Tetrahedron Letters No. 30, pp 2607 - 2610, 1974. Pergamon Press. Printed in Great Britain.

NOVEL REACTIONS IN THE PREPARATION OF ALKYLIDENE-2,3-DIHYDROFURANS

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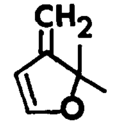
(Received in USA 9 April 1974; received in UK for publication 17 June 1974)

In the course of our recent investigations of potential rearrangement reactions related to the methylideneoxirane to cyclopropanone transformation,[1] we have had to develop methods for preparation of alkylidene-2,3-dihydrofurans of general structure 1. We would like to report here the observation of an abnormal reaction which leads to the formation of a stable derivative of 1 and offers the potential of being a general route to this sparsely studied series of compounds.[2] In addition, the results of a more rational synthetic entry into this series of compounds, involving reaction of the 2,3-dihydrofuranone 2, are reported. Specifically, 2,2-dimethyl-3-(benzoylformyl)-methylidene-5-phenyl-2,3-dihydrofuran (3)[3] has been synthesized by a modification of the reaction conditions used previously for preparation of bullatenone (2).[4] Also, we have successfully prepared and partially characterized the extremely labile 2,2-dimethyl-3-methylene-5-phenyl-2,3-dihydrofuran 4, obtained from 2 and methyl lithium, and have observed a transient dimeric intermediate in pathways for decomposition of 4.



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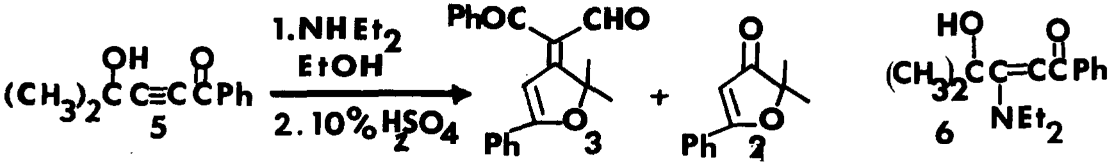
1-Phenyl-4-methyl-4-hydroxypent-2-ene-1-one (5)[6], when reacted with 0.5 equivalents of diethylamine in abs ethanol, followed by treatment with 10% aqueous sulfuric acid, yielded a mixture of the expected furanone 2[5] (29.7%) along with the alkylidenedihydrofuran 3[7] (34.4%). The structure of the novel dihydrofuran derivative was arrived at by a judicious utilization of an accumulation of spectral and analytical data.

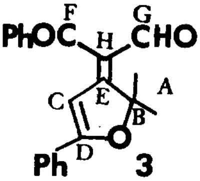


Microanalysis along with the mass spectrometrically derived molecular weight indicated that the formed alkylidenefuran had a molecular formula of $C_{21}H_{18}O_3$[8] and, thus, corresponded to a product of a reaction involving two molecules of acetylene 5 with loss of an acetone molecule. The proton nmr ($CDCl_3$) of this material displayed a 6H singlet at δ 1.98 (equivalent C-2 methyls), an 8H multiplet centered at δ 7.25 and a 2H multiplet at δ 8.06 (two phenyls with one being benzoyl), and 1H singlet at δ 8.28 (C-3 vinyl), and a 1H singlet at δ 10.55 (aldehyde). The infrared spectrum ($CHCl_3$ and CS_2) serves to strengthen the structural assignment of 3; major bands appear at 2755 (aldehyde C-H), 1660 (conjugated dienal C=O), 1645 (conjugated aryl dienone C=O), 1565 and 1538 cm^{-1} (C=C of conjugated dienone). Further support for the presence of the crossed conjugated diendione chromophore is found in the uv spectrum of 3 which displays (95% ethanol) maxima at 367 nm (23,800) and 246 nm (14,300). The mass spectrum contains a fragmentation pattern with major peaks at m/e 318 (P, 36%), 317 (-H, 36%), 303 ($-CH_3$, 28%), 289 (-CHO, 33%), 275 ($-CH_3CHCH_2$, 10%), 213 (-PhCO, 13%) and 105 (PhCO, 100%).

