Intramolecular Diels–Alder Reaction of New Building Blocks, *N*-Substituted 3,5-Dihydro-1*H*-thieno[3,4-*c*]-pyrrole *S,S*-Dioxides; a General Route to the Tricyclic Azanorbornane Framework

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In spite of the absence of activating groups for dienophiles, *N*-substituted 3,5-dihydro-1*H*-thieno[3,4-*c*]pyrrole *S,S*-dioxides **1** which contain terminal olefin substituents, undergo facile intramolecular Diels–Alder reaction and subsequent spontaneous desulfonylation to give the corresponding tricyclic azanorbornane framework **2** in good yields.

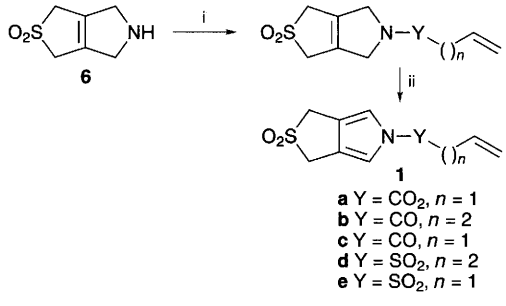
Recently, we reported the preparation of a new building block, 3,5-dihydro-1*H*-thieno[3,4-*c*]pyrrole *S,S*-dioxides (pyrrolesulfolenes) and their intermolecular Diels–Alder reactions.[1] In continuing our studies on the demonstration of the utility of pyrrolesulfolenes for organic synthesis we describe here that pyrrolesulfolenes **1** substituted on the nitrogens with non-activated terminal olefins smoothly undergo intramolecular Diels–Alder cycloaddition and subsequent spontaneous desulfonylation to give the corresponding tricyclic azanorbornanes **2** under both thermal and high-pressure conditions.

N-allyloxycarbonylpyrrolesulfolene **1a** (Y = CO_2, *n* = 1) was prepared from the readily available 3,4,5,6-tetrahydro-1*H*-thieno[3,4-*c*]pyrrole *S,S*-dioxide **6**[1a] by reaction with allyl chloroformate and subsequent oxidation with MnO_2.† Compounds **1b–e** were prepared similarly (Scheme 1).‡

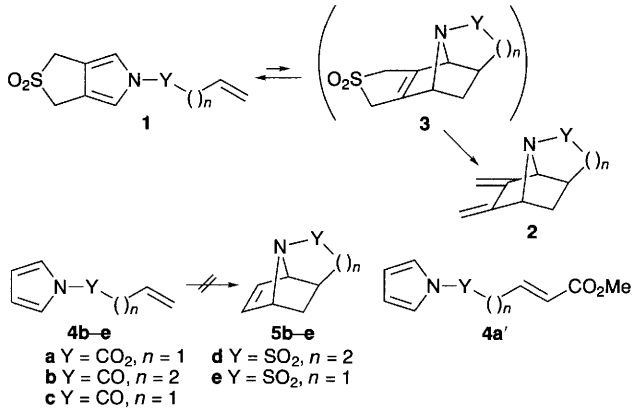
When a dilute benzene solution of **1a** (0.05 mol dm^{-3}) was heated at 150 °C for 24 h in a sealed tube, it underwent an intramolecular Diels–Alder reaction to afford a tricyclic carbamate **2a** (Y = CO_2, *n* = 1) in 46% isolated yield (Scheme 2, Table 1). The formation and isolation of the intramolecular Diels–Alder adduct **2a** is surprising in view of the absence of an activating group for the dienophile in **2a**. This result also contrasts with the failure of an activated dienophile carrier, the *N*-allyloxycarbonylpyrrole derivative **4a′**, to undergo an intramolecular Diels–Alder reaction.[2] Under the same conditions, *N*-(pent-4-enoyl)pyrrolesulfolene **1b** (Y = CO, *n* = 2) and the but-4-enoyl derivative **1c** (Y = CO, *n* = 1) gave the corresponding tricyclic six- [**2b** (Y = CO, *n* = 2)], and five-membered amide [**2c** (Y = CO, *n* = 1)], respectively. Furthermore, the same treatment of *N*-sulfonylpyrrolesulfolenes **1d** (Y = SO_2, *n* = 2) and **1e** (Y = SO_2, *n* = 1) afforded tricyclic sulfonamides **2d** (Y = SO_2, *n* = 2) and **2e** (Y = SO_2, *n* = 1) respectively. The structures of all the new compounds thus obtained were confirmed by ^1H NMR, IR and MS spectral data.§ In order to confirm the role of the sulfolene moiety in the intramolecular Diels–Alder reaction of *N*-substituted pyrrolesulfolene, we examined the reactions of the corresponding simple pyrroles **4b–e** under the same conditions (150 °C, 24 h, 0.05 mol dm^{-3} benzene solution, sealed tube) and found that **4b–e** did not give any Diels–Alder adducts (Table 1).

