Kurze Mitteilungen

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SCOOPY and Oxirane Reactions: α-Lithio-Ylids vs. Conventional Ylids*

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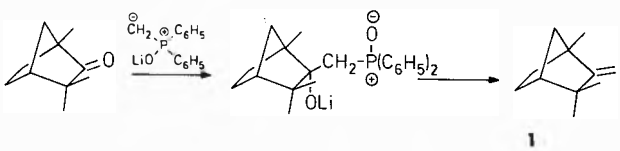
Abstract

Described for the first time in 1966, α-lithio-triphenyl-phosphonio-ylids have so far played only a marginal role in synthetic chemistry and this may well remain their fate in the future too. In *trans*-selective or "three-dimensional" (SCOOPY) *Wittig* reactions the conventional preparation of the "betaine-ylid" intermediates is generally superior to the α-lithio-ylid approach. Ordinary ylids react smoothly with most oxiranes provided soluble lithium salts are present. Again the use of α-lithio-ylids can be avoided.

Recently, triphenylphosphonio-α-lithio-alkylids [1] (or "ylenids" [2]) have been rediscovered by American authors [3], who recommend their use as "activated ylids". In particular, three types of α-lithio-ylid addition reactions were investigated: 1. to fenchone, a sterically most hindered ketone; 2. to aldehydes, opening a new access to betaine-ylids, the key intermediates in trans-selective and "three-dimensional" *Wittig* reactions [4], 3. to epoxides, considered to be not electrophilic enough to react with ordinary ylids. Although occasionally the α-lithio-ylid approach may indeed be competitive with or even superior to existing methods, we must warn not to overestimate its synthetic potential.

Fenchone easily combines with the PO-ylid obtained from methyldiphenylphosphine oxide upon deprotonation with butyllithium. The *Wittig/Horner*-sequence is terminated by hydrolysis and treatment with potassium hydride or *tert*-butoxide [5] to afford 72% 1,3,3-trimethyl-2-methylene-bicyclo[2.2.1]heptane **1**.

Scheme 1:



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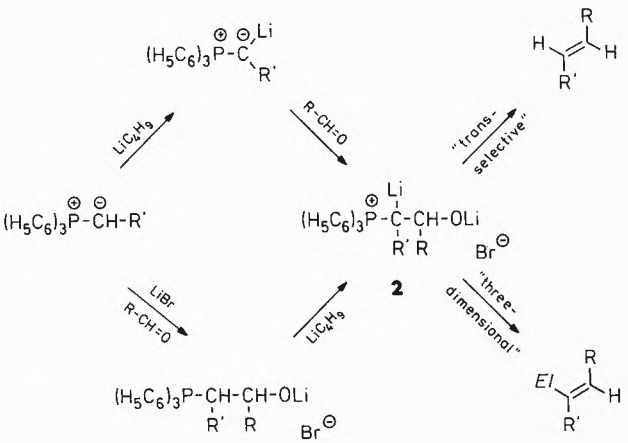
The α-lithio-ylid route to betaine-ylids **2** [6] is an operational reversal of their standard preparation by α-deprotonation of a betaine/lithium-halide adduct [7]. Whereas in the latter case phenyllithium, butyllithium or methyllithium suffice, *sec*- or *tert*-butyllithium are required to generate α-lithio-ylids. Even then no complete conversion is achieved [8]. Are these inconveniences compensated by any distinct advantage? We hoped to use α-lithio-ylids as precursors to betaine-ylids bearing an electron-withdrawing substituent in the α-position. They are inaccessible in the ordinary way, due to the instability of the corresponding betaine/lithium-halide intermediates. Thus, triphenylphosphonio-benzylid, -chloromethylid and -methoxymethylid were consecutively treated with *sec*-butyllithium, benzaldehyde and water (or hydrogen chloride in ether, followed by potassium *tert*-butoxide [7]). Stilbene, β-chloro-styrene and β-methoxystyrene were produced in modest yield and only as (*Z*/*E*)-mixtures.

Scheme 2:



Finally, the case of ylid reactions with oxiranes merits special attention. The literature, at first sight, appears to be contradictorious. On one hand, the inertness of oxiranes towards ylids is emphasized over and over again

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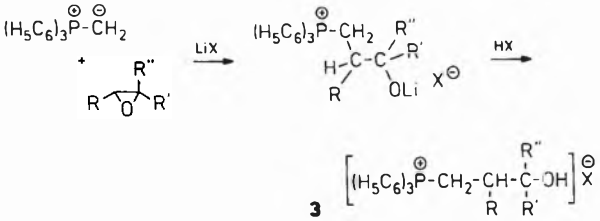
Table 1: γ-Hydroxyalkyl-phosphonium salts **3** obtained after reaction between oxiranes and triphenylphosphonio-methylid

$(H_5C_6)_3\overset{\oplus}{P}-CH_2-CH_2-\underset{R}{\overset{R'}{C}}-OH$	$\overset{\ominus}{X}$	mp [°C]	yield [a]
R = R' = H;	X = Br	219–220	61%
R = CH_3; R' = H;	X = Br	251–253 [b]	51%
R = R' = CH_3;	X = I	171–172 [b]	32%
R = CH_3; R' = CH=CH_2;	X = $B(C_6H_5)_4$	183–185	56%

[a] Yields refer to recrystallized products, the purity of which was testified by combustion analyses.
[b] Melting under decomposition.

