1-(α-bromovinyl)-2-(1-cyclohexen-1-yl)ethanol, 80376-64-3.

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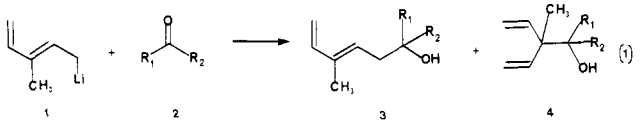
Received November 17, 1981

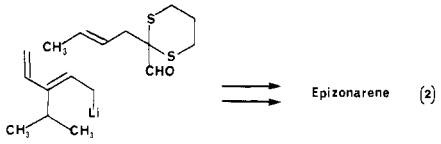
Acyl Silanes as Sterically Hindered Aldehydes: Additions, Oxidations, and Desilylations

Summary: Acyl trimethylsilanes can be used as sterically hindered synthons for aldehydes, whereby the trimethylsilyl group is removed via a Brook rearrangement.

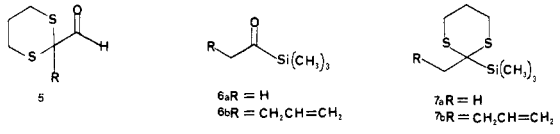
Sir: In connection with our studies of the pentadienyl anion pathway[1] to intramolecular Diels–Alder reactions we have examined several factors which control the regioisomer distributions of **3** and **4** (eq 1): (1) kinetic vs.



thermodynamic control,[2] (2) solvent and cation effects,[3] and (3) steric effects. The amount of desired 1,3-diene (**3**) was usually greatest when the substrate was hindered (i.e., **2**, R_1 and R_2 large). We required a method, however, to cause an aldehyde to *temporarily* appear more hindered to the approach of an organometallic reagent (**1**). After the desired 1,3-diene was formed, the steric "blocking group" must be removed. Thus we used for this purpose a dithiane carboxaldehyde **5** in a synthesis of epizonarene (eq 2). The bulky 1,3-dithiane group could subsequently be removed with Raney nickel.

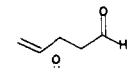
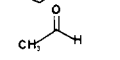
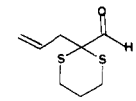
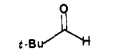
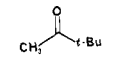
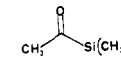
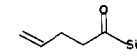


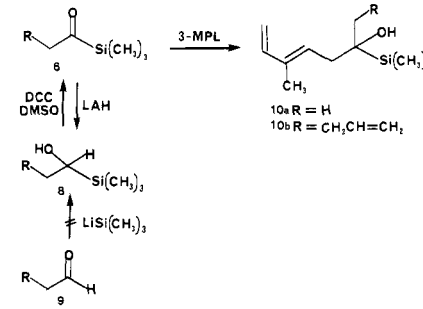
In this paper we discuss application of acyl silanes[4] such as **6a** or **6b** as sterically hindered aldehyde equivalents.



Acyl silanes **6a** or **6b** were prepared by hydrolysis[5] of the corresponding thioketals **7a** and **7b**. Acyl silanes **6a** and **6b** are stable to distillation and can be chromatographed. Compound **6b** was reduced with $LiAlH_4$ in ether to give the silyl carbinol **8**. Although we were able to oxidize **8** back to the ketone using DCC/Me_2SO methods,[6] we were not able to prepare **8** via addition of Me_3SiLi[7] to aldehyde **9**.

