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Aminolysis of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes: route to β-keto amides and β-enamino carboxamides

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Abstract—4-Alkoxy substituted 1,3,2-dioxaborinanes **1**, readily available from β-keto esters, undergo substitution reactions under mild reaction conditions with primary and secondary amines, deriving the 4-alkylamino analogue **2**. Reactions of **1** with substituted phenylhydrazines gave the corresponding hydrazones, or pyrazolones, and 5-alkoxy-1*H*-pyrazoles as a mixture of products.

1. Introduction

β-Keto amide and β-enamino carboxamide classes of compounds represent versatile and useful building blocks for the synthesis of natural products[1] and targets for pharmaceuticals.[2] Additionally, in the recent literature there are numerous examples of where β-keto amides and β-enamino carboxamides have been used for the synthesis of heterocyclic compounds, such as highly substituted furans,[3] pyrazolones,[4] pyrazoles,[5] *N*-hydroxyindoles,[6] diazepines,[7] 3-isoxazolols,[8] β-lactams,[9] 4-hydroxycoumarins[10] and indanones.[11] The enantioselective hydrogenation[12] of β-enamino carboxamides provides access to β-amino acids and their derivatives, which are the components of a variety of interesting natural products and targets for pharmaceutical research.[13] Other uses of β-keto amides and β-enamino carboxamides, as starting materials, include, for example, enantioselective halogenations,[14] the multicomponent domino reaction,[15] diastereoselective addition reactions,[16] the carbenoid-mediated chain extension,[17] spirolactamisation,[18] the synthesis of 2,3-diketo amides[19] and stereocontrolled cyclisation reactions.[20] Several methods have been reported for the synthesis of β-keto amides. The available methods can be classified according to the bond formed. The most general methods are based on the nucleophilic amidations of electrophiles such as β-keto acids (often prepared from protected β-keto esters),[21] β-keto esters,[22] β-keto thioesters,[23] ketene dimers,[24] dioxinones,[25] acylated Meldrum's acids or 2,2-dimethyl-2*H*,4*H*-1,3-dioxin-4-ones.[8] Other approaches include the condensation of ketone enolates with isocyanates[26] or activated carbamates,[27] the condensation of amide enolates with esters[28] or acyl chlorides,[29] the fragmentation of isoxazolium salts[30] and the enzymatic hydrolysis of β-keto nitriles.[31] Each of the above methods for the synthesis of β-keto amides has its own advantages and disadvantages, concerning the reaction conditions, the yields of the reactions or the availability of the starting material. A few years ago, we described a new synthetic route to pyrimidine *N*-oxides, starting from 1,3-diketones and carboxamide oximes.[32] We found that the reactions catalysed with $BF_3 \cdot Et_2O$ gave pyrimidine *N*-oxides in low yields. Later, we discovered that the low yields were due to the formation of 1,3-diketonatoboron difluorides, which were first described by Morgan and Tunstall,[33] and are known as interesting intermediates in organic synthesis.[34] As part of our research program, which is oriented at investigating the synthetic potential of 1,3-diketonatoboron difluorides and 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes, we have found that they can be successfully used for the synthesis of enaminones, pyrazoles, β-keto amides, β-enamino carboxamides and pyrazolones.[35] Additionally, Christoffers et al. reported on a regioselective enamine formation via β-diketonatoboron difluorides and their application in the asymmetric Michael reaction.[18a] Here, we report on our further research relating to the above-mentioned topic.

2. Results and discussion

The starting materials, 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes **1a–e**, are readily available from the corresponding β-keto esters.[17,35b,36] The treatment of β-keto esters in dry dichloromethane or toluene solutions with 2 equiv of $BF_3 \cdot Et_2O$ for 24 h is the most successful method in our hands (Chart 1). In the first stage, we examined the reactivity of **1a** in the presence of primary or secondary alkylamines. They undergo successful aminolysis in acetonitrile, forming

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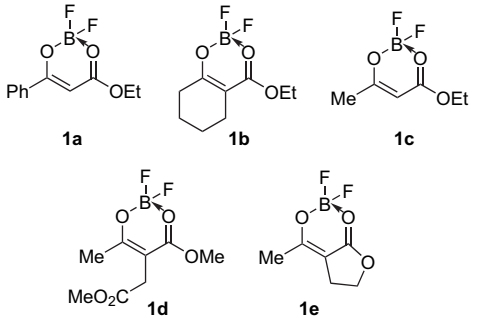
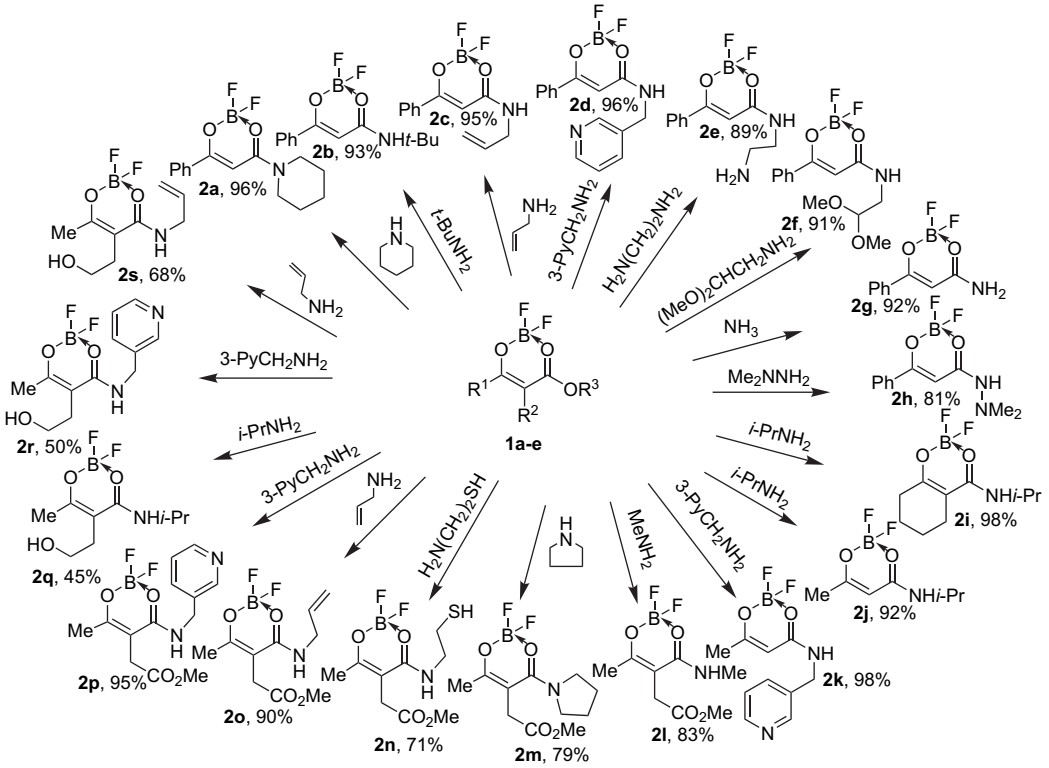


Chart 1. Preparation of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes **1**; $BF_3 \cdot Et_2O$ (2 equiv), CH_2Cl_2 or toluene, 25 °C.

their 4-alkylamino analogues **2**, and surprisingly the boronato moiety is retained during the conversion (Scheme 1).

The results are different from those of the well-known Lewis acid catalysed reaction of β-keto esters with amines forming β-enamino esters.[37] Initial studies on the aminolysis of **1a** indicated that when the reaction was carried out in acetonitrile and with a slight excess (1.3 equiv) of the corresponding amine at room temperature the desired 4-alkylamino analogues **2a–h** were isolated in excellent yields (81–98%). In less-polar solvents (CH_2Cl_2, Et_2O and toluene) the 1,3-keto ester by-products become more noticeable. The chemistry was applicable to a wide range of alkylamines (primary, secondary, *t*-$BuNH_2$ and allylamine), which gave the corresponding borinanes **2**. When using 1,1-dimethylhydrazine the resulting hydrazido boron complex was isolated (Scheme 1, e.g., **2h**). Similarly, the aminolysis of **1b** or **1c** led to the formation of **2**. Additionally, in the case of dimethyl 2-acetylsuccinate-derived borinane **1d** we were able to carry out the chemoselective introduction of an amido group to a multifunctional system (Scheme 1, e.g., **2l–2p**). The reaction of *i*-$PrNH_2$, 3-picolylamine and allylamine with **1e** (readily available by the treatment of 3-acetyldihydrofuran-2(3*H*)-one with $BF_3 \cdot Et_2O$) resulted in the cleavage of the lactone moiety, producing alcohol-functionalised amido complexes (Scheme 1, e.g., **2q–2s**). The method is, in general, readily applicable for the preparation of a wide range of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes **2**,[38] which Staskun has shown can be useful precursors for the selective N-alkylations, C-5 halogenations and the synthesis of quinolin-2-ones.[39]

The structure of **2** was confirmed by X-ray structural analysis and NMR spectroscopy, showing in the ^{13}C NMR spectrum, characteristic ^{19}F–^{13}C couplings in the range of 2.5–3.0 Hz for the =C–O–BF_2 bond sequence, and slightly smaller, 2.0–1.5 Hz coupling, for the –C=O→BF_2 bond sequence. Several observations regarding this preparation are worth mentioning. (1) The reactions were carried out under mild reaction conditions in the presence of a slight excess of amine, followed by the simple isolation of the products. (2) *t*-$BuNH_2$, cysteamine, 2-aminoethylamine and 2,2-dimethoxyethylamine underwent successful and chemoselective reactions, in the latter case yielding a carbonyl-protected amido derivative (Scheme 1, e.g., **2f**). (3) The problem associated with volatile or gaseous amines can be simply overcome, applying the described procedure, by passing ammonia or methylamine through the stirred acetonitrile solution of **1** (Scheme 1, e.g., **2g** and **2l**). The boronato difluoride moiety activates the ester carbonyl group towards the attack of an amine and the substitution products, amido complexes, are obtained. This reactivity can be explained by the fact that only the enol–borate structure is found in the solid form.



