New Building Blocks, 3,5-Dihydro-1*H*-thieno[3,4-*c*]pyrrole 2,2-Dioxides; Preparation and their Diels–Alder Reaction with Dimethyl Acetylenedicarboxylate

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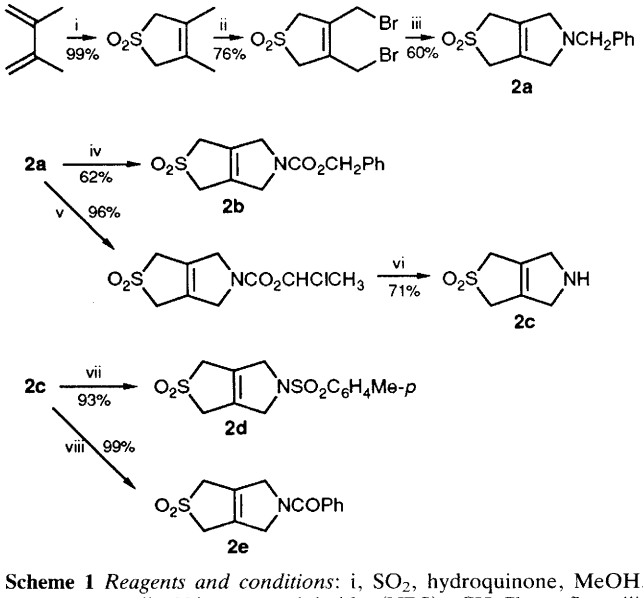
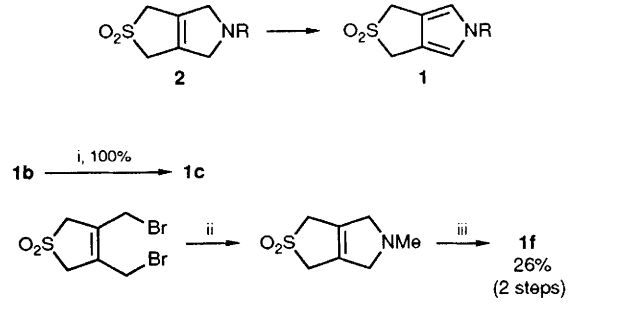
New building blocks, 3,5-dihydro-1*H*-thieno[3,4-*c*]pyrrole 2,2-dioxides **1**, have been prepared and react with dimethyl acetylenedicarboxylate to give new types of compound: 7-aza-2,3-dimethylenenorbornene **A**, the 1 : 2 adduct **B**, 1a,3a,6,9-tetrahydrobenz[*g*]indole **C**, and dihydroindolosulfolene **D** depending on the reaction conditions and the *N*-substituent.

In the course of our studies on the chemistry of 3-sulfolenes (2,5-dihydrothiophene 1,1-dioxides) annulated with five-membered heteroaromatic rings,[1] we have prepared a series of pyrrole-annulated 3-sulfolenes, the 3,5-dihydro-1*H*-thieno[3,4-*c*]pyrrole 2,2-dioxides **1**[2] containing a variety of *N*-substituents. The pyrrole and 3-sulfolene moieties in these molecules can both be readily functionalized and used as the diene component in Diels–Alder reactions. Pyrrole-annulated sulfolenes **1** were expected to undergo Diels–Alder reaction with two different types of dienophile and offer a rapid elaboration of multifunctional multicyclic systems. We now report general methods for preparation of the pyrrole-annulated 3-sulfolenes **1** and their Diels–Alder reactions with dimethyl acetylenedicarboxylate.

Compounds **2** were prepared as shown in Scheme 1. The derivatives **2a** and **2b** were prepared from 3,4-bis(bromomethyl)-2,5-dihydrothiophene 1,1-dioxide, which is easily obtained by brominating the cycloadduct of 2,3-dimethylbuta-1,3-diene and sulfur dioxide, by a modification of the literature method.[4] Cleavage of the benzyloxy carbonyl group



Scheme 1 *Reagents and conditions*: i, SO_2, hydroquinone, MeOH, room temp.; ii, *N*-bromosuccinimide (NBS), CH_2Cl_2, reflux; iii, $PhCH_2NH_2$, MeCN, room temp.; iv, $ClCO_2CH_2Ph$, C_6H_6, room temp.; v, $ClCO_2CHClMe$ in $ClCH_2CH_2Cl$, room temp.; vi, MeOH, 50 °C; vii, *p*-$MeC_6H_4SO_2Cl$; pyridine, room temp.; viii, PhCOCl, K_2CO_3, $CHCl_3$, room temp.



