pyrazole (**2e**).

This compound was obtained in 65% yield as an oil; n^D_{20} 1.5137; bp 70-72 °C/1 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 3.20 (s, 3H, CH_3O), 3.65 (t, 2H, CH_2O, J = 5.4 Hz), 4.25 (t, 2H, CH_2N, J = 5.4 Hz), 7.50 (s, 1H, C^3H), 7.80 (s, 1H, C^5H).

4-Bromo-1-(3,3-diethoxypropyl)-1*H*-pyrazole (**2g**).

This compound was obtained in 80% yield as an oil; n^D_{20} 1.4840; bp 98-100 °C/0.04 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 1.10 (t, 6H, CH_3, J = 6.0 Hz), 2.0 (m, 2H, CH_2CH), 3.40-3.60 (m, 4H, CH_2O), 4.10 (t, 2H, CH_2N, J = 6.6 Hz), 4.43 (t, 1H, O-CH-O, J = 5.8 Hz), 7.50 (s, 1H, C^3H), 7.95 (s, 1H, C^5H).

1-Isobutyl-1*H*-pyrazole (**9b**).

This compound was obtained in 64% yield as an oil; n^D_{20} 1.4614; bp 85-88 °C/20 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 0.82 (d, 6H, CH_3, 6.2 Hz), 2.05-2.14 (m, 1H, $CH(CH_3)_2$), 3.90 (d, 2H, CH_2N, J = 6.6 Hz), 6.20 (s, 1H, C^4H), 7.40 (s, 1H, C^3H), 7.64 (c, 1H, C^5H).

1-Propyl-1*H*-pyrazole (**9c**).

This compound was obtained in 66% yield as an oil; n^D_{20} 1.4668; bp 70-72 °C/20 mm Hg (the analytical data of **9c** are identical to those reported in [8e]).

1-(3-Methylbutyl)-1*H*-pyrazole (**9d**).

This compound was obtained in 63% yield as an oil; n^D_{20} 1.4641; bp 58-61 °C/1 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 0.88 (d, 6H, CH_3, *J* = 7.0 Hz), 1.40-1.50 (m, 1H, $(CH_3)_2CH$), 1.65 (m, 2H, CH_2CH_2N), 4.12 (t, 2H, CH_2N, J = 7.2 Hz), 6.18 (s, 1H, C^4H), 7.40 (s, 1H, C^3H), 7.70 (s, 1H, C^5H).

1-(3,3-Diethoxypropyl)-1*H*-pyrazole (**9e**).

This compound was obtained in 88% yield as an oil; n^D_{20} 1.4596; bp 90-92 °C/1 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 1.12 (t, 6H, CH_3, J = 6.6 Hz), 1.98-2.06 (m, 2H, CH_2CH), 3.35-3.60 (m, 4H, CH_2O), 4.10 (t, 2H, CH_2N, J = 6.6 Hz), 4.40 (t, 1H, O-CH-O, J = 5.4 Hz), 6.20 (s, 1H, C^4H), 7.42 (s, 1H, C^3H), 7.68 (s, 1H, C^5H).

4-Bromo-1,3,5-trimethyl-1*H*-pyrazole (**12a**).

This compound was obtained in 70% yield as a solid; mp 30-32 °C (the analytical data of **12a** are identical to those reported in [12]).

1-(2-Methoxyethyl)-1*H*-pyrazole (**25**).

This compound was obtained in 68% yield as an oil; n^D_{20} 1.4782; bp 102-104 °C/20 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 3.20 (s, 3H, CH_3O), 3.66 (t, 2H, CH_2O, J = 5.6 Hz), 4.25 (t, 2H, CH_2N, J = 5.4 Hz), 6.20 (s, 1H, C^4H), 7.40 (s, 1H, C^3H), 7.67 (s, 1H, C^5H).

General Procedure for the Alkylation of Pyrazole with Hydrochlorides of 2-Dimethylaminoethylchloride and 3-Dimethylaminopropylchloride.

2-Dimethylaminoalkylchloride hydrochloride (250 mmol) was slowly added to a solution of pyrazole **1** (200 mmol) and KOH (28 g, 500 mmol) in absolute ethanol (200 ml) with stirring. The reaction mixture was heated at reflux for 1.5 h and then cooled to room temperature. CH_2Cl_2 (400 ml) was added, the resulting mixture was filtered and the solvent was evaporated. The crude product was distilled *in vacuo* (1 mm Hg) to give 1-alkylpyrazole **2f** or **2h** as an oil.

3-(4-Bromo-1*H*-pyrazol-1-yl)-*N*,*N*-dimethylpropan-1-amine (**2f**).

This compound was obtained in 70% yield as an oil; n^D_{20} 1.5087; bp 107-108 °C/20 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 1.80-1.88 (m, 2H, $NCH_2CH_2CH_2N$), 2.15 (s, 6H, CH_3N), 2.20 (t, 2H, $CH_2N(CH_3)_2$, J = 7.0 Hz), 4.08 (t, 2H, $CH_2N_{pyrazole}$, J = 7.0 Hz), 7.50 (s, 1H, C^3H), 7.95 (s, 1H, C^5H).

2-(4-Bromo-1*H*-pyrazol-1-yl)-*N*,*N*-dimethylethanamine (**2h**).

