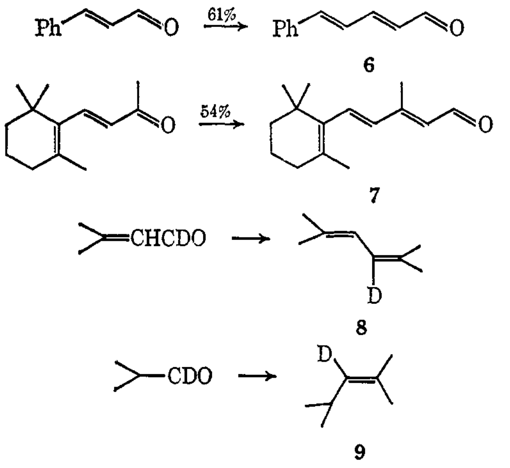
Table I. Formation of α,β-Unsaturated Aldehydes from Dihydro-1,3-oxazines[a]

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[c,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)[j]
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.

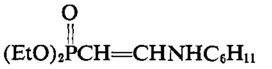


Acknowledgments. The authors wish to acknowledge partial financial assistance from the National Institutes of Health (RG-06248-09).

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).

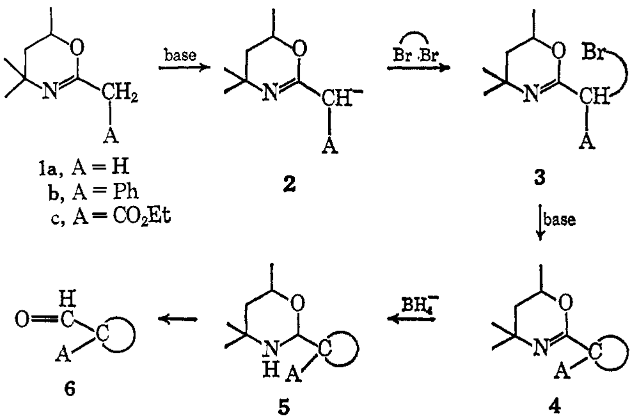
Table I. Formation of Cycloalkanecarboxaldehydes from Dihydro-1,3-oxazines

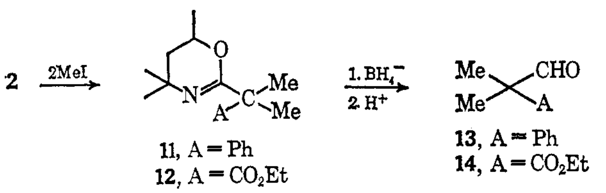
Entry	Dihalide	% **4**[a]	% **5**	**6**	% **6** over-all	2,4-DNP mp, °C
1	1-Bromo-2-chloroethane	85	90	Cyclopropanecarboxaldehyde	69[c]	184–185[h]
2	1,3-Dibromopropane	26[b]	90[b]	Cyclobutanecarboxaldehyde	20[c]	155–157[d]
3	1,4-Dibromobutane	55[b]	95[b]	Cyclopentanecarboxaldehyde	36[c]	153–154[e]
4	1,2-Dibromoethane	99	96	1-Phenylcyclopropanecarboxaldehyde	62	193–195[f]
5	1,3-Dibromopropane	76[b]	92[b]	1-Phenylcyclobutanecarboxaldehyde	49	156–158[f]
6	1,4-Dibromobutane	98	91	1-Phenylcyclopentanecarboxaldehyde	60	166–168[f]
7	1,4-Dibromobutane	90	95	Ethyl 1-formylcyclopentanecarboxylic acid	72	134–135[g]

