Synthesis and Diels–Alder reactions of 2-acetamido-3-phenylthiobuta-1,3-diene and its derivatives

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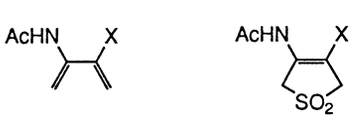
3-Acetamido-4-sulfur-substituted 3-sulfolenes 2a–c which are convenient precursors to the corresponding dienes 1a–c have been synthesized. The Diels–Alder reactions of the dienes 1a–c can be efficiently carried out by heating the 3-sulfolenes 2a–c with dienophiles. The reactions with unsymmetrical dienophiles demonstrate that the '*para*'-directing ability of the substituents on the 2,3-disubstituted 1,3-dienes follows the order AcNH > $PhSO_2$ > PhS > PhSO. However, Lewis acids can change significantly the regioselectivity of the reaction; for the diene 1a, the regiocontrol is even reversed. Semiempirical analyses of the diene FMO coefficients and the transition states involved in the cycloaddition provide some insight into the factors which affect the regioselectivity.

Diels–Alder reactions are widely used in the synthesis of complex cyclic molecules,[1] and in this connection much progress has been made in the preparation of highly functionalized dienes.[2] Recently,[3,4] 2,5-dihydrothiophene *S*,*S*-dioxides (3-sulfolenes) have been extensively used as stable precursors to substituted 1,3-dienes which are often quite sensitive to heat, light and acids. We have also used this method to synthesize some sulfur-substituted dienes.[5] One important feature of the Diels–Alder reaction which is of great interest to both theoretical[6] and synthetic[7–9] chemists is the regiochemical control exerted by different groups on the competing positions of the diene. The introduction of hetero substituents on the diene is especially useful because they further increase the reactivity of the diene as well as the synthetic versatility of the cycloadducts.[10] The attachment of two hetero substituents at the 2- and 3-positions of the diene has been reported.[9] We have also used 3-sulfolene chemistry to synthesize some 2,3-dihetero substituted buta-1,3-dienes and found that the regiocontrol of these substituents in the Diels–Alder reaction follows the order PhS > PhSO > $PhSO_2$ > Me_3Si.[11] This order was not the same as that predicted for 4-sulfur-substituted buta-1,3-diene-1-carbamates (RO_2C-NH > $PhSO_2$ > PhS > PhSO).[12] This variance may be attributable to the different substitution positions involved or the different interactions between the neighbouring substituents. To clarify this, we now report the first synthesis and Diels–Alder reactions of 2-acetamido-3-phenylthiobuta-1,3-diene **1a** and its sulfoxide **1b** and sulfone **1c** derivatives from the corresponding 3-sulfolene precursors **2a**, **2b** and **2c**.

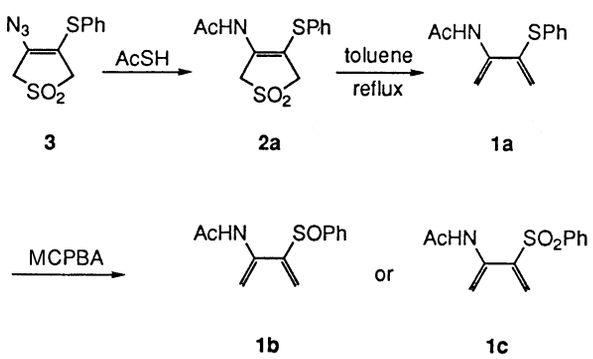


1 **a** X = PhS **2**
b X = PhSO
c X = $PhSO_2$

Results and discussion

Cycloadditions

Treatment of 3-azido-4-phenylthio-3-sulfolene **3**[9e] with thioacetic acid gave 3-acetamido-4-phenylthio-3-sulfolene **2a** (56%). Presumably the azido group was first reduced by thioacetic acid to the amino group which was subsequently acylated by thioacetic acid to give the amido sulfide **2a**.[13] Controlled oxidation of the sulfide **2a** with different amounts of *m*-chloroperbenzoic acid (MCPBA) gave the sulfoxide **2b** (55%) and the sulfone **2c** (80%). Compound **2a** underwent desulfonylation[14] in refluxing toluene to give the desired diene **1a** (72%). The thio-substituted diene **1a** was selectively oxidized to the corresponding sulfoxide **1b** or sulfone **1c** by using suitable amounts of MCPBA.



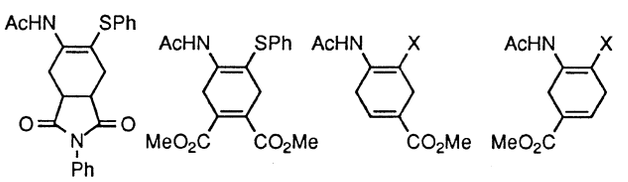
The new diene **1a** could be distilled *in vacuo* and was fully characterized by spectral methods, but the dienes **1b** and **1c** were rather unstable, and decomposed upon distillation. Thus, it was more convenient to use the 3-sulfolene precursor **2** directly for the Diels–Alder reactions. Compound **2** when heated with dienophiles in toluene in a sealed tube at 165 °C for 6 h yielded cyclization products (Table 1). The reactions of **2a** with *N*-phenylmaleimide (entry 1) and dimethyl acetylenedicarboxylate (entry 2) gave the cycloaddition products **4** (99%) and **5** (92%). This indicates that the diene **1a** is highly reactive, probably due to the two electron-donating groups attached. The reaction of 3-sulfolene **2a** with methyl propynoate gave two isomeric products **6a** and **7a** (2.5 : 1) in 89% yield (entry 3). Similar reactions of methyl propynoate with **2b** (entry 4) and with **2c** (entry 5) gave lower yields of an isomeric mixture of products **6** and **7**, consistent with the lower electron density of the dienes **1b** and **1c**. The reactions of **2a** and **2c** with methyl acrylate (entries 6, 7) and methyl vinyl ketone (entries 8, 9) gave similar cycloaddition products **8–11**. Compounds **6a** and **7a** were separated by HPLC, and oxidized by MCPBA (2.2 equiv.) to the corresponding sulfones **6c** and **7c** which were identical with those obtained from

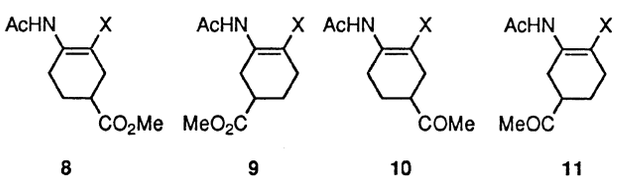
Table 1 Diels–Alder reactions of the 3-sulfolenes **2**