This compound was obtained in 61% yield as an oil; n^D_{20} 1.5197; bp 94-96 °C/20 mm Hg; ^1H NMR (DMSO-d_6, ppm): δ 2.15 (s, 6H, CH_3N), 2.62 (t, 2H, $CH_2N(CH_3)_2$, J = 5.6 Hz), 4.17 (t, 2H, $CH_2N_{pyrazole}$, J = 5.6 Hz), 7.50 (s, 1H, C^3H), 7.95 (s, 1H, C^5H).

General Procedure for the Synthesis of Pyrazol-4-ylboronic Acids **4a-g** and **14a**.

A solution of 100 mmol of 4-bromopyrazole (**2a-g** or **12a**) in 150 ml of dry THF was cooled to -90 °C. The 4-bromopyrazole (**2a-g** or **12a**) was lithiated by slowly adding 62.5 ml of a 1.6 *M* solution of *n*-butyllithium in hexane. During the addition, the temperature of the reaction mixture was kept below -80 °C. After the addition was complete, the solution was stirred at -90 °C for 1 h. A solution of 15 ml (132 mmol) of trimethylborate was added, and the reaction mixture was stirred at -70 °C for 0.5 h. After the reaction mixture was allowed to warm to -15 °C, it was neutralized with 150 ml of 15% aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature and was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with 100 ml of THF. The combined organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was washed with ether (2 × 50 ml) and dried *in vacuo* to give acids **4a-g** and **14a** as white solids.

1-Methyl-1*H*-pyrazol-4-ylboronic Acid (**4a**).

This compound was obtained in 38% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 3.80 (s, 3H, CH_3N), 7.60 (s, 1H, C^3H), 7.75 (s, 1H, C^5H), 7.8 (br s, 2H, $B(OH)_2$).

1-Ethyl-1*H*-pyrazol-4-ylboronic Acid (**4b**).

This compound was obtained in 44% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 1.32 (t, 3H, CH_3, J = 7.3 Hz), 4.10 (q, 2H, CH_2N, J = 7.3 Hz), 7.55 (br s, 2H, $B(OH)_2$), 7.65 (s, 1H, C^3H), 7.80 (s, 1H, C^5H).

1-Propyl-1*H*-pyrazol-4-ylboronic Acid (**4c**).

This compound was obtained in 51% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 0.77 (t, 3H, CH_3CH_2, J = 7.2 Hz), 1.70-1.84 (m, 2H, CH_2CH_3), 4.10 (t, 2H, CH_2N, J = 6.0 Hz), 7.5 (br s, 2H, $B(OH)_2$), 7.62 (s, 1H, C^3H), 7.77 (s, 1H, C^5H).

1-(3-Methylbutyl)-1*H*-pyrazol-4-ylboronic Acid (**4d**).

This compound was obtained in 41% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 0.80 (d, 6H, CH_3, J = 7.2 Hz), 1.42-1.50

(m, 1H, $(CH_3)_2CH$), 1.60-1.70 (m, 2H, CH_2CH_2N), 4.09 (t, 2H, CH_2N, J = 6.4 Hz), 7.6 (br s, 3H, $B(OH)_2$, C^3H), 7.81 (s, 1H, C^5H).

1-(2-Methoxyethyl)-1*H*-pyrazol-4-ylboronic Acid (**4e**).

This compound was obtained in 50% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 3.17 (s, 3H, CH_3O), 3.67 (t, 2H, CH_2O, J = 5.8 Hz), 4.20 (t, 2H, CH_2N, J = 5.8 Hz), 7.5 (br s, 2H, $B(OH)_2$), 7.62 (s, 1H, C^3H), 7.81 (s, 1H, C^5H).

1-[3-(Dimethylamino)propyl]-1*H*-pyrazol-4-ylboronic Acid (**4f**).

This compound was obtained in 38% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 1.80-1.95 (m, 2H, $NCH_2CH_2CH_2N$), 2.16 (s, 6H, CH_3N), 2.25 (t, 2H, $CH_2N(CH_3)_2$, J = 7.0 Hz), 4.07 (t, 2H, $CH_2N_{pyrazole}$, J = 7.0 Hz), 7.5 (br s, 2H, $B(OH)_2$), 7.62 (s, 1H, C^3H), 7.77 (s, 1H, C^5H).

1-(3,3-Diethoxypropyl)-1*H*-pyrazol-4-ylboronic Acid (**4g**).

This compound was obtained in 39% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 1.10 (t, 6H, CH_3, J = 6.1 Hz), 1.95-2.04 (m, 2H, CH_2CH), 3.45-3.65 (m, 4H, CH_2O), 4.10 (t, 2H, CH_2N, J = 6.8 Hz), 4.38 (t, 1H, O-CH-O, J = 5.8 Hz), 7.55 (br s, 2H, $B(OH)_2$), 7.62 (s, 1H, C^3H), 7.78 (s, 1H, C^5H).

1,3,5-Trimethyl-1*H*-pyrazol-4-ylboronic Acid (**14a**).

This compound was obtained in 25% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 2.12 (s, 3H, CH_3-C^3), 2.24 (s, 3H, CH_3-C^5), 3.54 (s, 3H, CH_3N), 7.7 (br s, 2H, $B(OH)_2$).