Scheme 1. Preparation of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes **2**; alkylamine (1.3 equiv) MeCN, 25 °C, 0.5–4 h.

Ponde et al. reported on transesterifications and transthioesterifications of β-keto esters using clay and proposed the β-keto enolate transition-state model.[40] On the other hand, reacting **1** with aliphatic or aromatic alcohols or H_2O (1–3 equiv) at room temperature in MeCN did not produce the expected transesterification products or the corresponding carboxylic acids. In contrast, only β-keto esters were isolated as the sole products. The same results were obtained by the treatment of **1** with 1–3 equiv of NH_2OH.

Compounds **2** can be thought of as protected β-keto amides, which can be obtained after a suitable deprotection. Indeed, the treatment of **2** with sodium acetate (5 equiv) in boiling 1:1 ethanol/water (v/v) afforded useful building blocks,[41] β-keto amides **3**, in acceptable yields (Scheme 2). After a careful crystallisation (CH_2Cl_2/light petroleum) of the crude mixture of tautomers **3g** and **3g′** we were able to isolate both tautomers, *N*-benzyl-2-oxo-1-cyclohexanecarboxamide (**3g**) and its enol form **3g′**, as pure compounds. In contrast, only a trace of enol tautomer was detected (according to ^{1}H NMR spectra) in the crude product **3f** (Scheme 2). In general, β-carbonyl compounds, such as β-keto amides, exist in solutions as both enol and keto tautomers. In the case of **3g** and **3g′**, we observed equilibrium in the DMSO-d_6 solutions after a few days at room temperature, while they remained unchanged in chloroform. The structure of **3g′** was also confirmed using X-ray analysis (Fig. 1).

A concise (one-step) approach was then designed to access the β-amino carboxamides. The reaction was performed in *n*-propanol using excess (5 equiv) of the corresponding amine. The results obtained from the reaction of three alkylamines and phenylhydrazine with **2** in *n*-propanol solutions at 130 °C in a sealed reaction vessel are summarised in Scheme 2. The reactions were completed in 12 h and the products **4a–4d** were isolated in good-to-moderate yields. The substrate **2o** reacts (under the same reaction conditions), for example, with benzylamine and propargylamine, providing the 3-(alkylaminoethylidene) pyrrolidine-2,5-dione derivatives **4b** and **4c** after condensation and subsequent cyclisation (Scheme 2).

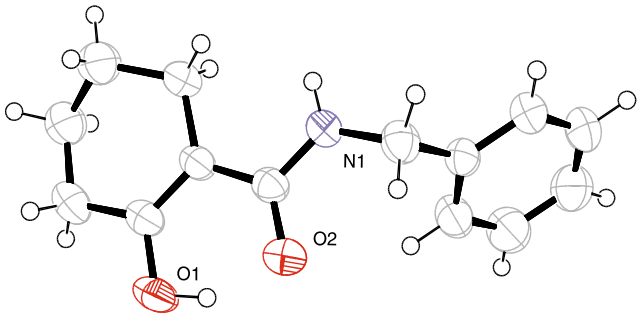
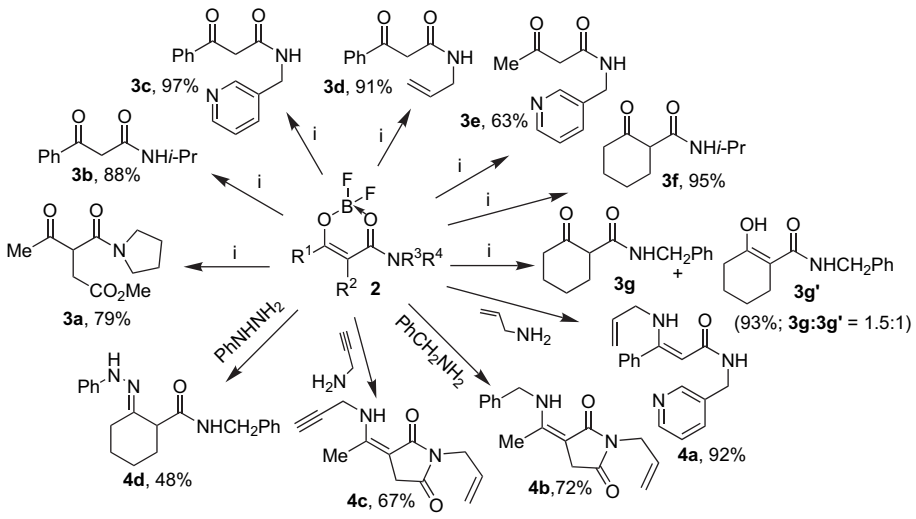


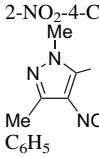
Figure 1. ORTEP diagram with the heteroatom numbering of **3g′**.

Our attention was then directed towards the arylhydrazino compounds as nitrogen nucleophiles. As mentioned above, reacting alkylhydrazines with **1a** resulted in the formation of the hydrazido boron complex (Scheme 1, e.g., **2h**). When using arylhydrazines such as 2,4-dinitrophenyl, 2-nitro-4-cyanophenyl and heteroaryl hydrazines, the corresponding β-hydrazono esters **5** were isolated (Table 1, entries 1–3, 9 and 11). When **1a** was treated with arylhydrazine hydrochlorides only traces of the products were detected in the ^{1}H NMR spectra of a crude reaction mixture after a prolonged reaction time. Since some of the arylhydrazines (i.e., 4-bromophenylhydrazine, 4-fluorophenylhydrazine) are commercially available as hydrochloride salts, the corresponding free hydrazines were obtained by neutralisation with Na_2CO_3 and subsequent extraction. However, a different reactivity was observed for the arylhydrazines. As mentioned, the reaction of arylhydrazines bearing an electron-withdrawing group (CN, NO_2) led exclusively to the formation of β-hydrazono esters **5**, whereas reactions with more nucleophilic phenylhydrazines resulted in the formation of a mixture of pyrazolones **6** and 5-alkoxy-1*H*-pyrazoles **7** (Scheme 3, Table 1). To test the solvent's effect on the product distribution and to establish possible synthetic applicability for the formation of 5-alkoxypyrazoles **7** (which can be accessed via the O-alkylation of 5-hydroxy derivatives in DMSO under basic conditions, albeit only in moderate yields),[42] we performed the reaction in several solvents and at different temperatures. The best results were



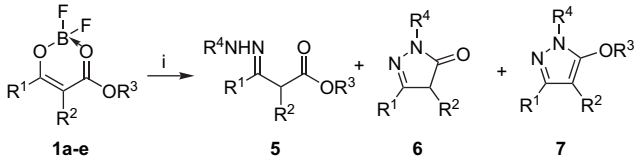
Scheme 2. Transformations of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinanes **2**; (i) AcONa (5 equiv), 1:1 EtOH/H_2O (v/v), reflux, 2–16 h.

Table 1. Reaction of **1** with hydrazines: products **5–7** produced via Scheme 3

Entry	R^1	R^2	R^4	**5** (Yield,[a] %)	**6** (Yield,[a] %)	**7** (yield,[a] %)
1	Ph	H	2,4-$NO_2C_6H_3$	**5a**[43] (96)	—	—
2	Ph	H	2-NO_2-4-CNC_6H_3	**5b** (93)	—	—
3	Ph	H		**5c** (95)	—	—
4	Ph	H	C_6H_5	—	**6a**[44] (44)	**7a**[45] (26)
5	Ph	H	4-FC_6H_4	—	**6b** (39)	**7b** (34)
6	Ph	H	2,5-FC_6H_3	—	**6c** (60)	**7c** (37)
7	Ph	H	4-BrC_6H_4	—	**6d** (53)	**7d** (27)
8	Ph	H	3-$CF_3C_6H_4$	—	**6e** (42)	**7e** (23)
9	Me	H	2-NO_2-4-CNC_6H_3	**5d** (89)	—	—
10	Me	H	4-BrC_6H_4	—	**6f** (49)	**7f** (16)
11	Me	MeO_2CCH_2	2-NO_2-4-CNC_6H_3	**5e** (87)	—	—

[a] Yields of isolated products are given.

obtained in acetonitrile, yielding 5-alkoxy-1*H*-pyrazoles **7** in the range of 16–37% (Table 1).

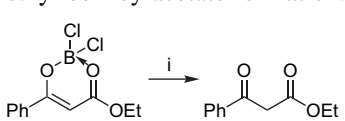


1a-e **5** **6** **7**

Scheme 3. Reactions of **1** with arylhydrazines; (i) R^4NHNH_2 (1.1 equiv), MeCN, 25 °C, 5–24 h.

The structural phenomena of the B–X π binding affinity and the resulting effect on the chemistry are suggested to be manifested in practise. However, the binding affinity of BF_3 to carbonyls is considerably different from that of BCl_3. The evidence came from a comparison of the reactivity of **1a** and its chloro analogue **8**. One would expect the 2,2-dichloro-1,3,2-dioxaborinane analogue **8** (a so-far undescribed compound) to have a lower activation barrier towards the aminolysis than **1a**. Arising from this fact, we considered whether **8** might react similarly and provide an extension of the methodology. The formation of **8** was achieved by the treatment of ethyl benzoylacetate with a solution of BCl_3 in dry toluene at 25 °C.

The treatment of 2,2-dichloro-1,3,2-dioxaborinane **1f** with benzylamine or diisopropylamine in dry MeCN or CH_2Cl_2 solutions quantitatively led to the formation of ethyl benzoylacetate (Scheme 4). It seems that in the case of 2,2-dichloro-1,3,2-dioxaborinanes the nucleophilic attack at the boron moiety is much more favourable than that at the carbonyl functionality, consequently resulting in decomplexation and ethyl benzoylacetate formation.



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Scheme 4. Reaction of 2,2-dichloro-1,3,2-dioxaborinane **1f** with alkylamines; (i) $PhCH_2NH_2$ or $(i\text{-Pr})_2NH$, dry MeCN or CH_2Cl_2, 25 °C.

