

Lithium secondary amide bases have been used to generate kinetic enolates from α,β -unsaturated ketones⁶ and 3-alkoxycyclohexenones.⁷ However, we have found that lithium hexamethyldisilazide (LHDS) is clearly superior to diisopropylamide or isopropylcyclohexylamide in methylation studies with 2-thioalkoxyenones.⁸

The following procedure is typical. A solution of **3** (10 g) in THF was added over 15 min at -78° to 1.1 equiv of LHDS (generated *in situ* from hexamethyldisilazane and *n*-butyllithium at ice bath temperature) in THF. HMPA (1.5 equiv), followed by methyl iodide (2 equiv), was added and the resulting solution was allowed to warm to room temperature and, after 1.2 hr, water was added. Analysis⁴ revealed that 2-thio-*n*-propyl-5,5,6-trimethyl-2-cyclohexen-1-one (**5**; 92% yield) and enone **4** (0.3%), along with dialkylated compounds **9** (2.7%) and **7** (1.6%), as well as recovered **3** (4.1%), were present. Thioalkoxyenone **5** [88% isolated yield, bp 120° (~ 0.3 Torr), *m/e* 212] displayed olefinic proton resonance centered at δ 6.58 ($J = 4.5$ Hz) and ir absorption at 5.96μ (film).

The ratio of α' to α alkylation using LHDS is vitally dependent upon the order in which HMPA and **3** are added to the base. Using conditions identical with those already described (in which **5** and **4** formed in a ratio of 300:1); except that HMPA was added to LHDS before **3**, resulted in a ratio **5**:**4** of 6:1. These results suggest that the basic properties of LHDS are modified in the presence of HMPA. Recently, a lithium diisopropylamide-HMPA complex has been reported to exhibit markedly reduced nucleophilicity when compared to lithium diisopropylamide alone.⁹

Construction of a wide variety of 2,6-dialkylated cyclohexenone derivatives should be possible by consecutive alkylation of 2-thioalkoxyenones. For example, methylation of enone **5** (methyl iodide, potassium *tert*-butoxide in *tert*-butyl alcohol) gave dialkylated enone **7** [88% yield, bp 100° (~ 0.3 Torr), *m/e* 226].

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(6) R. A. Lee, C. McAndrews, K. M. Patel, and W. Reusch, *Tetrahedron Lett.*, 965 (1973).

(7) G. Stork and R. L. Danheiser, *J. Org. Chem.*, **38**, 1775 (1973).

(8) Methylation studies with **3** and analogs using secondary amide bases under a variety of conditions always resulted in recovery of 15–30% thioalkoxyenone.

(9) J. L. Herrmann, G. R. Kieczkowski, and R. H. Schlessinger, *Tetrahedron Lett.*, 2433 (1973).

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N,N-Ditosylhydrazones. Synthesis and Some Unique Reactions with Alkylolithium Reagents

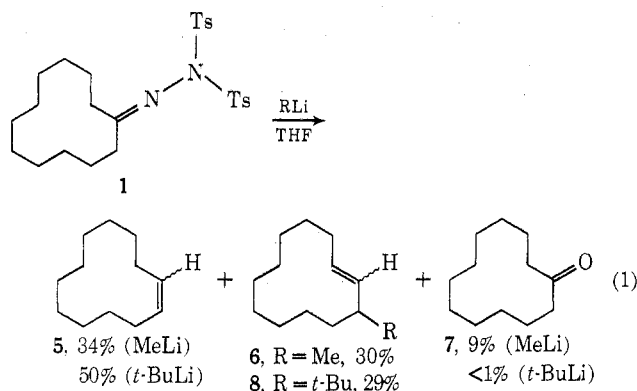
Summary: Several *N,N*-ditosylhydrazones have been synthesized and converted into either 3-alkyl olefins or simple alkylated hydrocarbons by reaction with methyl- and *tert*-butyllithium.

