Denitration of *α*-Nitroketones by Treatment of their Tosylhydrazones with Lithium Aluminium Hydride; New Applications of the Henry Reaction

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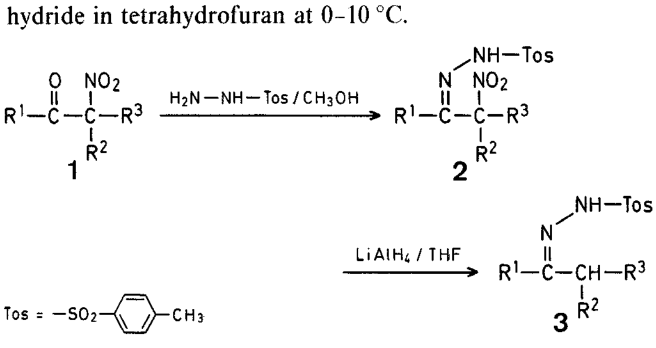
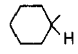
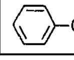
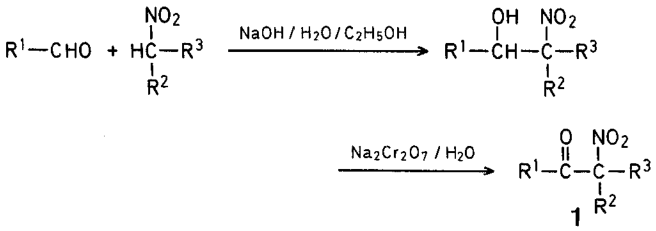
The use of aliphatic nitro compounds in organic synthesis has been well documented[1]. The synthetic application of nitroaliphatic compounds includes interconversions of functional groups as well as C—C bond forming processes. Without doubt, the replacement of nitro groups by hydrogen or its isotopes also is of practical interest. To our knowledge, only five methods[2-6] for this purpose have hitherto been reported.

We here describe a new and efficient indirect route for effecting denitration of *α*-nitroketones. Our method consists of the conversion of *α*-nitroketones (**1**) into the corresponding tosylhydrazones (**2**) followed by treatment with lithium aluminium hydride in tetrahydrofuran at 0-10 °C.

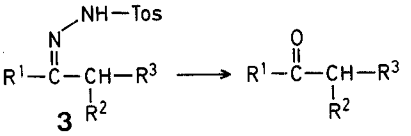


	R^1	R^2	R^3		R^1	R^2	R^3
a	$-(CH_2)_4-$		H				
b	$-(CH_2)_5-$		H	e	$-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-$		
c	$-CH_2-CH_2-\underset{C(CH_3)_3}{CH}-CH_2-$		H	f	n-C_3H_7	CH_3	H
d	$-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-\underset{CH_3}{\overset{CH_3}{C}}-$		H	g	i-C_3H_7	C_2H_5	H
				h		CH_3	H
				i	 $-CH_2-CH_2-$	CH_3	CH_3

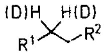
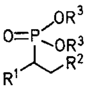
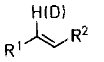
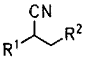
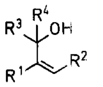
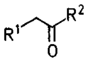
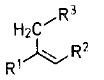
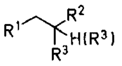
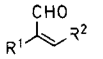
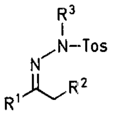
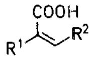
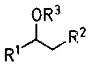
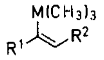
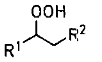
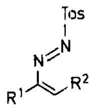
This reductive denitration procedure renders possible new applications of the Henry reaction[7] (nitroaldol reaction), a classical, recently improved[8,9] method for C—C bond formation, as well as of other preparatively interesting reactions of nitroalkanes such as *C*-acylation[10,11]. The first of these mentioned possibilities is illustrated by the facts that the starting *α*-nitro compounds **1** used by us are most conveniently prepared by the aldol-analogous addition of aldehydes to nitroalkanes (Henry reaction) and oxidation of the (isolated) *β*-nitroalcohols[7,12],



and that our product tosylhydrazones **3** may be readily cleaved to give the corresponding ketones[13].