3. Conclusion

In summary, a convenient two-step procedure for the conversion of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes to β-keto amides or β-enamino carboxamides, via their 4-alkylamino analogues, has been demonstrated. Additionally, when 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes react with arylhydrazines bearing electron-withdrawing substituents, the corresponding hydrazones are obtained in good yields, whereas the reaction with more nucleophilic arylhydrazines resulted in the formation of pyrazolones and 5-alkoxy-1*H*-pyrazoles.

4. Experimental

4.1. General

Solvents and starting compounds were obtained from commercial sources (Fluka, Sigma and Aldrich). All reactions were carried out in dry solvents. Light petroleum refers to the fraction with the boiling point 40–60 °C. Hydrazines (4-fluorophenylhydrazine and 4-bromophenylhydrazine) were obtained in the free form from the commercially available hydrochloride salts by neutralisation with Na_2CO_3 and subsequent extraction into CH_2Cl_2. TLC was carried out on Fluka silica gel TLC cards. All mps were determined on a hot stage apparatus and are uncorrected. IR spectra were recorded on a BioRad FTS 3000MX instrument. NMR spectra were recorded on a Bruker Avance 300 DPX spectrometer at 302 K. Chemical shifts are reported in δ ppm, referenced to an internal TMS standard for ^1H NMR and chloroform-*d* (δ 77.0) and DMSO-d_6 (δ 39.5) for ^{13}C NMR. The ^1H–^{13}C HMBC spectra were obtained with 512 time increments and 32 scans per t_1 increment. The ^{15}N NMR spectrum was obtained from ^1H–^{15}N GHMQC spectrum and is reported in δ ppm referenced to an external $MeNO_2$ standard. Microanalyses were performed on a Perkin–Elmer 2400 series II CHNS/O analyser. Mass spectra and high-resolution mass measurements were performed on a VG-Analytical Autospec EQ instrument.

4.2. General procedure for the preparation of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes 1a–d

To a solution of the corresponding 1,3-keto ester (1 mmol) in toluene (5 mL) boron trifluoride etherate (2 equiv) was added at room temperature. After being stirred at room temperature for 24 h, the reaction mixture was concentrated to 1/3 of its volume (in the case of ethyl benzoylacetate, ethyl

cyclohexanone-2-carboxylate and ethyl acetoacetate) and then cooled (–30 °C). The precipitated material was filtered off and washed with 5:1 petroleum ether/EtOAc (5 mL), yielding the pure product. In the case of 2-acetylbutyrolactone and dimethyl 2-acetylsuccinate the reaction mixture was evaporated to dryness, yielding a yellowish oil that was used in the next step without further purification.

Compounds **1a**, **1c** and **1d** were prepared according to the previously reported procedure.[18a,35a]

4.2.1. 2,2-Difluoro-4-ethoxy-5*H*,6*H*,7*H*,8*H*-1,3,2-benzodioxaborinane (1b). Brownish solid, yield 98%; mp 50–52 °C (from hexane). IR (KBr, ν cm^{-1}): 2949, 1605, 1531, 1492, 1462, 1377, 1342, 1289, 1210, 1166, 1047, 1001, 871, 826, 766. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.41 (t, 3H, J=7.2 Hz), 1.62–1.78 (m, 4H), 2.25 (t, 2H, J=6.4 Hz), 2.41 (t, 2H, J=6.4 Hz), 4.51 (q, 2H, J=7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 20.2, 21.2, 21.4, 31.0, 66.0, 95.3, 173.6 (t, J=2.3 Hz), 183.1 (t, J=1.7 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −141.8. MS (EI, 70 eV, *m/z* (%)): 218 (M^+, 27), 124 (100), 68 (57). HRMS (EI) *m/z* calcd for $C_9H_{13}BF_2O_3$: 218.0926, found: 218.0932.

4.2.2. 2,2-Difluoro-7-methyl-5*H*,6*H*-furo[2,3-*d*][1,3,2]dioxaborinane (1e). Colourless oil, yield 99%. IR (film, ν cm^{-1}): 3002, 1749, 1709, 1649, 1579, 1499, 1046, 920. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.15–2.18 (m, 3H), 3.07 (t, 2H, J=8.0 Hz), 4.85 (t, 2H, J=8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 22.4, 74.2, 95.0, 179.8 (t, J=2.3 Hz), 180.7 (t, J=1.7 Hz). MS (EI, 70 eV, *m/z* (%)): 176 (M^+, 70), 161 (100), 95 (65), 64 (87). HRMS (EI) *m/z* calcd for $C_6H_7BF_2O_3$: 176.0456, found: 176.0462.

4.3. General procedure for the reaction of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinanes 2a–e with amines

To a solution of the corresponding amine (1.3 mmol) in MeCN (5 mL), 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinane (1 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 0.5–4 h. When product precipitated from the reaction mixture, it was filtered off and washed with cold MeCN (3 mL), otherwise the reaction mixture was evaporated to dryness and the residue dissolved in CH_2Cl_2 or EtOAc (30 mL), washed with water (2× 10 mL), dried over $MgSO_4$ and evaporated to dryness. In some cases products were purified by flash chromatography.

4.3.1. 2,2-Difluoro-4-phenyl-6-(1-piperidinyl)-1,3,2-dioxaborinane (2a). White solid, yield 96%; mp 167–169 °C (from EtOAc). IR (KBr, ν cm^{-1}): 2949, 2856, 1612, 1494, 1368, 1304, 1248, 1108, 1072, 930, 764. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.66 (m, 6H), 3.72 (t, 2H, J=5.1 Hz), 3.82 (t, 2H, J=5.1 Hz), 6.64 (s, 1H), 7.49–7.62 (m, 3H), 8.02–8.06 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 32.2, 25.4, 25.7, 44.5, 46.9, 82.7, 126.9, 128.6, 132.2, 133.2, 164.5 (t, J=2.6 Hz), 171.0 (t, J=2.0 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −142.6. MS (EI, 70 eV, *m/z* (%)): 297 (M^+, 68), 262 (57), 214 (34), 174 (67), 105 (100), 77 (46). HRMS (EI) *m/z* calcd for $C_{14}H_{16}BF_2NO_2$: 297.1242, found: 297.1250. Anal. Calcd for $C_{14}H_{16}BF_2NO_2$: C, 60.25; H, 5.78; N, 5.02. Found: C, 59.91; H, 5.93; N, 5.43.

4.3.2. 6-(*tert*-Butylamino)-2,2-difluoro-4-phenyl-1,3,2-dioxaborinane (2b). White solid, yield 93%; mp 185–187 °C (from MeCN). IR (KBr, ν cm^{-1}): 3349, 2982, 1612, 1541, 1455, 1334, 1125, 1011, 920, 802, 770. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51 (s, 9H), 5.71 (s, 1H), 5.83 (br s, 1H), 7.40–7.53 (m, 3H), 7.82–7.86 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.9, 54.6, 85.1, 126.9, 128.6, 132.2, 133.1, 169.2, 172.3. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −142.6. MS (EI, 70 eV, *m/z* (%)): 267 (M^+, 61), 210 (100), 105 (92), 57 (88). HRMS (EI) *m/z* calcd for $C_{13}H_{16}BF_2NO_2$: 267.1242, found: 267.1251.

4.3.3. 6-(Allylamino)-2,2-difluoro-4-phenyl-1,3,2-dioxaborinane (2c). White solid, yield 95%; mp 104–106 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3337, 3204, 1627, 1536, 1419, 1457, 1310, 1239, 1015, 802, 772, 685. ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.00–4.04 (m, 2H), 5.20–5.30 (m, 2H), 5.89–5.97 (m, 1H), 6.16 (s, 1H), 7.50–7.59 (m, 3H), 7.82–7.85 (m, 2H), 9.99 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 42.3, 85.1, 117.2, 126.4, 128.9, 132.2, 132.6, 132.9, 168.0 (t, J=2.6 Hz), 169.8 (t, J=2.0 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −142.2. ^{15}N NMR (60.8 MHz, DMSO-d_6) δ −261.2. MS (EI, 70 eV, *m/z* (%)): 251 (M^+, 71), 250 (75), 232 (44), 196 (39), 105 (100). HRMS (EI) *m/z* calcd for $C_{12}H_{12}BF_2NO_2$: 151.0929, found: 151.0936.

4.3.4. 2,2-Difluoro-4-phenyl-6-(3-picolylamino)-1,3,2-dioxaborinane (2d). White solid, yield 96%; mp 184–186 °C (from MeCN). IR (KBr, ν cm^{-1}): 3440, 2957, 1617, 1526, 1335, 1283, 1078, 950, 760, 711, 679. ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.64 (s, 2H), 6.16 (s, 1H), 7.44 (dd, 1H, J_1=7.5 Hz, J_2=4.8 Hz), 7.51–7.61 (m, 3H), 7.76–7.84 (m, 3H), 8.54–8.60 (m, 2H), 10.09 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 42.2, 85.9, 124.6, 127.3, 129.8, 133.0, 133.2, 133.5, 136.6, 149.9, 150.1, 168.9 (t, J=2.6 Hz), 170.9 (t, J=2.0 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −141.8. MS (EI, 70 eV, *m/z* (%)): 302 (M^+, 43), 282 (61), 265 (100), 105 (67), 92 (68), 77 (42). Anal. Calcd for $C_{15}H_{13}BF_2N_2O_2$: C, 59.64; H, 4.34; N, 9.27. Found: C, 59.62; H, 4.57; N, 8.98.

