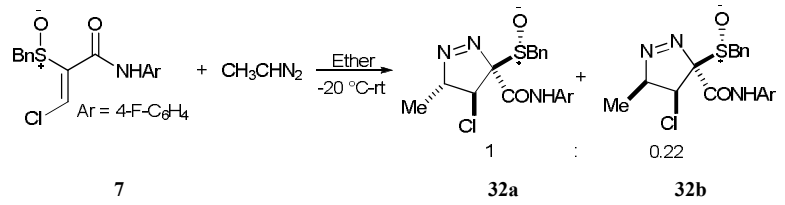
Supplementary Material for Manuscript

The cycloadditions were typically conducted using 1 mmol of the β-chloroacrylamide dipolarophile as a 0.05 M solution in ether. In some instances, 1–3 mL of acetone was required to solubilise the dipolarophile (see Experimental). Diazoethane and diazomethane were both generated at –20 °C, and an ethereal solution of the β-chloroacrylamide was then added to an excess of the dipole (7 equivalents) at –20 °C, the solution was allowed to slowly return to room temperature and was then stirred for 4–6 hours. As phenyldiazomethane was generated at –50 °C, an ethereal solution of the β-chloroacrylamide was added to the freshly prepared phenyldiazomethane (10 equivalents) at –50 °C, the solution was allowed to slowly return to room temperature and was then stirred for 16 hours. All cycloadditions in which trimethylsilyldiazomethane was employed as the dipole were conducted at room temperature, and the reaction time was dependant upon the nature of the dipolarophile; cycloadditions with the sulfoxide derivatives were complete within 6 hours using 5 equivalents of the dipole, while employment of the sulfide derivatives required reaction times of up to 48 hours and up to 15 equivalents of the dipole was necessary. The pyrazoline cycloadducts isolated from the cycloadditions of diazoalkanes to the β-chloroacrylamides are polar compounds and are very poorly soluble in the majority of organic solvents; in most instances, DMSO-d_6 was required to record the ^{13}C NMR spectra. This property did, however, facilitate isolation of the cycloadducts as the reaction mixture could simply be filtered at the end of the reaction. The pyrazoline and pyrazole cycloaddducts synthesised during this work are all novel compounds.

The dipolarophilic reactivity of the sulfoxide derivatives of the β-chloroacrylamides towards diazoethane as the 1,3-dipole was explored first, with initial investigations focusing on the benzylsulfinyl β-chloroacrylamides, and in particular the *N*-4-fluorophenyl derivative **7**. A solution of **7** in ether and acetone (a small quantity of acetone was required to solubilise **7**) was added dropwise to an excess of an ethereal solution of diazoethane at –20 °C. The reaction solution was allowed to return slowly to room temperature and a white solid precipitated out of solution as the reaction proceeded. Following stirring at room temperature for 4 hours, the solvent and excess diazoethane were evaporated under reduced pressure to yield the crude pyrazolines as a 1 : 0.22 mixture of the 2 diastereomers **32a** and **32b** (Scheme 1).



Scheme 1

Purification of the crude cycloadducts proved to be problematic in the early stages. When purification by column chromatography on silica gel was attempted, decomposition of the cycloadducts occurred and a very low recovery of the purified diasteromers resulted. For all subsequent pyrazoline cycloadducts that necessitated chromatographic purification, neutral alumina was used. Hot recrystallisation from solvents such as chloroform and ethyl acetate was also attempted, but the cycloadducts did not survive these conditions and decomposition was still observed. To circumvent decomposition problems, it was decided to isolate the product by filtration, instead of removing the solvent and excess dipole at the end of the reaction by concentration at reduced pressure. The reaction was repeated and again a white solid precipitated out of solution as the reaction proceeded. After stirring at room temperature for 4 hours and then open to the air for a further 0.5 hours to allow excess diazoethane to evaporate, the reaction solution was filtered to give a 1 : 0.21 mixture of the pyrazolines **32a** and **32b**. ^{1}H NMR spectroscopic analysis of the white solid indicated that the cycloadducts were isolated in a pure state, cleaner than by concentration of the reaction mixture, and in a very good yield of 94%.

For the diazoethane cycloadditions, the pyrazolines derived from the β-chloroacrylamides at the sulfide level of oxidation had greater solubility in most organic solvents than the sulfoxide analogues; it was possible to record the ^{13}C NMR spectra in $CDCl_3$. However, as a result of the greater solubility the isolation of pyrazoline cycloadducts at the sulfide level in pure form (with the exception of **19** and **20**) was less trivial than for the corresponding sulfoxide derivatives, which could be recovered by filtration of the product mixture.

The pyrazoles **51, 58–61** are very polar compounds, and use of DMSO-d_6 is required to record the ^{1}H and ^{13}C NMR spectra.

In cycloadditions of trimethylsilyldiazomethane with the α-thio-β-chloroacrylamides, the consumption of the sulfide was monitored by TLC analysis, and after 5 h and 24 h additional portions of five equivalents of trimethylsilyldiazomethane (15 equivalents in total) had to be added to the reaction mixture to force the cycloaddition

to completion. After stirring for 48 h, there was no evidence of any starting material remaining by TLC analysis.

For cycloadditions of diazomethane with α-sulfinyl-β-chloroacrylamides, a solution of the sulfoxide in ether (a small amount of acetone was also required to solubilise the benzylsulfinyl derivatives) was added dropwise to an excess of an ethereal solution of diazomethane at –20 °C. The solution was allowed to slowly return to room temperature while stirring for 4 hours. For the benzylsulfinyl and *N*-benzyl-*n*-butylsulfinyl derivatives, a white solid precipitated out of solution as the reaction proceeded and following filtration, each of the pyrazoline cycloadducts **66, 67, 68** and **69** was isolated as a single diastereomer. ^{1}H NMR spectroscopic analysis of the white solid collected by filtration indicated that the cycloadducts were pure.

Examination of the structure of the rearranged pyrazole **63** reveals a number of interesting features. In the solid state, the pyrazole **63** exists as the tautomer with the carboxamide group at the 3-position of the heterocycle rather than the 5-position (Figure 1). As discussed with the pyrazole **51**, it is believed that this tautomer is stabilised by an intramolecular hydrogen bond between the amide NH and N(2) of the heterocycle. The 4,5-substituted tautomer may be present in the solution state.

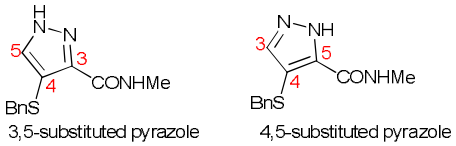


Figure 1

The hydrogen bonding networks are illustrated in Figure 2. There is an intramolecular hydrogen bond between the NH of the amide and the N(2) of the heterocycle with a bond length of 2.48 Å, an intermolecular hydrogen bond between the N(1)H of the heterocycle and the carbonyl group with a bond length of 1.86 Å, and an intermolecular hydrogen bond between the N(2) of the heterocycle and the amide NH with a bond length of 2.17 Å.

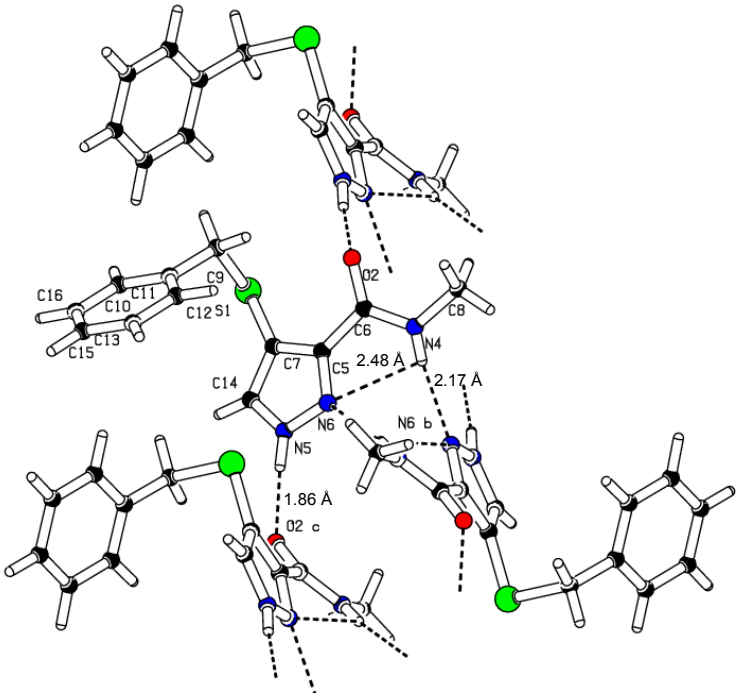


Figure 2

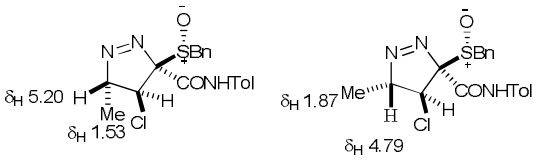
When the cycloaddition of phenyldiazomethane with the *N*-methyl substituted β-chloroacrylamide **9** was originally carried out, a very poor yield of 10% was obtained for the pyrazoline **77** on filtration. The mother liquor was then concentrated to yield a red oil with a complex ^{1}H NMR spectrum, and on purification of this residue by chromatography on silica gel the pyrazole **82** was isolated in 13% yield. The cycloaddition was then repeated under identical conditions and on filtration of the reaction mixture, the pyrazoline **77** was isolated in 37% yield on this occasion. The pyrazoline **77** was sufficiently soluble in $CDCl_3$ to record the ^{1}H and ^{13}C NMR spectrum in this solvent, with no evidence of decomposition. The ^{1}H NMR spectrum of **77** was also recorded in DMSO-d_6, and approximately 7% of the sample had decomposed to the pyrazole **82** [characteristic signals for **82** were evident at δ_H 2.78 ppm ($NHCH_3$) and δ_H 8.27 ppm (NH)]. The NMR spectra of the pyrazolines in $CDCl_3$ and DMSO-d_6 suggest different conformations, presumably due to different hydrogen-bonding systems.

The benzenesulfinyl substituted β-chloroacrylamides **16** and **14** were reacted with freshly prepared phenyldiazomethane, and following stirring at room temperature for 16 hours, the reaction mixtures were concentrated to give the crude products. After purification by column chromatography on silica gel, the pyrazoles **79** and **80** were isolated in yields of 56% and 79% respectively. Precipitates formed as the cycloaddition

of the benzenesulfinyl derivative **15** and the *n*-butylsulfinyl derivatives **27** and **31** with phenyldiazomethane proceeded, which were isolated by filtration through a sintered glass funnel following stirring at room temperature for 16 hours, to yield the pyrazoles **82, 79** and **80** as white solids.

Spectroscopic Interpretation of the Cycloadducts

The pyrazolines **32**–**37** and **44**–**50** have a characteristic absorption in the 1532–1552 cm^{-1} region of the IR spectra due to stretching of the N=N in the pyrazoline ring.[1,2] The ^1H NMR spectra of the pyrazolines **32**–**37** and **44**–**50** show some very interesting patterns. The methyl group attached to C(5) appears as a doublet at δ_H 1.46–1.66 ppm for the major diastereomer, whereas the corresponding signal appears further downfield for the minor diastereomer at δ_H 1.75–1.87 ppm. Another feature in each instance is that for the minor diastereomer, the signal in the ^1H NMR spectra for the proton attached to C(5) appears further upfield than that of the proton attached to C(4), whereas for the major diastereomer the signal for the proton attached to C(5) appears further downfield than the signal for the C(4) proton (for example, see Figure 3**)**.



33a **33b**

Figure 3

The regiochemistry of the 1,3-dipolar cycloadditions with diazoethane was confirmed by the appearance of the doublet of quartets for the proton attached to C(5) in the ^1H NMR spectra due to coupling to the methyl group at the 5-position and the proton attached to the carbon at the 4-position, and a doublet for the proton attached to C(4). If the opposite regioisomer was formed, then the signal for C(5)H would appear as a quartet due to coupling to the methyl group only and the signal for C(3)HCl would be evident as a singlet (Figure 4).

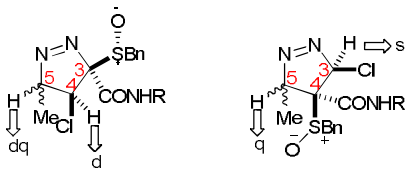


Figure 4

The *endo*/*exo* assignment of the diazoethane derived pyrazoline cycloadducts was confirmed by NOE experiments at 600 MHz on the *N*-tolyl substituted pyrazoline **33**. For the minor diastereomer **33b**, irradiation of C(5)C*H*$_3$ at 1.86 ppm resulted in an enhancement of C(5)*H* but not C(4)*H* [b, Figure 5], irradiation of C(5)*H* at 4.78 ppm led to an enhancement of C(4)*H* and C(5)C*H*$_3$ [c, Figure 5], while irradiation of C(4)*H* at 5.32 ppm led to an enhancement of C(5)*H* but not C(5)C*H*$_3$ [d, Figure 5]. These results are consistent with the *exo*-diasteromer.

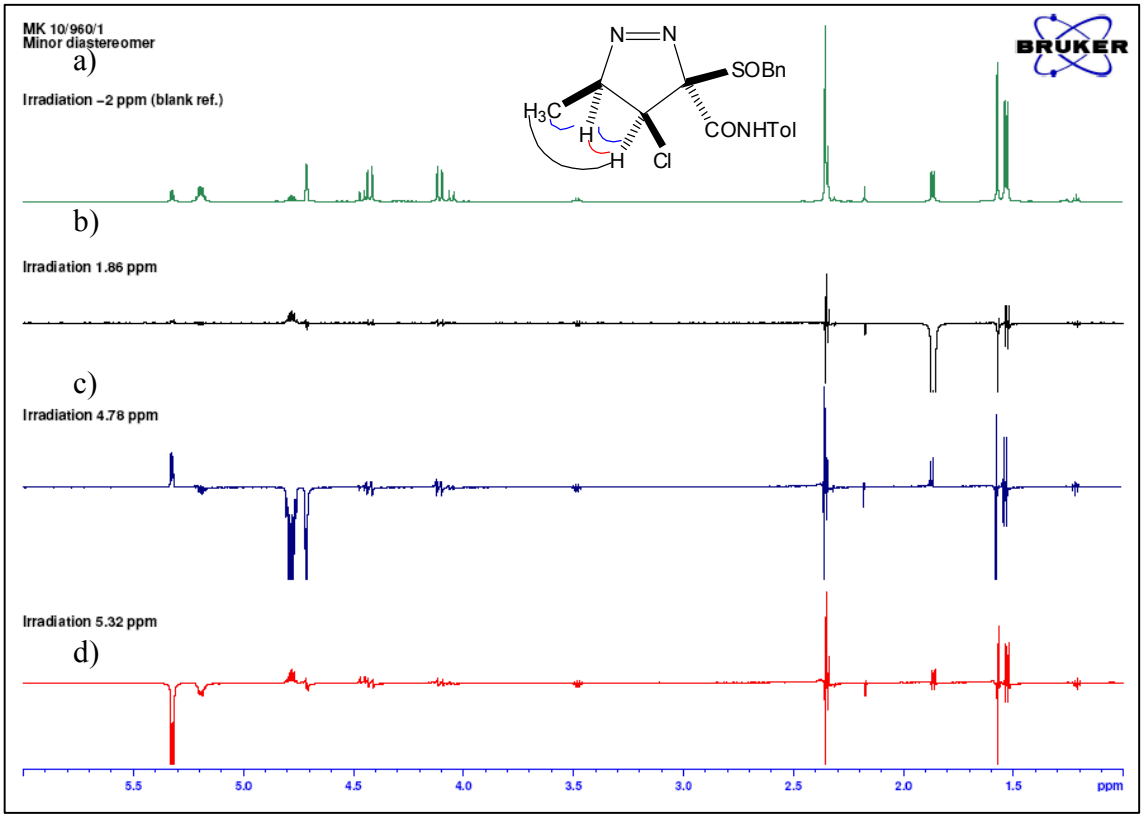


Figure 5 NOE spectra of ***33b*** *recorded at 600 MHz in CDCl*$_3$

The NOE experiment for the major diastereomer **33a** supported the assignment, although it was less convincing than the assignment of the minor due to the observation of enhancement between C(4)*H* and C(5)*H*. Irradiation of the methyl group attached to C(5) at 1.53 ppm led to an enhancement of C(4)*H* and C(5)*H* [b, Figure 6]. Irradiation of C(4)*H* at 4.71 ppm led to an enhancement of C(5)CH_3 [c, Figure 6], while irradiation of C(5)*H* at 5.19 ppm led to an enhancement of C(5)CH_3 [d, Figure 6]. These results are consistent with the *endo*-diastereomer. However, irradiation of C(4)*H* and C(5)*H* led to an enhancement of the other signal, indicating the proximity of these protons in space despite their *trans* orientation.

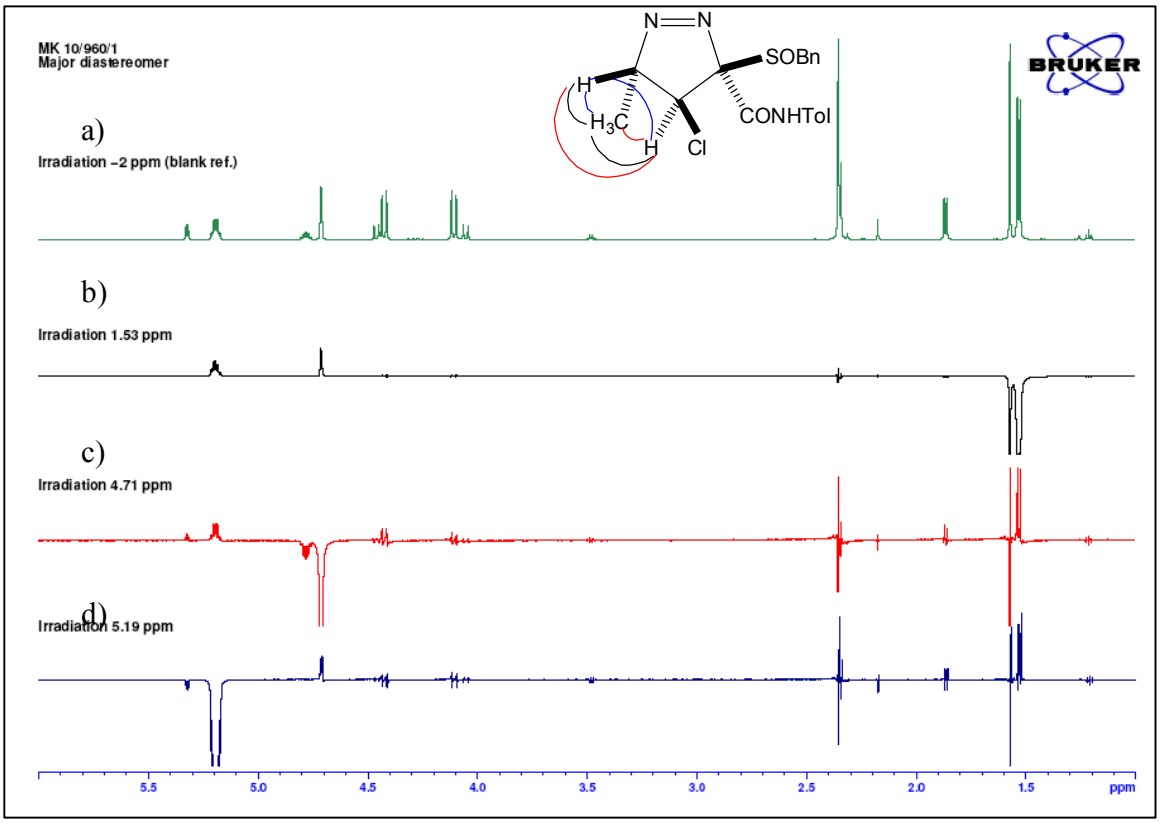


*Figure 6 NOE spectra of **33a** recorded at 600 MHz in $CDCl_3$*

For the diazoethane derived pyrazoles, a characteristic sharp singlet is seen in the ^{1}H NMR spectra in the region δ_H 6.43–6.68 ppm for the proton attached to C(4), with the corresponding signal in the ^{13}C NMR spectra observed at δ_C 104.3-105.7 ppm. The

absorption frequency of the carbonyl stretch in the IR spectra of the pyrazoles is reduced by 15–20 cm^{-1} when compared to the sulfoxide precursors.[3] This is due to the delocalisation of the lone pair of the pyrazole nitrogen into the carbonyl group (Figure 7). Two NH stretches (the amide NH and the NH of the pyrazole ring) were evident in the IR spectra of the pyrazoles in the region 3110–3390 cm^{-1}.

