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On the Perils of Unexpected Silane Generation

Abstract:

A number of functional group reductions reported in the literature utilize mixtures of triethoxysilane [(EtO_3SiH)] and Lewis acids. It should be noted that this combination can produce the highly pyrophoric and toxic gas, silane (SiH_4).

Over the past number of years, several safety alerts have been published concerning hazards related to the unexpected generation of silane, SiH_4, in chemical reactions. For example, see the reports in *Chemical & Engineering News* (C&EN).[1] These alerts are related to publications pertaining to the preparation of hydride-capped silicon nanoparticles by the reduction of $SiCl_4$ with $LiAlH_4$ in ethereal solvents.[2] The initial publications apparently failed to mention that this procedure could lead to the release of SiH_4, an extremely dangerous, toxic, pyrophoric, and explosive gas (TLV-TWA 5 ppm, flammable in air between 1 and 96% v/v).[3] Whilst this material can be generated and handled safely on a large scale with appropriate safety and engineering controls, its unexpected generation in a standard organic chemistry facility can lead to serious hazards to workers and risks to infrastructure. A 1% silane mix in nitrogen is flammable in air.[3] It is of interest to note that that the efficient generation of SiH_4, GeH_4, and SnH_4 from their respective tetrachlorides and $LiAlH_4$ was reported as long ago as 1947.[4] It would be assumed (hoped) that any competent and well-trained synthetic organic chemist would recognize the potential for SiH_4 generation from $SiCl_4$ and $LiAlH_4$. However, this highly hazardous material can also be generated by a less apparent, insidious pathway.

These C&EN news reports recall an incident several years ago in which a highly pyrophoric and explosive gas (presumed to be SiH_4) was unexpectedly generated.[5] The reaction under investigation was the selective reduction of methyl-11-bromo-undecanoic ester to 11-bromo-undecanol. This had been done successfully on pilot scale using $BH_3{-}THF$. However, for large-scale manufacture, a more economical but still selective reductant was sought. A paper was located describing the reduction of esters to alcohols in the presence of other reducible groups, including primary alkyl bromides, with $(EtO)_3SiH$ and $Ti(i\text{-}PrO)_4$ as a catalyst.[6] This procedure was tried on a millimolar scale. The reaction proceeded without incident, and the product was isolated in very high yield and excellent purity, exactly as described in the literature.[6] The reaction was then scaled up to multigram scale with quite a different outcome. Shortly after the reagents were mixed, an extremely exothermic reaction began with a highly pyrophoric gas being generated. The incident terminated when the reaction vessel exploded, resulting in the destruction of all the surrounding contents in the fume hood.[5] Whilst never unambiguously proven, the most likely cause of this incident was the disproportionation of the $(EtO)_3SiH$ to mixtures of $(EtO)_XSiH_Y$ including SiH_4.[5]

Occasionally the combination of $(EtO_3)SiH$ and Lewis acid has been reported for the reduction of functional groups other than esters. For example, phosphine oxides to phosphines [$(EtO)_3SiH + Ti(OiPr)_4$],[7] reductive etherification [$(EtO)_3SiH + InCl_3/TMSCl$],[8] reduction of ketones [$(EtO)_3SiH + ZnI_2$][9] and the latest being the reduction of amides to amines [$(EtO)_3SiH + Zn(OAc)_2$)][10]—a reaction that could be very attractive as a greener alternative to $LiAlH_4$ or BH_3 reduction for the synthesis of amines. It should be noted that the large-scale synthesis of SiH_4 is via the Lewis acid- or Lewis base-catalysed disproportion of $HSiCl_3$,[11,12] and there are reports in the literature of $(EtO)_3SiH$ as a SiH_4 precursor in the presence of various catalysts and in the absence of a reducible substrate.[13] However, it should ***never*** be assumed that reaction mixtures containing reducible substrates, $(EtO)_3SiH$ and Lewis acids, will not generate SiH_4, and the use and scale-up of any such process should be undertaken with great caution and with high regard for potential hazards of unexpected generation of SiH_4. Safer alternatives to $(EtO)_3SiH$ that cannot lead to SiH_4 generation should always be considered before the use of $(EtO)_3SiH$. Some examples are tetramethyldisiloxane[14] and polymethylhydrosiloxane.[7,15]

Note Added after Proof: A correction to reference 10 has just been published.[16]

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