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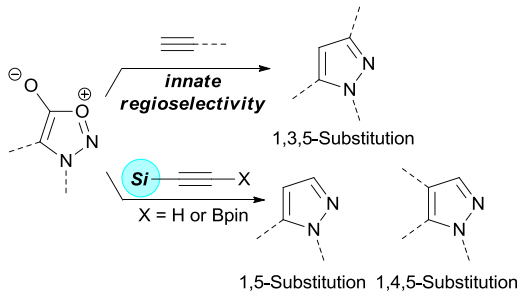
Expanding Available Pyrazole Substitution Patterns by Sydnone Cycloaddition Reactions

A. W. Brown and J. P. A. Harrity*

Department of Chemistry, University of Sheffield, Sheffield, S3 7HF (U.K.). j.harrity@sheffield.ac.uk

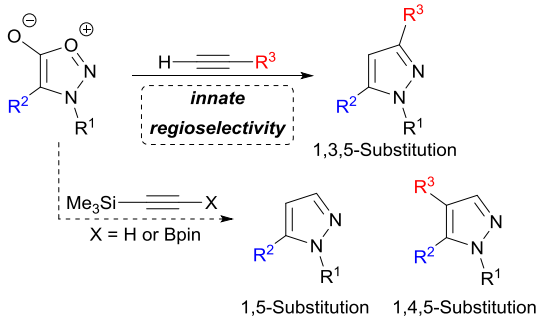
Abstract

We report the use of alkynylsilanes for the regiocontrolled synthesis of pyrazoles from functionalised sydnones. The strategies outlined herein allow a range of pyrazoles to be accessed with substitution patterns that are otherwise not directly obtained with high selectivity by alkyne cycloadditions. Moreover, this study serendipitously highlighted a simple and convenient procedure for the synthesis of aryl monofluoromethyl ethers through the combination of TBAF and dichloromethane.



Introduction

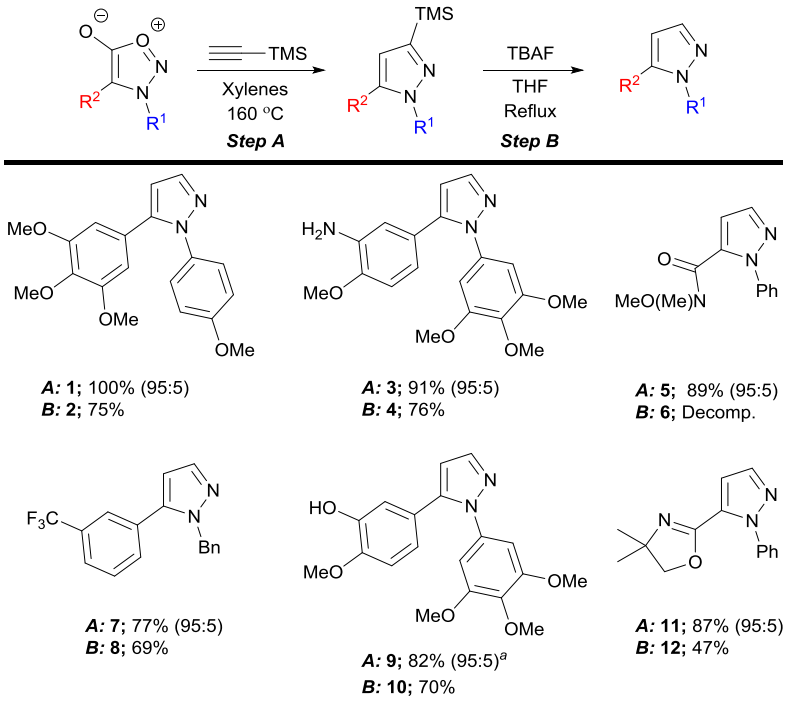
Pyrazoles are a privileged class of heteroaromatic compounds and they constitute the core motif of a number of compounds of medicinal and agrochemical significance.[1] Classical approaches to pyrazoles have broadly encompassed condensation and cycloaddition reactions.[2] Work in our labs has sought to exploit both strategies for the direct formation of borylated pyrazoles where the borate is introduced during annelation, rather than through ring functionalisation.[3] With respect to cycloadditions, sydnones have emerged as effective precursors to pyrazoles, and they offer a regiocontrolled route to 1,3-disubstituted and 1,3,5-trisubstituted diazoles when reacted with terminal alkynes.[4] This product substitution pattern is the result of the innate selectivity of alkyne cycloadditions with 4-H and 4-substituted sydnone substrates. We have been interested in developing strategies that overturn this innate selectivity, and report herein how alkynylsilanes can access alternative substitution patterns, thereby expanding the scope of sydnone cycloaddition methodology for pyrazole synthesis (Scheme 1).[5]



Scheme 1. Sydnone cycloadditions of alkynes to form pyrazoles.

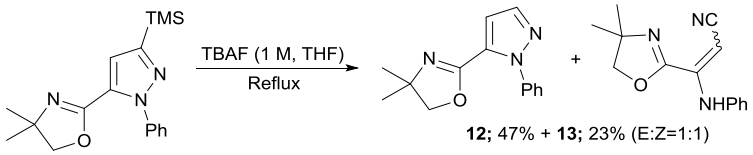
Results and Discussion

1,5-Disubstituted pyrazoles: We initially started our investigations into expanding the scope of the preparation of 1,5-disubstituted pyrazoles. Our strategy was to employ trimethylsilylacetylene as a non-gaseous acetylene equivalent in cycloaddition reactions of 4-substituted sydnones, which were in turn prepared by direct arylation[6] or by metalation chemistry. In all cases attempted, the cycloaddition proceeded efficiently and with high (albeit ultimately inconsequential) regioselectivity favouring the 3-substituted pyrazole (Scheme 2). In contrast, TBAF-mediated removal of the trimethylsilyl group proved somewhat less general. While pyrazoles **2**, **4** and **8** were successfully prepared in good yield (see below for discussion of compound **10**), Weinreb amide-substituted pyrazole **5** only afforded a complex mixture of products. Moreover, in the case of oxazoline-substituted pyrazole **11**, product **12** was afforded in only moderate yield.



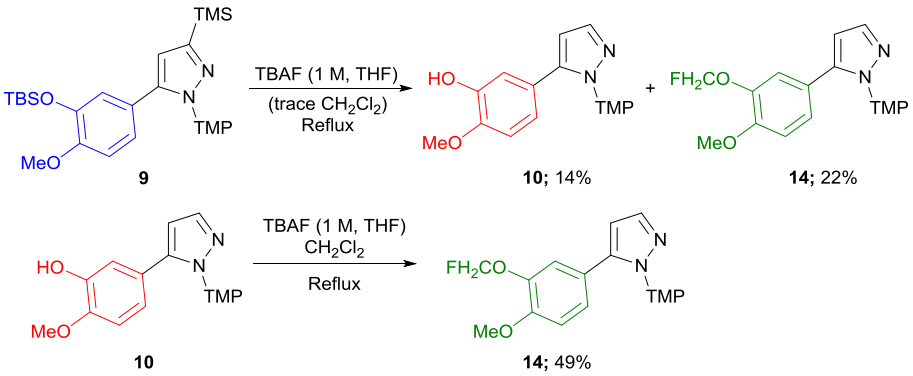
Scheme 2. Preparation of 1,5-disubstituted pyrazoles. [a]R^2 in the starting sydnone was used as the corresponding TBS-ether.

These studies highlighted some unexpected outcomes in the TBAF mediated protodesilylation of 3-trimethylsilylpyrazoles. With regard to the low yield observed in the synthesis of **12**, we were able to isolate (23%, 1:1 E:Z) and characterise a major by-product of this reaction which proved to be nitrile **13** (Scheme 3). The isolation and characterisation of **13** highlights the propensity of electron deficient pyrazoles to undergo elimination under strongly basic conditions.[7]



Scheme 3. TBAF-mediated elimination.

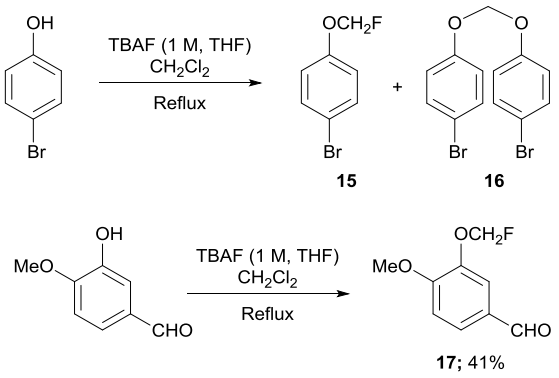
With regard to the conversion of **9**→**10**, we noted that significantly lower yields of product were observed in the presence of CH_2Cl_2 (carried over from chromatography). Specifically, when **9** was subjected to refluxing TBAF, a small amount of **10** was isolated together with mono-fluoromethylated phenol **14**. In addition, fluoromethylation product **14** could be generated in higher yield when the reaction vessel was charged with dichloromethane, TBAF and heated at reflux (Scheme 4).



Scheme 4. TBAF-mediated protodesilylation and monofluoromethylation studies. TMP:3,4,5-$(MeO)_3C_6H_2$.

Current interest in developing methods for the simple incorporation of fluorous hydrocarbons suggested that this method could represent a powerful tool in the synthesis of organofluorine compounds. Monofluoromethyl ethers are much less prevalent in the literature than their

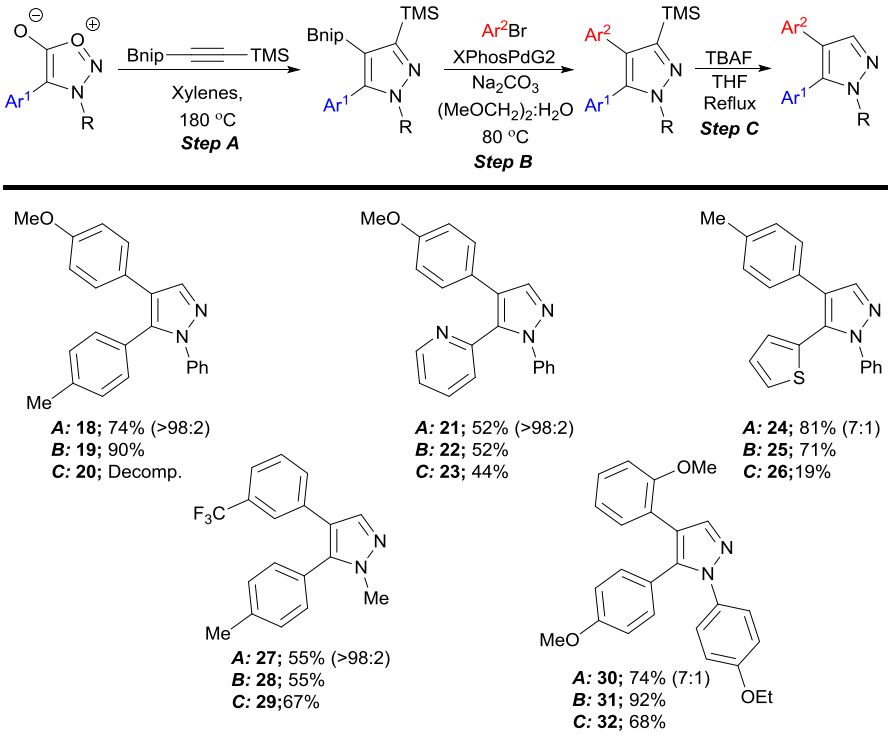
difluoro- and trifluoro- counterparts. However, Hu et al. recently reported the monofluoromethylation of phenols and other nucleophiles using fluoroalkyl sulfoximines.[8] In order to explore the generality of our method for the synthesis of monofluoromethyl ethers, we attempted to repeat the reaction shown in Scheme 4 on 4-bromophenol and 3-hydroxy-4-methoxybenzaldehyde, our results are depicted in Scheme 5. Subjecting 4-bromophenol to TBAF/CH_2Cl_2 led to fluoromethylation product **15**, as judged by ^{1}H NMR analysis of the crude reaction mixture. However, the product was found to be contaminated with the corresponding acetal **16**. Unfortunately, **15** and **16** could not be separated by chromatography. Furthermore, **15** was found to undergo conversion to acetal **16** on various chromatographic supports, or on standing. In this context, the instability of monofluoromethyl ethers has been noted by Hu and Sheng.[8,9] Interestingly however, **17** could be isolated cleanly after chromatography on florisil, albeit in modest yield (Scheme 5). These experiments suggested that the fluoromethyl ether formation outlined here may be useful, but only in cases where the final products undergo slow hydrolysis. Finally, with regard to the mechanism of fluoromethyl ether formation, Zhang et al. have shown that chlorofluoromethane is capable of alkylating phenols.[10] We therefore propose that CH_2Cl_2 and TBAF combine to form FCH_2Cl as an alkylating agent. The potential for fluoromethylation via an interrupted Reimer-Tiemann reaction[11] was discounted as CD_2Cl_2 provided the **d-17** with >95% D-incorporation.