Entry	Reactant	Dienophile	Product (ratio)[a]	Yield %[b]
1	**2a**	*N*-Phenylmaleimide	**4**	99
2	**2a**	$MeO_2CC{\equiv}CCO_2Me$	**5**	92
3	**2a**	$HC{\equiv}CCO_2Me$	**6a** + **7a** (2.5:1)	89
4	**2b**	$HC{\equiv}CCO_2Me$	**6b** + **7b** (3.8:1)	56
5	**2c**	$HC{\equiv}CCO_2Me$	**6c** + **7c** (2.1:1)	60
6	**2a**	$H_2C{=}CHCO_2Me$	**8a** + **9a** (2.3:1)	90
7	**2c**	$H_2C{=}CHCO_2Me$	**8c** + **9c** (1.6:1)	77
8	**2a**	$H_2C{=}CHCOMe$	**10a** + **11a** (2.5:1)	99
9	**2c**	$H_2C{=}CHCOMe$	**10c** + **11c** (1.7:1)	61
10	**1a**	$H_2C{=}CHCOMe$[c]	**10a** + **11a** (1:5)	69
11	**1b**	$H_2C{=}CHCOMe$[c]	**10c** + **11c** (2.2:1)[d]	46[e]
12	**1c**	$H_2C{=}CHCOMe$[c]	**10c** + **11c** (5.6:1)	31[f]

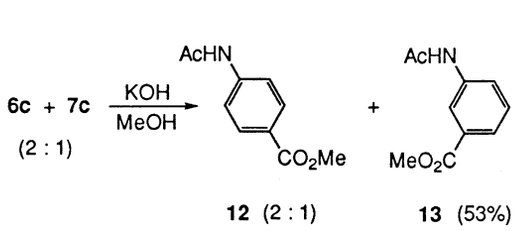
[a] The isomer ratio was determined by ^{1}H NMR spectroscopy of the crude product. [b] Isolated yield of purified products. [c] The reaction was carried out in the presence of zinc chloride (10 equiv.) and dichloromethane at room temperature for 2 d. [d] The diastereomeric mixture (2.7:1.6:1:1) of sulfoxides obtained from the Diels–Alder reaction was directly oxidized by MCPBA to the sulfones. [e] Combined yield of Diels–Alder reaction and MCPBA oxidation. [f] Combined yield of preparation of **1c** from **2c** and the Diels–Alder reaction of **1c**.

entry 5. The major product **6c** upon treatment with sodium hydroxide in methanol gave methyl 4-acetamidobenzoate **12**, whereas a mixture of **6c** and **7c** under similar conditions gave a mixture of **12** and methyl 3-acetamidobenzoate **13**. This demonstrates that the major isomers **6a–c** have the carboxylate group '*para*' to the acetamido group, and thus the acetamido group has a stronger directing effect than the phenylthio group in determining the regioselectivcity of the Diels–Alder reaction of dienes **1**. By comparing entries 3, 4 and 5, it can be seen that the '*para*'-directing ability of substituents in the Diels–Alder reactions of the dienes **1** follows the order AcNH > $PhSO_2$ > PhS > PhSO. The directing ability of AcNH > $PhSO_2$ > PhS can also be shown by comparing entry 6 with 7, and entry 8 with 9.





a, X = PhS, **b**, X = PhSO, **c**, X = $PhSO_2$



We have also carried out some Lewis acid-catalysed Diels–Alder reactions with the dienes **1a–c** (Table 1, entries 10–12). The reaction of **1a** with methyl vinyl ketone in the presence of zinc chloride at room temperature gave a mixture of **10a** and **11a** in a ratio of 1:5 (entry 10). It is interesting to note that the regioselectivity of the Lewis acid-catalysed reaction is controlled by the phenylthio group as opposed to the acetamido group in the thermal reaction (entry 8). On the other hand, similar Lewis acid-catalysed reactions of the dienes **1b** and **1c** with methyl vinyl ketone (entries 11 and 12) still showed regiocontrol by the acetamido group. The regioselectivity for the sulfone-substituted diene **1c** was considerably enhanced by the Lewis acid (compare entries 9 and 12).

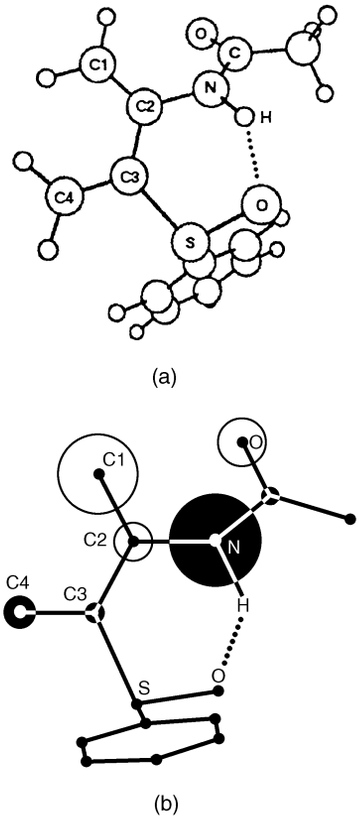


Fig. 1 Geometry optimized (PM3) for **1b** (a) and the orbital drawing for its HOMO (b). (a) Hydrogen bonding exists between H and O, which helps to keep the diene moiety co-planar. (b) The size of the circles is proportional to the amplitude of the conjugated p orbitals.

Semiempirical FMO analysis

The FMO coefficients and energies for compounds **1a–c** estimated by two semiempirical models[15] AM1 and PM3 are listed in Table 2. In all cases the acetamido substituent (at C-2) is shown to be a stronger *para*-directing group than the sulfur-containing substituents (at C-3), which is established by comparison of the coefficients $c_1^2 > c_4^2$. Variation in product ratios among these three compounds is not self-evident so that an analysis on their structural and electronic configurations was performed.

For **1b** and **1c** the HOMOs are composed mainly of the π-orbitals of the diene and the acetamido group but with minimal involvement of any orbitals localized on the sulfur moieties [Figs. 1(b) and 2]. As shown in Table 2, both the (c_1^2/c_4^2) ratios for sulfoxide **1b** ($0.54^2/0.19^2$) and sulfone **1c** ($0.56^2/0.19^2$) as calculated by the PM3 method predict a higher regiocontrol by the acetamido group for the cycloaddition (*cf.* 3.8/1.0 and 2.1/1.0 in Table 1). Estimations by AM1 are also given in Table 2, which are consistent with those of PM3.

In all the calculations listed in Table 2 the diene moieties are held at a pseudo *cis* conformation in order to normalize the parameters for better comparison. Even in the absence of such a constraint, the fully optimized geometries of **1b** and **1c** are primarily s-*cis* and planar with a small rotational barrier along C(2)–C(3). Intramolecular hydrogen bonding exists between the acetamido NH and the sulfoxide SO groups, which helps to maintain a six-membered ring conformation between the

Table 2 Semiempirical FMO calculations for compounds **1a–c**. The diene moieties (C-1 to C-4) are set to a pseudo-*cisoid* conformation, and all other atoms are allowed to optimize fully with key word PRECISE. The c_i values are coefficients for the vertical π-orbitals of the corresponding carbons in HOMOs and SHOMOs

