

A FACILE SYNTHESIS OF 4-PHENYLTHIO-2(5H)-FURANONE DERIVATIVES.

SYNTHESIS OF SESQUIROSE FURAN AND BULLATENONE

Yasuhiro Takahashi, Hisahiro Hagiwara, Hisashi Uda,*

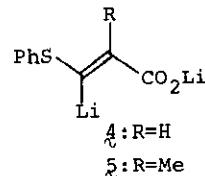
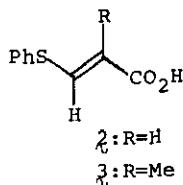
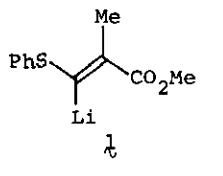
and Hiroshi Kosugi

Chemical Research Institute of Non-Aqueous Solutions,

Tohoku University, Katahira-2, Sendai 980, Japan

Condensation of the dianions derived from E-3-(phenylthio)-prop-2-enoic acid and its 2-methyl homologue with aldehydes and ketones provides a facile one step synthesis of 5-substituted 4-phenylthio-2(5H)-furanone derivatives. The application to the synthesis of sesquirose furan and bullatenone is described.

Recently, we reported that, upon treatment with lithium diisopropylamide (LDA), methyl E-2-methyl-3-(phenylthio)prop-2-enoate produced selectively the 3-lithio derivative (λ), which reacted with aldehydes and α, β -enoates to give functionalized 2-(5H)-furanones (α, β -butenolides) and cyclopentenones in one step.¹ It was found, however, that the carbanion λ did not react with ketones, and that parent methyl E-3-(phenylthio)prop-2-enoate (methyl ester of λ), unlike its corresponding 3-(1-pyrrolidinyl) ethyl ester,² could not be lithiated under the condition examined (LDA/THF, -80°C), decomposition or side-reaction took place. We have now found that the free acid λ ,³ as well as the 2-methyl derivative λ ,⁴ can produce selectively lithium 3-lithio-enoates λ and λ and reacted with aldehydes and ketones to give 5-substituted 4-phenylthio-2(5H)-furanones δ - λ .⁵



The dianion species λ and λ were easily generated by treating enoic acids λ and λ with two equivalents of LDA in THF at -80°C. From quenching experiment by

deuterium oxide, it was found that the dianion δ was stable even at room temperature, whereas the dianion γ decomposed above -40°C . The reactions with aldehydes were carried out at $-80\sim-40^{\circ}\text{C}$ for 3 h in the case of the dianion δ and at $-40\sim0^{\circ}\text{C}$ for 3 h in the dianion γ , respectively. Acid-catalyzed lactonization of the initial product gave, after preparative tlc, 2(5H)-furanones δ and γ in moderate to good yields.⁵ The results are summarized in Table 1. Several comments are in order. In both cases of δ and γ , in contrast to the case of the monoanion λ , normal addition procedure gave satisfactory results. In the reaction with crotonaldehyde, both δ and γ afforded selectively the 1,2-adducts. Furthermore, it is noted that the reaction of the dianion δ with crotonaldehyde gave only the 1:1 adduct $\gamma\delta$ in good yield, in contrast to the formation of a considerable amount (13%) of the 1:2 adduct in the case of the monoanion λ .¹

The dianion δ also reacted satisfactorily with acyclic and cyclic ketones under the identical condition to give directly 5,5-disubstituted 2(5H)-furanones δ as shown in Table 2. While, the dianion γ was found to be less reactive than δ but more reactive than the monoanion λ to ketones, giving 2(5H)-furanones $\gamma\delta$ in low yields.

Both dianions δ and γ were also acylated by an acid anhydride. Thus, treatment of δ and γ with acetic anhydride under the same condition afforded the corresponding 5-hydroxy derivative $\lambda\delta$ and $\lambda\gamma$ in 59 and 28% yields, respectively. Thus, the dianion species δ and γ offer advantages and lead to a generally applicable synthetic route to a variety of 5-substituted 4-phenylthio-2(5H)-furanones.