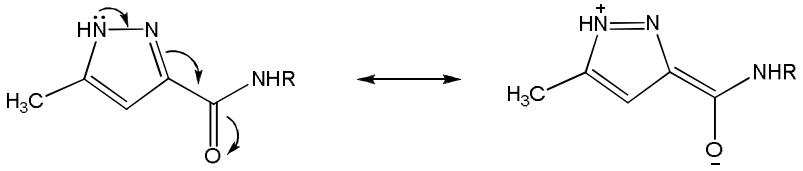


Figure 7

Similar patterns were evident in the ^{1}H NMR spectrum of the pyrazolines **55a** and **55b** derived from the β-chloroacrylate **54** as those observed for the β-chloroacrylamide derived pyrazolines; the methyl group attached to C(5) appears as a doublet at δ_H 1.47 ppm for the major diastereomer and the corresponding signal for the minor diastereomer appears further downfield at δ_H 1.78 ppm. For the minor diastereomer, the resonance in the ^{1}H NMR spectrum for the proton attached to C(5) appears further upfield than that of the proton attached to C(4), whereas for the major diastereomer the signal for the proton attached to C(5) appears further downfield than the signal for the C(4) proton. The major diastereomer was thus tentatively assigned as *endo* and the minor diastereomer was assigned as *exo*.

Another interesting feature of the ^{1}H NMR spectrum of **55a** and **55b** is the difference in the chemical shift of the methoxy protons; for the minor diastereomer, a 3H singlet is evident at δ_H 3.34 ppm, whereas the corresponding signal in the major diastereomer appears much further downfield at δ_H 3.62 ppm, signifying major conformational differences between the major and minor diastereomers.

Two characteristic broad signals are evident in the ^{1}H NMR spectra of the pyrazoles **51, 58–61** for the proton attached to C(4) and the proton attached to C(5); the C(4)H signal appears in the region δ_H 6.66–6.79 ppm and the C(5)H signal appears at δ_H 7.74–7.88 ppm. In most cases a broad singlet is observed, but on a few occasions

coupling between the C(4) and C(5) protons leads to fine splitting, and a broad doublet is evident, with a coupling constant of approximately 2 Hz. The analogous signals for C(4) and C(5) in the ^{13}C NMR spectra are at δ_C 104.7–106.0 ppm for C(4) and δ_C 129.8–131.5 ppm for C(5) (Figure 8).

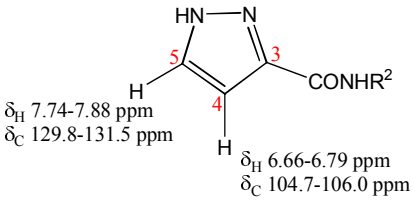


Figure 8

In each instance, the signal for the proton attached to C(5) is slightly broader in the ^{1}H NMR spectra than the corresponding signal for the proton attached to C(4). Likewise, the signal for C(5) is always broader than the signal for C(4) in the ^{13}C NMR spectra; the quadrupolar moment of the adjacent ^{14}N may be a contributing factor here. Significant broadening of the C(5) signal and the signal for the quaternary carbon at the 3-position of the heterocycle is observed in the ^{13}C NMR spectrum for the *N*-methylamido pyrazole **61**.

In the ^{13}C NMR spectra of the rearranged pyrazoles **62, 63** and **65**, broad signals are observed for the carbons at the 3-position and 5-position of the heterocycle. The quadrupolar moment of ^{14}N may be contributing to this broadening effect. Interestingly, sharp signals for C(3) and C(5) are observed in the ^{13}C NMR spectrum for the pyrazole **64**. The ^{13}C NMR spectra of **62, 63–65** also contain a quaternary carbon signal at δ_C 107–109 ppm, characteristic of the carbon at the 4-position of the heterocycle.

The ^{1}H NMR spectra of **64** and **65** were recorded in both $CDCl_3$ and DMSO-d_6, and the signals for the amide NH and the NH of the heterocycle appear further downfield in DMSO-d_6 (Table 1). Hydrogen bonding may account for these observations, as hydrogen bonding decreases the electron density around the proton and thus moves the proton to higher frequency. In $CDCl_3$, both the amide NH and NH of the heterocycle may participate in hydrogen bonding. When recorded in DMSO-d_6, the solvent may affect the

intermolecular hydrogen bonding network, and intermolecular hydrogen bonding with DMSO-d_6 may occur.

Table 1 δ_H values for NH protons of ***64***

	δ_H ($CDCl_3$) ppm	δ_H (DMSO-d_6) ppm
amide NH	9.44	10.06
N(1)H	11.33	13.75

In the ^{13}C NMR spectra of the diazomethane derived pyrazolines **66** and **67** (recorded in $CDCl_3$), the signal for the carbon attached to the chlorine [C(4)] appears at δ_C 51–52 ppm and the signal for C(5) appears at δ_C 87–88 ppm. It was anticipated that the signal for C(4) would experience a more significant deshielding effect and that its signal would appear further downfield. The observed effect indicates that the diazo group is more electron withdrawing than chlorine (Figure 9).

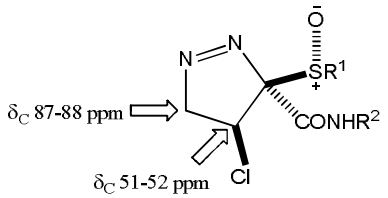


Figure 9

The diazomethane derived pyrazolines **66-69** had a characteristic absorption in the 1540–1550 cm^{-1} region of the IR spectra due to stretching of the N=N in the pyrazoline ring.[1,2]

The electron-withdrawing effect of the diazo group is again evident in the ^{13}C NMR spectra of the pyrazolines **70** and **73** (recorded in DMSO-d_6), with the signal for the carbon attached to the chlorine [C(4)] appearing at δ_C 57 ppm and the signal for C(5) evident at δ_C 84 ppm.

For the pyrazoline **77**, two characteristic doublets were evident in the ^1H NMR spectrum at δ_H 4.69 and 5.94 ppm for C(4)H and C(5)H. The deshielding effect of the diazo group on the carbon at the 5-position was again evident in the ^{13}C NMR spectrum, with the signal for the carbon at the 4-position appearing at δ_C 59.3 ppm and the carbon at

the 5-position appearing at δ_C 99.8 ppm. The structure of the pyrazoline was further confirmed by the presence of an absorption at 1532 cm^{-1}, characteristic of the N=N stretch in the pyrazoline system.[1,2]

The structure of the *N*-tolylamido pyrazoline **76** was confirmed by the presence of two characteristic doublets at δ_H 4.83 and 6.03 ppm in the ^{1}H NMR spectrum when recorded in $CDCl_3$ and by the presence of the N=N absorption at 1525 cm^{-1} in the IR spectrum. Due to the poor solubility of **76** in $CDCl_3$, DMSO-d_6 was necessary to record the ^{13}C NMR spectrum. The ^{1}H NMR spectrum of **76** was also recorded in DMSO-d_6 prior to the ^{13}C NMR spectrum, and there was some evidence for decomposition to the pyrazole **79**, confirmed by the comparison of the additional signals with a sample of **79** which was independently synthesised later. When the ^{13}C NMR spectrum was recorded in DMSO-d_6, total decomposition to the pyrazole **79** had occurred.

As the *N*-benzylamido pyrazoline **78** was insoluble in $CDCl_3$, its ^{1}H NMR spectrum was recorded in DMSO-d_6; approximately 53% of the sample had decomposed to the corresponding pyrazole **80**, confirmed by the agreement of the decomposition product with a genuine sample of the pyrazole **80**. It was thus not possible to obtain the ^{13}C NMR spectrum of **76** or **78**. The IR spectrum of **78** contained the characteristic N=N stretch at 1525 cm^{-1} and accurate elemental analysis was also obtained, thereby confirming the pyrazoline structure of **78** prior to dissolution in DMSO-d_6.

As mentioned above, two distinctive doublets were evident in the ^{1}H NMR spectra of **76–78**, at δ_H 4.85–5.12 ppm and δ_H 5.53–5.59 ppm in DMSO-d_6 and at δ_H 4.69–4.83 ppm and δ_H 5.94–6.03 ppm in $CDCl_3$. The upfield signal was assigned as the proton on the carbon attached to the chlorine [C(4)H] and the downfield signal was assigned as the C(5)H proton. The electron-withdrawing effect of the diazo group on the 5-position of the pyrazoline system was seen earlier for the diazomethane derived pyrazolines, and in the phenyldiazomethane derived pyrazolines the C(5)H is also benzylic, leading to a further deshielding of this proton. Interestingly, when the ^{1}H NMR spectra were recorded in $CDCl_3$, the two doublets were further apart. Also, the values of the coupling constants between the protons attached to C(4) and C(5) are very different in the two solvents; in $CDCl_3$, coupling constant values of 6.3–6.8 Hz are observed whereas the corresponding values in DMSO-d_6 are 8.7–9.0 Hz. Evidently, the pyrazolines adopt

different conformations in $CDCl_3$ and DMSO-d_6, presumably due to different hydrogen bonding systems.

A distinctive doublet is observed in the ^{1}H NMR spectra of **79, 80, 82** at approximately δ_H 7.80 ppm (when recorded in DMSO-d_6), assigned as the *ortho*-protons on the phenyl ring attached to the 5-position (Figure 10). Tensmeyer and Ainsworth have attributed this *ortho*-shift phenomenon to the magnetic anisotropy of the neighbouring ring; the *ortho*-phenyl protons reside preferentially near the plane of the pyrazole ring and are shifted downfield by the magnetic field of the pyrazole ring current.[4]

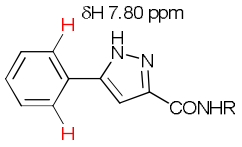


Figure 10

There is a dramatic difference in the position of the NH signal of the carboxamide in the ^{1}H NMR spectra of the pyrazoles **79, 80, 82** when recorded in $CDCl_3$ and DMSO-d_6, with the NH signal appearing further downfield by ~1.5 ppm in DMSO-d_6. This may be due to a change in the nature of the hydrogen bonding network from intramolecular hydrogen bonding in $CDCl_3$ to intermolecular hydrogen bonding with DMSO-d_6.

The values for the coupling constants of the C(4)H and C(5)H coupling in **86** are identical (7.6 Hz) in $CDCl_3$ and DMSO-d_6 (for the corresponding sulfoxide-derived pyrazolines a larger coupling constant is observed in DMSO-d_6), implying that the pyrazoline adopts similar conformations in $CDCl_3$ and DMSO-d_6, in contrast to what was seen above for the sulfoxide derived pyrazolines.

Experimental

(3*R,4*R**,5*R**,S_S*)-3-(Benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 33a and (3*R**,4*R**,5*S**,S_S*)-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 33b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.94 g, 8.0 mmol)] was added to a solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-

(benzylsulfinyl)propenamide **8** (0.40 g, 1.2 mmol) in ether (40 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **33a** and **33b** (**33a**: **33b** 1:0.27 by ^{1}H NMR spectroscopy) as a white solid (0.39 g, 84%), mp 158-160 °C; (Found C, 58.34; H, 5.26; N, 10.46; S, 8.22, Cl, 9.70. $C_{19}H_{20}ClN_3O_2S$ requires C, 58.53; H, 5.17; N, 10.78; S, 8.22, Cl, 9.09%); ν_{max}/cm^{-1} (KBr) 3292 (NH), 3026 (CH), 1671 (CO), 1609, 1543 (N=N), 1519, 1456, 1407;

Major diastereomer **33a**: δ_H (300 MHz, $CDCl_3$) 1.53 [3H, d, *J* 7.5, C(5)C*H*$_3$], 2.35 (3H, s, ArC*H*$_3$), 4.11 (1H, d, A of AB system, J_{AB} 12.7, SC*H*$_2$), 4.43 (1H, d, B of AB system, J_{AB} 12.7, SC*H*$_2$), 4.71 [1H, d, *J* 4.0, C(4)*H*], 5.20 [1H, dq, *J* 7.5, 4.0, C(5)*H*], 7.13-7.55 (9H, m, Ar*H*)*, 8.83 (1H, br s, N*H*).

δ_C (75.5 MHz, DMSO-d_6) (signals for major diastereomer **33a** only detected) 15.8 [C(5)*C*H$_3$], 20.9 (Ar*C*H$_3$), 54.2 (S*C*H$_2$), 61.4 [*C*(5)H], 90.0 [*C*(4)H], 107.2 [*C*(3)], 122.0 (aromatic *C*H), 128.7 (aromatic *C*H or aromatic *C*), 129.2, 129.4, 130.9 (3 × aromatic *C*H), 131.3 (aromatic *C*H or aromatic *C*), 134.5, 135.1 (aromatic *C*), 162.3 (*C*O);

Minor diastereomer **33b**: δ_H (300 MHz, $CDCl_3$) 1.87 [3H, d, *J* 7.3, C(5)C*H*$_3$], 2.34 (3H, s, ArC*H*$_3$), 4.05 (1H, d, A of AB system, J_{AB} 12.8, SC*H*$_2$), 4.46 (1H, d, B of AB system, J_{AB} 12.8, SC*H*$_2$), 4.75-4.82 [1H, m, C(5)*H*], 5.32 [1H, d, *J* 5.6, C(4)*H*], 7.13-7.55 (9H, m, Ar*H*)*, 9.06 (1H, br s, N*H*).

*The aromatic signals were indistinguishable for the two diastereomers.

HRMS (ES+): Exact mass calculated for $C_{19}H_{21}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 362.0982. Found 362.0973; m/z (ES+) 392.1 {[($C_{19}H_{20}N_3O_2S^{37}Cl$)+$H^+$], 6%}, 390.1 {[($C_{19}H_{20}N_3O_2S^{35}Cl$)+$H^+$], 12%}, 364.2 {[($C_{19}H_{20}NO_2S^{37}Cl$)+$H^+$], 20%}, 362.2 {[($C_{19}H_{20}NO_2S^{35}Cl$)+$H^+$], 46%}, 216 (100%).

(3*R,4*R**,5*R**,*S*$_S$*)-3-(Benzylsulfinyl)-4-chloro-4,5-dihydro-*N*,5-dimethyl-3*H*-pyrazole-3-carboxamide 34a and (3*R**,4*R**,5*S**,*S*$_S$*)-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-*N*,5-dimethyl-3*H*-pyrazole-3-carboxamide 34b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.96 g, 8.2 mmol)] was added to a solution of *N*-methyl-*Z*-3-chloro-2-

(benzylsulfinyl)propenamide **9** (0.30 g, 1.2 mmol) in ether (30 mL) and acetone (5 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature and while stirring for 4 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **34a** and **34b** (**34a**:**34b** 1:0.22 by ^{1}H NMR spectroscopy) as a white solid (0.24 g, 43%), mp 83-84 °C; (Found C, 48.79; H, 5.08; N, 13.14. $C_{13}H_{16}ClN_3O_2S$ requires C, 49.76; H, 5.14; N, 13.39%); ν_{max}/cm^{-1} (KBr) 3346 (NH), 3030 (CH), 2976 (CH), 1669 (CO), 1542 (N=N stretch), 1044 (SO);

Major diastereomer **34a**: δ_H (300 MHz, $CDCl_3$) 1.47 [3H, d, *J* 7.5, C(5)CH_3], 3.00 (3H, d, *J* 5.0, NHCH_3), 4.04 (1H, d, A of AB system, J_{AB} 12.8, SCH_2), 4.39 (1H, d, B of AB system, J_{AB} 12.8, SCH_2), 4.61 [1H, d, *J* 4.0, C(4)*H*], 5.13 [1H, dq, *J* 7.4, 4.0, C(5)*H*], 6.91 (1H, br s, N*H*), 7.28-7.43 (5H, m, Ar*H*)*; δ_C (75.5 MHz, DMSO-d_6) 15.8 [CH_3, C(5)*C*H_3], 26.6 (CH_3, NH*C*H_3), 54.2 (CH_2, S*C*H_2), 61.1 [CH, *C*(5)H], 90.2 [CH, *C*(4)H], 106.8 [C, *C*(3)], 128.6, 129.1, 130.8 (3 × CH, aromatic *C*H), 131.4, 131.5 (2 × C, aromatic *C*), 164.0 (C, *C*O).

Minor diastereomer **34b**: δ_H (300 MHz, $CDCl_3$) 1.84 [3H, d, *J* 7.3, C(5)CH_3], 2.92 (3H, d, *J* 4.9, NHCH_3), 3.98 (1H, d, A of AB system, J_{AB} 12.9, SCH_2), 4.44 (1H, d, B of AB system, J_{AB} 12.9, SCH_2), 4.60-4.70 [1H, m, C(5)*H*], 5.25 [1H, d, *J* 5.4, C(4)*H*], 6.96 (1H, br s, N*H*), 7.28-7.43 (5H, m, Ar*H*)*; δ_C (75.5 MHz, DMSO-d_6) 14.3 [CH_3, C(5)*C*H_3], 26.8 (CH_3, NH*C*H_3), 55.3 (CH_2, S*C*H_2), 59.3 [CH, *C*(5)H], 86.5 [CH, *C*(4)H], 109.9 [C, *C*(3)], 162.6 (C, *C*O) (the aromatic signals were not observed for the minor diastereomer).

