Reaction of Hydrazones with Methoxy(tosyloxy)iodobenzene (MTIB): Tosylate Formation under Oxidative Conditions

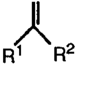
Christopher A. Ramsden,* Helen L. Rose

Department of Chemistry, Keele University, Keele, Staffordshire ST5 5BG, England

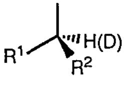
Received 18 October 1996

Abstract: Treatment of aromatic hydrazones **1** containing electron-withdrawing, reduction sensitive substituents with MTIB gives the corresponding tosylates **2** in high yield. When the tosylate is particularly reactive the thermodynamically more stable methyl ether **3** is isolated. Analogous reactions with DAIB give acetates **4** in high yield. Dialkyl hydrazones give olefinic products (e.g. **7** and **8**). (+)-Camphor hydrazone **1k** with either MTIB or DAIB gives both camphene **12** (major product) and tricyclene **11** (minor product) suggesting that a carbene pathway accounts for some of the material formed in these oxidations.

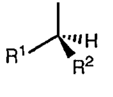
Unsubstituted hydrazones have been oxidised to diazo compounds and related products by a wide variety of reagents,[1] including lead tetraacetate (LTA)[1-3] and to a very limited extent diacetoxyiodobenzene (DAIB).[4] In the absence of base, the acetic acid generated by these reagents leads to formation of the corresponding acetate together with elimination of nitrogen. The reagents LTA and DAIB often give similar products but, as we have recently demonstrated,[5] this is not always the case. As a general reagent DAIB has significant advantages over LTA including its relative cost, stability and toxicity but investigations of its chemistry are still relatively limited. Another advantage of reagents based on iodine (III) is the opportunity to readily replace acetate by other ligands,[6] including tosyloxy.[7] For these and other reasons,[8] the synthetic applications of hypervalent iodine reagents merit further study. In this context, we now report the oxidation of a series of aromatic hydrazones by methoxy(tosyloxy)iodobenzene [MeO(TsO)IPh] (MTIB)[7] and demonstrate a method of generating tosylates under essentially oxidative conditions. This approach may be useful for selective reduction and further elaboration of polyfunctional aldehydes and ketones.[9]



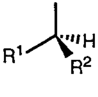
1



2

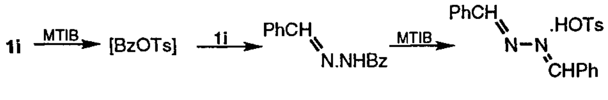


3



4

Reaction of acetophenone hydrazone **1a** with one equivalent of MTIB in CH_2Cl_2 solution gave, after chromatographic purification, 1-phenylethyl tosylate **2a** (Table 1). In a similar manner the tosylates **2b-e** containing reduction sensitive groups were obtained in good yield.[10] When the tosylate is more reactive, presumably as a result of favourable S_N1 dissociation to an ion pair,[11] the isolated products are the thermodynamically more stable methyl ethers (e.g. **3f-h**). In the case of benzaldehyde hydrazone **1i** the product was benzylideneazine tosylate (84%), presumably formed by rapid reaction of the transient benzyl tosylate with the hydrazine precursor and further oxidation (Scheme 1). All attempts to obtain benzyl tosylate were unsuccessful. In parallel experiments all the hydrazones **1a-i** reacted with DAIB to give the corresponding acetates **4** in high yield (Table 1). These reactions appear to be much cleaner than corresponding reactions using LTA.[3] Oxidative acetoxylation using DAIB therefore provides a good route to protected alcohols in the presence of sensitive functional groups, including other alcohols since these are not oxidised by DAIB under these conditions.



Scheme 1

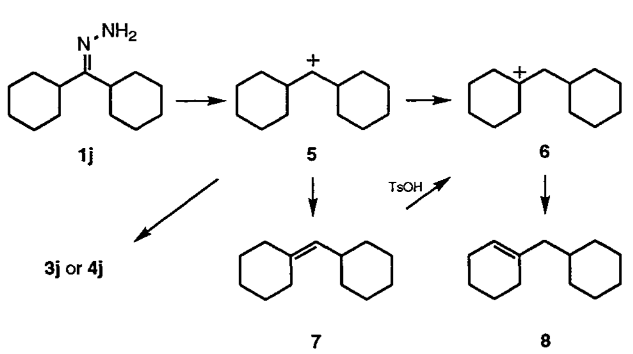
Hydrazone protons readily exchange in D_2O providing a mild and convenient method for α-deuteration. Thus, deuteration of 3-nitro acetophenone hydrazone **1b** using $CHCl_3$-D_2O gave the [^{2}H]hydrazone which upon MTIB oxidation gave the α-[^{2}H]tosylate **2b**.

