Pergamon

Tetrahedron Letters, Vol. 36, No. 31, pp. 5479-5482, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01078-5

Conversion of Saturated Ketones into 2-Lithiodienes *via* *N,N-Bis*-Tosylhydrazone Derivatives

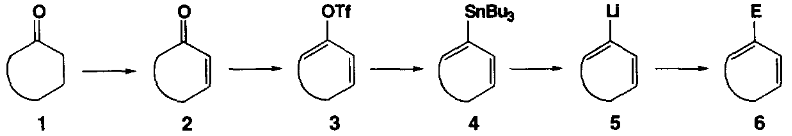
Philip Magnus* **and Michael B. Roe**

Department of Chemistry and Biochemistry, University of Texas at Austin, Austin, Texas 78712.

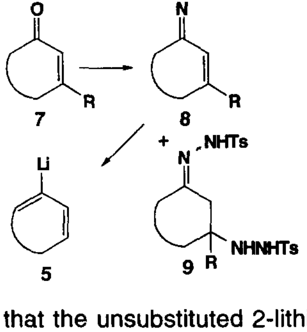
Abstract: Saturated *N*-tosylhydrazones can be converted into 2-lithiodienes *via N,N-bis*-tosylhydrazones and elimination to an α,β-unsaturated *N*-tosylhydrazone , followed by the Shapiro reaction.

The conversion of a saturated ketone into a 2-lithio-1,3-diene for subsequent treatment with an electrophile to give the derivative **6**, **Scheme 1**, is a lengthy sequence of reactions. The saturated ketone **1** has to be converted into the α,β-unsaturated ketone **2**, which is transformed into the enol triflate **3**, and then into the alkenyltrialkylstannane **4**. The stannane **4** can be transmetallated to give **5**, and quenching with an electrophile results in **6**,[1] or Pd° catalyzed insertion reactions lead directly to **6** (for example where E = CO_2Me).[2]

Scheme 1



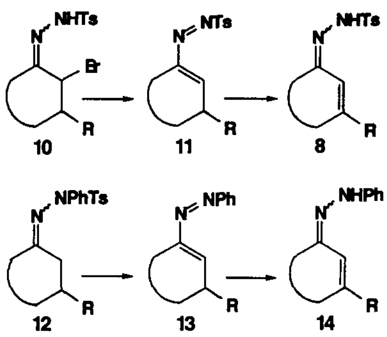
Scheme 2



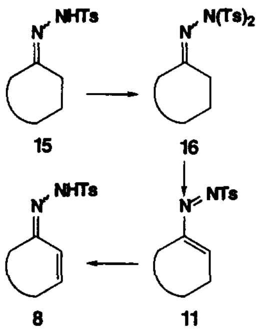
While studying the chemistry of *N*-tosylhydrazones we had occasion to examine the conversion of **1** into **6**. Before describing our results, it is pertinent to outline some of the restrictions that limit the applicability of *N*-tosylhydrazone chemistry combined with the Shapiro reaction. Treatment of an α,β-unsaturated ketone **7** with $TsNHNH_2$ only gives the hydrazone **8** if the β-substituent is sufficiently bulky to prevent conjugate addition, **Scheme 2**. For example if **7** (R = H) is treated with $TsNHNH_2$, the major product is the 1,4-adduct **9** rather than the desired 1,2-adduct **8**.[3] This means that the unsubstituted 2-lithiodiene **5** is not available *via* the usual methods for the preparation of **8**.[4] Consequently, we required a synthesis of **8** (R = H) that does not proceed through the normal α,β-unsaturated ketone **7** (R = H) pathway.

