

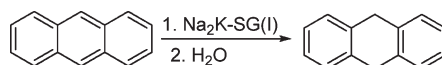
Birch Reductions at Room Temperature with Alkali Metals in Silica Gel (Na₂K-SG(I))

Partha Nandi, James L. Dye, and James E. Jackson*

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

jackson@chemistry.msu.edu

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11 entries, modest to high yields

Alkali metals in silica gel (the Na₂K-SG(I) reagent) cleanly effect Birch reductions of substrates with at least two or more aromatic rings. The reaction conditions are alcohol-free, ammonia-free, and achieve excellent yields and high selectivities at room temperature.

Conventional Birch reductions^{1–3} of aromatic compounds are performed with alkali metals in liquid ammonia (the so-called dissolving metal conditions) in the presence of alcohols at or below the $-33\text{ }^{\circ}\text{C}$ reflux temperature of liquid ammonia. These versatile reactions can be tuned by varying temperatures, metals,^{4–6} additives, proton sources, or quenching agents. They have also been combined with other reactions in tandem sequences.^{7–14} A cathodic Birch reduction has been reported for a limited class of substrates.¹⁵ The hydroxide ion has been used as an electron source for the photochemically activated Birch reduction of a naphthalene derivative.¹⁶ Birch reduction variants also include reactions in THF with gaseous ammonia as a solvent component and the reaction atmosphere.¹⁷

The class of substrates described herein can alternatively be reduced, with complementary selectivities, by hydrogenation

with transition metal^{18,19} or lanthanide²⁰ catalysts.²¹ However, toxicities and costs of many catalytic transition metals²² and the low temperature requirements of conventional Birch reductions remain areas of concern for process development and scale up.²³ Additionally, alkali metal–arenide salts can form stable complexes with ammonia, which can later cause violent reactions during quenching.²⁴

Alkali metals in silica gel^{25,26} (the so-called M-SG reagents) have been developed in our laboratories as dry, free-flowing powders.^{27,28} The usefulness of these reagents in replacing dissolved metal conditions has been illustrated in

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- (25) SiGNa chemistry has developed three categories of alkali metal nanostructured silica materials (M-SG): Stage 0 materials are strongly reducing pyrophoric powders; Stage I materials are nonpyrophoric, free-flowing black powders with reactivity equivalent to neat alkali metals, and Stage II is less reducing but reacts with water to produce hydrogen at pressures from ambient to several thousand psi. All three categories of M-SG, with different metals and metal alloys absorbed, are available commercially.
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- (28) Although these M-SG(I) reagents do not react with dry air, they can degrade rapidly in ordinary moist lab atmospheres. Thus, appropriate caution should be exercised in handling these materials. Like the pure alkali metals, these materials react vigorously and exothermically with water, giving off flammable hydrogen gas.

the context of several reductive cleavage reactions.^{29–31} They have also proven effective in reduction of functionalized aromatic compounds and esters.³² This latter extension of the classical Bouveault–Blanc reaction has turned out to be particularly simple and convenient, allowing M-SG materials to serve as alternatives to the hydride reagents.

We now present a study of applications of the Na₂K-SG(I) reagent in reductions of polyaromatic hydrocarbons and conjugated aromatic systems. In addition to conventional stirred-batch mode reaction conditions, we report on the feasibility of using Na₂K-SG(I) in flow reactor settings.

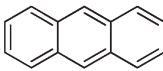
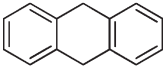
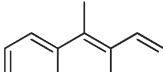
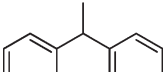
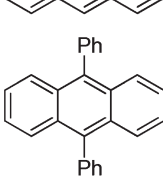
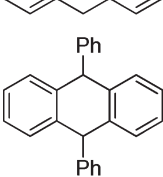
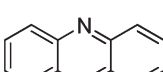
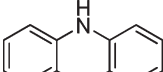
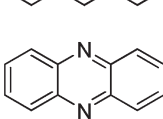
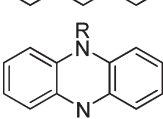
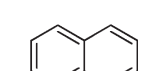
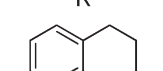
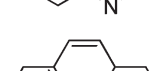
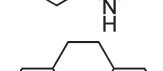
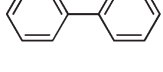
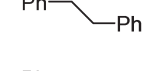
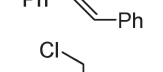
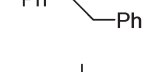
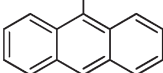
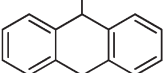
Table 1 shows representative examples of Birch reductions performed with Na₂K-SG(I) reagent. Some of the products (e.g., dialkylated phenazines³³) are attractive for photochromic and electrochromic applications.³⁴ Reduced acridine derivatives are important cores of therapeutic agents that target the central nervous system.³⁵