4-Bromo-1-[2-(dimethylamino)ethyl]-1*H*-pyrazol-5-ylboronic Acid (**8**).

A solution of 23.0 g (105 mmol) of 4-bromopyrazole (**2h**) in 250 ml of dry THF was cooled to -70 °C. The 4-bromopyrazole (**2h**) was lithiated by slowly adding 65.6 ml of a 1.6 *M* solution of *n*-butyllithium in hexane. After the addition was complete, the solution was stirred at -70 °C for 2 h. A solution of 16 ml (141 mmol) of trimethylborate was added, and the reaction mixture was stirred at -70 °C for 0.5 h. After the reaction mixture was allowed to warm to -15 °C, it was neutralized with 160 ml of 15% aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature and was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with 150 ml of THF. The combined organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was washed with ether (2 × 50 ml) and dried *in vacuo* to give 10.4 g (38%) of acid **8** as a white solid; purity 90% (based on ^1H NMR data). ^1H NMR (DMSO-d_6, ppm): δ 2.35 (s, 6H, CH_3N), 3.30 (t, 2H, $CH_2N(CH_3)_2$, J = 5.5 Hz), 4.15 (t, 2H, $CH_2N_{pyrazole}$, J = 5.5 Hz), 7.5 (br s, 2H, $B(OH)_2$), 7.45 (s, 1H, C^3H). MS, *m/z*: 172, 174 {[M-(C_4H_9N+H_2O)]$^+$, 1Br}.

General Procedure for the Synthesis of Pyrazol-5-ylboronic Acids (**17a-e**).

A solution of 100 mmol of 1-alkylpyrazole (**9a-e**) in 200 ml of dry THF was cooled to 5 °C with stirring. The 1-alkylpyrazole (**9a-e**) was lithiated by slowly adding 62.5 ml of a 1.6 *M* solution of *n*-butyllithium in hexane. After the addition was complete, the cooling bath was removed and the reaction mixture was stirred at 20 °C for 1 h. The reaction mixture was cooled to –70 °C, and a solution of 15 ml (132 mmol) of trimethylborate was added. The reaction mixture was stirred at -70 °C for 0.5 h. After the reaction mixture was allowed to warm to -15 °C, it was neutralized with 150 ml of 15% aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature and was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with 100 ml of THF. The combined organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was washed with ether (2 × 50 ml) and dried *in vacuo* to give acids (**17a-e**) as white solids.

1-Methyl-1*H*-pyrazol-5-ylboronic Acid (**17a**).

This compound was obtained in 38% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 3.90 (s, 3H, CH_3N), 6.62 (s, 1H, C^4H), 7.4 (br s, 2H, $B(OH)_2$), 7.75 (s, 1H, C^3H).

1-Isobutyl-1*H*-pyrazol-5-ylboronic Acid (**17b**).

This compound was obtained in 54% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 0.77 (d, 6H, CH_3, 5.8 Hz), 2.00-2.10 (m, 1H, $CH(CH_3)_2$), 4.12 (d, 2H, CH_2N, J = 6.4 Hz), 6.65 (s, 1H, C^4H), 7.35 (s, 1H, C^3H), 8.2 (br s, 2H, $B(OH)_2$).

1-Propyl-1*H*-pyrazol-5-ylboronic Acid (**17c**).

This compound was obtained in 52% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 0.77 (t, 3H, CH_3CH_2, J = 7.3 Hz), 1.70-1.82 (m, 2H, CH_2CH_3), 4.25 (t, 2H, CH_2N, J = 6.4 Hz), 6.63 (s, 1H, C^4H), 7.37 (s, 1H, C^3H), 7.5 (br s., 2H, $B(OH)_2$).

1-(3-Methylbutyl)-1*H*-pyrazol-5-ylboronic Acid (**17d**).

This compound was obtained in 63% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 0.83 (d, 6H, CH_3, J = 7.0 Hz), 1.38-1.46 (m, 1H, $(CH_3)_2CH$), 1.50-1.64 (m, 2H, CH_2CH_2N), 4.35 (t, 2H, CH_2N, J = 7.4 Hz), 6.65 (s, 1H, C^4H), 7.35 (s, 1H, C^3H), 7.6 (br s, 2H, $B(OH)_2$).

1-(3,3-Diethoxypropyl)-1*H*-pyrazol-5-ylboronic acid (**17e**).

This compound was obtained in 40% yield as a white solid; ^1H NMR (DMSO-d_6, ppm): δ 1.10 (t, 6H, CH_3, J = 6.7 Hz), 1.90-2.00 (m, 2H, CH_2CH), 3.25-3.55 (m, 4H, CH_2O), 4.30–4.50 (m, 3H, CH_2N, OCH_2O), 6.60 (s, 1H, C^4H), 7.48 (s, 1H, C^3H), 7.55 (br s, 2H, $B(OH)_2$).

1-Vinyl-1*H*-pyrazole (**29**).

