respectively. This method (as well as the extensions described in the subsequent articles) complements the synthesis described by Corey and Seebach[12] which adds one carbon in the conversion of alkyl halides to their corresponding aldehydes.[13] Further nucleophilic reactions of the anion **5** (A = H, Ph) are currently being examined with other substrates. Reactions, in high yield, have been observed using epoxides, esters, nitriles, and acid chlorides which provide a wide variety of alkylated oxazines **2** and in turn significantly increase the scope of this aldehyde synthesis.[14]

Table I. Formation of Aldehydes from Dihydro-1,3-oxazines[a]

RX	% 2[b]	% 3[b]	% 4 (over-all)	2,4-DNP mp, °C (lit.)
		A = H		
Methyl iodide	99	99	60	149–150 (142–148)[c]
n-Propyl iodide	98	90	65	102–104 (106)[c]
n-Butyl bromide	95	100	67	102–103 (104)[c]
Allyl bromide	90	90	53	116–118 (120)[c]
2-Bromoethyl ether	93	98	54	88–89 (88–89)[d]
Isopropyl iodide	99	90	47	121–122 (121–122)[c]
Benzyl bromide	88	100	54	153–154 (144–145)[c]
3-Bromocyclohexene	89	90	50	92–94 (97)[e]
		A = Ph		
Methyl iodide	91	96	70	137–138 (135)[f]
n-Propyl bromide	92	98	69	112–113 (115–116)[g]

[a] Deuterated aldehydes were obtained in comparable yields and were checked for isotopic purity using nmr. [b] Contained 95+% pure material. [c] I. Heilbron, "Dictionary of Organic Compounds," Oxford Press, New York, N. Y., 1965. [d] H. Adkins and G. Krsek, *J. Am. Chem. Soc.*, **71**, 3051 (1949). [e] C. W. Whitehead, *et al.*, *J. Org. Chem.*, **26**, 2814 (1961). [f] C. F. H. Allen and J. Van Allen, "Organic Syntheses," Coll. Vol. III, John Wiley & Sons, Inc., New York, N. Y., 1955. [g] Semicarbazone derivative, Beilstein, "Handbuch der Organische Chemie," Vol. 7, Julius Springer, Berlin, 1925, p 329.

Acknowledgments. The authors wish to acknowledge partial financial assistance from the National Institutes of Health (RG-06248-09).

(12) E. J. Corey and D. Seebach, *Angew. Chem. Intern. Ed. Engl.*, **4**, 1075, 1077 (1966).

(13) For recent reviews on other aldehyde syntheses see (a) J. Carnduff, *Quart. Rev.* (London), **20**, 169 (1966); (b) S. Patai, "Chemistry of the Carbonyl Group," John Wiley & Sons, Inc., New York, N. Y., 1966.

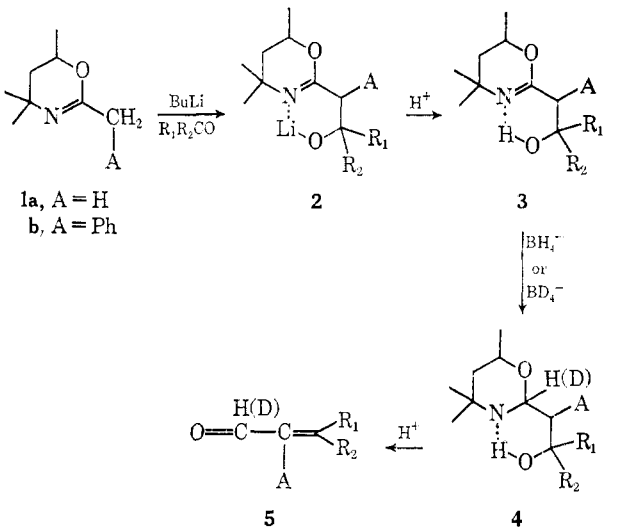
(14) The authors will provide complete experimental details to anyone requesting them.

A. I. Meyers, Aiko Nabeya
H. Wayne Adickes, Ieva Ruks Politzer
Department of Chemistry
Louisiana State University in New Orleans
New Orleans, Louisiana 70122
Received October 9, 1968

Aldehydes from Dihydro-1,3-oxazines. II. A New Synthesis of α,β-Unsaturated Aldehydes and Their C-1 Deuterated Derivatives

Sir:

It was previously shown[1] that the lithio salts of dihydro-1,3-oxazines (**1a,b**) are excellent nucleophiles and react efficiently with alkyl halides producing precursors to a variety of aliphatic aldehydes. We now wish to describe the reaction of these oxazine anions with a host of carbonyl compounds, giving rise to good yields of the adducts, **2**, which are useful precursors to conjugated aldehydes. Addition of aldehydes or ketones to the THF solution of the lithio salt of **1** (**a** or **b**) at −78° followed by hydrolytic work-up produces near quantitative yields of the oxazinyl alcohols, **3** (Table I). The crude adducts thus obtained are suitable for borohydride or borodeuteride reduction, as previously described,[1] leading to the tetrahydro-1,3-oxazines, **4**. Cleavage of **4** with aqueous oxalic acid gives 48–69% over-all yields of α,β-unsaturated aldehydes.[2] The complete scheme is therefore a three-step operation requiring no purification of intermediates



and can be accomplished, as in the case of aliphatic aldehydes,[1] in approximately 1.5 days from commercially available starting materials. In cases where the oxazinyl alcohols, **3**, were solids they could be readily purified by crystallization. However, if these products are liquids attempted purification by distillation results in reversal to the carbonyl compound and **1**.[3] The thermal instability of **3** is of no serious consequence in this synthesis since the "crude" material is formed in high yield and any impurities present do not interfere with the subsequent reduction step to **4**.

The alkylation of the anions **1** with ketones forming β,β-disubstituted acroleins is particularly valuable in this scheme since the aldehyde ylide reagents do not react with ketones.[4,5] Comparison of this method with that recently reported by Wittig indicates that the over-all yields[6] of unsaturated aldehydes appear to be comparable. The advantages of the present technique may be summarized as follows: (a) it permits labeling of the C-1 position with deuterium or tritium; (b) it starts with stable, commercially available materials;

(1) A. I. Meyers, A. Nabeya, H. W. Adickes, and I. R. Politzer, *J. Am. Chem. Soc.*, **91**, 763 (1969).

(2) The procedures mentioned in ref 1 are adaptable to the preparation of α,β-unsaturated aldehydes. Over-all yields are not necessarily optimum since many reactions were performed only once and on a 20–50-mmole scale.

(3) This behavior is not unexpected since aldol-type products are well known to reverse under the influence of heat and base. Note that **3** has a built-in basic site which obviously facilitates reversal to starting materials. The intramolecular hydrogen bonding in **3** and **4** was confirmed by infrared and nmr techniques.

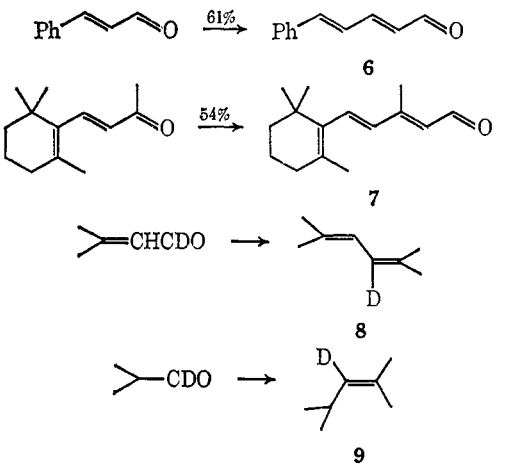
(4) A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., 1966, pp 152, 205.

Table I. Formation of α,β-Unsaturated Aldehydes from Dihydro-1,3-oxazines[a]

Carbonyl compound	R_1	R_2	% crude **3**	% crude **4**	% **5** over-all	2,4-DNP mp, °C (lit.)
		A = H				
n-Butyraldehyde	H	*n*-Butyl	95	90	61	144–145 (147)[b]
n-Heptaldehyde	H	*n*-Heptyl	87	90	48	124–125 (126)[b]
Benzaldehyde	H	Phenyl	97	99	64	200–201 (201)[b]
p-Tolualdehyde	H	*p*-Tolyl	99	99	57	40–42[c] (42)[b]
p-Anisaldehyde	H	*p*-Anisyl	100	98	61	58[c] (59)[b]
3,4-Dimethoxybenzaldehyde	H	3,4-Dimethoxyphenyl	93	88	54	83–84[d] (83[b])
Acetone	CH_3	CH_3	93	100	50	221–222[e] (222)[b]
Diethyl ketone	C_2H_5	C_2H_5	96	98	62	169[e] (169)[f]
Cyclohexanone	Cyclohexylidene		88	95	53	193–195[e] (198–200)[g]
Cyclopentanone	Cyclopentylidene		96	93	63	180–181 (176–177)[h]
3-Cholestanone	3-Cholestylidene		90	95	69	110–112[e,i,k]
Acetophenone	CH_3	Phenyl	100	85	50[l]	200–202 (208)[b]
p-Bromoacetophenone	CH_3	*p*-Bromophenyl	87	95	55[l]	181–182[i]
2-Acetylnaphthalene	CH_3	2-Naphthyl	92	99	62	217–219[i]
Benzophenone	Phenyl	Phenyl	91	99	62	197–198 (196)[i]
2-Acetylthiophene	CH_3	2-Thienyl	91	96	58[l]	118–126[i]
		A = Ph				
Benzaldehyde	H	Phenyl	99	93	63	239–240 (240–242)[b]
Cyclopentanone	Cyclopentylidene		93	93	54[m]	165–166[i]

