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ORTHO-LITHIATION OF TRIPHENYLPHOSPHONIO-METHYLID AND, ALSO, TRIPHENYLPHOSPHINE OXIDE

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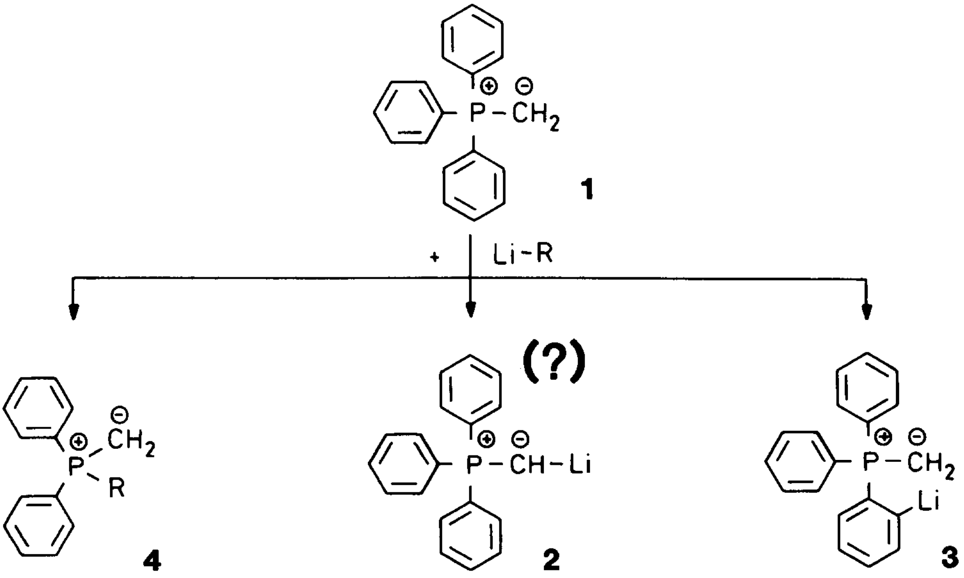
Summary: While upon treatment with methyl- or butyllithium triphenylphosphonio-methylid (1) undergoes extensive ligand exchange (leading to 4) it reacts with sec- or tert-butyllithium mainly at the ortho-position exchanging one hydrogen against a lithium atom (to give 3).

α-Lithio-ylids 2 [1] may be regarded as "activated" phosphorus ylids 1 . Recently, their use as key intermediates in Wittig and SCOOPY [2] reactions has been recommended [3]. We have demonstrated, however, that ordinary P^+ or PO ylids can serve the same purposes equally well or, actually, better [4]. Moreover, despite all attempts to repeat the work of Corey and Kang [3], we were unable to confirm the yields claimed by these authors. Rather than the reported 54 - 87% of pure products, we identified (by gas chromatography) product mixtures containing not more than 12 - 43% of the compounds which may, though even must not, be derived from an intermediate α-lithio ylid. We are now in the position to present firm evidence for two concomitant reactions that extensively compete with the α-metalation of ylids : ligand/ligand exchange at the phosphorus center and metalation at the *ortho*-position of a phenyl ring generating species 4 and 3 , respectively.



A precooled solution (-75°C; 0.5 M) of 20 mmol triphenylphosphonio-methylid (**1**) in 100 mL of tetrahydrofuran (THF) was added to methyllithium, butyllithium, *sec*-butyllithium or *tert*-butyllithium from which the former solvent had been stripped off. After keeping the mixture 2 - 5 h at a temperature between -35°C and +25°C, the reaction was quenched with hydrogen chloride in diethyl ether (DEE) and the mixture studied by ^{1}H- and, notably, ^{31}P-nmr [5]. Aryl/alkyl-ligand exchange [6] was found to occur to a considerable extent with methyllithium and butyllithium (see table) [7]. Parallel runs were treated with DCl/DEE [8]. As revealed by ^{2}H-nmr spectra [9], substantial amounts of deuterium were incorporated in the *ortho*-positions, especially when *sec*- or *tert*-butyllithium served as the reagent. Unfortunately the degree of both, *o*- and α-metalation, can be assessed only inaccurately. This is due in part to the presence of unreacted ylid **1** (each sample contained a total of 1.3 - 1.9 deuterium atoms per molecule). In addition, we have found evidence for a *relay protonation* of **3** : rapid addition of a deuteron (or another electrophile) to the sterically best accessible α-position, intramolecular proton transfer to the *o*-position and ultimate deuteration of the newly generated ylid. It is safe to say, however, that *sec*- and *tert*-butyllithium *mainly produce ortho-lithio ylid* **3** *and that α-lithio ylid* **2** *forms just as a by-product, if at all* (see table).