	Model	HF (kcal mol^{-1})	HOMO & SHOMO	(eV)	c_1	c_2	c_3	c_4
1a	PM3	26.96	HOMO	−8.86	0.47	0.28	−0.23	−0.42
			SHOMO	−9.20	0.27	0.18	0.16	0.24
	AM1	28.58	HOMO	−8.50	0.31	0.18	−0.26	−0.50
			SHOMO	−9.09	0.55	0.40	0.00	0.00
1b	PM3	−1.10	HOMO	−8.75	0.54	0.30	−0.07	−0.19
	AM1	−3.42	HOMO	−8.87	0.62	0.42	−0.14	−0.28
1c	PM3	−36.63	HOMO	−8.89	0.56	0.32	−0.08	−0.19
	AM1	−31.25	HOMO	−9.05	0.63	0.43	−0.14	−0.26

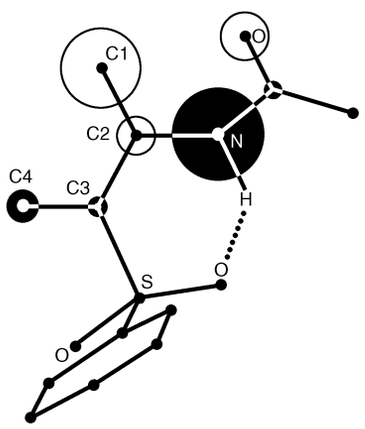


Fig. 2 Orbital drawing for the HOMO of **1c** calculated by PM3. A hydrogen bond is shown between H and O.

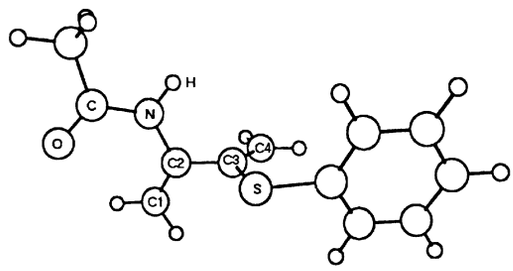


Fig. 3 The twisted geometry of **1a** is optimized by PM3 at its lowest energy, in which the dihedral angle C(1)–C(2)–C(3)–C(4) is estimated to be 84°

subsitituents [Fig. 1(a)]. When computed by MNDO where hydrogen bonding is not considered, the conformations of **1a–c** are in twisted forms with large values for the dihedral angle C(1)–C(2)–C(3)–C(4).

Unlike **1b** and **1c**, the conformation of **1a** is predicted to be non-planar since it is incapable of forming an internal hydrogen bond. The geometry of **1a** as fully optimized by PM3 (AM1 and MNDO likewise)[15] prefers a conformation with 84° for the dihedral angle C(1)–C(2)–C(3)–C(4) (Fig. 3). The N–C(2)–C(1) and C(4)–C(3)–S groupings are arranged nearly orthogonal so that their π-orbitals cannot delocalize across each other. However, the eigenvalues for either canonical orbitals are quite close, *i.e.* −8.94 and −8.98 eV for the HOMO and SHOMO, respectively (PM3). Both the acetamido and phenylthio groups resonate strongly with the conjugated C=C double bonds; in this form it is rather difficult to predict which group controls the regioselectivity.

For the convenience of comparison as mentioned above, the diene moiety of **1a** is held planar manually by setting up the dihedral angle C(1)–C(2)–C(3)–C(4) to 0°. The π-orbitals of the acetamido and phenylthio groups are forced to mix with each other and, as a consequence, the two energy levels split. The HOMO and SHOMO of **1a** change to −8.86 and −9.20 eV (PM3), respectively as shown in Table 2. The coefficient c_1^2 (0.47^2) of the HOMO is slightly larger than that of c_4^2 (0.42^2), showing that both substituents interact significantly with the π-orbitals of the diene. The coefficients calculated by AM1 are also shown in the table, where a reversed order is obtained, *i.e.* $c_1^2 < c_4^2$. These models therefore predict nearly equal regiodirecting abilities for the acetamido and phenylthio groups. The unexpected stronger regiodirecting power of the acetamido group as observed in experiments has also been recognized earlier by Overman *et al*. for 1,4-disubstituted dienes.[7c] It seems that in these cases the regioselectivity is not only governed by the HOMO coefficients, but also by electronic factors such as polarity of the molecule.[12]

A combined effect of both FMO coefficients and electrostatic potentials may be properly expressed by examining their transition states. A transition state modeling (AM1)[16] is performed for the adduct of **1a** and methyl vinyl ketone in the two orientations leading to **10a** and **11a**. In these calculations the dihedral angle C(1)–C(2)–C(3)–C(4) is constrained at 0° in order to hold the diene moiety co-planar. The dienophile is arranged in a pseudo *trans* conformation which approaches the diene according to the *endo* addition rule.[17] The estimated distances between the terminal carbons in the progress of bond formation are in the range of 2.0–2.2 Å (Fig. 4). It is interesting to find that the transition state for **10a** (**10a-T**, 26.03 kcal mol^{-1}) is slightly more stable than that for **11a** (**11a-T**, 26.58 kcal mol^{-1}). Some bonding parameters of **10a-T** and **11a-T** are listed in Table 3. This provides some evidence for our hypothesis that the regioselectivity of this reaction is not determined only by the FMO coefficients.

In Lewis acid-catalysed reactions, the primary effect of the Lewis acid is to lower the LUMO energy of the dienophile, along with some changes of the orbital coefficients. In a model study for methyl vinyl ketone, the LUMO potential is lowered by 1.03 eV upon co-ordinating to $ZnCl_2$.[16] The $(c_1/c_2)^2$ ratio of the LUMO for the vinylic carbons increases from 1.98 to 2.93. These changes will not only increase the rate of reaction, but also put more weight on the LUMO coefficients in determining the regioselectivity. This may be part of the reason for the enhancement of the product ratio **10c**/**11c** (5.6) in entry 12 catalysed by $ZnCl_2$ as compared with that in entry 9 (1.7).

The reversed regiodirecting behaviour for the acetamido group and the phenylthio group in entry 10 (**1a** with $ZnCl_2$) and entry 8 (**2a** without $ZnCl_2$) indicates that the Lewis acid can interact not only with the dienophile but also with the diene. The *endo* transition states **10a-T** and **11a-T** are more favourable because the diene can also interact with the acetyl group of the dienophile through a secondary orbital effect. In the transition state **11a-T** (Fig. 4), the acetyl oxygen and the acetamido group on the diene can co-ordinate simultaneously with the metal of the Lewis acid. We think that it is such chelating structures which determine the regioselectivity of the cycloaddition. The resulting product **11a** shows that the phenylthio group is

Table 3 Estimated heats of formation (HF) and selected bond lengths for the transition states of cycloaddition of **1a** with methyl vinyl ketone in two geometries referred to in Fig. 4 (unit of length in Å). Bonds in **bold** are in the progress of formation

	C(1)–C(2)	C(2)–C(3)	C(3)–C(4)	**C(4)–C(5)**	C(5)–C(6)	**C(6)–C(1)**	HF (kcal mol^{-1})	Final adduct
10a-T	1.40	1.43	1.38	**2.23**	1.39	**2.06**	26.03	**10a**
11a-T	1.40	1.43	1.38	**2.09**	1.38	**2.20**	26.58	**11a**