The literature reveals relatively little information other than the *N*-tosylhydrazone of an α-bromoketone **10** undergoes elimination under basic conditions to give the *N*-tosyldiazene **11** which tautomerizes to the more stable α,β-unsaturated *N*-tosylhydrazone **8**.[5] It has also been reported that *N*-phenyl-*N*-tosylhydrazone **12** on treatment with base eliminates *p*-toluene sulfinic acid to give **14** *via* **13**, **Scheme 3**.[6] The latter method appears to be the most readily applicable

Scheme 3

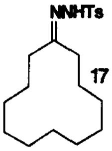
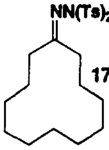
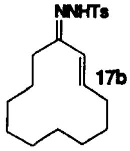
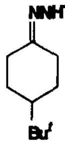
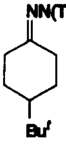
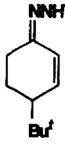
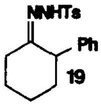
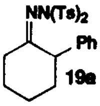
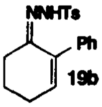
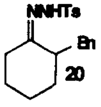
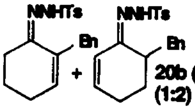


Scheme 4



to our requirements. Consequently, we decided to examine the conversion of saturated *N*-tosylhydrazones **15** into *N,N*-*bis*-tosylhydrazones **16**, and their transformation *via* the *N*-tosyldiazene intermediate **11** into the α,β-unsaturated *N*-tosylhydrazone **8**, **Scheme 4**. The only previous reference to the preparation of *N,N-bis*-tosylhydrazones **16** reports low to moderate yields.[7] Significant improvement was obtained by careful control of the reaction conditions. Typically, oil-free sodium hydride (1.4 eq) was suspended in DMF (ca. 1M, degassed) at 0°C, and the *N*-tosylhydrazone **15** (1.0 eq) was added.[8] After 15 min. *p*-toluenesulfonyl chloride (1.4 eq) was added. The mixture stirred at 0°C for 15 min. and at 25°C for 40 min. Water was added to precipitate the product. The *N,N-bis*-tosylhydrazones were purified by crystallization from ethanol.[9] The elimination was carried out by treating the *N,N-bis*-tosylhydrazones (1.0 eq) with 1,8-diazobicyclo[5.4.0]undec-7-ene (DBU) (3.0 eq) in chlorobenzene (ca. 0.25M) at 25°C. Heating caused extensive decomposition, and the reactions took several days to go to completion. The crude product was adsorbed onto silica gel and eluted through silica gel with dichloromethane to give pure α,β-unsaturated *N*-tosylhydrazone **17b-23b**, TABLE 1.

TABLE 1

ENTRY	SUBSTRATE	=NN(Ts)$_2$	PRODUCT
A	 NNHTs 17	 NN(Ts)$_2$ 17a (77%)	 NNHTs 17b (86%)
B	 NNHTs 18 Bu^t	 NN(Ts)$_2$ 18a (68%) Bu^t	 NNHTs 18b (95%) Bu^t
C	 NNHTs Ph 19	 NN(Ts)$_2$ Ph 19a (54%)	 NNHTs Ph 19b (56%)
D	 NNHTs Bn 20	 NN(Ts)$_2$ Bn 20a (66%)	 NNHTs Bn + NNHTs Bn 20b (84%) (1:2)

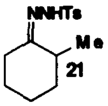
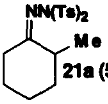
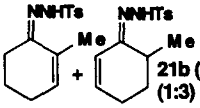
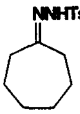
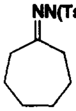
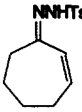
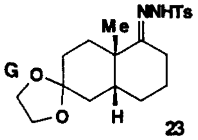
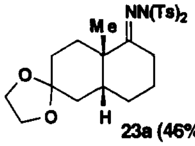
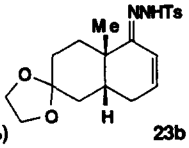
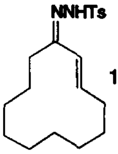
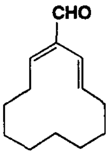
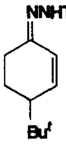
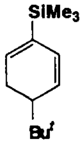
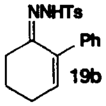
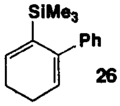
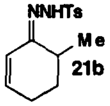
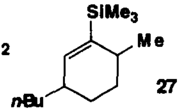
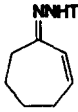
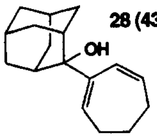
E	 21	 21a (50%)	 21b (76%) (1:3)
F	 22	 22a (49%)	 22b (65%)
G	 23	 23a (46%)	 23b (36%)

TABLE 2

ENTRY	SUBSTRATE	ELECTROPHILE	PRODUCT
A	 17b	DMF^{10}	 24 (65%)
B	 18b	Me$_3$SiCl^{11}	 25 (81%)
C	 19b	Me$_3$SiCl^{11}	 26 (25%)
D	 21b	Me$_3$SiCl$^{11, 12}$	 27 (95%)
E	 22b	Adamantanone	 28 (43%)

All of the *N,N-bis*-tosylhydrazones **17a-23a** are highly crystalline compounds, and the yields refer to recrystallized material. Entries D and E illustrate that the DBU mediated elimination give as the major product the less substituted *N*-tosylhydrazone, whereas entry C indicates that conjugation favors the thermodynamically more stable product.

