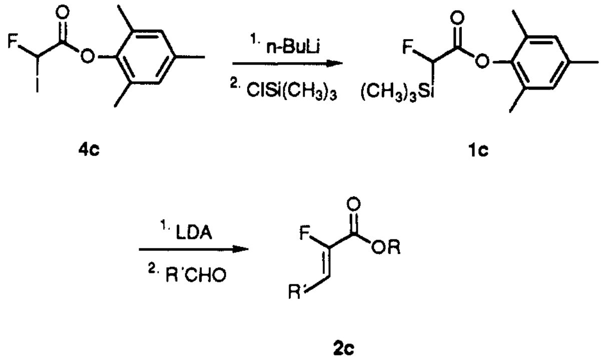
Transmetalation and silylation were easily effected to yield the TMP α-silyl-α-fluoroacetate which was easily purified by bulb-to-bulb distillation.[21] Deprotonation with LDA at −100 °C followed by addition of the aldehyde yielded on warming to −40 °C the (*Z*)-2-fluoroalkenoate with excellent stereoselectivity[22] in most cases. To test the stability of the products to the reaction conditions, an *E*/*Z* mixture of 2-fluorononenoates was treated with LDA at 0 °C for 1 h, conditions more rigorous than those of the reaction. The *E* to *Z* olefin ratios were unchanged under these harsh circumstances. This selectivity is in sharp contrast to the lack of selectivity previously reported in the reaction of *tert*-butyl α-silyl-α-chloroacetates.[23]

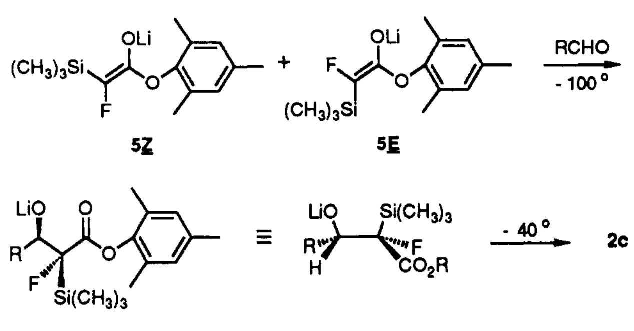


4c

1c

2c

Low-temperature ^{19}F NMR[24] spectroscopy of a solution of the anion **5** indicated that there was a mixture of enolates present. The relative proportion of the two enolates formed was invariant over the temperature range −80 to −40 °C. When benzaldehyde was added to the enolate mixture at −40 °C, olefin formation, and disappearance of the resonances attributed to the enolates, was immediate and the selectivity was equivalent to that reported in Table II. The remarkable preference for formation of the *Z* olefin requires an equally high bias for formation of the

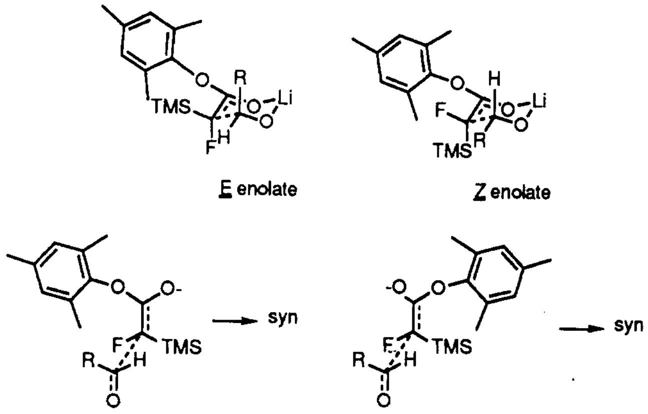


5Z

5E

6

syn[25] aldolate **6** if the commonly accepted syn elimination mechanism for the Peterson olefination reaction is invoked.[7a] Thus we tentatively propose that the high selectivity of the olefination reaction implies that a closed transition state[26] is not likely to be involved in the aldol reaction but rather that the reaction occurs via an open transition state of the type proposed by Noyori[27] where enolate geometry is not important. The bulk of the trimethylsilyl group controls the approach of the aldehyde with the result that only the required syn aldolate is formed irregardless of the enolate geometry.



Acknowledgment. Financial support of this work by the National Science Foundation Grant Number CHE-8520875 and DARPA under contract DAAL03-88-K-0198 is gratefully acknowledged.

