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LETTERS

Reduction of Olefins on Solid Support Using Diimide

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Abstract: The reduction of solid supported olefinic substrate using diimide is described. The diimide, prepared from sulfonylhydrazide, was found to efficiently reduce the olefinic substrates. Typically, the reaction proceeds in over 90% yield to afford the reduction product cleanly after cleavage from the Wang resin. © 1998 Elsevier Science Ltd. All rights reserved.

The use of solid phase organic synthesis (SPOS) for drug discovery has increased the last several years.[1,2] During this time, an increasing number of reactions has been adapted to solid phase synthesis. However, among the methods still not successfully applied to SPOS is the hydrogenation reaction, since the usual methods require reacting two heterogeneous entities together. Diimide reductions of olefins using sulfonylhydrazides is a well known process [3,4,5] but, to our knowledge, this reaction has not been applied to solid phase chemistry. Soluble catalysts [6,7] and resin-bound sulfonylhydrazides have also been reported,[8] but the use of these reagents is not useful for multistep sequences on polymer. We now wish to report herein the use of diimide for the reduction of resin-bound olefinic substrate.

Typically, the reductions were performed by mixing the Wang resin supported substrate and 3 equivalents of benzenesulfonylhydrazide (**1**) in DMF at 100°C overnight. The reactions were carried out in an open flask or sealed tube. The substrate was then cleaved from the resin using either 20% TFA in dichloromethane or sodium hydroxide in THF/MeOH (Table 1). Hence, under these conditions, resin-bound *trans*-stilbene was reduced to *p*-phenethylbenzoic acid in 91% yield after cleavage from the resin (entry 1). Electron deficient (entries 2-3) and electron rich (entry 4) olefins showed similar reactivity. Alkynes can also be reduced using this procedure. For example, hexynoate derivative (entry 5) was reduced to the corresponding alkane quantitatively. Trisubstituted olefins (entry 7) showed moderate reactivity compared to the less substituted olefins.

We also examined the reactivity of other sulfonylhydrazides, namely 4-fluorobenzenesulfonylhydrazide (**2**) and 2,3,5-trichloro benzenesulfonylhydrazide (**3**) in the reduction protocol. To determine their reactivity, experiments were run at three different temperatures (60°C, 80°C, 100°C) for each sulfonylhydrazide. From these experiments, we found that vinylbenzoic acid derivative was fully reduced at 60°C using the sulfonylhydrazide **3** compared to 63% and 72% yield with sulfonylhydrazide **1** and **2** respectively. Even though our standard conditions employed benzenesulfonylhydrazide (**1**) in DMF at 100°C, these

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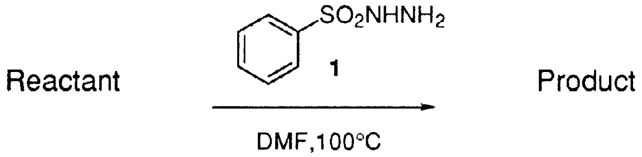
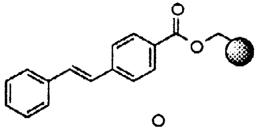
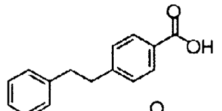
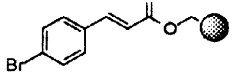
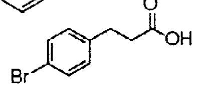
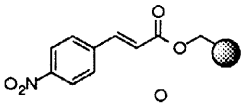
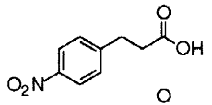
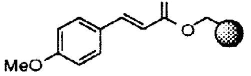
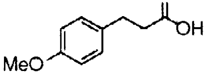
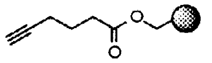
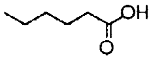
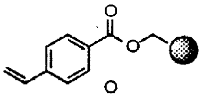
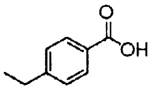
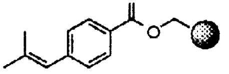
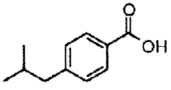
results suggest the possibility of using other sulfonylhydrazides which require lower temperatures to perform the reduction, hence providing a useful alternative for heat sensitive substrates.

Table 1: Diimide reductions of resin-bound alkenes and alkyne.



Entry	Reactant	Product	Recovered Yield (%)	Purity[a] (%)
1			>95	91
2			>95	>95
3			>95	>95
4			>95	92
5			>95	>95
6			>95	>95
7			>95	33

(a)Purity determined by ^{1}H NMR. In all cases the main contaminant was the starting material.

In conclusion, we report an effective, and convenient method for the reduction of olefins on solid support, and this reaction should find use in the synthesis of various libraries.

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