ARSONIOSILYLATION OF α,β -UNSATURATED CARBONYL COMPOUNDS. DIRECT SYNTHESIS OF FURANS FROM α,β -ENALS

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Summary : Arsoniosilylation reactions of α,β -enones and α,β -enals have been studied by the low temperature ¹H-NMR spectroscopy and direct synthesis of furans from α,β -enals via arsoniosilylation is discribed.

It has been previously reported that the phosphoniosilylation of α , β -unsaturated carbonyl compounds has proved to be an efficient method to generate synthetically important β -acyl vinyl or homoenolate anion equivalents.^{1,2} As the extension of this work, we have investigated the arsoniosilylation of α , β -unsaturated carbonyl compounds. When 2-cyclohexen-1-one was treated with triphenylarsine and trimethylsilyl triflate (TMSOTf) in dichloromethane at room temperature, no reaction took place. The result seems to be reasonable in view of the low nucleophilic nature of triphenylarsine, as compared with triphenylphosphine.³ Furthermore, it has been reported that attempts to obtain the arsonium salt from acrolein, triphenylarsine and hydrogen bromide were unsuccessful and the corresponding arsonium salt was prepared in an indirect manner.⁴



We have found that arsoniosilylation of α,β -enones occurred at low temperature via the 1,4-addition mode and the reaction was essentially reversible, depending upon the reaction temperature. The TMSOTf promoted addition of triphenylarsine to α,β -enones was carefully studied using the low temperature ¹H-NMR spectroscopy. When 4-hexen-3-one was reacted with 1.2 equiv of triphenylarsine and TMSOTf in d₈-THF at low temperatures, several noteworthy features have been found. First, the reaction went to approximately 90% and 50% completion at -80 °C and -40 °C, respectively. Second, the present reaction occurred via the 1,4-addition mode. Third, the reaction afforded a 3:2 ratio of *Z*- and *E*-isomer at -40 °C, whereas a

6:1 ratio of Z- and *E*-isomer was obtained at -80 °C.⁵ Finally, when arsonium salts in d_8 -THF at -80 °C was allowed to warm to room temperature, 4-hexen-3-one was regenerated, demonstrating the reversibility of the arsoniosilylation reaction. Furthermore, it is noteworthy that *E*-isomer was faster than *Z*-isomer in generating the starting enone. The similar result was obtained with 2-cyclohexen-1-one.

The arsoniosilylation of α , β -enals went to completion even at -20 °C via the 1,4-addition mode but it led to decomposition at room temperature. For instance, the arsoniosilylation of crotonaldehyde afforded a 3:1 ratio of Z- and E-isomer at -20 °C and 3:2 ratio of Z- and E-isomer at -50 °C.⁶

Generation of arsonium ylides gave initially discouraging results and it was turned out to be dependent on the nature of trialkylsilyl enol ethers and bases.⁷ After much experimentation, it was found that the use of triisopropylsilyl (TIPS) triflate and potassium bis(trimethylsilyl)amide gave the best results. The arsonium ylides bearing trimethylsilyl or triethylsilyl enol ether group were decomposed almost instantly, which were determined by the reaction with aldehydes.⁸ Attempts to generate arsonium ylides with TIPS group via arsoniosilylation of α,β -enones were unsuccessful due to the instability of arsonium ylides and the formation of diene enol ethers to some extent.⁹



We have studied the possibility of the use of the arsonium ylide 2 as α,β -formyl vinyl anion equivalent,⁴ as shown in scheme 1. Reaction of 2 (R=Me) with hydrocinnamaldehyde in tetrahydrofuran at - 78 °C for 10 min followed by quenching with aqueous sodium bicarbonate afforded γ -hydroxyenal 4a (R=Me, R'=CH₂CH₂Ph)^{10,11} in 40% yield, indicating the intermediacy of the epoxide 3.¹² The similar types of the epoxide 3 such as 3,4-epoxy enol ethers,¹³ enol thioethers¹⁴ and acetals¹⁵ under thermal or acidic conditions were known to be converted into furan derivatives.¹⁶ The reaction of 2 (R=n-C₆H₁₃) with benzaldehyde under the same conditions gave 22% of (3-benzoyl)nonyl aldehyde triisopropylsilyl enol ether along with 23% of *E*-3-(α hydroxybenzyl)-2-nonenal and 10% of 3-n-hexyl-2-phenylfuran. Apparently, the TIPS enol ether would be produced by the rearrangement of the epoxide ring¹⁷ and this problem was solved by