As for the direct construction of 7-azanorbornene frameworks from pyrrole derivatives and ethylenic dienophiles *via* Diels–Alder reaction, the thermal liability of the cycloadducts to undergo the retro reaction is the main factor limiting their availability.[3] As use of high pressure usually causes a large increase in the rate of cycloadduct formation, thereby permitting the use of lower temperature, we investigated the high-pressure reactions of the pyrrolesulfolenes **1a–e** and simple pyrroles **4b–e**. While the reaction of **1b** at 28 °C at 4 kbar for 72 h in CH_2Cl_2 (0.05 mol dm^{-3} solution) gave no cycloadduct but simply recovery of **1b** (91%), at 8 kbar, the cycloadduct **2b** was isolated in 16% yield accompanied with the recovery of **1b** (68%). Finally at 12 kbar for 72 h, a yield enhancement was observed (69%). While simple pyrroles **4** did not undergo intramolecular Diels–Alder reaction (to give **5**) even under 12 kbar, the same treatment of a series of pyrrolesulfolenes **1** also in no case produced isolable **3** (which can be regarded as analogous to **5**) but rather the desulfonylated product **2** (Table 1). These results suggest that the desulfonylation of **3** is the key step for the successful intramolecular Diels–Alder reaction of **1**. Due to the ready desulfonylation of **3** caused by the repulsion between the nitrogen lone-pair and π-orbital of the endocyclic olefin,[3c] conversion of the pyrrolesulfolene **1** to the cycloadducts **3** should be irreversible, in contast with the pyrrole **4** ⇌ cycloadduct **5** process (Scheme 2).

In conclusion, the sulfolene moiety of **1** serves not only as a *s-cis*-diene synthon in the syntheses of polycyclic polyfunctional aza compounds,[1] but also plays an important role in



Scheme 1 *Reagents and conditions*: For **1a**; i, allyl chloroformate, pyridine, 0 °C for 30 min. then room temp. (r.t.) for 3 h, yield 51%; ii, MnO_2, CH_2Cl_2, r.t. for 39 h, yield 43%. For **1b**; i, pent-4-enoyl chloride, triethylamine, CH_2Cl_2, −78 °C then r.t. for 4 h, yield 72%; ii, as for **1a**, yield 48%. For **1c**; i, but-3-enoyl chloride, triethylamine, CH_2Cl_2, −78 °C then r.t. for 4 h, yield 51%; ii, as for **1a**, yield 43%. For **1d**; but-3-enylsulfonyl chloride, pyridine, r.t. for 3.5 h, yield 45%; ii, as for **1a**, yield 48%. For **1e**; i, allylsufonyl chloride, pyridine, r.t. for 3.5 h, yield 42%, ii, as for **1a**, yield 40%.



