Synthesis and Diels–Alder reactions of 2*H*-azirine-3-carboxamides

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For Otto Meth–Cohn on his 65th birthday, with regards and best wishes
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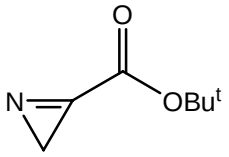
Abstract
Four 2-azidoacrylamides 5 have been prepared from the corresponding acrylamides 3 by reaction with bromine then with sodium azide. From three of these azides, compounds 5b–5d, 2*H*-azirine-3-carboxamides 2 were produced by pyrolysis in toluene. These azirines reacted with conjugated dienes at room temperature to give cycloadducts. The reaction of the chiral azirine amide 2d with cyclopentadiene showed no selectivity.

Keywords: Azirine, azide, Diels-Alder reaction

Introduction



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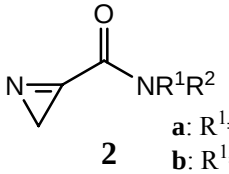

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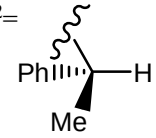
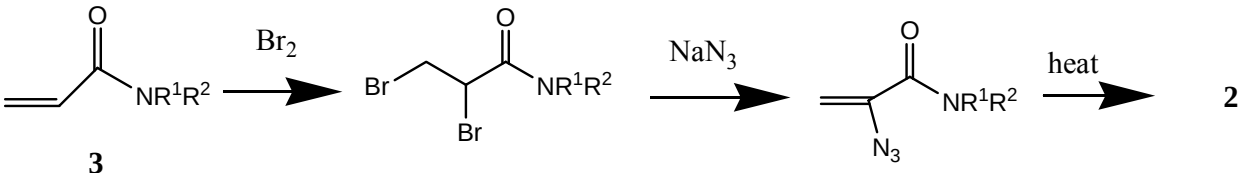
a: $R^1 = Bu^t$, $R^2 = H$
b: $R^1 = R^2 = Me$
C: $R^1R^2 = (CH_2)_4$
d: $R^1 = R^2 =$



The hetero Diels–Alder reaction is a useful method for the synthesis of six-membered heterocycles. The reactivity of imines as the 2p-electron component in cycloaddition reactions is low and largely restricted to imines bearing one or two electron withdrawing substituents. The ring strain in 2*H*-azirines increases the reactivity of the imine function and we have previously shown that 2*H*-azirines that are activated by an alkoxycarbonyl group on the C=N bond will undergo uncatalyzed Diels–Alder reactions with conjugated dienes at room temperature.[1,2] In

particular, the simple azirine ester 1 proved to be a good dienophile.[2] A disadvantage of this ester is that it is too unstable to be isolated, so that Diels–Alder reactions have to be carried out in hydrocarbon solutions of the azirine immediately after it has been generated. On the basis of an assumption that analogous amides 2 would be somewhat more stable but still sufficiently activated to undergo cycloaddition reactions we set out to prepare a series of these compounds and to study their chemistry.

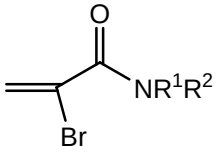


3 **4** **5**

The route used to generate the azirine 1 started from *tert*-butyl acrylate. This was converted into *tert*-butyl-2-azidoacrylate by successive reaction with bromine and sodium azide. The azide was then decomposed by heating in heptane or toluene to generate the azirine.[2] We have used the same approach to prepare the amides 2. No 2-azidoacrylamides have been described in the literature so the route to these compounds was designed to follow that used for the preparation of

2-Azidoacrylic esters

The first compound that was targeted was the *tert*-butyl amide 2a. *N*-*tert*-Butylacrylamide 3a is commercially available and so provided a convenient starting material with which to explore the series. Addition of bromine gave the dibromo amide 4a.[3] The reaction of this dibromo amide with sodium azide was carried out under a wide range of conditions in which the temperature, the reaction time and the number of equivalents of sodium azide were all varied in attempts to optimise the formation of the vinyl azide 5a. In all cases the azide was accompanied by a significant by-product, the 2-bromoacrylamide 6. The two components were separated by chromatography and, in the best conditions, the required vinyl azide 5a was obtained in 62% yield. The bromoacrylamide 6 was not converted into the vinyl azide 5a by further reaction with sodium azide. The formation of this by-product, which we had not seen in the corresponding ester preparation, obviously reduced the convenience and efficiency of the overall route.