Sir: The reactions of tosylhydrazones with alkyl-lithium reagents and other bases are well known, pro-

viding useful synthetic routes from ketones to a variety of compounds including olefins, allenes, acetylenes, diazo compounds, and carbenes.¹ This paper describes the preparation of several members of a new class of compounds, the *N,N*-ditosylhydrazones, and the reaction of representative members with methyl- and *tert*-butyllithium. While yields have not been optimized in any of the experiments described below, we consider the transformations sufficiently novel to report them at this time.²

Using Baumgarten's³ procedure for the preparation of *N,N*-ditosylamines, a dry DMF solution of cyclododecanone monotosylhydrazone, mp 154 – 156° , prepared by the method of Bamford and Stevens,⁴ was treated at 25° (N_2) with 1.2 equiv of sodium hydride followed by 1.0 equiv of toluenesulfonyl chloride. After water work-up cyclododecanone *N,N*-ditosylhydrazone (**1**), mp 152 – 153° , was obtained in 49% yield. The *N,N*-ditosylhydrazones listed in Table I were similarly prepared.

Reaction of ditosylhydrazone **1** with 2.5 equiv of methylolithium (2.0 *M* in hexane) in THF at 0° (N_2) followed by a water quench and ether extraction led to the mixture of products shown in eq 1 which was separated by preparative vpc.



The products were identified by direct comparison with authentic samples. Cyclododecene^{5,6} (**5**) was prepared by reaction¹ of cyclododecanone monotosylhydrazone with methylolithium. Authentic 3-methylcyclododecene^{5,7} (**6**) was prepared by treating 2-methylcyclododecanone monotosylhydrazone⁷ with methylolithium.

The formation of 3-methylcyclododecene (**6**) in this reaction was quite unexpected, suggesting that the reaction of ditosylhydrazones with other alkylolithium reagents might constitute a new 3-alkyl olefin synthesis. We were particularly intrigued by the use of *tert*-butyllithium since few examples of the direct introduction of a *tert*-butyl group into a molecule are known.⁸

(1) See, *inter alia*, L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley-Interscience, New York, N.Y., Vol. 2, 1969, pp 417–423, and Vol. 3, 1972, p 293; A. M. Foster and W. C. Agosta, *J. Org. Chem.*, **37**, 61 (1972).

(2) See paragraph at end of paper regarding supplementary material.

(3) P. J. DeChristopher, J. P. Adamek, G. D. Lyon, J. J. Galante, H. E. Haffner, R. J. Boggio, and R. J. Baumgarten, *J. Amer. Chem. Soc.*, **91**, 2384 (1969).

(4) W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 4735 (1952).

(5) A mixture of *cis* and *trans* isomers.

(6) V. Prelog and M. Speck, *Helv. Chim. Acta.*, **38**, 1786 (1955).

(7) J. Casanova and B. Waegell, *Bull. Soc. Chim. Fr.*, 1289 (1971).

(8) See, for example, G. H. Posner and J. J. Sterling, *J. Amer. Chem. Soc.*, **95**, 3076 (1973).

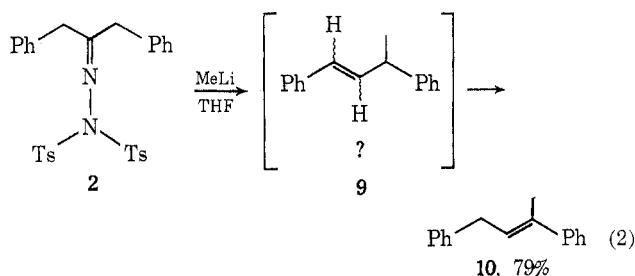
TABLE I
 MELTING POINT AND YIELD DATA FOR REPRESENTATIVE MONO- AND DITOSYLHYDRAZONES

Parent ketone	Monotosylhydrazone		Ditosylhydrazone		Compd no.
	Mp, °C	Yield, ^{a,b} %	Mp, °C	Yield, ^{b,c} %	
Cyclododecanone	154–156	75	152–153	49	1
Dibenzyl ketone	180–181	86	159–160	26	2
Cyclohexanone	152–153 ^d	81	149–150	50	3
4- <i>tert</i> -Butylcyclohexanone	144–145	62	169–170	36	4
Pentan-3-one	104–106	61	149–150	42	
Pinacolone	152–154 ^e	69	155–156	41	
Cholestan-3-one	171–173 ^f	44	171–172	19	

^a Based on starting ketone. ^b Satisfactory analytical data ($\pm 0.4\%$ for C, H, and N, the latter when determined) were reported for all new compounds listed in the table. ^c Based on starting monotosylhydrazone. ^d Lit.⁴ mp 156°. ^e Lit.⁴ mp 155°. ^f C. W. Shoppe, D. N. Jones, and G. H. R. Sumner, *J. Chem. Soc.*, 3100 (1957), reported mp 172–174°.