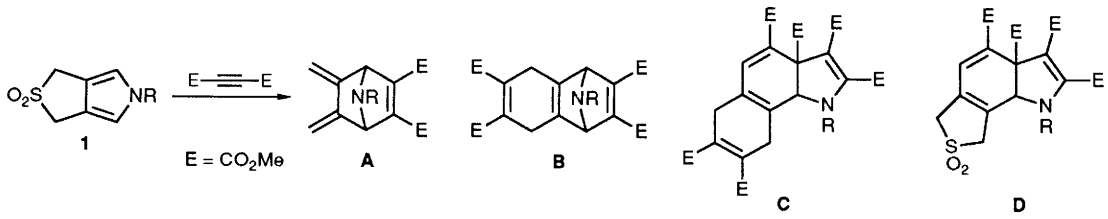
Scheme 2 *Reagents and conditions*: i, H_2, Pd/C, tetrahydrofuran, room temp.; ii, $MeNH_2$, MeCN, room temp.; iii, DDQ, C_6H_6, room temp.

Table 1 Oxidation of pyrrolinesulfolenes **2**

R		Reagent	Conditions[a]	Yield (%) **1**	Yield (%) **2**
CH_2Ph	**2a**	DDQ	Dioxane, 3 h	100	0
H	**2c**	DDQ	C_6H_6, 5 °C, 15 min	40	0
CO_2CH_2Ph	**2b**	CMD[b]	C_6H_6, 4 days	59	31
Ts[c]	**2d**	CMD	CH_2Cl_2, 5 days	50	22
COPh	**2e**	CMD	C_6H_6, 4 days	54	41

[a] Room temp. except for **2c**. [b] 'Chemical MnO_2' (CMD-U). [c] Ts = *p*-$MeC_6H_4SO_2$.

Table 2 Diels–Alder reaction of 3,5-dihydro-1*H*-thieno[3,4-*c*]pyrrole 2,2-dioxides **1** with DMAD

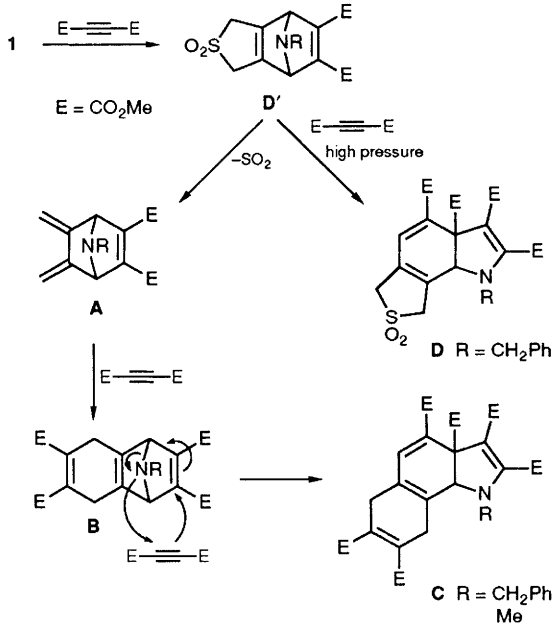


Entry	R		DMAD (equiv.)	Solvent	Temp./ °C	Time/ h	Pressure/ kbar	Yield (%) A	B	C	D	1
1	CH_2Ph	**1a**	3	Benzene	100	4		28	0.1	47		15
2	CH_2Ph	**1a**	4	Benzene	140	16				97		
3	CH_2Ph	**1a**	3	CH_2Cl_2	Room temp.	48	4			62		
4	CH_2Ph	**1a**	3	CH_2Cl_2	Room temp.	48	12				38	
5	Me	**1f**	3	Benzene	150	2				73		
6	CO_2CH_2Ph	**1b**	3	Benzene	150	13			85			
7	CO_2CH_2Ph	**1b**	3	CH_2Cl_2	Room temp.	48	12		52			16
8	Ts	**1d**	3	Benzene	170	14			97			
9	COPh	**1e**	3	Benzene	170	7	7		99			

of **2b** was attempted by the literature procedure[4] (15% HBr in glacial acetic acid), but the best yield was only 17% in our hands (lit.[4] 64%). Olofson *et al.* reported that α-chloroethyl chloroformate was a good reagent for the selective *N*-dealkylation of tertiary amines.[5] When the *N*-benzylpyrroline **2a** was treated with α-chloroethyl chloroformate in $ClCH_2CH_2Cl$ at 0 °C (15 min) and then room temperature (3 h), the chloroethyl carbamate was obtained in 96% yield. This chloroethylcarbamate was warmed to 50 °C in MeOH for 30 min to give **2c** (R = H) in 71% yield. *N*-(*p*-Tolylsulfonyl)- and *N*-benzoyl-pyrrolines **2d** and **2e** were prepared by treating **2c** with the corresponding chlorides in the presence of base in high yields.