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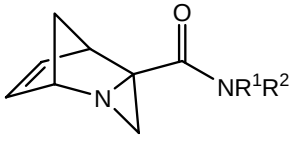
The vinyl azide 5a was pyrolysed in toluene but there was no evidence, from trapping experiments or from NMR analysis of the reaction mixture, that the azirine 2a was formed. There was some indication from the NMR spectra that a polymer was being generated. It is not clear why the reaction fails but we tentatively ascribe it to the choice of a secondary amide as the functional group. We had previously found that the azirine esters are very sensitive to nucleophilic attack, even by water, and a polar, hydrogen bonding functional group is likely to aid decomposition.

In order to test this hypothesis a tertiary amide was chosen as the next target. Commercially available *N*,*N*-dimethylacrylamide 3b was converted into the previously unknown dibromo amide 4b in high yield. This compound reacted smoothly with sodium azide to give the vinyl azide 5b without the side reaction that occurs with the *tert*-butyl amide. Because of the high polarity of the vinyl azide it proved difficult to isolate the compound efficiently from a DMF solution, so the reaction with sodium azide was best carried out in a two phase system with a phase transfer catalyst present. The vinyl azide 5b was fully characterized. It was then converted, by heating in toluene, into the azirine 2b. In contrast to the ester 1, this amide was stable enough to survive below 0 ºC for several weeks if stored in solution, and a good NMR spectrum could be obtained from a sample after evaporation of a portion of the solution. The azirine decomposed when heated in solution above 100 ºC for prolonged periods. Thus, as anticipated, the amide 2b was somewhat more stable than the ester 1.

Diels–Alder reactions were carried out with cyclopentadiene, 2,3-dimethylbutadiene and 1-methoxy-3-trimethylsilyloxybutadiene at room temperature. The adducts 7a, 8a, and 9 respectively, were obtained from these reactions and were characterized. These products are analogous to those obtained earlier from the azirine esters and these dienes.[1,2] All the compounds proved unexpectedly difficult to purify by column chromatography. They were absorbed so strongly on silica that solvent mixtures containing methanol were needed to elute them, and the isolated yields were reduced as a result. Other chromatographic supports were tried but without improvement.



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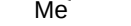
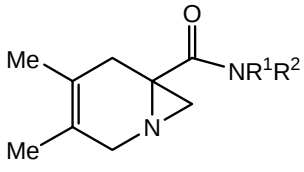
a:$R^1 = R^2$ =Me
b: R^1R^2= $(CH_2)_4$
c:R^1=R^2=





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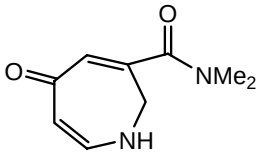
a: $R^1 = R^2$ = Me
b: $R^1R^2 = (CH_2)_4$



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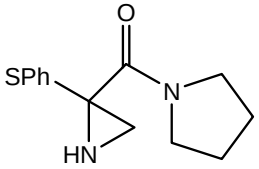

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In order to test whether this polarity characteristic was a peculiarity of the dimethyl amide series of compounds, a third series of reactions was carried out using the acryloylpyrrolidine 3c as the precursor. This amide is known[4] but it is not commercially available; it was prepared from pyrrolidine and acryloyl chloride. It was converted into the azirine 2c by way of the intermediates 4c and 5c without any problems, the conversion of the dibromo amide 4c into the vinyl azide 5c being fast and efficient. Again it proved possible to characterize the azirine 2c and to store it in solution. Reactions with cyclopentadiene and with 2,3-dimethylbutadiene gave the cycloadducts 7b and 8b, respectively. Although the compounds were slighly less polar than their analogues 7a and 8a, they were still difficult to purify by chromatography. A single reaction was also carried out between the azirine 2c and a nucleophile, thiophenol. This gave the expected aziridine 10 which, unlike the cycloadducts, was relatively non polar and therefore easy to purify.

The chemistry of a chiral azirine amide, compound 2d, was also investigated briefly. A chiral azirine ester had been prepared previously but was found to show little diastereoselectivity in the Diels–Alder reaction.[5] A chiral tertiary amide offers the possibility of introducing a twofold axis of symmetry into the side chain; thus it seemed worthwhile to explore whether this would be more selective in its cycloadditions. The azirine 2d was generated by the general route from the acrylamide 3d. This amide has not previously been reported but it was prepared from bis[(*S*)-1-phenylethyl]amine, which is commercially available as its hydrochloride, and acryloyl chloride. The azirine reacted well with cyclopentadiene but the reaction was completely unselective: an adduct 7c was obtained as a (partly separable) 1:1 mixture of diastereoisomers.

In summary, the 2-azidoacrylamides are simple to prepare from the corresponding acrylamides and those derived from tertiary acrylamides are converted into 2*H*-azirines on pyrolysis. These azirines combine useful characteristics of reasonable stability with good reactivity in the Diels–Alder reaction. The disadvantages are the high polarity of the cycloadducts and the lack of selectivity of the chiral azirine 2d in its reaction with cyclopentadiene.

Experimental Section

General Procedures. IR spectra were recorded on a Perkin-Elmer 883 spectrometer. Solid samples were run as Nujol mulls, and liquids as thin films. ^{1}H NMR spectra were recorded either on a Bruker AC 200 instrument at 200 MHz or on a Varian Gemini 2000 instrument at 300 MHz. Multiplicities are recorded as broad peaks (br), singlets (s), doublets (d), triplets (t), and multiplets (m). ^{13}C NMR spectra were recorded on a Varian Gemini instrument at 75.5 MHz. Mass spectra were recorded on a VG Micromass 7070E machine as electron impact (EI) (70 eV) or chemical ionization (CI) spectra. Microanalyses were performed in the University of Liverpool Microanalysis Laboratory.

Unless otherwise stated all commercial solvents and reagents were used as supplied. THF and ether were dried from benzophenone and sodium; dichloromethane and toluene were dried over calcium hydride and distilled. Light petroleum refers to the fraction bp 40–60 ºC.

2,3-Dibromo-*N*-*tert*-butylpropionamide (4a). To a solution of *N*-*tert*-butylacrylamide 3a (3.00 g, 23.6 mmol) in dry dichloromethane (70 mL) at 0 ºC bromine (3.83 g, 24.0 mmol) was added dropwise. When the starting material was no longer detected by TLC the reaction mixture was washed with 10 % aq. sodium metabisulfite (2 x 30 mL) and with water (50 mL), the organic layer was dried over $MgSO_4$ and evaporated *in vacuo*. The residue was crystallized to give 2,3-dibromo-*N*-*tert*-butylpropionamide 4a (4.9 g, 73 %) as colourless needles, mp 182–183 ºC (from dichloromethane) (lit.,[3] 185–187 ºC); IR (Nujol) 3295, 1659, 1559, 1454, 1365, 1223, 1168, and 960 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.37 (9 H, s), 3.80 (1 H, dd, *J* = 10.2 and 4.4 Hz), 3.95 (1 H, dd, *J* = 10.2 and 8.0 Hz), 4.34 (1 H, dd, *J* = 8.0 and 4.4 Hz), and 5.89 (1 H, bs, NH); MS (EI) 289 (1.4), 287 (2.9), 285 (M^+, 1.6), and 57 (100). Anal. Calcd for $C_7H_{13}Br_2NO$: C, 29.31; H, 4.56; N, 4.88. Found: C, 29.19; H, 4.48; N, 4.79.

2-Azido-*N*-*tert*-Butylacrylamide 5a and 2-Bromo-*N*-*tert*-butylacrylamide (6)

(a) With sodium azide in DMF. To a solution of 2,3-dibromo-*N*-*tert*-butylpropionamide 4a (1.70 g, 5.92 mmol) in DMF (60 mL) at rt was added sodium azide (1.15 g, 17.8 mmol). After 24 h when all the starting material had disappeared the reaction mixture was poured into water and extracted with dichloromethane. The organic extracts were washed with brine (2 x 50 mL), water (50 mL), and dried over $MgSO_4$ and evaporated *in vacuo*. The crude residue contained two compounds that were separated by column chromatography [light petroleum–ethyl acetate (10:1)] to give2-azido-*N*-*tert*-butylacrylamide 5a(0.61 g, 62%) as a pale yellow oil; IR (film) 3424, 2958, 2858, 2114, 1689, 1611, 1516, 1458, 1367, and 882 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.36 (9H, s), 5.09 (1H, d, *J* = 2.2 Hz), 6.08 (1H, d, *J* = 2.2 Hz), and 6.23 (1H, bs, NH); MS (CI) 186.1 ($[M + NH_4]^+$, 100) and 169.1 (M^+, 14). GC and MS showed that the sample contained a small amount of the dibromo compound 4a and it was not purified further. The other product was identified as 2-bromo-*N*-*tert*-butylacrylamide 6(0.37 g, 31 %); a colourless solid mp below rt; IR (film) 3338, 2975, 1696, 1615, 1538, 1453, 1364, 925, and 791 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.39 (9 H, s), 5.95 (1 H, d, *J* = 1.5 Hz), 6.50 (1 H, bs), and 6.93 (1 H, d, *J* = 1.5 Hz). Anal. Calcd for $C_7H_{12}BrNO$: C, 40.80; H, 5.87; N, 6.80. Found: C, 41.24; H, 5.98; N, 7.13.

(b) With Azidotrimethylsilane. To a solution of 2,3-dibromo-N-tert-butylpropionamide 4a (0.50 g, 1.74 mmol) in THF (40 mL) at rt was added azidotrimethylsilane (0.60 g, 5.22 mmol) and TBAF (10% in THF) (5.2 mL, 5.22 mmol). After 24 h when all the starting material had disappeared the reaction mixture was washed with 5% aq. H_2SO_4 (2 x 20 mL), sat. aq.$NaHCO_3$ (2 x 20 mL) and brine (20 mL). The organic layer was dried over $MgSO_4$ and evaporated in vacuo. The crude product was subjected to column chromatography [light petroleum–ethyl acetate (10:1)] to give 2-azido-N-tert-butylacrylamide 5a (0.17 g, 60%) and 2-bromo-N-tert-butylacrylamide 6 (0.15 g, 30%).

2,3-Dibromo-*N*,*N*-dimethylpropionamide (4b). This was prepared as for compound 4a from *N*,*N*-dimethylacrylamide (7.0 g, 70.6 mmol), and was isolated by crystallization as a pale yellow solid (17.8 g, 96 %), mp 43–44 ºC (from dichloromethane); IR (Nujol) 1669, 1414, 1119, and 912 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 3.00 (3 H, s), 3.06 (3 H, s), 3.64 (1 H, dd, *J* = 9.5 and 3.9 Hz), 4.11 (1 H, dd, *J* = 10.5 and 9.5 Hz), 4.66 (1 H, dd, *J* = 10.5 and 3.9 Hz), and 5.27 (1 H, s, NH); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 30.7, 36.4, 37.3, 38.9, and 166.4; MS (EI) 261 (1.46), 259 (2.81), 257 (M^+, 1.46), and 72 (100). Anal. Calcd for $C_5H_9Br_2NO$: C, 23.19; H, 3.50; N, 5.41. Found: C, 23.13; H, 3.55; N, 5.33.

2-Azido-*N*,*N*-dimethylacrylamide (5b). To a solution of 2,3-dibromo-*N*,*N*-dimethylpropionamide 4b(1.0 g, 3.9 mmol), tetrabutylammonium bromide (1.24 g, 3.96 mmol) and sodium azide (0.75 g, 11.6 mmol) in dichloromethane (10 mL) was added sat. aq. $NaHCO_3$ (10 mL). The two phase mixture was stirred vigorously at rt until no starting material could be detected by TLC (1 h). Ethyl acetate (50 mL) was added; the organic layer was separated and successively washed with sat. $NaHCO_3$, water (2 x 10 mL) and brine (2 x 10 mL). The combined extracts were dried over $MgSO_4$, filtered and evaporated *in vacuo* to afford 2-azido-*N*,*N*-dimethylacrylamide 5b (0.37 g, 67%) as a yellow oil; IR (film) 2113, 1661, 1614, 1403, and 889 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.98 (3 H, s), 3.09 (3 H, s), 4.99 (1 H, d, *J* = 2.0 Hz), and 5.07 (1 H, d, *J* = 2.0 Hz). Anal. Calcd for $C_5H_8N_4O$: C, 42.85; H, 5.75; N, 39.98. Found: C, 42.66; H, 5.80; N, 40.30.

2*H*-Azirine-3-*N*,*N*-dimethylcarboxamide 2b. A solution of 2-azido-*N*,*N*-dimethylacrylamide 5b (0.37 g, 2.6 mmol) in toluene (70 mL) was heated at 95 ºC until all the starting material had decomposed (3 h) (^1H NMR). After rapid evaporation of the solvent of a small sample an orange oil was obtained that was identified as the 2*H*-azirine-3-carboxamide 2b; IR (film) 2937, 1648, 1403, 1262, and 1136 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.82 (2 H, s), 3.11 (3 H, s), and 3.24 (3 H, s).

1-Pyrrolidin-1-yl-propenone (3c). To a solution of pyrrolidine (7.82 g, 110 mmol) in dry ether (60 mL) under N_2 was added dropwise during 30 min, acryloyl chloride (4.5 mL, 55 mmol) in ether (15 mL). After 20 h the solution was washed with water (2 x 20 mL), 10% HCl (20 mL) and water (20 mL). The organic layer was dried over $MgSO_4$, filtered and the solvent evaporated *in vacuo* to yield 1-pyrrolidin-1-yl-propenone[4] 3c as an oil (6.26 g, 91 %); IR (film) 2977, 2878, 1651, 1614, 1435, 980, and 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (4 H, m), 3.54 (4 H, t, *J* = 6.9 Hz), 5.66 (1 H, dd, *J* = 2.4 and 9.8 Hz), 6.35 (1 H, dd, *J* = 2.4 and 16.8 Hz), and 6.47 (1 H, dd, *J* = 9.8 and 16.8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 24.2, 26.0, 45.8, 46.5, 127.1, 128.8, and 164.5. Anal. Calcd for $C_7H_{11}NO$: M, 125.08406. Found (EI): M^+, 125.08426.

2,3-Dibromo-1-pyrrolidin-1-ylpropan-1-one 4c. This was prepared as for compound 4a from 1-pyrrolidin-1-yl-propenone 3c (6.26 g, 50.1 mmol) as a pale orange solid (5.29 g, 70%), mp 49–51 ºC (from dichloromethane); IR (Nujol) 2977, 2880, 1660, 1443, and 733 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.86–2.09 (4 H, m), 3.46–3.64 (4 H, m), 3.67 (1 H, dd, *J* = 4.2 and 9.6 Hz), 4.14 (1 H, dd, *J* = 9.6 and 10.8 Hz), 4.55 (1 H, dd, *J* = 4.2 and 10.8 Hz); MS (EI) 287 (0.76), 285

(1.60), 283 (M^+, 0.88), and 98 (100). Anal. Calcd for $C_7H_{11}Br_2NO$: C, 29.49; H, 3.89; N, 4.91; M, 282.92072. Found: C, 29.54; H, 3.95; N, 4.92; M^+ (EI), 282.92091.

2-Azido-1-pyrrolidin-1-yl-propenone (5c). This was prepared as compound 5b from 2,3-dibromo-1-pyrrolidin-1-yl-propan-1-one 4c (2.0 g, 7.0 mmol). 2-Azido-1-pyrrolidin-1-yl-propenone 5c was obtained as a yellow oil (1.0 g, 85.7 %); IR (Nujol) 2980, 2884, 2113, 1682, 1614, 143, 914, and 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.89–1.96 (4 H, m), 3.48–3.61 (4 H, m), 5.12 (1 H, d, *J* = 1.9 Hz), and 5.20 (1 H, d, *J* = 1.9 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 23.91, 26.09, 46.08, 48.70, 104.23, 140.77, and 162.47; MS (CI) 167 ($[M + H]^+$). Anal. Calcd for $C_7H_{13}N_4O$: M, 167.09329. Found (CI): $[M + H]^+$: 167.09308.

(2*H*-Azirin-3-yl)pyrrolidin-1-ymethanone (2c). A solution of 2-azido-1-pyrrolidin-1-ylpropenone 5c (1.80 g, 10.84 mmol) in toluene (100 mL) was heated at 95 ºC until all the starting material had decomposed (10 h) (^1H NMR). After rapid evaporation of the solvent of a small sample an orange oil was obtained that was identified as (2*H*-azirin-3-yl)pyrrolidin-1-yl-methanone 2c; IR (film) 2975, 2881, 1631 and 1445 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.82 (2 H, s), 1.86–2.04 (4 H, m), and 3.51–3.67 (4 H, m).

***N*,*N*-Bis[(*S*)-1-phenylethyl]acrylamide (3d).** This compound was prepared as described for the amide 3c from acryloyl chloride (0.35 g, 3.9 mmol), bis[(*S*)-1-phenylethyl]amine hydrochloride (Fluka) (1.0 g, 3.8 mmol) and triethylamine (0.85 g, 8.4 mmol). The amide was isolated as an oil (1.0 g, 94%); IR (film) 1644, 1605, 1433, 1248 and 697 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.73 (6 H, d, *J* = 7.0 Hz), 4.85–5.05 (2 H, br), 5.40 (1 H, dd, *J* = 10.0 and 2.4 Hz), 6.10 (1 H, dd, *J* = 16.8 and 10.0 Hz), 6.27 (1 H, dd, *J* = 16.8 and 2.4 Hz), and 6.85–7.25 (10 H, m); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.0 (br), 52.40, 126.85, 127.34, 128.35, 130.72, 134.65, 141.24, and 166.91. Anal. Calcd for $C_{19}H_{21}NO$: M, 279.16229. Found (EI): M^+, 279.16232.

2,3-Dibromo-*N*,*N*-bis[(*S*)-1-phenylethyl]propionamide (4d). Addition of bromine (0.60 g, 3.8 mmol) to the amide 3d (1.01 g, 3.60 mmol) gave the dibromo amide 4d (1.57 g, 99%) as an oil; IR (film) 1651, 1455, 1377 and 694 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.76 and 1.78 (together 3 H, each d, *J* = 7.2 Hz), 1.84 and 1.86 (together 3 H, each d, *J* = 7.2 Hz), 3.58–3.70 (1 H, m), 4.00–4.25 (1 H, m), 4.60–4.85 (1 H, m), 5.00–5.35 (2 H, m) and 7.00–7.40 (10 H, m). Integration of the methyl signals indicated that two diastereoisomers were present in a 1:1 ratio. The compound was not characterized further.

2-Azido-*N*,*N*-bis[(*S*)-1-phenylethyl]acrylamide (5d). The dibromo amide 4d (1.57 g, 3.57 mmol) and sodium azide (0.70 g, 10.8 mmol) gave, by the method described for the azide 5b, the azidoacrylamide 5d (0.68 g, 66%) as an oil; IR (film) 2105, 1644, 1439, 1251 and 698 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.76 (6 H, d, *J* = 7.0 Hz), 4.80–5.10 (2 H, br m), 4.99 (1 H, d, J = 2.3 Hz), 5.06 (1 H, d, *J* = 2.3 Hz), and 6.90–7.50 (10 H, m); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.41, 55.47, 101.55, 127.49, 128.05, 128.82, 139.93, 142.16, and 164.53. Anal. Calcd for $C_{19}H_{21}N_4O$: M, 321.17154. Found (CI): $[M + H]^+$, 321.17210.

2*H*-Azirine-3-*N*,*N*-Bis[(*S*)-1-phenylethyl]carboxamide (2d). A solution the vinyl azide 5d (0.56 g, 1.75 mmol) in toluene (50 mL) was heated at 95 ºC and the course of the reaction was

monitored by NMR (200 MHz, $CDCl_3$). New signals appeared at δ 1.59 (2 H, s) and 1.84 (6 H, dd, *J* = 7.4 and 1.2 Hz), replacing those of the vinyl azide at δ 1.76, 4.99, and 5.06. After 5 h these signals had reached a maximum. The azirine was not characterized further but was used directly in a reaction with cyclopentadiene.

Diels-Alder Reactions of 2*H*-Azirines. General procedure

A solution of the correspondent vinyl azide in toluene (100 mL) was heated at 95 ºC until all the starting material had decomposed (^{1}H-NMR or TLC). The solution was allowed to cool to rt and the diene was added (in large excess with 2,3-dimethylbutadiene and cyclopentadiene or 2 eq. of 1-methoxy-3-trimethylsilyloxybutadiene). The solution was left at rt for periods ranging from 1 day to several days, until the azirine could no longer be detected by TLC. The solvent was then removed and the products purified by flash column chromatography. The following compounds were isolated.

2-Azatricyclo[3.2.1.0^{2,4}]oct-6-ene-4-*N*,*N*-dimethylcarboxamide (7a). This was obtained from the pyrolysis of 2-azido-*N*,*N*-dimethylacrylamide 5b (0.60 g, 3.61 mmol) and cyclopentadiene (2.6 mL, 40 mmol) after reaction for 24 h, and was isolated as an oil (0.29 g, 42%) by flash chromatography (from dichloromethane–methanol 10:1); IR (film) 2985, 1645, 1504, 1397, 843, and 759 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.61 (1 H, s), 1.70 (1 H, dd, *J* = 2.4 and 3.0 Hz), 1.97 (1 H, d, *J* = 3.0 Hz), 2.50 (1 H, dt, *J* = 7.8 and 1.5 Hz), 2.98 (3 H, s), 3.05 (3 H, s), 3.05–3.08 (1 H, m), 4.14 (1 H, s), 5.71–5.74 (1 H, m), and 6.12–6.15 (1 H, m); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 35.37, 36.54, 41.07, 43.55, 47.89, 58.95, 65.62, 128.28, 130.83, and 170.96. Anal. Calcd for $C_{10}H_{14}N_2O$: M, 179.11844. Found (EI): M^+, 179.11822.

3,4-Dimethyl-1-azabicyclo[4.1.0]hept-3-ene-6-*N*,*N*-dimethycarboxamide (8). This was obtained by pyrolysis of 2-azido-*N*,*N*-dimethylacrylamide 5b (0.37 g, 2.6 mmol). 2,3-Dimethylbutadiene (2.9 mL, 26 mmol) was added and, after 6 days, compound 8 was isolated as an oil (0.16 g, 31%) by flash chromatography (dichloromethane–methanol 10:1); IR (film) 1643, 1501, 1401, 1138, 1059, and 678 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.55 (3 H, s), 1.65 (3 H, s), 1.84 (1 H, s), 1.96 (1 H, s), 2.32 (1 H, d, *J* = 16.8 Hz), 2.60 (1 H, d, *J* = 16.8 Hz), 3.00 (3 H, s), 3.12 (3 H, s), 3.19 (1 H, d, *J* = 16.8 Hz), and 3.65 (1 H, d, *J* = 16.8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 16.39, 18.51, 29.00, 31.48, 35.26, 37.31, 41.03, 51.71, 119.94, 120.26, and 171.59. Anal. Calcd for $C_{11}H_{19}N_2O$: M, 195.14974. Found (CI): $[M + H]^+$, 195.14965.

5-Oxo-2,5-dihydro-1*H*-azepine-3-*N*,*N*-dimethylcarboxamide (9). Pyrolysis of the vinyl azide 5b (0.21 g, 1.28 mmol) followed by the addition of 1-methoxy-3-trimethylsilyloxybutadiene (1.28 mL, 2mmol) gave, after 4 days, the azepinone 9 (0.07 g, 20%) as an oil by flash chromatography (dichloromethane–methanol 10:1); IR (film) 3339, 1613, 1516, 1408, and 1026 m^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.02 (3 H, s), 3.14 (3 H, s), 3.96 (2 H, d, *J* = 4.9 Hz, H-2) (coupling removed by D_2O shake), 5.26 (1 H, dd, *J* = 8.2 and 2.5 Hz, H-6), 6.27 (1 H, d, *J* =

2.2 Hz, H-4), 7.06 (1 H, br d, $J \approx 8$ Hz, H-7), and 7.40–7.60 (br, NH). Anal. Calcd for $C_9H_{12}N_2O_2$: M, 180.08987. Found (EI): M^+, 180.09020.

(2-Azatricyclo[3.2.1.0^{2,4}]oct-6-en-4-yl)pyrrolidin-1-ylmethanone (7b). This was obtained by pyrolysis of the vinyl azide 5c (1.80 g, 10.8 mmol) followed by the addition of cyclopentadiene (6.7 mL, 100 mmol). Compound 7c was isolated (0.84 g, 38%) as an oil after 2 days by flash chromatography (acetone–light petroleum 5:2 followed by dichloromethane–methanol 20:1); IR (film)1642, 1431, and 758 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.57 (1 H, d, J = 0.9 Hz), 1.69 (1 H, dd, J = 3.0 and 7.8 Hz), 1.81–1.96 (4 H, m), 1.98 (1 H, br dd, J = 1.2 and 3.3 Hz), 2.46 (1 H, dt, J = 7.8 and 1.8 Hz), 3.16–3.18 (1 H, m), 3.44–3.59 (4 H, m), 4.11–4.14 (1 H, br s), 5.70 (1 H, dd, J = 2.4 and 5.4 Hz),and 6.09–6.13 (1 H, m). Anal. Calcd for $C_{12}H_{16}N_2O$: M, 204.12627. Found (EI): M^+, 204.12620.

2-Azatricyclo[3.2.1.0^{2,4}]oct-6-ene-4-*N*,*N*-bis[(*S*)-1-phenylethyl]carboxamide (7c). The vinyl azide 5d (0.56 g, 1.75 mmol) was pyrolysed as described above and cyclopentadiene (1.16 g, 17.5 mmol) was added. After 24 h the reaction mixture was subjected to flash chromatography which gave (with toluene–ethyl acetate 1:1) the aziridines 7c. The mixture (0.34 g, 53%) contained two diastereoisomers, both oils, in a 1:1 ratio, which were partially separated by chromatography. *Isomer 1*: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.72 (1 H, s), 1.78 (6 H, d, J = 7.2 Hz), 1.76–1.78 (1 H, m), 2.18 (1 H, d, J = 3.6 Hz), 2.61 (1 H, dt, J = 7.4 and 1.0 Hz), 3.21 (1 H, br s), 4.14 (1 H, br s), 4.20–4.30 (1 H, br s), 5.45–5.70 (1 H, br), 5.73 (1 H, br dd, J = 5.1 and 2.3 Hz), 6.05–6.14 (1 H, m), and 7.00–7.30 (10 H, m). *Isomer 2*: ^1H NMR ($CDCl_3$, 200 MHz) δ 1.52–1.87 (8 H, m), 2.16 (1 H, d, J = 3.0 Hz), 2.58 (1 H, dt, J = 8.0 and 1.0 Hz), 3.28–3.30 (1 H, m), 4.13 (1 H, s), 4.20–4.30 (1 H, br s), 5.60–5.75 (1 H, br s), 5.71–5.73 (1 H, m), 6.12–6.15 (1 H, m), and 7.00–7.50 (10 H, m). Anal. (mixture) Calcd for $C_{24}H_{26}N_2O$: M, 358.20450. Found (EI): M^+, 358.20421.

(2-Phenylsulfanylaziridin-2-yl)pyrrolidin-1-ylmethanone (10). A solution of 2-azido-1-pyrrolidin-1-yl-propenone (0.53 g, 3.21 mmol) in toluene (80 mL) was heated at 95 ºC until all the starting material had decomposed (TLC). The solution was then allowed to cool to rt and thiophenol (0.35 g, 3.22 mmol) was added. The solution was left until no azirine could be detected by TLC (2 days). The disulfide 10 was isolated by flash chromatography (hexane–ethyl acetate 1:1) as a yellow oil (0.70 g, 88%); IR (film) 3257, 3060, 2975, 2879, 1630, 1431, 1187, 884, 741, and 691 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) (all signals broad and poorly resolved) δ 1.78–1.96 (4 H, m), 2.21–2.25 (2 H, m), 3.37–3.56 (4 H, m), 3.98 (1 H, br s), and 7.18–7.50 (5 H, m); MS (EI) 248 (M^+, 17.3), 249 (2.6), 250 (1.0), and 70 (100). Anal. Calcd for $C_{13}H_{16}N_2OS$: C, 62.87; H, 6.49; N, 11.28. Found: C, 62.60; H, 6.46; N, 11.34.

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