To a stirred and cooled (5 °C) solution of 1-(2-methoxyethyl)-1*H*-pyrazole (**25**) (16.3 g, 129 mmol) in 200 ml of dry THF, a solution (80.6 ml) of *n*-butyllithium (1.6 *M*) was added dropwise. After the addition was complete, the cooling bath was removed and the reaction mixture was stirred at 20 °C for 1 h. The reaction mixture was cooled to –70 °C, and a solution of 17 ml (150 mmol) of trimethylborate was added. The reaction mixture was stirred at -70 °C for 0.5 h. After the reaction mixture was allowed to warm to -15 °C, it was neutralized with 180 ml of 15% aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature and was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with 100 ml of THF. The combined organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure (50 mm Hg). The crude product was distilled *in vacuo* to give 4.7 g (39%) of pure **29** as an oil, n^D_{20} 1.5160; bp 67-69 °C/25 mm Hg, the analytical data of **29** are identical to those reported in [13].

1,3-Dimethyl-1*H*-pyrazol-5-ylboronic Acid (**23a**) and 3-Methyl-1-propyl-1*H*-pyrazol-5-ylboronic Acid (**23b**).

To a stirred solution of a mixture of pyrazoles (**20a** and **21a**) (based on ^1H NMR spectral data, the content of **20a** is equal to 57%, or 70.2 mmol) in 500 ml of dry THF, a solution (43.8 ml) of

n-butyllithium (1.6 *M*) was added dropwise at 20 °C. After the addition was complete, the reaction mixture was stirred at 20 °C for 1 h. The reaction mixture was cooled to –70 °C, and a solution of 10 ml (88 mmol) of trimethylborate was added. The reaction mixture was stirred at -70 °C for 0.5 h. After the reaction mixture was allowed to warm to -15 °C, it was neutralized with 100 ml of 15% aqueous ammonium chloride solution. The mixture was allowed to warm to room temperature and was stirred for 1 h. The organic layer was separated, and the aqueous layer was extracted with 150 ml of THF. The combined organic layer was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was washed with ether (2 × 50 ml) and dried *in vacuo* to give 3.9 g (40%) of acid (**23a**) as a white solid; ^{1}H NMR (DMSO-d_6, ppm): δ 2.10 (s, 3H, CH_3-C^3), 3.85 (s, 3H, CH_3N), 6.42 (s, 1H, C^{4}H), 7.5 (br s, 2H, $B(OH)_2$).

Analogously, from 22.2 g of a mixture of isomers **20b** and **21b** (based on ^{1}H NMR spectral data, the content of **20b** is equal to 68%, or 121.7 mmol), 17.4 g (58%) of acid **23b** were obtained; ^{1}H NMR (DMSO-d_6, ppm): δ 0.72 (t, 3H, CH_3CH_2, J = 7.0 Hz), 1.60-1.70 (m, 2H, CH_2CH_3), 2.10 (s, 3H, CH_3-C^3), 4.15 (t, 2H, CH_2N, J = 6.8 Hz), 6.40 (s, 1H, C^{4}H), 7.5 (br s, 2H, $B(OH)_2$).

General Procedure for the Synthesis of Pinacol Esters of Pyrazolylboronic Acids (**10a-g, 15, 18a-e** and **24a,b**).

A mixture of pyrazolylboronic acid (50 mmol), pinacone (5.9 g, 50 mmol) and molecular sieves 4 Å (1.0 g) in 100 of THF was stirred at room temperature for 2 h. The reaction mixture was filtered and the solvent was evaporated under reduced pressure. The crude residue was dissolved in 100 ml of hexane. The solution was washed with 80 ml of water, dried over Na_2SO_4, filtered and the solvent was evaporated *in vacuo* to give pure esters **10a-g, 15, 18a-e** and **24a,b** as oils or low-melting point solids. In several cases, the compounds were additionally purified by distillation *in vacuo* (0.01 mm Hg).

1-Methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10a**).

This compound was obtained in 80% yield as a solid; mp 67-69 °C; ^{11}B NMR ($CDCl_3$, ppm): δ+29.3; ^{1}H NMR (DMSO-d_6, ppm): δ 1.25 (s, 12H, $(CH_3)_2$C-O), 3.82 (s, 3H, CH_3N), 7.55 (s, 1H, C^{3}H), 7.80 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 24.6 ($(CH_3)_2$C-O), 38.1 (CH_3N), 82.5 ($(CH_3)_2C$-O), 137.0 (C^3), 143.9 (C^5); MS, *m/z*: 208 ([M]$^+$), 193 ([M-CH_3]$^+$), 109 ([M-$C_6H_{11}O$]$^+$). HRMS: Found, [M]$^+$, 208.13711. Calculated for $C_{10}H_{17}BN_2O_2$, 208.13830; dm (mmu) +1.2.

Anal. Calcd. for $C_{10}H_{17}BN_2O_2$: C, 57.72; H, 8.24; B, 5.20; N, 13.46. Found: (%): C, 58.02; H, 8.46; B, 5.49; N, 13.56.

1-Ethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10b**).

