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METAL-AMMONIA REDUCTION: THE RING REDUCTION OF AROMATIC CARBOXYLIC ESTERS

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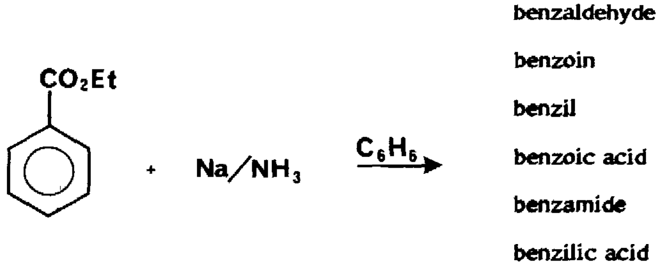
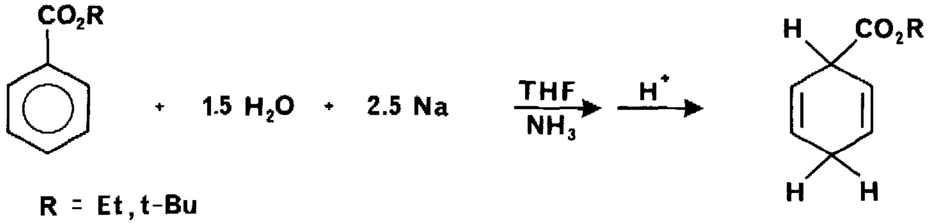
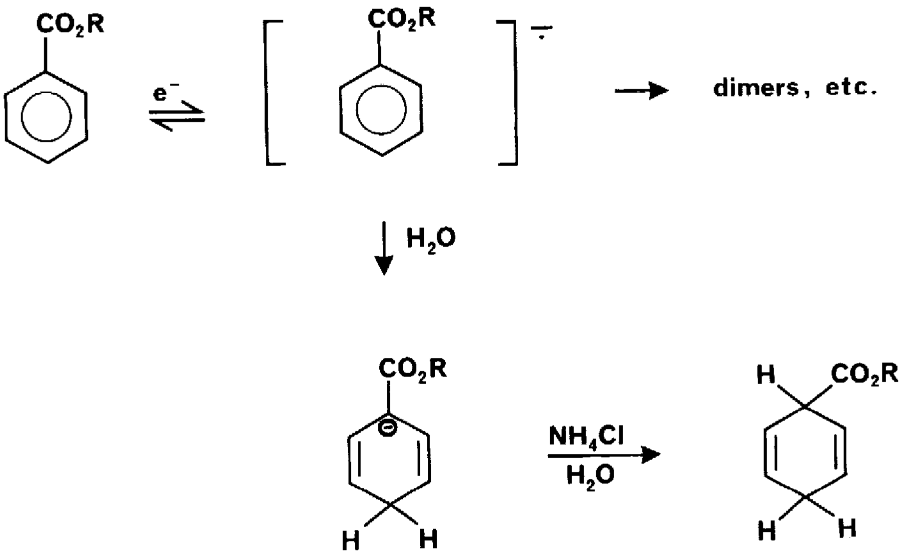
Aryl benzoates are reduced to 1,4-dihydroaromatics with Na/NH_3 in the presence of water.

The reduction of esters by sodium metal and alcohol in liquid ammonia is a familiar reaction known generally as the Bouveault-Blanc procedure.[1] Furthermore, Kharasch, et. al.,[2] investigated the reduction of ethyl benzoate with sodium/ammonia/benzene, and found a wide variety of products depending on reaction conditions. In all cases, however, only reduction involving the ester function was observed and attempts to effect ring reductions in aromatic esters are not evident in the literature. Hence, we regard the results reported herein as highly novel in that we have reduced alkyl benzoates to the corresponding 1,4-dihydro compounds in excellent yield. Moreover, we have found that some metal-ammonia additions can proceed efficiently with water present <u>before</u> metal addition,[3] and, in fact, with alkyl benzoates this appears to be the preferred procedure.

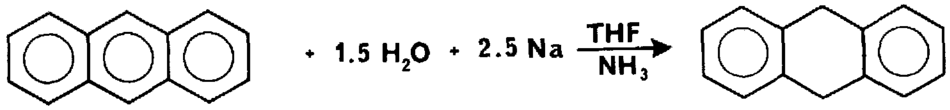




In view of the well known chemistry concerning the carbonyl based reduction of esters, coupled with numerous admonishments that metal-ammonia reductions must be carried out under strictly anhydrous conditions,[4] we were quite surprised to learn that ethyl benzoate may be reduced in over 90% yield[5] and t-butyl benzoate nearly quantitatively[6] by sodium-ammonia reduction in the presence of one to two equivalents water.[7] Since under comparable conditions (i.e., metal added last) Kharasch observed benzoin as the major product, we must presume that in the present case, water is acting to protonate the radical anion before dimerization takes place. Although alcohols have been used to protonate radical anions and shift the initial equilibrium, the <u>efficient</u> use of water[3] in this capacity appears to be rather unusual (preliminary results suggest that 1.5 eq t-butyl alcohol will also product satisfactory results, although not quite as good as water). An alternate possibility is that the radical anion is in equilibrium with a dianion, and that it is the dianion which is protonated removing it and the radical anion from the system. However, recent studies[8] with naphthalene and anthracene indicate that initially formed dianions from these hydrocarbons are protonated by ammonia itself to provide monoanions resistant to further protonation in the absence of proton source. Assuming that dianions in this presence case might follow a similar pathway, we tend to favor protonation of the radical anions as the likely course of the reaction.

