Tetrahedron Letters No. 44, pp 4297 - 4300.
©Pergamon Press Ltd. 1978. Printed in Great Britain.

0040-4039/78/1029-4297$02.00/0

A NEW SYNTHESIS OF γ-ALKYLIDENE-$\Delta^{\alpha,\beta}$-BUTENOLIDES

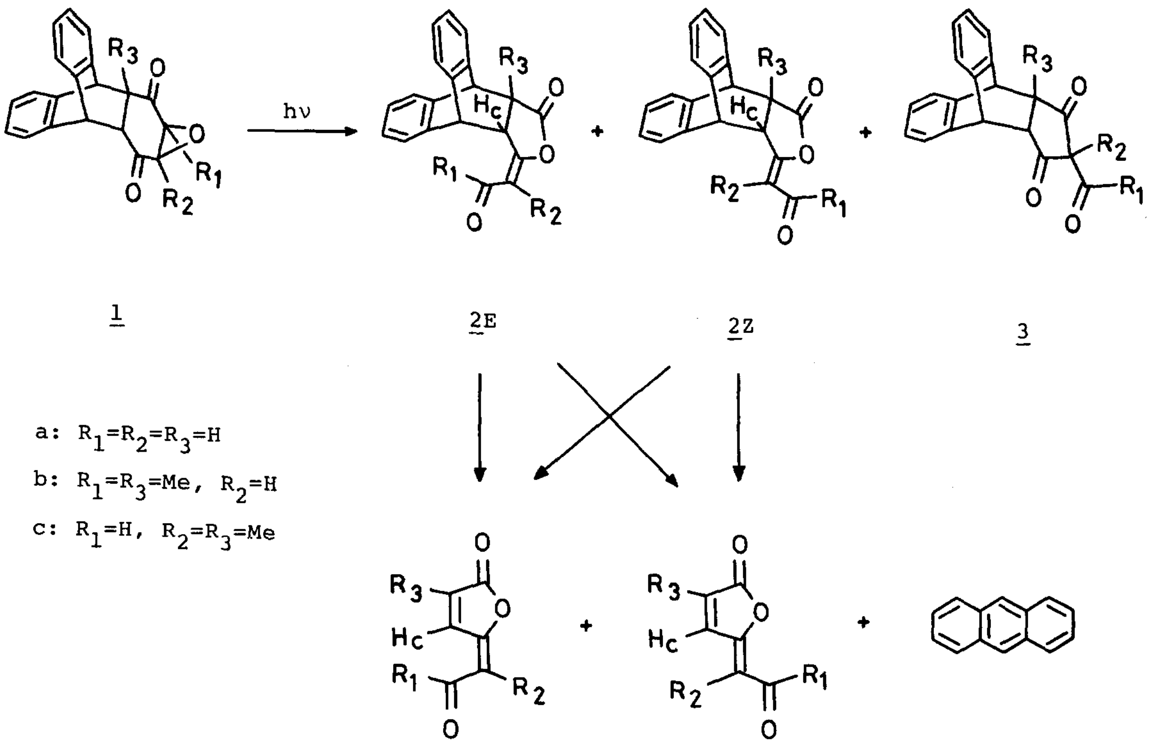
Tohru Kitamura, Yosihide Kawakami, Takeshi Imagawa, and Mituyosi Kawanisi
Department of Industrial Chemistry, Faculty of Engineering, Kyoto University,
Kyoto 606, Japan

The structural unit of γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolide occurs in a variety of natural products, such as patulin,1) protoanemonin,2) tetrenolin,3) freelingyne,4) and matricarialactone,5) possessing a wide range of biological activity. This fact has stimulated considerable research on the development of new synthetic methods for the construction of this structural unit.6)

We now wish to report a facile method for construction of the γ-alkylidene-$\Delta^{\alpha,\beta}$-butenolide moiety based on the recently reported photochemical rearrangement of 2,3-epoxy-1,4-cyclohexanediones into γ-alkylidene-γ-butyrolactones,7) combined with the retro-Diels-Alder reaction.

UV-irradiation of epoxy diketone 1a, derived from p-benzoquinone,8) for 20 hrs in acetone, using a 100-W high pressure Hg lamp (pyrex), gave a mixture of 2aE, 2aZ, 3a, and 1a in a ratio of 1 : 1 : 2.5 : 1 (NMR).9) Preparative TLC separation using phosphate-buffered silica gel layer gave lactones 2aE [10%; mp 198°(dec)] and 2aZ [13%; mp 191°(dec)], with 1a (13%) recovered. The triketone (3a), very liable to decompose on TLC, was the sole product on irradiation of 1a in AcOEt10) [80%; mp 163°(dec); δ_{CHO} 9.13].

Retro-Diels Alder reaction of 2aE at 230° (20 mmHg) and preparative TLC separation gave a 1 : 1 mixture of butenolides 4aE and 4aZ in 80% yield, along with anthracene (90%). The same ratio of the products was obtained from the reaction of 2aZ, indicating the isomerization of 4aE and 4aZ under reaction conditions.



