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REACTION OF ORGANIC AZIDES WITH SODIUM HYDRIDE[1]

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The alkali metal hydrides are not noted for their ability to reduce organic functional groups. Only a few reports have appeared concerning such reactions, usually involving reduction of halogen derivatives.[2] We wish to report that several classes of organic azides (alkyl, aryl, and arenesulfonyl) react readily with sodium hydride in refluxing tetrahydrofuran or 1,2-dimethoxyethane to give nearly quantitative yields of nitrogen and moderate (30-60%) yields of the corresponding amine. For example, treatment of 1.0 mmole of cyclohexyl azide with ca. 19 mmoles of NaH in 10 ml of THF for 2 hrs. at reflux yielded 43% of cyclohexylamine and a small amount of dicyclohexylamine. (The latter probably results from further reaction of the cyclohexylamide anion.[3]) Similar results from other alkyl and aryl azides are presented in Table I.

$$R\text{-}N_3 + NaH \xrightarrow{THF,\ \Delta} RNH^-, Na^+ + N_2$$

Arenesulfonyl azides also react readily with NaH in THF but the initial product, sulfonamide anion, is rapidly degraded to sulfinate ion under these conditons. However, carrying out the reaction in the presence of an excess (30:1 ratio) of methyl iodide affords a good yield of the corresponding N,N-dimethylsulfonamide (ca. 90% from tosyl azide). Addition of methyl iodide improved the yield of amine (mostly as dimethyl derivative) somewhat in the case of phenyl azide (note Table I) but had little effect on the alkyl azide reactions. Methyl sulfate was much less efficient at protecting the sulfonamide anion and trimethylsilyl chloride halts all reaction, apparently poisoning the hydride surface. (Such an effect of silyl chlorides has been noted previously with KH reactions in THF.[2e])

Even sodium azide reacts slowly with NaH in refluxing THF. After a 3 hr. period 1.0 mmole of NaN_3 is 25% destroyed on refluxing with 18-19 mmoles of NaH in 10 ml. of THF.[4] Ammonia could be easily detected after quenching the reaction mixture with water.

Table I

Reactions of Azides with Sodium Hydride in THF[a]

Azide	T, °C	Time to Completion[b]	Yield of Amine (%)[c]
n-butyl	66°	2 hrs.	39
n-octyl	66°	2 hrs.	35
Cyclohexyl	66°	2 hrs.	43[d]
	66°	25 min.[e]	--
Benzyl	66°	2 hrs.	48
	66°	15 min.	33[f]
Phenyl	40°	2.3 hrs.	--
	40°	15 min.[g]	--
p-tolyl	66°	15 min.	33

[a] Reactions were carried out by treating 1.0 mmole of azide with about 19 mmoles of commercial NaH in 10 ml of THF.

[b] Time at which azide could no longer be detected by gas chromatography.

[c] Measured by gas chromatography.

[d] Using DME as solvent, a 47% yield was obtained.

[e] Reaction catalyzed by 0.4 mmole of pre-formed cyclohexylamine anion (sodium salt).

[f] In the presence of 30 mmoles of CH_3I, a 57% yield of dimethylaniline was obtained.

[g] Reaction catalyzed by 0.4 mmole of aniline anion (sodium salt).

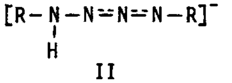
The azides are quite stable in refluxing THF in the absence of NaH. The presence of sodium metal, a common contaminant of commercial NaH, was not essential to the reaction since hydride purified by treatment with naphthalene in THF, exposure to air, and removal of hydrocarbon by washing gave the same results. Likewise, treatment of either n-octyl or p-tolyl azide (1.0 mmole) with sodium dispersion (0.15-0.20 mmole) in refluxing THF for 2 hrs. resulted in recovery of more than 90% of the azide and production of only traces of amine. Use of highly reactive NaH prepared by reaction of H_2 and sodium naphthalene in THF[6] resulted in a more rapid reaction (complete destruction of p-tolyl azide in 5-10 min. at reflux, formation of 68% p-toluidine) but no appreciable change in outcome. Commercial LiH in THF, or NaH in hydrocarbon solvents did not affect alkyl or aryl azides.

The reactions of alkyl and aryl azides (an probably NaN_3) are autocatalytic. Refluxing a mixture of aniline anion (sodium salt)[7] with phenyl azide in THF results in rapid destruction of the azide and an increase in aniline concentration. The presence of preformed amine anion (ca. 0.4 mmole) also greatly increased the rate of disappearance of phenyl and cyclohexyl azide when heated with NaH in THF, as shown in Table I. This is probably not the case with arenesulfonyl azides, however, since refluxing tosylamide anion with tosyl azide in THF for several hrs. does not result in appreciable destruction of the azide.

The reaction is probably initiated by attack of hydride ion on the terminal nitrogen of the azide in the manner of other soft bases (e.g., phosphines and carbanions).[8] The resulting triazene anion (I) must then decompose to N_2 and amide anion. (Monosubstituted, neutral, triazenes

$[R{-}N{=}N{=}N{-}H]^-$

I


$[R{-}\underset{H}{N}{-}N{=}N{=}N{-}R]^-$

II

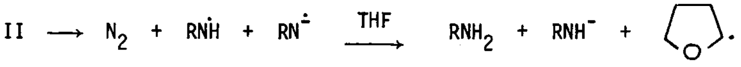
$[R{-}N{=}N{=}N{=}N{-}R]^{-2}$

III

are known to be quite unstable.)[9] Autocatalysis would be explained by rapid attack of amide anion on unreacted azide to yield tetrazene anion II and possibly, after deprotonation by NaH, dianion III. Evidence for the ease of formation of species such as II and III is the facile disproportionation of arylamine anion and aryl azide (eq. 1) observed on mixing these species in

$$ArNH^-, Na^+ + Ar'N_3 \xrightarrow{THF} \xrightarrow{H_2O} ArNH_2 + ArN_3 + Ar'NH_2 + Ar'N_3 \qquad (1)$$

THF at 25°, followed by addition of water.[10] Production of further quantities of amide anion must result from thermal breakdown of II and/or III to N_2 and amino radical species, followed by hydrogen atom abstraction from solvent, (eq. 2 and 3). Proton abstraction from THF is ruled out


$$II \longrightarrow N_2 + R\dot{N}H + R\dot{N}^- \xrightarrow{THF} RNH_2 + RNH^- +$$

(2)


$$III \longrightarrow N_2 + 2\,R\dot{N}^- \xrightarrow{THF} 2\,RNH^- +$$

(3)

(except possibly from the 3-position) by the lack of formation of ethylene in these reactions.[11] The rather low yield of amine in these systems is probably the result of numerous other reactions of these radical species, Nelsen and Heath noting a "plethora" of products from thermal decompositions of 1,4-diaryl-1,4-dimethyl-2-tetrazenes.[13] If our proposed mechanism is correct, it does suggest that the anionic tetrazenes (II and/or III) are much less stable than neutral 2-tetrazenes. Those studied by Nelsen and Heath, and tetramethyl-2-tetrazene[14] all required temperatures of well over 100° for appreciable rates of decomposition.

While these reactions apparently have little synthetic utility they do suggest interesting areas for amino radical research.

Footnotes and References

1. Supported in part by the Publich Health Service (Research Grant No. R01-AM-11419 from the National Institute of Arthritis and Metabolic Diseases), and by the Alfred P. Sloan Foundation.
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