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Synthetic Photochemistry. LXIX.¹⁾ The Structures of the Photocycloadducts of 2-Acetoxy-4,4-dimethylbutenolide with Cyclohexene: A Revision

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The photoaddition of 2-acetoxy-4,4-dimethylbutenolide was reinvestigated, and the two isomeric cycloadducts were isolated along with the reported one. The structure of the latter was revised to the cis-syn-cis adduct from the NOE study and the analysis of the coupling pattern of its ¹H-NMR spectrum.

Recently we reported the photocycloaddition reaction of α -hydroxy- γ,γ -dimethylbutenolide (enol form of γ,γ -dimethyl- α -tetronic acid: **1**),²⁾ and α -hydroxy- γ -methylbutenolide (**2**).³⁾ A stereochemical peculiarity of the reaction with **1**, compared with that with α -hydroxy- γ -methylbutenolide (**2**),³⁾ prompted us to further investigate the reaction of the derivatives derived from **1**, since there have been many examples for photochemical generation of trans-fused 6/4-ring system, and, therefore, the photoreaction of the derivatives of **1** with cyclohexene is expected to give such trans-adducts. Indeed, a reinvestigation of the reaction with the acetate of **1** (**3**) and cyclohexene led to isolate three cycloadducts, whose stereostructures were elucidated by careful NMR analyses including a positive nuclear Overhauser effect (NOE).⁴⁾

When **3** was irradiated with cyclohexene as similar to the previous study,³⁾ formation of three products (**4**, **5**, and **6**) were recognized, and the mixture was carefully separated with column chromatography and HPLC. The major product, **4**, was the already reported cycloadduct; previously, the cycloadduct **4** was tentatively assigned as the cis-anti-cis adduct on the basis of the ¹H NMR spectral similarity with the adduct of **1** (**7**). Thus, parallel formation of two other isomeric photocycloadducts, **5** and **6**, should recall the analysis of stereostructures of all the products.

Thus, the three methine protons of **4** on the ring juncture appeared at δ 2.68, 3.16, and 3.37 as a multiplet, double doublets of doublet, and a doublet, respectively, which could be assigned as 3b-, 7a- and 3a-protons, respectively. All these protons were less shielded than those of **7** as large as 0.7 ppm, and the mutual coupling constants, $J_{3a, 3b}=9.2$ Hz, $J_{3b, 7a}=11.4$ Hz, were somewhat larger than those of corresponding cis-anti-cis adducts of **1** (**7**) and of **2** (**8**, **9**), but not similar to those of the trans-adduct of **2** (**10**: $J_{3a, 3b}=6.2$ Hz, $J_{3b, 7a}=12$ Hz). However, the width of the 3b-proton signal (ca. 40 Hz) of **4** (see Table 1) suggests the different steric environment from that of **7**. In addition, the ¹³C NMR spectrum of **4** revealed a similarity with **7**, **8** or **9** except for the chemical shifts of C-3b and C-7b (Table 2).

The careful NOE experiments provided informations: the positive NOEs were observed between the protons at 3b-H and 7a-H (6%) and between 3a-H and 3b-H (6%).

These findings confirm not only the cis 3b,7a-configuration, but also cis-3a,3b-configuration.

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Structures of 2-Acetoxy-4,4-dimethylbutenolide-Cyclohexene Photoadducts

Table 1. The ^{13}C -NMR data of the cycloadducts of **1**, **2**, and **3**.