In view of their unique functionality, the furanones thus obtained would appear to serve as useful synthetic intermediates for elaboration of complex organic structures or of natural products. Typical reactions using the furanone $\delta\delta$ are exemplified in Scheme 1. Upon treatment with diisobutylaluminum hydride (DIBAH)⁶ at -70°C or with methylolithium at -80°C , the furanone $\delta\delta$ gave 3-phenylthio-2-propylfuran ($\lambda\delta$) and the 5-methyl derivative ($\lambda\gamma$) in 65 and 47% yields, respectively. Conjugate addition reaction with lithium dimethylcuprate at -90°C proceeded to furnish a 73% yield of the phenylthio-methyl group exchange product, 4-methyl-5-propyl-2(5H)-furanone ($\lambda\delta$).

Combination of the conjugate addition of lithium dimethylcuprate with DIBAH reduction would provide a strategy for the synthesis of sesquirose furan ($\lambda\delta$), one of the constituents of the leaf oil of Actinodaphne longifolia (Blume) Nakai

Table 1. Reaction of the dianion δ or ζ with aldehydes.^a

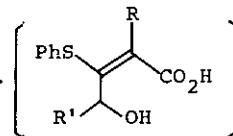
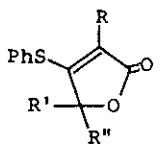
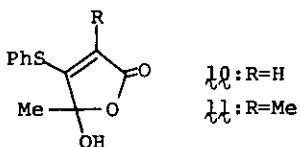
δ or ζ	$R'CHO$		Yield (%) ^b	
			$\delta: R=H$	$\zeta: R=Me$
a	MeCH ₂ CH ₂		98	67 (69) ^{c,d}
b	Me ₂ CH		74	78 (60) ^{c,d}
c	Ph		71	46 (55) ^{c,d}
d	MeCH=CH		80	64 (18) ^{c,d}
e	Me ₂ C=CH(CH ₂) ₂ ^{Me} C=CHCH ₂		48	

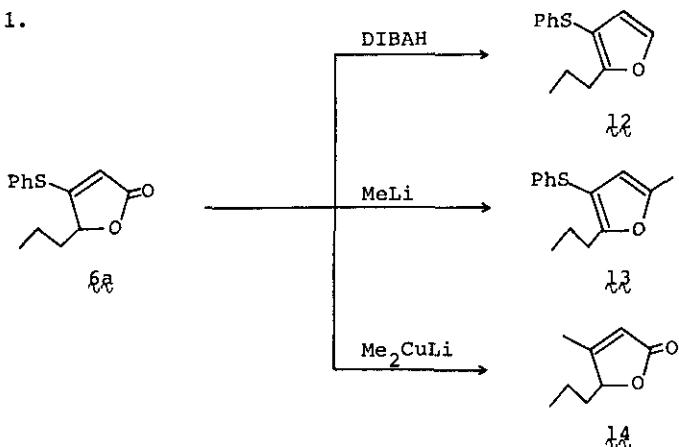
Table 2. Reaction of the dianion δ or ζ with ketones.^a

δ or ζ	$R'COR''$		Yield (%) ^b	
			$\delta: R=H$	$\zeta: R=Me$
a	Me Me(CH ₂) ₄		82	0
b	Me Me		65	16 ^e
c	-(CH ₂) ₅ -		53	36 ^e
d	-(CH ₂) ₆ -		45	10 ^e
e	-(CH ₂) ₃ CH=CH-		45	0

a) Ca. 1 mmol of δ or ζ was employed. b) Isolated yield of pure product. c) Yield in parenthesis is from the ester monoanion δ . See Ref. 1. d) According to inverse addition procedure at -80~60°C. e) Reaction was conducted at room temperature for 2 h.

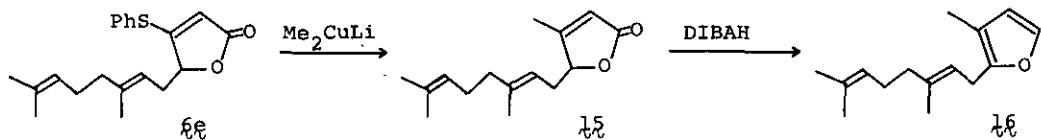


Scheme 1.



