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High Pressure Intramolecular Diels–Alder Reactions of Vinylsulfonates and Vinylsulfonamides

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Dedicated to Doz. Dr Wolf D. Habicher on the occasion of his 60th birthday

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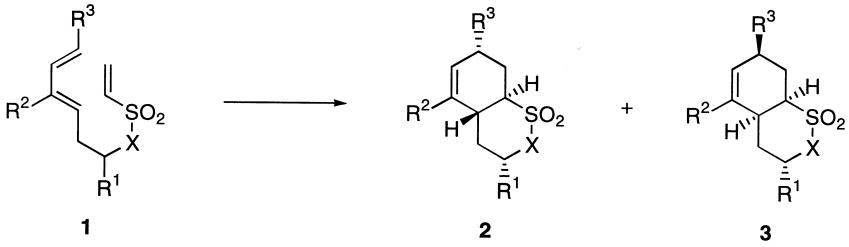
Abstract—Acceleration of the intramolecular Diels–Alder reaction of vinylsulfonic esters and amides bearing acyclic and carbocyclic 1,3-diene moieties by application of high pressure leads to excellent yields of sultones and sultams, respectively, at ambient temperature. The influence of pressure on the stereoselectivity of these processes has been investigated.

Since both the intermolecular as well as the intramolecular Diels–Alder reaction feature a negative volume of activation, application of high pressure causes a marked increase in rate for both versions.[1–7] We report our investigations on the influence of high pressure on yield and stereochemical outcome of the intramolecular [4+2] cycloaddition of vinylsulfonic esters and amides derived from hydroxyalkyl or aminoalkyl substituted 1,3-dienes, respectively.[8]

During our studies on the intramolecular Diels–Alder reaction of vinylsulfonates **1** (X=O), we found that reflux in



1 **2** **3**

Scheme 1.

Table 1. Intramolecular Diels–Alder reactions of vinylsulfonic acid derivatives **1**

1–3	X	R^1	R^2	R^3	13 kbar, CH_2Cl_2, room temp.		Toluene, BHT, reflux	
					2:**3**[a]	Yield (%)[b]	**2**:**3**[a]	Yield (%)[b]
a	O	H	H	H	1.0:2.3	88	1.0:1.0	76[c]
b	O	Me	H	Me	1.0:2.0	78	1.4:1.0	64[c]
c	O	*t*-Bu	Me	H	3.6:1.0	79	4.7:1.0	76[c]
d	NBn	H	H	H	1.0:1.6	79	1.0:1.0	76
e	NBn	Me	H	Me	1.0:1.9	81	1.6:1.0	61

[a] Determined by capillary GC on the crude products.
[b] Isolated yield.
[c] Ref. 9.

Keywords: Diels–Alder reactions; pressure; reactions under; sultones; sultams.
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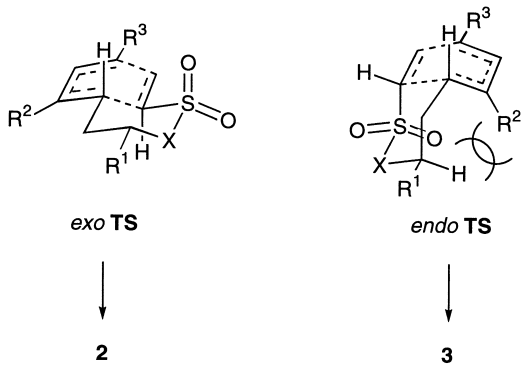


Figure 1. Transition states (TS) for the intramolecular Diels–Alder reaction of vinylsulfonic acid derivatives **1**.

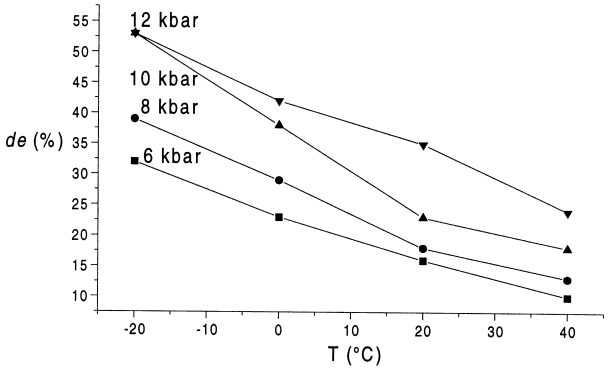


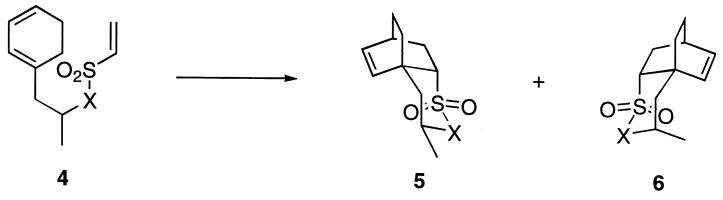
Figure 2. Dependence of diastereomeric excess on temperature and pressure for the cycloaddition of vinylsulfonate **1a** to *endo* sultone **3a**.

toluene was required for efficient cycloaddition at ordinary pressure.[9,10] In order to suppress side reactions at this elevated temperature, addition of a small amount of the radical scavenger BHT proved beneficial. While attempts to trigger cyclization of these substrates at lower temperature using different Lewis acids failed, application of high pressure[11] turned out to be effective. Thus, vinylsulfonates **1a–c** as well as vinylsulfonamides[12,13] **1d,e** smoothly cyclized at room temperature when a pressure of 13 kbar was applied. The presence of BHT is not necessary under these conditions, and the yields are significantly higher compared to those obtained in refluxing toluene at ambient pressure (Scheme 1, Table 1).