It is worthy of note that the tosylhydrazones **3** may be used as starting materials for a large series of preparatively useful further reactions[14]. This is exemplified by the following list of selected product types obtainable from ketone tosylhydrazones of the type **3a–h** ($R^3 = H$):

Product	Ref. 14	Product	Ref. 14
	a-f		o
	g, h, i		p, p
	g, j		r, s
	g, i		t, u
	g, k		v
	g		w
 M=Si, Ge, Sn	l, m		x
	n		

The applicability of the present reductive denitration is limited to such *α*-nitroketone tosylhydrazones (**2**) in which the nitro group is attached to a secondary or tertiary C-atom; thus for example, *α*-nitroacetophenone does not undergo the reaction.

All starting reagents were obtained commercially except for 2,4,4-trimethylcyclopentanone which was prepared according to a published procedure[15]. 2-Nitrocyclohexanone and 2-nitrocycloheptanone were prepared by treatment of cyclohexene and cycloheptene with dinitrogen tetroxide[16]. 4-*t*-Butyl-2-nitrocyclohexanone, 2-nitro-3,3,5,5-tetramethylcyclohexanone, and 2-nitro-2,4,4-trimethylcyclopentanone were prepared by nitration of the corresponding enol acetates as previously reported[17]. Analytical grade tetrahydrofuran was purified by the standard method[18].

α-Nitroketone Tosylhydrazones (2); General Procedure:

A solution of tosylhydrazine in methanol is added to a solution of the equimolecular amount of the *α*-nitroketone **1** in methanol, a few drops of sulfuric acid are added, and the mixture is allowed to stand at room temperature for 8-10 h. The crystalline tosylhydrazone **3** which crystallizes upon cooling of the solution is isolated by suction, dried in vacuo, and used in the reduction step without further purification. An analytical sample may be prepared by recrystallization from methanol or ethanol.

Denitration of Tosylhydrazones 2a-i; General Procedure:

Dry tetrahydrofuran (100 ml) is placed in a dried, nitrogen-flushed, 250 ml flask fitted with a septum inlet and a stirrer. Lithium alumi-

0039-7881/83/0232-0137-03 $ 03.00

Table 1. Preparation of Tosylhydrazones of α-Nitroketones **(2a–i)**

2	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	I.R. (KBr)[d] ν[cm⁻¹]			^{1}H-N.M.R. (CDCl$_3$/TMS$_{int}$)[e] δ [ppm]
				NH	SO$_2$	NO$_2$	
a	95	134°	$C_{13}H_{17}N_3O_4S$ (311.3)	3205	1170, 1340	1555	1.30–2.55 (m, 11 H); 5.02 (t, 1 H, J=3.8 Hz); 7.57 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.19[f] (bs, 1 H)
b	93	118–119°	$C_{14}H_{19}N_3O_4S$ (325.3)	3210	1168, 1320	1550	1.08–2.61 (m, 13 H); 5.15 (t, 1 H, J=7.5 Hz); 7.57 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.55[f] (bs, 1 H)
c	95	113–114°	$C_{17}H_{25}N_3O_4S$ (367.4)	3190	1168, 1330	1570	0.88 (s, 9 H); 1.05–2.40 (m, 7 H); 2.42 (s, 3 H); 5.09 (m, 1 H); 7.58 (AA'BB' pattern, 4 H, J=8.0 Hz); 7.98[f] (bs, 1 H)
d	93	138–139°	$C_{17}H_{25}N_3O_4S$ (367.4)	3230	1168, 1350	1550	0.72–2.00 (m, 16 H); 2.38 (s, 3 H); 4.80 (s, 1 H); 7.55 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.58[f] (s, 1 H)
e	90	130°	$C_{15}H_{21}N_3O_4S$ (339.3)	3212	1170, 1350	1542	1.00 (s, 3 H); 1.13 (s, 3 H); 1.78 (s, 3 H); 1.98 (s, 2 H); 2.33 (s, 2 H); 2.43 (s, 3 H); 7.57 (AA'BB' pattern, 4 H, J=8.0 Hz); 7.68[f] (bs, 1 H)
f	89	96–97°	$C_{13}H_{19}N_3O_4S$ (313.3)	3198	1180, 1345	1545	0.85 (t, 3 H, J=6.6 Hz); 1.02–2.00 (m, 2 H); 1.6 (d, 3 H, J=6.75 Hz); 2.22 (m, 2 H); 2.45 (s, 3 H); 5.14 (q, 1 H, J=6.75 Hz); 7.57 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.35[f] (s, 1 H)
g	85	111–112°	$C_{14}H_{21}N_3O_4S$ (327.3)	3215	1170, 1340	1548	0.86 (t, 3 H, J=6.7 Hz); 1.02 (dd, 6 H, J=6.7 Hz); 2.12 (m, 2 H); 2.44 (s, 3 H); 2.88 (qq, 1 H, J=6.7 Hz); 5.05 (t, 1 H, J=6.75 Hz); 7.58 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.52[f] (s, 1 H)
h	81	126–127°	$C_{16}H_{23}N_3O_4S$ (353.4)	3200	1171, 1345	1553	0.82–2.82 (m, 11 H); 1.62 (d, 3 H, J=6.3 Hz); 2.42 (s, 3 H); 5.24 (q, 1 H, J=6.3 Hz); 7.57 (AA'BB' pattern, 4 H, J=8.0 Hz); 8.52[f] (bs, 1 H)
i	65	142–143°	$C_{19}H_{23}N_3O_4S$ (389.4)	3198	1171, 1340	1553	1.68 (s, 6 H); 2.32–2.80 (m, 7 H); 6.98–7.83 (m, 10 H)

