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Spotlight 327

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Sodium Hydride

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Abha Verma was born in 1981 in Chandigarh, India. After obtaining her B.Sc. (Honors) in 2002 and her M.Sc. (Honors) in chemistry in 2004 from the Panjab University, Chandigarh, she worked for six months at the Dr. Reddy's Pharmaceutical Company, Hyderabad, India, before joining the Indian Institute of Science at Bangalore, India, where she worked for the Chemical Biology program for two years. In 2007, she joined the research group of Professor Mark L. Trudell at the University of New Orleans and is now working towards her Ph.D. degree.

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Dedicated to my research advisor Prof. Mark L. Trudell

Introduction

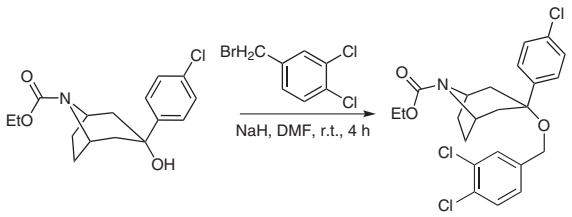
Sodium hydride (NaH)[1] is an important reagent for the synthesis of both organic and inorganic compounds. It is used as a base for the deprotonation of alcohols, phenols, amides, ketones, esters, and stannanes, and thus it is widely used to promote condensations of carbonyl compounds via the Dieckmann, Stobbe, Darzens and Claisen condensations. Under aprotic conditions NaH is an effective reducing agent for disulfides, disilanes, azides, and isoquinolines.

NaH is produced by the direct reaction of hydrogen and liquid sodium. Pure NaH is colorless (mp 800 °C), although samples generally appear grey, and commercially available either as free-flowing grey powder (95% dry hydride) or as grey powder dispersed in mineral oil. Because of its rapid and irreversible reaction with water, NaH can be used to dry some organic solvents. NaH-based hydrogen storage systems are also being developed for use in fuel-cell vehicles.

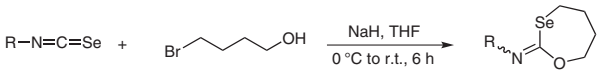
As sodium hydride can behave both as a base and a source of hydride, this dual ability in the presence of an electrophile and suitable solvents results in the formation of selective products.[2] An interesting selectivity between NaH and potassium hydride was observed in the preparation of Macroviracin A where NaH yielded the desired macrocyclic dilactone core.[2]

Abstracts

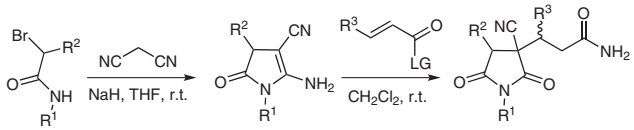
(A) A series of 3α-arylmethoxy-3β-arylnortropanes were synthesized by alkylation of the corresponding tertiary alcohols using NaH.[3]



(B) The first synthesis of 1,3-oxaselenepane derivatives by the reaction of aryl isoselenocyanates with 4-bromobutanol in the presence of sodium hydride as a one-pot reaction was reported recently where the *Z*/*E* isomerism for the exocyclic carbon nitrogen double bond in the selenium heterocycles was observed for the first time.[4]



(C) Despite their important physicochemical and therapeutic properties, until 2008 only two structures bearing 7-hexahydro-aza-indoles prototype nucleus were known in the literature.[5] An effective route involves the reaction of enaminonitrile γ-lactams derived from *N*-alkyl-α-bromoacetamides and malononitrile in the presence of NaH with acryloyl chloride derivatives.



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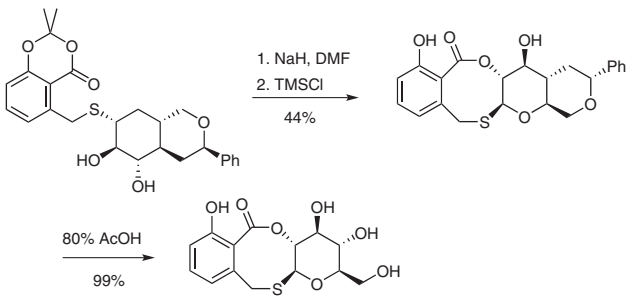
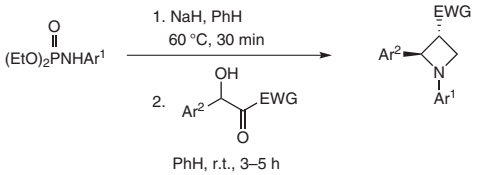
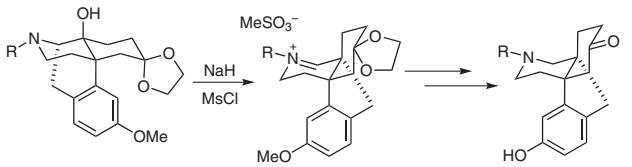
(D) A novel eight-membered polyhydroxylated salicylic acid lactone[6] was prepared from 2,6-dihydroxybenzoic acid and sodium thio-D-glucose. The key step involved a NaH-promoted intramolecular lactonization in the presence of excess TMSCl which led to the isolation of the 'natural product like' lactone.



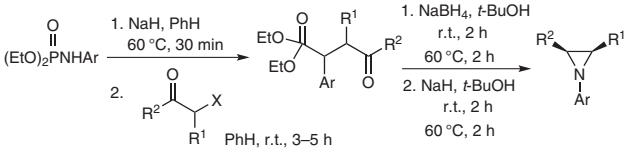
(E) In a one-pot procedure, diethyl *N*-arylphosphoramidates were treated with NaH to generate an anion in situ, which underwent an aza-Michael addition to Baylis–Hillman adducts followed by cyclization to afford the azetidine-3-carbonitriles/carboxylates.[7]



(F) The treatment of morphinan with NaH and MsCl provided a very stable iminium salt possessing a propellane skeleton.[8] The iminium ion is expected to be a key intermediate for the synthesis of novel opioid ligands.



(G) A novel and efficient aziridination of α-halo ketones with diethyl *N*-arylphosphoramidates affords diethyl *N*-aryl-*N*-(2-oxoalkyl)-phosphoramidates which undergo reductive cyclization with $NaBH_4$ followed by NaH to give highly diastereoselective 1,2-disubstituted and 1,2,3-trisubstituted aziridines.[9]



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