Analysis of the crude products by capillary GC confirmed that only diastereomers **2** and **3** were formed under both conditions. The relative configuration of the cycloadducts was determined by diagnostic ^{1}H NMR coupling constants and NOEs. By invoking transition states with equatorial orientation of the substituent R^1 on a chair-like folded tether (Fig. 1), the observed diastereoselectivities can be readily rationalized. For vinylsulfonates **1a**,**b** and vinylsulfonamides **1d**,**e** with R^2=H, the more compact *endo* transition state leading to *cis* fused products **3** is favored at high pressure, whereas there is either no (**1a**,**d**) *exo*/*endo* discrimination or a small *exo* preference (**1b**,**e**) at normal pressure. Interestingly, for substrate **1c** with R^2=Me, the unfavorable steric interaction between R^2 and the hydrogen atom on the carbinol center in the *endo* transition state still predominantly influences the stereochemical outcome at 13 kbar. As a consequence, diastereoselectivity decreases with increasing pressure in this case.

The degree of *endo* preference for the cycloaddition of vinylsulfonate **1a** was studied at different temperatures (−20, 0, 20°C: CH_2Cl_2; 40°C: toluene) and pressures (Fig. 2). For this substrate with R^2=H, simple diastereoselectivity increases with increasing pressure and decreasing temperature. Obviously, at a temperature of −20°C, a maximum *de* is already reached at 10 kbar.

In contrast to the situation with acyclic 1,3-dienes **1**, only *endo* adducts are formed from substrates **4a**[9,14] and **4b** incorporating a cyclic 1,3-diene unit at normal pressure already (Scheme 2, Table 2). This is probably due to nonbonding interactions involving a hydrogen atom on the saturated C_2-bridge *syn* to the six-membered heterocycle in the alternative *exo* transition states. At 13 kbar, the



Scheme 2.

Table 2. Intramolecular Diels–Alder reactions of vinylsulfonic acid derivatives **4**

4–6	X	13 kbar, CH_2Cl_2, room temp.		Toluene, BHT, reflux	
		5:**6**[a]	Yield (%)[b]	**5**:**6**[a]	Yield (%)[b]
a	O	54.6:1	92	10.2:1	58[c]
b	NBn	30.3:1	93	9.3:1	77

[a] Determined by capillary GC on the crude products.
[b] Isolated yield.
[c] Ref. 9.

preference for adducts **5** with equatorial methyl group is significantly enhanced. Stereochemical assignment for **5b** and **6b** rests on diagnostic ^{1}H NMR coupling constants and NOEs and was unambiguously established for **5b** by X-ray diffraction analysis (Fig. 3).[15]

The vinylsulfonates **1a–c** and **4a** used for this study were available from alcohols **7** and **9** as described,[9] while the vinylsulfonamides **1d**,**e** and **4b** were prepared by treatment of the *N*-benzylamines **8** and **10** derived from **7** and **9**, respectively, with vinylsulfonyl chloride (Scheme 3).[12]

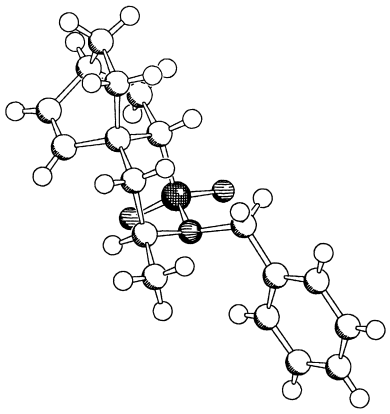
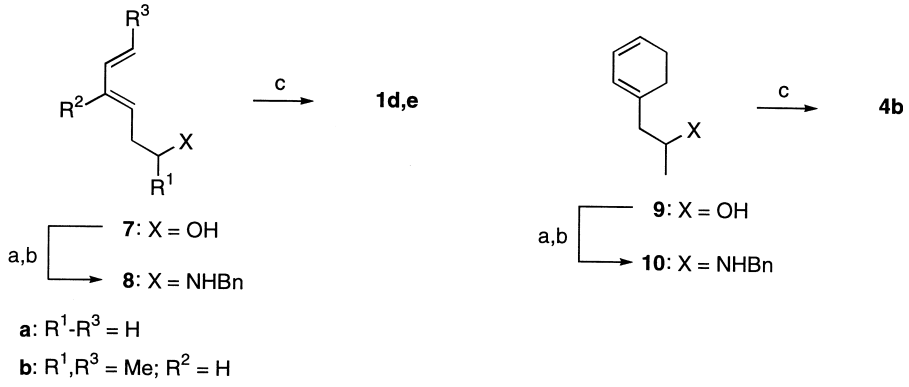


Figure 3. Crystal structure of sultam **5b**.[15,16]

with a Hewlett Packard 5972 detector+a Hewlett Packard 5890 GC (GC/MS) and a Finnigan MAT 95. Microanalyses were performed by the analytical laboratory of the Institut für Organische Chemie, Technische Universität Dresden. High pressure reactions were run in a Hofer apparatus.