Supplementary Material Available: Experimental data for compounds in this paper (5 pages). Ordering information is given on any current masthead page.

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(19) **3c** may be prepared in the following manner. To 8.47 g (0.075 mol) of α-chloro-α-fluoroacetic acid was added 18.02 g (1.2 equiv, 0.090 mol) of phthaloyl chloride. The mixture was heated together under reflux for 4 h and then was distilled (bp 65–67 °C) to yield 8.58 g (88%) of the α-chloro-α-fluoroacetyl chloride. 2,4,6-Trimethylphenol (3.63 g, 0.032 mol) dissolved in 50 mL of THF, which had been deprotonated at 0 °C with *n*-butyllithium (0.038 mol., 15.4 mL of a 2.5 M solution in hexane), was treated dropwise with α-chloro-α-fluoroacetyl chloride (5.00 g, 0.038 mol) at 0 °C. The mixture was allowed to warm to room temperature overnight with stirring. The reaction was quenched with saturated ammonium chloride (20 mL) and was extracted with ether (4 portions, 20 mL each). The combined organic extracts were washed with saturated sodium bicarbonate (4 portions, 20 mL each) and brine (20 mL) and were concentrated to yield 5.21 g (85%) of **3c**.

(20) mp 65–66 °C.

(21) bp 90–110 °C at 0.025 mm.

(22) Robinson, C. N.; Stablein, G. E.; Slater, C. D. *Tetrahedron* **1990**, *46*, 335–340.

(23) Chan, T. H.; Moreland, M. *Tetrahedron Lett.* **1978**, 515–518.

(24) ^{19}F NMR δ −220 and −218 ppm.

(25) Masamune, S.; Ali, S. A.; Snitman, D. L.; Garvey, D. S. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 557–558.

(26) Heathcock, C. H. In *Asymmetric Synthesis*, Morrison, J. D., Ed.; Academic: Orlando, 1984; Vol. 3, Part B, pp 111–212.

(27) Noyori, R.; Nishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1981**, *103*, 2106–2107.

A Simple Method for Producing Cycloalkenyllithiums from Cycloalkanones via Reductive Lithiation of Enol Phenyl Thioethers

Theodore Cohen* and Mary Dosch Doubleday

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Received May 29, 1990

Summary: Cyclohexenyl, cycloheptenyl, and cyclooctenyl phenyl sulfides, readily prepared from the corresponding cycloalkanones, are reductively lithiated by lithium *p,p'*-di-*tert*-butylbiphenylide to produce cycloalkenyllithiums in good yields.

Until recently, there has been virtually only a single method to generate the very synthetically useful cyclo-

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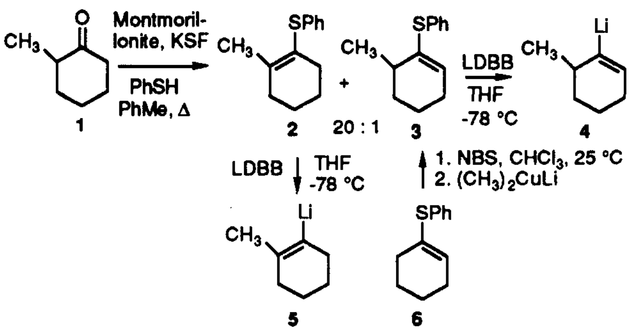
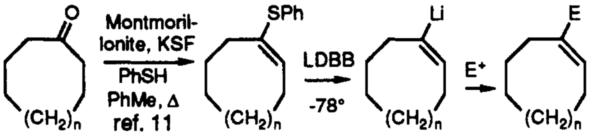
Scheme I



alkenyllithiums, the widely used Bond[1] modification of the Shapiro[2] reaction. This process, in which a (triisopropylphenyl)sulfonylhydrazone[3] of a ketone is treated with a butyllithium in a solvent usually containing tetramethylethylenediamine (TMEDA) suffers from the expense of the hydrazide reagent and of TMEDA when it is used and from the fact that cycloalkenyllithiums with certain substitution patterns cannot be generated in this way. Recently, Wulff[5] has developed a more general procedure that involves reaction of enol triflates of cyclic ketones with a higher order cuprate derived from a trialkylstannyllithium. The product is a cycloalkenyltrialkylstannane that can form a cycloalkenyllithium upon reaction with an alkyllithium.

