HIGH-PRESSURE INTERMOLECULAR DIELS-ALDER REACTIONS OF THE NOVEL BUILDING BLOCK; *4H,6H*-THIENO[3,4-*c*]FURAN 5,5-DIOXIDE

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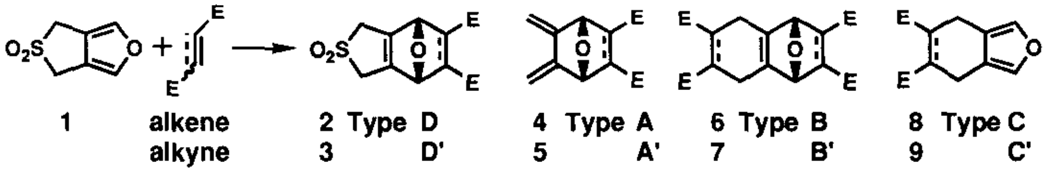
Abstract- At high pressure, the furansulfolene, 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (**1**), whose furan and 3-sulfolene moieties could be used as diene components in Diels-Alder reactions, reacted with the dienophiles at its furan moiety selectively.

The establishment of polycyclic systems from readily available precursors with a minimum number of steps and regio- and stereochemical control remains a synthetic challenge. One of the most important ring-forming reactions currently use for this purpose is cycloaddition. Tandem cycloaddition is an effective strategy for the rapid assembly of a wide variety of ring systems. To set up the reagents for this sequence, we constructed furan-fused sulfolene, 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (**1**) with careful attention directed to its chemistry. Under thermal conditions, its versatility was found to be bis-diene in the Diels-Alder reaction.[1] Scheme 1 illustrates schematically possible for Diels-Alder reactions of **1**. This paper reports the Diels-Alder reactions of **1** conducted at 4- 12 Kbar with the aim of selective Diels-Alder reaction at the furan moiety of **1**.

Scheme 1



For the Diels-Alder reaction of furansulfolene (**1**) with dimethyl maleate under atmospheric pressure, 3 equivalent mol of the dienophile and high temperature were necessary to obtain satisfactory yields of Diels-Alder adduct (**4a**) as approximately 85:15 ratios of *endo*/*exo* isomers (Table 1, Entries 1-4). Further addition of the dienophile (the type B adduct formation) was slower than that of the initial equivalent (the type D formation), but could not be avoided; at 120° C, the type B adduct (**6a**) was formed together with **4a** (Entry 2), and at 150° C, the type C compound (**8a**), the retro Diels-Alder product of **6a** was obtained (Entry 4). Under high pressure (12 Kbar), **1** reacted with dimethyl maleate (3 equiv. mol) in CH_2Cl_2 at 28 °C for 48 h to afford a type D (10-oxa-4-thiatricyclo[5.2.1.$0^{2,6}$]dec-2(6)-ene 4,4-dioxide) adduct (**2a**) in 81% yield (Entry 5). At 4 Kbar, the adduct (**2a**) was obtained in a lower yield (Entry 6). The ^{1}H nmr spectrum showed **2a** to be a single stereoisomer, *cis-endo*.[2] For the reaction of **1** with dimethyl maleate, the use of high pressure (12 Kbar) in

