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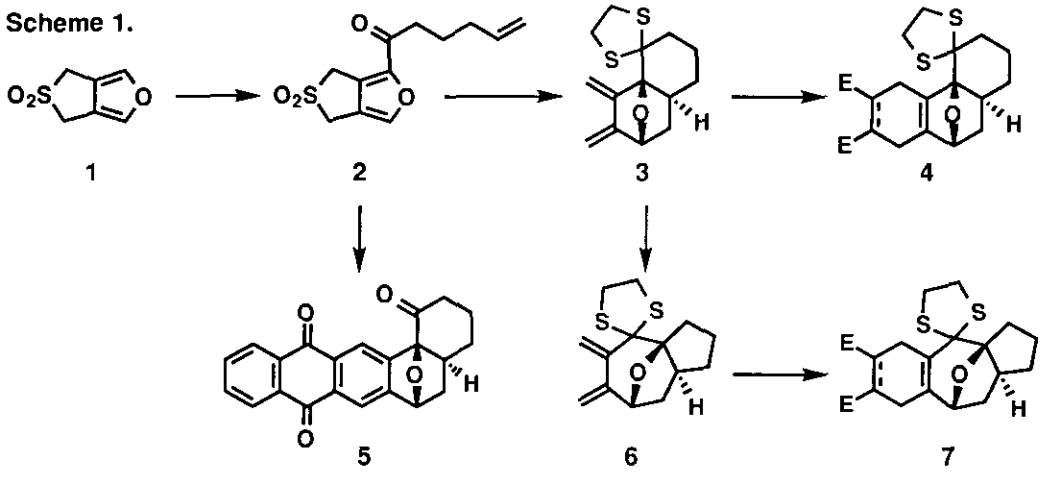
Abstract-----The tricyclic diene (**6**), readily accessible from a novel building block, 4*H*,6*H*-thieno[3,4-*c*]furan 5,5-dioxide (**1**), reacted with a variety of dienophiles to give the tetracyclic perhydroazulene derivatives (**7**) in good to high yield.

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 polycylic compound (**5**) in a single step.[4] Furthermore, the adduct (**3**) readily rearranges to furnish the tricyclic diene

Scheme 1.



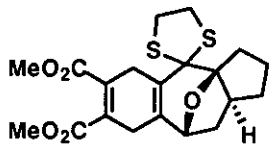
(**6**) *in high yield on treatment with Lewis acid.*[5] We report here the cycloaddition of **6** with a variety of dienophiles to construct the functionalized tetracyclic system (**7**).

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	*N*-Phenylmaleimide	A	1 h	**9a,b** (56, 8: 5)
4	*N*-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: Me_2AlCl (2 eq.) in benzene at room temperature; C: Me_2AlCl (2 eq.) in benzene at 50 °C; D: $EtAlCl_2$ (2 eq.) in benzene at room temperature; E: in CH_2Cl_2 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 ^{1}H-NMR. In Entries 7 and 8, **9e,f** and **9c,d** were separated each other by silica gel chromatography.



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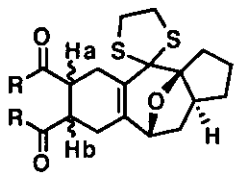
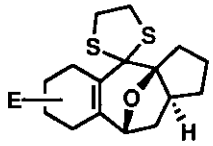
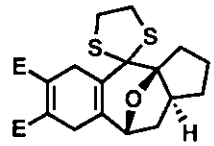


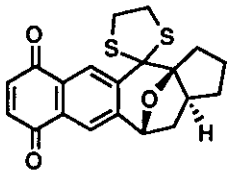
9 **a**, R=N-Ph, α-Ha, α-Hb
b, R=N-Ph, β-Ha, β-Hb
c, R=OMe, α-Ha, β-Hb
d, R=OMe, β-Ha, α-Hb
e, R=OMe, α-Ha, α-Hb
f, R=OMe, β-Ha, β-Hb
g, R= CH=CH



10 **a**, E=CO_2Me
b, E=CN, OAc
c, E=CHO



11 **a**, E=H, E'=CO_2Me
b, E=CO_2Me, E'=H



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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. Me_2AlCl 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, Me_2AlCl was also effective but elevated temperature was required (conditions C, Entries 6 and 8). $EtAlCl_2$ was better than Me_2AlCl for the cases of methyl acrylate and acrolein (conditions D, Entries 10 and 12). Using other Lewis acid such as $SnCl_4$ and $TiCl_4$ 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 here[7] 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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4. S. Maki, K. Konno, and H. Takayama, *J. Chem. Soc., Chem. Commun.*, 1995, 2025.
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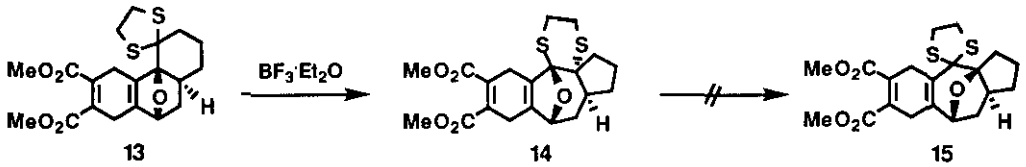
6. All new compounds were fully characterized by spectral (^{1}H-NMR, IR, MS, and HRMS) and/or combustion analyses.
7. In addition, all attempts to obtain **7** from **4** by Lewis acid catalyzed rearrangement as from **3** to **6**, nor **7** from **3** through **6** by tandem rearrangement-cycloaddition in a single step were unsuccessful. Interestingly, however, treatment of the compound (**13**) with BF_3Et_2O 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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