Scheme 5. TBAF-mediated monofluoromethylation of phenols.

1,4,5-Trisubstituted pyrazoles: We next turned our attention to the synthesis of more heavily decorated pyrazoles. We envisaged that an alkynylboronate bearing a trimethylsilyl group could provide general access to 1,4,5-substituted products, assuming appropriate regiochemical insertion of the alkyne. Specifically, the TMS-group could act as a surrogate

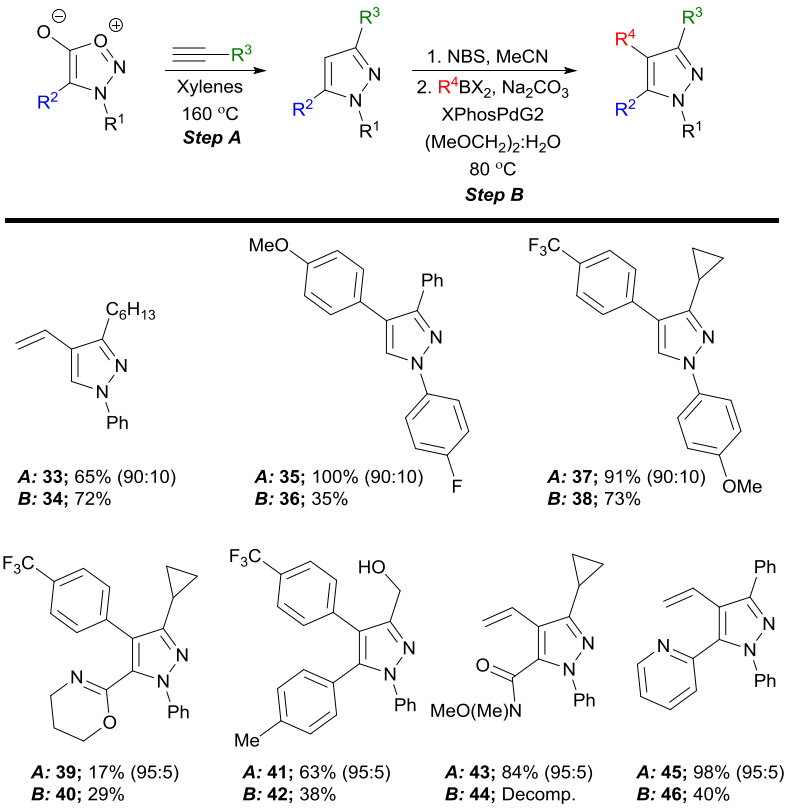
for a C3-H while the boronate would offer a means for diversifying at C4. Our results towards this objective are summarised in Scheme 6. The cycloaddition reactions generally proceeded in moderate to good yield and afforded single regioisomers in the cases of **18**, **21**, and **27**, in a similar manner to our previous report on alkynylboronate cycloadditions.[3(b),(c)] Interestingly, slightly lower regioselectivities were observed for products **24** and **30**, possibly due to the electron rich nature of the sydnone 4-substituents in these cases. Suzuki-Miyaura coupling of the cycloadducts proceeded smoothly for all examples, affording fully-substituted pyrazole cores. TBAF-mediated TMS cleavage successfully furnished products **23**, **29** and **32**, although a particularly low yield was isolated in the case of **26**. Unfortunately, **19** was not a viable substrate for this final step and desilylation resulted in a complex mixture of products.



Scheme 6. Preparation of 1,4,5-disubstituted pyrazoles.

Regiocontrolled 3,4-substituted pyrazole synthesis: Generally speaking, the employment of internal alkynes in sydnone cycloadditions results in a mixture of pyrazole regioisomers.[12] While this issue is somewhat alleviated by the employment of alkynylboronates, sydnones with a C4-substituent are typically required.[3(c)] As terminal alkynes generally undergo highly regioselective cycloadditions with sydnones, we envisioned that a bromination and cross-

coupling sequence would represent a more controlled and predictable strategy for the synthesis of 1,3,4- and 1,3,4,5-substituted pyrazoles. In order to investigate this approach, we subjected a small series of N-arylsydnones to cycloaddition, and these afforded **33**, **35** and **37** in good to high yield and high regioselectivity (Scheme 7). The cycloadducts were then brominated and immediately subjected to Suzuki-Miyaura cross-coupling with boronic acid derivatives. Gratifyingly, the 1,3,4-trisubsubstituted pyrazoles **34**, **36** and **38** were isolated in moderate to good yield. Furthermore, 4-substituted sydnones underwent cycloaddition with terminal alkynes with excellent regioselectivity. In the case of the oxazine-substituted sydnone, a significant amount of decomposition was observed resulting in a very low isolated yield of pyrazole **39**. Subsequent bromination and cross-coupling afforded fully-substituted pyrazoles **40**, **42** and **46**, albeit with generally low yields because of steric hindrance. Unfortunately, Weinreb amide **43** was not stable to the bromination/Suzuki-Miyaura strategy. Overall this strategy provides rapid access to fully-substituted pyrazole cores bearing useful functionality, with near complete control of regiochemistry. A quite diverse range of structures can be installed with predictable regiochemistry.



Scheme 7. Preparation of 1,3,4-trisubstituted- and 1,3,4,5-tetrasubstituted pyrazoles.

Conclusions

We have developed a flexible strategy for the synthesis of a diverse range of pyrazoles with high and predictable regiocontrol. A range of functional groups are tolerant of the cycloaddition conditions and a number of functionalised pyrazoles have been prepared. These studies have highlighted the potential of TBAF-CH_2Cl_2 mixtures to transfer fluoromethyl groups, although the generality of this process appears to be narrow at present due to instability in the resulting products.

Experimental Section

General Procedure A: Preparation of 3,4-diarylsydnones:

A mixture of sydnone (1 eq.), aryl halide (1.5 eq.), palladium acetate (5 mol %), XPhos (10 mol %) and potassium carbonate (2-3 eq.) in DMF (0.25 – 0.5 M) under an atmosphere of nitrogen was heated at 80 - 120 °C for 14 hours before the reaction was allowed to cool to ambient temperature and water was added. The resulting mixture was extracted with ethyl acetate:40-60 petroleum ether (9:1) and the combined organic layers dried over $MgSO_4$ and concentrated in vacuo. Flash silica chromatography (eluting solvent 20%-100% ethyl acetate in 40-60 petroleum ether) afforded the target 3,4-diarylsydnones. The compounds could be further purified by recrystallisation from ethanol or dichloromethane/petrol.

General Procedure B: Cycloadditions of Sydnones with Terminal Alkynes:

A Schlenk tube was charged with sydnone (1 eq.), alkyne (2-4 eq.) and xylenes (1 M). The tube was then sealed and heated at 160 ^{o}C for 24 hours. The mixture was allowed to cool to ambient temperature and loaded onto a short plug of silica and washed with 40-60 petroleum ether before elution with ethyl acetate. Volatiles were removed in vacuo and the crude residue purified by flash silica chromatography (gradient starting with 100% 40-60 petroleum ether and ending with 40% ethyl acetate in 40-60 petroleum ether) affording the target 1,3,5-trisubstituted pyrazoles as major products.

General Procedure C: Trimethylsilyl Group Cleavage:

A flask equipped with a reflux condenser was charged with pyrazole (1 eq.), and TBAF (10 eq. 1 M solution in THF) and heated at reflux under an inert atmosphere of nitrogen for 24 hours. The mixture was allowed to cool to ambient temperature, poured into water and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Flash silica chromatography (gradient starting with 100% 40-60 petroleum ether and ending with 60% ethyl acetate in 40-60 petroleum ether) afforded the target desilated pyrazoles.

General Procedure D: Thermal Cycloaddition of Sydnones with Alkynylboronates:

A Schlenk tube was charged with sydnone (1 eq.), alkyne (2 eq.) and xylenes (1 M). The tube was then sealed and heated at 180 ^{o}C for 48 hours. The mixture was allowed to cool to ambient temperature and loaded onto a short plug of silica and washed with 40-60 petroleum ether before elution with ethyl acetate. Volatiles were removed in vacuo and the crude residue purified by flash silica chromatography (gradient starting with 100% 40-60 petroleum ether and ending with 40% ethyl acetate in 40-60 petroleum ether) affording the target pyrazole boronic esters. The products were isolated as single regioisomers unless otherwise stated and contaminated with small amounts of protodeboronated by-product. ^{13}C NMR spectra of organoboron compounds are missing a signal for the carbon atom directly attached to the boron due to broadening arising from the quadrupolar relaxation effect.

General Procedure E: Suzuki-Miyaura Coupling of Pyrazole Boronic Acid Derivatives:

A flask equipped with a reflux condenser was charged with pyrazole boronic ester (1 eq.), XPhosPdG2 (0.1 eq.), sodium carbonate (2 eq.) and degassed 1,2-dimethoxyethane:water (1:1, 0.1 M) and heated at 80 ^{o}C under an inert atmosphere of nitrogen for 14 hours. The mixture was allowed to cool to ambient temperature, poured into water and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Flash silica chromatography (gradient starting with 100% 40-60 petroleum ether and ending with 40% ethyl acetate in 40-60 petroleum ether) afforded the target cross-coupled pyrazoles as an inseparable mixture of the target material and the product arising from protodeboronation. Only characterisation for the target material is reported.

General Procedure F: Bromination and Subsequent Suzuki-Miyaura Coupling of Pyrazoles:

To a flask containing pyrazole (1 eq.) was added a solution of N-bromosuccinamide (1 eq.) in acetonitrile (0.2 M). The resulting mixture was stirred for one hour at ambient temperature,

before being poured into water. The mixture was extracted with ethyl acetate and the combined organic layers washed with aqueous sodium hydroxide (1 M). The organic layer was dried over $MgSO_4$, filtered and volatiles removed in vacuo. The crude material was concentrated into a flask. The flask was then charged with aryl/vinyl boronate (1.5 eq.), XPhosPdG2 (10 mol %), sodium carbonate (2-3.5 eq.) and thoroughly degassed 1,2-dimethoxyethane:water (1:1, 0.1 M). The mixture was heated at 80 ^{o}C for 14 hours, cooled to ambient temperature, poured into water and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered and volatiles removed in vacuo. Flash silica chromatography (gradient starting with 100% 40-60 petroleum ether and ending with 100% ethyl acetate in 40-60 petroleum ether) afforded the target pyrazoles.

N-Methyl-, N-benzyl-, N-phenyl-, N-(4-methoxyphenyl)-, N-(4-fluorophenyl)-, and N-(3,4,5-trimethoxyphenyl)sydnone were prepared by standard methods (cyclodehydration of N-nitrosoamino acid with trifluoroacetic anhydride).[6] 4-(4-tolyl)-N-methylsydnone[1] and 4-(4-tolyl)-N-phenylsydnone[6] were prepared according to procedures described previously.

4-(3,4,5-Trimethoxyphenyl)-N-(4-methoxyphenyl)sydnone:

Following general procedure A using N-(4-methoxyphenyl)sydnone (100 mg, 0.521 mmol) and 5-bromo-1,2,3-trimethoxybenzene (193 mg, 0.781 mmol), the title compound was isolated as a yellow solid (132 mg, 71%).

M.p.: 155-157 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.65 (6H, s), 3.82 (3H, s), 3.89 (3H, s), 6.55 (2H, s), 7.06 (2H, d, J = 9.0 Hz), 7.44 (2H, d, J = 9.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$): δ 56.0, 56.1, 61.1, 104.2, 107.9, 115.3, 120.0, 126.6, 127.5, 138.5, 153.4, 162.3, 167.1. FTIR: ν_{max} 3116 (w), 3091 (w), 2944 (w), 2841 (w), 1729 (s), 1578 (s), 1125 (s), 991 (m); HRMS calculated for $C_{18}H_{19}N_2O_6$ (ES^+)($+H^+$): 359.1243. Found: 359.1239.