[a] Yield of isolated pure product.

[b] Uncorrected.

[c] Microanalyses were performed using C, H, N Analyzer Model 185 of Hewlett-Packard Co. The analyses were in satisfactory agreement with the calculated values: C, ±0.07; H, ±0.22; N, ±0.31.

[d] Recorded on a Perkin-Elmer 297 spectrometer.

[e] Recorded at 90 MHz using a Varian EM 390 spectrometer.

[f] Signal disappears on treatment with D$_2$O.

Table 2. Alkyl Ketone Tosylhydrazones **3a–i** prepared[e]

3	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c] or m.p. [°C] reported	I.R. (KBr)[d] ν [cm⁻¹]	
				NH	SO$_2$
a	88	154–155°	156°[19]	3250	1170, 1335
b	85	146–147°	148–149°[20]	3240	1170, 1325
c	88	152–154°	149–150°[14f]	3230	1163, 1335
d	89	158–160°	160–162°[14n]	3260	1165, 1340
e	81	90–92°	$C_{15}H_{22}N_2O_2S$ (294.3)	3243	1172, 1340
f	81	85–86°	$C_{13}H_{20}N_2O_2S$ (268.3)	3201	1162, 1335
g	86	119–121°	$C_{14}H_{22}N_2O_2S$ (282.3)	3220	1175, 1335
h	87	129–131°	$C_{16}H_{24}N_2O_2S$ (308.4)	3218	1170, 1345
i	94	85–86°	$C_{19}H_{24}N_2O_2S$ (344.4)	3220	1170, 1332

[a-d] See Table 1.

[e] The tosylhydrazones **3a–i** exhibited physical and spectral parameters in agreement with literature reports or with those of independently prepared specimens.

nium hydride (1.14 g, 30 mmol) is added and the mixture is cooled to 0 °C. A solution of the α-nitroketone tosylhydrazone (**2a–i**; 10 mmol) in dry tetrahydrofuran (25 ml) is added dropwise (*Caution:* hydrogen evolution). The mixture is stirred for 2 h, treated carefully with cold water, acidified with 2 normal sulfuric acid, and extracted with ether (2 × 100 ml). The ether layer is dried with sodium sulfate, the solvent removed under reduced pressure, and the product **3** recrystallized from methanol/water.

The authors thank the Italian Research Council (Roma) for financial support.

Received: July 22, 1982

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