More definitive proof of the alkylidenedihydrofuran structure for 3 comes from C-13 nmr spectral data. In Table I are summaries of the decoupled spectra of 3 ($CDCl_3$) and that of the model bullatenone (2). Characteristic resonances are found at 186 ppm for the aldehyde carbonyl and at 24, 96, 111 and 180 ppm for carbons at the positions assigned on the basis of comparison with the known 2.

This abnormal and novel reaction of acetylene 5 to produce the substituted alkylidenedihydrofuran 3 appears explainable in terms of a mechanism which involves the intermediacy of the enamine 6. In the bullatenone forming reaction, 6 survives until aqueous acid treatment which catalyzes dehydrative cyclization and hydrolysis. However, when excess acetylene 5 is present, condensation with the formed enamine occurs to yield an extended dienamine which then cyclizes and cleaves to the dihydrofuran 3 upon acid treatment.[9]

Table I. C-13 NMR Spectral Data of the Alkylidenedihydrofuran 3 and 4, and Bullatenone 2.



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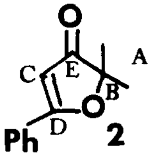

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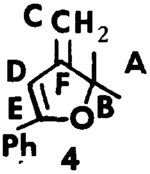

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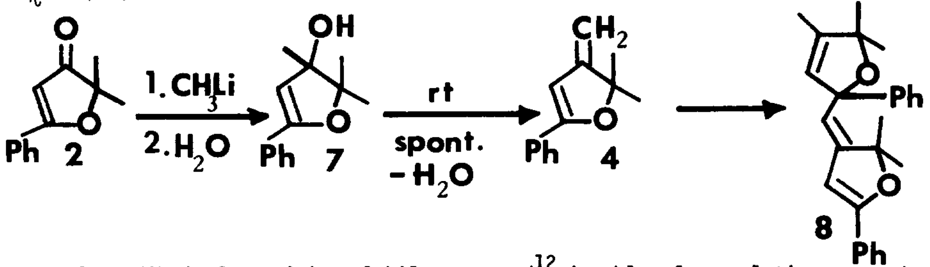
Carbon	Chem. Shift (ppm rel tms)	Mult.	Carbon	Chem. Shift (ppm rel tms)	Mult.	Carbon	Chem. Shift (ppm rel tms)	Mult.
A	24	q	A	23	q	A	28	q
B	96	s	B	89	s	B	88	s
C	111	d	C	99	d	C	95	t
D	180	s	D	183	s	D	100	d
E	161	s	E	206	s	E	158	s
aryls	139-128	-	aryls	133-127	-	F	160	s
F	190	s	-	--	-	aryls	125-131	-
G	186	d	-	--	-	-	--	-
H	175	s	-	--	-	-	--	-

Treatment of 2 with methyl lithium (1:2 molar ratio in ether) followed by normal aqueous work-up gave, after solvent concentration, a light yellow oil whose characterization as the hydroxyfuran 7 was made on the basis of the spectral data (ir, 3360 cm^{-1} (br); nmr, three methyl singlets, styryl aryl and vinyl and hydroxyl resonances). On standing for short periods (nearly complete after 1.5 hr) in $CHCl_3$ or neat, 7 disappears with simultaneous liberation of water and formation of 2,2-dimethyl-3-methylidene-5-phenyl-2,3-dihydrofuran (4). Characterization[11] of 4 is accomplished on the basis of spectral data. The proton nmr of 4 ($CDCl_3$) is characteristically simple and indicates the presence of two equivalent methyl groups, two nonequivalent vinyl methylene protons, one uncoupled vinyl and five aromatic protons. The position of the vinyl-methylene resonances (δ 4.37 and 4.71) suggests their location at the terminus of a dienol ether chain. The carbon-13 nmr results offer additional strong support; signals with proper multiplicities are seen in the expected approximate regions (see Table I).

The uv of 4 displays a maximum at 320 nm.