1-(4-Methoxyphenyl)-3-(trimethylsilyl)-5-(3,4,5-trimethoxyphenyl)-pyrazole, **1a** and 1-(4-methoxyphenyl)-4-(trimethylsilyl)-5-(3,4,5-trimethoxyphenyl)-pyrazole **1b**:

Following general procedure B using 4-(3,4,5-trimethoxyphenyl)-N-(4-methoxyphenyl)sydnone (200 mg, 0.558 mmol) and trimethylsilylacetylene (219 mg, 2.23 mmol) in xylenes (0.56 mL), an inseparable mixture of pyrazole **1a** and **1b** was isolated as a brown oil (230 mg, 100%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.36 (9H, s), 3.67 (6H, s), 3.80 (3H, s), 3.84 (3H, s), 6.41 (2H, s), 6.57 (1H, s), 6.87 (2H, d, J = 9.0 Hz), 7.26 (2H, d, J = 9.0 Hz); ^{13}C NMR (101 MHz,

$CDCl_3$) δ -0.8, 55.7, 56.1, 61.1, 106.1, 113.3, 114.2, 126.3, 127.1, 133.8, 137.8, 143.1, 153.1, 153.6, 159.0; FTIR: ν_{max} 2955 (w), 2835 (w), 1584 (m), 1514 (s), 1244 (s), 1125 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{29}N_2O_4Si$: 413.1897. Found: 413.1905.

1-(4-Methoxyphenyl)-5-(3,4,5-trimethoxyphenyl)-pyrazole, **2**:

Following general procedure C using a mixture of pyrazoles **1a** and **1b** (222 mg, 0.539 mmol, 95:5) and and TBAF in THF (5.4 mL, 5.4 mmol), pyrazole **2** was isolated as an orange solid (137 mg, 75%).

M.p.: 92-94 ^oC; ^1H NMR (400 MHz, $CDCl_3$) δ 3.66 (6H, s), 3.80 (3H, s), 3.84 (3H, s), 6.41 (2H, s), 6.47 (1H, d, J = 2.0 Hz), 6.87 (2H, d, J = 9.0 Hz), 7.23 (2H, d, J = 9.0 Hz), 7.67 (1H, d, J = 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.6, 56.1, 61.0, 106.1, 106.9, 114.1, 126.0, 126.9, 133.5, 138.0, 140.0, 142.9, 153.1, 159.0; FTIR: ν_{max} 2931 (w), 2835 (w), 1586 (m), 1514 (s), 1415 (m), 1241 (s), 1121 (s), 1002 (m), 835 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{21}N_2O_4$: 341.1501. Found: 341.1504.

4-(3-Amino-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone:

Following general procedure A using N-(3,4,5-trimethoxyphenyl)sydnone (100 mg, 0.396 mmol) and 5-bromo-2-methoxyaniline (120 mg, 0.595 mmol), the title compound was isolated as an orange solid (135 mg, 91%).

M.p.: 173-174 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.77 (6H, s), 3.80 (3H, s), 3.83 (2H, s), 3.90 (3H, s), 6.52 (1H, dd, J = 8.5, 2.0 Hz), 6.64 (1H, d, J = 8.5 Hz), 6.68 (2H, s), 6.85 (1H, d, J = 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.6, 56.6, 61.2, 102.5, 108.4, 110.2, 113.4, 117.1, 118.1, 130.1, 136.6, 140.5, 147.7, 154.0, 167.2; FTIR: ν_{max} 3471 (w), 3367 (w), 2941 (w), 2838 (w), 1732 (s), 1606 (m), 1224 (s), 1127 (s); HRMS calculated for $C_{18}H_{20}N_3O_6$ $(ES^+)(+H^+)$: 374.1352. Found: 374.1353.

1-(3,4,5-Trimethoxyphenyl)-3-(trimethylsilyl)-5-(3-amino-4-methoxyphenyl)-pyrazole, **3a** and 1-(3,4,5-trimethoxyphenyl)-4-(trimethylsilyl)-5-(3-amino-4-methoxyphenyl)-pyrazole, **3b**:

Following general procedure B using 4-(3-amino-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone (150 mg, 0.402 mmol) and trimethylsilylacetylene (158 mg, 1.61 mmol), an inseparable mixture of pyrazole **3a** and **3b** was isolated as a brown oil (156 mg, 91%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.35 (9H, s), 3.69 (6H, s), 3.76-3.81 (8H, m), 6.50 (1H, s), 6.53-6.58 (3H, m), 6.62 (1H, d, J = 2.0 Hz), 6.67 (1H, d, J = 8.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.9, 55.6, 56.1, 61.0, 103.2, 110.1, 113.5, 115.1, 119.1, 123.7, 136.1, 136.3, 137.1, 143.4, 147.2, 153.1, 153.6; FTIR: ν_{max} 3465 (br), 3372 (br), 2955 (w), 2836 (w), 1598 (m), 1505 (s), 1455 (m), 1418 (m), 1228 (s), 1125 (s), 980 (m), 835 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{30}N_3O_4Si$: 428.2006. Found: 428.2023.

1-(3,4,5-Trimethoxyphenyl)-5-(3-amino-4-methoxyphenyl)-pyrazole, **4**:

Following general procedure C using a mixture of pyrazoles **3a** and **3b** (156 mg, 0.365 mmol) and TBAF in THF (3.7 mL, 3.7 mmol), pyrazole **4** was isolated as a tan crystals (99 mg, 76%).

M.p.: 100-101 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (6H, s), 3.79 (2H, br), 3.84 (3H, s), 3.84 (3H, s), 6.40 (1H, d, J = 2.0 Hz), 6.56 (2H, s), 6.58 (1H, dd, J = 8.5, 2.0 Hz), 6.64 (1H, d, J = 2.0 Hz), 6.70 (1H, d, J = 8.5 Hz), 7.66 (1H, d, J = 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.7, 56.2, 61.1, 102.8, 107.4, 110.2, 115.2, 119.3, 123.5, 136.2, 136.2, 137.1, 140.1, 143.4, 147.4, 153.1; FTIR: ν_{max} 3444 (w), 3346 (w), 3303 (w), 3198 (w), 2934 (w), 2837 (w), 1598 (m), 1500 (s), 1463 (s), 1419 (s), 1229 (s), 1120 (s), 1029 (m), 991 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{22}N_3O_4$: 356.1610. Found: 356.1615.

4-Carboxylic acid-N-phenylsydnone:[13]

To a solution of N-phenylsydnone (3.55 g, 21.9 mmol) in THF (75 mL) at -78 ^{o}C was added a solution of n-butyl lithium (~2.17 M in hexanes, 11.1 mL, 24.1 mmol). The reaction mixture was stirred for 1 hour at -78 ^{o}C. The resulting solution was transferred by cannula to a flask containing excess solid CO_2 and stirred for 1 hour at -78 ^{o}C. The reaction was allowed to warm to room temperature (**caution extra venting required**) and stirred for a further 2 hours. The reaction was poured into water and the aqueous layer washed with ethyl acetate. The aqueous layer was then acidified to pH 1 and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$, filtered, and volatiles removed in vacuo to afford the title compound as an orange solid (4.11 g, 91%). The product could be further purified by recrystallisation from ethanol.

M.p.: 190-191 °C (lit.[13] 193 ^{o}C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56-7.83 (5H, m), 13.37 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 100.7, 125.7, 129.2, 132.0, 135.3, 157.9, 164.5; FTIR: ν_{max} 2944 (br), 2558 (br), 2159 (br), 2031 (w), 1807 (s), 1674 (s), 1489 (s), 1308 (m),

1212 (s), 1063 (m), 1027 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_9H_7N_2O_4$: 207.0406. Found: 207.0413.

4-[(N-Methoxy-N-methyl)amide]-N-phenylsydnone:

To a solution of 4-carboxylic acid-N-phenylsydnone (500 mg, 2.43 mmol) in CH_2Cl_2 (10 mL) at 0 ^oC was added oxalyl chloride (924 mg, 7.28 mmol) and DMF (3 drops) and the mixture stirred for 10 minutes at 0 ^oC. The reaction was allowed to warm to room temperature and stirred for a further 3 hours. Volatiles were then removed in vacuo and the resulting yellow solid dissolved in CH_2Cl_2 (10 mL). Triethylamine (541 mg, 5.35 mmol) and N,O-dimethylhydroxylamine hydrogen chloride (284 mg, 2.92 mmol) were added at 0 ^oC and the reaction stirred for 14 hours at RT. The reaction was poured into water, extracted with CH_2Cl_2, the combined organic layers were dried over $MgSO_4$ and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (gradient 100% 40-60 petroleum ether to 60% ethyl acetate) affording the title compound as a yellow oil (394 mg, 65%).

^1H NMR (400 MHz, $CDCl_3$) δ 3.28 (3H, s), 3.86 (3H, s), 7.50-7.61 (4H, m), 7.61-7.69 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 33.3, 62.2, 102.8, 124.0, 129.7, 132.3, 134.7, 157.3, 164.4; FTIR: ν_{max} 1765 (s), 1651 (m), 1480 (m), 1443 (w), 1269 (w), 1173 (w), 1051 (w), 990 (w); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{11}H_{11}N_3O_4$: 250.0822. Found: 250.0821.

1-(Phenyl)-3-(trimethylsilyl)-5-[(N-Methoxy-N-methyl)amide]-pyrazole, **5a** and 1-(phenyl)-4-(trimethylsilyl)-5-[(N-Methoxy-N-methyl)amide]-pyrazole, **5b**:

Following general procedure B using 4-[(N-methoxy-N-methyl)amide]-N-phenylsydnone (213 mg, 0.855 mmol) and trimethylsilylacetylene (336 mg, 3.42 mmol), an inseparable mixture of pyrazole **5a** and **5b** was isolated as an orange oil (231 mg, 89%, >95:5).

^1H NMR (400 MHz, $CDCl_3$) δ 0.34 (9H, s), 3.18 (3H, s), 3.53 (3H, s), 6.79 (1H, s), 7.31-7.39 (1H, m), 7.40-7.46 (2H, m), 7.47-7.53 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -1.0, 33.6, 61.5, 115.1, 123.8, 127.9, 129.2, 135.3, 140.5, 154.0, 162.4; FTIR: ν_{max} 2954 (w), 1650 (m), 1599 (m), 1499 (m), 1310 (m), 1113 (m), 977 (w), 836 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{15}H_{21}N_3O_2Si$: 304.1476. Found: 304.1481.

4-(3-trifluoromethylphenyl)-N-benzylsydnone:

Following general procedure A using N-benzylsydnone (500 mg, 2.84 mmol) and 3-bromotrifluoromethyl benzene (958 mg, 4.26 mmol), the title compound was isolated as a colourless solid (342 mg, 38%).

M.p.: 81-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 (2H, s), 7.15-725 (2H, m), 7.34-7.45 (3H, m), 7.50-7.60 (2H, m), 7.60-7.72 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.1, 106.4, 123.6 (q, J = 272.5 Hz), 125.1 (q, J = 3.5 Hz), 125.4, 126.1 (q, J = 3.5 Hz), 127.6, 129.6, 129.86, 129.91, 130.9, 131.65 (q, J = 33.0 Hz), 131.68, 167.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.9; FTIR: ν_{max} 2954 (w), 1732 (s), 1524 (m), 1432 (m), 1360 (m), 1321 (m), 1159 (s), 1112 (s), 1005 (s), 907 (s), 815 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{16}H_{12}F_3N_2O_2$: 321.0845. Found: 321.0848.

1-(Benzyl)-3-(trimethylsilyl)-5-(3-trifluoromethylphenyl)-pyrazole, **7a** and 1-(benzyl)-4-(trimethylsilyl)-5-(3-trifluoromethylphenyl)-pyrazole, **7b**:

Following general procedure B using 4-(3-trifluoromethylphenyl)-N-benzylsydnone (99 mg, 0.31 mmol) and trimethylsilylacetylene (104 mg, 1.06 mmol), an inseparable mixture of pyrazole **7a** and **7b** was isolated as an orange oil (89 mg, 77%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.36 (9H, s), 5.40 (2H, s), 6.50 (1H, s), 7.01 (2H, d, J = 6.5 Hz), 7.20-7.30 (3H, m), 7.40-7.51 (3H, m), 7.60 (1H, d, J = 7.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.9, 53.7, 113.7, 122.6 (s, q not distinguishable), 125.1 (q, J = 3.5 Hz), 125.8 (q, J = 3.5 Hz), 126.8, 127.7, 128.8, 129.2, 131.0 (q, J = 32.5 Hz), 131.9, 132.1, 137.6, 142.5, 153.0; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.3; FTIR: ν_{max} 2958 (w), 1455 (m), 1311 (s), 1248 (m), 1167 (s), 1125 (s), 1073 (s), 983 (m), 837 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{21}F_3N_2Si$: 375.1499. Found: 375.1508.