(3*E*)-3,5-Hexadien-1-yl methanesulfonate. To a solution of **7a**[17] (980 mg, 10 mmol) in dry THF (60 mL) cooled to 0°C is added dropwise triethylamine (1.11 g, 11 mmol) and freshly distilled mesyl chloride (1.25 g, 11 mmol) under argon. The mixture is stirred for 8 h at 0°C and treated with saturated aqueous NH_4Cl (8 mL). After extraction of the aqueous layer with diethyl ether (3×80 mL), washing of the combined organic layers with 2N HCl (80 mL), saturated aqueous $NaHCO_3$ (80 mL), and water (80 mL), drying over $MgSO_4$, and evaporation of the solvent in vacuo, the mesylate of **7a** (1.74 g, 99%) is obtained. R_f



Scheme 3. (a) MsCl, Et_3N, THF, 0°C, 99% from **7a** or MsCl, 2,6-lutidine, $CHCl_3$, 0°C, 92% from **7b** or MsCl, pyridine, $CHCl_3$, 0°C, 87% from **9**. (b) $BnNH_2$, 80°C, 62% **8a**, 66% **8b**, 75% **10**. (c) CH_2=$CHSO_2Cl$, 2,6-lutidine, CH_2Cl_2, 0°C, 87% **1d** or CH_2=$CHSO_2Cl$, Et_3N, CH_2Cl_2, 0°C, 85% **1e**, 95% **4b**.

Experimental

General experimental information

All reactions requiring exclusion of moisture were run under argon using flame-dried glassware. Solvents were dried by distillation from potassium (THF) or else CaH_2. Flash chromatography was performed on Merck silica gel 60 (40–63 μm). Capillary GC analyses were performed with a Shimadzu GC-14A or GC-14B, a Shimadzu C-R6A integrator, a HP 5 column, 25 m length, 0.25 mm i.d., 0.25 μm film. HPLC separations were performed with a Waters 616 pump, a Waters 2410 detector and a Nucleosil 100-5 (5 μm, 250 mm length, 4 mm i.d.) column (analytical scale), a Waters 600 pump, a Knauer K-2400 detector, and a Nucleosil 100-5 (5 μm, 250 mm length, 10 or 20 mm i.d.) or a Porasil 100-10 (10 μm, 250 mm length, 30 mm i.d.) column (semi-preparative scale), and a Waters Delta Prep 3000, a Knauer K-2400 detector, and a Porasil 125 (15–20 μm, 300 mm length, 50 mm i.d.) column (preparative scale). Melting points were determined on a Kofler microscope desk. ^{1}H NMR and ^{13}C NMR spectra were obtained on a Bruker ASP-300 (^{1}H: 300 MHz, ^{13}C: 75.47 MHz) or a Bruker DRX-500 (^{1}H: 500 MHz, ^{13}C: 125.8 MHz); m_c=multiplet centered at, br=broad. ^{13}C multiplicities were determined using DEPT pulse sequences. FT-IR spectra were obtained on a Nicolet 205; w=weak, s=strong, m=medium, br=broad. Mass spectra (70 eV) were recorded

***N*-Benzyl-*N*-[(3*E*)-3,5-hexadien-1-yl]amine (8a).** A solution of the mesylate of **7a** (1.5 g, 8.5 mmol) in benzylamine (80 mL) freshly distilled from $CaCl_2$ is stirred for 6 h at 80°C. After cooling, the mixture is treated with 2N NaOH (20 mL) and extracted with pentane (5×50 mL). The combined extracts are dried over $MgSO_4$, the solvent is removed in vacuo, and the residue is purified by flash chromatography (pentane/diethyl ether, 1:1,+1% triethylamine) to give **8a** (980 mg, 62%) as a colorless liquid. R_f 0.38 (pentane/diethyl ether, 1:1,+1% triethylamine); IR (neat): 3402 (br, w, N–H), 3027 (m), 3010 (m), 2927 (s), 2871 (s), 2836 (s), 2817 (s), 1650 (w), 1605 (w), 1495 (s), 1120 (m), 1028 (s), 901 (m), 734 (s), 698 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.42 (br s, 1H), 2.32 (m, 2H), 2.72 (t, J=6.9 Hz, 2H), 3.80 (s, 2H), 5.00 (d, J=10.1 Hz, 1H), 5.12 (d, J=16.7 Hz, 1H), 5.69 (dt, J_d=14.6 Hz, J_t=7.1 Hz, 1H), 6.12 (dd, J=14.7 Hz, J=10.2 Hz, 1H), 6.33 (ddd, J=16.7 Hz, J=10.2 Hz, J=10.2 Hz, 1H), 7.26 (m_c, 1H) 7.28–7.36 (m, 4H); ^{13}C NMR ($CDCl_3$): δ 33.0 (t), 48.4 (t), 53.8 (t), 115.4 (t),

0.27 (pentane/diethyl ether, 3:2); IR (neat): 3019 (w), 2868 (w), 1654 (w), 1603 (w), 1355 (s, SO_2OR), 1176 (s, SO_2OR), 1008 (m), 974 (s), 959 (s), 834 (m), 794 (m), 529 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.47 (q, J=6.7 Hz, 2H), 2.93 (s, 3H), 4.19 (t, J=6.7 Hz, 2H), 4.99 (d, J=10.2 Hz, 1H), 5.10 (d, J=16.7 Hz, 1H), 5.58 (dt, J_d=14.7 Hz, J_t=7.0 Hz, 1H), 6.12 (m, 1H), 6.26 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 32.2 (t), 37.3 (q) 68.9 (t), 116.8 (t), 127.7 (d), 134.3 (d), 136.3 (d).

126.8 (d), 128.0 (d), 128.3 (d), 132.3 (d), 132.7 (d), 136.9 (d), 140.3 (s). MS (GC/MS) *m/z* (relative intensity): 120 (35) [$M^+-C_5H_7$], 91 (100) [$C_7H_7^+$], 65 (16), 51 (5), 41 (12), 39 (12); HRMS Calcd for ($C_{13}H_{19}N+H^+$) [$M+H^+$]: 188.149. Found: 189.151.

