Tetrahedron Letters Vol. 21, pp 4417 - 4420
©Pergamon Press Ltd. 1980. Printed in Great Britain.

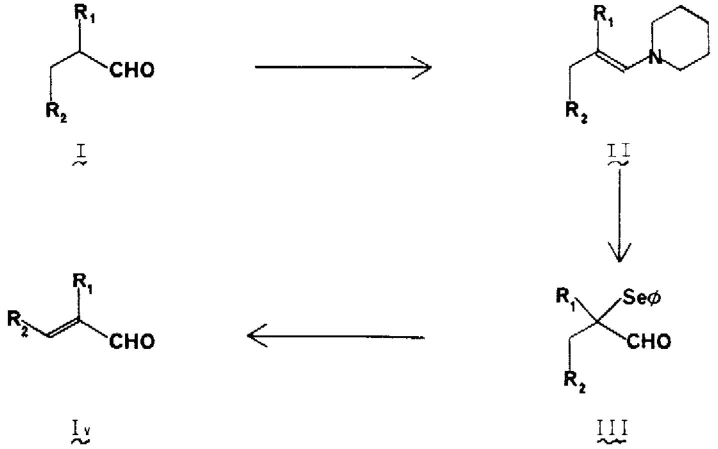
0040-4039/80/1108-4417$02.00/0

A MILD OXIDATION OF ALDEHYDES TO α,β-UNSATURATED ALDEHYDES

David R. Williams*[1] and Kiyoshi Nishitani
Dept. of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106
and
Department of Chemistry, Indiana University, Bloomington, Indiana 47405

Summary: Phenylselenenyl chloride reacts with enamines at -110° C to give α-phenylselenoaldehydes, and oxidative elimination yields α,β-unsaturated aldehydes.

In connection with a number of synthetic problems currently underway in our laboratories, an efficient and mild process to oxidatively transform an aldehyde R-CH_2-CH_2-CHO to its corresponding α,β-unsaturated isomer R-CH=CH-CHO was necessary. Moreover, we required reagents and conditions sufficiently selective to distinguish between functional groups in complex molecules. This note describes an expeditious method for effecting this oxidation as outlined below.[2]



Results of a number of aldehyde substrates chosen to illustrate the process are shown in Table I.[3] Enamine formation was conveniently accomplished using either of two procedures: (A) piperidine (1.1 mmol) was added to the aldehyde (1.0 mmol) in benzene solution and the mixture was stirred over molecular sieves (3A) (2-5 hr),[4] or (B) a benzene solution of aldehyde (1.0 mmol) and piperidine (1.1 mmol) was heated at reflux with a moisture trap (3-5 hr).[5]

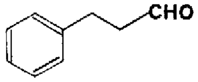
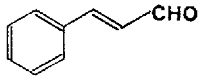
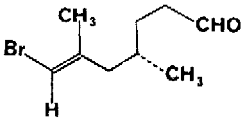
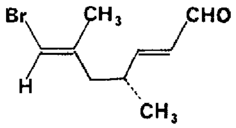
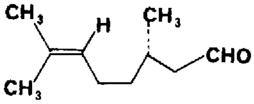
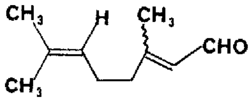
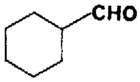
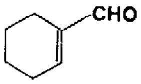
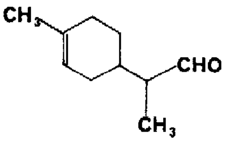
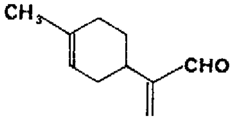
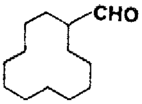
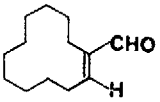
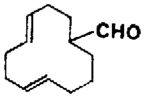
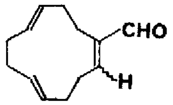
Phenylselenenylation occurred almost instantaneously when a solution of phenylselenenyl chloride in anhydrous tetrahydrofuran was added over 5 minutes to the crude enamines in THF at -110° C (ether-liquid nitrogen bath) under argon.[6] The mixture was allowed to warm to -80° C over 15 minutes, then quenched by addition of water (∿2 ml) and ether (∿10 ml), and warmed to room temperature with continued stirring for an additional 2-3 hrs to complete the hydrolysis and afford the crude α-phenylselenoaldehydes III. Isolation by filtration chromatography through silica gel gave 75-90% yields of pure III.

The formation of α-phenylselenoaldehydes has previously been achieved by formylation of α-lithioselenides,[7] and by direct selenenylation of simple aldehydes.[8] The latter process requires stirring starting aldehyde with phenylselenenyl chloride at room temperature for prolonged periods, and in our cases, led to unacceptable mixtures of products resulting from competing reactivity of olefinic residues. The sulfenylation of aldehyde enolates at low temperature has been reported;[9] however, adaptation of these conditions for reaction with phenylselenenyl chloride generally gave poorer yields of III. Likewise, anions derived from the corresponding imines also led to mixtures. Notably enol acetates and ethers have been recognized as excellent substrates for selenenyl reagents (RSe-X), but investigators have concentrated their efforts on utilizing ketone precursors.[10,11]

Finally, oxidative elimination to the desired α,β-unsaturated products IV was accomplished in the usual manner using either meta-chloroperbenzoic acid (method A) or sodium periodate (method B) giving overall yields of 50-80%. The crude selenides III were, in practice, carried forward without purification. Oxidation with buffered solutions of hydrogen peroxide led to mixtures of IV and the corresponding α,β-unsaturated carboxylic acids. Generally the procedure is more successful with α-disubstituted aldehydes, and, in fact, simple cases such as n-heptanal formed the intermediate selenide III in good yield, but attempted oxidations in buffered media repeatedly led to considerable decomposition, apparently resulting from the ease of available self-condensation reactions.