1-(Benzyl)- 5-(3-trifluoromethylphenyl)-pyrazole, **8**:

Following general procedure C using a mixture of pyrazoles **7a** and **7b** (81 mg, 0.22 mmol) and TBAF in THF (2.2 mL, 2.2 mmol), pyrazole **8** was isolated as a yellow oil (45 mg, 69%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 (2H, s), 6.40 (1H, d, J = 2.0 Hz), 7.01-7.10 (2H, m), 7.23-7.34 (3H, m), 7.46-7.57 (3H, m), 7.61-7.68 (2H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 53.7, 107.2, 123.9 (q, J = 272.5 Hz), 125.5 (q, J = 3.5 Hz), 126.0 (q, J = 3.5 Hz), 126.9, 127.9, 128.9, 129.3, 131.3 (q, J = 32.5 Hz), 131.6, 132.3, 137.3, 139.4, 142.6; ^{19}F NMR (377

MHz, $CDCl_3$) δ -62.8; FTIR: ν_{max} 2668 (w), 1340 (m), 1321 (s), 1166 (s), 1118 (s), 1072 (s), 928 (m), 906 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{13}F_3N_2$: 303.1104. Found: 303.1107.

4-(3-Hydroxy-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone:

Following general procedure A using N-(3,4,5-trimethoxyphenyl)sydnone (500 mg, 1.98 mmol) and 5-bromo-2-methoxyphenol (604 mg, 2.97 mmol). Flash silica chromatography (eluting solvent 10%-30% ethyl acetate in dichloromethane) afforded the title compound as a yellow solid (599 mg, 81%).

M.p.: 237-239 °C (dec.); ^{1}H NMR (400 MHz, DMSO-d_6): δ 3.73 (9H, s), 3.76 (3H, s), 6.71 (1H, dd, J = 8.5, 2.0 Hz), 6.88 (1H, d, J = 2.0 Hz), 6.91 (1H, d, J = 8.5 Hz), 7.13 (2H, s), 9.28 (1H, s); ^{13}C NMR (101 MHz, DMSO-d_6): δ 55.5, 56.5, 60.4, 103.9, 108.1, 112.0, 114.1, 117.0, 118.5, 129.9, 139.8, 146.3, 148.1, 153.5, 166.2; FTIR: ν_{max} 3415 (br), 3062 (w), 2947 (w), 1718 (s), 1605 (m), 1243 (s), 1125 (s), 1014 (s), 949 (m); HRMS calculated for $C_{18}H_{19}N_2O_7$ (ES^+)($+H^+$): 375.1192. Found: 375.1192.

4-(3-[(Tert-butyldimethylsilyl)oxy]-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone:

To a solution of 4-(3-hydroxy-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone (200 mg, 0.535 mmol) and TBSCl (161 mg, 1.07 mmol) in DMF (2 mL), under an atmosphere of nitrogen, was added DIPEA (138 mg, 1.07 mmol) and the reaction stirred at room temperature for 14 hours. Aqueous NH_4Cl was added and the mixture extracted with ethyl acetate. The organic phase was dried over $MgSO_4$ and the volatiles were removed in vacuo. Flash silica chromatography (gradient 100% 40-60 petroleum ether to 40% ethyl acetate) afforded the title compound as an orange solid (211 mg, 81%).

M.p.: 97-98 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.03 (6H, s), 0.90 (9H, s), 3.79 (6H, s), 3.80 (3H, s), 3.91 (3H, s), 6.67 (1H, d, J = 2.5 Hz), 6.68 (2H, s), 6.82 (1H, d, J = 8.5 Hz), 7.18 (1H, dd, J = 8.5, 2.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -4.7, 18.4, 25.7, 55.6, 56.6, 61.2, 102.6, 108.1, 112.2, 117.1, 119.7, 121.6, 130.1, 140.7, 145.1, 151.8, 154.2, 167.1; FTIR: ν_{max} 2933 (w), 1729 (m), 1606 (m), 1460 (m), 1225 (s), 1125 (s), 1015 (m), 999 (m), 946 (m), 837 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{24}H_{33}N_2O_7Si$: 489.2057. Found: 489.2081.

1-(3,4,5-Trimethoxyphenyl)-3-(trimethylsilyl)-5-(3-[(tert-butyldimethylsilyl)oxy]-4-methoxyphenyl)-pyrazole, **9a** and 1-(3,4,5-trimethoxyphenyl)-4-(trimethylsilyl)-5-(3-[(tert-butyldimethylsilyl)oxy]-4-methoxyphenyl) -pyrazole, **9b**:

Following general procedure B using 4-(3-[(tert-butyldimethylsilyl)oxy]-4-methoxyphenyl)-N-(3,4,5-trimethoxyphenyl)sydnone (150 mg, 0.307 mmol) and trimethylsilylacetylene (121 mg, 1.23 mmol), an inseparable mixture of pyrazoles **9a** and **9b** was isolated as a clear oil (136 mg, 82%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01 (6H, s), 0.35 (9H, s), 0.90 (9H, s), 3.70 (6H, s), 3.79 (3H, s), 3.81 (3H, s), 6.52 (1H, s), 6.54 (2H, s), 6.68 (1H, d, J = 2.0 Hz), 6.79 (1H, d, J = 8.5 Hz), 6.87 (1H, dd, J = 8.5, 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -4.8, -0.9, 18.4, 25.7, 55.6, 56.1, 61.0, 103.3, 111.8, 113.4, 121.4, 122.4, 123.6, 136.2, 137.2, 143.0, 144.8, 151.1, 153.2, 153.7; FTIR: ν_{max} 2954 (w), 2930 (w), 2857 (w), 1598 (m), 1496 (m), 1463 (m), 1415 (m), 1229 (s), 1127 (s), 1007 (m), 979 (m) 980 (m), 937 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{28}H_{43}N_2O_5Si_2$: 543.2711. Found: 543.2728.

1-(3,4,5-Trimethoxyphenyl)-5-(3-hydroxy-4-methoxyphenyl)-pyrazole, **10** and 1-(3,4,5-trimethoxyphenyl)-5-(3-fluoromethoxy-4-methoxyphenyl)-pyrazole, **14**:

Following general procedure C using a mixture of pyrazoles **9a** and **9b** (131 mg, 0.241 mmol, 95:5) and TBAF in THF (2.4 mL, 2.4 mmol), pyrazole **10** was isolated as a colourless solid (12 mg, 14%) and pyrazole **14** was isolated as a clear oil (21 mg, 22%).

10: M.p.: 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.68 (6H, s), 3.83 (3H, s), 3.86 (3H, s), 5.99 (1H, br), 6.42 (1H, d, J = 2.0 Hz), 6.53 (2H, s), 6.69 (1H, dd, J = 8.5, 2.0 Hz), 6.76 (1H, d, J = 8.5, Hz), 6.87 (1H, d, J = 2.0, Hz), 7.65 (1H, d, J = 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.0, 56.2, 61.1, 102.9, 107.9, 110.6, 115.2, 121.0, 123.8, 135.9, 137.2, 140.1, 142.9, 145.6, 146.8, 153.1; FTIR: ν_{max} 3133 (br), 2933 (w), 2840 (w), 1601 (m), 1499 (s), 1458 (m), 1420 (m), 1272 (m), 1232 (s), 1118 (s), 1010 (m), 1002 (m), 933 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{19}H_{21}N_2O_5$: 357.1445. Found: 357.1446.

14: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.70 (6H, d, J = 1.5 Hz), 3.84 (3H, d, J = 1.5 Hz), 3.88 (3H, d, J = 1.5 Hz), 5.58 (2H, dd, J = 54.5, 1.5 Hz), 6.48 (1H, t, J = 1.5 Hz), 6.53 (2H, d, J = 1.5 Hz), 6.88 (1H, dd, J = 8.5, 1.5 Hz), 6.98-7.05 (2H, m), 7.69 (1H, t, J = 1.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.2, 56.3, 61.1, 101.4 (d, J = 220.5 Hz), 103.2, 107.3, 112.1, 118.3, 123.4, 125.0, 135.8, 137.5, 140.2, 142.3, 145.4, 149.9, 153.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -149.1 (t, J = 54 Hz); FTIR: ν_{max} 2933 (w), 2838 (w), 1598 (m), 1505 (s), 1455 (m), 1417 (m), 1229 (s), 1119 (s), 1002 (m), 972 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{22}N_2O_5F$: 389.1513. Found: 389.1499.

1-(3,4,5-Trimethoxyphenyl)-5-(3-hydroxy-4-methoxyphenyl)-pyrazole, **10**:

Following general procedure C a mixture of pyrazoles **9a** and **9b** (100 mg, 0.184 mmol) and TBAF in THF (1.8 mL, 1.8 mmol), pyrazole **10** was isolated as a colourless solid (46 mg, 70%).

See above for characterisation data.

4-[N-(2-Hydroxy-1,1-dimethylethyl)amide]-N-phenylsydnone:

To a solution of 4-carboxylic acid-N-phenylsydnone (825 mg, 4.00 mmol) in CH_2Cl_2 (40 mL) at 0 ^oC was added oxalyl chloride (1.52 g, 12.0 mmol) and DMF (3 drops) and the mixture stirred for 10 minutes at 0 ^oC. The reaction was allowed to warm to room temperature and stirred for a further 3 hours. Volatiles were then removed in vacuo and the resulting yellow solid dissolved in CH_2Cl_2 (40 mL). Triethylamine (486 mg, 4.80 mmol) and 2-amino-2-methylpropanol (428 mg, 4.80 mmol) were added at 0 ^oC and the reaction stirred for 14 hours at RT. The reaction was poured into water, extracted with CH_2Cl_2, the combined organic layers were dried over $MgSO_4$ and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (eluting solvent 100% ethyl acetate) affording the title compound as a yellow solid (975 mg, 88%). The product could be further purified by recrystallisation from CH_2Cl_2/petrol.

M.p.: 184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (6H, s), 3.59 (2H, s), 4.03 (1H, br), 7.42 – 7.86 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 24.7, 56.8, 70.2, 102.2, 125.3, 129.4, 132.5, 134.6, 155.9, 167.3; FTIR: ν_{max} 3318 (br), 1751 (s), 1675 (s), 1494 (w), 1303 (w), 1059 (w); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{13}H_{16}N_3O_4$: 278.1141. Found: 278.1148.

4-(4,4-Dimethyl-2-oxazoline)-N-phenylsydnone:

Triethylamine (5.28 g, 52.2 mmol) and carbon tetrachloride (12.3 g, 80.0 mmol) were added respectively to a suspension of 4-[N-(2-hydroxy-1,1-dimethylethyl)amide]-N-phenylsydnone (964 mg, 3.48 mmol) and triphenylphosphine (3.65 g, 13.9 mmol) in acetonitrile (17 mL) at ambient temperature. The reaction was allowed to stir for 2 h before being diluted with ethyl acetate and washed with aqueous sodium hydrogen carbonate. The aqueous layer was extracted with ethyl acetate, the organics combined, dried over magnesium sulfate and the solvent removed in vacuo. The resulting residue was purified by flash silica chromatography (gradient 0 – 60% ethyl acetate in 40/60 petroleum ether) affording the title compound as a yellow solid (475 mg, 53%).

M.p.: 131-133 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, s), 3.87 (2H, s), 7.43 – 7.71 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.1, 68.2, 79.0, 98.8, 125.1, 129.5, 132.5, 135.0, 151.0, 165.5; FTIR: ν_{max} 1785 (s), 1754 (m), 1658 (m), 1485 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{13}H_{14}N_3O_3$: 260.1035. Found: 260.1039.

