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CARBENOID TYPE BASE INDUCED RING EXPANSION OF THE ADDUCTS OF CYCLIC KETONES WITH *BIS*(PHENYLTHIO)METHYLLITHIUM

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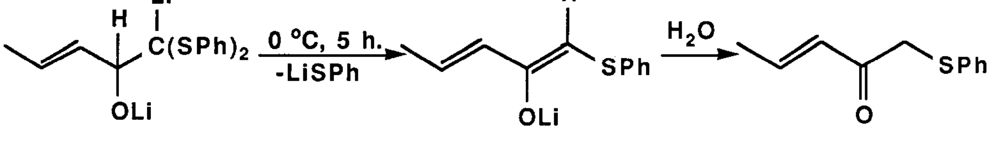
Abstract : In another application of the principle that metallo derivatives of *bis*(phenylthio)acetals behave as carbenoids when present in the same molecule with another anionic group, the adducts of cyclic ketones with *bis*(phenylthio)methyllithium react with an alkyllithium to yield the ring expanded α-(phenylthio)ketones.

An earlier report from this laboratory has disclosed a synthetically significant application of a pinacol-type ring expansion,[1] in which removal of thiophenoxide ion from compounds **1-3** and **6** by treatment with cuprous trifluoromethanesulfonate (triflate) generates a carbocation intermediate capable of rearranging (possibly *via* an epoxide intermediate) to compounds **7-9** and **12**, respectively, in good yields. Recently, Corey[2] used this type of ring expansion as a key step in his synthesis of retigeranic acid and modifications of the procedure have been explored by both Knapp[3] and Murray.[4] The method was unsuccessful, however, when applied to ring expansion of **4** to **10**.

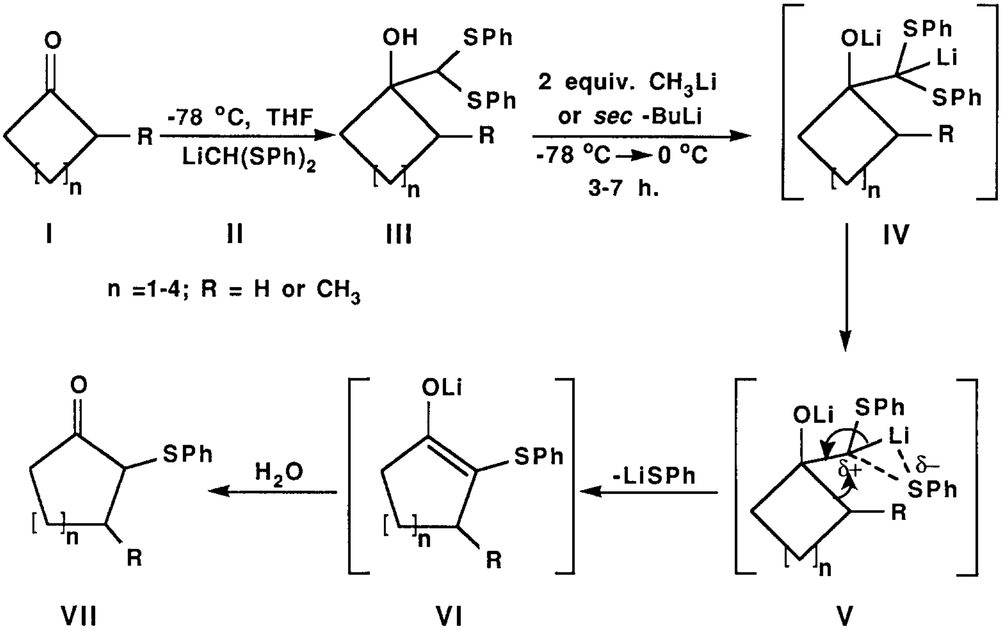
We now report a method which is superior in ease and generality to the ring expansion method described above and which occurs under basic rather than Lewis acid conditions. This new method is based on the recently enunciated principle whereby the conjugate base of a phenyl thioacetal exhibits carbenoid behavior when it exists in a molecule with a second negative charge; this principle has been used for ring closures of dilithio derivatives of both thioacetal alcohols and *bis*-thioacetals,[5] cyclopropanation of enolate carbenoids,[6] and, especially pertinent to the present work, CH insertion in lithio derivatives of thioacetals bearing an allylic oxyanion substituent[7] (see Scheme 1).