The selenoaldehydes III are also excellent precursors to β-hydroxy selenides which are conveniently transformed into vinyl selenides, epoxides, olefins, and allylic alcohols.[12] For example, the optically active aldehyde V was directly reduced with lithium tri-t-butoxyaluminum hydride (1.1 equivalent, -78° C, 1 hr) in tetrahydrofuran (99.4%), and oxidative elimination with sodium periodate (2 equivalents, methanolic aqueous THF at 25° C) gave only E-(trans)-allylic alcohol VI after chromatography on silica (76.8%).[13] The overall result allowed selective introduction of the carbon double bond while avoiding possible epimerization of the chiral methyl substituent.

TABLE I

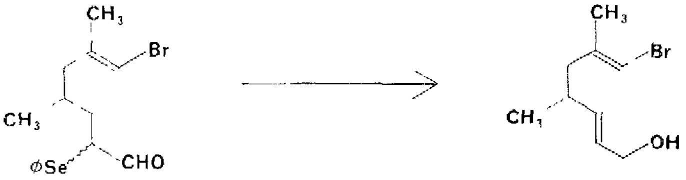
Starting Aldehyde	Enamine Method (Yield)	Selenide III	Oxidation Method	Product Aldehyde	Overall Yield[a]
	A (99%)		B		(68%)
	A (91%)	94%	A		(60%)
	A (99%)	80%	A		(44%)[b]
	B (99%)	82%	B		(67%)
	B (97%)		B		(50%)
	B (99%)		A		(80%)[c]
	B (93%)	74%	A		(76%)[d]

(a) Isolated yields after silica gel chromatography to remove diphenyl diselenide and highly polar by-products.

(b) Ratio of E:Z-isomers is 1:1.5.

(c) The crude 1-cyclododecenecarboxaldehyde shows E:Z ratio of 1:2, and purification by chromatography results in complete isomerization to the E-isomer. (NMR indicates chemical shifts of δ 9.37 and 6.50 and δ 10.17 and 6.61 for -C$\underline{H}$O and vinylic -$\underline{H}$ for E- and Z-isomers, respectively, in $CDCl_3$ solution.)

(d) Crude cyclododecatrienecarboxaldehyde gave E- and Z-isomers in 1:2 ratio (NMR (CDCl3)). δ 9.40 and 10.03 for -C$\underline{H}$O, respectively) for E and Z-compounds, and chromatography resulted in a 1:1 mixture.



V VI

Acknowledgement: The authors wish to thank the Research Corporation and the National Institute of Health for their generous support of our work.

References

1. Present address, Indiana University, Department of Chemistry, Bloomington, Indiana 47405.
2. The referee's comments are included to underscore the importance of our methodology: "α,β-Unsaturated aldehydes are extremely useful synthetic substrates and there presently exist relatively few methods for performing the reported conversion of aldehydes to α,β-unsaturated aldehydes. In fact, most α,β-unsaturated aldehydes are synthesized via condensation reactions of one sort or another. Since the requisite starting aldehydes are normally readily available, this present methodology makes accessible α,β-unsaturated aldehydes that would be difficult to prepare by other methods. Furthermore, the method is extremely mild as compared to the various condensation methods."
3. In each case purified products were characterized by infrared, nuclear magnetic resonance, and mass spectral analysis, the results of which were fully in accord with assigned structures.
4. K. Taguchi and F.H. Westheimer, J. Org. Chem., 36, 1570 (1971).
5. F.E. Heyl and M.F. Herr, J. Amer. Chem. Soc., 75, 1918 (1953); and G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, J. Amer. Chem. Soc., 85, 207 (1963).
6. Phenylselenenylation at -78°C usually reduced overall yields of final products by approximately 20%.
7. J.N. Denis, W. Dumont and A. Krief, Tetrahedron Letters, 453 (1976).
8. K.B. Sharpless, R.F. Lauer, and A.Y. Teranishi, J. Amer. Chem. Soc., 95, 6137 (1973).
9. D. Seebach and M. Teschner, Chem. Ber., 109, 1601 (1976).
10. H.J. Reich, J.M. Renga, and I.L. Reich, J. Amer. Chem. Soc., 97, 5435 (1975); and D.L.J. Clive, Chem. Comm., 695 (1973).
11. Electrolysis of ketones with diphenyl diselenide has recently been reported; S. Torii, K. Uneyama, and K. Handa, Tetrahedron Letters, 1863 (1980).
12. H.J. Reich, Accts. of Chem. Res., 12, 22 (1979); and D.L. Clive, Tetrahedron, 34, 1049 (1978).
13. The *syn*-elimination proceeds with complete regiospecificity, and, in this case, as expected, provides only the *E*-geometry, K.B. Sharpless and R.F. Lauer, J. Amer. Chem. Soc., 95, 2697 (1973).

(Received in USA 18 July 1980)