***N*-Benzyl-*N*-(3*E*)-3,5-hexadien-1-yl vinylsulfonamide (1d).** To a solution of amine **8a** (500 mg, 2.67 mmol) in CH_2Cl_2 (10 mL) cooled to 0°C are added dropwise under argon 2,6-lutidine (0.6 mL, 5.35 mmol) and vinylsulfonyl chloride[18] (0.5 mL, 5.35 mmol). After stirring for 12 h at 0°C, the mixture is diluted with diethyl ether (4 mL) and subjected to flash chromatography (pentane/diethyl ether, 1:1) to give **1d** (644 mg, 87%) as a slightly yellow liquid. R_f 0.8 (pentane/diethyl ether, 1:1); IR (neat): 3063 (m), 3033 (m), 3012 (m), 2929 (m), 1600 (w), 1496 (m), 1455 (m), 1339 (s, SO_2N), 1257 (m), 1149 (s, SO_2N), 1045 (m), 1007 (m), 969 (m), 939 (m), 905 (m), 791 (m), 764 (m), 744 (m), 700 (m), 655 (m), 560 (m), 542 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 2.18 (m_c, 2H), 3.10 (t, J=7.4 Hz, 2H), 4.26 (s, 2H), 4.92 (d, J=10.1 Hz, 1H), 5.02 (d, J=16.7 Hz, 1H), 5.69 (dt, J_d=14.7 Hz, J_t=7.1 Hz, 1H), 5.84 (d, J=9.8 Hz, 1H), 5.88 (dd, J=14.7 Hz, J=10.4 Hz, 1H), 6.15 (d, J=16.5 Hz, 1H), 6.16 (ddd, J=16.7 Hz, J=10.3 Hz, J=10.3 Hz, 1H), 6.36 (dd, J=16.5 Hz, J=9.8 Hz, 1H), 7.29 (m_c, 5H); ^{13}C NMR ($CDCl_3$): δ 31.6 (t), 46.7 (t), 51.2 (t), 116.1 (t), 126.4 (t), 127.9 (d), 128.3 (d), 128.6 (d), 130.2 (d), 133.3 (d), 135.3 (d), 136.0 (s), 136.6 (d).

(4*E*,6*E*)-4,6-Octadien-2-yl methanesulfonate. To a solution of **7b**[19] (2.85 g, 22.3 mmol) in dry $CHCl_3$ (40 mL) cooled to 0°C is added dropwise 2,6-lutidine (3.58 g, 33.5 mmol) and freshly distilled mesyl chloride (3.05 g, 26.8 mmol) under argon. The mixture is stirred overnight at 0°C and diluted with diethyl ether (25 mL). After washing with 2N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (20 mL), drying over $MgSO_4$, and evaporation of the solvent in vacuo at 0°C, the mesylate of **7b** (4.22 g, 92%) is obtained as a colorless oil. R_f 0.32 (cyclohexane/ethyl acetate, 3:1); IR (neat): 3654 (w), 2987 (s), 2929 (s), 2262 (m), 1598 (s), 1445 (s), 1354 (s, SO_2OR), 1176 (s, SO_2OR), 1096 (s), 1006 (s), 917 (s), 818 (s), 755 (s), 663 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.39 (d, J=6.2 Hz, 3H), 1.71 (d, J=6.9 Hz, 3H), 2.36–2.46 (m, 2H), 2.94 (s, 3H), 4.77 (m_c, 1H), 5.39–5.51 (m, 1H), 5.57–5.69 (m, 1H), 5.96–6.13 (m, 2H); ^{13}C NMR ($CDCl_3$): δ 18.0 (q), 20.8 (q), 38.6 (q), 39.7 (t), 79.5 (d), 124.3 (d), 129.0 (d), 130.9 (d), 134.5 (d). MS (GC/MS) *m/z* (relative intensity): 204 (1) [M^+], 134 (24) [$M^+-C_6H_9$], 108 (80) [$M-CH_3SO_3H$], 93 (100), 81 (71) [$C_6H_9^+$], 79 (77), 77 (19), 67 (20), 53 (19), 43 (20).

***N*-Benzyl-*N*-[(4*E*,6*E*)-4,6-octadien-2-yl]amine (8b).** A solution of the mesylate of **7b** (4.22 g, 20.5 mmol) in benzylamine (200 mL) freshly distilled from $CaCl_2$ is stirred for 12 h at 40°C and 2 h at 80°C. After cooling, the mixture is treated with 2N NaOH (40 mL) and extracted with pentane (5×100 mL). The combined extracts are dried over $MgSO_4$, the solvent is removed in vacuo, and the residue is purified by flash chromatography (cyclohexane/ethyl acetate, 3:1,+1% triethylamine) to give **8b** (2.94 g, 66%). R_f 0.39 (cyclohexane/ethyl acetate, 3:1,+1% triethylamine); IR (neat): 3398 (br, w, N–H), 3062 und 3026 (m), 2961 (m), 2872 (w), 1703 (m), 1644 (s), 1495 (m), 1452 (s), 1377 (m), 990 (s), 752 (s), 695 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.08 (d, J=6.2 Hz, 3H), 1.71 (d, J=6.2 Hz, 3H), 2.08–2.27 (m, 2H), 2.72 (m_c, 1H), 3.72 (d, J=13.1 Hz, 1H), 3.82 (d, J=13.1 Hz, 1H), 5.41–5.65 (m, 2H), 5.99–6.05 (m, 2H) 7.15–7.42 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 17.9 (q), 20.3 (q), 40.1 (t), 51.3 (d), 52.2 (t), 125.8 (d), 126.8 (d), 128.3 (d), 128.9 (d), 131.1 (d), 132.5 (d), 134.0 (d), 139.5 (s). MS (GC/MS) *m/z* (relative intensity): 215 (1) [M^+], 200 (1) [M^+-CH_3], 134 (100) [$M^+-C_6H_9$], 91 (100) [$C_7H_7^+$], 81 (5) [$C_6H_9^+$], 65 (17); HRMS Calcd for ($C_{15}H_{21}N+H^+$) [$M+H^+$]: 216.175. Found: 216.174.