[2, 9]. On the other hand, several examples of successful ylid additions to oxiranes are documented [10]. Actually, the apparent incongruity disappears as soon as one asks for the detailed reaction conditions. The addition takes readily place only in the presence of soluble lithium salts such as lithium bromide or iodide [11]. The interaction between the metal and the ring oxygen atom provides electrophilic assistance to ring-opening (*push-pull*-mechanism); the exceptional strenght of the developping O-Li bond constitutes the major driving force for the reaction.

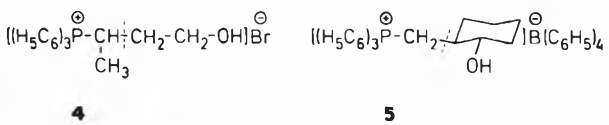
Scheme 3:



The few examples, summarized in the table, concern ylid reactions with oxiranes having at least one unsubstituted methylene group in the ring. In such cases the ring-opening proceeds particularly readily.

Branching at the reacting ylid or oxirane centers, however, does not seriously hinder the addition. Thus, triphenylphosphonio-ethylid and ethylene oxide combined smoothly to afford (3-hydroxy-1-methyl-propyl)-triphenylphosphonium bromide (**4**; 68%; mp. 233–235 °C), while triphenyl-phosphonio-methylid and cyclohexene oxide gave (*trans*-2-hydroxycyclohexyl-methyl)-triphenylphosphonium tetraphenylborate (**5**; 83%; mp. 215–219 °C) [12].

Scheme 4:



4 **5**

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4 (a) *M. Schlosser:* Topics Stereochem. *5,* 1 (1970); (b) *A. S. Arora* und *I. K. Ugi:* in Houben/Weyl, "Methoden der organischen Chemie" (Editor: *E. Müller*), Band *5/1b,* 887 (1972), G. Thieme Verlag, Stuttgart.

5 *M. Schlosser* and *Huynh Ba Tuong:* Chimia *30,* 197 (1976).

6 The term "β-oxido ylid" should be abolished as a misnomer. The former carbonyl oxygen atom is not present as a free anion, as this nomenclature suggests, but rather binds strongly with a lithium atom. Thus, "β-lithio-oxy ylid" (or "β-metallo-oxy ylid") is a correct synonym for the trivial name "betaine ylid".

7 *M. Schlosser* und *K. F. Christmann:* Justus Liebigs Ann. Chem. *708,* 1 (1967).

8 Although solid experimental proof is still lacking, we suspect the ylids to undergo, to some extent, metalation at the phenyl rings.

9 a) *G. Ohloff* and *M. Pawlak:* Helv. Chim. Acta *56* 1176 (1973); b) *N. Bensel, H. Marschall,* and *P. Weyerstahl:* Tetrahedron Lett. *1976,* 2293; c) *J. P. Marino* and *N. Hatanaka:* J. Org. Chem. *44,* 4467 (1979).

10 See, for example *R. R. Heath, R. E. Doolittle, P. E. Sonnet,* and *J. H. Tumlinson:* J. Org. Chem. *45,* 2910 (1980).

11 Styrene-oxide was, however, found to form a five membered cycloadduct of the oxyphospholane type even at room temperature when treated 4 days with "salt-free" triphenylphosphonio-methylid: *J. Wulff* and *R. Huisgen:* Chem. Ber. *102.* 1841 (1969). See also: *W. E. McEwen* and *A. P. Wolf:* J. Am. Chem. Soc. *84,* 676 (1962); *E. Zbiral:* Mh. Chemie *94,* 78 (1963).

12 General working procedure: Add to the oxirane (1.2 equivalents) concentrated solutions of the salt-free ylid (1.0 equiv.) in tetrahydrofuran and lithium bromide, iodide or tetraphenylborate (1.2 equiv.) in diethyl ether; after 3 h stirring neutralize with an non-aqueous acid; evaporate the solvents, wash the residue with cold water, dry and recrystallize twice from dichloromethane/ethyl acetate (bromides and, occasionally, iodides) or acetone/ethanol (tetraphenylborates and again, occasionally, iodides).