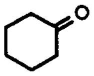
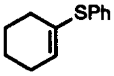
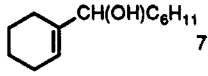
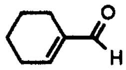
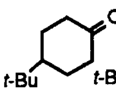
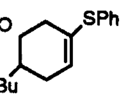
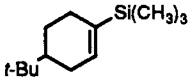
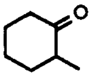
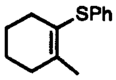
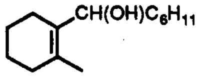
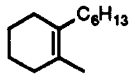
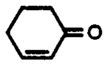
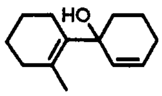
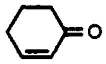
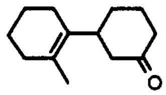
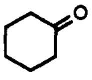
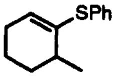
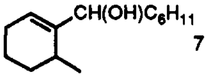
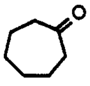
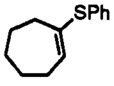
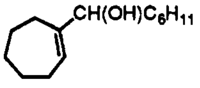
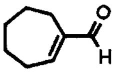
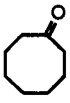
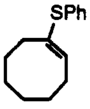
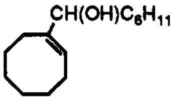
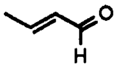
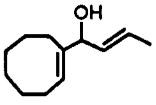
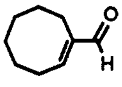
We now present a new procedure for the preparation of cyclohexenyl-, cycloheptenyl-, and cyclooctenyllithiums, starting from cyclic ketones or a number of other precursors of vinyl sulfides.[6] The method usually involves a two-pot process starting from cycloalkanones and involves the reductive lithiation[7] of cycloalkenyl phenyl sulfides by means of the radical anion lithium *p,p'*-di-*tert*-butylbiphenylide[8] (LDBB, eq 1). It has none of the



(1)

drawbacks of Bond's procedure, and it should be far cheaper[9] and in many cases simpler than Wulff's procedure. The only limitation that we have observed is that it is unsuccessful for the production of cyclopentenyllithiums; attempts to form the latter result instead in the production of phenyllithium.[10]

Table I. Preparation and Reductive Lithiation of Cycloalkenyl Sulfides

ketone	vinyl sulfide[a]	yield, %[b]	electrophile	product	yield, %[b]
		83	c-C_6H_{11}CHO		79
			Me_2NCHO		80
		67	Me_3SiCl		75
		73	c-C_6H_{11}CHO		80
			$C_6H_{13}I$[c]		71
					86[d]
					68[e]
		52[f]	c-C_6H_{11}CHO		75
		75	c-C_6H_{11}CHO		89
			Me_2NCHO		92
		86	c-C_6H_{11}CHO		75
					86[d]
			Me_2NCHO		88

[a] Vinyl sulfides prepared according to ref 11 unless noted otherwise. [b] Chromatographically pure; characterized by IR, ^{1}H NMR, MS, and HRMS data. [c] 2.2 equiv. [d] The silica was treated with triethylamine and the glassware with aqueous base. [e] After formation of the vinyl anion at -78 °C, the reaction mixture was cannulated into 1.2 equiv of CuBr-Me_2S in THF at -78 °C and stirred for 0.5 h prior to addition of 1.2 equiv of electrophile (ref 14). [f] Prepared according to ref 6.

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[1] Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147. Bond, F. T.; DiPietro, R. A. *J. Org. Chem.* **1981**, *46*, 1315.

[2] Shapiro, R. H. *Org. React.* (*N.Y.*) **1976**, *23*, 405. This reaction was apparently discovered independently by Shechter and Friedman: Kaufman, G.; Cook, F.; Shechter, H.; Bayless, J.; Friedman, L. *J. Am. Chem. Soc.* **1967**, *89*, 5736.

[3] An earlier version[4] using tosylhydrazones required a large excess of butyllithium and a correspondingly large excess of electrophile and it is only rarely used at present.

[4] Stemke, J. E.; Bond, F. T. *Tetrahedron Lett.* **1975**, 1815. Shapiro, R. H.; Lipton, M. F.; Kolonko, K. J.; Buswell, R. L.; Capuano, L. A. *Tetrahedron Lett.* **1975**, 1811.

