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DISSOLVING METAL REDUCTIONS WITH SODIUM POTASSIUM ALLOY IN THE PRESENCE OF 18-CROWN-6

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Abstract. The dissolving metal reduction of organic compounds can be performed in THF utilizing sodium potassium alloy in the presence of a catalytic amount of 18-crown-6.

The reaction of organic compounds with dissolving metals provides a method for the selective reduction of a number of functional groups.[1] Typically, alkali metals are employed for such reductions in liquid ammonia (with or without a cosolvent) although solvents such as amines and HMPT have also been utilized.[1]

Twenty years ago it was demonstrated that potassium metal or the sodium potassium alloy could be dissolved in polyethers to give blue solutions; however, the synthetic utility of these solutions was not examined.[2] More recently, Dye and co-workers have shown that the solubility of alkali metals in THF (and other solvents) can be greatly increased with the aid of an appropriate crown ether or cryptate.[3] They found that under suitable conditions these solutions contain high concentrations of alkali metal anions. Thus, the use of these solutions for the reduction of organic compounds would allow the range of solvents for dissolving metal reductions to be extended. Furthermore, these solutions should exhibit unique reducing properties when compared to classical dissolving metal reductions. Nevertheless, the exploration of the reducing ability of solutions containing alkali metals rendered soluble by crown ethers or cryptates has been limited to a few reports concerning the use of such solutions for the preparation of radical anions,[4] for the catalysis of anionic polymerization,[5] and for the reduction of benzene to cyclohexadiene.[6] The tedious procedure required for the preparation of such solutions has undoubtedly hindered progress in this area. A vacuum line distillation of the alkali metal is necessary in order to free it of any oxide and/or hydroxide coat.[3]

We have found that by employing the sodium potassium alloy (eutectic mixture[7]) intense blue solutions can be obtained in THF at 0°C with the aid of 18-crown-6 as a complexing agent. Since the alloy is a liquid at room temperature (and at 0°C; melting point -11°C), metal of sufficient purity for the preparation of such solutions can be obtained by withdrawing an aliquot of the alloy via a syringe. Distillation of the alloy is unnecessary. Preliminary spectroscopic examination of the blue solution (Cary-14) indicates that both the sodium anion and the potassium anion are present.[8]

We have found that blue solutions which contain the sodium potassium alloy suspended in THF in the presence of a catalytic amount of 18-crown-6 are capable of reducing organic compounds. These dissolving metal reductions were generally performed at 0°C in the presence of tert-butyl alcohol. As long as the blue solution was maintained at 0°C under a nitrogen atmosphere, its decomposition by tert-butyl alcohol was slow as evidenced by the fact that the blue color was not bleached (over a period of several hours) and by the fact that the rate of hydrogen evolution was very slow. Nonetheless, a slight excess of alloy was used for the reductions.

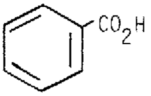
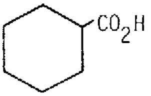
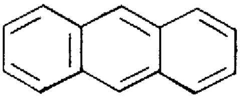
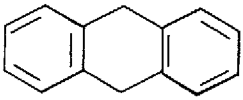
As is shown in the Table (entries 1-5), 4-octyne and 3-octyne can be reduced to the corresponding octenes (a mixture of cis and trans isomers). As expected,[9] when the reaction time was increased from 0.5 hrs. (entry 1 and 4) to 2 hrs. (entry 2 and 5), a substantial quantity of octane was also produced. Likewise, when the reaction mixture was allowed to warm to room temperature (entry 3), an appreciable amount of octane was produced. However, in all cases the ratio of trans isomer to cis isomer was 3:1. When the reduction of 4-octyne was attempted under the same conditions as described in the table for entry 2 but in the absence of crown ether,[10] only a trace amount of octenes could be detected by GC. Nonetheless, the trans:cis ratio remained at 3:1.