1-(Phenyl)-3-(trimethylsilyl)-5-(4,4-dimethyl-2-oxazoline)-pyrazole, **11a** and 1-(phenyl)-4-(trimethylsilyl)-5-(4,4-dimethyl-2-oxazoline)-pyrazole, **11b**:

Following general procedure B using 4-(4,4-dimethyl-2-oxazoline)-N-phenylsydnone (98 mg, 0.38 mmol) and trimethylsilylacetylene (149 mg, 1.51 mmol), an inseparable mixture of pyrazole **11a** and **11b** was isolated as an orange oil (103 mg, 87%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.31 (9H, s), 1.32 (6H, s), 3.94 (2H, s), 7.08 (1H, s), 7.34-7.51 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -1.0, 28.1, 67.8, 79.3, 118.0, 125.3, 128.1, 128.6, 131.6, 140.6, 154.2, 155.3; FTIR: ν_{max} 2961 (w), 2896 (w), 1667.0 (m), 1599 (m), 1500 (m), 1312 (m), 1248 (m), 1192 (m), 1068 (s), 1006 (m), 979 (m), 837 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{23}N_3OSi$: 314.1683. Found: 314.1696.

1-(Phenyl)-5-(4,4-dimethyl-2-oxazoline)-pyrazole, **12** and 3-(phenylamino)-3-(4,4-dimethyl-2-oxazoline)-2-propenenitrile (E+Z), **13**:

Following general procedure C using a mixture of pyrazoles **11a** and **11b** (102 mg, 0.325 mmol) and TBAF in THF (3.3 mL, 3.3 mmol), pyrazole **12** was isolated as an orange oil (37 mg, 47%) and nitrile **13** was isolated as an orange oil (18 mg, 23%, E:Z ~1:1).

`12: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (6H, s), 3.93 (2H, s), 6.89 (1H, d, J = 2.0 Hz), 7.35-7.48 (5H, m), 7.68 (1H, d, J = 2.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.0, 68.0, 79.2, 111.1, 125.1, 128.2, 128.6, 129.9, 131.5, 140.2, 154.7; FTIR: ν_{max} 2965 (w), 1662 (m), 1588 (s), 1499 (s), 1394 (m), 1355 (m), 1289 (m), 1084 (m), 999 (s), 955 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{14}H_{16}N_3O$: 242.1288. Found: 242.1290.

13 (1:1 mixture of E/Z isomers): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (3H, s), 1.38 (3H, s), 4.14 (1H, s), 4.29 (1H, s), 4.92 (0.5H, d, J = 1.5 Hz), 4.95 (0.5H, d, J = 1.5 Hz), 7.14 (0.5H, br), 7.15-7.25 (3.5H, m), 7.39 (1H, t, J = 7.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 28.3, 67.4, 68.3, 68.6, 69.0, 80.7, 81.2, 116.8, 118.7, 123.7, 125.0, 126.0, 126.5, 129.0, 129.9, 137.5, 137.9, 142.8, 144.3, 158.9, 159.2; FTIR: ν_{max} 2974 (w), 2200 (w), 1681 (m), 1587 (s), 1495 (m), 1448 (m), 1366 (m), 1300 (m), 962 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{14}H_{16}N_3O$: 242.1288. Found: 242.1288.

1-(3,4,5-Trimethoxyphenyl)-5-(3-hydroxy-4-methoxyphenyl)-pyrazole, **14**:

A flask was charged with pyrazole **10** (51 mg, 0.14 mmol), CH_2Cl_2 (0.5 mL) and TBAF in THF (1 M, 1.5 mL, 1.5 mmol) and the reaction heated at reflux for 14 h. The reaction was allowed to cool to ambient temperature and poured into aq. $NaHCO_3$, extracted with ethyl acetate and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (gradient 100% petroleum ether – 60% ethyl acetate in petroleum ether) affording **14** as a colourless oil (27 mg, 49%) and recovered pyrazole **10** (13 mg, 25%).

See above for characterisation data.

1-Bromo-4-fluoromethoxybenzene, **15** and 1,1'-[methylenebis(oxy)]bis[4-bromobenzene] **16**:[14]

A flask was charged with 4-bromophenol (100 mg, 0.585 mmol), CH_2Cl_2 (0.5 mL) and TBAF in THF (1 M, 6 mL, 6 mmol) and the reaction heated at reflux for 14 h. The reaction was allowed to cool to ambient temperature and poured into aq. $NaHCO_3$, extracted with ethyl acetate and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (gradient 100% petroleum ether – 10% ethyl acetate in petroleum ether) affording a mixture of **15** and **16** as a colourless oil (20 mg, 17%, 85:15). The mixture was characterised by ^1H and ^{19}F NMR only.

^1H NMR (400 MHz, $CDCl_3$) δ 5.68 (2H, d, J = 54.5 Hz), 6.91-7.04 (2H, m), 7.38-7.48 (2H, m); ^{19}F NMR (128 MHz, $CDCl_3$) δ -149.1 (t, J = 54.5 Hz).

3-Fluoromethoxy-4-methoxybenzaldehydebenzene, **17**:

A flask was charged with 3-hydroxy-4-methoxybenzaldehyde (50 mg, 0.33 mmol), CH_2Cl_2 (0.5 mL) and TBAF in THF (1 M, 3.3 mL, 3.3 mmol) and the reaction heated at reflux for 14 h. The reaction was allowed to cool to ambient temperature and poured into aq. $NaHCO_3$, extracted with ethyl acetate and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (gradient 100% petroleum ether – 40% ethyl acetate in petroleum ether) affording **17** as a colourless solid (25 mg, 41%).

M.p.: 59-61 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 3.97 (3H, s), 5.77 (2H, d, J = 54.0 Hz), 7.05 (1H, d, J = 8.5 Hz), 7.63 (1H, d, J = 8.5, 2.0 Hz), 7.66-7.67 (1H, m), 9.86 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.4, 101.0 (d, J = 221.0 Hz), 111.8, 116.4, 128.5, 130.2, 146.3 (d, J = 2.5 Hz), 155.1, 190.5; ^{19}F NMR (128 MHz, $CDCl_3$) δ -149.8 (t, J = 54.0 Hz); FTIR: ν_{max}

1686 (s), 1601 (m), 1587 (m), 1508 (s), 1439 (s), 1404 (m), 1262 (s), 1228 (s), 1173 (m), 1135 (s), 1079 (m), 1016 (s), 943 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_9H_9FO_3$: 184.0530. Found: 184.0526.

A flask was charged with 3-hydroxy-4-methoxybenzaldehyde (50 mg, 0.33 mmol), CH_2Cl_2 (0.5 mL) THF (3.3 mL) and the reaction heated at reflux for 14 h. The reaction was allowed to cool to ambient temperature and volatiles removed in vacuo, resulting in the recovery of starting material.

3-(1-Fluoro-1,1-dideuteromethoxy)-4-methoxybenzaldehydebenzene, d-**17**:

A flask was charged with 3-hydroxy-4-methoxybenzaldehyde (50 mg, 0.33 mmol), CD_2Cl_2 (0.5 mL) and TBAF in THF (1 M, 3.3 mL, 3.3 mmol) and the reaction heated at reflux for 14 h. The reaction was allowed to cool to ambient temperature and poured into aq. $NaHCO_3$, extracted with ethyl acetate and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (gradient 100% petroleum ether – 40% ethyl acetate in petroleum ether) affording d-**17** as a colourless solid (19 mg, 31%).

M.p.: 57-59 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.97 (3H, s), 7.05 (1H, d, J = 8.5 Hz), 7.64 (2H, m), 9.86 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 56.4, 98.5-102.1 (m), 111.8, 116.3, 128.5, 130.2, 146.3, 155.1, 190.5; ^{19}F NMR (128 MHz, $CDCl_3$) δ -151.1- -151.2 (m); FTIR: ν_{max} 1690 (s), 1603 (m), 1587 (m), 1508 (s), 1435 (s), 1266 (s), 1164 (m), 1129 (s), 1016 (s), 916 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_9H_7D_2FO_3$: 187.0734. Found: 187.0734.

1-(Phenyl)-3-(trimethylsilyl)-4-(pinacolatoborolane)-5-(4-tolyl)-pyrazole, **18**:[15]

Following general procedure D using 4-(4-tolyl)-N-phenylsydnone (200 mg, 0.793 mmol) and 4,4,5,5-tetramethyl-2-[2-(trimethylsilyl)ethynyl]-1,3,2-dioxaborolane (356 mg, 1.59 mmol), pyrazole **18** was isolated as a tan solid (187 mg, 74%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.41 (9H, s), 1.24 (12H, s), 2.34 (3H, s), 7.05 (2H, d, J = 8.0 Hz), 7.11 (2H, d, J = 8.0 Hz), 7.19-7.28 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.4, 21.5, 25.0, 83.2, 114.1, 125.5, 127.0, 128.4, 128.7, 130.6, 137.8, 140.3, 150.0, 159.6.

1-(Phenyl)-3-(trimethylsilyl)-4-(4-methoxyphenyl)-5-(4-tolyl)-pyrazole, **19**:

Following general procedure E using pyrazole **18** (200 mg, 0.462 mmol) and 4-bromoanisole (130 mg, 0.694 mmol), pyrazole **19** was isolated as a yellow solid (172 mg, 90%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.22 (9H, s), 2.27 (3H, s), 3.81 (3H, s), 6.82 (2H, d, J = 9.0 Hz), 6.89 (2H, d, J = 8.0 Hz), 6.97 (2H, d, J = 8.0 Hz), 7.10 (2H, d, J = 9.0 Hz), 7.21-7.34 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.3, 21.4, 55.2, 110.7, 113.4, 114.3, 119.5, 120.4, 125.2, 127.0, 128.8, 129.0, 130.2, 131.8, 137.5, 140.6, 152.6, 158.5; FTIR: ν_{max} 3050 (w), 2955 (w), 1598 (m), 1520 (m), 1492 (m), 1449 (s), 1325 (m), 1243 (s), 1037 (m), 990 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{26}H_{29}N_2OSi$: 413.2044. Found: 413.2042.

4-(2-Pyridyl)-N-phenylsydnone:[16]

Following general procedure A using N-phenylsydnone (1.50 g, 9.25 mmol) and 2-bromopyridine (2.19 g, 13.9 mmol), the title compound was isolated as colourless crystals (2.19 g, 99%).

M.p.: 111-112 °C (lit.[16] 142-143 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (1H, ddd, J = 7.5, 5.0, 1.0 Hz), 7.46-7.58 (4H, m), 7.60-7.66 (1H, m), 7.74 (1H, td, J = 8.0, 2.0 Hz), 8.09 (1H, dt, J = 8.0, 1.0 Hz), 8.23 (1H, ddd, J = 5.0, 2.0, 1.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 107.1, 121.8, 122.7, 125.1, 129.3, 131.6, 136.0, 136.8, 144.9, 149.1, 167.1.

1-(Phenyl)-3-(trimethylsilyl)-4-(pinacolatoborolane)-5-(2-pyridyl)-pyrazole, **21**:

Following general procedure D using 4-(2-pyridyl)-N-phenylsydnone (200 mg, 0.836 mmol) and 4,4,5,5-tetramethyl-2-[2-(trimethylsilyl)ethynyl]-1,3,2-dioxaborolane (375 mg, 1.67 mmol), pyrazole **21** was isolated as a yellow solid (184 mg, 52%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.41 (9H, s), 1.22 (12H, s), 7.16-7.28 (7H, m), 7.57 (1H, td, J = 7.5, 2.0 Hz), 8.56 (1H, ddd, J = 5.0, 2.0, 1.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.5, 25.1, 83.3, 115.4, 122.7, 125.2, 125.6, 127.2, 128.8, 135.5, 140.3, 149.1, 151.1, 159.5; FTIR: ν_{max} 2971 (w), 1593 (m), 1496 (m), 1410 (m), 1312 (m), 1140 (m), 1043 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{31}{}^{11}BN_3O_2Si$: 419.2309. Found: 419.2311.

1-(Phenyl)-3-(trimethylsilyl)-4-(4-methoxyphenyl)-5-(2-pyridyl)-pyrazole, **22**:

Following general procedure E using pyrazole **21** (158 mg, 0.377 mmol) and 4-bromoanisole (106 mg, 0.565 mmol), pyrazole **22** was isolated as a yellow solid (90 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.20 (9H, s), 3.80 (3H, s), 6.81 (2H, d, J = 9.0 Hz) 7.05 (1H, dt, J = 8.0, 1.0 Hz), 7.07-7.15 (3H, m), 7.20-7.25 (1H, m), 7.26-7.30 (4H, m), 7.50 (1H, td, J = 7.5, 2.0 Hz), 8.45 (1H, ddd, J = 5.0, 2.0, 1.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.3, 55.2, 113.4, 122.4, 124.8, 125.7, 126.6, 127.0, 128.7, 130.7, 131.7, 136.0, 139.3, 140.6, 149.7,

150.4, 152.6, 158.7; FTIR: ν_{max} 3047 (w), 2965 (w), 2836 (w), 1584 (m), 1500 (m), 1246 (s), 1175 (m), 1034 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{24}H_{26}N_3OSi$: 400.1840. Found: 400.1848

1-(Phenyl)-4-(4-methoxyphenyl)-5-(2-pyridyl)-pyrazole, **23**:

Following general procedure C using pyrazole **22** (83 mg, 0.21 mmol) and TBAF in THF (2.1 mL, 2.1 mmol), pyrazole **23** was isolated as a yellow crystalline solid (30 mg, 44%).