4.3.5. 6-[(2-Aminoethyl)amino]-2,2-difluoro-4-phenyl-1,3,2-dioxaborinane (2e). White solid, yield 89%; mp 136–137 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3372, 3300, 3059, 1591, 1566, 1481, 1333, 1269, 1147, 1059, 1024, 748, 693. ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 3.31 (t, 2H, J=6.6 Hz), 3.43–3.47 (m, 2H), 3.68–3.73 (m, 2H), 3.81 (t, 1H, J=6.6 Hz), 6.23 (s, 1H), 7.46–7.56 (m, 3H), 7.86–8.01 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 40.2, 43.2, 85.4, 126.2, 128.9, 132.0, 132.9, 167.7 (t, J=2.6 Hz), 168.8 (t, J=2.0 Hz). MS (EI, 70 eV, *m/z* (%)): 254 (M^+, 7), 213 (89), 105 (90), 77 (100). HRMS (EI) *m/z* calcd for $C_{11}H_{13}BF_2N_2O_2$: 254.1038, found: 254.1032.

4.3.6. 2,2-Difluoro-6-[(2,2-dimethoxyethyl)amino]-4-phenyl-1,3,2-dioxaborinane (2f). White solid, yield 91%; mp 124–125 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3292, 2957, 1630, 1536, 1494, 1458, 1298, 1233, 1129, 969, 890, 770. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.34 (s, 6H), 3.50 (d, 2H, J=5.1 Hz), 4.52 (t, 1H, J=5.1 Hz), 6.21 (s, 1H), 7.50–7.62 (m, 3H), 7.80–7.85 (m, 2H), 9.84 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.6, 53.7,

85.0, 101.2, 126.3, 128.9, 132.2, 132.7, 168.2 (t, J=2.3 Hz), 169.6 (t, J=2.3 Hz). MS (EI, 70 eV, m/z (%)): 299 (M^+, 3), 105 (32), 75 (100). HRMS (EI) m/z calcd for $C_{13}H_{16}BF_2NO_4$: 299.1140, found: 299.1152. Anal. Calcd for $C_{13}H_{16}BF_2NO_4$: C, 52.21; H, 5.39; N, 4.68. Found: C, 51.94; H, 5.63; N, 4.80.

4.3.7. 2,2-Difluoro-4-amino-6-phenyl-1,3,2-dioxaborinane (2g). White solid, yield 92%; mp 183–184 °C (from EtOAc). IR (KBr, ν cm^{-1}): 3460, 3366, 3285, 1660, 1609, 1574, 1532, 1487, 1369, 1121, 1036, 991, 918, 772, 689. ^1H NMR (300 MHz, DMSO-d_6): δ 5.93 (s, 1H), 7.33–7.45 (m, 3H), 7.75–7.78 (m, 2H), 8.41 (br s, 1H), 8.55 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 84.1, 126.2, 128.1, 131.6, 132.7, 170.5 (t, J=2.5 Hz), 171.3 (t, J=2.0 Hz). MS (EI, 70 eV, m/z (%)): 211 (M^+, 76), 210 (100), 105 (65), 77 (40). HRMS (EI) m/z calcd for $C_9H_8BF_2NO_2$: 211.0616, found: 211.0624. Anal. Calcd for $C_9H_8BF_2NO_2$: C, 51.24; H, 3.82; N, 6.64. Found: C, 50.77; H, 3.93; N, 6.93.

4.3.8. 2,2-Difluoro-6-(2,2-dimethylhydrazino)-4-phenyl-1,3,2-dioxaborinane (2h). White solid, yield 81%; mp 159–160 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3269, 1611, 1536, 1393, 1348, 1169, 1045, 974, 907, 865, 771. ^1H NMR (300 MHz, $CDCl_3$): δ 2.61 (s, 6H), 6.52 (s, 1H), 7.50–7.61 (m, 3H), 7.91–7.94 (m, 2H), 10.09 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 46.9, 81.6, 126.9, 128.9, 132.6, 132.8, 169.0 (t, J=2.6 Hz), 172.6 (t, J=2.0 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −142.0. MS (EI, 70 eV, m/z (%)): 254 (M^+, 35), 108 (100), 77 (41), 59 (79). HRMS (EI) m/z calcd for $C_{11}H_{13}BF_2N_2O_2$: 254.1038, found: 254.1046.

4.3.9. 2,2-Difluoro-4-(isopropylamino)-5*H*,6*H*,7*H*,8*H*-1,3,2-benzodioxaborinane (2i). White solid, yield 98%; mp 131–133 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3364, 2984, 1607, 1528, 1416, 1198, 1129, 1020, 883, 751, 656. ^1H NMR (300 MHz, DMSO-d_6): δ 1.28 (d, 6H, J=6.6 Hz), 1.71–1.75 (m, 4H), 2.12–2.17 (m, 2H), 2.33–2.37 (m, 2H), 4.21–4.33 (m, 1H), 5.98 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.0, 21.1, 21.3, 21.5, 30.0, 43.1, 94.7, 166.0 (J=2.6 Hz), 172.4 (J=2.0 Hz). ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −141.6. MS (EI, 70 eV, m/z (%)): 231 (M^+, 72), 173 (100), 123 (70). HRMS (EI) m/z calcd for $C_{10}H_{16}BF_2NO_2$: 231.1242, found: 231.1249.

4.3.10. 2,2-Difluoro-6-(isopropylamino)-4-methyl-1,3,2-dioxaborinane (2j). Colourless oil, yield 92%. IR (film, ν cm^{-1}): 3362, 2982, 1624, 1538, 1419, 1294, 1073, 1047, 981, 786. ^1H NMR (300 MHz, $CDCl_3$): δ 1.25 (d, 6H, J=6.6 Hz), 2.04 (s, 3H), 4.15–4.26 (m, 1H), 5.25 (s, 1H), 6.52 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.4, 22.9, 43.9, 88.0, 167.8, 177.5. MS (CI, m/z (%)): 191 (MH^+, 50), 176 (55), 133 (67), 92 (100), 85 (64), 69 (91). HRMS (CI) m/z calcd for $C_7H_{13}BF_2NO_2$: 190.0966, found: 190.0966.

4.3.11. 2,2-Difluoro-4-methyl-6-(3-picolylamino)-1,3,2-dioxaborinane (2k). White solid, yield 98%; mp 147–149 °C (from EtOAc). IR (KBr, ν cm^{-1}): 3249, 3109, 1603, 1533, 1464, 1422, 1334, 1190, 1053, 964, 885, 787, 712. ^1H NMR (300 MHz, DMSO-d_6): δ 2.01 (s, 3H), 4.54(d, 2H, J=5.7 Hz), 5.41 (s, 1H), 7.42 (dd, 1H, J_1=4.8 Hz, J_2=7.6 Hz), 7.71 (d, 1H, J=7.6 Hz), 8.52–8.56 (m, 2H), 10.02 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.0, 40.9, 87.2, 123.7, 132.2, 135.6, 148.8, 148.9, 167.4 (t, J=2.3 Hz), 176.5 (t, J=1.7 Hz). MS (CI, m/z (%)): 240 (MH^+, 51), 220 (31), 156 (56), 92 (100), 65 (44). HRMS (CI) m/z calcd for $C_{10}H_{12}BF_2N_2O_2$: 239.0918, found: 239.0918.

4.3.12. 2,2-Difluoro-5-(2-methoxy-2-oxoethyl)-4-methyl-6-(methylamino)-1,3,2-dioxaborinane (2l). White solid, yield 83%; mp 116–117 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3411, 2955, 1739, 1621, 1522, 1445, 1348, 1301, 1175, 1055, 861, 777, 737, 697, 655. ^1H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 3H), 3.06 (d, 3H, J=5.0 Hz), 3.20 (s, 2H), 3.75 (s, 3H), 7.37 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.9, 27.9, 31.5, 52.8, 91.5, 168.8 (t, J=2.7 Hz), 172.0, 176.5 (t, J=1.8 Hz). MS (EI, 70 eV, m/z (%)): 235 (M^+, 27), 216 (24), 176 (100), 110 (57), 97 (58). HRMS (EI) m/z calcd for $C_8H_{12}BF_2NO_4$: 235.0828, found: 235.0834. Anal. Calcd for $C_8H_{12}BF_2NO_4$: C, 40.89; H, 5.15; N, 5.96. Found: C, 40.96; H, 5.28; N, 6.19.

4.3.13. 2,2-Difluoro-5-(2-methoxy-2-oxoethyl)-4-methyl-6-(1-pyrrolidinyl)-1,3,2-dioxaborinane (2m). White solid, yield 79%; mp 98–100 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 2969, 2885, 1733, 1596, 1569, 1477, 1431, 1341, 1316, 1236, 1170, 1086, 772. ^1H NMR (300 MHz, $CDCl_3$): δ 1.92 (tt, 2H, J_1=J_2=6.6 Hz), 2.01 (tt, 2H, J_1=J_2=6.6 Hz), 2.11 (s, 3H), 3.41 (s, 2H), 3.65–3.74 (m, 4H), 3.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 23.2, 26.9, 32.0, 48.8, 50.3, 52.5, 91.9, 166.0 (t, J=2.0 Hz), 171.8, 179.5 (t, J=1.5 Hz). MS (EI, 70 eV, m/z (%)): 275 (M^+, 30), 256 (46), 216 (100), 147 (35), 118 (76), 97 (67), 70 (42), 55 (63). HRMS (EI) m/z calcd for $C_{11}H_{16}BF_2NO_4$: 275.1141, found: 275.1151.

4.3.14. 2,2-Difluoro-5-(2-methoxy-2-oxoethyl)-4-methyl-6-[(2-sulfanylethyl)amino]-1,3,2-dioxaborinane (2n). White solid, yield 71%; mp 66–68 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3395, 2956, 2577, 1736, 1602, 1522, 1438, 1347, 1299, 1197, 1051, 780. ^1H NMR (300 MHz, $CDCl_3$): δ 1.53 (t, 1H, J=8.6 Hz), 2.22 (s, 3H), 2.78 (dt, 2H, J_1=8.6 Hz, J_2=6.3 Hz), 3.23 (s, 2H), 3.67 (dt, 2H, J_1=J_2=6.1 Hz), 3.76 (s, 3H), 7.66 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.1, 23.7, 31.6, 44.0, 52.9, 91.5, 168.5 (t, J=2.0 Hz), 171.9, 177.7 (t, J=2.0 Hz). MS (EI, 70 eV, m/z (%)): 261 (M^+−HF, 76), 149 (97), 93 (86), 57 (100). Anal. Calcd for $C_9H_{14}BF_2NO_4S$: C, 38.46; H, 5.02; N, 4.98. Found: C, 38.40; H, 5.25; N, 4.88.