This compound was obtained in 78% yield as a white solid. mp 43-45 °C ; ^{11}B NMR ($CDCl_3$, ppm): δ+29.4; ^{1}H NMR (DMSO-d_6, ppm): δ 1.25 (s, 12H, $(CH_3)_2$C-O), 1.36 (t, 3H, CH_3CH_2, J = 7.3 Hz), 4.12 (q, 2H, CH_2N, J = 7.3 Hz), 7.55 (s, 1H, C^{3}H), 7.90 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 15.4 (CH_3CH_2), 24.6 ($(CH_3)_2$C-O), 45.8 (CH_2N), 82.5 ($(CH_3)_2C$-O), 135.4 (C^3), 143.7 (C^5); MS, *m/z*: 222 ([M]$^+$), 207 ([M-CH_3]$^+$), 123 ([M-$C_6H_{11}O$]$^+$). HRMS: Found, [M]$^+$, 222.15258. Calculated for $C_{11}H_{19}BN_2O_2$, 222.15395; dm (mmu) +1.4.

Anal. Calcd. for $C_{11}H_{19}BN_2O_2$: C, 59.48; H, 8.62; B, 4.87; N, 12.61. Found: C, 59.65; H, 8.72; B, 4.97; N, 12.55.

1-Propyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10c**).

This compound was obtained in 85% yield as an oil; n^D_{20} 1.4790; bp 100-102 °C/0.04 mm Hg; ^{11}B NMR ($CDCl_3$, ppm): δ+29.4; ^{11}B NMR ($CDCl_3$, ppm): δ+27.7; ^{1}H NMR (DMSO-d_6, ppm): δ 0.80 (t, 3H, CH_3CH_2, J = 7.4 Hz), 1.25 (s, 12H, $(CH_3)_2$C-O), 1.72-1.80 (m, 2H, CH_2CH_3), 4.05 (t, 2H, CH_2N, J = 6.2 Hz), 7.55 (s, 1H, C^{3}H), 7.77 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 10.9 (CH_3CH_2), 23.1 (CH_2CH_3), 24.6 ($(CH_3)_2$C-O), 52.4 (CH_2N), 82.5 ($(CH_3)_2C$-O), 136.1 (C^3), 143.8 (C^5); MS, *m/z*: 236 ([M]$^+$), 221 ([M-CH_3]$^+$), 208 ([M-C_2H_4]$^+$), 137 ([M-$C_6H_{11}O$]$^+$). HRMS: Found, [M]$^+$, 236.16882. Calculated for $C_{12}H_{21}BN_2O_2$, 236.16960; dm (mmu) +0.8.

Anal. Calcd. for $C_{12}H_{21}BN_2O_2$: C, 61.04; H, 8.96; B, 4.58; N, 11.86. Found: C, 60.99; H, 9.18; B, 4.33; N, 11.63.

1-(3-Methylbutyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10d**).

This compound was obtained in 88% yield as an oil; n^D_{20} 1.4766; ^{11}B NMR ($CDCl_3$, ppm): δ+29.4. ^{1}H NMR (DMSO-d_6, ppm): δ 0.82 (d, 6H, CH_3, J = 7.2 Hz), 1.25 (s, 12H, $(CH_3)_2$C-O), 1.42 (m, 1H, $(CH_3)_2CH$), 1.60-1.72 (m, 2H, CH_2CH_2N), 4.10 (t, 2H, CH_2N, J = 6.2 Hz), 7.55 (s, 1H, C^{3}H), 7.85 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 22.1 ($(CH_3)_2CH$), 24.5 ($(CH_3)_2$C-O), 24.8 ($(CH_3)_2CH$), 38.6 (CH_2CH_2N), 49.1 (CH_2N), 82.5 ($(CH_3)_2C$-O), 136.0 (C^3), 143.8 (C^5); MS, *m/z*: 264 ([M]$^+$), 249 ([M-CH_3]$^+$), 207 ([M-C_4H_9]$^+$), 165 ([M-$C_6H_{11}O$]$^+$). HRMS: Found, [M]$^+$, 264.19932. Calculated for $C_{14}H_{25}BN_2O_2$, 264.20090; dm (mmu) +1.6.

Anal. Calcd. for $C_{14}H_{25}BN_2O_2$: C, 63.65; H, 9.54; B, 4.09; N, 10.60. Found: C, 63.67; H, 9.85; B, 4.04; N, 10.80.

1-(2-Methoxyethyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10e**).

This compound was obtained in 72% yield as an oil; n^D_{20} 1.4827; ^{11}B NMR ($CDCl_3$, ppm): δ+29.5; ^{1}H NMR (DMSO-d_6, ppm): δ 1.25 (s, 12H, $(CH_3)_2$C-O), 3.20 (s, 3H, CH_3O), 3.68 (t, 2H, CH_2O, J = 5.8 Hz), 4.25 (t, 2H, CH_2N, J = 5.8 Hz), 7.57 (s, 1H, C^{3}H), 7.85 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 24.6 ($(CH_3)_2$C-O), 50.6 (CH_2N), 57.7 (CH_3O), 70.1 (CH_2O), 82.5 ($(CH_3)_2C$-O), 136.7 (C^3), 143.9 (C^5); MS, *m/z*: 252 ([M]$^+$), 237 ([M-CH_3]$^+$), 207 ([M-C_2H_5O]$^+$), 179 ([M-C_4H_9O]$^+$), 153 ([M-$C_6H_{11}O$]$^+$). HRMS: Found, [M]$^+$, 252.16582. Calculated for $C_{12}H_{21}BN_2O_3$, 252.16451; dm (mmu) –1.3.