Next, we set about oxidation of the pyrrolinesulfolenes **2** to pyrrolesulfolenes **1** (Table 1). The *N*-benzylpyrroline **2a** was converted into the pyrrole **1a** in 100% yield by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dioxane, but the reaction of **2c** (R = H) with DDQ was rather intractable and gave only a 40% yield of **1c** at best. Further, the reactions of **2b, 2d** and **2e**, which have electron-withdrawing substituents on the nitrogen, with DDQ did not give any pyrrolesulfolenes **1**. Oxidation of **2b, 2d** and **2e** was attempted by using NiO_2,[6] $(NH_4)_2Ce(NO_3)_6$[2] and active MnO_2.[7] Only active MnO_2 effected the desired transformation, giving low yields of the pyrrolesulfolenes **1**. Shioiri and Hamada[8] reported that 'chemical manganese dioxide' (CMD) gave much better results on oxidation of thiazolidines to thiazoles than the usually available activated manganese dioxide (Aldrich). CMD is industrially produced for batteries and readily commercially available. When the *N*-benzyloxycarbonylpyrrolinesulfolene **2b** was treated with CMD-U† (30 equiv.) in benzene at room temp. for 4 days, pyrrolesulfolene **1b** was obtained in 59% yield along with the starting material **2b** (31%). Although the reaction does not go to completion, the operation is easy and the starting material can be recycled. Compounds **2d** and **2e** were also oxidized by the same method to give **1d** and **1e**, respectively, in good yields. The *N*-benzyloxycarbonylpyrrole **1b** thus obtained was easily deprotected to give **1c** (R = H) in quantitative yield (Scheme 2). The

† Several CMDs are available from Chuo Denki Kogyo Co., Ltd., 272, Taguchi Myokokogen-machi, Nakabubiki-gun, Nigata Prefecture, Japan. We tried CMD-U, CMD-1 and CMD (IBA sample No. 32). CMD-U gave the best results, and CMD (IBA sample No. 32) was the second choice.



Scheme 3 Reaction mechanism

N-methylpyrrole **1f** was prepared from 2,3-bis(bromomethyl)buta-1,3-diene *via* DDQ oxidation.

The Diels–Alder reactions of the pyrrole-annulated sulfolenes **1** thus obtained with dimethyl acetylenedicarboxylate (DMAD) were studied (Table 2). When a solution of **1a** (R = CH_2Ph) in benzene was heated with DMAD (3 equiv.) at 100 °C in a sealed tube for 4 h, 7-aza-2,3-dimethylenenorbornene **A** (R = CH_2Ph) and 1a,3a,6,9-tetrahydrobenz[*g*]indole **C** (R = CH_2Ph) were obtained in 28 and 47% yields, respectively, along with the 1:2 adduct **B** (R = CH_2Ph, trace) and the starting pyrrole (15%) (entry 1). All attempts to get **A** selectively by decreasing the quantity of DMAD and/or lowering the reaction temperature were unsuccessful. For example, when **1a** was heated with 1.0 equiv. of DMAD at 90 °C, the ratio of **A** to **C** was 1:2.4. Reaction of 4 equiv. of DMAD with **1a** at 140 °C for 16 h gave **C** in 97% yield. Compound **C** was also obtained at 4 kbar. At 12 kbar, the dihydroindolosulfolene **D** was obtained. The reaction of the *N*-methylpyrrole **1f** with DMAD (3 equiv.) gave **C** (R = Me)

in 73% yield. Compounds **1b, 1d** and **1e**, which have electron-withdrawing substituents on the nitrogen, react with DMAD to give only the 1 : 2 adduct **B** in high yields.

These results can be reasonably explained by the mechanism in Scheme 3. The Diels–Alder reaction occurs on the pyrrole moiety to give compounds of type **D′**, which are instantaneously desulfonylated to give compounds **A**. Compounds **A** react with another DMAD molecule to give compounds of type **B**. If the substituent on the nitrogen is electron donating, **B** reacts further with another DMAD molecule to give **C** by a double Michael-type reaction. Under high-pressure conditions, compounds **D′** react with another DMAD molecule without desulfonylation to give **D**. The reaction of compound **A** (R = CH_2Ph) with DMAD (3 equiv., benzene, 100 °C, 5 h) to give **C** in 91% yield (7% recovery) supports this mechanism.

All new compounds described in this paper were characterized by ^1H NMR and mass spectroscopy, and elemental analysis and/or high-resolution mass spectrometry. Efforts to further expand the scope and utility of these reactions of pyrrole-annulated sulfolenes **1** are presently under active investigation.

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