[a] Deuterated aldehydes were obtained in comparable yields; crude **3** and **4** were found to be 90–95% pure by nmr and vpc. [b] I. Heilbron, "Dictionary of Organic Compounds," Oxford Press, New York, N. Y., 1965. [c] Melting point of aldehyde. [d] K. Friederich and W. Hartmann, *Ber.*, **94**, 839 (1961). [e] Semicarbazone derivative. [f] J. Cologne and A. Perrot, *Bull. Soc. Chim. France*, 660 (1957). [g] G. Wittig and P. Suchanek, *Tetrahedron Suppl.*, *B*, 347 (1966). [h] G. Saucy, R. Marbert, H. Lindlar, and O. Isler, *Helv. Chim. Acta*, **42**, 1945 (1959). [i] New compound, analytical data were satisfactory. [j] H. Lorenz and R. Wizinger, *Helv. Chim. Acta*, **28**, 600 (1945). [k] A mixture containing 15% of the β,γ-unsaturated isomer. [l] *cis–trans* mixture. [m] Purified by passing through an alumina column (Woelm, Activity I).

(c) it utilizes commercial butyllithium rather than lithium diisopropylamide, which must be prepared from the secondary amine and alkyllithium reagents; (d) it is devoid of any significant side reactions[6] during the hydrolysis to the final product. Other methods of preparing α,β-unsaturated aldehydes have been recently reviewed.[7] Another useful aspect of this method allows a stereospecific two-carbon chain extension of carbonyl compounds using anion **1a**. In this manner, we were able to convert cinnamaldehyde to the *trans*-dienal **6** in 61% over-all yield (mp 37–39°, lit.[8] mp 41–42°) and β-ionone to *trans*-β-ionylideneacetaldehyde (**7**) in 54% over-all yield (2,4-DNP mp 200–202°; lit.[9] mp 198–199°). Both reactions of the anion with conjugated carbonyl compounds proceeded without any detectable evidence of 1,4 addition. It is evident that this method of preparing unsaturated aldehydes may find some use in carotenoid syntheses.[10] The ease with which deuterated aldehydes are produced should also provide an entry into specifically deuterated olefins (**8** and **9**) when this method is coupled with the Wittig and related reactions. Studies are in progress to further extend this synthesis to such systems.



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A. I. Meyers, Aiko Nabeya, H. Wayne Adickes
J. Michael Fitzpatrick, G. Ray Malone, and Ieva Ruks Politzer
Department of Chemistry
Louisiana State University in New Orleans
New Orleans, Louisiana 70122
Received October 9, 1968

(5) A report has appeared [W. Nagata and Y. Hayase, *Tetrahedron Letters*, 4359 (1968)] after this paper was completed describing the use of an imine salt of diethylformylmethyl phosphonate and carbonyl compounds giving good yields of α,β-unsaturated aldehydes. The "two-step" sequence, however, requires two additional somewhat lengthy steps for the preparation of the unstable starting material, diethyl β-(cyclohexylimino)ethyl phosphate

$$(EtO)_2\overset{\overset{O}{\|}}{P}CH{=}CHNHC_6H_{11}$$

(6) G. Wittig and H. Reiff, *Angew. Chem. Intern. Ed. Engl.*, **7**, 7 (1968).
(7) J. Carnduff, *Quart. Rev.* (London), **20**, 169 (1966).
(8) D. Marshall and M. C. Whiting, *J. Chem. Soc.*, 4083 (1956).
(9) I. Heilbron, E. R. H. Jones, M. Julia, and B. C. L. Weedon, *ibid.*, 1827 (1949).
(10) A review on chain extension in carotenes has appeared: O. Isler and P. Schudel, *Advan. Org. Chem.*, **4**, 119 (1963).

Aldehydes from Dihydro-1,3-oxazines. III. A New Synthesis of Cycloalkanecarboxaldehydes

Sir:

The synthetic utility of dihydro-1,3-oxazines (**1**) as precursors to acyclic and unsaturated aldehydes has been described.[1] We wish to add further to the reper-

(1) A. I. Meyers, A. Nabeya, H. W. Adickes, and I. R. Politzer, *J. Am. Chem. Soc.*, **91**, 763 (1969); A. I. Meyers, A. Nabeya, H. W. Adickes, J. M. Fitzpatrick, G. R. Malone, and I. R. Politzer, *ibid.*, **91**, 764 (1969).