Entries 1–3 in Table 1 show reduction of anthracene and its alkyl- and aryl-substituted derivatives. In these cases, no other byproducts were observed. This finding, verified by deuterium oxide (D₂O) quenching, suggests formation of dianion salt intermediates, consistent with similar reports³⁶ with Li. For entry 3, the ratio of cis/trans isomers was 1:2.

Entries 4–6 show reduction of the N-heterocycles acridine, phenazine, and quinoline, respectively. The 5,10-dihydrophenazine in entry 5 was isolated as the dialkylated product to provide increased stability and ease of handling. Quinoline (entry 6) underwent smooth reduction to the tetrahydro analogue, in contrast to the reduction of naphthalene, which was relatively sluggish and gave only 1,4-dihydronaphthalene as product (determined by GC–MS) upon reduction with 3 equiv of Na₂K-SG(I). Entry 7 shows reduction of phenanthrene. Alkenes and alkynes conjugated to aromatic rings were shown to undergo reduction (entries 8 and 9) without any detectable reduction of aromatic rings. Presumably, these reactions occur via dianion salts as has been previously reported for stilbene and related olefins with sodium.³⁷ Interestingly, in the absence of a proton source, diphenyl acetylene underwent dimerization and cyclo-trimerization to give a mixture of 1,2,3,4-tetraphenyl butadiene (major) and hexaphenylbenzene (minor). Entry 10 shows dehalogenation–Birch reduction occurring in tandem. Entry 11 shows the reduction of indene. Additional information about the functional group compatibility of these reagents under essentially identical reaction conditions has been reported in previous publications.^{29–32}

When applied to biphenyl and related polyaromatic hydrocarbons such as pyrene and acenaphthene, the Na₂K-SG(I) reduction showed the characteristic colors of the arenide anions. The mixtures they form upon quenching can be understood in terms of the distribution of negative charges

TABLE 1. Birch Reductions Using Na₂K-SG(I)

Entry	Substrate	Product	Yield
1			97
2			86
3			96
4			92
5			87 ^a
6			74
7			95
8	Ph—C≡C—Ph		90 ^b
9	Ph—CH=CH—Ph		98
10			83 ^c
11			100 ^d

^aR = *n*-butyl. ^bReaction carried out in presence of HMDS (hexamethyldisilazane). ^cConversion by ¹H NMR. ^dConversion by GC–MS (done with 2.5 equiv of Na-SG), others are isolated yields.

among various positions in the dianions.³⁸ Not surprisingly, more electron-rich rings such as xylene and mesitylene did not undergo any detectable reduction. With 3,3'-dimethoxy biphenyl, in addition to the desired Birch reduction, cleavage of Me–OAr and MeO–Ar bonds was seen.

Some of the reactions above (entries 1 and 7) were carried out in small Pasteur pipet columns. In this method, a solution of the desired substrate in THF was passed through the column (containing a total of 7.5 metal equivalents) under an inert atmosphere. The collection flask contained enough water to quench the ether solutions of dianions (e.g., dianion of anthracene) generated in the column.

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Entries 1, 7, 8, and 9 were shown to be feasible with solid acids such as NH_4Cl and HCO_2NH_4 as in situ proton sources. However, in studies with anthracene and phenanthrene, when *t*-BuOH was used as a homogeneous proton source, the reactions, assembled with 2.5 equiv of metal, did not go to completion. They also showed degraded selectivity; even when the number of reducing equivalents was increased to 5, the expected dihydroaromatic products were accompanied by both starting material and several higher mass products ($M + 2$ and $M + 4$) of further reduction.