Anal. Calcd. for $C_{12}H_{21}BN_2O_3$: C, 57.16; H, 8.39; B, 4.29; N, 11.11. Found: C, 57.28; H, 8.52; B, 3.91; N, 11.38.

N,*N*-Dimethyl-3-[4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazol-1-yl]propan-1-amine (**10f**).

This compound was obtained in 70% yield as an oil; n^D_{20} 1.4828; bp 76-78 °C/0.01 mm Hg (decomposition at temperature higher than 80-85 °C); ^{11}B NMR ($CDCl_3$, ppm): δ+29.5; ^{1}H NMR (DMSO-d_6, ppm): δ 1.25 (s, 12H, $(CH_3)_2$C-O), 1.80-1.94 (m, 2H, $NCH_2CH_2CH_2N$), 2.10 (s, 6H, CH_3N), 2.17 (t, 2H, $CH_2N(CH_3)_2$, J = 7.0 Hz), 4.10 (t, 2H, $CH_2N_{pyrazole}$, J = 7.0 Hz), 7.56 (s, 1H, C^{3}H), 7.87 (s, 1H, C^{5}H); ^{13}C NMR (DMSO-d_6, ppm): δ 24.6 ($(CH_3)_2$C-O), 27.8 ($NCH_2CH_2CH_2N$), 44.9 (CH_3N), 49.05 ($CH_2N_{pyrazole}$), 55.8 ($CH_2N(CH_3)_2$), 70.1 (CH_2O), 82.5 ($(CH_3)_2C$-O), 136.1 (C^3), 143.9 (C^5); MS, *m/z*: 279 ([M]$^+$), 264 ([M-CH_3]$^+$), 235 ([M-C_2H_6N]$^+$), 221 ([M-C_3H_8N]$^+$), 207 ([M-$C_4H_{10}N$]$^+$). HRMS: Found, [M]$^+$,

279.21243. Calculated for $C_{14}H_{26}BN_3O_2$, 279.21179; dm (mmu) –0.6.

Anal. Calcd. for $C_{14}H_{26}BN_3O_2$: C, 60.22; H, 9.39; B, 3.87; N, 15.05. Found: C, 60.28; H, 9.57; B, 3.51; N, 15.43.

1-(3,3-Diethoxypropyl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**10g**).

This compound was obtained in 70% yield as an oil; n^D_{20} 1.4695; ^{11}B NMR ($CDCl_3$, ppm): δ+29.5; ^{1}H NMR (DMSO-d_6, ppm): δ 1.07 (t, 6H, CH_3, J = 6.2 Hz), 1.18 (s, 12H, $(CH_3)_2$C-O), 2.08 (m, 2H, CH_2CH), 3.42-3.66 (m, 4H, CH_2O), 4.10 (t, 2H, CH_2N, J = 6.8 Hz), 4.22 (t, 1H,O-CH-O, J = 5.8 Hz), 7.63 (s, 1H, C^3H), 7.77 (s, 1H, C^5H); ^{13}C NMR (DMSO-d_6, ppm): δ 15.2 (CH_3CH_2), 24.6 ($(CH_3)_2$C-O), 34.0 (CH_2CH), 47.0 (CH_2N), 60.7 (CH_2O), 82.5 ($(CH_3)_2C$-O), 99.7 (O-CH-O), 136.3 (C^3), 140.0 (C^5); MS, *m/z*: 324 ($[M]^+$), 309 ($[M-CH_3]^+$), 295 ($[M-C_2H_5]^+$), 279 ($[M-C_2H_5O]^+$), 251 ($[M-C_4H_9O]^+$), 207 ($[M-C_5H_{11}O_2]^+$). HRMS: Found, $[M-C_2H_5]^+$, 295.18372. Calculated for $C_{14}H_{24}BN_2O_4$, 295.18290; dm (mmu) –0.8.

Anal. Calcd. for $C_{16}H_{29}BN_2O_4$: C, 59.27; H, 9.02; B, 3.34; N, 8.64. Found: C, 59.31; H, 9.14; B, 3.51; N, 8.68.

1,3,5-Trimethyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**15**).

This compound was obtained in 65% yield as a solid; mp 98-100 °C; ^{11}B NMR ($CDCl_3$, ppm): δ+29.7; ^{1}H NMR (DMSO-d_6, ppm): δ 1.25 (s, 12H, $(CH_3)_2$C-O), 2.15 (s, 3H, CH_3-C^3), 2.28 (s, 3H, CH_3-C^5), 3.60 (s, 3H, CH_3N); ^{13}C NMR (DMSO-d_6, ppm): δ 10.8 (CH_3-C^3), 13.7 (CH_3-C^5), 24.6 ($(CH_3)_2$C-O), 35.1 (CH_3N), 82.0 ($(CH_3)_2C$-O), 146.6 (C^3), 152.2 (C^5); MS, *m/z*: 236 ($[M]^+$), 221 ($[M-CH_3]^+$), 108 ($[M-C_6H_{12}O]^+$). HRMS: Found, $[M]^+$, 236.17063. Calculated for $C_{12}H_{21}BN_2O_2$, 236.16960; dm (mmu) –1.0.

Anal. Calcd. for $C_{12}H_{21}BN_2O_2$: C, 61.04; H, 8.96; B, 4.58; N, 11.86. Found: C, 61.18; H, 9.27; B, 4.66; N, 11.84.

