yield (92%). To our surprise **6** failed to undergo the hypoiodite reaction[12] with HgO and I_2 to give the expected cyclic ether **8**; instead, a mixture (9:1; 3α:3β) of iodoexpoxides **7** was produced under these conditions. Subsequently, it was found that photolysis of a solution of **7**, hexabutylditin (0.1 equiv), and pyridine (1 equiv) in benzene with a sun lamp provided **8** in high yield (80% from **6**). The dynamics of this highly efficient transformation are shown in Scheme II. It should be noted that the rearrangement of the epoxycarbinyl radical to the allyloxy radical[13] and the atom-transfer radical reaction[14] are the key elements in this catalytic process cycle. Completion of this synthetic route was accomplished by simply treating **8** with 48% hydrofluoric acid in acetonitrile at 60 °C, a process which gave target metabolite **2a** in 58% yield along with a trace of the byproduct **11**.[15] The conversion of **8** to **2a** was shown to proceed in a stepwise manner via the sequence **8** → **9** → **2a** with the second step presumably proceeding via the intermediacy of a cationic species such as **10** which, upon regioselective deprotonation of the 5-position, affords **2a**.

In summary, a seven-step synthetic route has been developed for elaboratoring 6α-hydroxymethyl metabolite **2a** from simvastatin in 30% overall yield and used to prepare g-scale quantities of **2a**.

Acknowledgment. The authors wish to thank Dr. Paul S. Anderson for his encouragement during the course of this investigation.

Supplementary Material Available: Experimental procedures for the preparation of **5**, **6**, **7**, **8**, and **2a** and spectral and analytical data of the products (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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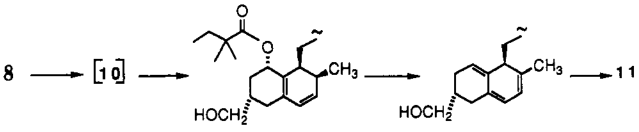
(12) For general reviews of the hypoiodite reaction, see: (a) Heusler, K.; Kalvoda, *J. Angew. Chem., Int. Ed. Engl.*, **1964**, *3*, 525–538. (b) Kalvoda, J.; Heusler, K. *Synthesis* **1971**, 501–526.

(13) For examples of synthetic applications using the rearrangement of an epoxycarbinyl radical to an allyloxy radical, see: (a) Carlson, R. G.; Huber, J. H. A.; Henton, D. E. *J. Chem. Soc., Chem. Commun.* **1973**, 223–224. (b) Barton, D. H. R.; Motherwell, R. S. H.; Motherwell, W. J., *J. Chem. Soc., Perkin Trans. 1* **1981**, 2363–2367. (c) Johns, A.; Murphy, J. A. *Tetrahedron Lett.* **1988**, *29*, 837–840. (d) Gash, R. C.; Maclorquodale, F., Walton, J. C. *Tetrahedron* **1989**, *45*, 5531–5538. (e) Rawal, V. H.; Newton, R. C.; Krishnamurthyl, V. *J. Org. Chem.* **1990**, *55*, 5181–5183.

(14) For a comprehensive review of the atom-transfer radical reaction, see: Curran, D. P. *Synthesis* **1988**, 489–513.

(15) Byproduct **11** is probably formed from **10** as indicated below:



Use of a Dilithiomethane Equivalent in a Novel One-Flask [2 + 1 + 2] Cyclopentannulation Reaction: A Highly Efficient Total Synthesis of (±)-Hirsutene

Keith Ramig,[1] Michael A. Kuzemko,[1] Kevin McNamara, and Theodore Cohen*

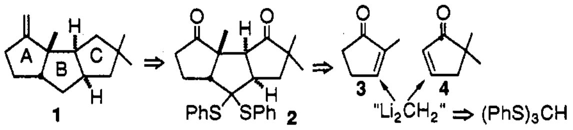
Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260

Received January 29, 1992

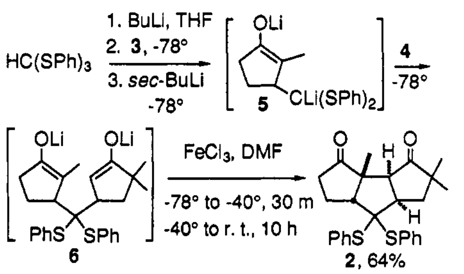
Summary: A brief synthesis of (±)-hirsutene demonstrates the novel use of tris(phenylthio)methane as a dilithiomethane equivalent capable of consecutive conjugate additions to different enones to form a dienolate which can be oxidized to a cyclopentane.

It has been shown that a variety of carbanion–carbenoids can be used in carbon–carbon bond forming processes in which the carbenoid function behaves as an electrophile.[2] Herein we report one of the most efficient total syntheses of the triquinane (±)-hirsutene[3] (**1**), by a process which utilizes the nucleophilic nature of the carbenoid function of a carbanion–carbenoid at low temperature. The synthesis features completely stereoselective construction of the triquinane nucleus by one-flask formation of three of the five carbon–carbon bonds of the B ring, using commercially available tris(phenylthio)methane as a dilithiomethane equivalent (Scheme I).