We have found that, if the $\text{Na}_2\text{K-SG(I)}$ reagent is handled quickly in lab air (~ 40 s), reactions give essentially the same results for anthracene reduction as those obtained with $\text{Na}_2\text{K-SG(I)}$ handled in a drybox. However, exposing the $\text{Na}_2\text{K-SG(I)}$ to lab air for 30 min caused a loss of about 1/3 of the reducing power (from 33 to 22% effective w/w Na_2K as determined by ethanol titration). As expected, these results are variable as a function of ambient humidity levels. Therefore, we recommend that the end user exercise standard precautions by handling this reagent like other air-sensitive materials such as LiAlH_4 , NaH , and Cu(I)Cl (e.g., storing in drybox or N_2 glovebag or in vacuum desiccator) or correct for the loss of reactivity by adding an excess of the reagent during use. These reductions can be also carried out with Na-SG(I)^{39} and $\text{K}_2\text{Na-SG(I)}$.

The procedure described here shows promise for development of flow reactors that could rapidly generate a solution of alkali metal carbanion species for reduction or other uses. Tandem reduction–alkylation (cf. entry 5, Table 1) and reduction–dehalogenation (entry 10) have also been shown to be feasible with the $\text{Na}_2\text{K-SG(I)}$ reagent. In summary, as an alternative to classical liquid ammonia conditions, we have provided a simple and convenient method for carrying out room-temperature Birch reductions of a series of polynuclear aromatic substrates in THF in the absence of co-reagents.

(39) Both Na-SG(I) and $\text{Na}_2\text{K-SG(I)}$ behaved similarly in terms of their stability in air. However, the reduction of anthracene and phenanthrene with $\text{Na}_2\text{K-SG(I)}$ in THF was found to be ~ 1.5 times faster than Na-SG(I) using identical procedures. As a result, for most subsequent studies, $\text{Na}_2\text{K-SG(I)}$ was used.

Experimental Section

General Procedure for M-SG Birch Reductions. In a 100 mL round-bottom flask equipped with a glass-coated magnetic stir bar and a rubber septum, anthracene (178 mg, 1 mmol, 1 equiv) and $\text{Na}_2\text{K-SG(I)}$ (420 mg, 40% w/w original loading of metal alloy in silica gel; titrated reducing capacity 4.9 mmol electrons = 2.45 equiv⁴⁰) were placed under an inert atmosphere (in a He drybox). To this flask was added 10 mL of anhydrous THF, and the mixture was stirred at room temperature for 6–8 h. The reaction color changed from colorless to dark blue. After this time, the reaction mixture was quenched with water (2 mL), added all at once. The resulting colorless mixture was then allowed to stir for 10 min. The organic layer was decanted, and the solid residues were washed with an additional 3×10 mL Et_2O . After separation, the combined organics were passed through a Celite pad in a sintered glass funnel to afford a clear solution that was concentrated on a rotary evaporator. The product 9,10-dihydroanthracene was obtained as a white solid (160–173 mg, yield = 88–97%). The product purity was verified by GC–MS ($m/z = 180$) and by ^1H and ^{13}C NMR: ^1H NMR (CDCl_3) δ 7.29 (m, 2H), 7.19 (m, 2H), 3.93 (s, 2H); ^{13}C NMR (CDCl_3) δ 136.5, 127.3, 126.0, 36.0.

Acknowledgment. Funding from SiGNa Chemistry Inc. for P.N.'s graduate assistantship is gratefully acknowledged.

Supporting Information Available: Detailed experimental procedures and ^1H and ^{13}C NMR spectra of prepared compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

(40) Reduction of one molecule of anthracene consumes two electrons. Since this paper's focus is effective two-electron reduction/ H_2 additions, the molar equivalency of the M-SG reactants is reckoned in terms of pairs of electrons, i.e., as 1/2 the total moles of alkali metal present. Thus, the above procedure's 4.9 mmol of electrons is referred to as 2.45 equiv. If reaction efficiency were perfect, 1 equiv of M-SG, so termed, would reduce 1 mol of aromatic, and its reaction with ethanol (2 mols) forms 1 mol of H_2 gas. This choice of terminology places the M-SG reagents on the same equivalence-counting scale as, for instance, lithium triethylborohydride or other single hydride donor reducing agents.