Table 1. Oxidation of Hydrazones using MTIB or DAIB[12]

Entry	Hydrazone		MTIB		DAIB
	R^1	R^2	**2**(%)	**3**(%)	**4**(%)
a	C_6H_5	CH_3	81	-	96
b	3-$NO_2C_6H_4$	CH_3	93	-	84
c	4-CNC_6H_4	CH_3	86	-	90
d	4-$NO_2C_6H_4$	H	92	-	97
e	C_6H_5	C_6H_5CO	97	-	89[a]
f	4-$CH_3OC_6H_4$	CH_3	-	68	92
g	C_6H_5	C_6H_5	-	86	99
h	C_6H_5	Cyclohexyl	-	77[b]	92
i	C_6H_5	H	-[c]	-	93
j	Cyclohexyl	Cyclohexyl	-	[20][d]	[45][d]
k	(+)-Camphor		-	-	[15][d]

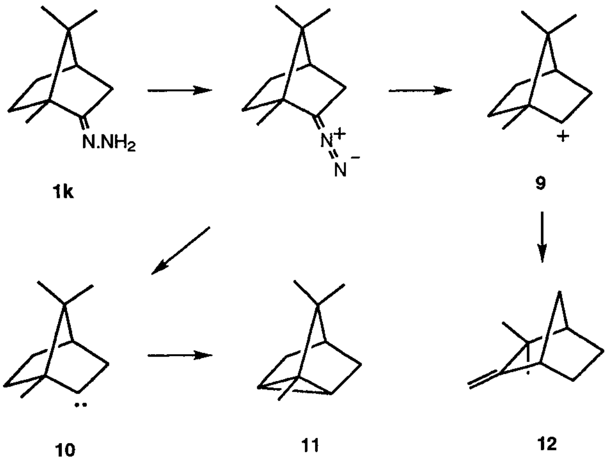
[a]reaction carried out under reflux (40 °C); [b]accompanied by some olefinic product; [c]the product was the azine tosylate (84%); [d]yields and product composition determined by GC and GC-MS: see text for discussion of additional products.

When dicyclohexylketone hydrazone **1j** was investigated only low yields of either the ether **3j** (MTIB) or the acetate **4j** (DAIB) were obtained and these were accompanied by the alkenes **7** and **8** (Scheme 2). Using DAIB the ratio of products was **4j**(45%):**7**(46%):**8**(7%) and this is virtually identical to the ratio observed by Barton and co-workers[2] [**4j**(43%):**7**(46%):**8**(8%)] using two equivalents of LTA in CH_2Cl_2-THF. One equivalent of LTA in CH_2Cl_2 also gave identical results. Use of MTIB gave the isomeric alkenes in the ratio of **7**(21%):**8**(45%). We ascribe this significant change in product ratio to protonation of the alkene **7** by tosic acid to give a tertiary carbocation **6** that deprotonates giving the isomer **8**. This mechanism is supported by the following observation. When the hydrazone **1j** was oxidised with one equivalent of DAIB and subsequently one equivalent of tosic acid was added, the initial isomer ratio of **7**(34%):**8**(6%) slowly changed over 20 hours to **7**(4%):**8**(36%). A control experiment without tosic acid showed no change in the isomer ratio over the same period.



Scheme 2

In the reactions of (+)-camphor hydrazone **1k** with either DAIB or MTIB both camphene **12** (63% or 25%) and tricyclene **11** (17% or 7%), identical by GC-MS with authentic samples, were identified in the product mixtures (Scheme 3). The observation of tricyclene **11** as a reaction product suggests that carbene intermediates (*e.g.* **10**), as well as carbocations (*e.g.* **5** and **9**), are partially involved in these I(III) oxidations. A previous report[2] suggests that LTA oxidation of the hydrazone **1k** gives only camphene **12** (60%), but an unidentified hydrocarbon (16%) may have been tricyclene. We detected both camphene (40-50%) and tricyclene (10-15%) when (+)-camphor hydrazone **1k** was oxidised with one or two equivalents of LTA under various conditions.