4.3.15. 6-(Allylamino)-2,2-difluoro-5-(2-methoxy-2-oxoethyl)-4-methyl-1,3,2-dioxaborinane (2o). White solid, yield 90%; mp 43–45 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3391, 2957, 1738, 1604, 1522, 1438, 1346, 1197, 1173, 1052. ^1H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 3H), 3.23 (s, 2H), 3.75 (s, 3H), 4.07–4.11 (m, 2H), 5.25–5.35 (m, 2H), 5.83–5.95 (m, 1H), 7.45 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.8, 31.3, 43.4, 52.7, 91.5, 118.3, 131.2, 168.0 (t, J=1.7 Hz), 171.8, 176.9 (t, J=1.9 Hz). MS (EI, 70 eV, m/z (%)): 261 (M^+, 32), 242 (28), 202 (100), 97 (62). HRMS (EI) m/z calcd for $C_{10}H_{14}BF_2NO_4$: 261.0984, found: 261.0991.

4.3.16. 2,2-Difluoro-5-(2-methoxy-2-oxoethyl)-4-methyl-6-(3-picolylamino)-1,3,2-dioxaborinane (2p). White solid, yield 95%; mp 132–134 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3233, 2966, 1730, 1614, 1518, 1432, 1308, 1225, 1206, 1143, 1054, 839, 710. ^1H NMR (300 MHz, $CDCl_3$): δ 2.22 (s, 3H), 3.21 (s, 2H), 3.71 (s, 3H), 4.66 (d, 2H, J=5.6 Hz), 7.34 (ddd, 1H, J_1=0.8 Hz, J_2=4.8 Hz, J_3=7.7 Hz), 7.68–7.73 (m, 1H), 7.92 (br s, 1H), 8.57 (d, 1H, J=1.9 Hz), 8.60 (dd, 1H, J_1=1.5 Hz, J_2=4.8 Hz). ^{13}C NMR (75 MHz, DMSO-d_6): δ 20.4, 29.6, 41.5, 51.8, 92.0, 123.5, 132.5, 135.0, 148.6, 148.7, 167.1 (t, J=2.5 Hz), 170.5, 175.7 (t, J=2.0 Hz). MS (EI, 70 eV, m/z (%)): 312 (M^+, 25), 253 (57), 92 (100). HRMS (EI) m/z calcd for $C_{13}H_{15}BF_2N_2O_4$: 312.1093, found: 312.1105.

4.3.17. 2,2-Difluoro-5-(2-hydroxyethyl)-6-(isopropylamino)-4-methyl-1,3,2-dioxaborinane (2q). The colourless oil obtained on workup was subjected to flash chromatography (5:3 light petroleum/EtOAc elution), colourless oil, yield 45%, R_f=0.25 (5:3 light petroleum/EtOAc). IR (film, ν cm^{-1}): 3559, 3383, 2978, 1601, 1520, 1466, 1285, 1200, 1049. ^1H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, 6H, J=6.9 Hz), 2.08 (s, 3H), 2.46 (t, 2H, J=5.4 Hz), 3.01 (br s, 1H), 3.80 (t, 2H, J=5.4 Hz), 4.14–4.23 (m, 1H), 7.90 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 22.2, 28.4, 43.7, 63.3, 96.7, 168.4, 174.0. ^{19}F NMR (282.4 MHz, $CDCl_3$): δ −142.0. MS (EI, 70 eV, m/z (%)): 235 (M^+, 3), 169 (40), 111 (100). HRMS (EI) m/z calcd for $C_9H_{16}BF_2NO_3$: 235.1191, found: 235.1201.

4.3.18. 2,2-Difluoro-5-(2-hydroxyethyl)-4-methyl-6-(3-picolylamino)-1,3,2-dioxaborinane (2r). The colourless oil obtained on workup was subjected to flash chromatography (5:3 light petroleum/EtOAc elution), white solid, yield 50%, R_f=0.21 (5:3 light petroleum/EtOAc); mp 70–72 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3308, 3237, 3058, 2911, 1697, 1607, 1480, 1427, 1402, 1362, 1232, 1138, 1090, 1021, 903, 793, 766, 712. ^1H NMR (300 MHz, $CDCl_3$): δ 1.90 (s, 3H), 2.83 (t, 2H, J=8.1 Hz), 3.27 (br s, 1H), 4.27 (t, 2H, J=8.1 Hz), 4.43 (d, 2H, J=6.3 Hz), 7.27 (ddd, 1H, J_1=1.0 Hz, J_2=4.8 Hz, J_3=7.9 Hz), 7.59–7.61 (m, 1H), 8.50–8.52 (m, 2H), 8.62 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.2, 26.3, 44.2, 65.1, 87.1, 123.6, 134.3 (2C), 148.3, 148.8, 156.1, 174.0. MS (EI, 70 eV, m/z (%)): 284 (M^+, 2), 218 (40), 92 (100). HRMS (EI) m/z calcd for $C_{12}H_{15}BF_2N_2O_3$: 284.1144, found: 284.1152.

4.3.19. 6-(Allylamino)-2,2-difluoro-5-(2-hydroxyethyl)-4-methyl-1,3,2-dioxaborinane (2s). The colourless oil obtained on workup was subjected to flash chromatography (1:10 MeOH/CH_2Cl_2 elution), colourless oil, yield 68%, R_f=0.20 (1:10 MeOH/CH_2Cl_2). IR (film, ν cm^{-1}): 3563, 3399, 2932, 1603, 1520, 1300, 1199, 1048. ^1H NMR (300 MHz, $CDCl_3$): δ 2.08 (s, 3H), 2.48 (t, 2H, J=5.4 Hz), 3.25 (br s, 1H), 3.77 (t, 2H, J=5.4 Hz), 4.00–4.04 (m, 2H), 5.18–5.29 (m, 2H), 5.78–5.29 (m, 1H), 8.22 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.8, 43.7, 63.0, 85.4, 97.1, 118.5, 132.1, 169.4, 174.8. MS (EI, 70 eV, m/z (%)): 233 (M^+, 23), 202 (7), 111 (100), 69 (47). HRMS (EI) m/z calcd for $C_9H_{14}BF_2NO_3$: 233.1035, found: 233.1030.

4.4. General procedure for the preparation of β-keto amides

A mixture of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinane (1 mmol), sodium acetate (5 mmol), ethanol (5 mL) and water (5 mL) was heated at reflux for 2–16 h. The solvent was then removed under reduced pressure and the residue dissolved in ethyl acetate (30 mL), washed with water (2×10 mL), dried over magnesium sulfate and evaporated to dryness. Products were in some cases purified by flash chromatography on a silica gel using 3:5 EtOAc/light petroleum as eluent.

4.4.1. Methyl 4-oxo-3-(1-pyrrolidinylcarbonyl)pentanoate (3a). Colourless oil, yield 79%. IR (film, ν cm^{-1}): 2955, 2880, 1725, 1638, 1436, 1360, 1248, 1165. ^1H NMR (300 MHz, $CDCl_3$): δ 1.77–1.97 (m, 4H), 2.10 (s, 3H), 2.82 (d, 2H, J=7.1 Hz), 3.36–3.65 (m, 4H), 3.58 (s, 3H), 3.89 (t, 1H, J=7.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 25.7, 27.6, 32.3, 46.1, 47.1, 51.7, 54.5, 166.7, 171.9, 202.0. MS (EI, 70 eV, m/z (%)): 227 (M^+, 35), 209 (37), 184 (38), 126 (70), 98 (45), 70 (100). HRMS (EI) m/z calcd for $C_{11}H_{17}NO_4$: 227.1158, found: 227.1163.

4.4.2. *N*-Isopropyl-3-oxo-3-phenylpropanamide (3b). White solid, yield 88%; mp 70–72 °C (from CH_2Cl_2/light petroleum). IR (KBr, ν cm^{-1}): 3297, 2973, 1690, 1641, 1551, 1450, 1045, 756, 689. ^1H NMR (300 MHz, $CDCl_3$): δ 1.19 (d, 6H, J=6.5 Hz), 3.93 (s, 2H), 4.03–4.23 (m, 1H), 6.19 (br s, 1H), 7.42–7.53 (m, 3H), 7.99–8.03 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.6, 41.6, 45.6, 128.5, 128.8, 134.0, 136.3, 164.7, 196.3. MS (EI, 70 eV, m/z (%)): 205 (M^+, 17), 190 (19), 105 (100), 77 (61), 58 (81). HRMS (EI) m/z: calcd for $C_{12}H_{15}NO_2$: 205.1103, found: 205.1110.

4.4.3. 3-Oxo-3-phenyl-*N*-(3-pyridinylmethyl)propanamide (3c). White solid, yield 97%; mp 100–102 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3219, 3046, 1679, 1655, 1578, 1428, 1325, 1221, 1034, 756, 721, 688. ^1H NMR (300 MHz, $CDCl_3$): δ 4.01 (s, 2H), 4.51 (d, 2H, J=6.3 Hz), 7.24 (dd, 1H, J_1=4.8 Hz, J_2=7.5 Hz), 7.41–7.74 (m, 5H), 7.96–8.00 (m, 2H), 8.50–8.54 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 41.0, 45.0, 123.5, 128.5, 128.9, 133.7, 134.2, 135.4, 136.0, 148.8, 149.1, 166.0, 195.9. MS (EI, 70 eV, m/z (%)): 254 (M^+, 34), 107 (100), 77 (62). HRMS (EI) m/z calcd for $C_{15}H_{14}N_2O_2$: 254.1055, found: 254.1063.

