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A New Generation of "Instant Ylids" : Powder Mixtures of Phosphonium Salts and Potassium Hydride as Storable Precursors to Wittig Reagents

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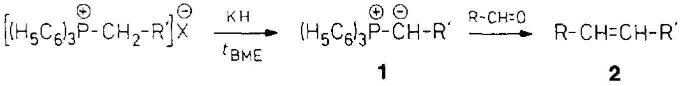
Abstract : Mixing a finely pulverized alkyltriphenylphosphonium salt and potassium hydride in 1 : 1 molar ratio gives a ready-to-use powder the components of which react rapidly when *tert*-butyl methyl ether is added under stirring. When, in general after a few minutes, the generation of the (triphenylphosphonio)alkanide is complete, it can be immediately used for the Wittig olefination of a carbonyl compound. Compared to sodium amide based "instant ylids", the new blends offer little advantage as long as simple phosphonium salts are ingredients but they extend considerably the shelf life of mixtures containing heterosubstituted derivatives such as methylthiomethyl- or picolyltriphenylphosphonium salts.

More than a decade ago we had made an amazing observation. Dry powders of phosphonium salts, moderate acids (typical pK_a range 10 - 15), can be mixed with finely dispersed sodium amide, a strong base (pK_a of ammonia in the range of 35 - 40), and as such conserved over months or years without notable decomposition. However, when an aromatic or ethereal solvent is added (even vapors may suffice !), a vigorous reaction starts and sets free the corresponding triphenylphosphonioalkanide. When the Wittig reagent thus generated is used for carbonyl olefination, it gives almost quantitative yields [1].

In the meantime such "instant ylid" mixtures have become popular tools of organic synthesis. They can be applied on a microscale [2] (< 1 mmol) and in 100 kg quantities [3] for industrial purposes. So far, however, it was only possible to store such mixtures indefinitely if the phosphonium salt did not contain heterosubstituents. (Chloromethyl)-, (methylthiomethyl)- and (8-hydroxyoctyl)triphenylphosphonium salts in the presence of sodium amide were found to have "shelf half lives" of only 5 - 10 weeks. Even more vulnerable proved to be the mixture of triphenyl(2-picolyl)phosphonium salt and sodium amide which after less than one month showed already a rapid decline in reactivity. We immediately suspected an addition of the base onto the heterocycle to be at the origin of the deterioration. We have indeed obtained nmr evidence for such a degradation process which obviously does not require solvent mediation and occurs already at 25 °C although Tchichibabin reactions in general are performed at temperatures around or above 100 °C.

With identical metals, hydrides are roughly as basic but less nucleophilic than amides. As we found, dry powder mixtures of simple or heterosubstituted phosphonium salts [4] with potassium hydride [5] are astonishingly stable and can be conserved at 0 °C over months or years (see Table). Only in the case of the mixture containing (fluoromethyl)triphenylphosphonium salt is it advisable to keep it in a deep-freezer at -25 °C (Table). In order to assess the olefination capacity as a function of storage time, a suspension of the given "instant ylid" (10 mmol) in *tert*-butyl methyl ether (20 mL) was vigorously stirred for 15 min at 25 °C before benzaldehyde (10 mmol) was added at 0 °C to the ylid **1** thus set free. The products **2** formed were identified by gas chromatographic comparison of their retention times (on at least two stationary phases of different polarity) with those of authentic samples [6] and quantified by their peak areas relative to a known amount of a reference compound ("internal standard").



$$[(H_5C_6)_3\overset{\oplus}{P}-CH_2-R']\overset{\ominus}{X} \xrightarrow[{}^tBME]{KH} \underset{\mathbf{1}}{(H_5C_6)_3\overset{\oplus}{P}-\overset{\ominus}{C}H-R'} \xrightarrow{R-CH=O} \underset{\mathbf{2}}{R-CH=CH-R'}$$

Table. Consecutive treatment of phosphonium salt/potassium hydride mixtures with *tert*-butyl methyl ether and benzaldehyde : yields of olefins **2** after given intervals of storage at 0 °C or, numbers in parentheses, at 25 °C.

Phosphonium side chain CH_2R'	Counter ion X	Yield of olefins **2** after varying storage periods			
		1 h [a]	3 months	6 months	12 months
CH_3	Br	92%	93% (90%)	93% (82%)	91% (64%)
$CH_2CH(CH_3)_2$	Br	91%	88% (89%)	90% (88%)	-
CH_2F [b]	BF_4	65%	55% (31%)	50% (22%)	-
CH_2Cl	Cl	87%	-	88% (84%)	87% (60%)
CH_2OCH_3	BF_4	87%	-	87% (62%)	79% (53%)
CH_2SCH_3	Cl	92%	-	91% (88%)	81% (75%)
2-picolyl	Cl	91%	-	92% (71%)	-
3-picolyl	Cl	90%	90% (89%)	88% (67%)	-
4-picolyl	Cl	90%	-	89% (77%)	-

a) No difference between exposure to 0 °C or 25 °C after 1 h.
b) At -25 °C : 67, 67 and 66% after storage during 1 h, 3 months and 6 months, respectively.

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