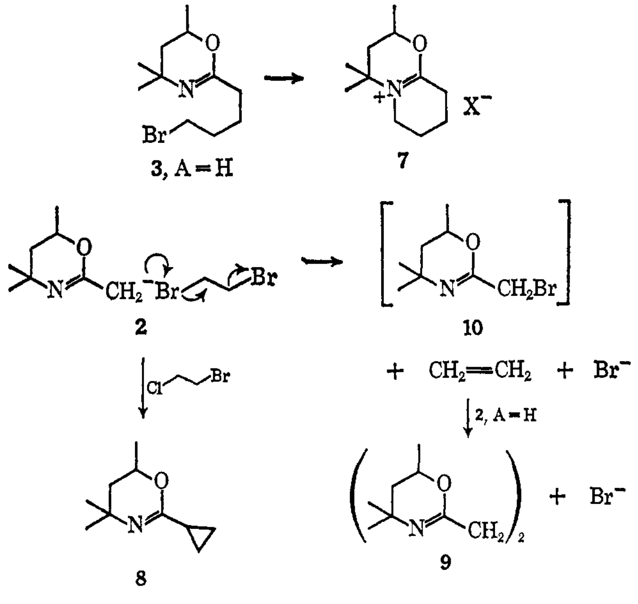
[a] Crude yields (estimated by nmr and vpc to be 90–95% pure) unless otherwise stated. [b] Pure distilled material. [c] Isolated as 2,4-DNP derivative. [d] H. C. Brown and B. C. S. Rao, *J. Am. Chem. Soc.*, **80**, 5377 (1958). [e] T. Taguchi and M. Ets, *Pharm. Bull.* (Tokyo), **5**, 88 (1957). [f] J. W. Wilt, J. M. Kosturik, and R. C. Orlowski, *J. Org. Chem.*, **30**, 1052 (1965). [g] New compound; analytical data satisfactory. [h] J. D. Roberts, *J. Am. Chem. Soc.*, **73**, 2959 (1951).

toire of this versatile heterocycle a general synthesis of alicyclic and α,α-disubstituted aldehydes by the technique of successive alkylation. Thus, by treatment of the 2-methyl- (**1a**),[2] 2-benzyl- (**1b**),[2] or 2-carbethoxymethyloxazine[3] (**1c**) with the appropriate base,[4] the corresponding anion, **2**, is readily prepared and can be alkylated with 1 equiv of an α,ω-dibromoalkane producing the bromoalkyloxazine **3**. Upon the addition of a second equivalent of base cyclization to the 2-cycloalkyloxazine **4** occurs (Table I).

Reduction of the cycloalkyloxazines with sodium borohydride or deuteride at −30° results in quantitative conversion to the 2-cycloalkyltetrahydro-1,3-oxazines **5** (Table I). The crude products of the reduction were directly cleaved[1] in the presence of aqueous oxalic acid, and steam distillation afforded the cycloalkylcarboxaldehydes **6** in 20–72% over-all yield (based on the dihalide).[5] The low yield of the 2-cyclobutyloxazine (entry 2) was due to the competing cyclization of **3** (A = H) to the quaternary salt **7** (X = Br). The latter was extremely hygroscopic and was readily converted to the perchlorate **7** (X = ClO_4), mp 200–201°, ir (KBr), 1635 cm^{-1} ($>$C=N$<^+$).[6] Although the anion **1b** reacted smoothly with 1,2-dibromoethane, producing the 2-cyclopropyloxazine **4** (A = Ph, entry 4), reaction of the anion **1a** failed to give the corresponding cyclopropyl derivative **8**. Instead, the bisoxazinylethane[7] **9** was isolated in 90% yield, undoubtedly the result of attack of the anion **2** on the bromomethyl derivative **10**. The potential utility of **9** as a precursor to succindialdehyde and its dideuterio







---

(2) Columbia Organic Chemicals, Columbia, S. C.

(3) A. I. Meyers and A. Nabeya, *Chem. Commun.*, 1163 (1967).

(4) The anions **2** (A = H, Ph) were generated as described in ref 1, whereas **2** (A = CO_2Et) was quantitatively formed using sodium hydride in THF.

(5) In order to determine whether it was necessary to purify the intermediates **4** and **5** prior to isolation of the aldehyde, several were purified by distillation (entries 2, 3, and 5 of Table I) whereas the others (entries 1, 4, 6, and 7) were crude materials. From the data in Table I it is apparent that the entire sequence can be carried out without purification of intermediates.

(6) The reaction of the anion **1a** with 1,3-dibromopropane, in a separate experiment, was intentionally allowed to proceed without a second equivalent of butyllithium and produced **7** in 85% yield (as the perchlorate).