***N*-Benzyl-*N*-[(4*E*,6*E*)-4,6-octadien-2-yl] vinylsulfonamide (1e).** To a solution of amine **8b** (200 mg, 0.927 mmol) in CH_2Cl_2 (8 mL) cooled to 0°C are added dropwise under argon triethylamine (0.13 mL, 0.93 mmol) and vinylsulfonyl chloride[18] (0.09 mL, 0.93 mmol). The mixture is stirred for 1 h at 0°C, filtered through a pad of silica gel, and diluted with diethyl ether (10 mL). After washing with ice-cold 2N HCl (10 mL), saturated aqueous $NaHCO_3$ (20 mL), and brine (10 mL), the organic layer is dried over $MgSO_4$. Evaporation of the solvent in vacuo at 0°C yields **1e** (242 mg, 85%) as a slightly yellow oil. R_f 0.64 (pentane/diethyl ether, 2:1); IR (neat): 3020 (w), 2977 (m), 2935 (m), 2916 (m), 1454 (m), 1338 (s, SO_2N), 1175 (s), 1145 (s, SO_2N), 991 (s), 921 (s), 734 (s), 656 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.11 (d, J=6.9 Hz, 3H), 1.40 (d, J=6.3 Hz, 3H), 2.29 (m, 1H), 2.42 (m, 1H), 3.85 (m, 1H), 4.30 (s, 2H), 5.41–5.71 (m, 2H), 5.85 (d, J=9.7 Hz, 1H), 5.99–6.05 (m, 2H), 6.18 (d, J=16.5 Hz, 1H), 6.40 (dd, J=16.5 Hz, J=9.7 Hz, 1H), 7.21–7.40 (m, 5H).

1-(1,3-Cyclohexadienyl)-propan-2-yl methanesulfonate. To a solution of **9**[9] (1.70 g, 12.3 mmol) in dry $CHCl_3$ (55 mL) cooled to 0°C is added dropwise pyridine (1.94 g, 24.6 mmol) and freshly distilled mesyl chloride (2.80 g, 24.6 mmol) under argon. The mixture is stirred for 2 days at 0°C and diluted with diethyl ether (55 mL). After washing with 2N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and water (20 mL), drying over $MgSO_4$, and evaporation of the solvent in vacuo, flash chromatography (cyclohexane/ethyl acetate, 2:1) gives the mesylate of **9** (2.32 g, 87%) as a colorless liquid. R_f 0.30 (cyclohexane/ethyl acetate, 2:1); IR (neat): 3038 (s), 2983 (w), 2938 (m), 2873 (w), 2827 (m), 1649 (w), 1591 (w), 1497 (w), 1455 (m), 1437 (m), 1426 (m), 1382 (m), 1352 (s, SO_2OR), 1338 (s, SO_2OR), 1241 (m), 1220 (w), 1172 (s, SO_2OR), 1126 (m), 1039 (m), 1009 (m), 972 (s), 925 (s), 899 (s), 796 (m), 751 (m), 695 (s), 528 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.41 (d, J=6.2 Hz, 3H), 2.05–2.22 (m, 6H), 2.30 (dd, J=6.1 Hz, J=14.0 Hz, 1H), 2.50 (dd, J=7.2 Hz, J=14.0 Hz, 1H), 2.90 (s, 3H), 4.88 (m_c, 1H), 5.71 (m, 2H), 5.85 (m_c, 1H, 3-H); ^{13}C NMR ($CDCl_3$): δ 21.2 (q), 22.7 (t), 22.8 (t), 38.6 (q), 44.6 (t), 78.4 (d), 122.7 (d), 124.3 (d), 125.0 (d), 133.4 (s). MS (GC/MS) *m/z* (relative intensity): 216 (3) [M^+], 121 (9), 120 (27) [$M^+-CH_3SO_3H$], 105 (34), 91 (100), 79 (46), 78 (55), 77 (32), 65 (12), 63 (5), 51 (8), 43 (6), 41 (8), 39 (13).

***N*-Benzyl-*N*-[1-(1,3-cyclohexadienyl)-propan-2-yl]amine (10).** A solution of the mesylate of **9** (1.8 g, 8.3 mmol) in benzylamine (15 mL) freshly distilled from $CaCl_2$ is stirred for 12 h at 80°C. After cooling, the mixture is treated with