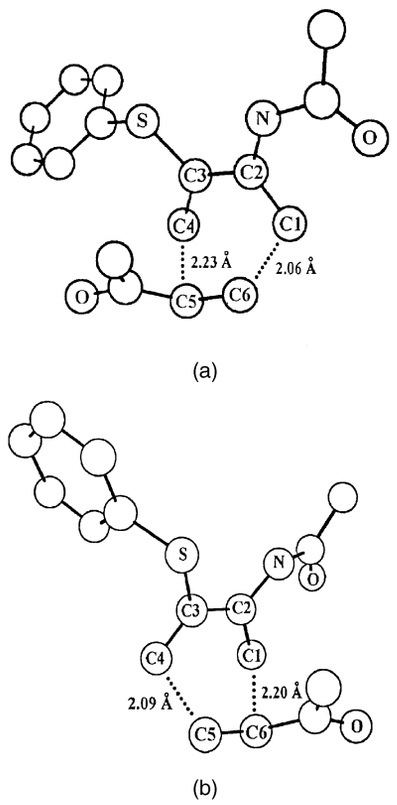


Fig. 4 Calculated transition state structures (AM1) for the cycloaddition of **1a** with methyl vinyl ketone in two orientations. Hydrogens are omitted for clarity. The structure **10a-T** which leads to adduct **10a** is predicted to be slightly more stable (26.03 kcal mol^{-1}) than **11a-T** which leads to **11a** (bottom, 26.58 kcal mol^{-1}).

located *para* to the acetyl group and is regarded as the regio-director, contrary to the thermal reaction. The situations for **1b** and **1c** are different from that of **1a**, because an oxygen atom on the sulfur increases the polarity of these substituents so that in the transition state the S–O group co-ordinates better with the zinc ion than the acetamido group. Therefore, the sulfoxide or the sulfone group is located preferably *meta* to the acetyl group to yield **10b** and **10c**. The observed regioselectivities for the Lewis acid-catalysed reactions of **1b** and **1c** are thus similar to those for the thermal reaction which can be estimated by the FMO coefficients.

From the above analysis, it can be seen that the *para*-directing ability of AcNH > $PhSO_2$, PhSO as exemplified by dienes **1b** and **1c** is clearly due to a more effective delocalization of the acetamido group in the HOMOs than the sulfur substituents. The directing ability of AcNH > PhS for diene **1a** agrees with a transition state analysis, in which electrostatic factors are also considered. In the presence of Lewis acid, the geometry of the transition state is determined by the formation of a better co-ordination between the metal and electronegative substituents. The attraction force between the metal and these groups is therefore responsible for the enhanced regioselectivity for **1c**, and the reversed order of regiodirecting ability in the case of **1a** (PhS > AcNH). While comparing the relative regiodirecting abilities of the sulfur substituents with or without the Lewis acid, the rule of additivity could be overshadowed by the complicated interactions between the substituents.[12]

Summary

We have synthesized 3-sulfolenes **2a–c** which are convenient precursors to the corresponding dienes **1a–c**. The Diels–Alder reactions of **1a–c** can be efficiently carried out by heating the 3-sulfolenes **2a–c** with dienophiles. The reactions with unsymmetrical dienophiles demonstrate that the '*para*'-directing ability of the substituents on the 2,3-disubstituted 1,3-dienes follows the order AcNH > $PhSO_2$ > PhS > PhSO which is the same as that predicted for 4-sulfur-substituted buta-1,3-diene-1-carbamates,[12] but is different from what we have observed for 2,3-disulfur-substituted 1,3-dienes (PhS > PhSO > $PhSO_2$).[11] However, a Lewis acid can change significantly the regioselectivity of the reaction. For the diene **1a**, the regiocontrol is reversed, and for the diene **1c**, the regioselectivity is enhanced. A semiempirical FMO analysis indicates that the effect of substituents on the regioselectivity of the Diels–Alder reaction is a combination of the influence of FMO coefficients and electrostatic factors, and that the Lewis acid can preferentially interact with different substituents on the diene.

Experimental

^{1}H and ^{13}C NMR spectra were measured in $CDCl_3$ at 300 and 75 MHz, respectively, with tetramethylsilane as the internal standard. HPLC was carried out with a LiChrosorb (Merck) column. The silica gel used for flash chromatography was made by Merck (60 H). All reagents were of reagent grade and were purified prior to use.[18]

3-Acetamido-4-phenylthio-2,5-dihydrothiophene *S*,*S*-dioxide 2a

A mixture of 3-azido-4-phenylthio-2,5-dihydrothiophene *S*,*S*-dioxide **3**[19] (0.97 g, 3.6 mmol) and thioacetic acid (2.7 cm^3, 36 mmol) was stirred at room temperature for 12 h. The excess of thioacetic acid was removed from the mixture *in vacuo*, and the crude product was purified by flash chromatography using hexane–ethyl acetate (3:1 to 1:1) as the eluent to give **2a** (0.57 g, 56%) as a white crystalline solid; mp 122–124 °C; ν_{max}(KBr)/cm^{-1} 3305 (NH), 1687 (CO), 1310 (SO_2) and 1130 (SO_2); δ_H(300 MHz; $CDCl_3$) 2.14 (3 H, s, Ac), 3.74 (2 H, t, *J* 1.2, 5-H), 4.58 (2 H, t, *J* 1.2, 2-H), 7.23–7.39 (5 H, m, Ph) and 8.00 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.9 (CH_3), 55.9 (5-C), 57.6 (2-C), 102.6 (4-C), 127.7 (Ph), 128.8 (Ph), 129.8 (Ph), 131.1 (3-C), 135.8 (Ph) and 168.1 (CO); *m*/*z* 283 (M^+, 10%) and 110 (100) (Found: M^+, 283.0339. $C_{12}H_{13}NO_3S_2$ requires *M*, 283.0338).

3-Acetamido-4-phenylsulfinyl-2,5-dihydrothiophene *S*,*S*-dioxide 2b

To a solution of **2a** (57 mg, 0.20 mmol) in dichloromethane (5 cm^3) at 0 °C was added MCPBA (42 mg, 0.22 mmol). The mixture was stirred at 0 °C for 1.5 h and then washed sequentially with aqueous sodium hydrogen carbonate (20 cm^3) and aqueous sodium thiosulfate (20 cm^3). The solvent was removed from the mixture by rotary evaporation, to give the product **2b** (33 mg, 55%) as a white crystalline solid after recrystallization from ethyl acetate–hexane; mp 187–189 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3250 (NH), 1692 (CO) and 1030 (SO); δ_H(300 MHz; $CDCl_3$–[$^2H_6$]acetone) 1.78 (3 H, s, Ac), 3.11 (1 H, d, *J* 15.2, 5-H), 3.26 (1 H, d, *J* 15.2, 5-H), 4.17 (1 H, d, *J* 13.8, 2-H), 4.19 (1 H, d, *J* 13.8, 2-H), 7.19–7.22 (3 H, m, Ph), 7.32–7.35 (2 H, m,

Ph) and 9.99 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.3 (CH_3), 51.8 (5-C), 58.8 (2-C), 107.9 (4-C), 125.5 (Ph), 130.3 (Ph), 133.1 (Ph), 137.2 (3-C), 140.6 (Ph) and 168.3 (CO); *m*/*z* 299 (M^+, 3%), 110 (100) and 78 (32) (Found: M^+, 299.0283. $C_{12}H_{13}NO_4S_2$ requires *M*, 299.0287).