[5] 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. Gilbertson, S. R.; Challener, C. A.; Bos, M. E.; Wulff, W. D. *Tetrahedron Lett.* **1988**, *29*, 4795.

[6] Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075.

[7] Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* **1989**, *22*, 152.

[8] Freeman, P. K.; Hutchinson, L. L. *J. Org. Chem.* **1980**, *45*, 1924; **1983**, *48*, 4705.

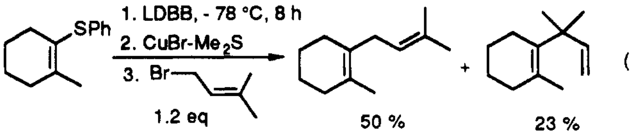
[9] A cost analysis based on the reagents required reveals that the reductive lithiation procedure is about 7.5 times less expensive than the method proceeding through stannanes. One factor in this comparison is that lithium is about one quarter of the cost per mole of the cheapest alkyllithium. Furthermore, *p,p'*-di-*tert*-butylbiphenyl can be recycled easily and if necessary the inexpensive thiophenol can also be recycled.

[10] Considering the mechanism of reductive lithiation,[7] the order of ease of reduction (cyclooctenyl and cycloheptenyl phenyl sulfides > cyclohexenyl and cyclopentenyl phenyl sulfides) and the fact that cyclooctenyl and cycloheptenyl phenyl sulfides cleave cleanly to give vinyl anions while cyclohexenyl phenyl sulfide gives a small amount and cyclopentenyl phenyl sulfides only phenyllithium may indicate that larger ring cycloalkenyl radicals are more stable than their smaller ring counterparts. However, the expected greater stability of the cyclopentenethiolate anion compared to that of the larger ring enolthiolate anions may also play a role in the direction of cleavage of cyclopentenyl phenyl sulfide.

As can be seen from Scheme I, 1-lithio-2-methylcyclohexene (**5**) can be readily produced by the new procedure. This compound cannot be generated by the Bond process since the sulfonylhydrazone of ketone **1** decomposes to the isomeric 1-lithio-6-methylcyclohexene (**4**). The latter is also available, albeit by a slightly longer route, involving the methylation of **6** (itself available from cyclohexanone, or via other routes) by Trost's procedure,[6] followed by reductive lithiation (Scheme I).

The reductive lithiation of vinyl phenyl sulfides (eq 1) with LDBB in THF occurs immediately at −78 °C for seven- and eight-membered rings and in 2 h for unsubstituted cyclohexenyl sulfides; substituted six-membered rings require 4–8 h to form the vinyllithiums. Reduction with lithium 1-(dimethylamino)naphthalenide (LDMAN),[12,13] which offers the advantage of an acid-extractable byproduct (DMAN), is very satisfactory for the production of cycloheptenyllithium ($^1/_2$ h reduction at −55 °C yields 92% of cycloheptene-1-carboxaldehyde) but it requires 6–12 h at −60 °C for six-membered rings and provides about 15% lower yields than LDBB; however, the reduction of substituted cyclohexenyl phenyl sulfides with this reagent is impractically slow.

As shown in Table I, attack of numerous electrophiles on the produced vinyllithiums results in good to excellent yields of desired products including allylic alcohols, vinylsilanes, and enals. Alkylation of **5** with 1-iodohexane proceeded in good yield but required 2.2 equiv of the alkylating agent due to the consumption of 1 equiv by the thiophenoxide ion; the products were easily separated by chromatography. In previous work on the methylation of an organolithium produced by reductive lithiation,[12] a heterocuprate[14] was used to avoid the necessity of an extra equivalent of methyl iodide. In the present case 1-iodohexane was too unreactive to alkylate the heterocuprate formed by treatment of **5** with $CuBr{-}Me_2S$ at temperatures below the decomposition point of the cuprate. However, the heterocuprate reacted instantaneously with allylic bromides at −78 °C (e.g. eq 2).



(2)

The heterocuprate was also extremely useful in providing exclusive 1,4 addition to enones,[15] whereas 1,2 addition to enals and enones was readily achieved with the vinyllithium (Table I). The latter reaction leads to synthetically useful precursors for Nazarov[16] rearrangements.

The brevity, low cost, and high yields obtained should make this procedure a particularly practical alternative to the Bond and Wulff processes for producing cyclohexenyl-, cycloheptenyl-, and cyclooctenyllithiums.[17] It should be particularly suitable as an industrial process.