	4 <i>cis-syn-cis</i>	5	7	8	9	6	10
		<i>cis-anti-cis</i>				<i>trans</i>	
$\delta(\text{Me})$	1.37- 1.51	1.39 1.48	1.34- 1.45	- 1.39	1.32 -	1.57 1.63	1.44 -
$\delta(3)$	-	-	-	4.45	4.82	-	4.75
$\delta(3a)$	3.37	2.69	2.66	2.65	2.88	2.89	2.53
$\delta(3b)$	2.68	2.25	2.00	1.90	2.07	2.2	2.37
$\delta(7a)$	3.16	2.85	2.41	2.47	2.44	-2.35	2.04
$\delta(\text{OH})$	-	-	3.39	3.15	2.9	-	3.6
$\delta(\text{Ac})$	2.08	2.11		-	-	2.18	-
$\delta(\text{CH}_2)$	1.05(1H) 1.35-1.72 (5H) 1.83(1H) 2.05(1H)	1.2-1.9 (10H)	1.14(1H) 1.30(1H) 1.5-1.85 (6H)	1.15(H) 1.35(1H) 1.45-1.8 (6H)	1.15(H) 1.35(1H) 1.5-1.8 (6H)	1.2-1.9 (10H)	1.20-1.45 (3H) 1.55-1.9 (5H)
$J(3,3a)$	0.0	-	-		4.5	-	7.0
$J(3a,3b)$	7.7	6.6	8.0	6.6	8.8	7.0	
$J(3b,7a)$	8.2	8	8	8	8		
$\Sigma J(3b,4)$	9		8		7.5		
$\Sigma J(7a,7)$	16	16	19		16		
$w(3b)$	25		24		24		
$w(7a)$	26		27		24		

The figures in italics are given in ± 1 Hz. Others are ± 0.4 Hz.

Table 2. The ^{13}C -NMR data of the cycloadducts of **1**, **2**, and **3**.

4 <i>cis-syn-cis</i>	5	7	8	9	6	10
	<i>cis-anti-cis</i>				<i>trans</i>	
173.3	173.8	180.0	180.6	180.1	172.7	177.6
86.3	84.2	85.9	80.8	77.6	84.1	76.5
51.2	52.7	52.9	50.1	48.2	52.0	51.6
30.3	28.0*	25.4	28.8	25.0	44.0	41.7
36.6	37.4	36.8	37.4	37.1	48.7	49.3
83.1	80.7	76.9	75.1	76.0	86.0	82.2
22.8	22.8	21.6	21.4	14.8	28.6*	22.5
28.7	28.6*	28.2	-	-	31.7	-
20.7, 24.0	21.6, 22.1	21.7(2C)	21.5(2C)	21.6(2C)	25.7, 26.2	25.6, 26.9
21.7(2C)	22.2, 22.8	22.0, 24.9	21.7, 24.6	21.9, 23.3	26.9, 27.0	26.0(2C)
169.1	168.7				170.0	
20.5*	20.9*				20.5	

*Figures denote the uncertain assignments, and might be exchangeable with the near signals.

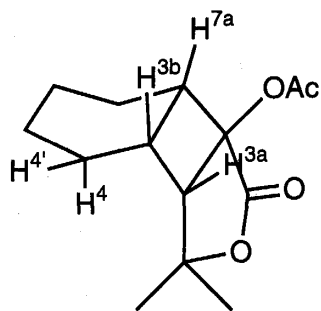


Fig. 1. Boat conformation of **4**. Dihedral angle for $\angle H^{3b}-C^{3b}-C^{7a} = 16.0^\circ$, $\angle H^{3b}-C^{3b}-C^4-H^{4a} = 173.6^\circ$

tion. Therefore **4** must be cis-syn-cis-adduct ($[3a\alpha, 3b\alpha, 7a\alpha, 7b\alpha]$ -7b-acetoxyoctahydro-3,3-dimethylbenzo[3,4]cyclobuta[1,2-*c*]-1*H* (3*H*)-furan-1-one), because the highly strained trans-4,5-ring contraction has to be ruled out.

This conclusion conflicts with the large coupling constant between 3b-H and 7a-H ($J = 11.4$ Hz), which is matching with trans-axial-axial coupling. Judging from the widths of their signals, *i.e.*, the sum of the coupling constants between 3b-H and two 4-methylene protons (19 Hz), and that between 7a-H and two 7-methylene protons (16 Hz), it was concluded that the conformation of cyclohexane part of **4** must not be chair form, but boat form. The conformation illustrated in Fig. 1 explains the coupling patterns of the methine protons of **4**.