Our attempted reduction of benzoic acid (3 hr. reaction time) with the sodium potassium alloy (3.5 meq/mmol of benzoic acid) in THF in the presence of 18-crown-6 (0.1 mmol/meq of alloy) and tert-butyl alcohol (3.5 mmol/mmol of benzoic acid) resulted in the formation of cyclohexane carboxylic acid as the major product along with unreacted benzoic acid. By employing an excess of the alloy (see Table, entry 6) and extending the reaction time to 18 hrs., cyclohexane carboxylic acid could be produced in good yield. Thus, in contrast to the classical dissolving metal reduction of benzoic acid,[1] the aromatic ring is reduced all the way to the saturated hydrocarbon stage. When the reduction was attempted in the absence of crown ether (but otherwise under the same conditions as described in the table for entry 6), unreacted benzoic acid (>99%) was isolated.

In order to further explore the ability of the alloy solution to reduce aromatic rings, the reduction of anthracene was attempted. Our preliminary studies have shown that in the absence of tert-butyl alcohol (see Table, entry 7) the reduction proceeds smoothly to give dihydroanthracene. Presumably, the two electron reduction of anthracene by the alloy produces the dianion which is inert to further reduction but is protonated during work-up to dihydroanthracene.[11] However, when the same reduction was attempted in the presence of tert-butyl alcohol as a proton source, a complex mixture was obtained. The NMR spectrum of the mixture indicated that dihydroanthracene was present along with products arising from further reduction. When the reduction was attempted in the absence of crown ether, a substantail quantity (60-65%) of dihydroanthracene was cleanly produced regardless of whether tert-butyl alcohol was present or not. It is not altogether surprising that anthracene can be reduced to the dihydro stage by the alloy in the absence of crown ether. However, it appears that further reduction is facilitated by the crown ether. We believe that for those reductions described above in which the crown ether is required, it functions as a phase transfer catalyst to transfer the alloy from the liquid metal phase to the organic phase.

The experimental procedure is convenient and is illustrated for the reduction of 4-octyne. A solution of 18-crown-6 (0.7 g, 2.7 mmol) and *tert*-butyl alcohol (1.9 g, 26 mmol) in 30 mL of dry THF[12] was stirred magnetically at 0°C under nitrogen while the sodium potassium alloy (1.0 mL 25 meq[13]) was introduced in one portion via a hypodermic syringe.[14] To the resulting deep blue solution was added 4-octyne (1.1 g, 10 mmol) dropwise as a solution in 20 mL of dry THF over a 10 minute period. The blue color faded somewhat during the addition; however, at no time was the blue color completely discharged. After an additional 20 minutes of stirring (when the intense blue color had just returned to the reaction mixture), the reaction was quenched by the *careful* addition of water (30 mL, dropwise!). Diethyl ether (50 mL) was added to the resulting solution and the layers were separated. The organic layer was extracted with 1 N HCl (3 X 50 mL), H_2O (3 X 50 mL) and sat'd NaCl (1 X 50 mL). The organic solution was dried over anhydrous Na_2SO_4 and the solvent was removed by distillation. The residue was subjected to short path (Kugelrohr) distillation (125-130°C, 1 atm.) to afford 1.5 g of material which still contained THF and *tert*-butyl alcohol. The yield of products (see Table, entry 1) was determined by GC analysis.[15]

Table. Reduction of Organic Compounds with Na-K in THF in the Presence of 18-Crown-6^a