Table 1. Diels-Alder Reactions of Furansulfolene (1) with Alkenes

Entry No	Dienophile (equiv.)	Reaction Conditions	Products(Yield, %)[a]				Total Yield
			Type D	Type A	Type B	Type C	
1	Dimethyl maleate (3 equiv.)	atmosphere, 28°C 48 h, CH_2Cl_2		no reaction			0 (94)[b]
2	Dimethyl maleate (3 equiv.)	sealed tube, 120°C 12 h, benzene		**4a** 61	**6a** 29		90
3	Dimethyl maleate (1 equiv.)	sealed tube, 120°C 12 h, benzene		**4a** 72			72 (24)[b]
4	Dimethyl maleate (3 equiv.)	sealed tube, 150°C 3 h, benzene		**4a** 63		**8a** 10	73
5	Dimethyl maleate (3 equiv.)	12 Kbar, 28°C 48 h, CH_2Cl_2	**2a** 81				81
6	Dimethyl maleate (3 equiv.)	4 Kbar, 28°C 48 h, CH_2Cl_2	**2a** 19				19 (75)[b]
7	Methyl *cis*-3-benzenesulfinylpropenoate (3 equiv.)	sealed tube, 90°C 20 h, Benzene		**4b** 82			82 (8)[b]
8	Methyl *cis*-3-benzenesulfinylpropenoate (3 equiv.)	12 Kbar, 28°C 48 h, CH_2Cl_2	**2b** 79	**4b** 5			84
9	Methyl *cis*-3-benzenesulfonylpropenoate (3 equiv.)	sealed tube, 120°C 20 h, benzene		**4c** 50			50
10	Methyl *cis*-3-benzenesulfonylpropenoate (3 equiv.)	12 Kbar, 28°C 48 h, CH_2Cl_2	**2c** 80	**4c** 7			87
11	Dimethyl fumarate (3 equiv.)	atmosphere, 28°C 48 h, CH_2Cl_2		no reaction			0 (96)[b]
12	Dimethyl fumarate (3 equiv.)	sealed tube, 150°C 2 h, benzene		**4a** 78	**6a** 11		89
13	Dimethyl fumarate (1 equiv.)	sealed tube, 150°C 2 h, benzene		**4a** 21			21 (72)[b]
14	Dimethyl fumarate (3 equiv.)	12 Kbar, 28°C 48 h, CH_2Cl_2	**2a** 41	**4a** 37			78 (12)[b]
15	*trans*-1,2-Bis(phenylsulfonyl)ethylene (3 equiv.)	12 Kbar, 28°C 48 h, CH_2Cl_2	**2d** 37	**4d** 35			72

a) Isolated yield. b) Recovery of **1**.

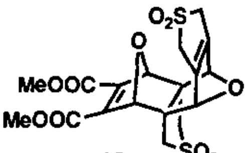
contrast to normal thermal conditions permitted the reaction to proceed at room temperature and stereoselectively. The isolated *endo*-**2a** with dimethyl maleate (1 equiv.) was kept at 12 Kbar and 28°C for 24 h, and no isomerization was observed by ^{1}H nmr measurement. This result is in accordance with the restricted retro Diels-Alder reaction under high pressure conditions.[3] Therefore, endo selectivity would be the result of kinetic control, and is probably due to large secondary orbital interactions.[4] At 12 Kbar pressure and 28° C, essentially the same reactions were observed when *cis*-acrylic ester derivatives such as methyl *cis*-3-benzenesulfinylpropenoate and methyl *cis*-3-benzenesulfonylpropenoate were used as dienophiles and the stereochemical integrity of the dienophiles was maintained in the cycloadducts: only the *cis-endo* isomer of **2** were produced. For the reaction of **1** and *trans*-alkenes, it was found that the cycloaddition at the furan moiety of **1** proceeded well at room temperature to give *trans*-**2** together with *trans*-**4** (Entries 14 and 15). At room temperature, these *trans* type D adducts underwent extrusion of SO_2 to give the corresponding type A adducts , while *cis-endo* adducts (**2**) were stable and the desulfonylation of them needed heating, for example, *cis-endo*-**2a** underwent desulfonylation to afford *cis-endo* **4a** at 120°C for 0.5 h (benzene, sealed tube) in 96% isolated yield. One reason of the extrusion of SO_2 of *trans*-type D adducts (**2**) may be due to the bicyclic ring strain caused by the repulsion between the oxabridge and the *exo*-substituent.

Table 2. Diels-Alder Reactions of Furansulfolene (1) with Alkynes

Entry No	Dienophile (equiv.)	Reaction Conditions	Products(Yield, %)[a]				Total Yield
			Type D'	Type A'	Type B'	Type C'	
1	Dimethyl acetylene-dicarboxylate(DMAD) (3 equiv.)	atmosphere, 28°C 7 days, CH_2Cl_2		**5a** 54	**7a** 39		93
2	Dimethyl acetylene-dicarboxylate(DMAD) (1 equiv.)	atmosphere, 28°C 7 days, CH_2Cl_2		**5a** 35			35 (61)[b]
3	Dimethyl acetylene-dicarboxylate(DMAD) (3 equiv.)	sealed tube, 120°C 1 h, benzene		**5a** 62	**7a** 29		91
4	Dimethyl acetylene-dicarboxylate(DMAD) (1 equiv.)	sealed tube, 120°C 1 h, benzene		**5a** 40	**7a** 3		43 (51)[b]
5	Dimethyl acetylene-dicarboxylate(DMAD) (3 equiv.)	4 Kbar, 28°C 24 h, CH_2Cl_2		**5a** 97	**7a** 3		100
6	*p*-Tolyl 2-(trimethyl-silyl)ethynyl sulfone (3 equiv.)	4 Kbar, 28°C 24 h, CH_2Cl_2		**5e** 73			73 (24)[b]

a) Isolated yield. b) Recovery of **1**

The result of the reaction of furansulfolene (**1**) with dimethyl acetylenedicarboxylate (DMAD) was shown in Table 2. Under atmospheric pressure, in fact, the cycloaddition of **1** with DMAD could be done at room temperature, but the reaction time were very long (Table 2, Entries 1 and 2). At 120° C, the reaction time was much shorter, however the tandem adduct (**7a**) was formed (Entries 3 and 4). Under high pressure, for the



10a

reaction of **1** with DMAD (3 equiv. mol), a sensitivity to pressure was found; at 12 Kbar and 28° C for 48 h, the furansulfolene was consumed and a adduct (**10a**), which was a 1:1 adduct of the type D' (**3a**) and **1**, was obtained as a single isomer in 53% yield, and at 6 Kbar for 24 h (28 °C) **10a** (23%) and tandem (type B') adduct **7a** (26%) were formed.[5] Under these conditions, the reaction of **1** with DMAD may first form the type D' adduct, which may then be more reactive toward **1** to produce **10a**. At 4 Kbar and room temperature, the reaction of **1** with DMAD (3 equiv. mol) was effected in a 97% yield of **5a** (Entry 5). Of particular interest was the finding that under pressure the reaction of **1** with alkynes did not yield type D' adducts (10-oxa-4-thiatricyclo[5.2.1.$0^{2,6}$]dec-2(6), 8-diene 4,4-dioxide) (**3**) but the corresponding type A' adducts (**5**)(Entries 5 and 6), indicating rapid desulfonylation attributable to two "*endo*-cyclic olefin-oxabridge" repulsions of the oxanorbornadiene moiety of **3**.[6] Desulfonylation should circumvent the release of one of them.[7]

In conclusion, the utilization of 12 Kbar pressure has proved to be an valuable technique for effecting cycloaddition of alkenes to the furan moiety of **1** stereoselectively. For the reaction of the furan moiety and alkynes as dienophiles, the use of 4 Kbar pressure in contrast to thermal conditions permitted the reaction to proceed in higher yield and in shorter reaction times.

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2. The configuration of all cycloadducts could be readily determined by inspection of the ^{1}H nmr spectra. The bridgehead protons of *exo*-isomers of cycloadducts appeared as singlets in the reasonable region, and those of *endo*-ones as doublets.
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5. Only one six-protons singlet for carbomethoxy at δ 3.60 in ^{1}H nmr (DMSO-d_6/TMS), one peak for the methyl carbon at δ 52.3 in its ^{13}C nmr together with one peak for carbonyl carbon at δ 170.56 showed this product to be one isomer of the 1:1 adducts of **1** and **3a**. As for the configuration of this adduct, the cycloaddition of endocyclic dienophilic unit in 7-oxanorbornyl compound like **3a** occurs preferentially at the exo face of its π-system[5a] and the non-bonding lone pairs on both oxygens may constitute an undesirable steric interaction due to their close proximity in the **10a'** (See below). Therefore, **1** molecule orients itself so that the oxygen atoms are anti to each other. a) P. R. Ashot, G. R. Brown, N. S. Isaacs, D. Giuffrida, F. H. Kohnke, J. P. Mathias, A. M. Z. Slawin, D. R. Smith, J. F. Stoddart, and D. J. Williams, *J. Am. Chem. Soc.*, 1992, **114**, 6330.
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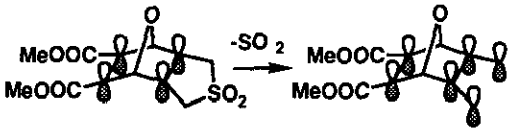
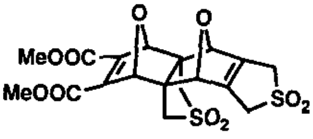


Type D' **Type A'**



10a'

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