In fact, the MM2 calculation of the cis-syn-cis-adduct showed the boat form is more stable than the half-chair form by 0.7 kcal/mol.⁵ Consequently, the stereochemistry of **4** should be assigned as the all cis-cycloadduct.

Contrary to this, the structure of the newly obtained cycloadduct **5** was concluded to be the cis-anti-cis-adduct by the simple comparison of the NMR data with those of **7**, **8** and **9**, compiled in Tables 1 and 2. And, similarly the remaining product **6** was assigned to be the trans-adduct by the NMR spectral comparison with **10**.

Obtaining the trans-fused stereoisomer as the photoproduct, the formation of these isomers is well interpreted in terms of steric effect (Fig. 2). In the reaction of **1**, syn-approach of **1** and cyclohexene is sterically disfavored because of the steric repulsion between cyclohexene ring and methyl group, and **7** was formed by anti-approach. The introduction of bulky acetoxy group lowered the energy difference between the syn- and anti-approach,

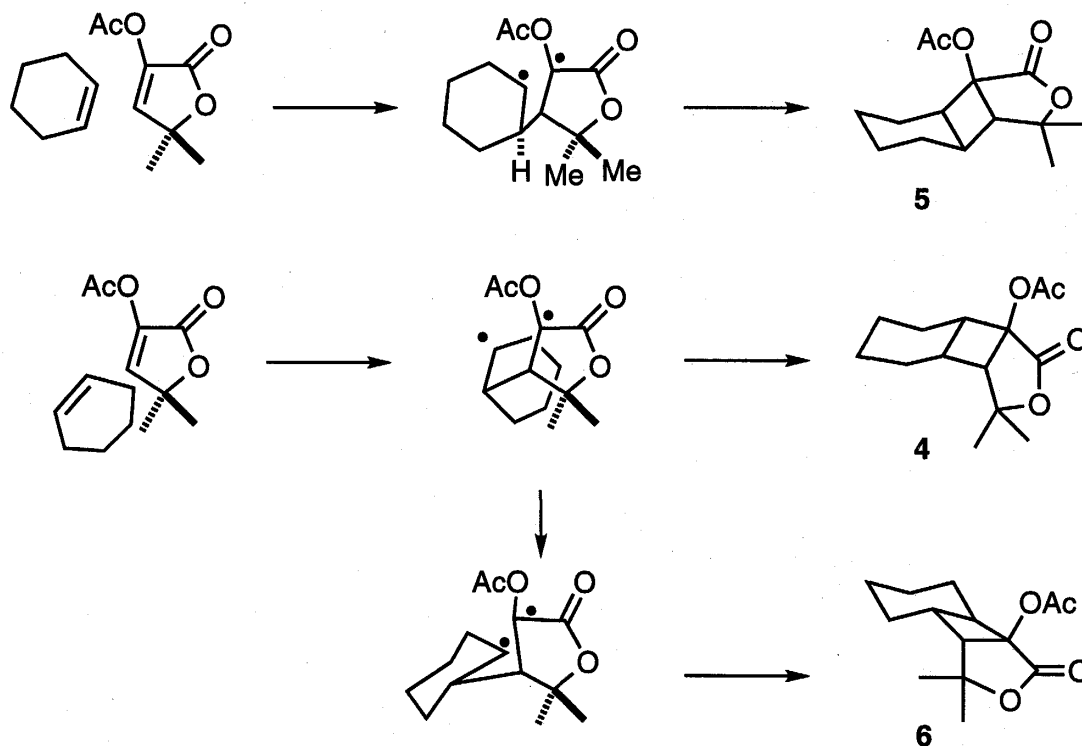
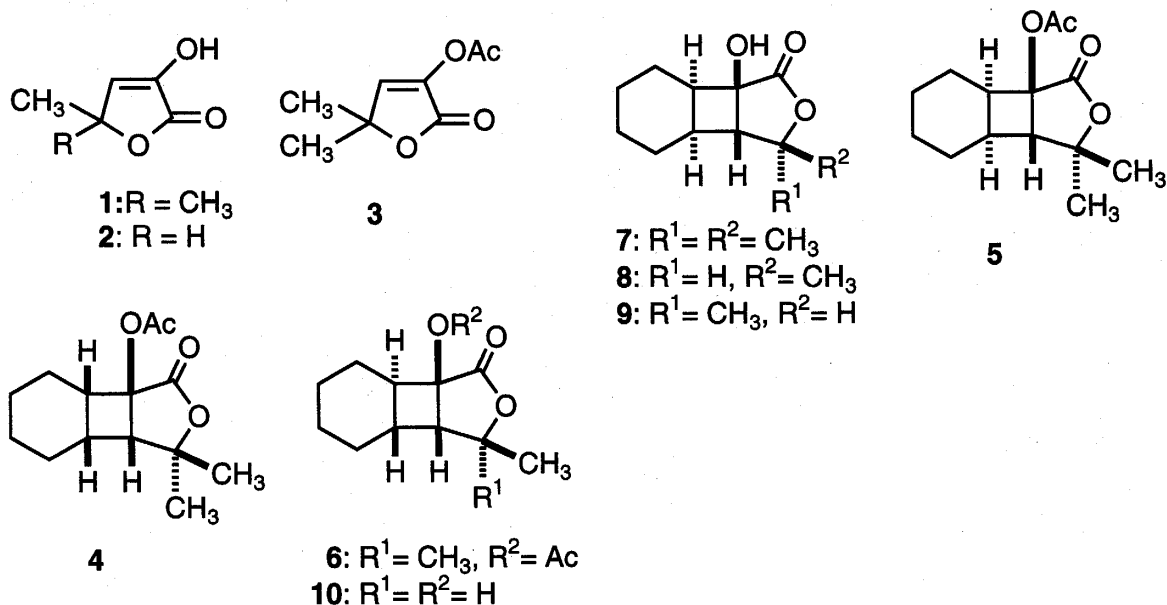


