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LETTERS

Caveat in Alkylative Fragmentation of Aldehyde Tosylhydrazones of Cyclic Ethers

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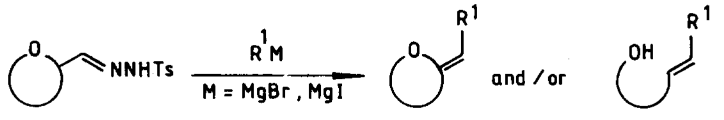
Abstract: Tosylhydrazones of aldehydes at the α-position of cyclic ethers when exposed to carbon nucleophiles produce either ring opened alkylated olefinic alcohols and/or cyclic alkylated vinyl ethers, the ratio of which is dependent on nature of hydrazone and nucleophile used.

Tosylhydrazones of ketones have been thoroughly exploited as versatile starting materials [1]. Mostly this class of compounds has been used as a source of vinyl anions [2] for alkylation with various electrophiles or for formation of olefins with specific geometries [3]. However it is rather surprising to note that aldehyde tosylhydrazones are still with few exceptions [4] an unexplored class of compounds. Our group has recently discovered a novel alkylative fragmentation of tosylhydrazones of aldehydes having α-epoxy [5] and isopropylidene groups [6] and also a reductive fragmentation [7] to produce chiral allyl alcohols. Also these hydrazones under the influence of Bamford-Stevens reaction conditions produce vinyl ethers [8]. In the course of further studies on alkylative fragmentation of aldehyde tosylhydrazones of cyclic ethers, we have observed unprecedented and unexpected findings, the results being described herein (equation 1).



(equation-1)

The tosylhydrazone **1** (Table **1**, entry 1) when exposed to three equivalents of PhMgBr in anhydrous THF, gave a very clean formation of the benzyl carbinol **1a** in 59%

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Table 1

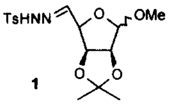
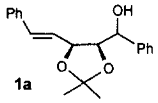
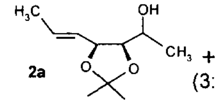
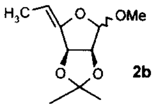
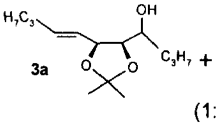
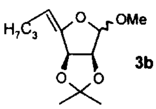
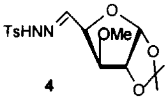
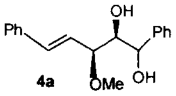
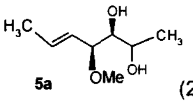
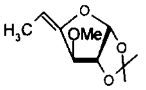
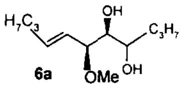
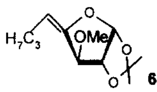
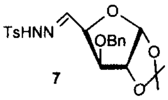
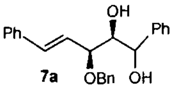
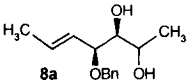
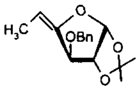
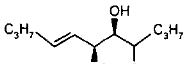
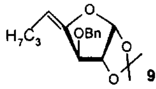
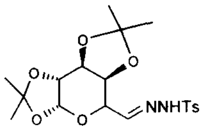
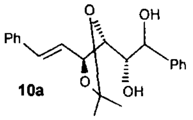
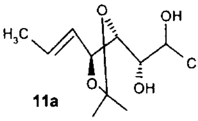
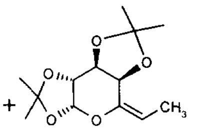
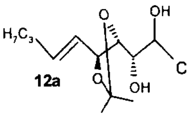
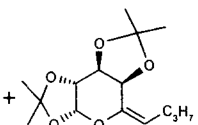
Entry	Substrate	Nucleophile	Products(Ratio)[a]	Overall Yields(%)[b]
1	 1	PhMgBr	 1a -	59
2	"	MeMgI	 2a + (3:1)  2b	86
3	"	PrMgBr	 3a + (1:2)  3b	72
4	 4	PhMgBr	 4a -	69
5	"	MeMgI	 5a + (2:1)  5b	68
6	"	PrMgBr	 6a + (1:2)  6b	65
7	 7	PhMgBr	 7a	54
8	"	MeMgI	 8a + (2:1)  8b	70
9	"	PrMgBr	 9a + (1:2)  9b	69