SCHEME 1



The application of this concept to the present ring expansions is shown in Scheme 2. Treatment of **III**, formed by adding cyclic ketones (**I**) to *bis*(phenylthio)methyllithium (**II**) in THF at -78 °C,[8] with two molar equivalents of an appropriate alkyllithium in THF at -78 °C and allowing the mixture to warm to 0 °C generates the dilithio derivative **IV**. The latter rearranges to the ring expanded enolate anion **VI**,[9] presumably through an intermediate of carbocationic character which may be approximated by structure **V** based on recent studies of Walborsky.[10] The advantages of this carbenoid type ring expansion over that induced by cuprous triflate are that the latter air and moisture sensitive salt is not required, that 0 °C is used instead of the reflux temperature of benzene, and that this method is successful in the rearrangement of compound **4**.

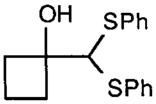
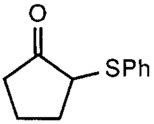
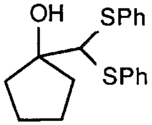
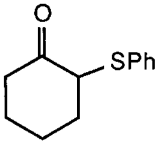
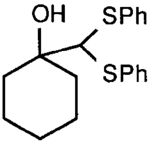
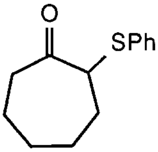
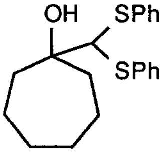
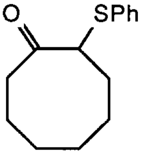
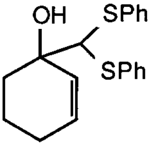
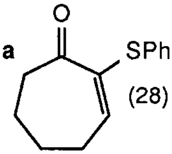
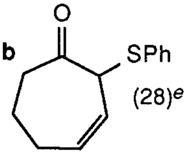
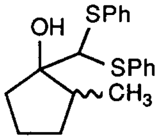
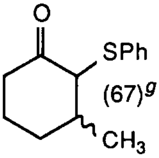
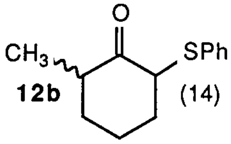
SCHEME 2



The rearrangement products (**7-12**) in the table indicate that a vinyl group migrates faster than an alkyl group and that the more highly substituted alkyl group preferentially migrates. The rearrangement of **5** forms the products of vinyl migration, **11a** and **11b**, in 56% total yield and **11b** gets quantitatively converted to **11a** with excess base. The rearrangement of **6** yields the products **12a** (67%) and **12b** (14%), revealing a 3.2 : 1 preference for migration of the most substituted alkyl group. These trends have also been seen in the lithium halocarbenoid rearrangements[11a-c] (see below) and in our previous copper(I)-induced ring expansion.[1]

For some unknown reason, the rearrangements to 5- and 6-membered cyclic α-(phenylthio)-ketones (**7**, **8**, **12a**, and **12b**) are best performed with methyllithium, whereas those to 7- and 8-membered cyclic α-(phenylthio)ketones (**9**, **10**, **11a**, and **11b**) require *sec*-butyllithium. When **3**, **4**, and

TABLE

Thioacetal (% yield from I)[a,b]			Alkyllithium Used	Time at 0 °C (h)[c]	Ketone Product (% yield)[a]		
1		(86)	CH_3Li	3	**7**		(70)
2		(72)	CH_3Li	4	**8**		(95)
3		(94)	*sec*-BuLi	3	**9**		(55)
4		(98)	*sec*-BuLi	3	**10**		(54)
5		(81)[d]	*sec*-BuLi	7	**11a** **11b**	 	(28) (28)[e]
6		(65)[f]	CH_3Li	3	**12a** **12b**	 	(67)[g] (14)