4.4.4. *N*-Allyl-3-oxo-3-phenylpropanamide (3d). White solid, yield 91%; mp 54–56 °C (from Et_2O/EtOAc). IR (KBr, ν cm^{-1}): 3300, 3078, 1690, 1641, 1551, 1449, 1330, 1281, 1212, 757, 689. ^1H NMR (300 MHz, DMSO-d_6): δ 3.73–3.77 (m, 2H), 3.96 (s, 2H), 5.05–5.23 (m, 2H), 5.75–5.87 (m, 2H), 7.49–7.67 (m, 3H), 7.97–8.00 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 41.9, 47.7, 116.0, 129.2, 129.5, 134.3, 135.9, 137.2, 167.0, 195.6. MS (EI, 70 eV, m/z (%)): 204 (MH^+, 15), 120 (25), 105 (100), 77 (72), 56 (87). HRMS (EI) m/z calcd for $C_{12}H_{13}NO_2$: 204.1025, found: 204.1030.

4.4.5. *N*-(3-Pyridinylmethyl)-3-oxo-3-phenylpropanamide (3e). Colourless oil, yield 63%. IR (film, ν cm^{-1}): 3268, 3092, 1719, 1655, 1564, 1452, 1362, 1163, 1038,

712. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.28 (s, 3H), 3.49 (s, 2H), 4.50 (d, 2H, J=6.0 Hz), 7.28 (dd, 1H, J_1=4.5 Hz, J_2=7.5 Hz), 7.55 (br s, 1H), 7.64–7.66 (m, 1H), 8.52–8.56 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.1, 41.0, 49.2, 123.6, 133.7, 135.5, 148.9, 149.1, 165.6, 204.6. MS (EI, 70 eV, *m/z* (%)): 192 (MH^+, 26), 107 (100), 92 (32). HRMS (EI) *m/z* calcd for $C_{10}H_{12}N_2O_2$: 192.0899, found: 192.0905.

4.4.6. *N*-Isopropyl-2-oxo-1-cyclohexanecarboxamide (3f). White solid, yield 95%; mp 101–103 °C (from CH_2Cl_2/light petroleum). IR (KBr, ν cm^{-1}): 3219, 3079, 2986, 2873, 1704, 1638, 1553, 1457, 1385, 1196, 1131, 1073, 1034, 911, 735. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.09 (d, 3H, J=6.4 Hz), 1.12 (d, 3H, J=6.4 Hz), 1.69–1.84 (m, 2H), 1.91–2.03 (m, 3H), 2.32–2.49 (m, 3H), 3.13 (dd, 1H, J_1=5.6 Hz, J_2=9.8 Hz), 4.02–4.14 (m, 1H), 6.80 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.60, 22.62, 24.1, 27.3, 31.4, 41.3, 42.1, 55.8, 167.8, 210.8. MS (EI, 70 eV, *m/z* (%)): 183 (M^+, 55), 125 (53), 114 (54), 98 (95), 58 (100). HRMS (EI) *m/z* calcd for $C_{10}H_{17}NO_2$: 183.1259, found: 183.1267.

4.4.7. *N*-Benzyl-2-oxo-1-cyclohexanecarboxamide (3g). Isolated after crystallisation of the mixture of compounds **3g** and **3g′** (CH_2Cl_2/light petroleum), white solid, yield 28%; mp 89–91 °C (from CH_2Cl_2/light petroleum). IR (KBr, ν cm^{-1}): 3252, 3080, 2945, 1706, 1639, 1558, 1385, 1247, 1192, 1130, 1077, 760, 738, 704. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.72–1.79 (m, 2H), 1.96–2.03 (m, 3H), 2.36–2.45 (m, 3H), 3.21 (dd, 1H, J_1=6.1 Hz, J_2=10.8 Hz), 4.47 (d, 2H, J=5.7 Hz), 7.26–7.34 (m, 5H), 7.36 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.2, 27.2, 31.5, 42.1, 43.3, 55.8, 127.3, 127.5, 128.6, 138.1, 168.9, 210.4. MS (EI, 70 eV, *m/z* (%)): 231 (M^+, 12), 106 (100), 91 (63). HRMS (EI) *m/z* calcd for $C_{14}H_{17}NO_2$: 231.1259, found: 231.1251. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.23; H, 7.58; N, 6.25.

4.4.8. *N*-Benzyl-2-hydroxy-1-cyclohexene-1-carboxamide (3g′). Also isolated after crystallisation of the mixture of compounds **3g** and **3g′** (CH_2Cl_2/light petroleum), white solid, yield 37%; mp 84–86 °C (from CH_2Cl_2/light petroleum). IR (KBr, ν cm^{-1}): 3389, 2945, 1645, 1606, 1546, 1382, 1306, 1233, 924, 743, 700. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.68–1.72 (m, 4H), 2.12–2.15 (m, 2H), 2.26–2.30 (m, 2H), 4.52 (d, 2H, J=5.7 Hz), 5.67 (br s, 1H), 7.28–7.40 (m, 5H), 14.09 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.9, 22.5, 22.7, 29.3, 43.1, 96.8, 127.6, 127.7, 128.8, 138.2, 170.6, 172.3. MS (EI, 70 eV, *m/z* (%)): 231 (M^+, 16), 106 (100), 91 (95). HRMS (EI) *m/z* calcd for $C_{14}H_{17}NO_2$: 231.1259, found: 231.1253.

4.5. General procedure for the preparation of β-carboxamido enamines

In a typical experiment the solution of 2,2-difluoro-4-alkylamino-1,3,2-dioxaborinane (1 mmol) and the corresponding amine (5 equiv) in *n*-PrOH (5 mL) was heated with stirring in Ace pressure tube at 130 °C. After heating for 12 h, the reaction mixture was evaporated under reduced pressure and the residue purified by flash chromatography.

4.5.1. (2*Z*)-3-(Allylamino)-3-phenyl-*N*-(3-picolyl)-2-propenamide (4a). The colourless oil obtained on workup was subjected to flash chromatography (1:1 light petroleum/EtOAc), colourless oil, yield 92%, R_f=0.20 (1:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 3273, 2921, 1618, 1592, 1541, 1497, 1426, 1310, 1210, 1030, 922, 771, 703. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62–3.66 (m, 2H), 4.50 (d, 2H, J=5.7 Hz), 4.50 (s, 1H), 5.07–5.25 (m, 2H), 5.47 (br s, 1H), 5.73–5.86 (m, 1H), 7.24–7.40 (m, 6H), 7.67–7.71 (m, 1H), 8.50 (dd, 1H, J_1=1.7 Hz, J_2=4.5 Hz), 8.57 (d, 1H, J=1.7 Hz), 9.12 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 40.2, 46.6, 88.2, 115.4, 123.4, 127.6, 128.1, 128.8, 135.1, 135.3, 135.6, 136.3, 148.1, 148.7, 162.3, 170.2. MS (ESI^+, *m/z* (%)): 294 (MH^+), 255. HRMS (ESI^+) *m/z* calcd for $C_{18}H_{20}N_3O$: 294.1606, found: 294.1614.

4.5.2. (*Z*)-1-Allyl-3-(1-(benzylamino)ethylidene)pyrrolidine-2,5-dione (4b). The colourless oil obtained on workup was subjected to flash chromatography (5:3 light petroleum/EtOAc elution), white solid, yield 72%, R_f=0.27 (5:3 light petroleum/EtOAc); mp =65–68 °C (from light petroleum/Et_2O). IR (KBr, ν cm^{-1}): 3302, 2918, 1736, 1660, 1614, 1388, 1223, 1186, 1091, 935, 886, 745. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.93 (s, 3H), 3.21 (s, 2H), 4.11–4.14 (m, 2H), 4.45 (d, 2H, J=6.3 Hz), 5.13–5.17 (m, 2H), 5.77–5.90 (m, 1H), 7.26–7.38 (m, 5H), 8.93 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.0, 33.5, 40.0, 46.9, 87.8, 117.1, 126.7, 127.5, 128.9, 132.0, 138.2, 155.8, 171.3, 174.6. MS (EI, 70 eV, *m/z* (%)):270 (M^+, 83), 106 (53), 91 (100). HRMS (EI) *m/z* calcd for $C_{16}H_{18}N_2O_2$: 270.1368, found: 270.1376. Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.27; H, 6.93; N, 10.43.

4.5.3. (*Z*)-1-Allyl-3-(1-(prop-2-ynylamino)ethylidene)-pyrrolidine-2,5-dione (4c). The colourless oil obtained on workup was subjected to flash chromatography (5:3 light petroleum/EtOAc), white solid, yield 67%, R_f=0.18 (5:3 light petroleum/EtOAc); mp=102–104 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3294, 3249, 2925, 1725, 1668, 1597, 1480, 1433, 1397, 1318, 1273, 1217, 1134, 1107, 1063, 922, 766. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.04 (s, 3H), 2.29 (t, 1H, J=2.5 Hz), 3.21 (s, 2H), 3.99 (dd, 2H, J_1=2.5 Hz, J_2=6.3 Hz), 4.10–4.13 (m, 2H), 5.13–5.23 (m, 2H), 5.78–5.87 (m, 1H), 8.60 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.7, 32.4, 33.4, 40.0, 72.2, 79.5, 89.3, 117.2, 131.8, 154.7, 171.3, 174.4. MS (EI, 70 eV, *m/z* (%)): 218 (M^+, 53), 135 (54), 107 (100). HRMS (EI) *m/z* calcd for $C_{12}H_{14}N_2O_2$: 218.1055, found: 218.1062. Anal. Calcd for $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 65.81; H, 6.52; N, 13.14.

