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One-pot transformation of nitriles into aldehyde tosylhydrazones

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Abstract—Reduction of various nitriles with Raney nickel and sodium hypophosphite in aqueous acetic acid and pyridine in the presence of tosylhydrazine gave the corresponding aldehyde tosylhydrazones in good yield.

Hydrazones are readily available compounds which can be transformed into a large variety of other structures, and have many industrial and biological applications.[1] Tosylhydrazones are a similarly valuable subclass of hydrazones whose most important synthetic uses are (a) nucleophilic additions to the C=N double bond; (b) electrophilic additions to hydrazone derived azaenolates; (c) Bamford–Stevens and Shapiro reactions, and (d) reductions, just to mention a few.[2] The most widely applied general method to obtain hydrazone derivatives is the condensation of an aldehyde or ketone with an (un)substituted hydrazine in the presence of an acidic catalyst. With acid sensitive aldehydes this condensation can be performed under neutral conditions as well.[1] Carboxylic acid derivatives such as imino-esters and orthoesters were also converted to hydrazones.[1]

In the course of a project on the synthesis of glycomimetics we needed tosylhydrazones of 2,6-anhydro-aldoses (*C*-glycopyranosyl aldehydes). Although several syntheses were published for such aldehydes,[3] these compounds are still not readily accessible because of the lengthiness of the preparative procedures. The most straightforward way to get *C*-glycosyl aldehydes is reduction of the easily available glycosyl cyanides with Raney nickel–sodium hypophosphite in aqueous acetic acid and pyridine.[4,5] However, under these conditions the product must be trapped as an imidazolidine derivative by 1,2-dianilino-ethane, otherwise, in the absence of this auxiliary, subsequent elimination of acetic acid results in a 2,6-anhydro-ald-2-enose (1-formyl glycal).[6] The aldehyde function can be unmasked from the imidazolidine by acid catalyzed hydrolysis.[4,5] To the best of our knowledge this procedure was not used with any other nitriles.

Since the above sequence also seemed lengthy with respect to the planned tosylhydrazone synthesis, we investigated a modification based on the following reasoning. The position of the equilibrium in hydrazone forming reactions is known to be shifted well to the product side.[7] This might allow an aldehyde to be trapped in situ by a hydrazine derivative similar to the above mentioned case. Therefore, the reduction of various nitriles **1** was investigated in the presence of tosylhydrazine. These experiments proved that our hypothesis was right, and the corresponding aldehyde tosylhydrazones[†] **2** were isolated in good yield (Table 1). The transformation could be performed in the presence of various functional groups and was extended to the per-*O*-acetylated-β-D-glucopyranosyl cyanide[8] **1h** as well. Several experiments were carried out with aliphatic nitriles (such as acetonitrile, propionitrile, 4-chlorobutyronitrile, ethyl cyanoacetate). In these cases clean transformations could be detected by TLC, how-

Keywords: hydrazones; nitriles; reduction; sulfonyl compounds; trapping reactions.

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[†] **General procedure for the synthesis of aldehyde tosylhydrazones 2**: Raney nickel (1.5 g, from an aqueous suspension, Merck) was added at room temperature to a vigorously stirred solution of pyridine (5.7 mL), acetic acid (3.4 mL), and water (3.4 mL). Then sodium hypophosphite (0.74 g, 8.4 mmol), tosylhydrazine (0.32 g, 1.7 mmol), and the corresponding nitrile **1** (1 mmol) were added to the mixture. When the reaction was complete (TLC, eluent: ethyl acetate–hexane 1:1) the insoluble materials were filtered off with suction, and washed with dichloromethane (10 mL). The organic layer of the filtrate was separated, washed with cold water (2×3 mL) and was concentrated under reduced pressure. Residual pyridine was removed by repeated co-evaporations with toluene. The residue was purified by crystallization or by column chromatography (eluent: ethyl acetate–hexane 1:1 or 1:2) to give the title compounds.

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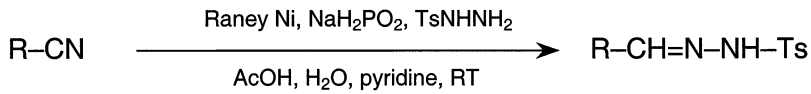
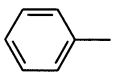
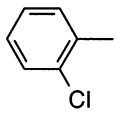
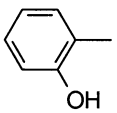
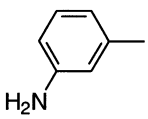
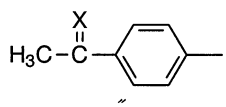
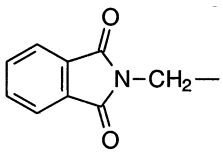
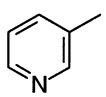
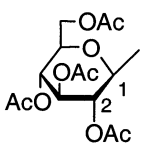
Table 1. Preparation and characterization of aldehyde tosylhydrazones[a] **2**



