

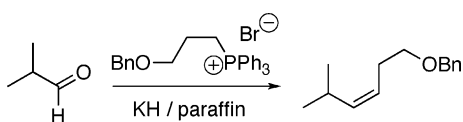
Potassium Hydride in Paraffin: A Useful Base for Organic Synthesis

Douglass F. Taber* and Christopher G. Nelson

Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716

taberdf@udel.edu

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The preparation of potassium hydride as a 1:1 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 *tert*-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)”.

(1) For early reports of the utility of KH as a reagent for organic synthesis, see (a) Brown, C. A. *J. Org. Chem.* **1974**, *39*, 1324. (b) Brown, C. A.; Yamashita, A. *J. Am. Chem. Soc.* **1975**, *97*, 891.

(2) For an early review of organic synthesis applications of KH, see Pinnick, H. W. *Org. Prep. Proced. Int.* **1983**, *15*, 199.

(3) As of this writing, more than 4000 pages of this journal have been published in 2006. The use of KH has been reported just 12 times: (a) Kumaraswamy, G.; Padmaja, M.; Markondaiah, B.; Jena, N.; Sridhar, B.; Kiran, M. U. *J. Org. Chem.* **2006**, *71*, 337. (b) Naya, S.; Ohtoshi, H.; Nitta, M. *J. Org. Chem.* **2006**, *71*, 176–184. (c) Chai, C. L. L.; Elix, J. A.; Moore, F. K. E. *J. Org. Chem.* **2006**, *71*, 992. (d) Kim, H. S.; Lee, S. Y.; Lee, H.; Bae, J. Y.; Park, S. J.; Cheong, M.; Lee, J. S.; Lee, C.-H. *J. Org. Chem.* **2006**, *71*, 911. (e) Ghosh, A. K.; Gong, G. *J. Org. Chem.* **2006**, *71*, 1085–1093. (f) Arns, S.; Barriault, L. *J. Org. Chem.* **2006**, *71*, 1809. (g) Lysen, M.; Hansen, H. M.; Begtrup, M.; Kristensen, J. L. *J. Org. Chem.* **2006**, *71*, 2518. (h) Johnsson, R.; Mani, K.; Cheng, F.; Ellervik, U. *J. Org. Chem.* **2006**, *71*, 3444. (i) O’Neal, W. G.; Roberts, W. P.; Ghosh, I.; Wang, H.; Jacobi, P. A. *J. Org. Chem.* **2006**, *71*, 3472. (j) Kadota, I.; Nishii, H.; Ishioka, H.; Takamura, H.; Yamamoto, Y. *J. Org. Chem.* **2006**, *71*, 4183. (k) Casarini, D.; Coluccini, C.; Lunazzi, L.; Mazzanti, A. *J. Org. Chem.* **2006**, *71*, 4490. (l) Hagiwara, H.; Takeuchi, F.; Kudou, M.; Hoshi, T.; Suzuki, T.; Hashimoto, T.; Asakawa, Y. *J. Org. Chem.* **2006**, *71*, 4619.

TABLE 1. Wittig Homologation Using KH(P)

| Aldehyde | Phosphonium Salt | Alkene | Yield(%) |
|----------|------------------|--------|----------|
| | | | 80 |
| | | | 48 |
| | | | 91 |
| | | | 66 |
| | | | 90 |

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 with normal handling. It is easily cut and weighed in the air. Indeed, we have stored a sample in air for 4 months and have observed no loss of titer. The titer was determined by addition of *n*-butanol and by volumetric measurement of the evolved hydrogen.

We were pleased to observe (Table 1) that the KH(P) prepared in this fashion 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 equiv of KH(P) and 2.0 equiv of phosphonium salt.

(4) The coating of air-sensitive catalysts with paraffin is a common industrial practice with many references in the patent literature. For examples, see (a) Fang, Y.; Liu, Y.; Ke, Y.; Guo, C.; Zhu, N.; Mi, X.; Ma, Z.; Hu, Y. *Appl. Catal. A* **2002**, *235*, 33. (b) Kosak, K. M.; Kosak, M. K. U.S. Patent 5 413 924, 1995. We have used this approach to stabilize sensitive catalysts: (c) Taber, D. F.; Frankowski, K. J. *J. Org. Chem.* **2003**, *68*, 6047. (d) Taber, D. F.; Li, H.-Y. U.S. Pat. Appl. Publ. US 2005288257, 2005.

(5) For the use of dry combinations of phosphonium salts and KH to generate ylides, see El-Khoury, M.; Wang, Q.; Schlosser, M. *Tetrahedron Lett.* **1996**, *37*, 9047.

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

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 (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 homogeneous 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 H₂ evolution. To a slurry of KH(P) (78.2 mg, 39.1 mg of KH) in 5 mL of 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 was expected).

Representative Procedure—Preparation of Alkene 7. To a 25 mL flask were added phosphonium salt **4** (982 mg, 2.0 mmol), KH(P) (144 mg of 50% w/w mixture of KH/paraffin, 1.8 mmol of KH), and 4 mL of dry THF. The suspension was stirred for 20 min, changing to a yellow-orange color, and 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 CH₂Cl₂ and, sequentially, H₂O, saturated aqueous NaH-

(6) KH(P) prepared by the method outlined here is commercially available from Wilmington PharmaTech.

CO₃, 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, 1H), 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; found, 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; found, 206.0944.

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Supporting Information Available: General experimental procedures, 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>.

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(7) ¹³C multiplicities were determined with the aid of a JVERT pulse sequence, differentiating the signals for methyl and methine carbons as “d” and for methylene and quaternary carbons as “u”.