2N NaOH (15 mL) and extracted with pentane (5×10 mL). The combined extracts are dried over $MgSO_4$, the solvent is removed in vacuo, and the residue is purified by flash chromatography (pentane/ethyl acetate, 1:1,+1% triethylamine) to give **10** (1.41 g, 75%) as a slightly yellow liquid. R_f 0.19 (pentane/diethyl ether, 1:1,+1% triethylamine); IR (neat): 3320 (w, N–H), 3031 (m), 2962 (m), 2926 (s), 2870 (s), 2824 (s), 1650 (w), 1600 (w), 1494 (m), 1465 (s), 1453 (s), 1372 (m), 1345 (m), 1195 (m), 1140 (m), 1117 (m), 1028 (m), 733 (s), 697 (s) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.09 (d, J=6.2 Hz, 3H), 1.77 (br s., 1H), 1.97 (m_c, 2H), 2.10 (m_c, 3H), 2.23 (dd, J=13.7 Hz, J=7.9 Hz, 1H), 2.81 (m_c, 1H), 3.72 (d, J=13.2 Hz, 1H), 3.87 (d, J=13.2 Hz, 1H), 5.68 (m_c, 2H), 5.86 (m_c, 1H), 7.28 (m_c, 5H); ^{13}C NMR ($CDCl_3$): δ 20.5 (q), 22.9 (t), 26.3 (t), 45.6 (t), 49.9 (d), 51.3 (t), 121.4 (d), 124.1 (d), 124.6 (d), 126.8 (d), 128.1 (d), 128.4 (d), 136.8 (s), 140.6 (s). MS (GC/MS) *m/z* (relative intensity): 226 (0.2) [M^+-H], 135 (5), 134 (50) [$M^+-C_7H_9$], 92 (9), 91 (100) [$C_7H_7^+$], 77 (9), 65 (13), 39 (6). Anal. Calcd for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.17. Found C, 84.36; H, 9.23; N, 6.55.

***N*-Benzyl-*N*-[1-(1,3-cyclohexadienyl)-propan-2-yl] vinylsulfonamide (4b).** To a solution of amine **10** (100 mg, 0.44 mmol) in CH_2Cl_2 (3 mL) cooled to 0°C are added dropwise under argon triethylamine (0.07 mL, 0.44 mmol) and vinylsulfonyl chloride[18] (0.05 mL, 0.44 mmol). After stirring for 1 h at 0°C, the mixture is diluted with diethyl ether (3 mL) and subjected to flash chromatography (cyclohexane/diethyl ether, 1:1) to give **4b** (133 mg, 95%) as a colorless oil. R_f 0.22 (cyclohexane/diethyl ether, 1:1); IR (neat): 3031 (m), 2935 (m), 2870 (w), 1650 (w), 1430 (m), 1510 (m), 1358 (s, SO_2N), 1305 (m), 1172 (s, SO_2N), 977 (m), 920 (s), 899 (s), 784 (m), 748 (m), 550 (m) cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.05 (d, J=6.8 Hz, 3H), 1.91 (m_c, 2H), 2.04 (m_c, 3H), 2.27 (dd, J=13.5 Hz, J=5.4 Hz, 1H), 2.81 (m_c, 1H), 4.21 (d, J=16.0 Hz, 1H), 4.28 (d, J=16.0 Hz, 1H), 5.48 (m_c, 1H), 5.58 (m_c, 1H), 5.73 (m_c, 1H), 5.79 (d, J=9.8 Hz, 1H), 6.12 (d, J=16.5 Hz, 1H), 6.35 (dd, J=16.5 Hz, J=9.8 Hz, 1H), 7.18 (m_c, 3H), 7.30 (m_c, 2H).

General procedure for intramolecular Diels–Alder reactions

Thermal: A solution of the vinylsulfonate or the vinylsulfonamide (0.4 mmol) in toluene (15 mL) is added rapidly via canula to a refluxing solution of BHT (5 mg) in toluene (15 mL) under argon. The resultant solution is vigorously stirred for the time indicated.

High pressure: A solution of the vinylsulfonate or the vinylsulfonamide (0.4 mmol) in CH_2Cl_2 (10 mL) is added to a Teflon® vial. The vial is closed, inserted into the high pressure apparatus, and subjected to a pressure of 13 kbar at room temperature for the time indicated.

Workup: The reaction mixture is filtered through a pad of silica gel and concentrated in vacuo at a temperature not exceeding 40°C. Diastereomeric ratios were determined by capillary gas chromatography (FID detection, 300°C detector temperature, 200°C injector temperature, temperature program 10°C min^{-1} from 80 to 300°C) on a sample of the crude products. Flash chromatography using the solvent systems listed in the individual entries with the R_f values yields the pure cycloadducts.

For thermal reactions of vinylsulfonates **1a–c**, **4a** and data of the sultones **2**/**3a–c**, **5a**, see Ref. 9. The reaction times for the high pressure reactions were as follows: **2a**/**3a** from **1a** (24 h), **2b**/**3b** from **1b** (12 h), **2c**/**3c** from **1c** (12 h), **5a**/**6a** from **4a** (12 h).

Sultams 2d/3d from 1d

Thermal reaction: 12 h; high pressure reaction: 24 h. Preparative separation of the diastereomers could not be achieved by chromatography or crystallization. The mixture generated under high pressure was used for assignment of the NMR signals. *Diastereomeric mixture.* R_f 0.55 (pentane/diethyl ether, 1:2); IR (KBr): 3024 (w), 2971 (w), 2944 (m), 2929 (w), 2879 (w), 1651 (w), 1494 (m), 1455 (m), 1331 (s, SO_2N), 1318 (s, SO_2N), 1262 (w), 1148 (s, SO_2N),1138 (s, SO_2N), 922 (w), 863 (m), 728 (m), 709 (m), 698 (m), 608 (w) cm^{-1}. Anal. Calcd for $C_{15}H_{19}NO_2S$: C, 64.95; H, 6.90; N, 5.05. Found C, 64.67; H, 6.97; N, 5.45.

