This Week's Citation Classic

Caglioti L & Grasselli P. A new method for the reduction of aldehydes and ketones to CH_2 under mild conditions. *Chem. Ind. London* **1964**:153.
[Istituto di Chimica Generale, Centro per lo Studio delle Sostanze Naturali del CNR, Politecnico, Milano, Italy]

The reaction of tosylhydrazones of ketones and aldehydes with $NaBH_4$ in MeOH or in dioxane solution is reported. The reaction results in short time (from a few minutes to 1-2 hours) and in mild conditions (no drastic agents such as acids or bases are employed) in CH_2 compounds. [The *SCI*® indicates that this paper has been cited in over 100 publications since 1964.]

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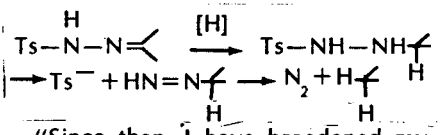
"My activity in the field of tosylhydrazones chemistry began in a quite casual way. Actually, I was searching for a reference on the chemistry of *Olea europea* terpenes when my attention was attracted by the Bamford-Stevens[1] reaction, reported in an old issue of *Journal of the Chemical Society*.

"The Bamford-Stevens reaction allows through a basic treatment the transformation of ketones' tosylhydrazones into olefins. At that time, I had some experience with the Wolff-Kishner reaction, modified by Huang-Milong, to transform an hydrazone of a carbonylic compound into a saturated compound. So if tosylhydrazones can give rise to olefins and hydrazones can provide for saturated compounds, I felt tempted to test what would happen by reducing a tosylhydrazone before its treatment with a strong alkaline agent (see figure on the right). My attempt was surprisingly successful: during the first experiment, carried out with the 3-keto-17b-hydroxy-androstane, I obtained the corresponding saturated compound.

"I worked for several years on this reaction and different reactions which could be carried out with tosylhydrazones. First of all, the reduction reaction appeared to be quite a good method to reduce keto groups to CH_2 groups in very mild conditions. This reduction reaction is particularly useful when multifunctional compounds (carbohydrates, β- and α-hydroxy ketones, etc.) are employed. $NaBH_4$, BH_3, $LiAlH_4$, and obviously the numberless variations of these hydrides are the most commonly used reagents. The reaction mechanism confirms the initial hypothesis: the tosylhydrazone molecule is reduced to a substituted tosylhydrazone, which in turn provides the saturated final product through formation of an unstable diimide:



"Since then, I have broadened my study of this versatile and interesting class of compounds and other reactions were developed: azoalkenes formation, osazones formation mechanism, etc. This effect started from a lucky opening, to a given page, of *Journal of the Chemical Society*. For further articles in this field see the references below.[2-4]

"In my opinion, this paper has been cited so many times because of the fact that it describes, in one page on a highly diffused journal in English, a very simple way to solve a difficult problem."

1. **Bamford W R & Stevens T S.** The decomposition of toluene-*p*-sulphonylhydrazones by alkali. *J. Chem. Soc.* **1952**:4735-40.
2. **Caglioti L.** The reduction of tosylhydrazones and of acyl tosylhydrazides. *Tetrahedron* **22**:487-93, 1966.
3. **Caglioti L, Ciranni G, Rosini G & Selva A.** The course of the reduction of acyl-tosylhydrazides with $LiAlH_4$. *Ricerca Scientifica* **37**:1146-8, 1967.
4. **Cacchi S, Caglioti L & Paolucci G.** The mechanism of the reduction of tosylhydrazones with B_2H_6 and $NaBH_4$ in aprotic solvents. *Bull. Chem. Soc. Jpn.* **47**:2323-4, 1974.