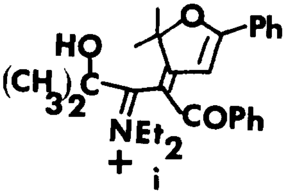
The methylene dihydrofuran 4 is a labile compound[12] in chloroform solution or neat at -10° (*ca.* lifetime of 1 day). Interestingly, its ensuing reaction is reasonably selective and leads to another only partially characterized material.[13] On the basis of limited spectral data and reasonable mechanistic considerations, we propose the dimer 8 as the structure of the intermediate in the polymerizing decomposition of 4.

We have attempted to construct a potentially more stable analog of 4 having methyl substituents at the exocyclic-methylene to block dimerization. However, reaction of isopropyl lithium and the furanone 2 appears to adopt an alternate course involving 1,4-addition and giving a 2-oxacyclopentanone. Attempts to prepare less labile alkylidenedihydrofurans are continuing as is our study of the chemistry of this class of compounds.

Acknowledgement. Grateful appreciation is expressed to the Petroleum Research Fund of the ACS for its initial support of this work and to the Robert A. Welch Foundation for its generous continuing support. Michael Peters would like to thank the Welch Foundation for an undergraduate fellowship.

References

1. J. K. Crandall and W. H. Machleder, *J. Amer. Chem. Soc.*, 90, 7292 (1968).
2. Our search of the literature has uncovered only one preparation of a 2-alkylidene-2,3-dihydrofuran (R. Filler, E. Piasek and L. Mark, *J. Org. Chem.*, 26, 2659 (1961).
3. One of the two diastereomers is formed exclusively. The stereochemistry about the exocyclic π-bond of 3, however, cannot be assigned on the basis of our data.
4. Bullatenone (2) is a natural product previously synthesized by Parker, *et al.*,[5] using acetylene 5 and diethyl amine in equimolar quantities.
5. W. Parker, R. A. Raphael and D. I. Wilkinson, *J. Chem. Soc.*, 3871 (1958).
6. This material was synthesized by the procedure of Parker, *et al.*[5]
7. Separation of the two materials was accomplished by silica gel chromatography. Further purification of 2 was by recrystallization from hexane, yielding a yellow crystalline solid, mp 108-109°; mono-2,4-DNP (by nmr), mp 196-201° decomp.
8. *Anal.* Calcd. for $C_{21}H_{18}O_3$: C, 79.23; H, 5.70. Found: C, 79.03; H, 5.65.
9. The cleavage of the proposed penultimate iminium salt i to 3 appears to have little literature precedence. However, loss of acetone from i would generate the highly stabilized carbene ii whose ensuing reaction with water would lead to 3. A possible analogous reaction is found in studies of Walborski[10] of the conversion of silyl amino alcohols to aldehydes.



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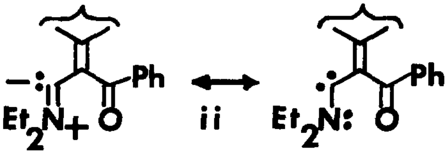

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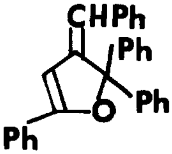
10. G. E. Niznik, W. H. Morrison and H. M. Walborsky, J. Org. Chem., 39, 600 (1974).

11. No attempt has been made to obtain analyses of the alcohol 7, methylene furan 4 or dimer 8.

12. The only other similarly structured methylidenedihydrofuran we have been able to find described in the literature is the tetraphenyl analog iii.[2] No note of abnormal instability of this material is made even though pathways for formation of a dimer similar to 8 are possible. This suggests that steric bulk at the methylidene carbon will increase the stability of this class of compounds.

13. When this reaction is followed by proton-nmr ($CDCl_3$ at r.t.), the resonances at δ 1.40, 4.37, 4.71 and 5.97 collapse at the same rate as appearance of signals at δ 1.33, 1.39, 1.45, 1.73, 5.05 and 5.60. The formed product can be isolated by rapid alumina chromatography, the semi-pure material obtained in this way is crystalline, mp 87-91°.



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