HRMS (ES+): Exact mass calculated for $C_{13}H_{17}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 286.0669. Found 286.0675; m/z (ES+) 316.1 {[$(C_{13}H_{16}N_3O_2S^{37}Cl)+H^+$], 12%}, 314.1 {[$(C_{13}H_{16}N_3O_2S^{35}Cl)+H^+$], 26%}, 288.1 {[$(C_{13}H_{16}NO_2S^{37}Cl)+H^+$], 24%}, 366.2 {[$(C_{13}H_{16}NO_2S^{35}Cl)+H^+$], 58%}, 231.2 (100%).

This compound decomposed readily at room temperature to give the pyrazole **40**, with characteristic peaks at δ_H (300 MHz, DMSO-d_6) 2.25 [3H, s, C(5)CH_3], 2.73 (3H, s, NHCH_3), 6.40 [1H, s, C(4)*H*], 8.07 (1H, br s, N*H* of carboxamide), in agreement with data for pure **40** (see below).

(3*R,4*R**,5*R**,*S*$_S$*)-*N*-benzyl-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 35a and (3*R**,4*R**,5*S**,*S*$_S$*)-*N*-benzyl-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 35b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.75 g, 6.4 mmol)] was added to a solution of *N*-benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **10** (0.30 g, 0.9 mmol) in ether (30 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **35a** and **35b** (**35a**:**35b** 1:0.33 by ^{1}H NMR spectroscopy) as a white solid (0.27 g, 77%), mp 100-101 °C; ν_{max}/cm^{-1} (KBr) 3350 (NH), 3043 (CH), 2975 (CH), 1666, 1537 (N=N stretch), 1496, 1455, 1260, 1048 (SO);

Major diastereomer **35a**: δ_H (300 MHz, $CDCl_3$) 1.46 [3H, d, *J* 7.5, C(5)C*H*$_3$], 3.91 (1H, d, A of AB system, J_{AB} 12.8, SC*H*$_2$), 4.24 (1H, d, B of AB system, J_{AB} 12.8, SC*H*$_2$), 4.40-4.71 [3H, m, NHC*H*$_2$ & C(4)*H* (observed as a doublet at 4.62, *J* 4.0)], 5.13 [1H, dq, *J* 7.5, 4.0, C(5)*H*], 7.16-7.50 (11H, m, N*H* & Ar*H*)*; δ_C (75.5 MHz, DMSO-d_6) 15.8 [CH_3, C(5)*C*H$_3$], 43.3 (CH_2, NH*C*H$_2$), 54.4 (CH_2, S*C*H$_2$), 61.0 [CH, *C*(5)H], 90.4 [CH, *C*(4)H], 106.9 [C, *C*(3)], 163.5 (C, *C*O)[§].

Minor diastereomer **35b**: δ_H (300 MHz, $CDCl_3$) 1.84 [3H, d, *J* 7.3, C(5)C*H*$_3$], 3.85 (1H, d, A of AB system, J_{AB} 12.8, SC*H*$_2$), 4.32 (1H, d, B of AB system, J_{AB} 12.8, SC*H*$_2$), 4.40-4.71 [3H, m, NHC*H*$_2$ & C(5)*H*], 5.26 [1H, d, *J* 5.5, C(4)*H*], 7.16-7.40 (10H, m, Ar*H*)*, 7.61 (1H, br s, N*H*); δ_C (75.5 MHz, DMSO-d_6) 14.2 [CH_3, C(5)*C*H$_3$], 43.5 (CH_2, NH*C*H$_2$), 55.2 (CH_2, S*C*H$_2$), 59.2 [CH, *C*(5)H], 86.7 [CH, *C*(4)H], 109.8 [C, *C*(3)], 162.0 (C, *C*O)[§].

*The aromatic signals were indistinguishable for the two diastereomers in the ^{1}H NMR.

[§]The aromatic signals were not distinguishable for the two diastereomers in the ^{13}C NMR and were seen at δ_C 127.4, 127.5, 128.1, 128.3, 128.7, 128.8, 129.1, 129.2, 130.6, 130.7 (aromatic *C*H), 131.3, 138.7 (aromatic *C*).

HRMS (ES+): Exact mass calculated for $C_{19}H_{21}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 362.0982. Found 362.0989; m/z (ES+) 392.2 {[$(C_{19}H_{20}N_3O_2S^{37}Cl)+H^+$], 14%}, 390.2

{[($C_{19}H_{20}N_3O_2S^{35}Cl$)+$H^+$], 32%}, 364.2 {[($C_{19}H_{20}NO_2S^{37}Cl$)+$H^+$], 42%}, 362.2 {[($C_{19}H_{20}NO_2S^{35}Cl$)+$H^+$], 100%}, 216.2 (78%).

(3*R,4*R**,5*R**,*S*$_S$*)-3-(Benzylsulfinyl)-*N*-*n*-butyl-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 36a and (3*R**,4*R**,5*S**,*S*$_S$*)-3-(benzylsulfinyl)-*N*-*n*-butyl-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 36b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.90 g, 7.7 mmol)] was added to a solution of *N*-*n*-butyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **11** (0.33 g, 1.1 mmol) in ether (30 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **36a** and **36b** (**36a**:**36b** 1:0.11 by ^{1}H NMR spectroscopy) as a white solid (0.13 g, 33%), mp 69-70 °C; (Found C, 48.15; H, 5.56; N, 10.28. $C_{16}H_{22}ClN_3O_2S$ requires C, 54.00; H, 6.23; N, 11.81%)-as this compound decomposed readily at room temperature, it was not possible to get accurate micro analysis; ν_{max}/cm^{-1} (KBr) 3345 (NH), 3029 (CH), 2978 (CH), 1662 (CO), 1538 (N=N stretch), 1456, 1260, 1228, 1049 (SO);

Major diastereomer **36a**: δ_H (300 MHz, $CDCl_3$) 0.96 [3H, t, *J* 7.3, C(4′)*H*], 1.32-1.52 [7H, m, C(3′)H_2, C(2′)H_2 & C(5)CH_3; C(5)CH_3 could be distinguished as a doublet at 1.47 ppm, *J* 7.5], 3.27-3.55 (2H, sym m, NHCH_2), 4.05 (1H, d, A of AB system, J_{AB} 12.8, SCH_2), 4.38 (1H, d, B of AB system, J_{AB} 12.8, SCH_2), 4.62 [1H, d, *J* 3.8, C(4)*H*], 5.06-5.20 [1H, m, C(5)*H*], 6.96 (1H, br s, N*H*), 7.18-7.52 (5H, m, Ar*H*); δ_C (75.5 MHz, DMSO-d_6) (signals for major diastereomer **36a** only detected) 14.0 [*C*(4′)H_3], 15.9 [*C*(5)H_3], 19.9 [*C*(3′)H_2], 31.0 [*C*(2′)H_2], 40.1 [NH*C*H_2], 54.3 (S*C*H_2), 61.2 [*C*(5)H], 90.2 [*C*(4)H], 107.0 [*C*(3)], 128.7, 129.2, 130.7, 131.5 (aromatic *C*H & aromatic *C*), 163.5 (*C*O).

Minor diastereomer **36b**: δ_H (300 MHz, $CDCl_3$) 1.84 [3H, d, *J* 7.0, C(5)CH_3], 5.25 [1H, d, *J* 4.7, C(4)*H*].

HRMS (ES+): Exact mass calculated for $C_{16}H_{23}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 328.1138. Found 328.1145; m/z (ES+) 358.2 {[($C_{16}H_{22}N_3O_2S^{37}Cl$)+$H^+$], 18%}, 356.2

{[($C_{16}H_{22}N_3O_2S^{35}Cl$)+$H^+$], 44%}, 330.2 {[($C_{16}H_{22}NO_2S^{37}Cl$)+$H^+$], 36%}, 328.2 {[($C_{16}H_{22}NO_2S^{35}Cl$)+$H^+$], 92%}, 182.2 (100%).

(3*R,4*R**,5*R**,*S*$_S$*)-3-(Benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 37a and (3*R**,4*R**,5*S**,*S*$_S$*)-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 37b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (1.23 g, 10.5 mmol)] was added to a solution of *Z*-3-chloro-2-(benzylsulfinyl)propenamide **12** (0.34 g, 1.4 mmol) in ether (30 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **37a** and **37b** (**37a**:**37b** 1:0.20 by ^{1}H NMR spectroscopy) as a white solid (0.32 g, 75%), mp 92-93 °C; ν_{max}/cm^{-1} (KBr) 3379 (NH), 3028 (CH), 2975 (CH), 1670 (CO), 1538 (N=N), 1498, 1457, 1375, 1232, 1044 (SO);

Major diastereomer **37a**: δ_H (300 MHz, $CDCl_3$) 1.50 [3H, d, *J* 7.5, C(5)C*H*$_3$], 4.14 (1H, d, A of AB system, J_{AB} 12.6, SC*H*$_2$), 4.42 (1H, d, B of AB system, J_{AB} 12.8, SC*H*$_2$), 4.58 [1H, d, *J* 4.0, C(4)*H*], 5.09-5.16 [1H, m, C(5)*H*], 5.89 (1H, br s, N*H*), 6.98 (1H, br s, N*H*), 7.32-7.48 (5H, m, Ar*H*)*; δ_C (75.5 MHz, DMSO-d_6) 15.9 [*C*(5)H$_3$], 54.3 (S*C*H$_2$), 61.2 [CH, *C*(5)H], 90.1 [CH, *C*(4)H], 106.9 [*C*(3)], 128.7, 129.2, 130.8 (3 × CH, 3 × aromatic *C*H), 131.6 (aromatic *C*), 165.8 (C, *C*O).

Minor diastereomer **37b**: δ_H (300 MHz, $CDCl_3$) 1.85 [3H, d, *J* 7.3, C(5)C*H*$_3$], 4.07 (1H, d, A of AB system, J_{AB} 12.8, one of SC*H*$_2$), 4.45 (1H, d, B of AB system, J_{AB} 13.0, one of SC*H*$_2$), 4.61-4.74 [1H, m, C(5)*H*], 5.21 [1H, d, *J* 5.4, C(4)*H*], 5.78 (1H, br s, N*H*), 7.15 (1H, br s, N*H*), 7.32-7.48 (5H, m, Ar*H*)*; δ_C (75.5 MHz, DMSO-d_6) 14.3 [*C*(5)H$_3$], 55.4 (S*C*H$_2$), 59.3 [CH, *C*(5)H], 86.5 [CH, *C*(4)H], 164.1 (C, *C*O) (aromatic signals not observed for minor diastereomer).

HRMS (ES+): Exact mass calculated for $C_{12}H_{15}NO_2S^{35}Cl$ [(M+H)$^+$ – N_2], 272.0512. Found 272.0525; m/z (ES+) 274.1 {[($C_{12}H_{14}NO_2S^{37}Cl$)+H^+], 4%}, 272.1 {[($C_{12}H_{14}NO_2S^{35}Cl$)+H^+], 12%}.

_N_-Benzyl-5-methyl-1_H_-pyrazole-3-carboxamide 39

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.80 g, 6.8 mmol)] was added to a solution of *N*-benzyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **14** (0.31 g, 1.0 mmol) in ether (30 mL) and acetone (10 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. A white solid precipitated out of solution as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give the *pyrazole* **39** as a yellow solid (0.12 g, 58%), mp 140-142 °C (As this compound decomposed at room temperature it was not possible to get accurate micro analysis); ν_{max}/cm^{-1} (KBr) 3184 (NH), 3113 (NH), 3029 (CH), 2920 (CH), 1646 (CO), 1562, 1492, 1434, 1293; δ_H (300 MHz, DMSO-d_6) 2.26 [3H, s, C(5)CH_3], 4.42 (2H, d, *J* 6.3, NHCH_2), 6.46 [1H, s, C(4)*H*], 7.15-7.44 (5H, m, Ar*H*), 8.72 (1H, br t, N*H* of carboxamide); δ_H (300 MHz, $CDCl_3$) (**39** is very poorly soluble in $CDCl_3$) 2.44 [3H, s, C(5)CH_3], 4.61 (2H, d, *J* 5.9, NHCH_2), 6.68 [1H, s, C(4)*H*], 7.26-7.37 (5H, m, Ar*H*), 7.64 (1H, br t, N*H* of carboxamide), a broad signal was also observed at 2.01 ppm (water signal normally observed at 1.60 ppm); δ_C (75.5 MHz, DMSO-d_6) 11.1 [CH_3, C(5)*C*H_3], 42.2 (CH_2, NH*C*H_2), 104.5 [CH, *C*(4)H], 127.0, 127.6, 128.5 (3 × CH, 3 × aromatic *C*H), 140.2 (C, aromatic *C*), 141.4, 145.6 [2 × C, *C*(3) & *C*(5)], 161.7 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{12}H_{14}N_3O$ $[M+H]^+$, 216.1137. Found 216.1136; m/z (ES+) 216.2 {[($C_{12}H_{13}N_3O$)+H^+], 100%}, 90.9 (16%).

_N_,5-dimethyl-1_H_-pyrazole-3-carboxamide 40

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (1.01 g, 8.7 mmol)] was added to a solution of *N*-methyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **15** (0.30 g, 1.2 mmol) in ether (30 mL) and acetone (5 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to slowly return to room temperature while stirring for 2 h. The solvent was removed by evaporation at reduced pressure to give **40** as a yellow oil. Recrystallisation from chloroform gave the *pyrazole* **40** as a white solid (0.12 g, 71%), mp 115-117 °C; ν_{max}/cm^{-1} (KBr) 3430 (br, NH), 3088 (CH), 2956 (CH), 1649 (CO), 1569, 1407, 1261; δ_H (300 MHz, DMSO-d_6) 2.25 [3H, s, C(5)CH_3], 2.73 (3H, s, NHCH_3), 6.43 [1H, s, C(4)*H*],

8.15 (1H, br s, N*H* of carboxamide), a broad signal for water was also observed at 5.85 ppm due to exchange with N(1)*H* (water signal normally observed at 3.40 ppm); δ_C (75.5 MHz, DMSO-d_6) 11.1 [CH_3, C(5)*C*H_3], 25.8 (CH_3, NH*C*H_3), 104.3 [CH, *C*(4)H], 141.4, 145.6 [2 × C, *C*(3) & *C*(5)], 162.0 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_6H_{10}N_3O$ $[M+H]^+$, 140.0824. Found 140.0829; m/z (ES+) 140.1 {[($C_6H_9N_3O$)+H^+], 100%}.

Elemental analysis resulted in an underestimation of the carbon, hydrogen and nitrogen content, possibly indicating decomposition or the presence of an inorganic impurity.

5-Methyl-*N*-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide 41

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.62 g, 5.3 mmol)] was added to a solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **16** (0.24 g, 0.8 mmol) in ether (30 mL) and acetone (5 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 4 h. A white solid precipitated out of solution as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give the *pyrazole* **41** as a low melting white solid (0.11 g, 67%); ν_{max}/cm^{-1} (KBr) 3320 (NH), 3135 (NH), 1664 (CO), 1603, 1556, 1317; δ_H (300 MHz, DMSO-d_6) 2.27 [3H, s, C(5)CH_3 or ArCH_3], 2.30 [3H, s, C(5)CH_3 or ArCH_3], 6.55 [1H, s, C(4)*H*], 7.13 (2H, d, *J* 7.8, Ar*H*), 7.68 (2H, d, *J* 7.8, Ar*H*), 9.88 (1H, br s, N*H* of carboxamide), a broad water signal was also observed at 3.77 ppm due to exchange with N(1)*H* (water signal normally observed at 3.40 ppm); δ_H (300 MHz, $CDCl_3$) 2.33 [3H, s, C(5)CH_3 or ArCH_3], 2.39 [3H, s, C(5)CH_3 or ArCH_3], 6.67 [1H, s, C(4)*H*], 7.16 (2H, d, *J* 8.2, Ar*H*), 7.58 (2H, d, *J* 8.2, Ar*H*), 8.60 (1H, br s, N*H* of carboxamide), 9.86 [br s, N(1)*H*, integrates for less than 1H]; δ_C (75.5 MHz, DMSO-d_6) 11.1 [CH_3, C(5)*C*H_3], 20.8 (CH_3, NH*C*H_3), 105.0 [CH, *C*(4)H], 120.4, 129.3 (2 × CH, 2 × aromatic *C*H), 132.6, 136.6 (2 × C, 2 × aromatic *C*), 141.5, 146.2 [2 × C, *C*(3) & *C*(5)], 160.4 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{12}H_{14}N_3O$ $[M+H]^+$, 216.1137. Found 216.1138; m/z (ES+) 216.2 {[($C_{12}H_{13}N_3O$)+H^+], 100%}.

Elemental analysis resulted in an underestimation of the carbon, hydrogen and nitrogen content, possibly indicating decomposition or the presence of an inorganic impurity.

_N_-_n_-Butyl-5-methyl-1_H_-pyrazole-3-carboxamide 42

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.85 g, 7.3 mmol)] was added to a solution of *N*-*n*-butyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **17** (0.30 g, 1.0 mmol) in ether (30 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give **42** as a colourless oil. Following purification by column chromatography using hexane: ethyl acetate (gradient elution 20-80% ethyl acetate) as eluent, the *pyrazole* **42** was obtained as a white solid (0.05 g, 27%), mp 122-123 °C; (Found C, 59.64; H, 8.40; N, 22.65. $C_9H_{15}N_3O$ requires C, 59.64; H, 8.34; N, 23.19%); ν_{max}/cm^{-1} (KBr) 3390 (NH), 3186 (NH), 2962 (CH), 1632 (CO), 1589, 1459, 1407, 1260; δ_H (300 MHz, $CDCl_3$) 0.94 [3H, t, *J* 7.4, C(4′)H_3], 1.31-1.49 [2H, m, C(3′)H_2], 1.51-1.64 [2H, m, C(2′)H_2], 2.35 [3H, s, C(5)CH_3], 3.42 [2H, overlapping dt (appears as a q), *J* 7.0, 7.0, NHCH_2], 6.56 [1H, s, C(4)*H*], 6.79 (1H, br s, N*H* of carboxamide), a broad signal for water was also observed at ~2 ppm due to exchange with N(1)*H* (water signal normally observed at 1.60 ppm); δ_C (75.5 MHz, $CDCl_3$) 11.5 [CH_3, C(5)*C*H_3], 14.2 [CH_3, C(4′)H_3], 20.5 [CH_2, C(3′)H_2], 32.1 [CH_2, C(2′)H_2], 39.3 (CH_2, NH*C*H_2), 105.2 [CH, *C*(4)H], 141.8, 147.1 [2 × C, *C*(3) & *C*(5)], 162.8 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_9H_{16}N_3O$ $[M+H]^+$, 182.1293. Found 182.1292; m/z (ES+) 182.2 {[($C_9H_{15}N_3O$)+H^+], 100%}.

