The Preparation of Sulfonamides by Reduction of N-Hydroxysulfonamides

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The reduction of oximes and hydroxamic acids to the corresponding amines with lithium aluminum hydride is well known[1,2]. In certain cases, however, this reduction proceeds only with difficulty, and in the case of some N-hydroxy compounds the reduction with lithium aluminum hydride has completely failed[3]. The reduction of hydroxamic acids to the corresponding amides cannot be achieved by catalytic hydrogenation using Raney nickel at atmospheric pressure[4].

We have found that N-hydroxysulfonamides (**1a–f**) are reduced by lithium aluminum hydride in tetrahydrofuran to give the corresponding sulfonamides (**2**) in good yields. This fact is in contrast to the results obtained in the analogous reduction of sulfonyl halides[5] and sulfoxides[6]; in these cases, the reduction proceeds further to give mercaptans and sulfides, respectively.

$$\underset{\mathbf{1}}{Ar-SO_2-NHOH} \xrightarrow{LiAlH_4 \text{ or } H_2/Ni} \underset{\mathbf{2}}{Ar-SO_2-NH_2}$$

We also made attempts to reduce N-hydroxysulfonamides (**1**) by catalytic hydrogenation at ambient temperature and pressure. Of the catalysts used (Pd, PdO_2, PtO_2, and Raney nickel), only Raney nickel was effective. In the case of PtO_2, the catalyst became inactive after the initial uptake of hydrogen and no further reduction was observed.

According to Horner et al.[7], in the hydrogenation of cyclohexene in ethanol even a small quantity of N-hydroxybenzenesulfonamide (**1a**) used as a deactivator was sufficient to poison the catalyst to an extent of 21–47%. However, we have found that in the presence of excess Raney nickel compounds **1a–f** can be reduced at ambient temperature and pressure to give the corresponding sulfonamides (**2a–f**) in 64–80% yields.

Reduction of N-Hydroxyarenesulfonamides with Lithium Aluminum Hydride:

A solution of **1** (0.02 mol) in tetrahydrofuran (~30 ml) was added, in small portions with stirring, to a suspension of lithium aluminum hydride (1 g) in tetrahydrofuran (100 ml) at 20–40°. The mixture was stirred for 2 hr, then evaporated to a small volume, diluted with ether (50 ml) (except for **e** and **f**), and acidified with dilute hydrochloric acid. The aqueous layer was twice extracted with ether and the extract evaporated. The residue was recrystallized from water or aqueous ethanol to give the pure sulfonamide.

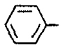
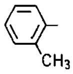
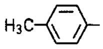
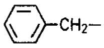
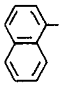
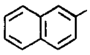
In the case of the N-hydroxynaphthalenesulfonamides (**1e**, **1f**), the reduction was carried out as above, except that no ether was used for dilution; upon the addition of dilute hydrochloric acid, the crude sulfonamides precipitated. The products were recrystallized from ethanol.

Reduction of N-Hydroxyarenesulfonamides with Hydrogen/Raney Nickel:

Raney nickel (~0.3 g; prepared from Ni—Al alloy, 42:58%)[8] was added to a solution of **1** (0.3 g) in ethanol (25 ml) and the mixture was shaken with hydrogen at ambient temperature and pressure. Hydrogen uptake was complete within 30 min. The catalyst was removed, ethanol evaporated, and the residue recrystallized from water or aqueous ethanol.

The I.R. spectra of compounds **2** were identical with those of authentic samples. The elemental analyses of compounds **2** were in good agreement with the calculated values.

Table. Reduction of N-Hydroxysulfonamides (**1**) to Sulfonamides (**2**)

	Ar	Yield %		m.p. of **2**[a]
		Reduction with $LiAlH_4$	Reduction with H_2/Ni	
a		82	73	153°
b		87	80	152°
c		82	80	138°
d		54	80	104°
e		93	78	150°
f		93	64	216°

[a] m. p. and mixture m. p. with authentic sample.

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