M.p.: 138-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.81 (3H, s), 6.60 (2H, d, J = 7.5 Hz), 6.75 (1H, s), 6.90 (2H, d, J = 9.0 Hz), 7.06-7.11 (2H, m), 7.33 (1H, ddd, J = 6.0, 5.0, 2.5 Hz), 7.45 (2H, d, J = 9.0 Hz), 7.67-7.76 (2H, m), 8.72 (1H, dt, J = 5.0, 1.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.5, 91.4, 114.8, 120.7, 121.2, 123.2, 124.8, 125.3, 125.6, 129.0, 130.1, 136.9, 140.4, 150.0, 151.3, 152.5, 159.5; FTIR: ν_{max} 2925 (w), 1580 (m), 1509 (s), 1377 (m), 1282 (m), 1109 (s), 944 (s),; HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{21}H_{17}N_3O$: 328.1444. Found: 328.1449.

4-(2-Thiophenyl)-N-phenylsydnone:

Following general procedure A using N-phenylsydnone (500 mg, 3.08 mmol) and 2-chlorothiophene (549 mg, 4.63 mmol), the title compound was isolated as a yellow solid (636 mg, 85%).

M.p.: 168-170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (1H, dd, J = 5.0, 4.0 Hz), 7.24 (1H, dd, J = 5.0, 1.0 Hz), 7.29 (1H, dd, J = 4.0, 1.0 Hz), 7.55-7.60 (2H, m), 7.64-7.70 (2H, m), 7.73-7.80 (1H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 106.5, 125.6, 126.0, 126.3, 126.6, 127.6, 130.4, 132.8, 133.9, 165.9; FTIR: ν_{max} 3108 (w), 3077 (w), 1725 (s), 1703 (m), 1250 (s), 1046 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{12}H_9N_2O_2S$: 245.0385. Found: 245.0376.

1-(Phenyl)-3-(trimethylsilyl)-4-(pinacolatoborolane)-5-(2-thiophenyl)-pyrazole, **24a** and 1-(Phenyl)-3-(pinacolatoborolane)-4-(trimethylsilyl)-5-(2-thiophenyl)-pyrazole, **24b**:

Following general procedure D using 4-(2-thiophenyl)-N-phenylsydnone (200 mg, 0.819 mmol) and 4,4,5,5-tetramethyl-2-[2-(trimethylsilyl)ethynyl]-1,3,2-dioxaborolane (367 mg, 1.64 mmol), pyrazole **24a** isolated as a yellow solid (221 mg, 64%) and pyrazole **24b** was isolated as a brown oil (21 mg, 6%).

24a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.42 (9H, s), 1.27 (12H, s), 6.95 (1H, dd, J = 5.0, 3.5 Hz), 7.00 (1H, dd, J = 3.5, 1.0 Hz), 7.25-7.33 (6H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.4, 25.0, 83.4, 125.7, 126.5, 127.3, 127.6, 128.8, 129.9, 131.5, 140.1, 143.0, 159.8; FTIR: ν_{max} 2979 (w), 1596 (w), 1496 (s), 1440 (m), 1317 (m), 1241 (s), 1137 (s), 1020 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{30}{}^{11}BN_2O_2SSi$: 424.1921. Found: 424.1923.

24b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (9H, s), 1.38 (12H, s), 6.91 (1H, dd, J = 3.5, 1.0 Hz), 6.95 (1H, dd, J = 5.0, 3.5 Hz), 7.22-7.33 (6H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.5, 25.1, 84.2, 125.1, 126.0, 126.7, 127.7, 127.9, 128.5, 130.8, 132.5, 139.9, 141.1; FTIR: ν_{max} 2976 (w), 1598 (w), 1456 (m), 1245 (s), 1221 (m), 1137 (s), 1030 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{28}H_{30}{}^{11}BN_2O_2SSi$: 424.1921. Found: 424.1918.

1-(Phenyl)-3-(trimethylsilyl)-4-(4-tolyl)-5-(2-thiophenyl)-pyrazole, **25**:

Following general procedure E using pyrazole **24a** (202 mg, 0.476 mmol) and 4-bromotoluene (122 mg, 0.714 mmol), pyrazole **25** was isolated as a yellow solid (131 mg, 71%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (9H, s), 2.37 (3H, s), 6.65 (1H, dd, J = 3.5, 1.0 Hz), 6.84 (1H, dd, J = 5.0, 3.5 Hz), 7.10-7.17 (4H, m), 7.20 (1H, dd, J = 5.0, 1.0 Hz), 7.29-7.43 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.4, 21.4, 110.7, 119.3, 120.3, 125.6, 126.8, 127.1, 127.6, 128.7, 128.8, 128.9, 130.6, 134.0, 136.7, 140.2, 152.5; FTIR: ν_{max} 3067 (w), 2955 (w), 1595 (w), 1498 (s), 1310 (m), 991 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{25}N_2SSi$: 389.1502. Found: 389.1500.

1-(Phenyl)4-(4-tolyl)-5-(2-thiophenyl)-pyrazole, **26**:

Following general procedure C using pyrazole **25** (129 mg, 0.332 mmol) and TBAF in THF (3.3 mL, 3.3 mmol), pyrazole **26** was isolated as an orange crystalline solid (20 mg, 19%).

M.p.: 150-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (3H, s), 6.40 (1H, s), 6.70 (2H, d, J = 7.5 Hz), 6.95-7.00 (1H, m), 7.09 (1H, dd, J = 5.0, 3.5 Hz), 7.12-7.23 (4H, m), 7.39 (2H, d, J = 7.5 Hz), 7.44 (1H, dd, J = 5.0, 1.0 Hz), 7.70 (1H, dd, J = 3.5, 1.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.4, 91.7, 102.5, 121.5, 123.3, 127.7, 128.4, 129.2, 129.9, 130.2, 130.5, 132.0, 136.0, 138.3, 141.2, 146.4; FTIR: ν_{max} 2950 (w), 1575 (s), 1509 (s), 1493 (s), 1421 (s), 1234 (m), 1109 (m), 947 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{17}N_2S$: 317.1107. Found: 317.1106.

1-(Methyl)-3-(trimethylsilyl)-4-(pinacolatoborolane)-5-(4-tolyl)-pyrazole, **27**:

Following general procedure D using 4-(4-tolyl)-N-methylsydnone (150 mg, 0.789 mmol) and 4,4,5,5-tetramethyl-2-[2-(trimethylsilyl)ethynyl]-1,3,2-dioxaborolane (354 mg, 1.58 mmol), pyrazole **27** was isolated as a yellow solid (162 mg, 55%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.38 (9H, s), 1.19 (12H, s), 2.41 (3H, s), 3.78 (3H, s), 7.20 (2H, d, J = 8.0 Hz), 7.25 (2H, d, J = 8.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.4, 21.5, 24.9, 37.1, 82.9, 112.6 (br), 128.5, 130.2, 138.1, 151.1, 158.7; FTIR: ν_{max} 2976 (w), 2897 (w), 1497 (s), 1301 (s), 1239 (s), 1141 (s), 1039 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{32}{}^{11}BN_2O_2Si$: 370.2357. Found: 370.2358.

1-(Methyl)-3-(trimethylsilyl)-4-(4-tolyl)-5-(3-trifluoromethylphenyl)-pyrazole, **28**:

Following general procedure E using pyrazole **27** (162 mg, 0.437 mmol) and 3-trifluoromethylbromobenzene (147 mg, 0.656 mmol), pyrazole **28** was isolated as a yellow solid (93 mg, 55%)

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.19 (9H, s), 2.35 (3H, s), 3.86 (3H, s), 7.07 (2H, d, J = 8.0 Hz), 7.15 (2H, d, J = 8.0 Hz), 7.24 (1H, d, J = 8.0 Hz), 7.31 (1H, t, J = 7.5 Hz), 7.46 (1H, d, J = 8.0 Hz), 7.50 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.2, 21.4, 37.5, 110.7, 119.9 (d, J = 99.5 Hz), 123.2 (dd, J = 7.5, 3.5 Hz), 124.3 (q, J = 272.5 Hz), 126.9, 127.2-127.5 (m), 129.7 (d, J = 52.5 Hz), 130.24 (q, J = 32.0 Hz), 133.6, 136.2, 138.5, 141.6, 150.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.7; FTIR: ν_{max} 2956 (w), 1733 (m), 1580 (m), 1510 (m), 1325 (m), 1309 (m), 1157 (s), 1117 (s), 1014 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{21}H_{24}F_3N_2Si$: 389.1655. Found: 389.1652.

1-(Methyl)-4-(3,trifluoromethylphenyl)-5-(4-tolyl)-pyrazole, **29**:

Following general procedure E using pyrazole **28** (93 mg, 0.24 mmol) and TBAF in THF (2.4 mL, 2.4 mmol), pyrazole **29** was isolated as a colourless solid (51 mg, 67%).

M.p.: 72 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 (3H, s), 3.78 (3H, s), 7.18 (2H, d, J = 8.0 Hz), 7.24-7.30 (4H, m), 7.35-7.40 (1H, m), 7.45 (1H, s), 7.76 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5, 37.4, 119.7, 122.7 (d, J = 3.5 Hz), 124.0 (d, J = 3.5 Hz), 124.2 (q, J = 272.0 Hz), 127.0, 128.9, 129.9, 130.0, 130.4, 130.9 (q, J = 32.0 Hz), 134.2, 137.5, 139.3, 140.6; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.9; FTIR: ν_{max} 2923 (w), 1520 (m), 1364 (m), 1314 (s), 1156

(s), 1119 (s), 991 (m), 905 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{18}H_{16}F_3N_2$: 317.1260. Found: 317.1258.

4-(4-Methoxyphenyl)-N-(4-ethoxyphenyl)sydnone:

Following general procedure A using N-(4-ethoxyphenyl)sydnone (500 mg, 2.42 mmol) and 4-bromoanisole (680 mg, 3.64 mmol), the title compound was isolated as a tan solid (566 mg, 75%).

M.p.: 169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (3H, t, J = 7.0 Hz), 3.78 (3H, s), 4.10 (2H, q, J = 7.0 Hz), 6.82 (2H, d, J = 9.0 Hz), 7.00 (2H, d, J = 9.0 Hz), 7.24 (2H, d, J = 9.0 Hz), 7.37 (2H, d, J = 9.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.7, 55.4, 64.3, 108.0, 114.4, 115.6, 117.1, 126.3, 127.3, 129.0, 159.8, 161.5, 167.4; FTIR: ν_{max} 2980 (w), 2936 (w), 1737 (s), 1608 (m), 1533 (m), 1516 (m), 1251 (s), 1185 (m), 1013 (m), 998 (m), 971 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{17}N_2O_4$: 313.1188. Found: 313.1177.

1-(4-Ethoxyphenyl)-3-(trimethylsilyl)-4-(pinacolatoborolane)-5-(4-methoxyphenyl)-pyrazole, **30a** and 1-(4-ethoxyphenyl)-3-(pinacolatoborolane)-4-(trimethylsilyl)-5-(4-methoxyphenyl)-pyrazole, **30b**:

Following general procedure D using 4-(4-methoxyphenyl)-N-(4-ethoxyphenyl)sydnone (177 mg, 0.567 mmol) and 4,4,5,5-tetramethyl-2-[2-(trimethylsilyl)ethynyl]-1,3,2-dioxaborolane (254 mg, 1.13 mmol), pyrazole **30a** was isolated as a brown solid (179 mg, 64%) and pyrazole **30b** was isolated as a brown oil (28 mg, 10%, ~85% purity).