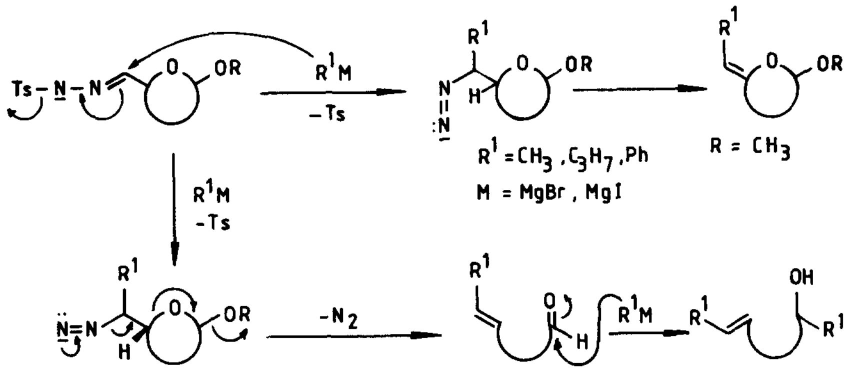
Table 1. (Contd...)

Entry	Substrate	Nucleophile	Products(Ratio)[a]	Overall Yields (%)[b]
10	 10	PhMgBr	 10a	50
11	,,	MeMgI	 11a + (1:1)  11b	69
12	,,	PrMgBr	 12a + (1:2)  12b	71

a) The olefin geometry of ring open products has found to be trans, however for ring unopened products the geometry is not determined.

b) Yields calculated after column chromatography of the products.

isolated yield. The formation of this product may be rationalized based on our previous findings [5,6,7]. Mechanistically, the first equivalent of nucleophile, viz. PhMgBr acts as a base whereas the second and third equivalents add to C-1 and C-5 (furanose nomenclature) [9]. Hydrazone **1** was also treated with methylmagnesium iodide and propylmagnesium bromide (entries 2 and 3). These experiments yielded to our surprise, the alkylated cyclic vinyl ethers (**2b** and **3b)** in substantial quantities along with expected products **2a** and **3a**. This unexpected result prompted us to study other cyclic ether tosylhydrazones (entries 4-12). Accordingly the tosylhydrazone **4**, when exposed to three equivalents of methylmagnesium iodide, gave a mixture of **5a** and **5b** in 68% overall yield. Similar observations were made with propylmagnesium bromide (entry 6). However, exposure of **4** to three equivalents of phenylmagnesium bromide furnished the benzyl carbinol **4a** in 69% yield. Identical results were drawn from tosylhydrazone **7** (entries 7,8 and 9). Changing the cyclic ether from five-membered to six-membered (entries 10,11 and 12) had no influence on the product formation except for a little variation in the ratio of the products. These results may be rationalized as shown in equation 2.



(equation - 2)

In conclusion, a new observation has been made on the chemistry of cyclic ethers having tosylhydrazone functionality at their α-position. The ring-opened products form important building blocks for C-glycoside synthesis [10], whereas the viny1 ethers may be useful starting materials for synthesis of constano lactone[11] and related compounds.

Spectral data:

1a). ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.20-7.40(m, 10H), 6.45(d, 1H, J=15.8Hz), 6.18(dd, 1H, J=15.8Hz, 7.4Hz), 4.60-4.85 (m, 2H), 4.45(t, 1H, J=6.3Hz), 1.62(s, 3H) and 1.40(s, 3H).

3b). ^{1}H NMR (200 MHz, $CDCl_3$): δ 4.95.(s, 1H), 4.92(dd, 1H, J=4.4Hz, 1Hz), 4.50(d, 1H, J=4.5Hz), 4.35(d, 1H, J=4.0 Hz), 3.30(s, 3H), 2.40-2.55(m, 2H), 1.5-1.7(m, 2H), 1.40(s, 3H), 1.25(s, 3H) and 0.98(t, 3H, J=7.4Hz).

6b). ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.0(d, 1H, J=4Hz), 4.52(dist t, 2H), 4.0(d, 1H, J=4Hz), 3.32(s, 3H), 2.50-2.60(m, 2H), 1.60-1.65(m, 2H), 1.50(s, 3H), 1.32(s, 3H) and 0.95(t, 3H, J=6.6Hz).

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[9] The absolute stereochemistry at the newly generated carbinol (C-1 carbohydrate) is not determined.

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