5-Methyl-_N_-phenyl-1_H_-pyrazole-3-carboxamide 43

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (1.31 g, 11.2 mmol)] was added to a solution of *N*-phenyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **18** (0.49 g, 1.6 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give **43** as a colourless oil. Following purification by column chromatography using hexane: ethyl acetate (gradient elution 10-80% ethyl acetate) as eluent, the *pyrazole* **43** was obtained as a yellow solid (0.21 g, 64%), mp 93-95 °C; ν_{max}/cm^{-1} (KBr) 3376 (NH), 3199 (NH), 3137 (CH), 2921 (CH), 1658 (CO), 1597, 1540, 1440, 1317; δ_H (300

MHz, $CDCl_3$) 2.39 [3H, s, C(5)CH_3], 6.68 [1H, s, C(4)*H*], 7.05-7.19 (1H, m, Ar*H*), 7.30-7.43 (2H, m, Ar*H*), 7.62-7.74 (2H, m, Ar*H*), 8.76 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, $CDCl_3$) 11.4 [CH_3, C(5)*C*H_3], 105.7 [CH, *C*(4)H], 120.1, 124.5, 129.4 (3 × CH, 3 × aromatic *C*H), 138.2 (C, aromatic *C*), 160.5 (C, *C*O)*; HRMS (ES+): Exact mass calculated for $C_{11}H_{12}N_3O$ $[M+H]^+$, 202.0980. Found 202.0987; m/z (ES+) 202.2 {[($C_{11}H_{11}N_3O$)+H^+], 100%}.

*C(3) and C(5) were not detected in the ^{13}C NMR spectrum.

(3*R,4*R**,5*R**)-3-(Benzylthio)-4-chloro-*N*-(4-fluorophenyl)-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 44a and (3*R**,4*R**,5*S**)-3-(benzylthio)-4-chloro-*N*-(4-fluorophenyl)-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 44b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.71 g, 6.1 mmol)] was added to a solution of *N*-(4-fluorophenyl)-*Z*-3-chloro-2-(benzylthio)propenamide **19** (0.28 g, 0.9 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 6 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **44a** and **44b** (**44a**:**44b** 1:0.08 by ^1H NMR spectroscopy) as a white solid (0.24 g, 74%), mp 220-221 °C; ν_{max}/cm^{-1} (KBr) 3241 (NH), 1663 (CO), 1526 (N=N stretch), 1507;

Major diastereomer **44a**: δ_H (300 MHz, $CDCl_3$) 1.66 [3H, d, *J* 7.3, C(5)CH_3], 4.04 (1H, d, A of AB system, J_{AB} 12.1, SCH_2), 4.10 (1H, d, B of AB system, J_{AB} 12.2, SCH_2), 4.21 [1H, d, *J* 7.4, C(4)*H*], 4.64-4.78 [1H, m, C(5)*H*], 6.97-7.09 (2H, m, Ar*H*)*, 7.16-7.52 (7H, m, Ar*H*)*, 8.64 (1H, br s, N*H*).

*These signals were indistinguishable for the two diastereomers.

δ_C (75.5 MHz, $CDCl_3$) (signals for major diastereomer **44a** only detected) 13.7 [CH_3, C(5)*C*H_3], 33.2 (CH_2, S*C*H_2), 59.5 [CH, *C*(5)H], 89.4 [CH, *C*(4)H], 96.2 [C, *C*(3)], 114.0 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3′)H], 119.8 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H], 126.0, 127.0, 127.3, (3 × CH, 3 × aromatic *C*H), 130.8, 133.6 (2 × C, 2 × aromatic *C*), 158.0 [C, d, $^1J_{CF}$ 245, aromatic *C*(4′)], 162.5 (C, *C*O).

Minor diastereomer **44b**: δ_H (300 MHz, $CDCl_3$) 1.77 [3H, d, *J* 7.4, C(5)C*H*$_3$], 4.15 (2H, d, *J* 3.4, SC*H*$_2$), 4.64-4.78 [1H, m, C(5)*H*]*, 4.98 [1H, d, *J* 6.5, C(4)*H*], 6.97-7.09 (2H, m, Ar*H*)*, 7.16-7.52 (7H, m, Ar*H*)*, 8.37 (1H, br s, N*H*).

*These signals were indistinguishable for the two diastereomers.

HRMS (ES+): Exact mass calculated for $C_{18}H_{18}NOS^{35}ClF$ $[(M+H)^+ - N_2]$, 350.0782. Found 350.0783; m/z (ES+) 352.1 {[($C_{18}H_{17}NOS^{37}ClF$)+H^+], 12%}, 350.2 {[($C_{18}H_{17}NOS^{35}ClF$)+H^+], 26%}.

Elemental analysis resulted in a significant underestimation of the carbon, hydrogen and nitrogen content, possibly indicating decomposition or the presence of an inorganic impurity.

(3*R,4*R**,5*R**)-3-(Phenylthio)-4-chloro-*N*-(4-fluorophenyl)-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 47a and (3*R**,4*R**,5*S**)-3-(phenylthio)-4-chloro-*N*-(4-fluorophenyl)-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 47b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.79 g, 6.7 mmol)] was added to a solution of *N*-(4-fluorophenyl)-*Z*-3-chloro-2-(phenylthio)propenamide **22** (0.30 g, 1.0 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by concentration at reduced pressure to give the crude products **47a** and **47b** (**47a**:**47b** 1:0.28 by ^{1}H NMR spectroscopy) as a pale yellow oil. Crystallisation from ether/hexane gave **47a** and **47b** (**47a**:**47b** 1:0.20 by ^{1}H NMR spectroscopy) as a white solid (0.26g, 75%), mp 87-88 °C; (Found C, 56.07; H, 4.22; N, 11.51; S, 8.50; Cl, 9.97; F, 5.57. $C_{17}H_{15}ClFN_3OS$ requires C, 56.12; H, 4.16; N, 11.55; S, 8.81; Cl, 9.74; F, 5.22%); ν_{max}/cm^{-1} (KBr) 3288 (NH), 3014 (CH), 2980 (CH), 1681 (CO), 1516 (N=N stretch);

Major diastereomer **47a**: δ_H (300 MHz, $CDCl_3$) 1.57 [3H, d, *J* 7.3, C(5)C*H*$_3$], 4.28 [1H, d, *J* 6.7, C(4)*H*], 4.57-4.67 [1H, sym m, C(5)*H*], 6.91-6.97, 7.13-7.18, 7.29-7.48, 7.66-7.85 (10H, m, Ar*H* & N*H*)*; δ_C (75.5 MHz, $CDCl_3$) 16.0 [CH_3, C(5)*C*H$_3$], 60.7 [CH, *C*(5)H], 91.6 [CH, *C*(4)H], 98.7 [C, *C*(3)]§, 116.0 [CH, d, $^2J_{CF}$ 23, aromatic *C*(3′)H]§, 122.1 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H]§, 128.3 (C, aromatic *C*)§, 129.6, 130.9 (2 × CH, 2 × aromatic

*C*H), 132.7 (C, aromatic *C*)[§], 138.0 (CH, aromatic *C*H), 160.1 [C, d, $^{1}J_{CF}$ 245, aromatic *C*(4′)][§], 164.5 (C, *C*O)[§].

Minor diastereomer **47b**: δ_H (300 MHz, $CDCl_3$) 1.80 [3H, d, *J* 7.3, C(5)CH_3], 4.46-4.55 [1H, sym m, C(5)*H*] , 5.06 [1H, d, *J* 5.9, C(4)*H*], 6.91-7.85 (10H, m, Ar*H* & N*H*)*; δ_C (75.5 MHz, $CDCl_3$) 14.1 [CH_3, C(5)*C*H_3], 61.2 [CH, *C*(5)H], 86.2 [CH, *C*(4)H], 129.7, 130.7 (2 × CH, 2 × aromatic *C*H), 137.4 (CH, aromatic *C*H).

*These signals were indistinguishable for the two diastereomers.

[§]The analogous signals were not detected for the minor diastereomer.

HRMS (ES+): Exact mass calculated for $C_{17}H_{16}NOS^{35}ClF$ [$(M+H)^+ - N_2$], 336.0625. Found 336.0630; m/z (ES+) 338.2 {[$(C_{17}H_{15}NOS^{37}ClF)+H^+$], 44%}, 336.2 {[$(C_{17}H_{15}NOS^{35}ClF)+H^+$], 100%}, 220.2 (16%), 88.0 (48%).

1,5-Dimethyl-*N*-phenyl-1*H*-pyrazol-3-carboxamide 52[5]

5-Methyl-*N*-phenyl-1*H*-pyrazole-3-carboxamide **43** (0.12 g, 0.6 mmol) in acetonitrile (15 mL) was added to a stirring solution of potassium carbonate (0.12 g, 0.8 mmol) in acetonitrile (5 mL). Methyl iodide (0.05 mL, 0.8 mmol) was added slowly *via* a syringe. Following stirring under nitrogen at room temperature for 16 h, the reaction mixture was filtered through a sintered glass funnel (grade 3) to remove the excess potassium carbonate. The solid was washed with dichloromethane (10 mL) and the solvent was then removed from the filtrate by evaporation under reduced pressure to give **52** as an orange oil. Following purification by column chromatography using hexane: ethyl acetate (gradient elution 20-80% ethyl acetate) as eluent, the *pyrazole* **52** was obtained as a white solid (0.07 g, 62%), mp 135-137 °C (Lit.,[5] 142-144 °C); (Found C, 65.52; H, 5.91; N, 18.84. $C_{12}H_{13}N_3O$ requires C, 66.96; H, 6.09; N, 19.52%); ν_{max}/cm^{-1} (KBr) 3281 (NH), 1660 (CO), 1596, 1538, 1495, 1429, 1319; δ_H (300 MHz, $CDCl_3$) 2.32 [3H, s, C(5)CH_3], 3.83 (3H, s, NCH_3), 6.64 [1H, s, C(4)*H*], 7.05-7.16 (1H, m, Ar*H*), 7.29-7.41 (2H, m, Ar*H*), 7.63-7.74 (2H, m, Ar*H*), 8.65 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, $CDCl_3$) 11.7 [CH_3, C(5)*C*H_3], 37.0 (CH_3, N*C*H_3), 106.8 [CH, *C*(4)H], 119.9, 124.2, 129.4 (3 × CH, 3 × aromatic *C*H), 138.5 (C, aromatic *C*), 141.1, 145.6 [2 × C, *C*(3) & *C*(5)], 160.5 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{12}H_{14}N_3O$ $[M+H]^+$, 216.1137. Found 216.1137; m/z (ES+) 216.2 {[$(C_{12}H_{13}N_3O)+H^+$], 100%}.

(3*R,4*R**,5*R**)-3-(Benzylthio)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 45a and (3*R**,4*R**,5*S**)-3-(benzylthio)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 45b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.71 g, 6.1 mmol)] was added to a solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(benzylthio)propenamide **20** (0.28 g, 0.9 mmol) in ether (20 mL) cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 6 h. A precipitate formed as the reaction progressed. The products were collected by filtration through a sintered glass funnel (grade 3) to give **45a** and **45b** (**45a**:**45b** 1:0.04 by ^{1}H NMR spectroscopy) as a white solid (0.22 g, 68%), mp 114-115 °C; ν_{max}/cm^{-1} (KBr) 3350 (NH), 3017 (CH), 1676 (CO), 1594, 1520 (N=N stretch);

Major diastereomer **45a**:δ_H (300 MHz, $CDCl_3$) 1.65 [3H, d, *J* 7.3, C(5)C*H*$_3$], 2.34 (3H, s, ArC*H*$_3$), 4.08 (2H, s, SC*H*$_2$), 4.24 [1H, d, *J* 7.2, C(4)*H*], 4.64-4.78 [1H, m, C(5)*H*], 7.15-7.61 (9H, m, Ar*H*)*, 8.63 (1H, br s, N*H*).

δ_C (75.5 MHz, $CDCl_3$) (signals for major diastereomer **45a** only detected) 16.0 [CH_3, C(5)*C*H$_3$], 21.3 (CH_3, Ar*C*H$_3$), 35.5 (CH_2, S*C*H$_2$), 61.7 [CH, *C*(5)H], 91.7 [CH, *C*(4)H], 98.8 [C, *C*(3)], 120.3, 128.2, 129.2, 129.6, 130.0 (5 × CH, 5 × aromatic *C*H), 134.5, 135.5, 135.8 (3 × C, 3 × aromatic *C*), 164.6 (C, *C*O);

Minor diastereomer **45b**: δ_H (300 MHz, $CDCl_3$) 1.76 [3H, d, *J* 7.4, C(5)C*H*$_3$], 2.34 (3H, s, ArC*H*$_3$), 4.15 (2H, s, SC*H*$_2$), 4.64-4.78 [1H, m, C(5)*H*]*, 5.00 [1H, d, *J* 6.4, C(4)*H*], 7.15-7.61 (9H, m, Ar*H*)*, 8.33 (1H, br s, N*H*).

*These signals were indistinguishable for the two diastereomers.

HRMS (ES+): Exact mass calculated for $C_{19}H_{21}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 346.1032. Found 346.1031; m/z (ES+) 348.0 {[($C_{19}H_{20}NOS^{37}Cl$)+H^+], 36%}, 346.0 {[($C_{19}H_{20}NOS^{35}Cl$)+H^+], 88%}, 244.1 (100%).

Elemental analysis resulted in an underestimation of the carbon, hydrogen and nitrogen content, possibly indicating decomposition or the presence of an inorganic impurity.

(3*R,4*R**,5*R**)-3-(Benzylthio)-*N*-*n*-butyl-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 46a and (3*R**,4*R**,5*S**)-3-(benzylthio)-*N*-*n*-butyl-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 46b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.97 g, 8.3 mmol)] was added to a solution of *N*-*n*-butyl-*Z*-3-chloro-2-(benzylthio)propenamide **21** (0.34 g, 1.2 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give the crude products **46a** and **46b** (**46a**:**46b** 1:0.16 by ^{1}H NMR spectroscopy) as a colourless oil. Crystallisation from ether/hexane gave **46a** and **46b** (**46a**:**46b** 1:0.10 by ^{1}H NMR spectroscopy) as a white solid (0.17g, 42%), mp 61-62 °C; ν_{max}/cm^{-1} (KBr) 3355 (NH), 3017 (CH), 2953 (CH), 1664 (CO), 1521 (N=N stretch);

Major diastereomer **46a**: δ_H (300 MHz, $CDCl_3$) 0.86-0.99 [3H, m, *J* 7.4, C(4′)*H*$_3$]*, 1.23-1.68 [7H, m, C(3′)*H*$_2$, C(2′)*H*$_2$ & C(5)C*H*$_3$]*, 3.16-3.38 (2H, m, NHC*H*$_2$)*, 3.99 (1H, d, A of AB system, J_{AB} 11.5, SC*H*$_2$), 4.03 (1H, d, B of AB system, J_{AB} 11.7, SC*H*$_2$), 4.17 [1H, d, *J* 7.0, C(4)*H*], 4.56-4.72 [1H, m, C(5)*H*]*, 6.89 (1H, br s, N*H*), 7.22-7.44 (5H, m, Ar*H*)*; δ_C (75.5 MHz, $CDCl_3$) 12.0, 13.9 [2 × CH_3, *C*(4′)H$_3$ & *C*(5)H$_3$], 18.4 [CH_2, *C*(3′)H$_2$], 29.7 [CH_2, *C*(2′)H$_2$], 33.3[§], 38.2 (2 × CH_2, S*C*H$_2$ & NH*C*H$_2$), 59.8 [CH, *C*(5)H][§], 89.5 [CH, *C*(4)H][§], 96.5 [*C*(3)][§], 164.6 (C, *C*O)[§].

Minor diastereomer **46b**: δ_H (300 MHz, $CDCl_3$) 0.86-0.99 [3H, m, *J* 7.4, C(4′)*H*$_3$]*, 1.23-1.68 [4H, m, C(3′)*H*$_2$ & C(2′)*H*$_2$]*, 1.75 [3H, d, *J* 7.3, C(5)C*H*$_3$], 3.16-3.38 (2H, m, NHC*H*$_2$)*, 4.10 (2H, d, *J* 3.4, SC*H*$_2$), 4.56-4.72 [1H, m, C(5)*H*]*, 4.92 [1H, d, *J* 6.0, C(4)*H*], 6.59 (1H, br s, N*H*), 7.22-7.44 (5H, m, Ar*H*)*; δ_C (75.5 MHz, $CDCl_3$) 12.1 [CH_3, *C*(4′)H$_3$ or *C*(5)H$_3$], 18.5 [CH_2, *C*(3′)H$_2$], 29.5 [CH_2, *C*(2′)H$_2$], 37.8 (CH_2, S*C*H$_2$).

*These signals were indistinguishable for the two diastereomers in the ^{1}H NMR spectrum.

[§]The analogous signals were not detected for the minor diastereomer.

The aromatic signals were not distinguished in the ^{13}C NMR for the two diastereomers and were seen at δ_C 126.1, 126.4, 127.1, 127.2, 127.6 (5 × CH, 5 × aromatic *C*H), 134.0 (C, aromatic *C*).

HRMS (ES+): Exact mass calculated for $C_{16}H_{23}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 312.1189. Found 312.1193; m/z (ES+) 314.2 {[($C_{16}H_{22}NOS^{37}Cl$)+H^+], 42%}, 312.2 {[($C_{16}H_{22}NOS^{35}Cl$)+H^+], 100%}, 214.1 (10%).

(3*R,4*R**,5*R**)-*N*-Benzyl-3-(phenylthio)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 48a and (3*R**,4*R**,5*S**)-*N*-benzyl-3-(phenylthio)-4-chloro-4,5-dihydro-5-methyl-3*H*-pyrazole-3-carboxamide 48b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.87 g, 7.5 mmol)] was added to a solution of *N*-benzyl-*Z*-3-chloro-2-(phenylthio)propenamide **23** (0.32 g, 1.1 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give the crude products **48a** and **48b** (**48a**:**48b** 1:0.27 by ^{1}H NMR spectroscopy) as a colourless oil. Crystallisation from ether/hexane gave **48a** and **48b** (**48a**:**48b** 1:0.22 by ^{1}H NMR spectroscopy) as a white solid (0.31 g, 80%), mp 73-74 °C; (Found C, 59.51; H, 4.94; N, 11.82. $C_{18}H_{18}ClN_3OS$ requires C, 60.07; H, 5.04; N, 11.68%); ν_{max}/cm^{-1} (KBr) 3357 (NH), 3058 (CH), 2978 (CH), 1673 (CO), 1518 (N=N stretch);

Major diastereomer **48a**: δ_H (300 MHz, $CDCl_3$) 1.50 [3H, d, *J* 7.4, C(5)C*H*$_3$], 4.08 (1H, dd, A of ABX, J_{AB} 14.6, J_{AX} 5.4, one of NHC*H*$_2$), 4.24 [1H, d, *J* 6.5, C(4)*H*], 4.30 (1H, dd, B of ABX, J_{AB} 14.6, J_{BX} 5.9, one of NHC*H*$_2$), 4.48-4.57 [1H, sym m, C(5)*H*], 6.38 (1H, br s, N*H*), 7.18-7.46 (8H, m, Ar*H*)*, 7.59-7.68 (2H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 15.9 [C(5)*C*H$_3$], 44.4 (NH*C*H$_2$), 61.0 [*C*(5)H], 91.3 [*C*(4)H], 99.1 [*C*(3)][§], 166.4 (*C*O).