Fig. 2. Anti and syn approach in the cycloaddition reaction of **3**, and paths to the products.



and makes the syn-approach possible. Then were given **4** and the trans-adduct **6**.

In the reaction with **2**, the syn-approach could also occur, because the elimination of the inner methyl group decreases the steric repulsion, and the biradical intermediate having less bulky hydroxyl group could more easily rotate than that from **3** and close the ring to give the trans-adduct **10**.

In conclusion, the steric course of the photoreaction of tetronic acid derivatives is affected by the bulkiness of the substituents, and the acetate **3** gave the cis-syn-cis- and trans-adduct through syn-approach in addition to the cis-anti-cis-adduct through anti-approach.

Experimental

Photochemical Cycloaddition of 3 with Cyclohexene. The acetate **3** (281 mg) and cyclohexene (3.0g) were dissolved in EtOAc and irradiated for 10 h by means of 400 W-high pressure Hg-lamp through a 10%-NiSO₄ solution (thickness: 1 cm). Silica-gel chromatography (Wakogel C 300) of the mixture afforded **4** (23 %) and **5** and **6** (47% in combined yield, 2.5 : 1). Analytically-pure sample of **5** (colorless oil, ν : 1780, 1760, 1370, 1220, 1070, 1040, and 920 cm⁻¹; m/z 252(M⁺, 2%), 210(15%), 192(12%), 182(22%), 166(30%), 151(42%), 148(20%), 137(100%), 83(59%)) was obtained after HPLC separation, but **6** was obtained in only as a mixture with **5**.

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- 4) The ¹H- and ¹³C-NMR spectra were measured in CDCl₃ with a GSX-270 spectrometer (JEOL).
- 5) Licensed from Cambridge Science Computing, Inc. (Ser. No. 13274).