1-Methyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**18a**).

This compound was obtained in 84% yield as a solid; mp 74-75 °C; ^{11}B NMR ($CDCl_3$, ppm): δ+27.7; ^{1}H NMR (DMSO-d_6, ppm): δ 1.30 (s, 12H, $(CH_3)_2$C-O), 3.93 (s, 3H, CH_3N), 6.60 (s, 1H, C^4H), 7.42 (s, 1H, C^3H); ^{13}C NMR (DMSO-d_6, ppm): δ 24.5 ($(CH_3)_2$C-O), 39.0 (CH_3N), 84.0 ($(CH_3)_2C$-O), 115.4 (C^4), 137.8 (C^3); MS, *m/z*: 208 ($[M]^+$), 193 ($[M-CH_3]^+$), 109 ($[M-C_6H_{11}O]^+$). HRMS: Found, $[M]^+$, 208.13957. Calculated for $C_{10}H_{17}BN_2O_2$, 208.13830; dm (mmu) –1.3.

Anal. Calcd. for $C_{10}H_{17}BN_2O_2$: C, 57.72; H, 8.24; B, 5.20; N, 13.46. Found: C, 58.00; H, 8.38; B, 5.26; N, 13.40.

1-Isobutyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**18b**).

This compound was obtained in 88% yield as a solid; mp 40-42 °C; ^{11}B NMR ($CDCl_3$, ppm): δ+27.8; ^{1}H NMR (DMSO-d_6, ppm): δ 0.80 (d, 6H, $(CH_3)_2$CH, J = 5.4 Hz), 1.28 (s, 12H, $(CH_3)_2$C-O), 2.00-2.10 (m, 1H, $CH(CH_3)_2$), 4.15 (d, 2H, CH_2N, J = 6.2 Hz), 6.60 (s, 1H, C^4H), 7.45 (c, 1H, C^3H); ^{13}C NMR (DMSO-d_6, ppm): δ 19.6 ($(CH_3)_2$CH), 24.5 ($(CH_3)_2$C-O), 30.1 ($CH(CH_3)_2$), 58.1 (CH_2N), 83.9 ($(CH_3)_2C$-O), 115.2 (C^4), 137.9 (C^3); MS, *m/z*: 250 ($[M]^+$), 235 ($[M-CH_3]^+$), 203 ($[M-C_3H_7]^+$). HRMS: Found, $[M]^+$, 250.18680. Calculated for $C_{13}H_{23}BN_2O_2$, 250.18525; dm (mmu) –6.2.

Anal. Calcd. for $C_{13}H_{23}BN_2O_2$: C, 62.41; H, 9.27; B, 4.32; N, 11.19. Found: C, 62.42; H, 9.42; B, 4.41; N, 11.40.

1-Propyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**18c**).

This compound was obtained in 82% yield as an oil; n^D_{20} 1.4739; bp 78-80 °C/0.02 mm Hg; ^{11}B NMR ($CDCl_3$, ppm): δ+27.8; ^{1}H NMR (DMSO-d_6, ppm): δ 0.75 (t, 3H, CH_3CH_2, J = 7.4 Hz), 1.26 (s, 12H, $(CH_3)_2$C-O), 1.70-1.80 (m, 2H, CH_2CH_3), 4.28 (t, 2H, CH_2N, J = 6.3 Hz), 6.60 (s, 1H, C^4H), 7.40 (s, 1H, C^3H); ^{13}C NMR (DMSO-d_6, ppm): δ 10.8 (CH_3CH_2), 24.1 (CH_2CH_3), 24.5 ($(CH_3)_2$C-O), 52.6 (CH_2N), 83.8 ($(CH_3)_2C$-O), 115.2 (C^4), 137.9 (C^3); MS, *m/z*: 236 ($[M]^+$), 221 ($[M-CH_3]^+$), 208 ($[M-C_2H_4]^+$). HRMS: Found, $[M]^+$, 236.16839. Calculated for $C_{12}H_{21}BN_2O_2$, 236.16960; dm (mmu) +1.2.

Anal. Calcd. for $C_{12}H_{21}BN_2O_2$: C, 61.04; H, 8.96; B, 4.58; N, 11.86. Found: C, 61.09; H, 9.13; B, 4.54; N, 12.08.

1-(3-Methylbutyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**18d**).

This compound was obtained in 90% yield as an oil; n^D_{20} 1.4718; ^{11}B NMR ($CDCl_3$, ppm): δ+27.7; ^{1}H NMR (DMSO-d_6, ppm): δ 0.87 (d, 6H, CH_3, J = 7.2 Hz), 1.30 (s, 12H, $(CH_3)_2$C-O), 1.40-1.50 (m, 1H, $(CH_3)_2CH$), 1.60-1.68 (m, 2H,CH_2CH_2N), 4.34 (t, 2H, CH_2N, J = 7.2 Hz), 6.60 (s, 1H, C^4H), 7.45 (s, 1H, C^3H); ^{13}C NMR (DMSO-d_6, ppm): δ 22.2 ($(CH_3)_2$CH), 24.5 ($(CH_3)_2$C-O), 25.1 (,$(CH_3)_2CH$), 39.8 (CH_2CH_2N), 49.6 (CH_2N), 83.7 ($(CH_3)_2C$-O), 114.9 (C^4), 137.4 (C^3); MS, *m/z*: 264 ($[M]^+$), 249 ($[M-CH_3]^+$), 207 ($[M-C_4H_9]^+$). HRMS: Found, $[M]^+$, 264.20232. Calculated for $C_{14}H_{25}BN_2O_2$, 264.20090; dm (mmu) –1.4.