Minor diastereomer **48b**: δ_H (300 MHz, $CDCl_3$) 1.77 [3H, d, *J* 7.2, C(5)C*H*$_3$], 3.77 (1H, dd, A of ABX, J_{AB} 14.7, J_{AX} 5.1, one of NHC*H*$_2$), 4.14 (1H, dd, B of ABX, J_{AB} 14.7, J_{BX} 6.4, one of NC*H*$_2$), 4.32-4.40 [1H, sym m, C(5)*H*], 5.01 [1H, d, *J* 5.8, C(4)*H*], 5.65 (1H, br s, N*H*), 6.79-6.87 (2H, m, Ar*H*), 7.18-7.46 (6H, m, Ar*H*)*, 7.72-7.79 (2H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 14.1 [C(5)*C*H$_3$], 44.6 (NH*C*H$_2$), 62.0 [*C*(5)H], 85.8 [*C*(4)H], 165.1 (*C*O).

*The aromatic signals were indistinguishable for the two diastereomers in the ^{1}H NMR spectrum.

[§]The analogous signal was not detected for the minor diastereomer.

The aromatic signals were not distinguished in the ^{13}C NMR spectrum for the two diastereomers and were seen at δ_C 128.18, 128.24, 128.4, 128.7, 129.1, 129.5, 129.6, 130.4, 130.6, 136.9, 137.6 (aromatic *C*H & aromatic *C*).

HRMS (ES+): Exact mass calculated for $C_{18}H_{19}NOS^{35}Cl$ $[(M+H)^+ - N_2]$, 332.0876. Found 332.0887; m/z (ES+) 334.2 {$[(C_{18}H_{18}NOS^{37}Cl)+H^+]$, 24%}, 332.2 {$[(C_{18}H_{18}NOS^{35}Cl)+H^+]$, 40%}, 88.0 (26%).

(3*R,4*R**,5*R**)-3-(Phenylthio)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 49a and (3*R**,4*R**,5*S**)-3-(phenylthio)-4-chloro-4,5-dihydro-5-methyl-*N*-(4-methylphenyl)-3*H*-pyrazole-3-carboxamide 49b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.76 g, 6.5 mmol)] was added to a solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(phenylthio)propenamide **24** (0.28 g, 0.9 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give the crude products **49a** and **49b** (**49a**:**49b** 1:0.27 by ^1H NMR spectroscopy) as a pale yellow oil. Purification by column chromatography on neutral alumina (activity II) using hexane-ethyl acetate 98:2 gave **49a** as a low melting white solid (0.16 g, 46%) and a single diastereomer; ν_{max}/cm^{-1} (KBr) 3376 (NH), 2979 (CH), 1689 (CO), 1522 (N=N stretch);

Major diastereomer **49a**: δ_H (300 MHz, $CDCl_3$) 1.55 [3H, d, *J* 7.4, C(5)C*H*$_3$], 2.29 (3H, s, ArC*H*$_3$), 4.30 [1H, d, *J* 6.6, C(4)*H*], 4.57-4.67 [1H, m, C(5)*H*], 7.01-7.11 (4H, m, Ar*H* & N*H*), 7.27-7.44 (3H, m, Ar*H*), 7.63-7.74 (3H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 16.1 [CH_3, C(5)*C*H$_3$], 21.5 (CH_3, Ar*C*H$_3$), 61.0 [CH, *C*(5)H], 91.8 [CH, *C*(4)H], 99.0 [C, *C*(3)], 120.5 (CH, aromatic *C*H), 128.5 (C, aromatic *C*), 129.8, 130.0, 131.0 (3 × CH, 3 × aromatic *C*H), 134.2, 135.4 (2 × C, 2 × aromatic *C*), 138.1 (CH, aromatic *C*H), 164.5 (C, *C*O).

The minor diastereomer **49b** was seen in the ^1H NMR spectrum of the crude product (ratio of major to minor 1:0.27 by ^1H NMR spectroscopy): δ_H (300 MHz, $CDCl_3$) 1.79

[3H, d, *J* 7.2, C(5)CH_3], 2.29 (3H, s, ArCH_3), 4.44-4.55 [1H, m, C(5)*H*], 5.08 [1H, d, *J* 5.9, C(4)*H*], 6.89-7.86 (10H, m, Ar*H* & N*H*).

HRMS (ES+): Exact mass calculated for $C_{18}H_{19}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 332.0876. Found 332.0891; m/z (ES+) 334.2 {[$(C_{18}H_{18}NOS^{37}Cl)+H^+$], 42%}, 332.2 {[$(C_{18}H_{18}NOS^{35}Cl)+H^+$], 100%}.

(3*R,4*R**,5*R**)-3-(Phenylthio)-4-chloro-4,5-dihydro-*N*,5-dimethyl-3*H*-pyrazole-3-carboxamide 50a and (3*R**,4*R**,5*S**)-3-(phenylthio)-4-chloro-4,5-dihydro-*N*,5-dimethyl-3*H*-pyrazole-3-carboxamide 50b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (1.20 g, 10.3 mmol)] was added to a solution of *N*-methyl-*Z*-3-chloro-2-(phenylthio)propenamide **25** (0.33 g, 1.5 mmol) in ether (25 mL) cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 6 h. The solvent was removed by evaporation at reduced pressure to give the crude products **50a** and **50b** (**50a**:**50b** 1:0.30 by ^{1}H NMR spectroscopy) as a white solid. Crystallisation from ether/hexane gave **50a** and **50b** (**50a**:**50b** 1:0.10 by ^{1}H NMR spectroscopy) as a white solid (0.20 g, 47%), mp 75-76 °C; (Found C, 50.94; H, 4.92; N, 15.32; Cl, 10.21; S, 11.94. $C_{12}H_{14}ClN_3OS$ requires C, 50.79; H, 4.97; N, 14.81; Cl, 12.49; S, 11.30%); ν_{max}/cm^{-1} (KBr) 3343 (NH), 2951 (CH), 1672 (CO), 1544 (N=N stretch);

Major diastereomer **50a**: δ_H (300 MHz, $CDCl_3$) 1.47 [3H, d, *J* 7.2, C(5)CH_3], 2.56 (3H, d, *J* 4.8, NHCH_3), 4.25 [1H, d, *J* 6.3, C(4)*H*], 4.55 [1H, dq, *J* 7.2, 6.3, C(5)*H*], 6.00 (1H, br s, N*H*), 7.33-7.50 (3H, m, Ar*H*)*, 7.62-7.73 (2H, m, Ar*H*)*; δ_C (75.5 MHz, $CDCl_3$) 16.0 [CH_3,C(5)*C*H_3], 26.7 (CH_3, NH*C*H_3)[§], 60.7 [CH, *C*(5)H], 91.5 [CH, *C*(4)H], 99.6 [C, *C*(3)][§], 129.0 (C, aromatic *C*)[§], 129.5, 130.7, 137.8 (3 × CH, 3 × aromatic *C*H), 167.1 (C, *C*O)[§].

Minor diastereomer **50b**: δ_H (300 MHz, $CDCl_3$) 1.77 [3H, d, *J* 7.2, C(5)CH_3], 2.33 (3H, d, *J* 5.1, NHCH_3), 4.32 [1H, dq, *J* 7.2, 5.7, C(5)*H*], 5.00 [1H, d, *J* 5.7, C(4)*H*], 5.25 (1H, br s, N*H*), 7.33-7.50 (2H, m, Ar*H*)*, 7.62-7.73 (2H, m, Ar*H*)*, 7.74-7.81 (1H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 14.0 [CH_3, C(5)*C*H_3], 61.9 [CH, *C*(5)H], 85.6 [CH, *C*(4)H], 129.4, 130.5, 137.3 (3 × CH, 3 × aromatic *C*H).

*The aromatic signals were indistinguishable for the two diastereomers.

[§]The analogous signals were not detected for the minor diastereomer.

HRMS (ES+): Exact mass calculated for $C_{12}H_{15}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 256.0563. Found 256.0571; m/z (ES+) 258.1 {[$(C_{12}H_{14}NOS^{37}Cl)+H^+$], 40%}, 256.2 {[$(C_{12}H_{14}NOS^{35}Cl)+H^+$], 100%}, 220.2 (52%).

(3*R,4*R**,5*R**)-4-Chloro-4,5-dihydro-*N*,5-dimethyl-3-(phenylthio)-3*H*-pyrazole-3-carboxamide 55a & (3*R**,4*R**,5*S**)-4-chloro-4,5-dihydro-*N*,5-dimethyl-3-(phenylthio)-3*H*-pyrazole-3-carboxamide 55b**

An excess of an ethereal solution of diazoethane [prepared from *N*-ethyl-*N*-nitrosourea **91** (0.80 g, 6.8 mmol)] was added to a solution of methyl *Z*-3-chloro-2-(phenylthio)propenoate **54** (0.25 g, 1.0 mmol) in ether (25 mL) at –20 °C. The reaction solution was allowed to return slowly to room temperature and then stirred for 6 h. The solvent was removed by evaporation at reduced pressure to give the crude products **55a** and **55b** as a colourless oil and a 1:0.23 mixture of diastereomers. Purification by column chromatography on a short column of neutral alumina (activity II) using hexane-ethyl acetate 98:2 as eluent gave the major diastereomer **55a** as a clear oil (0.13 g, 48%); ν_{max}/cm^{-1} (KBr) 2953 (CH), 1738 (CO), 1250; δ_H 1.47 [3H, d, *J* 7.5, C(5)C*H*$_3$], 3.62 (3H, s, OC*H*$_3$), 4.17 [1H, d, *J* 6.3, C(4)*H*], 4.47 [1H, overlapping dq, *J* 7.5, 6.3, C(5)*H*], 7.32-7.47 (3H, m, Ar*H*), 7.66-7.76 (2H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 15.5 [CH_3, C(5)*C*H$_3$], 53.4 (CH_3, O*C*H$_3$), 61.0 [CH, *C*(5)H], 90.5 [CH, *C*(4)H], 99.3 [C, *C*(3)], 128.1 (C, aromatic *C*), 129.0, 130.3, 137.2, (3 × CH, aromatic *C*H), 167.4 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{12}H_{13}N_2O_2S$ [$(M+H)^+$ – HCl], 249.0698. Found 249.0705; m/z (ES+) 287.1 {[$(C_{12}H_{13}N_2O_2S^{37}Cl)+H^+$], 16%}, 285.1 {[$(C_{12}H_{13}N_2O_2S^{35}Cl)+H^+$], 28%}, 249.1 {[$(C_{12}H_{12}N_2O_2S)+H^+$], 30%}.

The minor diastereomer **55b** was evident in the ^{1}H NMR spectrum of the crude product: δ_H 1.78 [3H, d, *J* 7.2, C(5)C*H*$_3$], 3.34 (3H, s, OC*H*$_3$), 4.42-4.51 [1H, m, C(5)*H*], 4.82 [1H, d, *J* 5.4, C(4)*H*], 7.32-7.47 (3H, m, Ar*H*)*, 7.80-7.91 (2H, m, Ar*H*).

*These signals were overlapping with the signals for the major diastereomer **55a**.

***N*-Benzyl-1*H*-pyrazole-3-carboxamide 58**

a) Prepared from N-benzyl-Z-3-chloro-2-(benzylsulfinyl)propenamide **10** *and trimethylsilyldiazomethane*

An ethereal solution of trimethylsilyldiazomethane (1.53 mL of a 2M solution, 3.1 mmol) was added to a stirring solution of *N*-benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **10** (0.20 g, 0.6 mmol) in ether (25 mL) and acetone (4 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred for 6 h. The solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as a yellow solid. Purification by column chromatography using hexane-ethyl acetate (gradient elution 20-40% ethyl acetate) gave **58** as a white solid (0.08 g, 66%), mp 149-150 °C; (Found C, 65.20; H, 5.43; N, 19.97. $C_{11}H_{11}N_3O$ requires C, 65.66; H, 5.51; N, 20.88%); ν_{max}/cm^{-1} (KBr) 3292 (NH stretch), 1641 (CO), 1555, 1351; δ_H (300 MHz, DMSO-d_6) 4.45 (2H, d, *J* 6.3, NHCH_2), 6.68 [1H, br s, C(4)*H*], 7.18-7.36 (5H, m, Ar*H*), 7.82 [1H, br s, C(5)*H*], 8.68 (1H, br s, N*H* of carboxamide), 13.24 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 42.2 (CH_2, NH*C*H_2), 105.4 [CH, *C*(4)H], 127.0, 127.6, 128.6, 130.3 [4 × CH, aromatic *C*H & *C*(5)H], 140.3 (C, aromatic *C*), 146.9 [C, *C*(3)], 162.2 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{11}H_{12}N_3O$ $[M+H]^+$, 202.0980. Found 202.0980; m/z (ES+) 202.2 {[($C_{11}H_{11}N_3O$)+H^+], 100%}, 90.9 (18%).

b) Prepared from N-benzyl-Z-3-chloro-2-(benzenesulfinyl)propenamide **14** *and trimethylsilyldiazomethane*

The title compound was also prepared using an ethereal solution of trimethylsilyldiazomethane (2.21 mL of a 2M solution, 4.4 mmol) and *N*-benzyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **14** (0.28 g, 0.9 mmol) in ether (25 mL) and acetone (4 mL). Following stirring at room temperature for 6 h and removal of the solvent and excess trimethylsilyldiazomethane, the crude product was obtained as a yellow solid. Following purification by column chromatography using hexane-ethyl acetate (gradient elution 20-40% ethyl acetate), **58** was obtained as a white solid (0.04 g, 25%), with IR and ^{1}H NMR spectroscopic details identical to above, except signals at δ_H 6.68 and 7.82 are notably sharper and appear as two doublets (*J*, 2.1) and NH signal is split into a broad triplet (*J*, 5.7).

c) Prepared from N-benzyl-Z-3-chloro-2-(benzenesulfinyl)propenamide **14** *and diazomethane*

The title compound was also prepared by adding a solution of *N*-benzyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **14** (0.16 g, 0.5 mmol) in ether (15 mL) and acetone (4 mL) to an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The reaction solution was slowly allowed to return to room temperature, and following stirring for 6 h and removal of the solvent and excess diazomethane, the crude product was obtained as a yellow oil. Following purification by column chromatography using hexane-ethyl acetate (gradient elution 20-40% ethyl acetate), **39** was obtained as a white solid (0.04 g, 40%), with IR and ^{1}H NMR spectroscopic details identical to above, except the signal at δ_H 6.68 ppm was notably sharper.

_N_-(4-Fluorophenyl)-1_H_-pyrazole-3-carboxamide 59

a) Prepared from N-(4-fluorophenyl)-Z-3-chloro-2-(benzylsulfinyl)propenamide **7** *and trimethylsilyldiazomethane*

An ethereal solution of trimethylsilyldiazomethane (1.51 mL of a 2M solution, 3.0 mmol) was added to a stirring solution of *N*-(4-fluorophenyl)-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **7** (0.20 g, 0.6 mmol) in ether (25 mL) and acetone (1.5 mL). Following stirring at room temperature for 6 h under a nitrogen atmosphere in the dark, the solvent and excess trimethylsilyldiazomethane were removed by concentration under reduced pressure to give the crude product as a yellow solid. Following purification by column chromatography on silica gel using hexane-ethyl acetate (gradient elution 20-40 % ethyl acetate), **59** was obtained as a white solid (0.07 g, 58%), mp 151-153 °C; (Found C, 58.44; H, 4.01; N, 19.52; F, 9.64. $C_{10}H_8FN_3O$ requires C, 58.53; H, 3.93; N, 20.48; F, 9.26%); ν_{max}/cm^{-1} (KBr) 3180 (NH), 2959 (CH), 1656 (CO), 1567, 1508, 1321; δ_H (300 MHz, DMSO-d_6) 6.79 [1H, br s, C(4)*H*], 7.09-7.27 (2H, m, Ar*H*), 7.73-7.97 [3H, m, C(5)*H* & Ar*H*], 10.13 (1H, br s, N*H* of carboxamide), 13.41 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 106.0 [CH, *C*(4)H], 115.4 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3′)H], 122.3 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H], 130.8 [CH, *C*(5)H], 135.6 (C, aromatic *C*), 146.9 [C, *C*(3)], 158.5 [C, d, $^1J_{CF}$ 239, aromatic *C*(4′)], 160.8 (C, CO); HRMS (ES+): Exact mass calculated for $C_{10}H_9N_3OF$ $[M+H]^+$, 206.0730. Found 206.0729; m/z (ES+) 206.2 {[($C_{10}H_8N_3OF$)+H^+], 100%}.

b) Prepared from N-(4-fluorophenyl)-Z-3-chloro-2-(benzenesulfinyl)propenamide **13** *and trimethylsilyldiazomethane*

The title compound was also synthesised using an ethereal solution of trimethylsilyldiazomethane (1.54 mL of a 2M solution, 3.1 mmol) and *N*-(4-fluorophenyl)-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **13** (0.20 g, 0.6 mmol) in ether (20 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred for 6 h. The solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as a yellow solid. Purification by column chromatography using hexane-ethyl acetate (gradient elution 20-60% ethyl acetate) gave **59** as a white solid (0.02 g, 16%), with IR and ^{1}H NMR spectroscopic details identical to above.

_N_-_n_-Butyl-1_H_-pyrazole-3-carboxamide 60

b) Prepared from N-n-butyl-Z-3-chloro-2-(benzylsulfinyl)propenamide **11** *and trimethylsilyldiazomethane*

An ethereal solution of trimethylsilyldiazomethane (2.41 mL of a 2M solution, 4.8 mmol) was added to a stirring solution of *N*-*n*-butyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **11** (0.29 g, 1.0 mmol) in ether (25 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred for 6 h. The solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as a yellow oil. Purification by column chromatography using hexane-ethyl acetate (gradient elution 20-80% ethyl acetate) gave **60** as a low melting white solid (0.08 g, 52%); (Found C, 57.69; H, 7.88; N, 24.56. $C_8H_{13}N_3O$ requires C, 57.46; H, 7.84; N, 25.13%); ν_{max}/cm^{-1} (KBr) 3292 (NH), 3135 (CH), 2955 (CH), 1641 (CO), 1559, 1313; δ_H (300 MHz, DMSO-d_6) 0.89 [3H, t, *J* 7.2, C(4′)H_3], 1.30 [2H, sextet, *J* 7.2, C(3′)H_2], 1.48 [2H, quintet, *J* 7.2, C(2′)H_2], 3.23 [2H, dt, *J* 6.9, 6.9, NHCH_2], 6.66 [1H, br s, C(4)*H*], 7.74 [1H, br s, C(5)*H*], 8.12 (1H, br s, N*H* of carboxamide), 13.18 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 13.7 [CH_3, *C*(4′)H_3], 19.6 [CH_2, *C*(3′)H_2], 31.4 [CH_2, *C*(2′)H_2], 38.0 (CH_2, NH*C*H_2), 104.8 [CH, *C*(4)H], 129.8 [CH, *C*(5)H], 146.8 [C, *C*(3)], 161.6 (C, CO); HRMS (ES+): Exact mass calculated for $C_8H_{14}N_3O$ $[M+H]^+$, 168.1137. Found 168.1138; m/z (ES+) 168.2 {[($C_8H_{13}N_3O$)+H^+], 100%}.

b) Prepared from N-n-butyl-Z-3-chloro-2-(benzenesulfinyl)propenamide **17** *and trimethylsilyldiazomethane*

The title compound was also prepared using an excess of an ethereal solution of trimethylsilyldiazomethane (1.85 mL of a 2M solution, 3.7 mmol) and *N*-*n*-butyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **17** (0.21 g, 0.7 mmol) in ether (20 mL). Following stirring at room temperature for 6 h and removal of the solvent and excess trimethylsilyldiazomethane, the crude product was obtained as a yellow oil. After purification by column chromatography using hexane-ethyl acetate (gradient elution 20-80% ethyl acetate), **60** was obtained as a low melting white solid (0.03 g, 28%), with IR and ^{1}H NMR spectroscopic details identical to above.