Table. Reaction between triphenylphosphonio-methylid (**1**) [a] and various organolithium reagents LiR in THF [b] : ligand exchange (→ **4**), *o*-metalation (→ **3**) and, possibly also, α-metalation (→ **2**).

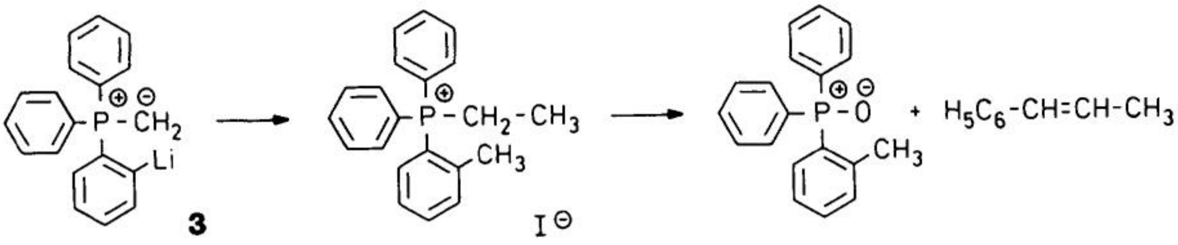
reagent LiR	reaction time (temperature)	phosphonium salt recov'd [c]	ratio (**2** + **3**) : **4**	ratio **3** : **2**
$LiCH_3$	5 h (+25°C)	26%	1 : 3	> 3 : 7
$Li\text{-}C_4H_9$	3 h (+25°C)	42%	3 : 1	> 3 : 7
$Li\text{-}CH(CH_3)C_2H_5$	2 h (-30°C)	82%	25 : 1	> 1 : 1
$Li\text{-}C(CH_3)_3$	2 h (-35°C)	86%	> 25 : 1	> 1 : 1

a) Spectroscopically (^{1}H- and ^{31}P-nmr) pure solution prepared from methyl-triphenylphosphonium bromide and NaH in THF, filtered under nitrogen and stored in a Schlenk burette.

b) A change in the solvent (*e.g.*, from THF to DEE) or addition of LiBr alters the product ratios only slightly and never profoundly. On the other hand, in view of the poor solubility of *o*-lithio ylid **3** at low temperatures (notably in DEE), low concentrations (about 0.2 M) and monitoring the progress of the reaction by means of an internal standard may help to improve the reproducibility of results.

c) Collected after addition of DCl/DEE and an saturated aqueous solution of NaBr and crystallized from dichloromethane/ethyl acetate (typical m.p. 217 - 221°C dec.; m.p. of pure compound 227 - 228°C dec.).

The *ortho*-specificity of the ring metalation was established rigorously. A solution of lithiated ylids was added dropwise to excess methyl iodide. The phosphonium salts thus obtained were consecutively treated with butyllithium and benzaldehyde. The resulting mixture of triphenylphosphine oxide (31%) and diphenyl-*o*-tolylphosphine oxide (58%) was separated by chromatography (silica gel; diethyl ether + acetonitrile 9 : 1) and each individual component identified by mp (mixture mp) and nmr comparison with authentic samples (diphenyl-*o*-, -*m*-, and -*p*-tolylphosphine oxide : mp 121 - 122°, 122 - 123° and 127 - 129°C; δ_{CH_3} : 2.44, 2.33 and 2.36 ppm : J_{P,CH_3} always < 0.5 Hz).