4.5.4. *N*-Benzyl-2-(2-phenylhidrazono)cyclohexanecarboxamide (4d). The precipitated product from the reaction mixture was filtered off to give pure product, a white solid, yield 48%; mp=170–174 °C. IR (KBr, ν cm^{-1}): 3315, 3225, 2938, 1661, 1604, 1543, 1495, 1447, 1427, 1360, 1208, 1148, 1096, 978, 890, 744, 696. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62–2.02 (m, 5H), 2.21–2.47 (m, 3H), 3.32 (t, 1H, J=5.5 Hz), 4.49 (d, 2H, J=6.0 Hz), 6.83–6.94 (m, 4H), 7.18–7.35 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.3, 24.5, 25.0, 29.2, 43.6, 49.9, 112.9, 120.0, 127.3, 127.7, 128.6, 129.2, 138.5, 145.2, 147.9, 171.6. MS

(EI, 70 eV, *m/z* (%)): 321 (M^+, 16), 214 (100), 91 (38). HRMS (EI) *m/z* calcd for $C_{20}H_{23}N_3O$: 321.1841, found: 321.1850. Anal. Calcd for $C_{20}H_{23}N_3O$: C, 74.74; H, 7.21; N, 13.07. Found: C, 75.01; H, 7.25; N, 13.30.

4.6. General procedure for the preparation of hydrazones

To a stirred solution of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinane (1 mmol) in MeCN (5 mL) the corresponding arylhydrazine (1.05 mmol) was added, which promptly dissolved. The reaction mixture was stirred at room temperature for 5–12 h. The precipitated material was filtered off, washed with cold MeCN (3 mL) and then recrystallised.

4.6.1. Ethyl 3-[(4-cyano-2-nitrophenyl)hydrazono]-3-phenylpropenoate (5b). Yellow solid, yield 93%; mp 144–145 °C (from EtOH). IR (KBr, ν cm^{-1}): 3294, 2220, 1742, 1618, 1564, 1412, 1278, 1150, 922, 820, 760. ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, 3H, J=7.2 Hz), 3.93 (s, 2H), 4.26 (q, 2H, J=7.2 Hz), 7.43–7.48 (m, 3H), 7.72 (dd, 1H, J_1=1.5 Hz, J_2=9.0 Hz), 7.89–7.93 (m, 2H), 8.11 (d, 1H, J=9.0 Hz), 8.53 (d, 1H, J=1.5 Hz), 11.71 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.9, 33.9, 61.5, 100.4, 117.1, 117.9, 126.5, 128.7, 130.0, 131.2, 131.4, 136.5, 138.1, 143.3, 147.7, 167.6. MS (EI, 70 eV, *m/z* (%)): 352 (M^+, 60), 306 (58), 147 (48), 77 (53). HRMS (EI) *m/z* calcd for $C_{18}H_{16}N_4O_4$: 352.1172, found: 352.1184.

4.6.2. Ethyl 3-[(1,3-dimethyl-4-nitro-1*H*-pyrazol-5-yl)hydrazono]-3-phenylpropanoate (5c). Yellow solid, yield 95%; mp 100–102 °C (from EtOH). IR (KBr, ν cm^{-1}): 3215, 1724, 1605, 1443, 1301, 764. ^1H NMR (300 MHz, $CDCl_3$): δ 1.29 (t, 3H, J=7.2 Hz), 2.52 (s, 3H), 3.91 (s, 2H), 4.13 (s, 3H), 4.28 (q, 2H, J=7.2 Hz), 7.43–7.46 (m, 3H), 7.77–7.81 (m, 2H), 10.76 (br s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.0 (2C), 33.6, 40.0, 61.5, 117.4, 126.2, 128.8, 129.8, 136.4, 142.6, 143.7, 147.5, 167.7. MS (EI, 70 eV, *m/z* (%)): 345 (M^+, 100), 225 (35), 103 (91), 77 (68). HRMS (EI) *m/z* calcd for $C_{16}H_{19}N_5O_4$: 345.1437, found: 345.1450.

4.6.3. Ethyl 3-[(4-cyano-2-nitrophenyl)hydrazono]butanoate (5d). The crude product was purified by silica gel chromatography (5:3 light petroleum/EtOAc elution), yellow solid, yield 89%, R_f=0.20 (1:1 light petroleum/EtOAc); mp 110–113 °C. IR (KBr, ν cm^{-1}): 3329, 3113, 2982, 2222, 1736, 1623, 1564, 1528, 1410, 1287, 1180, 1069, 923, 856. ^1H NMR (300 MHz, DMSO-d_6): δ 1.23 (t, 3H, J=7.2 Hz), 2.09 (s, 3H), 3.52 (s, 2H), 4.14 (q, 2H, J=7.2 Hz), 7.78 (d, 1H, J=9.0 Hz), 7.93 (dd, 1H, J_1=9.0 Hz, J_2=1.9 Hz), 8.57 (d, 1H, J=1.9 Hz), 10.66 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 14.0, 15.9, 43.8, 60.6, 99.5, 166.3, 117.8, 130.4, 131.3, 138.0, 143.3, 151.6, 169.1. MS (EI, 70 eV, *m/z* (%)): 290 (M^+, 100), 199 (95), 102 (78). HRMS (EI) *m/z* calcd for $C_{13}H_{14}N_4O_4$: 290.1015, found: 290.1024.

4.6.4. Dimethyl 2-[*N*-(4-cyano-2-nitrophenyl)ethanehydrazono]succinate (5e). Yellow solid, yield 87%; mp 102–103 °C (from light petroleum/EtOAc). IR (KBr, ν cm^{-1}): 3318, 2954, 2226, 1734, 1624, 1567, 1524, 1283, 1157, 998, 918, 762. ^1H NMR (300 MHz, DMSO-d_6): δ 2.11 (s, 3H), 2.93 (d, 2H, J=6.9 Hz), 3.62 (s, 3H), 3.69 (s, 3H), 3.94 (t, 1H, J=6.9 Hz), 7.72 (d, 1H, J=9.0 Hz), 7.97 (dd, 1H, J_1=1.8 Hz, J_2=9.0 Hz), 8.57 (d, 1H, J=1.8 Hz), 10.63 (br s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 15.4, 33.0, 49.4, 51.6, 52.3, 99.8, 116.1, 117.8, 130.6, 131.3, 138.1, 143.3, 152.6, 170.7, 171.4. MS (EI, 70 eV, *m/z* (%)): 348 (M^+, 30), 317 (30), 256 (100), 210 (23). HRMS (EI) *m/z* calcd for $C_{15}H_{16}N_4O_6$: 348.1070, found: 348.1081.

4.7. General procedure for the preparation of pyrazol-3-ones and 1*H*-pyrazoles

To a stirred solution of 2,2-difluoro-4-alkoxy-1,3,2-dioxaborinane (1 mmol) in MeCN (5 mL) the corresponding arylhydrazine (1.1 mmol) was added, which promptly dissolved. The reaction mixture was stirred at room temperature for 24 h. The solution was concentrated under reduced pressure, and the residue purified by silica gel chromatography (5:1 light petroleum/EtOAc elution).

4.7.1. 2,5-Diphenyl-2,4-dihydro-3*H*-pyrazol-3-one (6a).[44] After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6a** was isolated as a white solid, yield 44%, R_f=0.14 (5:1 light petroleum/EtOAc); mp 129.5–132 °C. IR (KBr, ν cm^{-1}): 2957, 1710, 1593, 1495, 1333, 1181, 1120, 895, 756, 688. ^1H NMR (300 MHz, $CDCl_3$): δ 3.85 (s, 2H), 7.19–7.26 (m, 1H), 7.41–7.49 (m, 5H), 7.76–7.80 (m, 2H), 7.96–8.00 (m, 2H).

4.7.2. 2-(4-Fluorophenyl)-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (6b). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6b** was isolated, yellowish solid, yield 39%, R_f=0.10 (5:1 light petroleum/EtOAc); mp 149–153 °C. IR (KBr, ν cm^{-1}): 1705, 1654, 1501, 1335, 1211, 1173, 1113, 836, 760, 691. ^1H NMR (300 MHz, $CDCl_3$): δ 3.86 (s, 2H), 7.09–7.15 (m, 2H), 7.45–7.47 (m, 3H), 7.75–7.78 (m, 2H), 7.93–7.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.4, 115.4 (d, J=22.5 Hz), 120.6 (d, J=8.0 Hz), 125.9, 128.9, 130.6, 130.7, 134.2 (d, J=3.0 Hz), 154.7, 159.9 (d, J=244.5 Hz), 169.9. MS (EI, 70 eV, *m/z* (%)): 254 (M^+, 100), 109 (52), 103 (60). HRMS (EI) *m/z* calcd for $C_{15}H_{11}FN_2O$: 254.0855, found: 254.0864.

4.7.3. 2-(2,5-Difluorophenyl)-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (6c). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6c** was isolated as a yellowish solid, yield 60%, R_f=0.14 (5:1 light petroleum/EtOAc); mp 111–112.5 °C. IR (KBr, ν cm^{-1}): 3063, 1728, 1624, 1509, 1449, 1342, 1249, 1206, 1121, 858, 759, 687. ^1H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 2H), 7.00–7.08 (m, 1H), 7.15–7.22 (m, 1H), 7.26–7.32 (m, 1H), 7.43–7.48 (m, 3H), 7.72–7.75 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.0, 113.6 (dd, J=26.0, 1.5 Hz), 115.6 (dd, J=24.0, 8.0 Hz), 117.6 (dd, J=22.5, 9.5 Hz), 125.42 (dd, J=14.5, 10.5 Hz), 125.9, 128.9, 130.6, 130.9, 152.4 (dd, J=249.5, 3.0 Hz), 155.8, 158.2 (dd, J=244.0, 2.5 Hz), 170.1. MS (EI, 70 eV, *m/z* (%)): 272 (M^+, 100), 230 (19), 127 (23), 103 (50). HRMS (EI) *m/z* calcd for $C_{15}H_{10}F_2N_2O$: 272.0761, found: 272.0770.

4.7.4. 2-(4-Bromophenyl)-5-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (6d). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6d** was isolated as a white solid, yield 53%, R_f=0.10 (5:1 light petroleum/EtOAc); mp 142–145 °C. IR (KBr, ν cm^{-1}): 2961, 1709, 1481, 1329, 1115, 1069, 820, 759, 687, 646. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.86 (s, 2H), 7.45–7.56 (m, 5H), 7.76–7.79 (m, 2H), 7.89–7.94 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.5, 118.0, 120.2, 125.9, 128.9, 130.6, 130.8, 131.8, 137.2, 154.8, 170.0. MS (EI, 70 eV, *m*/*z* (%)): 314 (M^+, 100), 169 (36), 103 (85). HRMS (EI) *m*/*z* calcd for $C_{15}H_{11}BrN_2O$: 314.0055, found: 314.0046.