_N_-Methyl-1_H_-pyrazole-3-carboxamide 61

An ethereal solution of trimethylsilyldiazomethane (2.56 mL of a 2M solution, 5.1 mmol) was added to a stirring solution of *N*-methyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **9** (0.26 g, 1.0 mmol) in ether (25 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred for 6 h. The solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as a yellow oil. Purification by column chromatography using hexane-ethyl acetate (gradient elution 20-80% ethyl acetate) gave **61** as a white solid (0.09 g, 73%), mp 128-129 °C; ν_{max}/cm^{-1} (KBr) 3294 (NH), 1648 (CO), 1565, 1311; δ_H (300 MHz, DMSO-d_6) 2.76 (3H, d, *J* 4.8, NHCH_3), 6.66 [1H, br d, *J* 2.4, C(4)*H*], 7.76 [1H, br d, *J* 2.1, C(5)*H*], 8.16 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, DMSO-d_6) 25.5 (CH_3, NH*C*H_3), 104.7 [CH, *C*(4)H], 131.5 [CH, br, *C*(5)H], 145.3 [C, br, *C*(3)], 161.7 (C, br, *C*O); HRMS (ES+): Exact mass calculated for $C_5H_8N_3O$ $[M+H]^+$, 126.0667. Found 126.0668; m/z (ES+) 126.0 {[($C_5H_7N_3O$)+H^+], 100%}.

(3_R_*,4_R_*,_S_$_S$*)-_N_-Benzyl-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-3_H_-pyrazole-3-carboxamide 67

A solution of *N*-benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **10** (0.18 g, 0.5 mmol) in ether (15 mL) and acetone (2 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath

while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give **67** as a white solid (0.13 g, 62%) as a single diastereomer, mp 87-88 °C; (Found C, 57.49, H, 4.93, N, 10.95, S, 8.76, Cl, 9.20; $C_{18}H_{18}ClN_3O_2S$ requires C, 57.52, H, 4.83, N, 11.18, S, 8.53, Cl, 9.43%); ν_{max}/cm^{-1} (KBr) 3326 (NH), 3030 (CH), 2976 (CH), 1666 (CO), 1541 (N=N), 1496, 1455, 1265, 1035 (SO); δ_H (300 MHz, $CDCl_3$) 3.87 (1H, d, A of AB system, *J* 12.6, SC*H*$_2$), 4.26 (1H, d, B of AB system, *J* 12.9, SC*H*$_2$), 4.41 (1H, dd, A of ABX, J_{AB} 14.7, J_{AX} 5.4, NHC*H*$_A$H$_B$), 4.62 (1H, dd, B of ABX, J_{AB} 14.9, J_{BX} 6.6, NHCH$_A$*H*$_B$), 4.83-4.93 [1H, m, one of C(5)*H*$_2$], 5.16-5.25 [2H, m, C(4)*H* & one of C(5)*H*$_2$], 7.16-7.40 (10H, m, Ar*H*), 7.71 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 44.4 (CH_2, NH*C*H$_2$), 51.8 [CH, *C*(4)H], 56.5 (CH_2, S*C*H$_2$), 87.4 [CH_2, *C*(5)H$_2$], 108.6 [C, *C*(3)], 127.9, 128.0, 128.88, 128.91, 129.1 (5 × CH, 5 × aromatic *C*H), 129.6 (C, aromatic *C*), 130.4 (CH, aromatic *C*H), 137.0 (C, aromatic *C*), 159.9 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{18}H_{19}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 348.0825. Found 348.0815; m/z (ES+) 350.1 {[($C_{18}H_{18}NO_2S^{37}Cl$)+H^+], 4%}, 348.1 {[($C_{18}H_{18}NO_2S^{35}Cl$)+H^+], 10%}, 87.9 (100%).

(3*R,4*R**,*S*$_S$*)-3-(Benzylsulfinyl)-4-chloro-4,5-dihydro-*N*-methyl-3*H*-pyrazole-3-carboxamide 68 & *N*-Methyl-1*H*-pyrazole-3-carboxamide 61**

A solution of *N*-methyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **9** (0.15 g, 0.6 mmol) in ether (15 mL) and acetone (2 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give **68** as a white solid (0.10 g, 55%), mp 58-59 °C; ν_{max}/cm^{-1} (KBr) 3342 (NH), 3052 (CH), 2921 (CH), 1671 (CO), 1550 (N=N), 1039 (SO); δ_H (300 MHz, $CDCl_3$) 2.93 (3H, d, *J* 4.8, NHC*H*$_3$), 4.02 (1H, d, A of AB system, *J* 12.9, SC*H*$_2$), 4.41 (1H, d, B of AB system, *J* 12.9, SC*H*$_2$), 4.83-4.92 [1H, m, one of C(5)*H*$_2$], 5.18-5.27 [2H, m, C(4)*H* & one of C(5)*H*$_2$], 7.15 (1H, br s, N*H*), 7.24-7.43 (5H, m, Ar*H*); In DMSO-d_6 **68** decomposed rapidly to give the pyrazole **61** with characteristic peaks at δ_H (300 MHz, DMSO-d_6) 2.75 (3H, s, NHC*H*$_3$),

6.66 [1H, d, *J* 2.1, C(4)*H*], 7.27-7.50 (5H, m, Ar*H*), 7.75 [1H, d, *J* 2.1, C(5)*H*], 8.15 (1H, br s, N*H*); δ_C (75.5 MHz, DMSO-d_6) 25.5 [CH_3, NH*C*H_3], 104.7 [CH, *C*(4)H], 131.5 [CH, *C*(5)H], 144.8 [C, *C*(3)], 161.7 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{12}H_{15}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 272.0512. Found 272.0520; m/z (ES+) 300.1 {[$(C_{12}H_{14}N_3O_2S^{35}Cl)+H^+$], 8%}, 348.1 {[$(C_{12}H_{14}NO_2S^{35}Cl)+H^+$], 6%}, 87.9 (100%).

(3*R,4*R**,*S*$_S$*)-3-(*n*-Butylsulfinyl)-4,5-dihydro-*N*-benzyl-3*H*-pyrazole-3-carboxamide 69 & *N*-benzyl-1*H*-pyrazole-3-carboxamide 58**

A solution of *N*-benzyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)propenamide **27** (0.17 g, 0.6 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. Following filtration of the reaction mixture through a sintered glass funnel (grade 3), **69** was obtained as a low melting white solid (0.15 g, 77%) as a single diastereomer. The ^{1}H NMR spectrum of the crude product was very clean; ν_{max}/cm^{-1} (KBr) 3328 (NH), 3035 (CH), 2932 (CH), 1671 (CO), 1540 (N=N), 1046 (SO); δ_H (300 MHz, $CDCl_3$) 0.94 [3H, t, *J* 7.5, C(4′)H_3], 1.33-1.56 [2H, m, C(3′)H_2], 1.74-1.92 [2H, m, C(2′)H_2], 2.82 (1H, ddd, *J* 12.6, 8.4, 6.0, one of SCH_2), 2.92 (1H, ddd, *J* 12.6, 8.7, 7.8, one of SCH_2), 4.40 (1H, dd, A of ABX, J_{AB} 15.0, J_{AX} 5.7, one of NCH_2), 4.54 (1H, B of ABX, J_{AB} 14.7, J_{BX} 6.3, one of NCH_2), 4.86 [1H, A of ABX, J_{AB} 18.9, J_{AX} 6.0, one of C(5)H_2], 5.06 [1H, dd, *J* 6.0, 1.8, C(4)*H*], 5.17 [1H, B of ABX, J_{AB} 18.9, J_{BX} 1.8, one of C(5)H_2], 7.22-7.40 (5H, m, Ar*H*), 7.68 (1H, br s, N*H*).

In DMSO-d_6 **68** decomposed rapidly to give the pyrazole **58** with characteristic peaks at δ_H (300 MHz, DMSO-d_6) 4.44 (2H, d, *J* 6.3, NHCH_2), 6.71 [1H, d, *J* 2.4, C(4)*H*], 7.78 [1H, d, *J* 2.1, C(5)*H*], 8.78 (1H, br t, *J* 6.0, N*H* of carboxamide), a broad signal was also observed at 5.38 ppm (water signal normally observed at 3.40 ppm); δ_C (75.5 MHz, DMSO-d_6) 42.2 (CH_2, NH*C*H_2), 105.4 [CH, *C*(4)H], 127.0, 127.6, 128.6, 130.3 [4 × CH, aromatic *C*H & *C*(5)H], 140.3 (C, aromatic *C*), 146.9 [C, *C*(3)], 162.2 (C, *C*O); m/z (ES+) 202.0 {[$(C_{11}H_{11}N_3O)+H^+$], 100%} (eliminated pyrazole).

(3*R,4*R**)-3-(Benzylthio)-4-chloro-*N*-(4-fluorophenyl)-4,5-dihydro-3*H*-pyrazole-3-carboxamide 70**

A solution of *N*-(4-fluorophenyl)-*Z*-3-chloro-2-(benzylthio)propenamide **19** (0.18 g, 0.6 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 6 h. Following removal of the solvent and excess diazomethane by evaporation under reduced pressure, **70** was obtained as a white solid (0.17 g, 79%) as a single diastereomer (the ^{1}H NMR spectrum of the crude product was very clean), mp 69-70 °C; (Found C, 56.63; H, 4.11; N, 11.58; Cl, 10.40. $C_{17}H_{15}ClN_3OSF$ requires C, 56.12; H, 4.16; N, 11.55; Cl, 9.74%); ν_{max}/cm^{-1} (KBr) 3268 (NH), 3021 (CH), 1668 (CO), 1508 (N=N); δ_H (300 MHz, $CDCl_3$) 4.09 (1H, d, A of AB system, J_{AB} 12.0, one of SCH_2), 4.13 (1H, d, B of AB system, J_{AB} 12.0, one of SCH_2), 4.90 [1H, dd, C of ABC, J_{AC} 6.6, J_{BC} 4.2, C(4)*H*], 4.96 [1H, A of ABC, J_{AB} 18.8, J_{AC} 4.2, one of C(5)H_2], 5.04 [1H, B of ABC, J_{AB} 18.8, J_{BC} 6.6, one of C(5)H_2], 6.97-7.07 (2H, m, Ar*H*), 7.17-7.45 (7H, m, Ar*H*), 8.54 (1H, br s, N*H*); δ_C (75.5 MHz, DMSO-d_6) 34.8 (CH_2, S*C*H_2), 57.0 [CH, *C*(4)H], 84.2 [CH_2, *C*(5)H_2], 100.1 [C, *C*(3)], 115.1 [CH, d, $^2J_{CF}$ 22, aromatic *C*(3′)H], 123.2 [CH, d, $^3J_{CF}$ 8, aromatic *C*(2′)H], 127.4, 128.6, 129.2 (3 × CH, 3 × aromatic *C*H), 134.0, 135.9 (2 × C, 2 × aromatic *C*), 158.8 [C, d, $^1J_{CF}$ 242, aromatic *C*(4′)], 163.7 (C, CO); HRMS (ES+): Exact mass calculated for $C_{17}H_{15}N_3OSF$ [$(M+H)^+$ – HCl], 328.0920. Found 328.0927; m/z (ES+) 328.2 {[$(C_{17}H_{14}N_3OSF)+H^+$], 34%}, 87.9 (100%).

4-(Benzylthio)-*N*-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide 62

An ethereal solution of trimethylsilyldiazomethane (1.94 mL of a 2M solution, 3.9 mmol) was added to a stirring solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(benzylthio)propenamide **20** (0.25 g, 0.8 mmol) in ether (25 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred at room temperature and the reaction progress was monitored by TLC analysis. After stirring for 5 h, TLC analysis showed that a lot of starting material still remained and a further 1.94 mL of trimethylsilyldiazomethane solution was added. Following stirring for 24 h, a further 1.94 mL of trimethylsilyldiazomethane solution was added to the reaction mixture. After

stirring for 48 h, TLC analysis indicated complete consumption of the starting material and the solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as an off-white solid. Purification by column chromatography using hexane-ethyl acetate (gradient elution 10-20% ethyl acetate) gave **62** as a white solid (0.16 g, 63%), mp 150-151 °C; (Found C, 66.34; H, 5.39; N, 12.91; S, 10.18. $C_{18}H_{17}N_3OS$ requires C, 66.85; H, 5.30; N, 12.99; S, 9.91%-C catalyst added); ν_{max}/cm^{-1} (KBr) 3267 (NH), 3150 (NH), 3030 (CH), 2919 (CH), 1652 (CO), 1601, 1551, 1515, 1316; δ_H (300 MHz, $CDCl_3$) 2.35 (3H, s, ArC*H*$_3$), 3.94 (2H, s, SC*H*$_2$), 7.01-7.24 (7H, m, Ar*H*), 7.45 (2H, d, *J* 8.4, Ar*H*), 7.64 [1H, s, C(5)*H*], 9.56 (1H, br s, N*H* of carboxamide), 12.40 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, $CDCl_3$) 21.0 (CH_3, Ar*C*H_3), 42.7 (CH_2, S*C*H_2), 107.9 [C, *C*(4)], 120.2, 127.7, 128.71, 128.73, 129.6 [4 × CH, aromatic *C*H], 134.3, 134.9, 136.8 [3 × C, aromatic *C* & *C*(3)], 142.4 [CH, br, *C*(5)H], 157.7 (C, *C*O); δ_C (75.5 MHz, DMSO-d_6) 20.5 (CH_3, Ar*C*H_3), 38.0 (CH_2, S*C*H_2), 113.3 [C, *C*(4)], 119.9, 126.9, 128.3, 128.8, 128.9 (4 × CH, aromatic *C*H), 132.3, 136.2, 137.8 [3 × C, aromatic *C* & *C*(3)], 143.2 [CH, br, *C*(5)H], 159.8 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{18}H_{18}N_3OS$ $[M+H]^+$, 324.1171. Found 324.1183; m/z (ES+) 324.2 {[($C_{18}H_{17}N_3OS$)+H^+], 100%}, 647.3 {[($C_{36}H_{34}N_6O_2S_2$)+H^+], 22%}.

_N_-(4-Methylphenyl)-4-(phenylthio)-1_H_-pyrazole-3-carboxamide 64

An ethereal solution of trimethylsilyldiazomethane (1.80 mL of a 2M solution, 3.6 mmol) was added to a stirring solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(phenylthio)propenamide **24** (0.22 g, 0.7 mmol) in ether (20 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred at room temperature and the reaction progress was monitored by TLC analysis. After stirring for 5 h, TLC analysis showed that a lot of starting material still remained and a further 1.80 mL of trimethylsilyldiazomethane solution was added. Following stirring for 24 h, a further 1.80 mL of trimethylsilyldiazomethane solution was added to the reaction mixture. After stirring for 48 h, TLC analysis indicated complete consumption of the starting material and the solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as an off-white solid. Recrystallisation from ethyl acetate gave **64** as a white solid (0.11 g, 50%), mp 181-183 °C; (Found C, 65.64; H,

4.88; N, 13.35; S, 10.46. $C_{17}H_{15}N_3OS$ requires C, 66.00; H, 4.89; N, 13.58; S, 10.36%); ν_{max}/cm^{-1} (KBr) 3298 (NH), 3120 (NH), 2919 (CH), 1683 (CO), 1603, 1540, 1314; δ_H (300 MHz, $CDCl_3$) 2.32 (3H, s, ArC*H*$_3$), 7.14 (2H, d, *J* 8.1, Ar*H*), 7.17-7.34 (5H, m, Ar*H*), 7.43 (2H, d, *J* 8.4, Ar*H*), 7.76 [1H, s, C(5)*H*], 9.44 (1H, br s, N*H* of carboxamide), 11.33 [1H, br s, N(1)*H*]; δ_H (300 MHz, DMSO-d_6) 2.27 (3H, s, ArC*H*$_3$), 7.06-7.35 (7H, m, Ar*H*), 7.65 (2H, d, *J* 8.1, Ar*H*), 7.98 [1H, s, C(5)*H*], 10.06 (1H, br s, N*H* of carboxamide), 13.75 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 20.4 (CH_3, Ar*C*H$_3$), 108.7 [C, *C*(4)], 119.9, 125.9, 127.6, 128.9, 129.0 [5 × CH, aromatic *C*H or *C*(3)H], 132.3 (C, aromatic *C*), 134.7 [CH, aromatic *C*H or *C*(5)H], 136.2, 137.3 (2 × C, 2 × aromatic *C*), 146.2 [C, *C*(3)], 159.6 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{17}H_{16}N_3OS$ $[M+H]^+$, 310.1014. Found 310.1018; m/z (ES+) 310.2 {[($C_{17}H_{15}N_3OS$)+H^+], 100%}, 619.3 {[($C_{34}H_{30}N_6O_2S_2$)+H^+], 4%}.