The α,β-unsaturated *N*-tosylhydrazone **8** was subjected to the Shapiro reaction conditions [*n*-BuLi/hexanes or MeLi/Et_2O (4.0-4.5 eq), TMEDA, -60°C to 25°C, 2-8h].[4] The resulting 2-lithiodiene **5** was trapped by a variety of electrophiles to give **24-28**, **TABLE 2**.[10,11] Interestingly, treatment of the 6-methylhydrazone **21b** in the same manner resulted in conjugate addition of *n*-BuLi, eventually leading to **27** (95%). The analogous 1,2-addition process to a saturated *N*-tosylhydrazone has been observed in steroid chemistry.[12]

This new variation on *N*-tosylhydrazone chemistry provides a simple method for the synthesis of α,β-unsaturated *N*-tosylhydrazones without the complications of competitive conjugate addition.

Acknowledgments. The National Science Foundation and the Welch Foundation are thanked for their support of this research.

References and footnotes

1. Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K. S.; Faron, K. L.; Gilbertson, S. R.; Kaesler, R. W.; Yang, D. C.; Murray, C. K., *J. Org. Chem.* **1986**, *51*, 277.
2. Baillargeon, V. P.; Stille, J. K., *J. Am. Chem. Soc.* **1986**, *108*, 452.
3. Kirmse, W.; Ruetz, L., *Liebigs Ann. Chem.* **1969**, *726*, 30.
4. Dauben, W. G.; Lorber, M. E.; Vietmeyer, N. D.; Shapiro, R. H.; Duncan, J. H.; Tomer, K., *J. Am. Chem. Soc.* **1968**, *90*, 4762. Dauben, W. G.; Rivers, G. T.; Zimmerman, W. T., *J. Am. Chem. Soc.* **1977**, *99*, 3414. "Comprehensive Organic Synthesis", Ed. Trost, B. M.; Fleming, I. Vol. 6, p. 779. Pergamon, **1991**.
5. Dondoni, A.; Rosini, G.; Mossa, G.; Cagioti, L., *J. Chem. Soc. (B).* **1968**, 1404. Caglioti, L.; Grasselli, P.; Morlacchi, F.; Rosini, G., *Chem. Ind. (London).* **1968**, 25. Rosini, G.; Baccolini, G.,*J. Org. Chem.* **1974**, *39*, 826.
6. Schantl, J. G.; Hebeisen, P., *Tetrahedron.* **1990**, *46*, 395. Caglioti, L.; Grasselli, P.; Rosini, G., *Tetrahedron Lett.* **1965**, 4545. Angelucci, F.; Cacchi, S.; Caglioti, L.; Rosini, G., *Chim. Ind. (Milan).* **1968**, *50*, 262.
7. Keana, J. F. W.; Dolata, D. P.; Ollerenshaw, J., *J. Org. Chem.* **1973**, *38*, 3815.
8. Hutchins, R. O.; Milewski, C. A.; Maryanoff, B. E., *J. Am. Chem. Soc.* **1973**, *95*, 3662.
9. All new compounds gave satisfactory ^1H NMR, IR, MS, HRMS.
10. Traas, P. C.; Boelens, H.; Takken, H. J., *Tetrahedron Lett.* **1976**, *26*, 2287.
11. Chamberlin, A. R.; Stemke, J. E.; Bond, F. T., *J. Org. Chem.* **1978**, *43*, 147.
12. Herz, J. E.; Ortiz, C. V., *J. Chem. Soc. (C).* **1971**, 2294.

(*Received in USA* 29 *March* 1995; *revised* 1 *June* 1995; *accepted* 9 *June* 1995)