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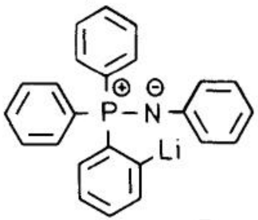
So far, no *ortho*-metalation of a phosphorus ylid has ever been reported. An analogy, however, does exist : phenyllithium or butyllithium converts the *N*-(triphenylphosphonio-)anilid into compound 5 [10]. Finally, also triphenylphosphine oxide undergoes an *ortho*-hydrogen/lithium exchange when treated in tetrahydrofuran with phenyllithium (after 3 h at 25°C : 89% 6) or *tert*-butyllithium (after 2 h at -35°C : 44% 6 + 46% *tert*-butyldiphenylphosphine oxide, mp 127 - 129°C, half of which was *o*-lithiated [11]). Thus, *ortho*-substituted phosphine oxides and hence also, after reduction, the corresponding phosphines become conveniently accessible. Starting with triphenylphosphine oxide, which was dissolved in a 0.7 M ether solution of phenyllithium (1 equiv., LiBr-containing) and kept 75 h at -25°C (deep freezer), we prepared for example diphenyl-*o*-tolyl-phosphine oxide (7 , 72%, mp 121 - 122°C), *o*-(1-hydroxy-ethyl)-phenyl-diphenyl-phosphine oxide (8 , 68%, mp 110 - 111°C) and 2-diphenylphosphoryl-benzoic acid (9 , 53%, 258 - 260°C).



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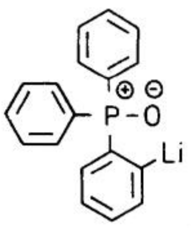

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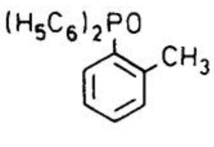

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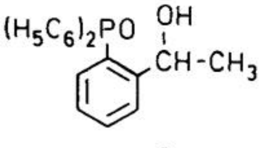

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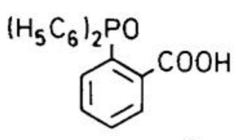

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3 E.J. Corey & J. Kang, *J. Am. Chem. Soc.* 1982, *104*, 4724.

4 M. Schlosser, Huynh Ba Tuong, J. Respondek & B. Schaub, *Chimia* 1983 , *37*, 10.

5 Bruker CXP-200 operating at 81.0 MHz and with deuterium lock : broadband and selectively (in the aromatic region) H-decoupled spectra were recorded of ylids (0.3 M in tetrahydrofuran/perdeuterobenzene 4 : 1, 10 mm tubes), and, after quenching with HCl/DEE, phosphonium salts (raw products, 0.3 M in deuterochloroform/methanol 4 : 1 mixtures, 10 mm tubes); chemical shifts (δ) : triphenylphosphonio-methylid 18.5; methyldiphenylphosphonio-methylid 9.1; butyldiphenylphosphonio-methylid 16.4; methyltriphenylphosphonium bromide 22.8; dimethyldiphenylphosphonium bromide 19.7; butyl-methyl-diphenylphosphonium bromide 22.9 ppm.

6 Previous examples of ligand/ligand exchange reactions at the phosphorus atom of ylids : (a) D. Seyferth & D.E. Welch, *J. Organomet. Chem.* 1964 , *2*, 1; (b) M. Schlosser, *Angew. Chem.* 1962 , *74*, 291.

7 Ylids 4 , if R = CH_3, C_4H_9 or $CH(CH_3)C_2H_5$, can get deprotonated for their part and afford α'-lithiated ylids ("phosphonio-diylids"[2b] or "ylid anions"; see L.E. Manzer, *Inorg. Chem.* 1976 , *15*, 2567).

8 M. Schlosser & K.F. Christmann, *Justus Liebigs Ann. Chem.* 1967 , *708*, 1, spec. page 24.

9 Bruker CXP-200 operating at 30.7 MHz without lock; 10 mm wide tubes filled with 0.3 M solutions of the samples in methanol; deuterium contents determined by integration in comparison with a known amount of $[^2H_{12}]$cyclohexane (difference in the response factors of the sample and the internal standard due to differences in their relaxation times being corrected after calibration).

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11 Previous ligand/ligand exchange reactions of phosphine oxides : (a) D. Seyferth, D.E. Welch & J.K. Heeren, *J. Am. Chem. Soc.* 1964 , *86*, 1100; (b) W. Smadja, M. Simalty-Simiatycki & C. Prévost, *Bull. Soc. Chim. Fr.* 1966 , 971.

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