Treatment of ditosylhydrazone **1** with 3.5 equiv of *tert*-butyllithium (2.54 M in pentane) in THF at -78° (N_2) followed by slow warm up to 25° , water quench, ether extraction, and preparative vpc led in 29% yield to *trans*-3-*tert*-butylcyclododecene (**8**). The position of the *tert*-butyl group was assigned by analogy to methyl olefin **6** and the *trans* isomer was indicated⁹ by the presence of strong absorption at 968 cm^{-1} and the lack of pronounced absorption in the region of 690 cm^{-1} . Also produced in this experiment in 50% yield was a mixture of *cis*- and *trans*-cyclododecene in a ratio of 41:59. The major component was identified as *trans*-cyclododecene by comparison with an authentic sample prepared by the method of Smith and Mennon.¹⁰

The reaction of methylithium with dibenzyl ketone *N,N*-ditosylhydrazone (**2**) gave predominantly *cis*-1,3-diphenylbutene-2 (**10**) in 79% crude yield (eq 2), the spectral properties of which corresponded to those reported for the substance by Cram.¹¹ Olefin **10** was probably produced by base-catalyzed isomerization¹¹ of the initially formed 1,3-diphenylbutene **9** and likely contained some of the other olefin isomers. Cram¹¹ has shown that olefin **10** is the most stable isomer in an equilibrium established through catalysis by *tert*-butyl alcohol-potassium *tert*-butoxide.

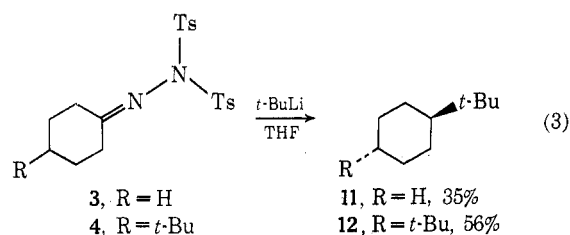


We next examined the reaction of *tert*-butyllithium with the *N,N*-ditosylhydrazones **3** and **4** of cyclohexa-

(9) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 33.
 (10) G. V. Smith and M. C. Mennon, *Ann. N. Y. Acad. Sci.*, **158**, 501 (1969).

(11) S. W. Ela and D. J. Cram, *J. Amer. Chem. Soc.*, **88**, 5777 (1966). The *trans* structure has also been assigned to olefin **9**; see R. M. Parkhurst, J. O. Rodin, and R. M. Silverstein, *J. Org. Chem.*, **28**, 120 (1963).

none and 4-*tert*-butylcyclohexanone, expecting to obtain, respectively, 3-*tert*-butylcyclohexene and 3,5-di-*tert*-butylcyclohexene. We were surprised to observe formation of *tert*-butylcyclohexane (**11**) in 35% yield from the first reaction and the analogous product, *trans*-1,4-di-*tert*-butylcyclohexane (**12**), in 56% yield from the second reaction (eq 3). The *tert*-butylcyclohexane (preparative vpc) was identified by direct comparison with a commercially available sample, while the *trans*-1,4-di-*tert*-butylcyclohexane (preparative vpc) showed physical and spectral properties identical with those reported for the substance by Kuss.¹²



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Supplementary Material Available.—Mechanistic rationalizations, together with experimental details, will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 20 × reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D. C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-1973-3815.

(12) E. Kuss, P. Pollsman, and H. Stegemeyer, *J. Mol. Structure*, **1**, 61 (1967).

(13) Alfred P. Sloan Fellow, 1972–1974; John Simon Guggenheim Fellow, 1972–1973; recipient of an NIH Research Career Development Award, 1972–1977.

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