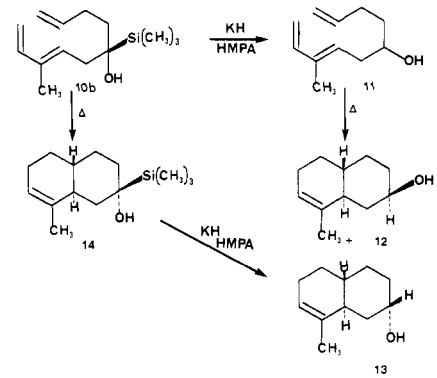
Table I. Steric Effects on the Regiochemistry of Additions of (3-Methylpentadienyl)lithium in THF (eq 1)

entry	compd 2	ratio 3/4, %
1		21/73
2		25/73
3		88/12
4		85/15
5		100/0
6		100/0
7		100/0

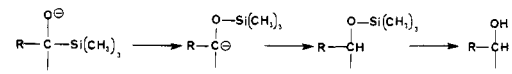


When 3-MPL (**1**, (3-methylpentadienyl)lithium) is allowed to react with **6a** or **6b**, only the conjugated isomers **10a** or **10b** are formed. The relative steric bulk of the Me_3Si group with respect to carbonyl additions can be seen from the regioisomer ratios in Table I. Analogy to a *tert*-butyl group seems reasonable.

The Me_3Si group, having served its purpose, could be removed by treatment of the alcohol with KH in HMPA.[8]



(1) (a) Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1978**, *100*, 6289–6291. (b) Wilson, S. R.; Mao, D. T. *J. Org. Chem.* **1979**, *44*, 3093–3094.
(2) Wilson, S. R.; Mao, D. T.; Jernberg, K. M.; Ezmirly, S. T. *Tetrahedron Lett.* **1977**, 2559–2562.
(3) Wilson, S. R.; Misra, R. N. *J. Org. Chem.* **1980**, *45*, 5079–5081.
(4) Reich, H. J.; Rusek, J. J.; Olson, R. E. *J. Am. Chem. Soc.* **1979**, *101*, 2225–2227.
(5) (a) Brook, A. G.; Duff, J. M.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431–434. (b) Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 431–436.
(6) Brook, A. G. *Adv. Organomet. Chem.* **1968**, *7*, 96–155.
(7) Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063–3064.
(8) The Brook arrangement has been observed for aryl-substituted α-hydroxy silanes as well as those where R = alkyl,[9] vinyl,[10] or acetylene:[11] Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77–84. In general, anion stabilizing



R groups enhance the rearrangement rate. In this case the lithium salt of **10a** is stable, whereas the potassium salt in HMPA or in the presence of 18-crown-6 rearranges.

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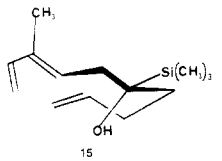
The product 11 has been reported earlier[1a] to undergo intramolecular Diels–Alder reaction leading to a mixture of 12 and 13. If **10b** is heated at 180 °C for 20 h, cyclization occurs. The product (mainly one isomer) is assigned structure 14 (equatorial Me_3Si) based on the assumption that the bulky Me_3Si group must occupy an equatorial position in the Diels–Alder transition state 15.[12] When 14 was treated with KH/HMPA, a stereospecific[13] Brook rearrangement[8] led to exclusive axial alcohol 13.



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In conclusion, we point out that the efficient desilylation of silyl carbinols makes their acyl silane precursors equivalent to aldehydes that are sterically hindered. Two additional advantages are the following: (1) acyl silanes are less prone to self-condensation than aldehydes and thus give higher overall yields and (2) the bulky Me_3Si substituent can be used to control the stereochemistry of subsequent reactions.

Acknowledgment. We thank the National Institues of Health (GM-26039) and the Petroleum Research Fund (11243-ACl) for financial assistance.