4.7.5. 5-Phenyl-2-[3-(trifluoromethyl)phenyl]-2,4-dihydro-3*H*-pyrazol-3-one (6e). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6e** was isolated as a brownish solid, yield 42%, R_f=0.15 (5:1 light petroleum/EtOAc); mp 123–126 °C. IR (KBr, ν cm^{-1}): 3050, 2959, 1717, 1492, 1466, 1340, 1164, 1117, 1073, 893, 799, 756, 691. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.89 (s, 2H), 7.45–7.57 (m, 5H), 7.78–7.81 (m, 2H), 8.25–8.28 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 39.6, 115.4 (q, J=4.0 Hz), 121.5 (m, 2C), 123.9 (q, J=272.5 Hz), 126.1, 129.0, 129.3, 130.5, 131.0, 131.3 (q, J=32.5 Hz), 138.6, 155.1, 170.2. MS (EI, 70 eV, *m*/*z* (%)): 304 (M^+, 100), 159 (35), 103 (93). HRMS (EI) *m*/*z* calcd for $C_{16}H_{11}F_3N_2O$: 304.0824, found: 304.0830.

4.7.6. 2-(4-Bromophenyl)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (6f). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **6f** was isolated as a yellow oil, yield 49%, R_f=0.19 (5:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 3230, 1625, 1585, 1492, 1400, 1362, 1333, 1148, 1007, 799, 761. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.22 (s, 3H), 3.42 (s, 2H), 7.47–7.50 (m, 2H), 7.77–7.80 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.0, 43.1, 117.8, 120.2, 131.8, 137.2, 156.6, 170.5. MS (EI, 70 eV, *m*/*z* (%)): 252 (M^+, 100), 183 (28), 174 (50), 155 (42), 90 (37). HRMS (EI) *m*/*z* calcd for $C_{10}H_9BrN_2O$: 251.9898, found: 251.9892.

4.7.7. 5-Ethoxy-1,3-diphenyl-1*H*-pyrazole (7a).[45] After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7a** was isolated as a colourless oil, yield 26%, R_f=0.37 (5:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 3062, 2983, 1594, 1559, 1503, 1458, 1393, 1265, 1152, 1048, 951, 759, 692. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48 (t, 3H, J=7.0 Hz), 4.24 (q, 2H, J=7.0 Hz), 6.00 (s, 1H), 7.24–7.34 (m, 2H), 7.38–7.45 (m, 4H), 7.81–7.87 (m, 4H).

4.7.8. 5-Ethoxy-1-(4-fluorophenyl)-3-phenyl-1*H*-pyrazole (7b). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7b** was isolated as a yellowish oil, yield 34%, R_f=0.25 (5:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 2984, 2940, 1561, 1514, 1477, 1389, 1213, 1157, 1043, 951, 835, 735, 694. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48 (t, 3H, J=7.0 Hz), 4.23 (q, 2H, J=7.0 Hz), 5.99 (s, 1H), 7.11–7.17 (m, 2H), 7.31–7.45 (m, 3H), 7.77–7.87 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.6, 68.1, 83.6, 115.5 (d, J=22.5 Hz), 123.7 (d, J=8.5 Hz), 125.4, 128.0, 128.5, 133.4, 135.1 (d, J=3.0 Hz), 150.5, 155.1, 160.8 (d, J=245.5 Hz). MS (EI, 70 eV, *m*/*z* (%)): 282 (M^+, 100), 253 (62), 102 (33), 95 (42). HRMS (EI) *m*/*z* calcd for $C_{17}H_{15}FN_2O$: 282.1168, found: 282.1177.

4.7.9. 1-(2,5-Difluorophenyl)-5-ethoxy-3-phenyl-1*H*-pyrazole (7c). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7c** was isolated as a white solid, yield 37%, R_f=0.45 (5:1 light petroleum/EtOAc); mp 47.5–49 °C. IR (KBr, ν cm^{-1}): 3066, 2986, 1626, 1562, 1514, 1387, 1250, 1178, 1027, 912, 868, 816, 760, 694. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.42 (t, 3H, J=7.0 Hz), 4.23 (q, 2H, J=7.0 Hz), 5.97 (s, 1H), 7.03–7.11 (m, 1H), 7.13–7.21 (m, 1H), 7.29–7.43 (m, 4H), 7.79–7.83 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 68.2, 83.0, 115.4 (d, J=26.0 Hz), 115.9 (dd, J=23.0, 8.0 Hz), 117.2 (dd, J=23.0, 9.0 Hz), 125.5, 126.8 (dd, J=14.5, 10.5 Hz), 128.2, 128.5, 133.2, 152.3, 152.7 (dd, J=249.5, 3.0 Hz), 156.0, 158.2 (dd, J=244.0, 2.5 Hz). MS (EI, 70 eV, *m*/*z* (%)): 300 (M^+, 100), 272 (85), 102 (50). HRMS (EI) *m*/*z* calcd for $C_{17}H_{14}F_2N_2O$: 300.1074, found: 300.1067.

4.7.10. 5-Ethoxy-1-(4-bromophenyl)-3-phenyl-1*H*-pyrazole (7d). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7d** was isolated as a yellowish solid, yield 27%, R_f=0.40 (5:1 light petroleum/EtOAc); mp 88–90 °C. IR (KBr, ν cm^{-1}): 2982, 1587, 1558, 1501, 1471, 1377, 1155, 1043, 827, 735. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.49 (t, 3H, J=7.0 Hz), 4.25 (q, 2H, J=7.0 Hz), 5.98 (s, 1H), 7.30–7.44 (m, 3H), 7.52–7.57 (m, 2H), 7.72–7.77 (m, 2H), 7.81–7.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.1, 68.6, 84.4, 119.6, 123.6, 125.9, 128.6, 129.0, 132.2, 133.7, 138.5, 151.3, 155.8. MS (EI, 70 eV, *m*/*z* (%)): 342 (M^+, 100), 315 (45), 155 (40), 102 (73). HRMS (EI) *m*/*z* calcd for $C_{17}H_{15}BrN_2O$: 342.0368, found: 342.0378.

4.7.11. 5-Ethoxy-3-phenyl-1-[3-(trifluoromethyl)-phenyl]-1*H*-pyrazole (7e). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7e** was isolated as a yellow oil, yield 23%, R_f=0.37 (5:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 3063, 2986, 1566, 1503, 1454, 1384, 1331, 1159, 1115, 892, 799, 741, 691. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52 (t, 3H, J=7.0 Hz), 4.28 (q, 2H, J=7.0 Hz), 7.32–7.60 (m, 6H), 7.84–7.88 (m, 2H), 8.06–8.09 (m, 1H), 8.17–8.20 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 68.3, 84.1, 118.3 (q, J=4.0 Hz), 122.2 (q, J=4.0 Hz), 124.4 (q, J=1.0 Hz), 123.9 (q, J=272.5 Hz), 125.5, 128.2, 128.5, 129.3, 131.3 (q, J=32.5 Hz), 133.1, 139.4, 151.1, 155.6. MS (EI, 70 eV, *m*/*z* (%)): 332 (M^+, 100), 304 (87), 145 (70), 102 (90). HRMS (EI) *m*/*z* calcd for $C_{18}H_{15}F_3N_2O$: 332.1137, found: 332.1146.

4.7.12. 1-(4-Bromophenyl)-5-methoxy-3-methyl-1*H*-pyrazole (7f). After the usual workup and chromatography (using 5:1 light petroleum/EtOAc as eluent), the title compound **7f** was isolated as a yellow oil, yield 16%, R_f=0.35 (5:1 light petroleum/EtOAc). IR (film, ν cm^{-1}): 2936, 1587, 1562, 1509, 1488, 1449, 1404, 1198, 1149, 1070, 1047, 1009, 827. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 3H), 3.91 (s,

3H), 5.49 (s, 1H), 7.48–7.51 (m, 2H), 7.57–7.60 (m, 2H). MS (EI, 70 eV, *m/z* (%)): 266 (M^+, 100), 155 (57), 75 (43). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.5, 58.8, 86.1, 118.9, 123.0, 124.0, 131.8, 149.1, 155.9. HRMS (EI) *m/z* calcd for $C_{11}H_{11}BrN_2O$: 266.0055, found: 266.0061.

4.8. 2,2-Dichloro-4-ethoxy-6-phenyl-1,3,2-dioxaborinane (8)

To a solution of ethyl benzoylacetate (1.92 g, 10 mmol) in toluene (60 mL) borontrichloride (1 M, 11 mL, 11 mmol) was added at room temperature. After being stirred at room temperature for 24 h, the reaction mixture was evaporated to dryness and the residue was treated with Et_2O (30 mL) and the precipitated material was filtered off yielding pure product, white hygroscopic solid, 2.43 g (89%); mp 123–126 °C (dec). IR (KBr, ν cm^{-1}): 2924, 1599, 1568, 1508, 1462, 1378, 1334, 1233, 1094, 1057, 947. ^1H NMR (300 MHz, $CDCl_3$): δ 1.50 (t, 3H, J=7.0 Hz), 4.64 (q, 2H, J=7.0 Hz), 6.11 (s, 1H), 7.48–7.53 (m, 2H), 7.62–7.67 (m, 1H), 7.94–7.97 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 67.6, 84.4, 128.0, 129.0, 131.1, 134.4, 174.5, 178.3. MS (EI, 70 eV, *m/z* (%)): 237 (M^+-Cl, 75), 209 (74), 105 (100). HRMS (EI) *m/z* calcd for $C_{11}H_{11}BClO_3$ $[M-Cl]^+$: 237.0490, found: 237.0490.

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