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[a] All yields are of purified materials which have been characterized by 300 MHz ^1H NMR, IR, and mass spectrometry. Elemental compositions were determined for new compounds by exact mass determination. [b] Yields of adducts were not optimized. [c] The time for which the reaction mixture was stirred at 0 °C before being quenched. [d] Cyclohexenone was treated with bis-(phenylthio)methyllithium in 2:1 hexane/THF at 0 °C for 1 min.[12] [e] Converted quantitatively to **11a** by excess base. [f] Two stereoisomers (54% and 11%); the major one was used in the rearrangement. [g] Total yield of 3:2 trans/cis ratio (by NMR) of two inseparable stereoisomers.

5 were each treated with either methyllithium or methyllithium/TMEDA, starting materials were recovered along with low yields (10-20%) of the desired cyclic α-(phenylthio)ketone.

The carbenoid type ring expansion described here is related to that reported by Nozaki,[11a] Villieras,[11b] and Köbrich,[11c] in which the adduct of a cyclic ketone with dichloromethyllithium or dibromomethyllithium is treated with a base (an alkylithium or a lithiated piperidine) to yield a ring expanded product; the chloro-compounds undergo deprotonation, followed by rearrangement to α-chlorocyclic ketones in moderate yields, while the bromo-compounds undergo Li/Br exchange to produce cyclic ketones in good yields. Overall, our method is comparable and produces stable and useful sulfur-functionalized ketones and, since it is performed under basic conditions, it nicely complements our earlier Lewis acid induced procedure and is somewhat more general than the latter.

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References and Notes

1. Cohen, T.; Kuhn, D.; Falck, J. *J. Am. Chem. Soc.* **1975**, *97*, 4749.
2. Corey, E. J.; Desai, M.; Engler, T. *J. Am. Chem. Soc.* **1985**, *107*, 4339.
3. Knapp, S.; Trope, A. F.; Theodore, M. S.; Hirata, N.; Barchi, J. J. *J. Org. Chem.* **1984**, *49*, 608.
4. Murray, R.; Israel, R. *J. Org. Chem.* **1985**, *50*, 1573.
5. Cohen, T.; Ouellette, D.; Daniewski, M. *Tetrahedron* **1978**, *34*, 5063. Cohen, T.; Ritter, R.; Ouellette, D. *J. Am. Chem. Soc.* **1982**, *104*, 7142. Cohen, T.; Ritter, R. *J. Am. Chem. Soc.* **1986**, *108*, 3718.
6. Cohen, T.; Yu, L.-C. *J. Am. Chem. Soc.* **1983**, *105*, 2811.
7. Cohen, T.; Yu, L.-C. *J. Org. Chem.* **1984**, *49*, 605. An analogous rearrangement had been reported earlier; Kuwajima, I.; Kurata, Y. *Chem. Lett.* **1972**, 291.
8. Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097.
9. We have shown in numerous cases[5-7] that a dilithio species with carbanionic properties is a precursor of the intermediate or transition state in which that same carbon atom manifests cationic properties.
10. Rachon, J.; Goedken, V.; Walborsky, H. M. *J. Am. Chem. Soc.* **1986**, *108*, 7435, and references cited therein.
11. (a) Nozaki, H.; Taguchi, H.; Yamamoto, H. *Tetrahedron* **1972**, *28*, 4661. Nozaki, H.; Taguchi, H.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1592. (b) Villieras, J.; Bacquet, C.; Normant, J.F. *J. Organomet. Chem.* **1972**, *40*, C1. Villieras, J.; Bacquet, C.; Normant, J.F. *J. Organomet. Chem.* **1975**, *97*, 325. (c) Köbrich, G.; Grosser, J. *Chem. Ber.* **1973**, *106*, 2626.
12. Unpublished work by Abraham, W. and Myers, M.

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