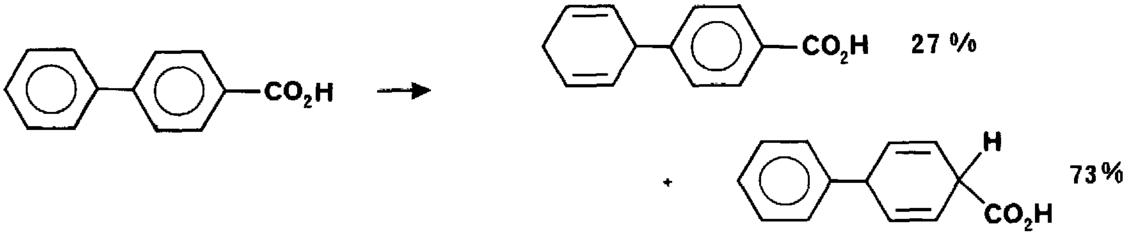


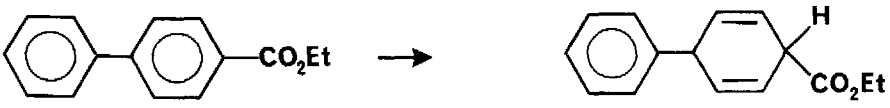
Thus, these results indicate that electron addition must be taking place more rapidly than destruction of the metal by water. If this is true, it should be observable in other systems as well provided a similar level of



reactivity towards electron addition. In order to test this hypothesis, we added sodium metal (2.5 mg-atm per mmol hydrocarbon) to anthracene in ammonia/THF (2:1) containing 1.5 equivalents water. After ten minutes, the solution was inverse quenched[8] into dilute ammonium chloride and product workup by ether extraction afforded 9,10-dihydroanthracene in quantitative yield.

The application of this procedure to polynuclear systems appears quite exciting and promises considerable synthetic potential. For example, although the sodium-ammonia reduction of biphenyl-4-carboxylic acid affords two products,[9] the ethyl ester provides regiospecific reduction to afford only a single product by the method described herein.[6] Hence it appears as though the ester function can be used to greatly enhance the regioselectivity (and presumably the reactivity) of aromatic carboxylic acid systems. Applications of this type are a matter for our continued investigations.





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References and Notes

(1) H. O., House, Modern Synthetic Reactions, 2d ed., W. A. Benjamin, Inc., Menlo Park, CA 1972, pp. 150-151.

(2) M. S. Kharasch, E. Sternfeld, F. R. Mayo, J. Am. Chem. Soc., 62, 362 (1940).

(3) Although metal-ammonia reductions are usually done under strictly anhydrous conditions, Wooster examined the reduction of toluene in the presence of water in 1937. He reports "a highly unsaturated liquid product which boils over the range 110-115, chars with fuming sulfuric acid, reacts vigorously with liquid bromine and rapidly decolorizes a solution of bromine in carbon disulfide." We have examined the reaction of sodium with toluene in ammonia containing varying amounts of water, and analysis by nmr indicates the product to be primarily toluene with some amount of reduction products only a part of which appears to be 1-methyl-1,4-cyclohexadiene. c.f., C. B. Wooster, K. L. Godfrey, J. Am. Chem. Soc., 59, 596 (1937).

(4) a. A. J. Birch, and G. Subba, Rao, Advances in Organic Chemistry, Methods and Results, E. C. Taylor, ed., Wiley-Interscience: New York, 1972.

b. H. Smith Chemistry in Nonaqueous Ionizing Solvents, G. Jander, H. Spandau, and C. C. Addison ed., Interscience: New York, Vol. I, part 2 1963.

c. R. G. Harvey Synthesis 161 (1970).

(5) This product has been prepared by the esterification of 1,4-dihydrobenzoic acid. See H. Plieninger, G. Ege, F. Jung, W. Maier-Borst. Chem. Ber., 94, 2088 (1961). All new compounds gave satisfactory analytical data. For a review of the nmr characteristics of 1,4-dihydroaromatics, see P. W. Rabideau. Acc. Chem. Res. 11, 141 (1978).

(6) The sodium (1.25 eq.) is added last to the ester in ammonia/THF (-78°) contaiing 1.5 eq. water. The reaction mixture is inverse quenched[8] into aqueous NH_4Cl after 15 minutes although the deep color generally only persists for about 10 minutes.

(7) In a report concerning the metal-ammonia reduction of acetophenone under a wide variety of conditions, one experiment was performed with water present before metal addition in the case of lithium. However, a variety of products were obtained with little ring reduction. See M. Narisada, F. Watanabe. J. Org. Chem, 38, 3887 (1973)

(8) P. W. Rabideau, E. G. Burkholder. J. Org. Chem. 43, 4283 (1978).

(9) P. W. Rabideau, S. J. Nyikos, D. L. Huser, E. G. Burkholder. Chem. Comm., in press. See also D. Franks, M. C. Grossel, R. C. Hayward, L. J. S. Knutsen Chem. Comm., 941 (1978).

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