3-Acetamido-4-phenylsulfonyl-2,5-dihydrothiophene *S*,*S*-dioxide 2c

To a solution of the sulfide **2a** (57 mg, 0.20 mmol) in dichloromethane (5 cm^3) at 0 °C was added MCPBA (84 mg, 0.44 mmol). The mixture was stirred at 0 °C for 1 h, and then worked up and purified as for **2b** to give the sulfone **2c** (50 mg, 80%) as a white crystalline solid; mp 201–203 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3345 (NH), 1720 (CO), 1327 (SO_2) and 1142 (SO_2); δ_H(300 MHz; $CDCl_3$) 2.03 (3 H, s, Ac), 3.54 (2 H, s, 5-H), 4.43 (2 H, s, 2-H), 7.40–7.44 (2 H, m, Ph), 7.50–7.58 (1 H, m, Ph), 7.68–7.72 (2 H, m, Ph) and 10.01 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.0 (CH_3), 51.8 (5-C), 75.3 (2-C), 106.5 (4-C), 126.9 (Ph), 129.4 (Ph), 134.3 (Ph), 138.3 (3-C), 139.3 (Ph), 167.9 (CO); *m*/*z* 315 (M^+, 2%) and 110 (100) (Found: M^+, 315.0239. $C_{12}H_{13}NO_5S_2$ requires *M*, 315.0236).

2-Acetamido-3-phenylthiobuta-1,3-diene 1a

A solution of the 3-sulfolene **2a** (57 mg, 0.20 mmol) in toluene (3 cm^3) was heated at reflux under nitrogen for 8 h and then evaporated *in vacuo*. The crude product was purified by flash chromatography using hexane–ethyl acetate (2:1) as the eluent to give **1a** (32 mg, 72%) as an oil; ν_{max}(neat)/cm^{-1} 3278 (NH) and 1675 (CO); δ_H(300 MHz; $CDCl_3$) 1.99 (3 H, s, Ac), 5.23 (1 H, br s, 1-H), 5.37 (1 H, s, 4-H), 5.69 (1 H, s, 4-H), 5.82 (1 H, br s, 1-H), 6.99 (1 H, br s, NH) and 7.26–7.38 (5 H, m, Ph); δ_C(75 MHz; $CDCl_3$) 24.4 (CH_3), 104.4 (1-C), 118.4 (4-C), 127.8 (Ph), 129.2 (×2, 2-C and Ph), 131.4 (Ph), 132.7 (3-C), 141.7 (Ph), 168.4 (CO); *m*/*z* 219 (M^+, 14%), 144 (37), 110 (100) and 109 (26) (Found: M^+, 219.0722. $C_{12}H_{13}NOS$ requires *M*, 219.0719).

2-Acetamido-3-phenylsulfinylbuta-1,3-diene 1b

To a solution of **1a** (70 mg, 0.32 mmol) in dichloromethane (2 cm^3) at 0 °C was added dropwise a solution of MCPBA (50%; 110 mg, 0.32 mmol) in dichloromethane (3 cm^3). The mixture was stirred at 0 °C for 2.5 h, after which 10% aqueous sodium thiosulfate (5 cm^3) and 10% aqueous sodium hydrogen carbonate (5 cm^3) were added to it. The mixture was then extracted with dichloromethane (10 cm^3 × 3) and the combined extracts were dried ($MgSO_4$), and concentrated by rotary evaporation. The crude product was purified by flash column chromatography using hexane–ethyl acetate (2:1) as eluent to give **1b** (74 mg, 98%) as a viscous liquid; δ_H(300 MHz; $CDCl_3$) 1.98 (3 H, s, Ac), 4.73 (1 H, br s, 1-H), 5.77 (1 H, br s, 1-H), 6.01 (1 H, s, 4-H), 6.12 (1 H, s, 4-H), 7.46–7.50 (3 H, m, Ph), 7.55–7.60 (2 H, m, Ph) and 8.12 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.3 (CH_3), 104.6 (1-C), 121.1 (4-C), 124.7 (Ph), 129.1 (×2, 2-C and Ph), 131.3 (Ph), 135.7 (3-C), 141.4 (Ph) and 168.8 (CO).

2-Acetamido-3-phenylsulfonylbuta-1,3-diene 1c

Similar reaction conditions and work-up procedure were employed as for **1b** except that twice the amount of MCPBA (2.5 equiv.) was used, and the solvent was not completely removed to avoid the dimerization of **1c**. Since neat **1c** is not stable, this concentrated solution of **1c** in dichloromethane was directly used for the Lewis acid-catalysed Diels–Alder reaction.

General procedure for the Diels–Alder reactions of 2a–c

A mixture of the 3-sulfolene **2** (0.23 mmol), dienophile (0.46 mmol) and hydroquinone (3 mg) in toluene (1 cm^3) was heated in a sealed tube at 165 °C for 6 h. The solvent was removed from the reaction mixture by rotary evaporation, and the crude product was purified by flash chromatography using hexane–ethyl acetate (1:1) as the eluent. The regioisomers were then separated by HPLC using hexane–ethyl acetate (gradient) as the eluent.

***N*-Phenyl-4-acetamido-5-phenylthio-1,2,3,6-tetrahydrophthalimide 4.** A white crystalline solid, mp 139–141 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3338 (NH) and 1670 (CO); δ_H(300 MHz; $CDCl_3$) 2.03 (3 H, s, Ac), 2.64–2.82 (2 H, m, 6-H), 3.03 (1 H, dd, *J* 16.8, 8.2, 3-H), 3.21–3.30 (1 H, m, 2-H), 3.32–3.41 (1 H, m, 1-H), 3.61 (1 H, dd, *J* 16.8, 1.8, 3-H), 7.13–7.22 (3 H, m, SPh), 7.22–7.31 (2 H, m, SPh), 7.35–7.51 (5 H, m, NPh) and 7.63 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.9 (CH_3), 27.6 (6-C), 30.5 (3-C), 39.8 (2-C), 40.1 (1-C), 111.8 (5-C), 126.2 (Ph), 127.2 (Ph), 128.5 (Ph), 129.0 (Ph), 129.3 (Ph), 129.7 (Ph), 131.9 (4-C), 132.9 (Ph), 139.7 (Ph), 168.7 (CO), 177.5 (CO) and 177.6 (CO); *m*/*z* 392 (M^+, 24%) and 283 (100) (Found: M^+, 392.1194. $C_{22}H_{20}N_2O_3S$ requires *M*, 392.1196).