(7) A. I. Meyers, *J. Org. Chem.*, **25**, 2231 (1960).

derivative as well as other dialdehydes is currently under investigation.[8]

Treatment of **1a** with 1-bromo-2-chloroethane under the usual cycloalkylation conditions resulted in an 85% yield of **8** which was reduced and subsequently cleaved to cyclopropanecarboxaldehyde in 65% over-all yield.

As a further extension of the successive alkylation of dihydro-1,3-oxazines, the anions **2** were alkylated using methyl iodide followed by a second equivalent of base and then a second equivalent of halide. In this manner the dimethyloxazines **11** and **12** were obtained in 76 and 85% yields, respectively.[9] Hydride (or deuteride) reduction of both products proceeded in 90–95% yields and cleavage in oxalic acid solution afforded the dimethyl derivatives **13** (53% over-all, semicarbazone mp 177–178°; (lit.[10] mp 178–179°) and **14** (66% over-all, 2,4-DNP mp 99–100°).[11]

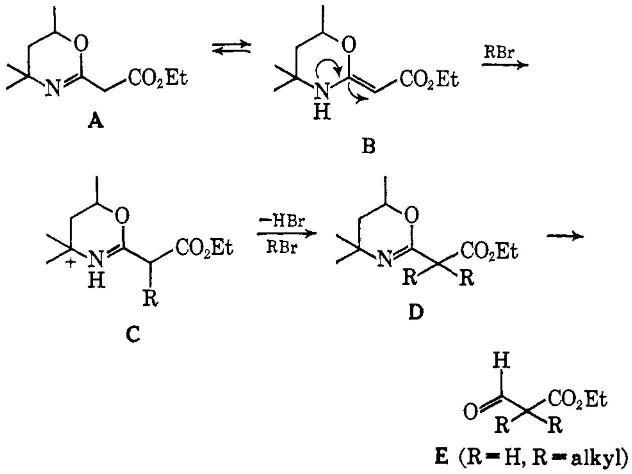
Additional studies are in progress to assess fully the potential of this synthetic method for obtaining a wide variety of aldehydes including those possessing additional functional groups.

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

---

[8] The reaction of **2** and dibromoethane was found to also give a high yield of **9** after the omission of the second equivalent of butyllithium. The formation of **10** in this manner now provides us with a highly useful intermediate, generated *in situ*, which should react with other organometallic reagents (RLi, RMgX) affording a route to otherwise inaccessible dihydro-1,3-oxazines and, ultimately, aldehydes. This behavior will be the subject of a future paper.

[9] Current studies in this laboratory have revealed that the oxazine ester **1c** which exists as a tautomeric mixture (A ⇆ B) can efficiently be alkylated with alkyl bromides in refluxing acetonitrile to the monoalkyl oxazine C. The latter can, after neutralization, undergo further alkylation to the dialkyloxazine D. Hence, the oxazine ester behaves as an enamine which exhibits the expected C-alkylation. This technique should likewise be useful in preparing mono- and dialkyl ester aldehydes E.



[10] N. H. Cromwell and H. H. Eby, *J. Am. Chem. Soc.*, **74**, 4201 (1952).

[11] The structures of all intermediates and final products were consistent (as were all the other examples in Table I) with their infrared, nmr, and mass spectra. All new compounds gave satisfactory analyses.

A. I. Meyers, H. Wayne Adickes
Ieva Ruks Politzer, Warren N. Beverung
Department of Chemistry
Louisiana State University in New Orleans
New Orleans, Louisiana 70122

Received October 9, 1968

Allenic–Propargylic and Allylic Rearrangements Accompanying Sulfur Dioxide Insertion into Carbon–Tin Bonds

Sir:

The chemistry of allenic[1] and allylic derivatives[2] of group IVb elements and the details of sulfur dioxide insertion into carbon–metal bonds[3–6] are subjects of current interest, and in this communication we wish to describe results pertinent to both areas.