Entry	Substrate	Time (hr.)	Products	%Yield
1	$CH_3(CH_2)_2C{\equiv}C(CH_2)_2CH_3$	0.5	$CH_3(CH_2)_2CH{=}CH(CH_2)_2CH_3$ $CH_3(CH_2)_6CH_3$	$83^{b,c}$ 1^{b}
2	$CH_3(CH_2)_2C{\equiv}C(CH_2)_2CH_3$	2	$CH_3(CH_2)_2CH{=}CH(CH_2)_2CH_3$ $CH_3(CH_2)_6CH_3$	$76^{b,c}$ 14^{b}
3	$CH_3(CH_2)_2C{\equiv}C(CH_2)_2CH_3$	0.5^{d}	$CH_3(CH_2)_2CH{=}CH(CH_2)_2CH_3$ $CH_3(CH_2)_6CH_3$	$70^{b,c}$ 9^{b}
4	$CH_3CH_2C{\equiv}C(CH_2)_3CH_3$	0.5	$CH_3CH_2CH{=}CH(CH_2)_3CH_3$ $CH_3(CH_2)_6CH_3$	$81^{b,c}$ 1^{b}
5	$CH_3CH_2C{\equiv}C(CH_2)_3CH_3$	2	$CH_3CH_2CH{=}CH(CH_2)_3CH_3$ $CH_3(CH_2)_6CH_3$	$72^{b,c}$ 18^{b}
6		18^{e}		$86^{f,g,h}$
7		1		$67^{g,i}$

(a) Reductions were performed at 0°C with Na-K (2.5 meq[13]/mmol of substrate) in the presence of 18-crown-6 (0.1 mmol/meq of Na-K) and t-BuOH (1.0 mmol/meq of Na-K); spectral data (NMR and IR) were consistent with the assigned structures of the products. (b) Product contained THF and t-BuOH; yields were determined by GC. (c) Trans:cis, 3:1. (d) After 10 min. the reaction mixture was allowed to warm to room temp. (e) After 1 hr. the reaction mixture was allowed to warm to room temp. (f) Amount of Na-K was 9 meq/mmol of benzoic acid. (g) Isolated yield. (h) Purity: 95% by GC. (i) The reaction was performed in the absence of t-BuOH.

In summary, we have demonstrated that by using the sodium potassium alloy in the presence of 18-crown-6, the dissolving metal reduction of organic compounds can be conveniently performed in THF. Yields for the octyne reductions are comparable to those obtained by classical procedures[16] although the stereoselectivity is not as high. The reduction of aromatic compounds to the saturated hydrocarbon stage generally involves catalytic hydrogenation[1] and thus our procedure provides an alternative method for the reduction of benzoic acid to cyclohexane carboxylic acid. We are currently investigating a modification of reaction conditions which will allow for the complete reduction of anthracene (and other aromatic compounds) and will allow an increase in the stereoselectivity of the octyne reductions.

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References and Notes

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8. For a discussion of the Visible-IR spectra of solutions containing alkali metal anions, see: M. K. Lok, F. J. Tehan and J. L. Dye, J. Phys. Chem., 76, 2975 (1972).
9. H. O. House and E. F. Kinloch, J. Org. Chem., 39, 747 (1974).
10. In the absence of crown ether very faint blue solutions are obtained.
11. It has previously been shown that in the absence of a proton donor the dissolving metal reduction of anthracene (Li, ammonia) affords dihydroanthracene. See, for example: R. G. Harvey and K. Urberg, J. Org. Chem., 33, 2570 (1968).
12. All glassware was oven dried (110°C) and the THF was dried and deoxygenated by distillation, under nitrogen, from the sodium benzophenone ketyl.
13. From the % composition and the known density (at 100°C; see: "Handbook of Chemistry and Physics", CRC Press, Cleveland, OH) it was estimated that approximately 40 mL of alloy = 1 eq. (i.e. 40 mL of alloy is equivalent to 1 g-atom of either pure Na or pure K; thus, the $2e^-$ reduction of 4-octyne, for example, requires 2 meq of alloy/mmol of 4-octyne). Destruction of a known volume of the alloy with 95% EtOH followed by the addition of water and titration with standardized HCl confirmed this estimate.
14. The alloy was stored under cyclohexane and aliquots were withdrawn from beneath the surface of the metal.
15. GC columns for the analysis of mixtures of the n-octenes have been previously described. See: N. C. G. Cambell, J. R. P. Clarke, R. R. Hill, P. Oberhansli, J. H. Parish, R. M. Southam and M. C. Whiting, J. Chem. Soc. (B), 349 (1968).
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