1 2E 2Z 3

a: $R_1=R_2=R_3=H$
b: $R_1=R_3=Me$, $R_2=H$
c: $R_1=H$, $R_2=R_3=Me$

4E 4Z

This success encouraged us to apply this method to the synthesis of butenolide 4bZ,11) a key intermediate for synthesis of freelingyne, a furanosesquiterpenoid. Irradiation of 1b, derived from 2,6-dimethyl-p-benzoquinone,12) in acetone led to a mixture of 2bE, 2bZ, and 3b in a ratio of 1 : 1.4 : 2.5. Other possible products, aldehydes 2c and 3c, were not detected. Preparative TLC (buffered) gave 2bE (12%; mp 174-176°), 2bZ (15%; mp 167-168°), and 3b13) (15%).

Pyrolytic treatment14) of the crude photolysate gave butenolides 4bE (17% from 2b; mp 88.5-89.5°, lit.11) mp 88-89°) and 4bZ (6%; mp 124-125°, lit.11) mp 124-125°), in addition to anthracene. These two compounds have been already prepared by tedious and low-yield procedures.11)

The stereochemistry of each of the E,Z-isomers was determined on the basis of the facts that allylic protons cis to the carbonyl function in α,β-unsaturated carbonyl compounds, or olefinic protons cis to the lactone oxygen atom resonate at a lower field than their trans counterparts.15) The NMR data are shown in the Table.

Table. NMR chemical shifts of 2 and 4.

		R_1	R_2	H_c	R_3
2aE	$R_1=R_2=R_3=H$	9.99	5.80	4.02	3.36
2aZ		9.68	5.49	3.65	3.28
2bE	$R_1=R_3=Me$, $R_2=H$	2.28	5.95	3.54	1.20
2bZ		2.15	5.45	3.03	1.23
4aE	$R_1=R_2=R_3=H$	9.93	8.14	6.63	6.15
4aZ		10.23	7.59	6.48	5.62
4bE	$R_1=R_3=Me$, $R_2=H$	2.31	7.96	6.13	2.06
		(2.3)	(8.0)	(6.1)	(2.1)
4bZ		2.60	7.16	5.50	2.13
		(2.5)	(7.1)	(5.4)	(2.15)

The values in parentheses donate the literature values.11)

References and Notes

1) R. B. Woodward and G. Singh, J. Am. Chem. Soc., 71, 758 (1949).

2) E. Shaw, J. Am. Chem. Soc., 68, 2510 (1946).

3) G. G. Gallo, C. Coronelli, A. Vigevani, and G. C. Lancini, Tetrahedron, 25, 5677 (1969).

4) R. A. Massy-Westropp, G. D. Reynolds, and T. M. Spotswood, Tetrahedron Letters, 1939 (1966).

5) F. Bohlmann, Fortsch. Chem. Org. Naturst., 25, 5677 (1969).

6) Y. S. Rao, Chem. Rev., 76, 625 (1976).

7) T. Kitamura, T. Imagawa, and M. Kawanisi, Tetrahedron Letters, 0000 (1978).

8) P. Yates and P. Eaton, J. Am. Chem. Soc., 82, 4436 (1960).

9) Irradiation at lower temperature (about -70°) resulted in slight increase of the ratio of (2aE+2aZ)/3.

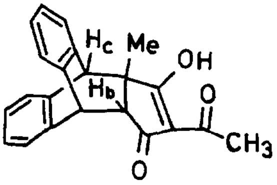
10) Irradiation of 1a in a variety of solvents such as benzene, CH_2Cl_2, CH_3CN,

and EtOH led to 3a in addition to a trace amount of 2aE and 2aZ.

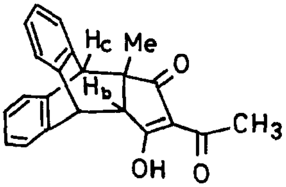
11) C. F. Ingham, R. A. Massy-Westropp, and G. D. Reynolds, Aust. J. Chem., 28, 2499 (1975), 27, 1477 (1974).

12) The epoxy diketone 1b (mp 185-186°) was prepared by epoxydation with basic hydrogen peroxide of the AlCl$_3$-catalyzed Diels-Alder adduct (mp 150.5-151.5°) between 2,6-dimethy-p-benzoquinone and anthracene.

13) As a tautomeric mixture of i and ii (1 : 1); NMR: Me, 1.03(s) and 1.20(s), COCH$_3$, 2.20, H$_b$, 2.42(d) and 2.73 (d), H$_c$, 4.32(s) and 4.27(s), aromatic H, 6.9-7.5(m).



i



ii

14) The other product 3b remained as the still residue.

15) L. M. Jackman and S. Sternhell, Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, 2nd Ed., Pergamon Press, New York, London, p. 222 (1969).

(Received in Japan 26 July 1978)