Dimethyl 4-acetamido-5-phenylthiocyclohexa-1,4-diene-1,2-dicarboxylate 5. A white crystalline solid, mp 117–118 °C; ν_{max}(KBr)/cm^{-1} 3350 (NH), 1734 (CO), 1716 (CO) and 1697 (CO); δ_H(300 MHz; $CDCl_3$) 2.05 (3 H, s, Ac), 3.21 (2 H, t, *J* 8.1, 6-H), 3.72 (3 H, s, 1-Me), 3.80 (3 H, s, 2-Me), 3.96 (2 H, t, *J* 8.1, 3-H), 7.19–7.34 (5 H, m, Ph) and 8.08 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.6 (4-Me), 30.8 (6-C), 32.5 (3-C), 52.39 (1-Me), 52.44 (2-Me), 105.5 (5-C), 126.8 (Ph), 128.2 (Ph), 129.5 (Ph), 130.7 (2-C), 132.1 (4-C), 132.8 (1-C), 137.4 (Ph), 167.0 (CO), 167.5 (CO) and 168.6 (CO); *m*/*z* 361 (M^+, 17%) and 220 (100) (Found: M^+, 361.0972. $C_{18}H_{19}NO_5S$ requires *M*, 361.0985).

Methyl 4-acetamido-5-phenylthiocyclohexa-1,4-dienecarboxylate 6a. A white crystalline solid, mp 117–118 °C; ν_{max}(KBr)/cm^{-1} 3359 (NH) and 1720 (CO); δ_H(300 MHz; $CDCl_3$) 2.03 (3 H, s, Ac), 3.13 (2 H, dt, *J* 1.7, 8.1, 6-H), 3.69 (3 H, s, CO_2Me), 3.83 (2 H, dt, *J* 3.8, 8.1, 3-H), 6.90–6.95 (1 H, m, 2-H), 7.18–7.33 (5 H, m, Ph) and 8.15 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.7 (4-Me), 30.4 (6-C), 30.7 (3-C), 51.7 (1-Me), 107.0 (5-C), 126.5 (Ph), 128.1 (Ph), 129.4 (×2, Ph), 133.4 (1-C), 134.6 (2-C), 137.8 (Ph), 166.4 (CO), 168.6 (CO); *m*/*z* 303 (M^+, 7%) and 194 (100) (Found: M^+, 303.0922. $C_{16}H_{17}NO_3S$ requires *M*, 303.0930).

Methyl 5-acetamido-4-phenylthiocyclohexa-1,4-dienecarboxylate 7a. A white crystalline solid, mp 131–132 °C; ν_{max}(KBr)/cm^{-1} 3355 (NH) and 1720 (CO); δ_H(300 MHz; $CDCl_3$) 2.04 (3 H, s, Ac), 3.06 (2 H, dt, *J* 3.8, 8.0, 3-H), 3.75 (3 H, s, CO_2Me), 3.81 (2 H, t, *J* 8.0, 6-H), 6.84–6.87 (1 H, m, 2-H), 7.18–7.31 (5 H, m, Ph) and 7.97 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.6 (5-Me), 28.8 (3-C), 32.4 (6-C), 51.8 (1-Me), 126.6 (Ph), 127.0 (Ph), 128.3 (1-C), 129.4 (×2, 2-C and Ph), 133.2 (5-C), 134.9 (Ph), 166.6 (CO) and 167.3 (CO); *m*/*z* 303 (M^+, 8%), 194 (100) and 162 (23) (Found: M^+, 303.0916. $C_{16}H_{17}NO_3S$ requires *M*, 303.0930).

Methyl 4-acetamido-5-phenylsulfinylcyclohexa-1,4-dienecarboxylate 6b. A white crystalline solid, mp 106–108 °C; ν_{max}(KBr)/cm^{-1} 3230 (NH), 1695 (CO) and 1670 (CO); δ_H(300 MHz; $CDCl_3$) 2.12 (3 H, s, Ac), 2.84–2.96 (2 H, m, 6-H), 3.61–3.72 (2 H, m, 3-H), 3.73 (3 H, s, 1-Me), 6.81–6.87 (1 H, m, 2-H), 7.50–7.60 (3 H, m, Ph), 7.65–7.82 (2 H, m, Ph) and 10.26 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.3 (4-Me), 24.5 (6-C), 31.4 (3-C), 51.8 (1-Me), 116.8 (5-C), 125.1 (Ph), 125.6 (1-C), 129.6 (Ph), 131.6 (Ph), 134.3 (2-C), 139.6 (4-C), 141.6 (Ph), 166.0 (CO) and 169.1 (CO); *m*/*z* 319 (M^+, 23%), 260 (72), 228 (26), 194 (76), 151 (100), 125 (58) and 120 (89) (Found: M^+, 319.0876. $C_{16}H_{17}NO_4S$ requires *M*, 319.0879).

Methyl 5-acetamido-4-phenylsulfinylcyclohexa-1,4-dienecarboxylate 7b. A white crystalline solid, mp 114–116 °C; ν_{max}(KBr)/cm^{-1} 3240 (NH), 1703 (CO) and 1030 (SO); δ_H(300 MHz; $CDCl_3$) 2.16 (3 H, s, Ac), 2.58–2.73 (1 H, m, 3-H), 2.98–3.16 (1 H, m, 3-H), 3.42–3.54 (2 H, m, 6-H), 3.73 (3 H, s, 1-Me), 6.79–6.83 (1 H, m, 2-H), 7.48–7.56 (3 H, m, Ph), 7.74–7.78 (2 H, m, Ph) and 9.48 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.2 (5-Me), 29.7 (3-C), 30.3 (6-C), 51.9 (1-Me), 121.0 (4-C), 125.1 (Ph), 126.6 (1-C), 129.4 (Ph), 131.3 (Ph), 133.6 (2-C), 139.8 (5-C), 141.0 (Ph), 165.9 (CO) and 169.2 (CO); *m*/*z* 319 (M^+, 32%), 260 (55), 194 (63), 193 (55), 151 (84), 120 (82), 84 (100) and 77 (38) (Found: M^+, 319.0873. $C_{16}H_{17}NO_4S$ requires *M*, 319.0879).

Methyl 4-acetamido-5-phenylsulfonylcyclohexa-1,4-dienecarboxylate 6c. A white crystalline solid, mp 141–143 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3317 (NH), 1710 (CO), 1675 (CO), 1365 (SO_2) and 1133 (SO_2); δ_H(300 MHz; $CDCl_3$) 2.16 (3 H, s, Ac), 3.08 (2 H, dt, *J* 1.7, 6.1, 6-H), 3.69 (3 H, s, 1-Me), 3.85 (2 H, dt, *J* 3.8, 6.1, 3-H), 6.75 (1 H, br s, 2-H), 7.50–7.67 (3 H, m, Ph), 7.79–7.88 (2 H, m, Ph) and 10.58 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 25.0 (4-Me), 25.4 (6-C), 30.7 (3-C), 51.8 (1-Me), 110.3 (5-C), 125.6 (1-C), 127.1 (Ph), 129.4 (Ph), 133.0 (2-C), 133.8 (Ph), 139.7 (4-C), 142.6 (Ph), 165.7 (CO) and 168.5 (CO); *m*/*z* 335 (M^+, 21%), 293 (37), 292 (51), 291 (59), 260 (52), 225 (50), 194 (93), 193 (69), 167 (64), 162 (50), 152 (76), 151 (80), 149 (97), 120 (100) and 93 (84) (Found: M^+, 335.0814. $C_{16}H_{17}NO_5S$ requires *M*, 335.0828).