Scheme 3

References and Notes

1. Holton, T.L.; Shechter, H. *J.Org.Chem.*, **1995**, *60*, 4725; Takeda, T.; Sasaki, S.; Nakamura, A.; Yamauchi, S.; Fujiwara, T. *Synlett*, **1996**, 273.
2. Barton, D.H.R.; McGhie, J.F.; Batten, P.L. *J.Chem.Soc.(C)*, **1970**, 1033.
3. Stojiljkovic, A.; Orbovic, N.; Sredojevic, S.; Mihailovic, M.Lj. *Tetrahedron*, **1970**, *26*, 1101.
4. Smith, P.A.S.; Bruckmann, E.M. *J.Org.Chem.*, **1974**, *39*, 1047; Lapatsanis, L.; Milias, G.; Paraskewas, S. *Synthesis*, **1985**, 513.
5. Ramsden, C.A.; Rose, H.L. *J.Chem.Soc.,Perkin Trans. 1*, **1995**, 615; See also Campbell, C.D.; Rees, C.W. *J.Chem.Soc.(C)*, **1969**, 752; Houghton, P.G.; Rees, C.W. *J.Chem.Res.(S)*, **1980**, 303.
6. Zhdankin, V.V.; Tykwinski, R.; Williamson, B.L.; Stang, P.J.; Zefirov, N.S. *Tetrahedron Lett.*, **1991**, *32*, 733; Magnus, P.; Lacour, J.; Evans, P.A. *Janssen Chimica Acta*, **1993**, *11*, 3; Kita, Y.; Okuno, T.; Hirofumi, T.; Akai, S. *Tetrahedron Lett.*, **1994**, *35*, 2717; Weiss, R.; Seubert, J. *Angew.Chem.Int.Ed. Engl.*, **1994**, *33*, 891.
7. Moriarty, R.M.; Vaid, R.K.; Koser, G.F. *Synlett*, **1990**, 365; Koser, G.F.; Wettach, R.H. *J.Org.Chem.*, **1980**, *45*, 4988.
8. Ramsden, C.A. *Chem.Soc.Revs*, **1994**, 111.
9. Hagiwara, T.; Tanaka, K.; Fuchikami, T. *Tetrahedron Lett.*, **1996**, *37*, 8187.
10. Typical procedure: to a stirred solution of MTIB (2.03g, 5 mmol) in dry CH_2Cl_2 (25ml) was added dropwise a solution of 4-cyanoacetophenone hydrazone **1c** (0.80g, 5 mmol) in CH_2Cl_2 (25ml). After 1h the solvent was removed and the solid product collected, recrystallised from MeCN-EtOH (9:1) and identified as *1-(4-cyanophenyl)ethyl tosylate* **2c** (86%), m.p. 102-3 °C. υ_{max}(KBr)/cm^{-1} 3068, 2988, 2224, 1600, 1452, 1416, 1362, 1212, 1180, 1096, 1054; δH(270 MHz,$CDCl_3$ + d_6-DMSO), 7.66 (2H, d, *J* 8.3), 7.56 (2H, d, *J* 8.3), 7.33 (2H, d, *J* 8.3), 7.25 (2H, d, *J* 8.3), 5.58 (1H, q, *J* 6.35), 2.42 (3H, s), 1.58 (3H, d, *J* 6.35); *m/z* 301 (M^+); Found: C, 63.72; H, 5.01; N, 4.74. $C_{16}H_{15}NO_3S$ requires C, 63.77; H, 5.02; N, 4.65.
11. Tsuji, Y.; Kim, S.H.; Saeki, Y.; Yatsugi, K.; Fujio, M.; Tsuno, Y. *Tetrahedron Lett.*, **1995**, *36*, 1465.
12. Unless otherwise stated, all products and novel precursors were analytically pure and their structures fully supported by spectroscopic data.