Acknowledgment. We thank the National Institutes of Health for financial support and Dr. Kasi Somayajula for recording the mass spectra.

Supplementary Material Available: Typical experimental procedures and spectral data for the products (6 pages). Ordering information is given on any current masthead page.

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(11) Labiad, B. Villemin, D. *Synthesis* **1989**, 143.

(12) Cohen, T.; Matz, J. R. *Synth. Commun.* **1980**, *10*, 311.

(13) For a description of the preparation and use of this reagent, see: Cohen, T.; Sherbine, J. P.; Hutchins, R. R.; Lin, M.-T. *Organomet. Synth.* **1986**, *3*, 361.

(14) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788.

(15) Kende first reported the preparation of a vinylcuprate by a Bond type reaction by using *tert*-butyllithium in order to avoid the use of TMEDA: Kende, A. S.; Jungheim, L. N. *Tetrahedron Lett.* **1980**, *21*, 3849. However, surprisingly, Heathcock appears to have been successful in preparing a vinyllithium for Cu^I-induced conjugate addition by the use of *n*-butyllithium in THF rather than in a solvent containing TMEDA: Hoagland, S.; Morita, Y.; Bai, D. L.; Märki, H.-P.; Kees, K.; Brown, L.; Heathcock, C. H. *J. Org. Chem.* **1988**, *53*, 4730.

(16) Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, 429.

(17) Lithium di-*tert*-butylbiphenylide is prepared as follows. To an oven-dried three-neck round-bottom flask, equipped with a glass stirring bar, rubber septum, and argon inlet, is added THF (7 mL) and di-*tert*-butylbiphenyl (DBB, 0.85 g, 3.2 mmol). Lithium ribbon is prepared by scraping the dark oxide coating off the surface while it is immersed in mineral oil. The metal is dipped in pentane, in order to remove the oil, and then weighed (24 mg, 3.4 mmol) in a tared beaker containing mineral oil. The metal is cut into small very shiny pieces while immersed in mineral oil. The small lithium pieces are dipped again in pentane and quickly added to the THF/DBB mixture while the flask is rapidly being purged with argon. The mixture is cooled to 0 °C and vigorously stirred for 4–5 h. The dark green-blue color of the radical anion appears within 10 min and formation is complete in 4–5 h. This procedure produces a 0.45 M solution of radical anion. A typical reductive lithiation procedure follows. To a solution of LDBB (5.25 mL of a 0.40 M solution in THF, 2.1 mmol) at −78 °C, 1-(phenylthio)-1-cyclohexene (0.190 g, 1.00 mmol) in THF (4 mL) is slowly added via syringe pump over a 0.50-h period. The deep blue-green reaction mixture is stirred at −78 °C for 2 h, during which time the color slowly changes to red. Cyclohexanecarboxaldehyde (0.133 mL, 0.123 g, 1.10 mmol) in THF (2 mL) is added dropwise until the mixture turns yellow. The reaction is quenched at −78 °C with brine, and the mixture is warmed to room temperature. Following extraction with ether (3 × 20 mL), the combined organic layer is washed with 10% NaOH (3 × 10 mL, or at least until all of the thiophenol is removed) and brine. The organic layer is dried ($MgSO_4$), and the solvent is removed by rotary evaporation. Radial chromatography with hexane is used to recover DBB from the reaction mixture, followed by 5% ethyl acetate/hexane to give a 79% yield of 1-(1′-cyclohexenyl)-1-cyclohexylmethanol.

Oxidative Cyclization of δ,ϵ- and ϵ,ζ-Unsaturated Enol Silyl Ethers

Barry B. Snider* and Taesoo Kwon

Department of Chemistry, Brandeis University, Waltham, Massachusetts 02254-9110

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Summary: Oxidative cyclization of δ,ϵ- and ϵ,ζ-unsaturated enol silyl ethers of aryl ketones with cupric triflate and cuprous oxide or ceric ammonium nitrate and sodium bicarbonate in acetonitrile provides tricyclic ketones stereoselectively.

We have recently described oxidative free-radical cyclizations which are initiated by oxidation of a β-dicarbonyl compound with $Mn(OAc)_3 \cdot 2H_2O$.[1] The scope of this reaction would be extended if the reaction could be initiated

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