A New Method for obtaining Epoxides from Aldehydes and Ketones

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Summary Oxirans may be obtained by treating carbonyl compounds in tetrahydrofuran with methylene bromide and lithium or lithium amalgam.

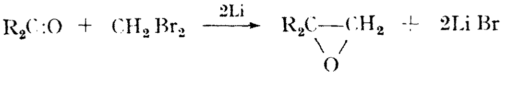
RECENTLY we reported that methylene magnesium halides obtained from methylene bromide or iodide and magnesium amalgam in ether–benzene (1 : 1) react easily with aldehydes and ketones yielding the corresponding methylenic olefins:[1]

$$CH_2(MgX)_2 + R_2C:O \rightarrow R_2C:CH_2$$

The same olefins are also obtained if the organometallic species is generated *in situ* in diethylether at room temperature in the presence of the carbonyl compounds.

We find that, if lithium or lithium amalgam is used instead of magnesium, the *in situ* reaction can take a different course.

When an equimolecular solution of a carbonyl compound and methylene bromide in freshly distilled tetrahydrofuran was treated under nitrogen between $-78°$ and room temperature with two gram atoms of lithium or the corresponding quantity of a diluted lithium amalgam, an oxiran was formed:



$$R_2C:O + CH_2Br_2 \xrightarrow{2Li} R_2C\underset{O}{-}CH_2 + 2LiBr$$

Epoxides were produced by this process from a variety of aldehydes and ketones (Table). Certain ketones, particularly α,β-unsaturated ones, do not react, at least under the conditions chosen, probably as a consequence of enolate ion formation. Such resistance to oxiran formation may of course prove useful in cases where selectivity is required. The yields are generally of the order of 40—50%, but, since a considerable amount of unchanged starting carbonyl compound was always recovered, the actual yield on the carbonyl compound converted was correspondingly higher.

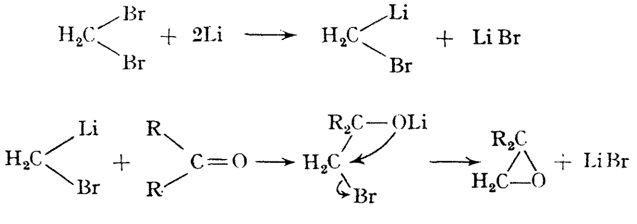
TABLE[a]

	Yield[b]
Lauraldehyde	35%
Benzaldehyde	37%
Cyclohexanone	48%
Methyl hexyl ketone	52%
5α-Cholest-3-one	95%
Pregnenolone acetate	40%

[a] All products completely characterised. [b] Yield of isolated, purified compounds.

The carbenoid species α-bromomethyl-lithium, resulting from the interaction of two atoms of lithium with a molecule of methylene bromide is probably the first intermediate in this reaction. Halogeno-metal compounds of this kind are known to behave under appropriate conditions as normal alkyl-lithiums do towards carbonyl compounds, yielding the corresponding halohydrin salts.[2]

These compounds then eliminate irreversibly a molecule of lithium bromide, yielding the final products.



The epoxides are also obtained on treating an equimolar solution of the carbonyl compound and methylene bromide in tetrahydrofuran with a molar amount of n-butyl-lithium at $-78°$.

In this case, however, the yields are considerably lowered as a consequence of the concurrent direct addition of butyllithium to the carbonyl group with formation of the corresponding n-butyl carbinol.

Work is in progress in our laboratories in order to ascertain the scope and mechanism of this reaction which is, in certain respects, related to the well known epoxide synthesis of Corey.[3]

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[1] G. Cainelli, F. Bertini, P. Grasselli, and G. Zubiani. *Tetrahedron Letters,* 1967, 5153.

[2] *cf. e.g.* G. Köbrich and R. H. Fischer, *Tetrahedron* 1968, **24**, 4343; G. Köbrich and W. Werner, *Tetrahedron Letters,* 1969, 2181.

[3] E. J. Corey, M. Chaykovsky, *J. Amer. Chem. Soc.,* 1965, **87**, 1353.