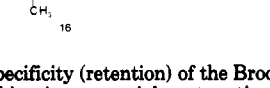
Registry No. 1, 51852-87-0; 2 (R_1 = Me; R_2 = H), 75-07-0; 2 (H_2C=$CHCH_2$—$C_4H_6S_2$; R_2 = H), 75266-68-1; 2 (R_1 = *t*-Bu; R_2 = H), 630-19-3; 2 (R_1 = Me; R_2 = *t*-Bu), 13411-48-8; 3 (R_1 = Me; R_2 = H), 80387-36-6; 3 (H_2C=$CHCH_2$—$C_4H_6S_2$; R_2 = H), 80387-37-7; 3 (R_1 = *t*-Bu; R_2 = H), 80387-38-8; 3 (R_1 = Me; R_2 = *t*-Bu), 80387-39-9; 4 (R_1 = H_2C=$CHCH_2CH_2$; R_2 = H), 80387-40-2; 4 (R_1 = Me; R_2 = H), 80387-41-3; 4 (H_2C=$CHCH_2$—$C_4H_6S_2$; R_2 = H), 80387-42-4; 4 (R_1 = *t*-Bu; R_2 = H), 80387-43-5; **6a**, 13411-48-8; **6b**, 80387-44-6; 8, 80387-45-7; 9, 2100-17-6; **10a**, 80387-46-8; **10b**, 80387-47-9; 11, 80387-48-0; 13, 80433-07-4; 14, 80387-49-1.

(9) Brook, A. G.; Warner, C. M.; Mcgriskin, M. E. *J. Am. Chem. Soc.* **1959**, *81*, 981–983.

(10) Kuwajima, I.; Kato, M. *J. Chem. Soc., Chem. Commun.* **1979**, 708–709.

(11) Reich, H. J.; Olson, R. E.; Clark, M. C. *J. Am. Chem. Soc.* **1980**, *102*, 1423–1424.

(12) Additional support for the equatorial disposition of the Me_3Si group comes from the addition of Me_3SiLi[7] to known[1a] ketone 16 which gives 14.



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(13) The stereospecificity (retention) of the Brook rearrangement[8] can be rationalized by kinetic equatorial protonation of the anionic intermediate. A related aliphatic Brook rearrangement has also been reported (Hudlick, P., Howard University, personal communcation) to occur with retention.

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Received August 21, 1981

Bifunctional Cyclopropyl Reagents: Stereocontrolled Approach to Vinyl Sulfides and Chemodifferentiated 1,4-Dicarbonyl Systems

Summary: The use of (*E*)-2-(hydroxymethyl)cyclopropyl phenyl sulfide as a useful conjunctive reagent, particularly in a stereocontrolled synthesis of vinyl sulfides, is reported.

Sir: The immense importance of the carbonyl group in structural elaboration stems from the ability to add nucleophiles to the carbonyl carbon atom and, most importantly, the ability to functionalize at the α carbon atom through the intermediacy of enols or enolates. Stereocontrolled methods for enol or enolate formation, which are generally lacking, would greatly enhance the utility of such synthetic intermediates. Vinyl sulfides not only have the possibility of serving as enol substitutes but, due to a myriad of other reactions involving direct replacement of sulfur or isomerizations to allylic systems, also may provide a much diverse reactivity profile. Thus, stereocontrolled syntheses of vinyl sulfides are particularly important but virtually nonexistent. We report herein that the bifunctional conjunctive reagent, 2-(hydroxymethyl)-cyclopropyl phenyl sulfide (1),[1] provides a novel stereocontrolled approach to such systems which can greatly enhance the utility of this functionality. Furthermore, it additionally allows transformation into several important building blocks—particularly chemodifferentiated 1,4-dicarbonyl systems.

The reagent 1 (bp 110–111 °C (0.07 torr),[2,3] which has been made on multimole scale, is available in 45% overall yield from thiophenol and γ-butyrolactone as outlined in Scheme I. The pyrrophoric dilithium reagent 2, which forms readily in contrast to the metalation of 2-methylcyclopropyl phenyl sulfide, forms as a suspension in hexane.[4-6] For synthetic purposes, two volumes of THF are

(1) For a few recent examples of small ring conjunctive reagents, see: Trost, B. M.; Nishimura, Y.; Yamamoto, K. *J. Am. Chem. Soc.* **1979**, *101*, 1328. Trost, B. M.; Bogdanowicz, M. J.; Frazee, W. J.; Salzmann, T. N. *Ibid.* **1978**, *100*, 5512. Trost, B. M.; Scudder, P. H. *Ibid.* **1977**, *99*, 7601. Trost, B. M.; Frazee, W. J. *Ibid.* **1977**, *99*, 6124. