

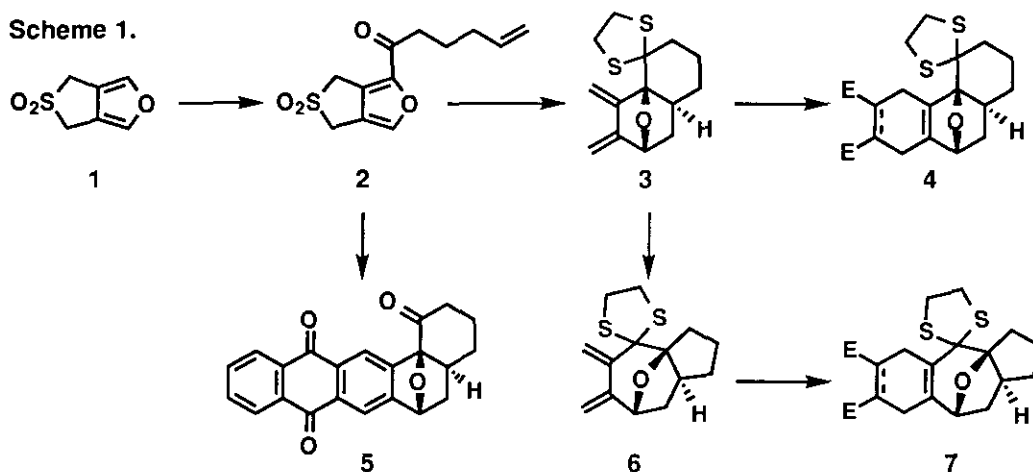
A NOVEL APPROACH TO FUNCTIONALIZED POLYCYCLIC SYSTEMS; SYNTHESIS OF TETRACYCLIC COMPOUNDS BY SEQUENTIAL REARRANGEMENT-CYCLOADDITION REACTIONS OF 7-OXA-2,3-DIMETHYLENENORBORNENE DERIVATIVE[†]

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Abstract-----The tricyclic diene (**6**), readily accessible from a novel building block, 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (**1**), reacted with a variety of dienophiles to give the tetracyclic perhydroazulene derivatives (**7**) in good to high yield.

We have synthesized a novel building block, 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (**1**), and demonstrated its utility in organic synthesis.¹ In particular, polycyclic ring systems are readily accessible from **1** via its 2-acyl derivative (**2**) as shown in Scheme 1. The intramolecular Diels-Alder reaction of **2** affords stereoselectively the tricyclic adduct (**3**),² which on subsequent intermolecular Diels-Alder reaction gives a tetracyclic compound (**4**) in good yield.³ Tandem cycloaddition of **2** also proceeds to afford a polycyclic compound (**5**) in a single step.⁴ Furthermore, the adduct (**3**) readily rearranges to furnish the tricyclic diene



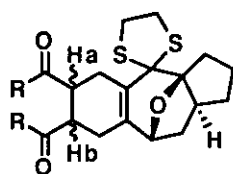
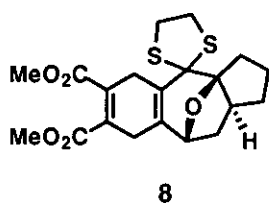
(6) in high yield on treatment with Lewis acid.⁵ We report here the cycloaddition of 6 with a variety of dienophiles to construct the functionalized tetracyclic system (7).

Table 1 summarizes the results. In the thermal conditions shown as conditions A, most of the dienophiles reacted smoothly with 6 to give the corresponding adducts (8-11)⁶ in good to high yield (Entries 1, 3, 5, 7,

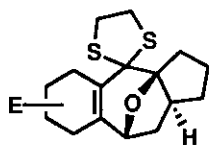
Table 1, Cycloaddition of the tricyclic diene (6) with dienophiles.

Entry	Dienophiles ^a	Conditions ^b	Time	Products (% yield, ratio) ^c
1	DMAD	A	1 h	8 (83)
2	DMAD	B	12 h	8 (62)
3	<i>N</i> -Phenylmaleimide	A	1 h	9a,b (56, 8: 5)
4	<i>N</i> -Phenylmaleimide	B	30 min	9a,b (57, 3: 2)
5	Dimethyl fumarate	A	8 h	9c,d (83, 4: 1)
6	Dimethyl fumarate	C	9 days	9c,d (38, 10: 1)
7	Dimethyl maleate	A	14 h	9e,f (60, 1: 1), 9c,d (27, 1: 1)
8	Dimethyl maleate	C	4 days	9e,f (42, 5: 4), 9c,d (9, 1: 1)
9	Methyl acrylate	A	13 h	10a (86, 3: 3: 2)
10	Methyl acrylate	D	2 h	10a (51, 10: 7)
11	Acrolein	A	8 h	10b (79, 8: 7: 5: 3)
12	Acrolein	D	5 min	10b (26, 4: 4: 4: 1)
13	1-Cyanovinyl acetate	A	3 days	10c (84, 4: 3: 2: 1)
14	Methyl propiolate	A	3 h	11a,b (89, 4: 3)
15	Benzoquinone	E	5 days	12 (40), 9g (15)

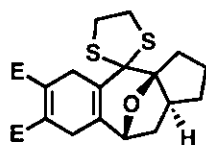
a) Three equiv. of dienophile was used for each experiment. b) A: in toluene at reflux; B: Me₂AlCl (2 eq.) in benzene at room temperature; C: Me₂AlCl (2 eq.) in benzene at 50 °C; D: EtAlCl₂ (2 eq.) in benzene at room temperature; E: in CH₂Cl₂ at 28 °C under high pressure (2.5 kbar). c) Except for Entries 1, 2, 7 and 8, the adducts were obtained as an inseparable mixture and the ratio was determined by ¹H-NMR. In Entries 7 and 8, 9e,f and 9c,d were separated each other by silica gel chromatography.



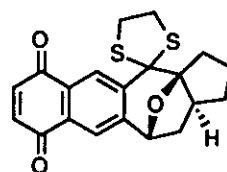
- 9** a, R=N-Ph, α -Ha, α -Hb
 b, R=N-Ph, β -Ha, β -Hb
 c, R=OMe, α -Ha, β -Hb
 d, R=OMe, β -Ha, α -Hb
 e, R=OMe, α -Ha, α -Hb
 f, R=OMe, β -Ha, β -Hb
 g, R=CH=CH



- 10** a, E=CO₂Me
 b, E=CN, OAc
 c, E=CHO



- 11** a, E=H, E'=CO₂Me
 b, E=CO₂Me, E'=H



12

9, 11, 13, and 14). These results are comparable to those reported previously for the reaction of **3** to produce **4**.³ Accordingly, the diene moiety of **6** has almost the same reactivity to that of **3** in thermal cycloaddition. In contrast, they are quite different in Lewis acid catalyzed conditions. The compound (**3**) gives no adducts when subjected to Lewis acid catalyzed conditions, but instead affords the rearrangement product (**6**) in high yield.⁵ In the case of **6**, however, the desired adducts (**8-11**) were obtained in fair to good yield. The most effective catalyst and conditions depended on the dienophiles used. Me₂AlCl at room temperature (conditions B) was good for the highly reactive dienophiles DMAD and *N*-phenylmaleimide (Entries 2 and 4). For dimethyl fumarate and dimethyl maleate, Me₂AlCl was also effective but elevated temperature was required (conditions C, Entries 6 and 8). EtAlCl₂ was better than Me₂AlCl for the cases of methyl acrylate and acrolein (conditions D, Entries 10 and 12). Using other Lewis acid such as SnCl₄ and TiCl₄ resulted in a complex mixture. Although the yields were lower than those in the corresponding thermal conditions, the stereoselectivity and the regioselectivity were somewhat improved.

In thermal cycloaddition of the diene (**3**), quinones smoothly react to give corresponding adducts in high yield.³ In marked contrast, however, the reaction of benzoquinone with **6** did not afford any adduct in any conditions described above. Therefore, a procedure using high pressure conditions (conditions E) was attempted to this particular dienophile. It turned out to be successful and the adduct (**9g**) along with its auto-oxidation product (**12**) were obtained in good yield (Entry 15).

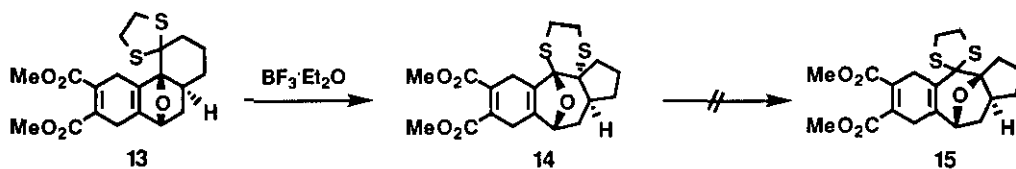
Thus, the tricyclic diene (**6**) was found to be highly reactive for cycloaddition and afforded the functionalized tetracyclic compound (**7**) in good to high yield both in thermal and in Lewis acid catalyzed conditions, which further demonstrated the versatility of **1** as a building block. The ready accessibility of **7**

as described here⁷ should be applicable to synthesis of complex natural products or compounds of biological interest with this polycyclic skeleton.

REFERENCES AND NOTES

† This paper is dedicated to Professor Koji Nakanishi on the occasion of his 75th birthday.

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5. K. Konno, S. Maki, and H. Takayama, *Tetrahedron Lett.*, 1995, **36**, 1865.
6. All new compounds were fully characterized by spectral (¹H-NMR, IR, MS, and HRMS) and/or combustion analyses.
7. In addition, all attempts to obtain **7** from **4** by Lewis acid catalyzed rearrangement as from **3** to **6**, nor **7** from **3** through **6** by tandem rearrangement-cycloaddition in a single step were unsuccessful. Interestingly, however, treatment of the compound (**13**) with BF₃·Et₂O at room temperature for 4 h gave the compound (**14**), which should be an intermediate for rearrangement to the desired product (**15**), in 27 % yield.



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