Methyl 5-acetamido-4-phenylsulfonylcyclohexa-1,4-dienecarboxylate 7c. A white crystalline solid, mp 132–134 °C; ν_{max}(KBr)/cm^{-1} 3325 (NH), 1710 (CO), 1675 (CO), 1365 (SO_2) and 1130 (SO_2); δ_H(300 MHz; $CDCl_3$) 2.19 (3 H, s, Ac), 3.00–3.15 (2 H, m, 3-H), 3.73 (3 H, s, 1-Me), 3.86–3.98 (2 H, m, 6-H), 6.80–6.88 (1 H, m, 2-H), 7.43–7.72 (3 H, m, Ph), 7.79–7.98 (2 H, m, Ph) and 10.49 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 25.4 (5-Me), 26.9 (3-C), 28.9 (6-C), 51.9 (1-Me), 109.1 (4-C), 126.0 (1-C), 127.0 (Ph), 129.4 (Ph), 132.8 (2-C), 133.8 (Ph), 139.8 (5-C), 144.4 (Ph), 165.7 (CO) and 168.3 (CO); *m*/*z* 335 (M^+, 2%), 194 (37), 167 (32), 151 (31), 149 (100) and 77 (31) (Found: M^+, 335.0820. $C_{16}H_{17}NO_5S$ requires *M*, 335.0828).

Methyl 4-acetamido-3-phenylthiocyclohex-3-enecarboxylate 8a and methyl 3-acetamido-4-phenylthiocyclohex-3-enecarboxylate 9a. These two compounds could not be separated by HPLC, and were viscous liquids. The following data were measured for the mixture: ν_{max}(film)/cm^{-1} 3350 (NH), 1737 (CO), 1731 (CO), 1691 (CO) and 1666 (CO); δ_H(300 MHz; $CDCl_3$) 1.72–1.90 (m), 2.02 (s), 2.08–2.20 (m), 2.25–2.38 (m), 2.40–2.57 (m), 2.60–2.83 (m), 2.85–3.16 (m), 3.20–3.35 (m), 3.66 (s), 3.70 (s), 7.10–7.35 (m), 7.88 (br s) and 7.99 (br s); *m*/*z* 305 (M^+, 14%) and 196 (100) (Found: M^+, 305.1075. $C_{16}H_{19}NO_3S$ requires *M*, 305.1085). The two isomers have distinct ^{1}H NMR absorptions at δ 3.65 and 3.70, respectively, for the methoxycarbonyl group. The ^{13}C NMR signals were quite distinctive so that the following assignments could be made.

Compound **8a**: δ 24.9 (4-Me), 27.3 (2-C), 32.5 (5-C), 39.6 (1-C), 51.8 (1-Me), 107.6 (3-C), 126.3 (Ph), 127.8 (Ph), 129.3 (Ph), 133.9 (4-C), 142.0 (Ph), 168.3 (CO) and 174.8 (CO).

Compound **9a**: δ 24.1 (6-C), 24.7 (4-Me), 29.3 (5-C), 30.6 (2-C), 39.1 (1-C), 51.8 (1-Me), 109.7 (4-C), 126.3 (Ph), 127.9 (Ph), 129.2 (Ph), 134.0 (3-C), 140.2 (Ph), 168.3 (CO) and 174.8 (CO).

Methyl 4-acetamido-3-phenylsulfonylcyclohex-3-enecarboxylate 8c. A viscous liquid; ν_{max}(film)/cm^{-1} 3300 (NH), 1738 (CO), 1674 (CO), 1367 (SO_2) and 1170 (SO_2); δ_H(300 MHz; $CDCl_3$) 1.56–1.71 (1 H, m, 6-H), 1.93–2.05 (1 H, m, 6-H), 2.14 (3 H, s, Ac), 2.29–2.40 (1 H, m, 1-H), 2.42–2.58 (2 H, m, 2-H), 2.87–3.02 (1 H, m, 5-H), 3.09–3.22 (1 H, dt, *J* 19.6, 4.3, 5-H), 3.59 (3 H, s, 1-Me), 7.50–7.67 (3 H, m, Ph), 7.80–7.85 (2 H, m, Ph) and 10.52 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.1 (6-C), 25.4 (4-Me), 26.5 (2-C), 27.8 (5-C), 38.1 (1-C), 51.9 (1-Me), 111.3 (3-C), 127.1 (Ph), 129.3 (Ph), 133.7 (Ph), 140.0 (Ph), 147.7 (4-C), 168.1 (CO) and 174.0 (CO); *m*/*z* 337 (M^+, 17%), 294 (100), 218 (41), 196 (67), 154 (88), 153 (61), 110 (41) and 95 (70) (Found: M^+, 337.0981. $C_{16}H_{19}NO_5S$ requires *M*, 337.0985).

Methyl 3-acetamido-4-phenylsulfonylcyclohex-3-enecarboxylate 9c. A viscous liquid; ν_{max}(film)/cm^{-1} 3307 (NH), 1738 (CO), 1682 (CO), 1370 (SO_2) and 1171 (SO_2); δ_H(300 MHz; $CDCl_3$) 1.50–1.71 (1 H, m, 6-H), 1.84–1.95 (1 H, m, 6-H), 2.15 (3 H, s, Ac), 2.17–2.26 (2 H, m, 5-H), 2.48–2.59 (1 H, m, 1-H), 3.15 (1 H, dd, *J* 19.0, 8.6, 2-H), 3.28 (1 H, dd, *J* 19.0, 4.7, 2-H), 3.63 (3 H, s, 1-Me), 7.48–7.67 (3 H, m, Ph), 7.77–7.84 (2 H, m, Ph) and 10.45 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.4 (6-C), 24.1 (5-C), 25.3 (3-Me), 30.6 (2-C), 38.3 (1-C), 51.9 (1-Me), 112.7 (4-C), 127.0 (Ph), 129.3 (Ph), 133.6 (Ph), 140.2 (Ph), 145.6 (3-C), 168.2 (CO) and 178.9 (CO); *m*/*z* 337 (M^+, 19%), 294 (100), 218 (48), 196 (60), 154 (88), 153 (60), 110 (45) and 95 (60) (Found: M^+, 337.0982. $C_{16}H_{19}NO_5S$ requires *M*, 337.0985).

1-Acetamido-4-acetyl-2-phenylthiocyclohexene 10a. A white crystalline solid, mp 35–37 °C (from ether–hexane); ν_{max}(KBr)/cm^{-1} 3357 (NH), 1701 (CO) and 1655 (CO); δ_H(300 MHz; $CDCl_3$) 1.60–1.66 (1 H, m, 5-H), 1.95 (3 H, s, 4-Ac), 2.01–2.11 (1 H, m, 5-H), 2.08 (3 H, s, 1-Ac), 2.23–2.50 (2 H, m, 3-H), 2.57–2.68 (1 H, m, 4-H), 2.80–3.08 (2 H, m, 6-H), 7.11–7.15 (3 H, m, Ph), 7.19–7.26 (2 H, m, Ph) and 7.99 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.44 (5-C), 24.49 (1-Me), 27.5 (3-C), 27.9 (4-Me), 31.9 (6-C), 47.5 (4-C), 108.0 (2-C), 126.3 (Ph), 127.9 (Ph), 129.2 (Ph), 134.0 (1-C), 141.7 (Ph), 168.2 (CO) and 209.5 (CO); *m*/*z* 289 (M^+, 10%), 180 (100) and 155 (97) (Found: M^+, 289.1127. $C_{16}H_{19}NO_2S$ requires *M*, 289.1138).