(1*R,2*R**)-*N*-Benzyl-2-ethyl-3-cyclohexene-1,2′-sultam (2d).** ^1H NMR ($CDCl_3$): δ 1.52 (m_c, 2H), 1.84 (m_c, 1H), 2.12–2.24 (m, 2H), 2.38 (m_c, 1H), 2.79 (m_c, 1H), 2.85 (m_c, 1H), 3.02 (ddd, J=13.8 Hz, J=4.2 Hz, J=2.5 Hz, 1H), 3.40 (ddd, J=13.7 Hz, J=13.4 Hz, J=2.7 Hz, 1H), 4.21 (d, J=14.3 Hz, 1H), 4.42 (d, J=14.3 Hz, 1H), 5.42 (m_c, 2H), 7.29 (m_c, 5H); ^{13}C NMR ($CDCl_3$): δ 19.7 (t), 23.9 (t), 29.3 (t), 38.6 (d), 47.2 (t), 50.2 (t), 60.5 (d), 127.2 (d), 127.8 (d), 128.3 (d), 128.4 (d), 128.6 (d), 136.1 (s). MS (GC/MS) *m/z* (relative intensity): 278 (0.1) [M^++H], 277 (0.6) [M^+], 213 (7) [M^+-SO_2], 212 (5), 121 (7), 120 (73), 118 (7), 92 (10), 91 (100) [$C_7H_7^+$], 79 (19), 77 (14), 67 (11), 65 (13), 41 (6), 39 (7).

(1*R,2*S**)-*N*-Benzyl-2-ethyl-3-cyclohexene-1,2′-sultam (3d).** ^1H NMR ($CDCl_3$): δ 1.60 (m_c, 2H), 1.94 (m_c, 1H), 2.12–2.24 (m, 2H), 2.28 (m_c, 1H), 2.97 (m_c, 2H), 3.22 (ddd, J=5.1 Hz, J=5.1 Hz, J=2.9 Hz, 1H), 3.28–3.38 (m, 1H), 4.11 (d, J=14.4 Hz, 1H), 4.48 (d, J=14.4 Hz, 1H), 5.70 (m_c, 2H), 7.29 (m_c, 5H); ^{13}C NMR ($CDCl_3$): δ 18.7 (t), 24.6 (t), 25.8 (t), 35.0 (d), 46.8 (t), 49.8 (t), 58.0 (d), 127.0 (d), 127.7 (d), 127.9 (d), 128.3 (d), 128.9 (d), 136.4 (s). MS (GC/MS) *m/z* (relative intensity): 277 (2.4) [M^+], 213 (4) [M^+-SO_2], 212 (8), 186 (5), 132 (5), 122 (6), 120 (6), 118 (9), 107 (5), 106 (6), 105 (13), 92 (12), 91 (100) [$C_7H_7^+$], 79 (22), 78 (6), 77 (15), 67 (5), 65 (13), 51 (5), 41 (6), 39 (7).

Sultams 2e/3e from 1e

Thermal reaction: 12 h; high pressure reaction: 12 h. Preparative separation of the diastereomers could not be achieved by chromatography. However, fractional crystallization yielded a sample highly enriched in **2e** that allowed assignment of the NMR signals. *Diastereomeric mixture.* R_f 0.37 (pentane/diethyl ether, 2:1); IR (KBr): 3023 (w), 2959 (m), 2873 (w), 1496 (m), 1456 (m), 1331 (s, SO_2N), 1313 (s, SO_2N), 1146 (s, SO_2N), 922 (w), 843 (w), 735 (m) cm^{-1}.

(1*R,2*R**,5*R**,2′*R**)-*N*-Benzyl-5-methyl-2-propyl-cyclohex-3-ene-1,2′-sultam (2e).** ^{1}H NMR ($CDCl_3$): δ 1.07 (d, J=7.2 Hz, 3H), 1.08 (d, J=7.0 Hz, 3H), 1.40 (m_c, 1H), 1.64 (ddd, J=13.7 Hz, J=2.5 Hz, J=2.5 Hz, 1H), 1.99 (m_c, 1H), 2.09 (m_c, 1H), 2.53 (m_c, 1H), 2.70 (m_c, 1H), 2.75 (m_c, 1H), 4.07 (ddq, J_d=12.3 Hz, J_q=7.0 Hz, J_d=2.5 Hz, 1H), 4.24 (d, J=16.4 Hz, 1H), 4.51 (d, J=16.4 Hz, 1H), 5.38 (m_c, 1H), 5.63 (m_c, 1H), 7.23–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 20.1 (q), 21.4 (q), 26.5 (t), 29.2 (d), 36.5 (t), 38.1 (d), 46.9 (t), 55.3 (d), 55.4 (d), 127.0 (d), 127.2 (d), 127.3 (d), 128.2 (d), 133.1 (d), 139.4 (s).

(1*R,2*S**,5*S**,2′*R**)-*N*-Benzyl-5-methyl-2-propyl-cyclohex-3-ene-1,2′-sultam (3e).** ^{1}H NMR ($CDCl_3$): δ 1.08 (d, J=6.7 Hz, 3H), 1.34 (d, J=7.1 Hz, 3H), 1.40 (m_c, 1H), 1.48 (ddd, J=15.8 Hz, J=3.1 Hz, J=3.1 Hz, 1H), 1.72 (ddd, J=15.8 Hz, J=6.9 Hz, J=6.9 Hz, 1H), 2.30 (m_c, 2H), 3.19 (m_c, 1H), 3.22 (ddd, J=6.3 Hz, J=2.7 Hz, J=2.7 Hz, 1H), 3.38 (ddq, J_q=7.1 Hz, J_d=6.9 Hz, J_d=3.1 Hz, 1H), 4.14 (d, J=14.9 Hz, 1H), 4.51 (d, J=14.9 Hz, 1H), 5.56 (m_c, 1H), 5.60 (dd, J=10.2 Hz, J=5.0 Hz, 1H), 7.23–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 16.4 (q), 21.3 (q), 26.4 (t), 30.3 (d), 31.1 (d), 31.5 (t), 48.8 (t), 52.8 (d), 57.8 (d), 127.1 (d), 127.2 (d), 127.6 (d), 128.0 (d), 133.8 (d), 137.0 (s).