30a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.41 (9H, s), 1.24 (12H, s), 1.39 (3H, t, J = 7.0 Hz), 3.80 (3H, s), 3.99 (2H, q, J = 7.0 Hz), 6.74-6.81 (4H, m), 7.09-7.17 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.3, 14.9, 25.0, 55.3, 63.7, 83.1, 113.0, 114.4, 123.8, 126.8, 132.0, 133.5, 149.8, 157.9, 159.3, 159.4; FTIR: ν_{max} 2977 (w), 2898 (w), 1615 (w), 1543 (w), 1515 (s), 1410 (m), 1238 (s), 1139 (s), 1042 (s), 1033 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{27}H_{38}{}^{11}BN_2O_4Si$: 492.2725. Found: 492.2722.

30b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (9H, s), 1.33-1.40 (15H, m), 3.78 (3H, s), 3.95 (2H, q, J = 7.0 Hz), 6.69 (2H, d, J = 9.0 Hz), 6.78 (2H, d, J = 8.5 Hz), 7.03 (2H, d, J = 8.5 Hz), 7.09 (2H, d, J = 9.0 Hz).

1-(4-Ethoxyphenyl)-3-(trimethylsilyl)-4-(2-methoxyphenyl)-5-(4-methoxyphenyl)-pyrazole, **31**:

Following general procedure E using pyrazole **30a** (150 mg, 0.305 mmol) and 2-bromoanisole (85 mg, 0.47 mmol), pyrazole **31** was isolated as a yellow oil (132 mg, 92%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.18 (9H, s), 1.43 (3H, t, J = 7.0 Hz), 3.62 (3H, s), 3.74 (3H, s), 4.03 (2H, q, J = 7.0 Hz), 6.68 (2H, d, J = 9.0 Hz), 6.81-6.86 (3H, m), 6.89 (1H, dd, J = 7.5, 1.0 Hz), 6.94 (2H, d, J = 9.0 Hz), 6.89 (1H, dd, J = 7.5, 1.5 Hz), 7.24-7.29 (3H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ -0.6, 14.9, 55.1, 55.3, 63.7, 110.6, 113.5, 114.5, 120.1, 123.4, 124.1, 125.1, 126.6, 128.6, 130.0, 131.0, 133.0, 133.8, 140.4, 152.3, 157.8, 158.8; FTIR: ν_{max} 2950 (w), 1518 (m), 1477 (m), 1314 (s), 1243 (m), 1156 (s), 1118 (s), 991 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{28}H_{33}N_2O_3Si$: 473.2255. Found: 473.2260.

1-(4-Ethoxyphenyl)-3-4-(2-methoxyphenyl)-5-(4-methoxyphenyl)-pyrazole, **32**:

Following general procedure E using pyrazole **31** (106 mg, 0.224 mmol) and TBAF in THF (2.2 mL, 2.2 mmol), pyrazole **32** was isolated as a colourless solid (61 mg, 68%). Note: product was contaminated with significant amounts of protodeboronated product from the previous steps.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (3H, t, J = 6.0 Hz), 3.76 (3H, s), 3.89 (3H, s), 4.01 (2H, q, J = 6.0 Hz), 6.74 (2H, d, J = 9.0 Hz), 6.79-6.84 (2H, m), 6.95-7.00 (4H, m), 7.13-7.20 (2H, m), 7.88 (1H, s), 7.90 (2H, d, J = 9.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.9, 15.1, 55.3, 55.4, 55.7, 55.9, 63.8, 63.8, 64.2, 206.8, 111.1, 112.5, 113.8, 114.0, 114.2 114.5, 114.7, 115.8, 116.5, 117.8, 120.6, 121.6, 122.2, 123.3, 124.2, 126.1, 126.8, 128.1, 130.1, 130.8, 131.4, 131.9, 133.5, 136.4, 139.9, 140.0, 140.1, 142.9, 156.9, 157.9, 159.2, 159.5, 160.5, 164.2; FTIR: ν_{max} 2980 (w), 2935 (w), 2837 (w), 1597 (s), 1512 (s), 1244 (m), 1168 (m), 1025 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{25}H_{25}N_2O_3$: 317.1260. Found: 317.1258.

1-(Phenyl)-3-(n-hexyl)-pyrazole, **33a** and 1-(phenyl)-4-(n-hexyl)pyrazole, **33b**:

Following general procedure B using N-phenylsydnone (200 mg, 1.23 mmol) and 1-octyne (544 mg, 4.93 mmol), an inseparable mixture of pyrazole **33a** and **33b** was isolated as a yellow oil (182 mg, 65%, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83-0.94 (3H, m), 1.26-1.46 (6H, m), 1.64-1.76 (2H, m), 2.66-2.78 (2H, m), 6.26 (1H, d, d, J = 2.5 Hz), 7.20-7.29 (1H, m), 7.37-7.48 (2H, m), 7.62-7.69 (2H, m), 7.82 (1H, d, J = 2.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) 14.2, 22.8, 28.6, 29.3, 29.8, 31.8, 106.6, 119.1, 126.0, 127.4, 129.5, 140.4, 155.6; FTIR: ν_{max} 2925 (m), 2854 (m),

1600 (s), 1530 (s), 1503 (s), 1457 (m), 1389 (s), 1324 (m), 1224 (m), 1042 (s), 946 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{15}H_{21}N_2$: 229.1699. Found: 229.1700.

1-(Phenyl)-3-(n-hexyl)-4-vinylpyrazole, **34**:

Following general procedure F using pyrazoles **33a** and **33b** (182 mg, 0.797 mmol), NBS (142 mg, 0.797 mmol), vinyllboronic acid pinacol ester (184 mg, 1.20 mmol), XPhosPdG2 (63 mg, 0.08 mmol) and Na_2CO_3 (169 mg, 1.59 mmol) for 17 hours, pyrazole **34** was isolated as an orange oil (146 mg, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84-0.95 (3H, m), 1.25-1.48 (6H, m), 1.65-1.76 (2H, m), 2.68-2.79 (2H, m), 5.36 (1H, dd, J = 11.0, 1.5 Hz), 5.47 (1H, dd, J = 17.5, 1.5 Hz), 6.57 (1H, dd, J = 17.5, 11.0 Hz), 7.20-7.28 (1H, m), 7.39-7.58 (2H, m), 7.65 (2H, dd, J = 7.5, 1.0 Hz), 7.93 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 14.2, 22.8, 27.3, 29.4, 29.5, 31.8, 112.9, 119.0, 124.3, 126.2, 126.8, 129.5, 140.1, 141.1, 153.3; FTIR: ν_{max} 2924 (m), 2854 (m), 1599 (m), 1554 (m), 1503 (s), 1463 (m), 1383 (m), 1219 (m), 1053 (s), 953 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{23}N_2$: 255.1856. Found: 255.1862.

1-(4-Fluorophenyl)-3-(phenyl)pyrazole, **35a** and 1-(4-fluorophenyl)-4-(phenyl)-pyrazole, **35b**:[17]

Following general procedure B using N-(4-fluorophenyl)sydnone (200 mg, 1.10 mmol) and phenylacetylene (453 mg, 4.44 mmol), an inseparable mixture of pyrazole **35a** and **35b** was isolated as a yellow solid (264 mg, 100%, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.78 (1H, d, J = 2.5 Hz), 7.13-7.21 (2H, m), 7.31-7.38 (1H, m), 7.44 (2H, t, J = 7.5 Hz), 7.71-7.77 (2H, m), 7.88-7.94 (3H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.3, 116.4 (d, J = 23.0 Hz), 121.0 (d, J = 8.5 Hz), 126.0, 128.3, 128.8, 130.2, 133.1, 136.7, 153.2, 161.2 (d, J = 246.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.1.

1-(4-Fluorophenyl)-3-(phenyl)-4-(4-methoxyphenyl)pyrazole, **36**:

Following general procedure F using pyrazoles **35a** and **35b** (264 mg, 1.10 mmol), NBS (197 mg, 1.10 mmol), 4-methoxyphenylboronic acid (253 mg, 1.67 mmol), XPhosPdG2 (87 mg, 0.11 mmol) and Na_2CO_3 (353 mg, 3.33 mmol) for 17 hours, pyrazole **36** was isolated as an amorphous orange solid (135 mg, 35%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.84 (3H, s), 6.90 (2H, d, J = 9.0 Hz), 7.17 (2H, dd, J = 9.0, 8.5 Hz), 7.25-7.30 (2H, m), 7.33-7.42 (3H, m), 7.62-7.64 (m, 2H), 7.75 (2H, ddd, J = 10.5,

5.0, 3.0 Hz), 7.90 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 55.3, 110.7, 114.1, 116.3 (d, J = 23.0 Hz), 120.7 (d, J = 8.5 Hz), 122.8, 125.1, 126.5, 128.0, 128.5, 130.0, 133.2, 136.5 (d, J = 2.5 Hz), 150.5, 158.9, 161.2 (d, J = 245.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.2 - -116.0 (m); FTIR: ν_{max} 2835 (w), 1556 (m), 1499 (s), 1448 (m), 1290 (m), 1245 (s), 1175 (s), 1027 (s), 958 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{18}FN_2O$: 345.1398. Found: 345.1398.

1-(4-Methoxyphenyl)-3-(cyclopropyl)pyrazole, **37a** and 1-(4-Methoxyphenyl)-4-(cyclopropyl)pyrazole, **37b**:

Following general procedure B using N-(4-methoxyphenyl)sydnone (200 mg, 1.04 mmol) and cyclopropylacetylene (275 mg, 4.16 mmol), an inseparable mixture of pyrazole **37a** and **37b** was isolated as a yellow oil (203 mg, 91%, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.73-0.83 (2H, m), 0.93-1.02 (2H, m), 2.04 (1H, tt, J = 8.5, 5.0 Hz), 3.83 (3H, s), 6.07 (1H, d, J = 2.5 Hz), 6.94 (2H, d, J = 9.0 Hz), 7.54 (2H, d, J = 9.0 Hz), 7.68 (1H, d, J = 2.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.2, 9.4, 55.7, 103.6, 114.6, 120.6, 120.7, 127.5, 156.7, 158.0; FTIR: ν_{max} 3007 (w), 1530 (m), 1512 (s), 1382 (m), 1299 (m), 1242 (s), 1180 (m), 1108 (m), 1026 (s), 949 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{13}H_{15}N_2O$: 215.1179. Found: 215.1176.

1-(4-Methoxyphenyl)-3-(cyclopropyl)-4-(4-trifluoromethylphenyl)pyrazole, **38**:

Following general procedure F using pyrazoles **37a** and **37b** (191 mg, 0.891 mmol), NBS (159 mg, 0.891 mmol), 4-trifluomethylphenylboronic acid (254 mg, 1.34 mmol), XPhosPdG2 (70 mg, 0.089 mmol) and Na_2CO_3 (189 mg, 1.78 mmol) for 17 hours, pyrazole **38** was isolated as an amorphous orange solid (234 mg, 73%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96-1.04 (2H, m), 1.06-1.15 (2H, m), 2.00 (1H, tt, J = 8.5, 5.0 Hz), 3.84 (3H, s), 6.96 (2H, d, J = 9.0 Hz), 7.58 (2H, d, J = 9.0 Hz), 7.67 (2H d, J = 8.5 Hz), 7.73 (2H d, J = 8.5 Hz), 7.91 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.1, 8.6, 55.7, 110.7, 114.7, 120.7, 121.3 (q, J = 260.5 Hz), 125.7 (q, J = 3.5 Hz), 125.8, 127.9, 128.5 (q, J = 32.5 Hz), 133.8, 137.1, 152.5, 158.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.3; FTIR: ν_{max} 3011 (w), 2834 (w), 1620 (w), 1522 (s), 1321 (s), 1252 (m), 1163 (m), 1104 (s), 1065 (s), 1021 (s), 956 (m), 849 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{18}F_3N_2O$: 359.1366. Found: 359.1376.

4-[N-(3-Hydroxypropyl)amide]-N-phenylsydnone:

To a solution of 4-carboxylic acid-N-phenylsydnone (2.00 g, 9.70 mmol) in CH_2Cl_2 (50 mL) at 0 ^oC was added oxalyl chloride (3.69 g, 29.1 mmol) and DMF (3 drops) and the mixture stirred for 10 minutes at 0 ^oC. The reaction was allowed to warm to room temperature and stirred for a further 3 hours. Volatiles were then removed in vacuo and the resulting yellow solid dissolved in CH_2Cl_2 (50 mL). Triethylamine (982 mg, 9.70 mmol) and 3-aminopropanol (874 mg, 11.6 mmol) were added at 0 ^oC and the reaction stirred for 14 hours at RT. The reaction was poured into water, extracted with CH_2Cl_2, the combined organic layers were dried over $MgSO_4$ and volatiles removed in vacuo. The resulting crude material was purified by flash silica chromatography (eluting solvent 100% ethyl acetate) affording the title compound as a colourless solid (2.00 g, 78%). The product could be further purified by recrystallisation from CH_2Cl_2/petrol.

