Tetrahedron Letters, Vol.22, No.43, pp 4269 - 4270, 1981
Printed in Great Britain

0040-4039/81/434269-02$02.00/0

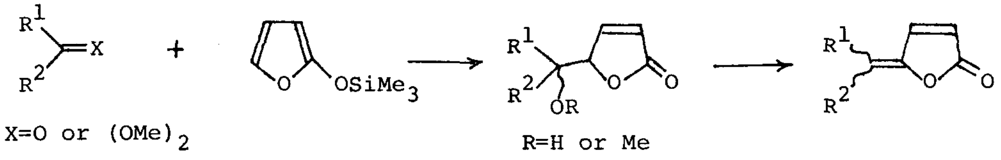
SYNTHESIS OF 4-YLIDENEBUTENOLIDES FROM 2-TRIMETHYLSILOXYFURAN

Morio ASAOKA, Noboru YANAGIDA, Keiji ISHIBASHI, and Hisashi TAKEI*
Department of Life Chemistry, Tokyo Institute of Technology
Nagatsutacho, Midoriku, Yokohama 227, Japan

Summary: Dehydration or dealkoxylation of the reaction products of various aldehydes, ketones, and acetals with 2-trimethylsiloxyfuran gave corresponding 4-ylidenebutenolides in good to high overall yields.

4-Ylidenebutenolides, which have been frequently encountered in natural products, display some interesting biological activities.[1,2] While some synthetic methods are available,[1-4] more convenient and widely applicable methods are desired.

In this paper we will report a two-step synthetic method of 4-ylidenebutenolides utilizing 2-trimethylsiloxyfuran.



1 2 3 4

In the presence of tin(IV) chloride, 2-trimethylsiloxyfuran(2) reacted with various aldehydes, ketones, and acetals to give the corresponding products(3) in good to high yields.[5] Acid(p-TsOH or HBr) catalyzed dehydration or dealkoxylation of 3 in refluxing benzene gave the 4-ylidenebutenolides in the range of 38-76% yields. But the following four methods (A-D) according to the type of 3 gave more successful results. Method A: Adducts of aldehyde(3a-f) were treated with 2-3 equivalents of acetic anhydride and triethylamine in the presence of 4-pyrrolidinopyridine(PPY) in dichloromethane at room temperature for 1-2.5h. Method B: In the case of the adduct of ketone(3g), trifluoroacetic anhydride was used instead of acetic anhydride in the method A at room temperature for 0.5h. Method C: The condensation products of ketone acetals(3h,3i) were treated with 2 equivalents of DBU in dichloromethane at room temperature for 15 minutes. Method D: The condensation product of aldehyde acetal(3j) was treated with 2 equivalents of sodium acetate in refluxing acetic acid for 1h.

Table Synthesis of 4-Ylidenebutenolides

	R^1	R^2	X	Yield(**3**) (%)	Method	Yield(**4**)[a)] (%)	E/Z ratio
1a	Ph	H	O	95	A	91	1[b)]
1b	$CH_3(CH_2)_4$-	H	O	94	A	94	1[b)]
1c	$PhCH_2CH_2$-	H	O	90	A	96	3/5[b)]
1d	2-Thienyl	H	O	96	A	91	1/2[c)]
1e	5-Methyl-2-thienyl	H	O	92	A	92	1/2[c)]
1f	$CH_3(CH_2)_2C \equiv C$-	H	O	70	A	90	5/2[c)]
1g	$-(CH_2)_5-$		O	95	A	9	-
	$-(CH_2)_5-$		O	-	B	97	-
1h	$-(CH_2)_5-$		$(OMe)_2$	66	C	85	-
1i	$PhCH_2CH_2$-	Me	$(OMe)_2$	77	C	90	-[d)]
	$PhCH_2CH_2$-	Me	$(OMe)_2$	-	D	73	-[d)]
1j	$PhCH_2CH_2$-	H	$(OMe)_2$	92	D	80	3/7[b)]

a) All of these compounds were confirmed by spectral data and elemental analyses. b) The ratio was determined by nmr. c) The ratio was determined by tlc isolation. d) The ratio could not be determined.

Typical procedure: To a solution of 2-trimethylsiloxyfuran(306 mg, 1.96 mmol) and benzaldehyde(180 mg, 1.7 mmol) in dry dichloromethane(3 ml), catalytic amount of tin(IV) chloride was added at -78°C and the reaction mixture was stirred for 2h at that temperature. After the addition of 1M hydrochloric acid(1 ml), the mixture was left to warm to room temperature. Usual work-up and subsequent isolation by tlc gave corresponding adduct(**3a**) in 95% yield. The adduct(194 mg, 1.02 mmol) was treated with triethylamine (289 mg, 2.86mmol) and acetic anhydride(216 mg, 2.12 mmol) in dichloromethane(5 ml) in the presence of catalytic amount of PPY at room temperature for 1h. Isolation by tlc gave **4a** in 91% yield.

References

1) G. Pattenden, Progress in the Chemistry of Organic Natural Products, p.133, Springer-Verlage, Wien (1978).
2) M. Yamamoto, Yuki Gosei Kagaku Kyokai Shi, 39, 25 (1981).
3) M. D'Auria, G. Piancattelli, and A. Scettri, Tetrahedron, 36, 3071 (1980).
4) a) J. E. T. Corrie, Tetrahedron Lett., 1971, 4873.
   b) G. A. Kraus and H. Sugimoto, Chem. Commun., 1978, 30.
5) a) M. Asaoka, K. Miyake, and H. Takei, Chem. Lett., 1977, 167.
   b) M. Asaoka, N. Sugimura, and H. Takei, Bull. Chem. Soc. Jpn., 52, 1953 (1977).
   c) E. Yoshii, T. Koizumi, E. Kitatsuji, T. Kawazoe, and T. kaneko, Heterocycles, 4, 1663 (1976).

(Received in Japan 30 June 1981)