Scheme I



Scheme II



The synthesis begins with conjugate addition of tris(phenylthio)methyllithium[4] to commercially available 2-methyl-2-cyclopentenone (**3**) at −78 °C, followed by sul-

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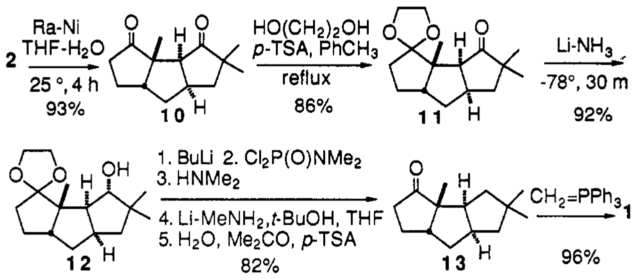
(1) Current address: Synthesis Development Department, Hoffmann-La Roche, Inc., 340 Kingsland St., Nutley, NJ 07110.

(2) (a) Ramig, K.; Bhupathy, M.; Cohen, T. *J. Org. Chem.* **1989**, *54*, 4404 and references cited therein. (b) Cohen, T.; Yu, L.-C., *Ibid.* **1985**, *50*, 3266.

(3) Leading references to previous syntheses of hirsutene: (a) Plamondon, L.; Wuest, J. D. *J. Org. Chem.* **1991**, *56*, 2076. (b) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986**, *108*, 3443. For triquinanes in general, see: Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry*; Springer-Verlag: Berlin, Heidelberg, Germany, 1987; p 184. See also: Curran, D. P. *Advances in Free Radical Chemistry*; JAI Press: Greenwich 1990; Vol. 1, p 121.

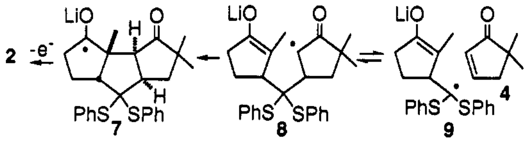
(4) Smith, R. A. J.; Lal, A. R. *Aust. J. Chem.* **1979**, *32*, 353. Cohen, T.; Nolan, S. M. *Tetrahedron Lett.* **1978**, 3533. Manas, A. R.-B.; Smith, R. A. J. *J. Chem. Soc., Chem. Commun.* **1975**, 216. Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 443.

Scheme III



fur–lithium exchange by treatment of the conjugate adduct with *sec*-butyllithium[2b] at the same temperature (Scheme II). It had previously been shown that analogues of the resulting enolate carbenoid **5**, when warmed to −45 °C, provide good yields of cyclopropyl ketones, an example of the carbenoid function behaving as an electrophile.[2a] Treatment of **5** with 5,5-dimethyl-2-cyclopentenone (**4**)[5] at −78 °C generates the dienolate **6**. The triquinane nucleus was completed by oxidative coupling of the enolate groups with anhydrous ferric chloride in DMF.[6] The single diastereomer of the triquinane isolated was the desired cis,anti,cis isomer **2** as indicated by the subsequent conversion to hirsutene.

Since there is no reason to expect a highly stereoselective conjugate addition of **5** to enone **4**, it is reasonable to speculate that the remarkable and gratifying stereoselectivity of this coupling reaction is a result of a reversible fragmentation of the enolate radical (e.g., **8**), formed upon 1-electron oxidation of **6**, to, e.g., **9** and enone **4**; that diastereomer of **8** that can comfortably close to the ketyl **7** then does so resulting in the most stable configuration of the coupling product **7**.[7]



Facile conversion of triquinane **2** to (±)-hirsutene is readily accomplished (Scheme III). Desulfurization of triquinane **2** with Raney nickel[8] gives dione **10**. Mehta et al.[3b] have converted dione **10** to hirsutene, but the yield was only 13%. We have devised a different set of reactions which allows hirsutene to be obtained from dione **10** in 62% yield. Protection of the least hindered carbonyl group by formation of an ethylene ketal gives ketone **11**, which is reduced by Li/NH_3 to give alcohol **12**.[9] Deoxygenation of the hindered alcohol function in **12** is accomplished by reduction of the derived phosphorodiamidate.[10] Ketone **13** is then converted to (±)-hirsutene (**1**) by Wittig methylenation.[11] Its ^1H and ^{13}C NMR spectra and mass spectrum were identical with those of an authentic sample kindly supplied by Professor Dennis Curran.

This synthesis appears to be one of the most efficient ever reported, requiring only eight steps (including those used to produce the known[5] enone **4**) and producing an 18% overall yield of (±)-hirsutene from commercially available starting materials. The scope of this new cyclopentane ring-forming process is under investigation.

Acknowledgment. We thank the National Science Foundation for financial support and Professors Tadhg Begley (Cornell University) and Peter Wipf for helpful suggestions.

Supplementary Material Available: Experimental procedures, spectral data, and NMR spectra of **1**, **2**, and **7–10** (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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