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KH in Paraffin - KH(P): A Useful Base for Organic Synthesis

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Abstract



The preparation of KH as a one:one homogenate with paraffin, termed KH(P), is reported. KH(P), a solid at room temperature, is stable without special handling. On suspension in THF with a phosphonium salt, KH(P) rapidly generates the ylide. Wittig condensation with aromatic, aliphatic and α , β -unsaturated aldehydes proceeds with high *Z*-selectivity. KH(P) should be a generally useful base for organic synthesis.

Sodium hydride (NaH), potassium *t*-butoxide and *n*-BuLi have long been the workhorse bases for organic synthesis. Potassium hydride (KH), although it is a powerful base and much faster kinetically than NaH, has not been so widely used.¹⁻³ Largely, this is because it comes commercially as a slurry in mineral oil, and it is operationally difficult to dispense precisely. We report the preparation of KH in a more convenient form, as a 50% by weight homogenate in paraffin.⁴ We have termed this new reagent "KH(P)".

There was the real concern that the heat from the reaction of surface KH with ambient moisture would be sufficient to initiate melting, leading to rapid decomposition. In fact, we have found that the KH(P) is stable to normal handling. It is easily cut and weighed in the air. Indeed, we have stored a sample in air for four months, and have observed no loss of titer. The titer was determined by addition of *n*-butanol and volumetric measurement of the evolved hydrogen.

We were pleased to observe (Table 1) that the KH(P) so prepared readily generated ylides from phosphonium salts.⁵ The alkenes formed from the non-stabilized phosphoranes were predominantly Z, while the alkene (Entry 5) from the stabilized phosphorane was E. The yields in Table 1 refer to reactions employing 1.8 equivalents of KH(P) and 2.0 equivalents of phosphonium salt.

We expect that KH(P), easily handled and measured and stable to storage, will have wide utility in organic synthesis.⁶

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Supporting Information available: General experimental procedures, and ¹H and ¹³C spectra and other data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

Experimental Section

Potassium hydride in paraffin

In a nitrogen atmosphere (grade 4.8) drybox, KH (35 % w/w dispersion in mineral oil) was washed with cyclohexane and filtered. Paraffin wax (paraffin wax for canning, mp = 48 - 50 °C, 2.00 g) was warmed to melting in a small cylindrical clear glass vial via a heating mantle. To the melted wax was added KH (2.00 g, 50 mmol) and the slurry was rapidly stirred to homogeneity with a Teflon® coated magnetic stir bar while still warm. Magnetic stirring was continued until the mixture began to solidify, at which time the vial was rolled on its side on a flat surface until the mixture was completely solid. The homogenous 50% w/ w dispersion of KH in paraffin was then capped and removed from the drybox for storage in the laboratory without further protection. [Caution: While we have never had any difficulty following this procedure, others have observed sparking when washing KH under "house" nitrogen.]

The KH(P) was titrated with an apparatus for measuring H_2 evolution. To a slurry of KH(P) (78.2 mg, 39.1 mg KH) in 5 mL heptane was slowly added a solution of excess 1-butanol in 5 mL of heptane. The gas evolved in the titration was then read from a volumetric buret as 23.5 mL (24.4 mL expected).

Representative procedure - preparation of alkene 7

To a 25 mL flask was added phosphonium salt **4** (982 mg, 2.0 mmol), KH(P) (144 mg of 50% w/w mixture of KH/paraffin, 1.8 mmol KH) and 4 mL of dry THF. The suspension was stirred for 20 min, changing to a yellow-orange color, then cooled to 0 °C. Aldehyde **1** (0.122 mL, 1.0 mmol) was then added and the mixture was stirred for 2 h at 0 °C. The mixture was then partitioned between CH_2Cl_2 and, sequentially, H_2O , saturated aqueous NaHCO₃ and brine. The combined organic extracts were dried (Na₂SO₄) and concentrated. The residue was chromatographed to give **7** as a colorless oil (214 mg, 0.80 mmol, 80% yield): TLC R_f (MTBE/petroleum ether = 1:10) = 0.52; ¹H NMR δ 2.65 (dq, J=6.8,1.5 Hz, 2H), 3.56 (t, J=6.8 Hz, 2H), 3.76 (s, 3H), 4.50 (s, 2H), 5.72 (dt, J=11.5, 7.2 Hz, 1H), 6.48 (d, J=11.5 Hz, 1H), 6.87 (dd, J=8.3, 2.7 Hz, 1H), 6.77 (s, 1H), 6.87 (d, J=7.7 Hz, 1 H), 7.20-7.34 (m, 6H); ¹³C NMR⁷ δ d 55.2, 112.4, 114.4, 121.34, 127.3, 127.6, 127.7, 128.4, 129.1, 129.4, 130.5; u 29.5, 69.9, 73.0, 138.5, 138.8, 159.5; IR 2852, 1598, 1101 cm⁻¹; MS *m/z* 268 (12), 162 (27), 147 (100), 134 (60), 115 (27). HRMS calcd for C₁₈H₂₀O₂ 268.1463, obsd 268.1457.

Alkene 11

Yield; 185 mg, 0.90 mmol, 90%; TLC R_f (MTBE/petroleum ether/CH₂Cl₂ = 4:20:1) = 0.56; ¹H NMR δ 1.13 (t, J=7.1 Hz, 3H), 3.81 (s, 3H), 4.26 (q, J=7.2 Hz, 2H), 6.42 (d, J=16.0 Hz, 1H), 6.91 (dd, J=8.3, 2.7 Hz, 1H), 7.03 (s, 1H), 7.10 (d, J=7.9 Hz, 1H), 7.28 (t, J=7.9 Hz, 1H), 7.64 (d, J=16.0 Hz, 1H); ¹³C NMR δ d 14.3, 55.2, 112.9, 116.1, 118.6, 120.7, 129.9, 144.5; u 60.5, 135.9, 160.0, 166.9; IR 2980, 1713, 1640 cm⁻¹; MS *m/z* 206 (64), 178 (11), 161 (100), 134 (18), 118 (24); HRMS calcd for C₁₂H₁₄O₃ 206.0943, obsd 206.0944.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Wittig homologation using KH(P)



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