_N_-Methyl-4-(phenylthio)-1*H*-pyrazole-3-carboxamide 65

a) Prepared from N-methyl-Z-3-chloro-2-(benzenethio)propenamide **25** *and trimethylsilyldiazomethane*

An ethereal solution of trimethylsilyldiazomethane (2.62 mL of a 2M solution, 5.2 mmol) was added to a stirring solution of *N*-methyl-*Z*-3-chloro-2-(phenylthio)propenamide **25** (0.24 g, 1.1 mmol) in ether (20 mL) under nitrogen at room temperature in the dark. The reaction solution was then stirred at room temperature and the reaction progress was monitored by TLC analysis. After stirring for 5 h, TLC analysis showed that a lot of starting material still remained and a further 2.62 mL of trimethylsilyldiazomethane solution was added. Following stirring for 24 h, a further 2.62 mL of trimethylsilyldiazomethane solution was added to the reaction mixture. After stirring for 48 h, TLC analysis indicated complete consumption of the starting material and the solvent and excess trimethylsilyldiazomethane were removed by evaporation at reduced pressure to give the crude product as an off-white solid. Recrystallisation from ethyl acetate gave **65** as a white solid (0.15 g, 62%), mp 203-204 °C; ν_{max}/cm^{-1} (KBr) 3334 (NH), 3111 (NH), 2920 (CH), 1649 (CO), 1566, 1478, 1353; δ_H (300 MHz, $CDCl_3$) 2.97 (3H, d, *J* 5.1, NHC*H*$_3$), 7.09-7.32 (5H, m, Ar*H*), 7.64 (1H, br s, N*H* of carboxamide), 7.72 [1H, s, C(5)*H*], 11.64 [1H, br s, N(1)*H*]; δ_H (300 MHz, DMSO-d_6) 2.73 (3H, d, *J* 4.5,

NHC*H*$_3$), 7.12-7.38 (5H, m, Ar*H*), 7.85 [1H, s, C(5)*H*], 8.08 (1H, br d, *J* 3.6, N*H* of carboxamide), 13.56 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 24.4 (CH_3, NH*C*H$_3$), 106.9 [C, *C*(4)], 124.6, 126.4, 127.8, 133.2 (br) [4 × CH, aromatic *C*H & *C*(5)H], 136.4 (C, aromatic *C*), 144.8 [C, br, *C*(3)], 160.5 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{11}H_{12}N_3OS$ $[M+H]^+$, 234.0701. Found 234.0711; m/z (ES+) 234.1 {[($C_{11}H_{11}N_3OS$)+H^+], 100%}, 467.2 {[($C_{22}H_{22}N_6O_2S_2$)+H^+], 24%}.

b) Prepared from N-methyl-Z-3-chloro-2-(phenylthio)propenamide **25** *and diazomethane*

The title compound was also prepared by addition of a solution of *N*-methyl-*Z*-3-chloro-2-(benzenethio)propenamide **25** (0.20 g, 0.9 mmol) in ether (15 mL) to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The reaction mixture was allowed to return slowly to room temperature and then stirred for 4 h. Following removal of the solvent and excess diazomethane, the crude product was obtained as a yellow solid. After purification by column chromatography on silica gel using hexane-ethyl acetate (gradient elution 20-40% ethyl acetate), **65** was obtained as a white solid (0.02 g, 10%), with IR and ^{1}H NMR spectroscopic details identical to above.

(3*R,4*R**)-*N*-Benzyl-3-(benzylthio)-4-chloro-4,5-dihydro-3*H*-pyrazole-3-carboxamide 72 & *N*-benzyl-4-(benzylthio)-1*H*-pyrazole-3-carboxamide 71**

A solution of *N*-benzyl-*Z*-3-chloro-2-(benzylthio)propenamide **28** (0.18 g, 0.6 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 6 h. Following removal of the solvent and excess diazomethane by evaporation under reduced pressure, **72** was obtained as a white solid (0.17 g, 84%) as a single diastereomer. The ^{1}H NMR spectrum of the crude product was very clean. {Note: This compound decomposed before full analysis could be carried out, with characteristic signals for **71** seen at δ_H 3.81 (s, SC*H*$_2$), 4.47 (d, *J* 6.3, NHC*H*$_2$), 7.47 [s, C(5)*H*], 8.07 (s, N*H*)}; δ_H (300 MHz, $CDCl_3$) 3.98 (1H, d, A of AB system, J_{AB} 11.7, one of SC*H*$_2$), 4.03 (1H, d, B of AB system, J_{AB} 11.7, one of SC*H*$_2$), 4.35 (1H, A of ABX, J_{AB} 14.4, J_{AX} 6.0, one of NC*H*$_2$), 4.45 (1H, B of

ABX, J_{AB} 14.4, J_{BX} 6.0, one of NCH_2), 4.87 [1H, dd, *J* 5.4, 4.5, C(4)*H*], 4.94-4.96 [2H, m, C(5)H_2], 7.17 (1H, br s, N*H*), 7.22-7.42 (10H, m, Ar*H*).

(3*R,4*R**)-*N*-Benzyl-3-(phenylthio)-4-chloro-4,5-dihydro-3*H*-pyrazole-3-carboxamide 73**

A solution of *N*-benzyl-*Z*-3-chloro-2-(phenylthio)propenamide **23** (0.20 g, 0.7 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The solution was allowed to return slowly to room temperature while stirring for 4 h. A precipitate formed as the reaction progressed. Following filtration of the reaction mixture through a sintered glass funnel (grade 3), **73** was obtained as a white solid (0.19 g, 91%), mp 87-89 °C; (Found C, 59.04; H, 4.55; N, 11.79; Cl, 10.27; S, 8.93. $C_{17}H_{16}ClN_3OS$ requires C, 59.04; H, 4.66; N, 12.15; Cl, 10.25; S, 9.27%); ν_{max}/cm^{-1} (KBr) 3321 (NH), 3014 (CH), 1660 (CO), 1518 (N=N); δ_H (300 MHz, $CDCl_3$) 3.92 (1H, dd, A of ABX, J_{AB} 14.6, J_{AX} 5.4 one of NCH_2), 4.20 (1H, dd, B of ABX, J_{AB} 14.6, J_{BX} 5.7, one of NCH_2), 4.72 [1H, dd, A of ABC, J_{AB} 19.2, J_{AC} 6.9, one of C(5)H_2], 4.88 [1H, dd, B of ABC, J_{AB} 19.2, J_{BC} 3.3, one of C(5)H_2], 4.91 [1H, dd, C of ABC, J_{AC} 6.9, J_{BC} 3.3, C(4)*H*], 5.98 (1H, br s, N*H*), 6.86-6.93 (2H, m, Ar*H*), 7.21-7.46 (6H, m, Ar*H*), 7.68-7.75 (2H, m, Ar*H*); δ_C (75.5 MHz, DMSO-d_6) 42.9 (CH_2, NH*C*H_2), 57.3 [CH, *C*(4)H], 83.7 [CH_2, *C*(5)H_2], 101.5 [C, *C*(3)], 126.6, 127.0, 128.1, 129.0, 129.3 (5 × CH, 5 × aromatic *C*H), 129.5 (C, aromatic *C*), 134.8 (CH, aromatic *C*H), 138.3 (C, aromatic *C*), 164.1 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{17}H_{17}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 318.0719. Found 318.0704; m/z (ES+) 318.2 {[$(C_{17}H_{16}NOS^{35}Cl)+H^+$], 8%}, 87.9 (100%).

***N*-Benzyl-4-(*n*-butylthio)-1*H*-pyrazole-3-carboxamide 74**

A solution of *N*-benzyl-*Z*-3-chloro-2-(*n*-butylthio)propenamide **92** (0.18 g, 0.6 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 4 h. Following removal of the solvent and excess diazomethane, the crude product was obtained as a pale yellow oil. After purification by column chromatography on silica gel

using hexane-ethyl acetate (gradient elution 20-80% ethyl acetate), **74** was obtained as a white solid (0.07 g, 38%), mp 120-122 °C; (Found C, 61.66; H, 6.46; N, 14.24. $C_{15}H_{19}N_3OS$ requires C, 62.25; H, 6.62; N, 14.52%); ν_{max}/cm^{-1} (KBr) 3275 (NH), 3109 (NH), 2951 (CH), 1644 (CO), 1555; δ_H (300 MHz, $CDCl_3$) 0.82 [3H, t, *J* 7.5, C(4′)H_3], 1.21-1.36 [2H, m, C(3′)H_2], 1.37-1.57 [2H, m, C(2′)H_2], 2.63 (2H, t, *J* 7.2, SCH_2), 4.65 (2H, d, *J* 5.7, NHCH_2), 7.22-7.39 (5H, m, Ar*H*), 7.62 [1H, s, C(5)*H*], 8.35 (1H, br s, N*H*), 11.23 [1H, br s, N(1)*H*]; δ_C (75.5 MHz, $CDCl_3$) 13.6 [CH_3, *C*(4′)H_3], 21.7 [CH_2, *C*(3′)H_2], 31.3 [CH_2, *C*(2′)H_2], 37.4 (CH_2, S*C*H_2), 43.4 (CH_2, NH*C*H_2), 109.2 [C, *C*(4)], 127.6, 127.8, 128.7 (3 × CH, aromatic *C*H), 137.8 (C, aromatic *C*), 140.2 [CH, br, *C*(5)H], 160.2 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{15}H_{20}N_3OS$ $[M+H]^+$, 290.1327. Found 290.1339; m/z (ES+) 290.2 {[($C_{15}H_{19}N_3OS$)+H^+], 100%}, 579.3 {[($C_{30}H_{38}N_6O_2S_2$)+H^+], 10%}.

4-(*n*-Butylthio)-*N*-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide 75

A solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(*n*-butylthio)propenamide **30** (0.21 g, 0.7 mmol) in ether (15 mL) was added to an excess of an ethereal solution of diazomethane [prepared from Diazald® (0.84 g, 3.9 mmol)] cooled in an ice-salt bath while stirring. The reaction solution was allowed to return slowly to room temperature while stirring for 4 h. Following removal of the solvent and excess diazomethane, the crude product was obtained as a pale yellow oil. After purification by column chromatography on silica gel using hexane-ethyl acetate (gradient elution 20-80% ethyl acetate), **75** was obtained as a white solid (0.04 g, 20%), mp 131-132 °C; ν_{max}/cm^{-1} (KBr) 3286 (NH), 3110 (NH), 2923 (CH), 1685 (CO), 1602, 1541; δ_H (300 MHz, $CDCl_3$) 0.89 [3H, t, *J* 7.2, C(4′)H_3], 1.41 [2H, sextet, *J* 7.2, C(3′)H_2], 1.52-1.67 [2H, m, C(2′)H_2]*, 2.34 (3H, s, ArCH_3), 2.76 (2H, dd, *J* 7.5, 7.2, SCH_2), 7.20 (2H, d, *J* 8.4, Ar*H*), 7.57 (2H, d, *J* 8.1, Ar*H*), 7.70 [1H, s, C(5)*H*], 9.90 (1H, br s, N*H*); δ_C (75.5 MHz, $CDCl_3$) 13.6 [CH_3, *C*(4′)H_3], 21.0 (CH_3, Ar*C*H_3), 21.7 [CH_2, *C*(3′)H_2], 31.3 [CH_2, *C*(2′)H_2], 37.6 (CH_2, S*C*H_2), 108.7 [C, *C*(4)], 120.2, 129.7 (2 × CH, aromatic *C*H), 134.4, 135.2 (2 × C, aromatic *C*), 140.5 [C, br, *C*(3)], 158.6 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{15}H_{20}N_3OS$ $[M+H]^+$,

290.1327. Found 290.1319; m/z (ES+) 290.2 {[($C_{15}H_{19}N_3OS$)+H^+], 100%}, 579.3 {[($C_{30}H_{38}N_6O_2S_2$)+H^+], 8%}.

*This signal sharpened in the ^{1}H NMR spectrum with a D_2O shake to give a quintet at 1.60 ppm (*J* 7.2).

_N_-(4-Methylphenyl)-5-phenyl-1_H_-pyrazole-3-carboxamide 79[6]

a) Prepared from N-(4-methylphenyl)-Z-3-chloro-2-(benzenesulfinyl)propenamide **16**

A solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **16** (0.20 g, 0.7 mmol) in ether (10 mL) and acetone (2 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.67 g, 6.0 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. After removal of the solvent by evaporation at reduced pressure, the crude product was obtained as an orange solid. Following purification by column chromatography on silica gel using hexane-ethyl acetate (gradient elution 10-40% ethyl acetate) as eluent, **79** was obtained as a pale yellow solid (0.10 g, 56%), mp 228-230 °C; ν_{max}/cm^{-1} (KBr) 3378 (NH), 3198 (NH), 2919 (CH), 1660 (CO), 1596; δ_H (300 MHz, DMSO-d_6) 2.30 (3H, s, ArCH_3), 7.01-8.01 [10H, m, Ar*H* & C(4)*H* (tentatively assigned as a br s at 7.28 ppm)], 10.07 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, DMSO-d_6) 20.5 (CH_3, Ar*C*H_3), 102.9 [CH, *C*(4)H], 120.2, 125.3, 128.3, 129.0 (4 × CH, 4 × aromatic *C*H), 132.5, 136.1 (2 × C, 2 × aromatic *C*), 159.2 (C, *C*O). There was a broad signal in the region 127-131 ppm and the signals for C(3), C(5), one aromatic C and one aromatic CH were not detected in the ^{13}C NMR spectrum; HRMS (ES+): Exact mass calculated for $C_{17}H_{16}N_3O$ $[M+H]^+$, 278.1293. Found 278.1306; m/z (ES+) 278.0 {[($C_{17}H_{15}N_3O$)+H^+], 100%}.

b) Prepared from N-(4-methylphenyl)-Z-3-chloro-2-(n-butylsulfinyl)propenamide **31**

The title compound was also prepared by addition of a solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(*n*-butylsulfinyl)propenamide **31** (0.15 g, 0.5 mmol) in ether (10 mL) to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.55 g, 5.6 mmol)]. A precipitate formed as the reaction progressed. Following stirring at room temperature for 16 h the reaction was filtered through a sintered glass funnel (grade 4) to give **79** as a white solid (0.05 g, 38%), mp 228-230 °C; (Found C, 73.02; H, 5.35; N,

15.17. $C_{17}H_{15}N_3O$ requires C, 73.63; H, 5.45; N, 15.15%); ν_{max}/cm^{-1} (KBr) 3379 (NH), 3195 (NH), 3017 (CH), 2917 (CH), 1661 (CO), 1597; δ_H (300 MHz, $CDCl_3$) 2.35 (3H, s, ArC*H*$_3$), 7.16 [1H, s, C(4)*H*], 7.18 (2H, d, *J* 8.4, Ar*H*), 7.38-7.52 (3H, m, Ar*H*), 7.55-7.66 (4H, m, Ar*H*), 8.63 (1H, br s, N*H* of carboxamide); δ_H (300 MHz, DMSO-d_6) 2.29 (3H, s, ArC*H*$_3$), 7.17 (2H, d, *J* 8.4, Ar*H*), 7.27 [1H, br s, C(4)*H*], 7.37-7.55 (3H, m, Ar*H*), 7.68 (2H, d, *J* 8.4, Ar*H*), 7.84 (2H, d, *J* 7.2, Ar*H*). There was an additional set of signals present at δ_H (300 MHz, DMSO-d_6) 5.72 (s), 8.27 (s), 10.04 (br s); δ_C (75.5 MHz, DMSO-d_6) 20.5 (CH_3, Ar*C*H$_3$), 102.9 [CH, *C*(4)H], 120.2, 125.3, 128.3, 128.97, 128.99 (5 × CH, 5 × aromatic *C*H), 132.6, 136.1 (2 × C, 2 × aromatic *C*), 159.2 (C, *C*O). The signals for C(3) and C(5) were not detected in the ^{13}C NMR spectrum.
HRMS (ES+): Exact mass calculated for $C_{17}H_{16}N_3O$ $[M+H]^+$, 278.1293. Found 278.1282; m/z (ES+) 278.0 {[($C_{17}H_{15}N_3O$)+H^+], 100%}.

(3*R,4*R**,5*R**,*S*$_S$*)-3-(Benzylsulfinyl)-4-chloro-4,5-dihydro-*N*-methyl-5-phenyl-3*H*-pyrazole-3-carboxamide 77 & *N*-methyl-5-phenyl-1*H*-pyrazole-3-carboxamide 82**

The reaction was conducted by addition of a solution of *N*-methyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **9** (0.18 g, 0.7 mmol) in ether (10 mL) to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.40 g, 5.0 mmol)] cooled to −50 °C using a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. A precipitate formed as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give **77** as a white solid (0.10 g, 37%) as a single diastereomer, mp 76-78 °C; (Found C, 55.90; H, 4.91; N, 10.58. $C_{18}H_{18}ClN_3O_2S$ requires C, 57.52; H, 4.83; N, 11.18%); ν_{max}/cm^{-1} (KBr) 3320 (NH), 3034 (CH), 2931 (CH), 1671 (CO), 1532 (N=N), 1047 (SO); δ_H (300 MHz, $CDCl_3$) 3.02 (3H, d, *J* 4.8, NHC*H*$_3$), 4.21 (1H, d, A of AB system, *J* 12.8, one of SC*H*$_2$), 4.40 (1H, d, B of AB system, *J* 12.8, one of SC*H*$_2$), 4.69 [1H, d, *J* 6.8, C(4)*H*Cl], 5.94 [1H, d, *J* 6.4, C(5)*H*Ph], 7.00 (1H, br t, N*H*), 7.20-7.50 (14H, m, Ar*H*); δ_C (75.5 MHz, $CDCl_3$) 26.8 (CH_3, NH*C*H$_3$), 56.3 (CH_2, SC*H*$_2$), 59.3 [CH, *C*(4)HCl], 99.8 [CH, *C*(5)HPh], 107.5 [C, *C*(3)], 127.0, 128.9, 129.1, 129.2, 129.3 (5 × CH, 5 × aromatic *C*H), 129.9 (C, aromatic *C*), 130.5 (CH, aromatic *C*H), 134.2 (C, aromatic *C*), 162.8 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{18}H_{19}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 348.0825.

Found 348.0816; m/z (ES+) 350.0 {[($C_{18}H_{18}NO_2S^{37}Cl$)+H^+], 8%}, 348.2 {[($C_{18}H_{18}NO_2S^{35}Cl$)+H^+], 20%}, 202.2 {[($C_{11}H_{11}N_3O$)+H^+], 8%}, 87.9 (100%).

(3*R,4*R**,5*R**,*S*$_S$*)-*N*-Benzyl-3-(benzylsulfinyl)-4-chloro-4,5-dihydro-5-phenyl-3*H*-pyrazole-3-carboxamide 78 & *N*-benzyl-5-phenyl-1*H*-pyrazole-3-carboxamide 80**

A solution of *N*-benzyl-*Z*-3-chloro-2-(benzylsulfinyl)propenamide **10** (0.21 g, 0.6 mmol) in ether (12 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.61 g, 5.9 mmol)] cooled to −50 °C using a cryocooler. The solution was slowly allowed to return to room temperature and the reaction mixture was then stirred for 16 h. A precipitate formed as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give **78** as a white solid (0.18 g, 64%) as a single diastereomer, mp 99-100 °C; (Found C, 63.14; H, 4.76; N, 9.30. $C_{24}H_{22}ClN_3O_2S$ requires C, 63.78; H, 4.91; N, 9.30%); ν_{max}/cm^{-1} (KBr) 3310 (NH), 3029 (CH), 2983 (CH), 1678 (CO), 1525 (N=N), 1049 (SO); δ_H (300 MHz, DMSO-d_6) 4.17 (1H, d, A of AB system, J_{AB} 12.6, one of SCH_2), 4.27 (1H, d, A of AB system, J_{AB} 12.6, one of SCH_2), 4.31 (1H, dd, A of ABX, J_{AB} 14.4, J_{AX} 5.7, one of NHCH_2), 4.59 (1H, dd, A of ABX, J_{AB} 14.4, J_{BX} 6.6, one of NHCH_2), 4.86 [1H, d, *J* 8.7, C(4)*H*Cl], 5.59 [1H, d, *J* 8.7, C(5)*H*Ph], 7.11-7.56 (15H, m, Ar*H*), 9.44 (1H, br t, *J* 6.3, N*H*). There was also evidence for decomposition to the pyrazole **80**, with characteristic peaks at δ_H (300 MHz, DMSO-d_6) 4.48 (2H, d, *J* 6.0, NHCH_2), 7.18 [1H, s, C(4)*H*], 7.81 (2H, d, *J* 8.4, Ar*H*), 8.89 (1H, br t, *J* 6.0, N*H* of carboxamide), a broad signal for water was also observed at 3.61 ppm (water signal normally observed at 3.40 ppm). When the ^{1}H NMR spectrum was re-run after 20 hours, complete decomposition to the pyrazole **80** had occurred, with spectroscopic details consistent with a genuine sample of **80**.