The allenic tin compound I (from "propargyl Grignard reagent"[7] and $(CH_3)_3SnCl$) reacts very rapidly with gaseous SO_2 to yield a colorless air-stable product, mp 83–84°, analyzing well[8] for a monoinsertion product, formulated as II on the basis of spectral data (given in Table I).

$$\underset{\text{I}}{(CH_3)_3SnCH{=}C{=}CH_2} \xrightarrow{SO_2} \underset{\text{II}}{(CH_3)_3SnSO_2CH_2C{\equiv}CH}$$

Thus insertion is accompanied by rearrangement of the allenic to the propargyl moiety. The dimethyltin compound III undergoes diinsertion to yield IV.

$$\underset{\text{III}}{(CH_3)_2Sn(CH{=}C{=}CH_2)_2} \xrightarrow{SO_2} \underset{\text{IV}}{(CH_3)_2Sn(SO_2{-}CH_2{-}C{\equiv}CH)_2}$$

The propargyltin compound V (from triphenyltin iodide and "propargyl Grignard reagent") rapidly inserts SO_2 to yield the rearranged allene VI.

$$\underset{\text{V}}{(C_6H_5)_3SnCH_2C{\equiv}CH} \xrightarrow{SO_2} \underset{\text{VI}}{(C_6H_5)_3SnSO_2CH{=}C{=}CH_2}$$

In a predominantly $CDCl_3$-CD_3COOD solvent V slowly isomerizes[9] to yield the allene isomer VII which reacts with SO_2 to produce the rearranged acetylene VIII.

$$\underset{\text{VII}}{(C_6H_5)_3SnCH{=}C{=}CH_2} \xrightarrow{SO_2} \underset{\text{VIII}}{(C_6H_5)_3SnSO_2CH_2C{\equiv}CH}$$

---

[1] H. G. Kuivila and J. C. Cochran, *J. Amer. Chem. Soc.*, **89**, 7152 (1967).

[2] H. G. Kuivila and J. A. Verdone, *Tetrahedron Letters*, 119 (1964).

[3] J. P. Bibler and A. Wojcicki, *J. Amer. Chem. Soc.*, **88**, 4862 (1966), and subsequent papers.

[4] N. A. D. Carey and H. C. Clark, *Can. J. Chem.*, **46**, 643 (1968).

[5] G. B. Deacon and P. W. Felder, *J. Amer. Chem. Soc.*, **90**, 493 (1968). ν_{S-O} in metal S-sulfinates ordinarily arise (when M–S π bonding is unimportant) in the regions 1200–1100 and 1000–1050 cm^{-1}, while in $Cu(H_2O)_4(p\text{-}OS(O)C_6H_4CH_3)_2$, known[5] to contain CuOS(O) bonds, ν_{S-O} arises at 979 and 954 cm^{-1} (D. A. Langs and C. R. Hare, *Chem. Commun.*, 853 (1967)). Chemical and ir evidence favors the O-sulfinate structure for $(C_6H_5)_3SnOSOC_6H_5$ (F. A. Hartman and A. Wojcicki, *Inorg. Chem.*, **7**, 1508 (1968)) prepared from triphenyltin hydride and benzenesulfinic acid (M. Pang and E. I. Becker, *J. Org. Chem.*, **29**, 1948 (1964)). It is not yet clear that SO_2 insertion into tetraphenyltin yields the same product as that prepared by Pang and Becker above.

[6] W. Kitching and B. F. Hegarty, Abstracts of Papers, Symposium on Organometallic Chemistry, Melbourne, May 1968.

[7] The actual structure of this Grignard reagent is not certain, although one report (B. J. Benaim, *Compt. Rend.*, 262, 937 (1966)) suggests that the propargyl structure is retained. Formation of allenic products then can be rationalized on the basis of rearrangement mechanisms, which would be more facile for more electrophilic reactions; *e.g.*, compare contrasting behavior of $(CH_3)_3SnCl$ and $(C_6H_5)_3SnI$ reported here. The actual nature of "propargyl Grignard reagent" will be discussed elsewhere.

[8] All products reported here had satisfactory elemental analyses and nmr and ir spectral data. Nmr spectra integrated satisfactorily.

[9] Substitution of triphenyltin for a trimethyltin group appears to slow down considerably (factor of 10^2) electrophilic cleavage reactions of allylic and allenic tin compounds.[1,2]