Anal. Calcd. for $C_{14}H_{25}BN_2O_2$: C, 63.65; H, 9.54; B, 4.09; N, 10.60. Found: C, 63.40; H, 9.62; B, 3.73; N, 10.88.

1-(3,3-Diethoxypropyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**18e**).

This compound was obtained in 70% yield as an oil; n^D_{20} 1.4670; ^{11}B NMR ($CDCl_3$, ppm): δ+27.9; ^{1}H NMR (DMSO-d_6, ppm): δ 1.05 (t, 6H, CH_3, J = 6.2 Hz), 1.18 (s, 12H, $(CH_3)_2$C-O), 1.98-2.10 (m, 2H, CH_2CH), 3.42-3.58 (m, 4H, CH_2O), 4.18 (t, 2H, CH_2N, J =6.9 Hz), 4.22 (t, 1H, O-CH-O, J = 5.4 Hz), 6.60 (s, 1H, C^4H), 7.46 (s, 1H, C^3H); ^{13}C NMR (DMSO-d_6, ppm): δ 15.2 (CH_3CH_2), 24.5 ($(CH_3)_2$C-O), 34.8 (CH_2CH), 47.4 (CH_2N), 60.5 (CH_2O), 83.9 ($(CH_3)_2C$-O), 100.0 (O-CH-O), 115.4 (C^4), 138.0 (C^3); MS, *m/z*: 324 ($[M]^+$), 295 ($[M-C_2H_5]^+$), 279 ($[M-C_2H_5O]^+$), 251 ($[M-C_4H_9O]^+$). HRMS: Found, $[M-C_2H_5]^+$, 295.18118. Calculated for $C_{14}H_{24}BN_2O_4$, 295.18290; dm (mmu) +1.7.

Anal. Calcd. for $C_{16}H_{29}BN_2O_4$: C, 59.27; H, 9.02; B, 3.34; N, 8.64. Found: C, 59.36; H, 9.23; B, 2.99; N, 8.84.

1,3-Dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**24a**).

This compound was obtained in 80% yield as an oil; n^D_{20} 1.4782; ^{11}B NMR ($CDCl_3$, ppm): δ+27.6; ^{1}H NMR (DMSO-d_6, ppm): δ 1.27 (s, 12H, $(CH_3)_2$C-O), 2.12 (s, 3H, CH_3-C^3), 3.86 (s, 3H, CH_3N), 6.35 (s, 1H, C^4H); ^{13}C NMR (DMSO-d_6, ppm): δ 12.7 (CH_3-C^3), 24.5 ($(CH_3)_2$C-O), 38.5 (CH_3N), 83.6 ($(CH_3)_2C$-O), 114.4 (C^4), 145.7 (C^3); MS, *m/z*: 222 ($[M]^+$), 207 ($[M-CH_3]^+$), 122 ($[M-C_6H_{12}O]^+$). HRMS: Found, $[M]^+$, 222.15251. Calculated for $C_{11}H_{19}BN_2O_2$, 222.15395; dm (mmu) +1.4.

Anal. Calcd. for $C_{11}H_{19}BN_2O_2$: C, 59.48; H, 8.62; B, 4.87; N, 12.61. Found: C, 59.66; H, 8.84; B, 4.95; N, 12.58.

3-Methyl-1-propyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1*H*-pyrazole (**24b**).

This compound was obtained in 88% yield as an oil; n^D_{20} 1.4726; bp 90-92 °C/0.02 mm Hg; ^{11}B NMR ($CDCl_3$, ppm): δ+27.7. ^{1}H NMR (DMSO-d_6, ppm): δ 0.75 (t, 3H, CH_3CH_2, J = 6.8 Hz), 1.26 (s, 12H, $(CH_3)_2$C-O), 1.60-1.70 (m, 2H, CH_2CH_3), 2.15 (s, 3H, CH_3-C^3), 4.18 (t, 2H, CH_2N, J = 6.8 Hz), 6.35 (s, 1H, C^{4}H); ^{13}C NMR (DMSO-d_6, ppm): δ 10.8 (CH_3CH_2), 12.8(CH_3-C^3) 24.0 (CH_2CH_3), 24.5 ((CH_3)$_2$C-O), 52.2 (CH_2N), 83.5 ((CH_3)$_2$*C*-O), 114.2 (C^4), 145.8 (C^3); MS, *m/z*: 250 ([M]$^+$), 221 ([M-C_2H_5]$^+$), 207 ([M-C_3H_7]$^+$). HRMS: Found, [M]$^+$, 250.18584. Calculated for $C_{13}H_{23}BN_2O_2$, 250.18525; dm (mmu) –0.6.

Anal. Calcd. for $C_{13}H_{23}BN_2O_2$: C, 62.41; H, 9.27; B, 4.32; N, 11.19. Found: C, 62.38; H, 9.41; B, 3.98; N, 11.40.

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