Scheme 2

Table 1 Intramolecular Diels–Alder reactions of pyrrolesulfolenes **1**

	Reaction Conditions				Yield (%)	
Pyrrolesulfolene	*T*/°C	Pressure	*t*/h	Product	Product	Recovery of **1** (**4**)
1a (Y = CO_2, *n* = 1)	150	Sealed tube[a]	24	**2a** (Y = CO_2, *n* = 1)	46	0
	28	12 kbar[b]	72	**2a**	66	0
1b (Y = CO, *n* = 2)	150	Sealed tube	24	**2b** (Y = CO, *n* = 2)	45	0
	28	4 kbar	72	None	0	91
	28	8 kbar	72	**2b**	16	68
	28	12 kbar	72	**2b**	69	0
4b (Y = CO, *n* = 2)	150	Sealed tube	24	None	0	87
	28	12 kbar	72	None	0	91
1c (Y = CO, *n* = 1)	150	Sealed tube	24	**2c** (Y = CO, *n* = 1)	48	0
	28	12 kbar	72	**2c**	54	0
4c (Y = CO, *n* = 1)	150	Sealed tube	24	None	0	88
	28	12 kbar	72	None	0	92
1d (Y = SO_2, *n* = 2)	150	Sealed tube	24	**2d** (Y = SO_2, *n* = 2)	49	0
	28	12 kbar	72	**2d**	54	0
4d (Y = SO_2, *n* = 2)	150	Sealed tube	24	None	0	85
	28	12 kbar	72	None	0	93
1e (Y = SO_2, *n* = 1)	150	Sealed tube	24	**2e** (Y = SO_2, *n* = 1)	43	0
	28	12 kbar	72	**2e**	52	0
4e (Y = SO_2, *n* = 1)	150	Sealed tube	24	None	0	86
	28	12 kbar	72	None	0	93

[a] Reactions in benzene. [b] Reactions in CH_2Cl_2

promoting the intramolecular Diels–Alder reaction of the pyrrole part of **1** to give 2-azatricyclo[4.4.$0^{2,8}$]decane and 2-azatricyclo[4.3.$0^{2,7}$]nonane derivatives.

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Footnotes

† A mixture of *N*-substituted 3,4,5,6-tetrahydro-1*H*-thieno[3,4-*c*]pyrrole *S,S*-dioxide and 20 equiv. of MnO_2 in CH_2Cl_2 was stirred at room temp. for 3 h. A further portion of MnO_2 (20 mol equiv.) was added and stirring continued for an additional 36 h.

‡ *Spectral data.* **1a**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 7.35 (2H, t, *J* = 1.0 Hz), 6.02 (1H, ddt, *J* = 16.5, 11.0, 6.3 Hz), 5.28 (1H, dd, *J* = 16.5, 1.8 Hz), 5.18 (1H, dd, *J* = 11.0, 1.8 Hz), 4.78 (2H, m), 4.24 (4H, d, *J* = 1.0 Hz); MS *m/z* 241 (M^+), 177 ($M^+ - SO_2$); IR ($CHCl_3$) 1737, 1382, 1115 cm^{-1}. **1b**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 7.38 (2H, t, *J* = 1.0 Hz), 5.84 (1H, ddt, *J* = 17.0, 10.5, 7.0 Hz), 5.08 (1H, dd, *J* = 17.0, 1.5 Hz), 5.01 (1H, dd, *J* = 10.5, 1.5 Hz), 4.20 (4H, d, *J* = 1.0 Hz), 2.35 (2H, m), 2.15 (2H, t, *J* = 8.0 Hz); MS *m/z* 239 (M^+), 175 ($M^+ - SO_2$), 156; IR ($CHCl_3$) 3122, 1690, 1325, 1125 cm^{-1}. **1c**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 7.39 (2H, t, *J* = 1.2 Hz), 5.92 (1H, ddt, *J* = 16.0, 10.5, 7.0 Hz), 5.15 (1H, dd, *J* = 16.0, 1.7 Hz), 5.03 (1H, dd, *J* = 10.5, 1.7 Hz), 4.23 (4H, d, *J* = 1.2 Hz), 3.26 (2H, d, *J* = 7.0 Hz); MS *m/z* 225 (M^+), 161 ($M^+ - SO_2$), 156 ($M^+ - SO_2$); IR ($CHCl_3$) 3120, 1688, 1327, 1119 cm^{-1}. **1d**: ^{1}H NMR (90 MHz, $CDCl_3$ $SiMe_4$) δ 7.20 (2H, t, *J* = 0.5 Hz), 5.85 (1H, ddt, *J* = 16.0, 10.7, 7.0 Hz), 5.12 (1H, dd, *J* = 16.0, 2.0 Hz), 5.01 (1H, dd, *J* = 10.7, 2.0 Hz), 4.13 (4H, d, *J* = 0.5 Hz), 3.28 (2H, t, *J* = 7.0 Hz), 2.56 (2H, m); MS *m/z* 275 (M^+), 211 ($M^+ - SO_2$); IR ($CHCl_3$) 1370, 1327, 1190, 1113 cm^{-1}. **1e**: ^{1}H NMR (90 MHz, CDCl, $SiMe_4$) δ 7.18 (2H, t, *J* = 0.7 Hz), 6.02 (1H, ddt, *J* = 16.5, 10.7, 7.0 Hz), 5.10 (1H, dd, *J* = 16.5, 1.5 Hz), 5.02 (1H, dd, *J* = 10.7, 1.5 Hz), 4.18 (4H, d, *J* = 0.7 Hz), 3.82 (2H, d, *J* = 7.0 Hz); MS *m/z* 261 (M^+), 197 ($M^+ - SO_2$); IR ($CHCl_3$) 1382, 1325, 1185, 1114 cm^{-1}.