α,β-Enal	Aldehyde	Product	Yield (%)	α,β-Enal	Aldehyde	Product	Yield (%)
H	PhCHO) 60	С Ч С Н	С , Сно) 5	53
Me	Ph~~CHC	P Ph	40	C ₄ ng	С-сно			51
	ł PhCHO	C ₆ H ₁₃	85		p-Cl-PhCHO	p-Cl-Ph	Me 5	55
	Ph CHC	C ₆ H ₁₃	62	Me	С-сно		Me 5	54
C	CHO	C ₆ H ₁₃	75	C	C4H9 CHO	Me C4H9	Me 7	7

Table 1. Synthesis of Furans from α,β -Enals via Arsoniosilylation

quenching with tetra-n-butylammonium fluoride (TBAF). Treatment with TBAF afforded the lactol 5 as a major product together with a small amount of 4a and 6, suggesting that the isomerization of 4a into 4b took place under the present conditions. Thus, treatment of a mixture of 4a, 5 and 6 with 10% hydrochloric acid at room temperature for 20 min gave 3-n-hexyl-2-phenylfuran in 85% yield. Table 1 summarizes our experimental results and shows the scope and applicability of the present method. The method works well with α , β -disubstituted enal and with both aromatic and aliphatic aldehydes.

A typical procedure is illustrated as follows. To a solution of triphenylarsine (215 mg, 0.70 mmol) and trans-2-nonenal (97 mg, 0.69 mmol) in tetrahydrofuran (4 ml) was added triisopropylsilyl triflate (214 mg, 0.70 mmol) at - 78 °C. After being stirred at -78 °C for 30 min, 1.52 ml of 0.5 M potassium bis(trimethylsilyl)amide was added dropwise to give a black ylide solution. The reaction mixture was stirred for 20 min at -78 °C and treated with benzaldehyde (87 mg, 0.82 mmol) at -78 °C. After being stirred at -78 °C for 1 hr, the resulting solution was treated with 0.83 ml of 1 M tetra-n-butylammonium fluoride, warmed to room temperature over 1hr, and then quenched using 2 ml of 10% hydrochloric acid. The reaction mixture was stirred at room temperature for 20 min and followed by dilution with diethyl ether (30 ml). The organic layer was washed with saturated sodium bicarbonate (8 ml) and dried. Removal of solvent and purification on silica gel gave 3-n-hexyl-2-phenylfuran (134 mg, 85%).

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- ¹H-NMR(300MHz, d₈-THF, -80 °C) δ 0.14(trans) (s,1.29H), 0.34(cis) (s, 7.71H), 0.67(trans) (t, J=7.07 Hz, 0.43H), 0.86(cis) (t, J=7.16 Hz, 2.57H), 1.49(trans) (d, J=7.05 Hz, 0.43H) 1.58(cis) (d, J=7.0 Hz, 2.57H), 2.05(cis) (m, 1.71H), 2.20(trans) (m, 0.29H), 4.43(cis) (d, J=10.4 Hz, 0.86H), 4.50(trans) (m, 0.16H), 5.41(cis) (m, 0.86H), 5.44(trans) (m, 0.16H), 7.35 (m, 15H).
- ¹H-NMR(300MHz, CDCl₃, -50 °C) δ 0.19(trans) (s, 3.6H), 0.25(cis) (s, 5.4H), 1.59(trans) (d, J=6.8 Hz, 1.2H), 1.66(cis) (d, J=7.0 Hz, 1.8H), 4.43(cis) (d-d, J=5.7 Hz, 10.8 Hz, 0.6H), 4.75(trans) (t, J=11.3 Hz, 0.4H), 5.07(cis) (m, 0.6H), 5.26(trans) (m, 0.4H), 7.36 (m, 15H).
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- 8. The reactions with several aldehydes did not give any of 4 and 5. Furthermore, the yellow color of the ylide at 78°C, generated by treatment with KN(SiMe₃)₂, was instantly disappeared.
- 9. In the case of 4-hexen-3-one, 22% of 3-triisopropylsilyloxy-2,4-hexadiene was isolated.
- 10. The structure of γ-hydroxyenal 4a was determined as follows. The ¹H-NMR spectral data of the diol, the reduction product of 4a, was different from that of the Z-diol, which was obtained from 6 by the known procedure (Rice, K. C.; Dyer, J. R. J. Heterocycl. Chem. 1975,12, 1325.). 4a could be converted into the corresponding furan under acidic and basic conditions.
- 11. In addition to 4a, 5 was formed to an observable extent (< 10%). However, it is unclear whether 4b was directly produced from 3 or 4a was isomerized to 4b under the present conditions.
- 12. We were unable to dectect the formation of the epoxide 3 due to its instability.
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