1 **2**

Starting compound		Product (**2**)			
				NMR[b]	
1	R	Yield (%)	Mp (°C)	C*H* (*C*H)	N*H*
a		96	124–125 (dec.) Lit.[9] 127–128	7.92 (146.9)	11.46
b		85	140–143 (dec.) Lit.[10] 142–144	8.26 (142.7)	11.76
c		88	149–152 Lit.[11] 149–151	8.19 (146.2)	10.23
d		83	Syrup	7.62 (148.4) $CDCl_3$	8.2–8.8 (br s) $CDCl_3$
e	 X = O in the starting material X = NNHTs in the product	80[c]	198–199 (dec.)	7.91 (146.2)	10.61, 11.55
f		75	160–161 (dec.)	7.26 (t, $J=3$) (144.5)	11.17
g		20[d]	154–156 (dec.) Lit.[12] 149–151	7.97 (144.1)	11.69
h		60	Syrup[e] $[\alpha]_D$ −8 (*c* 1.33, $CHCl_3$)	7.00 (d, $J_{H\text{-}1,CH}=6.3$) (143.7) $CDCl_3$	9.16 $CDCl_3$

[a] Each new compound gave correct elemental analysis.

[b] For DMSO-d_6 solutions, δ [ppm], J [Hz].

[c] The reaction was performed with 3 equivalents of tosylhydrazine.

[d] In spite of the clean reaction indicated by TLC several attempts failed for isolating this substance in higher yield. The probable reason for this may be a strong complexation of the product with Ni(II) salts.[1]

[e] ^1H NMR ($CDCl_3$): δ (ppm) 9.16 (s, 1H, NH), 7.80 (d, 2H, $J=7.9$ Hz, Ts), 7.34 (d, 2H, $J=7.9$ Hz, Ts), 7.00 (d, 1H, $J=6.3$ Hz, CH=N), 5.26 (pseudo t, 1H, $J=9.4$, 9.5 Hz, H-2) 5.05 (pseudo t, 1H, $J=9.4$, 10.0 Hz, H-3), 4.98 (pseudo t, 1H, $J=9.5$, 10.0 Hz, H-4), 4.24 (dd, 1H, $J=5.3$, 12.2 Hz, H-6), 4.07 (dd, 1H, $J=1.8$, 12.2 Hz, H-6′), 3.99 (dd, 1H, $J=6.3$, 9.5 Hz, H-1), 3.72 (ddd, 1H, $J=1.8$, 5.3, 9.5 Hz, H-5), 2.42 (s, 3H, Ts-CH_3), 2.07, 2.03, 2.01, 1.72 (4s, 12H, 4 OAc); ^{13}C NMR ($CDCl_3$): δ (ppm) 170.8, 170.6, 170.2, 169.6 (C=O), 144.3, 135.5 (Ts quaternary carbons), 143.7 (CH=N), 129.8, 128.0 (Ts), 77.8, 75.9, 73.1, 69.6, 68.3 (C-1 to C-5), 62.1 (C-6), 21.6 (Ts-CH_3), 20.8, 20.7, 20.3 (CH_3).

ever, the products decomposed during work-up. The configuration of the C=N double bond has not been investigated in compounds **2**.‡

In summary, we have found a simple, high yielding, one-pot procedure for the transformation of nitriles into aldehyde tosylhydrazones. This method can be advantageous when the corresponding nitrile, but not the aldehyde, is easily available.

Acknowledgements

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References

1. Dumić, M.; Korunčev, D.; Kovačević, K.; Polak, L.; Kolbah, D. In *Methoden der organischen Chemie (Houben-Weyl)*; Klamann, D.; Hagemann, H., Eds.; Thieme: Stuttgart, 1990; Vol. E14b, pp. 434–631.
2. Chamberlin, A. R.; Sheppeck II, J. E. *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; John Wiley & Sons: Chichester, 1995; Vol. 7, pp. 4953–4958.
3. Somsák, L. *Chem. Rev.* **2001**, *101*, 81–135.
4. Albrecht, H. P.; Repke, D. B.; Moffatt, J. G. *J. Org. Chem.* **1973**, *38*, 1836–1840.
5. Dettinger, H.-M.; Kurz, G.; Lehmann, J. *Carbohydr. Res.* **1979**, *74*, 301–307.
6. Schmidt, R. R.; Frische, K. *Bioorg. Med. Chem. Lett.* **1993**, *8*, 1747–1750.
7. Tennant, G. In *Comprehensive Organic Chemistry*; Sutherland, I. O., Ed.; Pergamon: Oxford, 1979; Vol. 2, pp. 385–590.
8. Myers, R. W.; Lee, Y. C. *Carbohydr. Res.* **1986**, *154*, 145–163.
9. Freudenberg, K.; Blümmel, F. *Liebigs Ann.* **1924**, *440*, 45–59.
10. McMahon, R. J.; Abelt, C. J.; Chapman, O. L.; Johnson, J. W.; Kreil, C. L.; LeRoux, J. P.; Mooring, A. M.; West, P. R. *J. Am. Chem. Soc.* **1987**, *109*, 2456–2469.
11. Bhati, A. *J. Chem. Soc.* **1965**, 1020–1023.
12. Street, J. D.; Baradarani, M. M.; Beddoes, R. L.; Mills, O. S.; Joule, J. A. *J. Chem. Res. (M)* **1987**, 1246–1254.

‡ In the case of a D-arabinose derived compound analogous to **2h** a single crystal X-ray structure determination indicated the configuration of the C=N double bond to be *E*.