§ 9,10-*Bis(methylene)*-4-*oxa*-2-*azatricyclo*[4.4.$0^{2,8}$]*decan*-3-*one* **2a**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 5.51 (1H, s), 5.32 (1H, s), 5.22 (1H, s), 5.04 (1H, s), 4.80 (2H, m), 4.30 (1H, t, *J* = 4.0 Hz), 4.14 (1H, s), 3.08–2.65 (3H, m); MS *m/z* 177 (M^+), 119; IR ($CHCl_3$) 1735 cm^{-1}. 9,10-*Bis(methylene)*-2-*azatricyclo*[4.4.$0^{2,8}$]*decan*-3-*one* **2b**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 5.40 (1H, s), 5.34 (1H, s), 5.26 (1H, s), 5.05 (1H, s), 4.20 (1H, t, *J* = 4.0 Hz), 4.11 (1H, s), 2.80–2.35 (3H, m), 2.20 (2H, m), 1.60–1.40 (2H, m); MS *m/z* 175 (M^+), 119; IR ($CHCl_3$) 1702 cm^{-1}. 8,9-*Bis(methylene)*-4-*oxa*-2-*azatricyclo*[4.3.$0^{2,7}$]*nonan*-3-*one* **2c**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 5.41 (1H, s), 5.35 (1H, s), 5.20 (1H, s), 5.08 (1H, s), 4.23 (1H, t, *J* = 4.0 Hz), 4.10 (1H, s), 3.10–2.75 (3H, m), 2.20 (2H, m); MS *m/z* 161 (M^+), 119; IR ($CHCl_3$) 1720 cm^{-1}. 9,10-*Bis(methylene)*-3-*thia*-2-*azatricyclo*[4.4.$0^{2,8}$]*decane* S,S-*dioxide* **2d**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 5.39 (1H, s), 5.34 (1H, s), 5.18 (1H, s), 5.10 (1H, s), 4.25 (1H, t, *J* = 4.0 Hz), 4.12 (1H, s), 3.20 (2H, m), 2.60–2.35 (3H, m), 1.50–1.10 (2H, m); MS *m/z* 211 (M^+), 119; IR ($CHCl_3$) 1380, 1184 cm^{-1}. 8,9-*Bis(methylene)*-3-*thia*-2-*azatricyclo*[4.3.$0^{2,7}$]*nonane* S,S-*dioxide* **2e**: ^{1}H NMR (90 MHz, $CDCl_3$, $SiMe_4$) δ 5.43 (1H, s), 5.34 (1H, s), 5.24 (1H, s), 5.01 (1H, s), 4.26 (1H, t, *J* = 4.2 Hz), 4.15 (1H, s), 3.80 (2H, m), 3.05–2.50 (3H, m); MS *m/z* 197 (M^+), 119; IR ($CHCl_3$) 1387, 1180 cm^{-1}.

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