M.p.: 84-86 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74 (2H, td, J = 12.0, 6.0 Hz), 2.64 (1H, t, J = 6.0 Hz), 3.49 (2H, dd, J = 12.0, 6.0 Hz), 3.62 (2H, q, J = 6.0 Hz), 7.53-7.62 (4H, m), 7.68 (1H, ddt, J = 8.0, 6.5, 1.5 Hz), 7.75 (1H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 32.3, 35.8, 59.5, 101.9, 125.3, 129.4, 132.5, 134.6, 156.4, 167.3; FTIR: ν_{max} 3449 (br), 3335 (m), 2930 (w), 1759 (s), 1653 (s), 1534 (s), 1493 (w), 1291 (m), 1215 (m), 956 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{12}H_{14}N_3O_4$: 264.0984. Found: 264.0974.

4-[2-(5,6-Dihydro-4H-1,3-oxazine)]-N-phenylsydnone:

To a solution of triphenylphosphine oxide (1.90 g, 6.84 mmol) in CH_2Cl_2 (35 mL) at 0 ^oC was added triflic anhydride (804 mg, 2.85 mmol) and the reaction stirred for 30 minutes at 0 ^oC. A solution of 4-[N-(3-hydroxypropyl)amide]-N-phenylsydnone (500 mg, 1.90 mmol) in CH_2Cl_2 (15 mL) was slowly added at 0 ^oC and the reaction allowed to warm to room temperature and stirred for 14 hours. The reaction mixture was poured into water and the organic layer discarded. The aqueous layer was basified with $NaHCO_3$ and extracted with ethyl acetate. The combined organic layers were dried over $MgSO_4$ and volatiles removed in vacuo. The crude material was purified by flash silica chromatography (eluting solvent 100% ethyl acetate) affording the title compound as a colourless solid (243 mg, 52%).

M.p.: 97-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (2H, dt, J = 11.5, 6.0 Hz), 3.47 (2H, t, J = 6.0 Hz), 4.04-4.09 (2H, m), 7.47-7.73 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.8, 42.5, 65.5, 103.0, 124.7, 129.4, 131.9, 135.6, 146.6, 166.2; FTIR: ν_{max} 3061 (w), 2959 (w), 2856 (w), 1766 (s), 1754 (s), 1657 (s), 1635 (s), 1480 (s), 1437 (m), 1275 (s), 1140 (s), 1078 (s),

1024 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{12}H_{12}N_3O_3$: 246.0879. Found: 246.0886.

1-(Phenyl)-3-(cyclopropyl)-5-[2-(5,6-dihydro-4H-1,3-oxazine)]pyrazole, **39a** and 1-(phenyl)-4-(cyclopropyl)-5-[2-(5,6-dihydro-4H-1,3-oxazine)]pyrazole, **39b**:

Following general procedure B using 4-[2-(5,6-dihydro-4H-1,3-oxazine)]-N-phenylsydnone (155 mg, 0.632 mmol) and cyclopropylacetylene (167 mg, 2.53 mmol), an inseparable mixture of pyrazole **39a** and **39b** was isolated as an orange oil (29 mg, 91%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70-0.81 (2H, m), 0.85-0.99 (2H, m), 1.82-1.94 (2H, m), 1.99 (1H, tt, J = 8.5, 5.0 Hz), 3.47 (2H, t, J = 6.0 Hz), 4.07 (2H, t, J = 5.5 Hz), 6.37 (1H, s), 7.26-7.35 (1H, m), 7.35-7.47 (4H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.1, 9.2, 21.8, 42.6, 65.2, 105.6, 124.7, 127.4, 128.6, 137.5, 141.0, 150.0, 155.7; FTIR: ν_{max} 2952 (w), 2837 (w), 1664 (s), 1596 (m), 1543 (m), 1502 (s), 1377 (m), 1338 (m), 1231 (m), 1121 (m), 1097 (s), 994 (s), 760 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{16}H_{18}N_3O$: 268.1444. Found: 268.1448.

1-(Phenyl)-3-(cyclopropyl)-4-(4-trifluoromethylphenyl)-5-[2-(5,6-dihydro-4H-1,3-oxazine)]-pyrazole, **40**:

Following general procedure F using pyrazoles **39a** and **39b** (27 mg, 0.10 mmol), NBS (18 mg, 0.10 mmol), 4-trifluomethylphenylboronic acid (29 mg, 0.15 mmol), XPhosPdG2 (8 mg, 0.01 mmol) and Na_2CO_3 (32 mg, 0.30 mmol) for 17 hours, pyrazole **40** was isolated as a colourless solid (12 mg, 29%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85-0.95 (2H, m), 1.00-1.06 (2H, m), 1.80-2.92 (3H, m), 3.42 (2H, t, J = 6.0 Hz), 4.07 (2H, t, J = 5.5 Hz), 7.33 (1H, t, J = 7.5 Hz), 7.43 (2H, t, J = 8.0 Hz), 7.49-7.56 (2H, m), 7.67 (4H, s); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.0, 8.2, 21.7, 26.1, 43.0, 65.7, 123.9, 124.5 (q, J = 271.5), 125.2 (q, J = 3.5), 127.6, 129.0, 129.80 (q, J = 36.0), 129.81, 135.0, 136.6, 140.3, 150.0, 152.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4; FTIR: ν_{max} 2957 (w), 1671 (m), 1619 (m), 1596 (m), 1498 (m), 1381 (m), 1324 (s), 1231 (m), 1162 (s), 1122 (s), 1069 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{23}H_{21}F_3N_3O$: 412.1631. Found: 412.1636.

1-(Phenyl)-3-(methanol)-5-(4-tolyl)pyrazole, **41a** and 1-(phenyl)-4-(methanol)-5-(4-tolyl)pyrazole, **41b**:

Following general procedure B using 4-(4-tolyl)-N-phenylsydnone (200 mg, 0.793 mmol) and propargylalcohol (178 mg, 3.17 mmol), an inseparable mixture of pyrazole **41a** and **41b** was isolated as a brown oil (132 mg, 63%, 95:5).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (3H, s), 2.36 (1H, br), 4.78 (2H, s), 6.49 (1H, s), 7.20 (4H, s), 7.26-7.37 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.4, 59.2, 106.1, 125.4, 127.56, 127.63, 128.7, 129.1, 129.3, 138.5, 140.1, 144.5, 152.9; FTIR: ν_{max} 3340 (br), 2928 (w), 1596 (m), 1498 (s), 1442 (m), 1374 (s), 1184 (m), 1035 (s), 1000 (s), 970 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{17}H_{17}N_2O$: 265.1335. Found: 265.1342.

1-(Phenyl)-3-(methanol)-4-(4-trifluoromethylphenyl)-5-(4-tolyl)pyrazole, **42**:

Following general procedure F using pyrazoles **41a** and **41b** (143 mg, 0.541 mmol), NBS (96 mg, 0.54 mmol), 4-trifluomethylphenylboronic acid (154 mg, 0.812 mmol), XPhosPdG2 (43 mg, 0.054 mmol) and Na_2CO_3 (115 mg, 1.08 mmol) for 17 hours, pyrazole **42** was isolated as a colourless solid (77 mg, 38%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (3H, s), 4.78 (2H, s), 6.93 (2H, d, J = 8.0 Hz), 7.05 (2H, d, J = 8.0 Hz), 7.26-7.37 (7H, m), 7.54 (2H, d, J = 8.0 Hz) (OH not observed); ^{13}C NMR (101 MHz, $CDCl_3$) δ 21.5, 57.8, 119.7, 124.4 (q, J = 272.0 Hz), 125.35, 125.42 (q, J = 3.5 Hz), 126.4, 127.7, 128.7 (q, J = 32.5 Hz), 129.0, 129.6, 130.1, 130.2, 136.5, 138.8, 139.7, 141.6, 150.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.4; FTIR: ν_{max} 3346 (br), 2877 (w), 1618 (w), 1595 (w), 1496 (m), 1378 (m), 1323 (s), 1166 (m), 1108 (s), 1068 (s), 1018 (m), 1004 (m), 855 (s); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{24}H_{20}F_3N_2O$: 409.1522. Found: 409.1529.

1-(Phenyl)-3-(cyclopropyl)-5-[(N-methoxy-N-methyl)amide]-pyrazole, **43a** and 1-(phenyl)-4-(cylcopropyl)-5-[(N-methoxy-N-methyl)amide]-pyrazole, **43b**:

Following general procedure B using 4-[(N-methoxy-N-methyl)amide]-N-phenylsydnone (150 mg, 0.602 mmol) and cyclopropylacetylene (159 mg, 2.41 mmol), an inseparable mixture of pyrazole **43a** and **43b** was isolated as an orange oil (138 mg, 84%, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) 0.78-0.86 (2H, m), 0.92-1.06 (2H, m), 1.95-2.11 (1H, m), 3.17 (3H, s), 3.52 (3H, s), 6.37 (1H, s), 7.28-7.54 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$) δ 8.3, 9.2, 33.6, 61.5, 105.7, 123.5, 127.6, 129.1, 135.5, 140.4, 155.8, 161.8; FTIR: ν_{max} 1648 (s), 1596 (m), 1544 (m), 1501 (s), 1372 (s), 1307 (m), 1183 (m), 1153 (m), 973 (s), 868 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{15}H_{18}N_3O_2$: 272.1394. Found: 272.1398.

1-(Phenyl)-3-(phenyl)-5-(2-pyridyl)pyrazole, **45a** and 1-(phenyl)-4-(phenyl)-5-(2-pyridyl)pyrazole, **45b**:

Following general procedure B using 4-(2-pyridyl)-N-phenylsydnone (200 mg, 0.836 mmol) and phenylacetylene (342 mg, 3.34 mmol), an inseparable mixture of pyrazole **45a** and **45b** was isolated as a brown oil (244 mg, 98%, 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) 7.16-7.23 (2H, m), 7.28-7.54 (8H, m), 7.64 (1H, td, J = 8.0, 1.5 Hz), 7.94 (2H, d, J = 7.0 Hz), 8.65 (1H, d, J = 4.0 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 106.5, 122.9, 123.7, 125.6, 126.0, 127.9, 128.2, 128.8, 129,1, 133.0, 136.5, 139.8, 140.5, 143.6, 149.8, 152.2; FTIR: ν_{max} 2957 (w), 1587 (m), 1496 (m), 1456 (m), 1441 (m), 1359 (m), 1216 (w), 1069 (w), 995 (w); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{20}H_{15}N_3$: 298.1339. Found: 298.1349.

1-(Phenyl)-3-(phenyl)-4-vinyl-5-(2-pyridyl)pyrazole, **46**:

Following general procedure F using pyrazoles **45a** and **45b** (244 mg, 0.821 mmol), NBS (146 mg, 0.821 mmol), vinyllboronic acid pinacol ester (190 mg, 1.23 mmol), XPhosPdG2 (65 mg, 0.08 mmol) and Na_2CO_3 (261 mg, 2.46 mmol) for 17 hours, pyrazole **46** was isolated as an amorphous orange solid (106 mg, 40%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (1H, dd, J = 11.5, 1.5 Hz), 5.13 (1H, dd, J = 18.0, 1.5 Hz), 6.69 (1H, dd, J = 18.0, 11.5 Hz), 7.23-7.32 (7H, m), 7.38 (1H, ddd, J = 7.5, 3.5, 1.5 Hz), 7.42-7.48 (2H, m), 7.66 (1H, td, J = 7.5, 2.0 Hz), 7.73-7.77 (2H, m), 8.70 (1H, dd, J = 5.5, 1.5 Hz); ^{13}C NMR (101 MHz, $CDCl_3$) δ 116.8, 118.5, 123.2, 125.0, 126.2, 126.8, 127.4, 128.1, 128.5, 128.9, 129.0, 133.6, 136.5, 139.9, 140.0, 150.1, 150.3, 151.1; FTIR: ν_{max} 2927 (w), 1592 (m), 1497 (m), 1447 (m), 1419 (m), 1360 (m), 992 (m), 974 (m); HRMS (ESI-TOF) m/z $[M+H]^+$ calculated for $C_{22}H_{18}N_3$: 324.1495. Found: 324.1507.

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