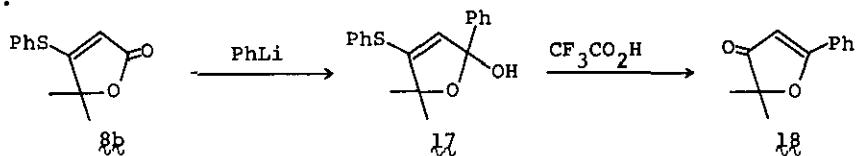
(Baribari).^{7,8} The furanone $6e$, derived from the reaction of the dianion 4 with homogeranylaldehyde, underwent smoothly the conjugate addition of lithium dimethylcuprate at -80°C to give a 70% yield of the sulfur-free furanone 15 , which is transformed by DIBAH reduction at -80°C to sesquirose furan (16) in 69% yield, identical with natural material spectroscopically (ir and nmr) (Scheme 2).

Scheme 2.



Bullatenone (18) is the 3-furanone derivative isolated from the blistered-leaf myrtle Myrtus bullata,^{9,10} and already four syntheses have been reported.^{10,11} Reaction of the furanone $8b$ at -90°C with phenyllithium gave the phenylated half-acetal 17 in 62% yield. Hydrolysis of 17 with trifluoroacetic acid in chloroform at room temperature furnished bullatenone (18) in 51% yield, identical with a sample of synthetic material by Smith and Jerris spectroscopically (ir and nmr) (Scheme 3).

Scheme 3.



ACKNOWLEDGEMENT We thank Professor N. Hayashi for identification of sesquirose furan and Professor A. B. Smith, III for bullatenone. This work supported partially by Grants-in-Aid for Scientific Research (No. 464171 for HH) and for Co-operative Research (No. 434027 for HU) from the Ministry of Education, Science, and Culture of Japan.

REFERENCES

- 1) K. Isobe, M. Fuse, H. Kosugi, H. Hagiwara, and H. Uda, Chem. Letters, 1979, 785.
- 2) R. R. Schmidt and J. Talbiersky, Angew. Chem., 1978, 90, 220; Angew. Chem. Int. Ed. Engl., 1978, 17, 204.
- 3) Mp 124-126°C (lit. mp 127-128°C). F. Montanari and A. Negrini, Boll. sci. fac. chim. ind. Bologna, 1956, 14, 71; Chem. Abstr., 1957, 51, 5695f.
- 4) Mp 131-132°C (lit. mp 132°C). L. Legrand and N. Lozac'h, Bull. soc. chim. France, 1958, 953. Prepared by alkaline hydrolysis of the methyl ester. The stereochemistry of the methyl ester has been determined by us. See Ref.1.
- 5) All products were characterized by combustion analysis or mass spectroscopy as well as by ir and ¹Hnmr spectroscopy.
- 6) H. Minato and T. Nagasaki, J. Chem. Soc. (C), 1966, 1866; 1968, 621; S. W. Pelletier, Z. Djarmati, S. D. Lajšić, I. V. Nićović, and D. T. C. Yang, Tetrahedron, 1975, 31, 1659.
- 7) N. Hayashi, H. Komae, S. Eguchi, M. Nakayama, S. Hayashi, and T. Sakao, Chem. and Ind., 1972, 572.
- 8) Recently, sesquirose furan has been synthesized. H. Kotake, K. Inomata, H. Kinoshita, S. Aoyama, and Y. Sakamoto, Heterocycles, 1978, 10, 105.
- 9) C. W. Brandt, W. I. Taylor, and B. R. Thomas, J. Chem. Soc., 1954, 3245.
- 10) W. Parker, R. A. Raphael, and D. I. Wilkinson, J. Chem. Soc., 1958, 3871.
- 11) A. Takeda, S. Tsuboi, and T. Sakai, Chem. Letters, 1973, 425; J. E. Baldwin, R. C. Thomas, L. I. Kruse, and L. Silberman, J. Org. Chem., 1977, 42, 3846; A. B. Smith, III and P. J. Jerris, Synth. Commun., 1978, 8, 421.

Received, 13th June, 1980