2-Acetamido-4-acetyl-1-phenylthiocyclohexene 11a. A white crystalline solid, mp 48–51 °C (from ether–hexane); ν_{max}(KBr)/cm^{-1} 3266 (NH), 1704 (CO) and 1645 (CO); δ_H(300 MHz; $CDCl_3$) 1.55–1.71 (1 H, m, 5-H), 1.88–1.98 (1 H, m, 5-H), 1.95 (3 H, s, 4-Ac), 2.10 (3 H, s, 2-Ac), 2.15–2.26 (2 H, m, 6-H), 2.68–2.71 (1 H, m, 4-H), 2.83–2.92 (1 H, m, 3-H), 3.12–3.24 (1 H, m, 3-H), 7.09–7.16 (3 H, m, Ph), 7.19–7.26 (2 H, m, Ph) and 7.88 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 24.5 (5-C), 25.1 (2-Me), 27.9 (4-Me), 29.5 (6-C), 29.7 (3-C), 46.9 (4-C), 110.6 (1-C), 126.3 (Ph), 128.1 (Ph), 129.3 (Ph), 134.2 (2-C), 140.2 (Ph), 168.4 (CO) and 209.6 (CO); *m*/*z* 289 (M^+, 12%), 180 (100) and 155 (95) (Found: M^+, 289.1125. $C_{16}H_{19}NO_2S$ requires *M*, 289.1138).

1-Acetamido-4-acetyl-2-phenylsulfonylcyclohexene 10c. A white crystalline solid, mp 77–79 °C (from ether–hexane); ν_{max}(KBr)/cm^{-1} 3319 (NH), 1708 (CO), 1700 (CO), 1371 (SO_2) and 1138 (SO_2); δ_H(300 MHz; $CDCl_3$) 1.97–2.10 (1 H, m, 5-H), 2.11 (3 H, s, 4-Ac), 2.16 (3 H, s, 1-Ac), 2.21–2.33 (2 H, m, 3-H and 5-H), 2.41–2.60 (2 H, m, 3-H and 4-H), 2.91–3.06 (1 H, m, 6-H), 3.18 (1 H, dt, *J* 18.1, 4.7, 6-H), 7.54–7.70 (3 H, m, Ph), 7.84–7.87 (2 H, m, Ph) and 10.53 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.7 (5-C), 25.4 (4-Me), 25.7 (1-Me), 27.9 (3-C), 30.9 (6-C), 45.7 (4-C), 111.4 (2-C), 127.1 (Ph), 129.4 (Ph), 133.7 (Ph), 140.1 (Ph), 146.8 (1-C), 168.3 (CO) and 208.7 (CO); *m*/*z* 321 (M^+, 38%), 278 (86), 236 (69), 180 (57), 138 (56) and 81 (100) (Found: M^+, 321.1027. $C_{16}H_{19}NO_4S$ requires *M*, 321.1030).

2-Acetamido-4-acetyl-1-phenylsulfonylcyclohexene 11c. A white crystalline solid, mp 80.5–81.5 °C (from ether–hexane); ν_{max}(KBr)/cm^{-1} 3300 (NH), 1716 (CO), 1709 (CO), 1371 (SO_2) and 1138 (SO_2); δ_H(300 MHz; $CDCl_3$) 1.52–1.67 (1 H, m, 5-H), 1.80–1.95 (1 H, m, 5-H), 2.12 (3 H, s, 4-Ac), 2.16 (3 H, s, 2-Ac), 2.20–2.35 (2 H, m, 6-H), 2.53–2.62 (1 H, m, 4-H), 2.90–3.05 (1 H, m, 3-H), 3.15–3.30 (1 H, m, 3-H), 7.52–7.70 (3 H, m, Ph), 7.80–7.86 (2 H, m, Ph), 10.46 (1 H, br s, NH); δ_C(75 MHz; $CDCl_3$) 23.5 (×2, 4-Me, 5-C), 25.4 (2-Me), 27.9 (6-C), 29.8 (3-C), 45.8 (4-C), 112.6 (1-C), 126.9 (Ph), 129.3 (Ph), 133.6 (Ph), 140.2 (Ph), 146.0 (2-C), 168.3 (CO) and 208.4 (CO); *m*/*z* 321 (M^+, 36%), 278 (86), 236 (67), 180 (55), 167 (25), 138 (53) and 81 (100) (Found: M^+, 321.1025. $C_{16}H_{19}NO_4S$ requires *M*, 321.1030).

General procedure for the Lewis acid-catalysed Diels–Alder reactions of 1a–c

Dichloromethane (1 cm^3) and methyl vinyl ketone (0.12 cm^3) were added sequentially to zinc chloride (200 mg, 1.5 mmol) which had been flame-dried *in vacuo* and then purged three times with nitrogen. After the mixture had been vigorously stirred for 20 min, a solution of each of the dienes **1a–c** (0.15 mmol) in dichloromethane (2 cm^3) was added dropwise at room temperature to the reaction mixture. After this had been stirred for 48 h it was quenched with water (5 cm^3) and extracted with dichloromethane (10 cm^3 × 3). The combined extracts were dried ($MgSO_4$), and concentrated by rotary evaporation to give the crude product. The ^{1}H NMR spectrum of the crude product was used to determine the ratio of the regioisomers. The crude

product was then purified by flash column chromatography to confirm the structure of the products and to determine the yield of the reaction. For the reaction of **1b**, a mixture of four diastereoisomers (2.7:1.6:1:1) was obtained. To determine the regiochemistry of the reaction, the crude product was oxidized by MCPBA (2.0 equiv.) to give a mixture of two diastereoisomers **10c** and **11c** (2.2:1).

Conversion of 6c and 7c into methyl 4-acetamidobenzoate 12 and methyl 3-acetamidobenzoate 13

To a 2:1 mixture of **6c** and **7c** (53 mg) was added a solution of potassium hydroxide (46 mg) in methanol (5 cm^3). The mixture was stirred at room temperature for 2 h after which the solvent was removed by rotary evaporation. The residue was dissolved in dichloromethane (25 cm^3), and the solution was washed with water (20 cm^3) and brine (20 cm^3), and dried ($MgSO_4$). After evaporation of the solution, the crude product was purified by flash chromatography using hexane as the eluent to give a 2:1 mixture of **12** and **13** (38 mg, 53%), the structures and ratios of which were determined from the ^{1}H NMR spectrum. The data obtained matched well with the literature values.[20,21] Using a similar procedure pure **6c** gave **12** only.

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