HRMS (ES+): Exact mass calculated for $C_{24}H_{23}NO_2S^{35}Cl$ [$(M+H)^+ - N_2$], 424.1138. Found 424.1136; m/z (ES+) 424.2 {[($C_{24}H_{22}NO_2S^{35}Cl$)+H^+], 4%}, 278.2 {[($C_{17}H_{15}N_3O$)+H^+], 16%}, 87.9 (100%).

N-Benzyl-5-phenyl-1*H*-pyrazole-3-carboxamide 80

a) Prepared from N-benzyl-Z-3-chloro-2-(benzenesulfinyl)propenamide **14** *(^{1}H NMR spectrum recorded in DMSO-d_6)*

A solution of *N*-benzyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **14** (0.19 g, 0.6 mmol) in ether (10 mL) and acetone (1 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.67 g, 6.0 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. After removal of the solvent by evaporation at reduced pressure, the crude product was obtained as a red oil. Following purification by column chromatography on silica gel using hexane: ethyl acetate (gradient elution 10-40% ethyl acetate), **80** was isolated as a white solid (0.13 g, 79%), mp 178-180 °C; ν_{max}/cm^{-1} (KBr) 3410 (NH), 3127 (NH), 3064 (CH), 2924 (CH), 1645 (CO), 1553; δ_H (300 MHz, DMSO-d_6) 4.49 (2H, d, *J* 6.3, NHCH_2), 7.18 [1H, s, C(4)*H*], 7.22-7.55 (8H, m, Ar*H*), 7.81 (2H, d, *J* 7.8, Ar*H*), 8.89 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, DMSO-d_6) 42.0 (CH_2, NH*C*H_2), 102.4 [CH, *C*(4)H], 125.2, 126.7, 127.3, 128.15, 128.22, 128.9 (6 × CH, 6 × aromatic *C*H), 139.6 (C, aromatic *C*), 160.6 (C, br, *C*O). The signals for C(3), C(5) and one aromatic C were not detected in the ^{13}C NMR spectrum.

HRMS (ES+): Exact mass calculated for $C_{17}H_{16}N_3O$ $[M+H]^+$, 278.1293. Found 278.1297; m/z (ES+) 278.3 {[($C_{17}H_{15}N_3O$)+H^+], 100%}.

b) Prepared from N-benzyl-Z-3-chloro-2-(n-butylsulfinyl)propenamide **27** *(^{1}H NMR spectrum recorded in $CDCl_3$ and DMSO-d_6)*

The title compound was also prepared by addition of a solution of *N*-benzyl-*Z*-3-chloro-2-(*n*-butylsulfinyl)propenamide **27** (0.10g, 0.3 mmol) in ether (10 mL) to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.56 g, 5.6 mmol)]. A precipitate formed as the reaction progressed. Following stirring at room temperature for 16 h the reaction was filtered through a sintered glass funnel (grade 4) to give **80** as a white solid (0.03 g, 36%), mp 177-178 °C; ν_{max}/cm^{-1} (KBr) 3410 (NH), 3128 (NH), 3066 (CH), 2924 (CH), 1643 (CO), 1554; δ_H (300 MHz, $CDCl_3$) 4.66 (2H, d, *J* 6.0, NHCH_2), 7.08 [1H, s, C(4)*H*], 7.13 (1H, br s, N*H* of carboxamide), 7.22-7.51 (8H, m, Ar*H*), 7.60 (2H, d, *J* 7.5, Ar*H*); δ_H (300 MHz, DMSO-d_6) 4.48 (2H, d, *J* 6.0, NHCH_2), 7.09 [1H, br s, C(4)*H*], 7.18-7.56 (8H, m, Ar*H*), 7.80 (2H, d, *J* 7.5, Ar*H*), 8.75 (1H, br s, N*H* of

carboxamide). HRMS (ES+): Exact mass calculated for $C_{17}H_{16}N_3O$ $[M+H]^+$, 278.1293. Found 278.1307; m/z (ES+) 278.3 {$[(C_{17}H_{15}N_3O)+H^+]$, 100%}.

_N_-Methyl-5-phenyl-1_H_-pyrazole-3-carboxamide 82 & (3_R_*,4_R_*,5_R_*,S_S*)-4-Chloro-4,5-dihydro-_N_-methyl-5-phenyl-3-(benzenesulfinyl)-3_H_-pyrazole-3-carboxamide 81

A solution of *N*-methyl-*Z*-3-chloro-2-(benzenesulfinyl)propenamide **15** (0.21 g, 0.9 mmol) in ether (10 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.67 g, 6.0 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature and the reaction mixture was then stirred for 16 h. A precipitate formed as the reaction progressed. The crude product was collected by filtration through a sintered glass funnel (grade 3) to give a mixture of **82** and **81** (**82**:**81** 9:1 by ^{1}H NMR spectroscopic analysis) as white solid (0.18 g, 64%). Following trituration in ether, **82** and **81** were obtained as a pale yellow solid (0.03 g, 17%) (**82**:**81** 9:1 by ^{1}H NMR spectroscopy**)**, mp 161-162 °C; ν_{max}/cm^{-1} (KBr) 3401 (NH), 3272 (NH), 3044 (CH), 1669 (CO), 1571;

82: δ_H (300 MHz, $CDCl_3$) 3.00 (3H, d, *J* 4.8, NHC*H*$_3$), 6.99 (1H, br s, N*H* of carboxamide), 7.07 [1H, s, C(4)*H*], 7.33-7.51 (3H, m, Ar*H*), 7.58-7.70 (2H, m, Ar*H*), a broad water signal was observed at 2.88 ppm (water signal is normally seen at 1.60 ppm); δ_H (300 MHz, DMSO-d_6) 2.78 (3H, br s, NHC*H*$_3$), 7.01-7.54 [4H, m, C(4)*H* & Ar*H*], 7.75-7.84 (2H, br m, Ar*H*), 8.33 (1H, br s, N*H* of carboxamide). N(1)*H* of pyrazole was unresolved in both $CDCl_3$ and DMSO-d_6; δ_C (75.5 MHz, DMSO-d_6) 25.5 (CH_3, NH*C*H$_3$), 102.2 [CH, *C*(4)H], 125.1, 128.1, 128.9 (3 × CH, 3 × aromatic *C*H), 130.3 (C, aromatic *C*), 144.6, 145.8 [2 × C, *C*(3) & *C*(5)], 161.1 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{11}H_{12}N_3O$ $[M+H]^+$, 202.0980. Found 202.0984; m/z (ES+) 202.0 {$[(C_{11}H_{11}N_3O)+H^+]$, 100%}.

Characteristic peaks for **81** were seen at δ_H (300 MHz, $CDCl_3$) 4.68 [1H, d, *J* 10.8, C(4)*H*Cl], 5.53 [1H, d, *J* 10.5, C(5)*H*Ph], 9.24 (1H, br s, N*H*) and at δ_H (300 MHz, DMSO-d_6) 5.04 [1H, br s, C(4)*H*Cl], 5.55 [1H, d, *J* 10.0, C(5)*H*Ph], 8.98 (1H, br s, N*H*).

_N_-Benzyl-4-(benzylthio)-5-phenyl-1_H_-pyrazole-3-carboxamide 83

A solution of *N*-benzyl-*Z*-3-chloro-2-(benzylthio)propenamide **28** (0.20 g, 0.6 mmol) in ether (10 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.51 g, 5.4 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. Following removal of the solvent and excess phenyldiazomethane by evaporation under reduced pressure, the crude product was obtained as a red oil. The ^{1}H NMR spectrum of the crude product was very complex, with evidence for the pyrazoline at δ_H 5.60 [d, *J* 8.4, C(5)*H*Ph]. Purification by column chromatography using hexane-ethyl acetate (gradient elution 10-20% ethyl acetate) gave **83** as a white solid (0.05 g, 19%), mp 157-158 °C; ν_{max}/cm^{-1} (KBr) 3264 (NH), 3181 (NH), 2924 (CH), 1645 (CO), 1602, 1559; δ_H (300 MHz, $CDCl_3$) 3.65 (2H, s, SCH_2), 4.48 (2H, d, *J* 5.8, NHCH_2), 6.73-6.82 (2H, m, Ar*H*), 7.04-7.50 (11H, m, Ar*H*), 7.93 (2H, dd, *J* 8.1, 1.8, Ar*H*), 8.19 (1H, br t, N*H* of carboxamide); δ_C (75.5 MHz, $CDCl_3$) 41.0, 43.4 (2 × CH_2, S*C*H_2 & NH*C*H_2), 105.3 [C, *C*(4)], 127.5, 127.7, 127.85, 127.88, 128.2, 128.5, 128.6, 128.8, 129.1 (9 × CH, 9 × aromatic *C*H), 131.8, 136.5, 137.5 (3 × C, 3 × aromatic *C*), 158.9 (C, *C*O), the signals for C(3) and C(5) were not detected in the ^{13}C NMR spectrum; HRMS (ES+): Exact mass calculated for $C_{24}H_{22}N_3OS$ $[M+H]^+$, 400.1484. Found 400.1497; m/z (ES+) 400.0 {[($C_{24}H_{21}N_3OS$)+H^+], 100%}.

4-(Benzylthio)-5-phenyl-*N*-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide 84

A solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(benzylthio)propenamide **20** (0.17 g, 0.5 mmol) in ether (10 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.54 g, 5.5 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. Following removal of the solvent and excess phenyldiazomethane by evaporation under reduced pressure, the crude product was obtained as a red oil. In the ^{1}H NMR spectrum of the crude product, there was evidence for the pyrazoline at δ_H 4.49 [d, *J* 8.4, C(4)*H*Cl], 5.63 [d, *J* 8.4, C(5)*H*Ph]. Purification by column chromatography using hexane-ethyl acetate (gradient elution 10-15% ethyl acetate) gave **84** as a white solid (0.05 g, 24%), mp 191-192 °C; (Found C, 71.98; H, 5.58; N, 10.12; S, 8.09. $C_{24}H_{21}N_3OS$ requires C, 72.15; H, 5.30; N, 10.52; S, 8.03%); ν_{max}/cm^{-1} (KBr) 3398 (NH), 3190 (NH), 2921 (CH), 1660 (CO), 1604, 1525; δ_H (300 MHz, $CDCl_3$) 2.35 (3H, s, ArCH_3), 3.78

(2H, s, SC*H*$_2$), 6.85-6.96 (2H, m, Ar*H*), 7.03-7.12 (3H, m, Ar*H*), 7.16 (2H, d, *J* 8.1, Ar*H*), 7.38-7.52 (5H, m, Ar*H*), 7.95 (2H, br d, *J* 6.3, Ar*H*), 9.70 (1H, br s, N*H* of carboxamide), 11.65 [1H, v br s, N(1)*H*]; δ_C (75.5 MHz, DMSO-d_6) 20.4 (CH_3, Ar*C*H$_3$), 40.0 (CH_2, S*C*H$_2$), 106.5 [C, br, *C*(4)], 120.0, 126.8, 128.0, 128.1, 128.3, 128.7, 129.1 (7 × CH, 7 × aromatic *C*H, 7 signals for 8 carbons), 132.7, 136.0, 137.6 (3 × C, 3 × aromatic *C*), 146.4, 149.5 [2 × C, *C*(3) and *C*(5)], 160.4 (C, *C*O); HRMS (ES+): Exact mass calculated for $C_{24}H_{22}N_3OS$ $[M+H]^+$, 400.1484. Found 400.1476; m/z (ES+) 400.0 {[($C_{24}H_{21}N_3OS$)+H^+], 100%}.

(3*R,4*R**,5*R**)-4-Chloro-4,5-dihydro-*N*-methyl-5-phenyl-3-(phenylthio)-3*H*-pyrazole-3-carboxamide 86, *N*-methyl-5-phenyl-1*H*-pyrazole-3-carboxamide 82[47] & *N*-methyl-5-phenyl-4-(phenylthio)-1*H*-pyrazole-3-carboxamide 90**

A solution of *N*-methyl-*Z*-3-chloro-2-(phenylthio)propenamide **25** (0.15 g, 0.7 mmol) in ether (10 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.57 g, 5.6 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. A precipitate formed as the reaction progressed. The product was collected by filtration through a sintered glass funnel (grade 3) to give **86** as a white solid (0.06 g, 25%) as a single diastereomer, mp 93-94 °C; ν_{max}/cm^{-1} (KBr) 3399 (NH), 2945 (CH), 1667 (CO), 1528 (N=N); δ_H (300 MHz, $CDCl_3$) 2.65 (3H, d, *J* 5.0, NHC*H*$_3$), 4.48 [1H, d, *J* 7.6, C(4)*H*Cl], 5.40 [1H, d, *J* 7.6, C(5)*H*Ph], 6.28 (1H, br s, N*H*), 7.21-7.29 (2H, m, Ar*H*), 7.35-7.51 (6H, m, Ar*H*), 7.66-7.73 (2H, m, Ar*H*); δ_H (400 MHz, DMSO-d_6) 2.49 (3H, d, *J* 4.4, NHC*H*$_3$), 4.62, 5.59 [2 × 1H, 2 × d, *J* 7.6, C(5)*H*Ph & C(4)*H*Cl], 7.27-7.32 (2H, m, Ar*H*), 7.40-7.55 (6H, m, Ar*H*), 7.61-7.68 (2H, m, Ar*H*), 8.08 (1H, br q, *J* 4.4, N*H*); HRMS (ES+): Exact mass calculated for $C_{17}H_{17}NOS^{35}Cl$ [$(M+H)^+ - N_2$], 318.0719. Found 318.0730; m/z (ES+) 320.0 {[($C_{17}H_{16}NOS^{37}Cl$)+H^+], 16%}, 318.0 {[($C_{17}H_{16}NOS^{35}Cl$)+H^+], 34%}, 87.8 (100%).

This compound decomposed in DMSO-d_6 to the rearranged pyrazole **90** and the pyrazole **82** (ratio of **90:82** 1.5:1) with characteristic peaks for **90** seen at δ_H (300 MHz, DMSO-d_6) 2.79 (3H, d, *J* 4.4, NHC*H*$_3$), 8.30 (1H, br q, *J* 4.4, N*H* of carboxamide) and at δ_C (75.5 MHz, DMSO-d_6) 25.5 (CH_3, NH*C*H$_3$), 102.1 [C, *C*(4)], 125.1, 128.1, 128.9 (3 × CH, 3 ×

aromatic *C*H), 130.3 (C, aromatic *C*), 144.6, 145.8 [2 × C, *C*(3) & *C*(5)], 161.1 (C, *C*O); and characteristic peaks for **82** seen at δ_H (300 MHz, DMSO-d_6) 2.74 (3H, d, *J* 4.4, NHCH_3), 8.23 (1H, br q, *J* 4.8, N*H* of carboxamide) and at δ_C (75.5 MHz, DMSO-d_6) 27.7 (CH_3, NH*C*H_3), 102.2 [CH, *C*(4)H], 124.1, 125.3 (2 × CH, aromatic *C*H), 125.0 (C, aromatic *C*), 127.6, 129.0, 129.3, 129.6 (4 × CH, aromatic *C*H), 130.5, 138.1, 143.6 [3 × C, aromatic *C*, *C*(3) or *C*(5)], 160.9 (C, *C*O). Spectroscopic details agreed with a genuine sample of **82**.

4-(Phenylthio)-5-phenyl-*N*-(4-methylphenyl)-1*H*-pyrazole-3-carboxamide 85

A solution of *N*-(4-methylphenyl)-*Z*-3-chloro-2-(phenylthio)propenamide **24** (0.20 g, 0.7 mmol) in ether (10 mL) was added dropwise to an excess of phenyldiazomethane [generated from benzaldehyde tosylhydrazone (1.55 g, 5.5 mmol)] cooled to –50 °C with a cryocooler. The solution was allowed to return slowly to room temperature while stirring for 16 h. Following removal of the solvent and excess phenyldiazomethane by evaporation under reduced pressure, the crude product was obtained as an orange oil. The ^{1}H NMR spectrum of the crude product was very complex, with evidence for the pyrazoline at δ_H 5.53 [d, *J* 8.1, C(5)*H*Ph]. Purification by column chromatography using hexane-ethyl acetate (gradient elution 10-20% ethyl acetate) gave **85** as a white solid (0.05 g, 20%), mp 187-188 °C; (Found C, 70.99; H, 5.04; N, 11.27; S, 8.10. $C_{23}H_{19}N_3OS$ requires C, 71.66; H, 4.97; N, 10.90; S, 8.32%); ν_{max}/cm^{-1} (KBr) 3392 (NH), 3189 (NH), 2918 (CH), 1661 (CO), 1602, 1523; δ_H (300 MHz, $CDCl_3$) 2.32 (3H, s, ArCH_3), 7.10-7.30 (7H, m, Ar*H*), 7.36-7.45 (5H, m, Ar*H*), 7.82 (2H, dd, *J* 7.8, 1.8, Ar*H*), 9.75 (1H, br s, N*H* of carboxamide); δ_C (75.5 MHz, $CDCl_3$) 20.9 (CH_3, Ar*C*H_3), 103.1 [C, *C*(4)], 120.3, 126.3, 126.5, 128.1, 128.5, 128.9, 129.6 (7 × CH, 7 × aromatic *C*H, 7 signals for 8 carbons), 134.5, 134.8, 135.6 (3 × C, 3 × aromatic *C*), 141.2 [C, br, *C*(3) or *C*(5)], 156.6 (C, *C*O). The signal for either C(3) or C(5) was not detected; HRMS (ES+): Exact mass calculated for $C_{23}H_{20}N_3OS$ $[M+H]^+$, 386.1327. Found 386.1338; m/z (ES+) 771.2 {[($C_{46}H_{38}N_6O_2S_2$)+H^+], 26%}, 386.0 {[($C_{23}H_{19}N_3OS$)+H^+], 100%}.

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