Sultams 5b/6b from 4b

Thermal reaction: 3 h; high pressure reaction: 12 h. By HPLC (analytical scale) a sample highly enriched in **6b** could be secured from the product mixture of the thermal reaction.

(1*R,2*S**,4*S**,2′*S**)-*N*-Benzyl-1-propylbicyclo[2.2.2]oct-5-ene-2,2′-sultam (5b).** Mp 124°C; R_f 0.23 (pentane/diethyl ether, 1:1); IR (neat): 3052 (m), 2983 (m), 2947 (s), 2935 (s); 2914 (m), 2870 (m), 1650 (w), 1450 (m), 1440 (w), 1382 (m), 1354 (s, SO_2N), 1338 (s), 1326 (s), 1296 (m), 1197 (m), 1172 (s, SO_2N), 1139 (m), 1099 (m), 1051 (m), 943 (m), 915 (m), 899 (s), 891 (s), 871 (s), 801 (s), 736 (m), 711 (m), 593 (s), 573 (m), 549 (m), 466 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.10 (d, J=6.9 Hz, 3H), 1.25 (m_c, 1H), 1.35 (m_c, 1H), 1.42 (m_c, 1H), 1.48–1.65 (m, 3H), 1.79 (ddd, J=10.3 Hz, J=5.8 Hz, J=2.9 Hz, 1H), 2.05 (ddd, J=10.3 Hz, J=9.8 Hz, J=2.9 Hz, 1H), 2.72 (m_c, 1H), 2.97 (dd, J=9.7 Hz, J=5.9 Hz, 1H), 4.17 (d, J=16.4 Hz, 1H), 4.26 (ddq, J_d=11.7 Hz, J_q=6.9 Hz, J_d=2.5 Hz, 1H), 4.53 (d, J=16.3 Hz, 1H), 6.07 (d, J=8.0 Hz, 1H), 6.40 (dd, J=8.0 Hz, J=8.0 Hz, 1H), 7.23–7.39 (m, 5H); ^{13}C NMR ($CDCl_3$): δ 20.2 (q), 24.3 (t), 27.9 (d), 29.4 (d), 34.6 (t), 38.5 (s) 38.6 (t), 46.4 (t), 52.4 (d), 57.8 (d), 127.0 (d), 127.2 (d), 128.4 (d), 132.9 (d), 134.0 (d), 139.5 (s). MS (GC/MS) m/z (relative intensity): 317 (0.2) [M^+], 132 (5), 105 (5), 104 (3), 103 (4), 93 (12), 92 (88), 91 (100) [$C_7H_7^+$], 79 (6), 78 (6), 77 (13), 65 (15), 51 (4). Anal. Calcd for $C_{18}H_{23}NO_2S$: C, 68.10; H, 7.30; N, 4.41. Found C, 67.99; H, 7.63; N, 4.37.

(1*S,2*R**,4*R**,2′*S**)-*N*-Benzyl-1-propylbicyclo[2.2.2]oct-5-ene-2,2′-sultam (6b).** R_f 0.21 (pentane/diethyl ether, 1:1); IR (neat): 3048 (m), 2981 (m), 2945 (s), 2927 (s), 2919 (m), 2878 (m), 1651 (w), 1378 (m), 1350 (s, SO_2N), 1341 (s), 1331 (s), 1292 (m), 1194 (m), 1168 (s, SO_2N), 1142 (m), 1102 (m), 1048 (m), 941 (m), 912 (m), 902 (s), 890 (s), 868 (s), 799 (s), 590 (s), 568 (m), 542 (m), 448 (m) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.24 (m_c, 1H), 1.35 (m_c, 1H), 1.42 (m_c, 2H), 1.49 (d, J=7.5 Hz, 3H), 1.78 (m_c, 2H), 1.79 (ddd, J=13.1 Hz, J=5.8 Hz, J=2.7 Hz, 1H), 2.05 (ddd, J=13.1 Hz, J=10.0 Hz, J=3.1 Hz, 1H), 2.72 (m_c, 1H), 3.14 (dd, J=10.0 Hz, J=5.8 Hz, 1H), 3.51 (ddq, J_d=8.4 Hz, J_q=7.5 Hz, J_d=2.7 Hz, 1H), 4.13 (d, J=14.8 Hz, 1H), 4.66 (d, J=14.8 Hz, 1H), 6.22 (d, J=8.4 Hz, 1H), 6.35 (dd, J=8.3 Hz, J=8.3 Hz, 1H), 7.23–7.39 (m, 5H).

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R=0.048 and wR^2=0.104, largest difference peak and hole 0.30 and −0.39 e Å^{-3}. The data set was collected with a Nonius KappaCCD diffractometer using a rotating anode generator FR591. Programs used: data collection Collect (Nonius, B. V., 1994), data reduction Denzo-SMN (Otwinowski, Z., Minor, W. *Methods in Enzymology* **1997**, *276*, 307–326), absorption correction SORTAV (Blessing, R. H. *Acta Cryst.* **1995**, *A51*, 33–37; Blessing, R. H. *J. Appl. Cryst.* **1997**, *30*, 421–426), structure solution SHELXS-97 (Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467–473), structure refinement SHELXL-97 (Sheldrick, G. M., Universität Göttingen, 1997). Crystallographic data of **5b** were deposited with the Cambridge Crystallographic Data Centre.

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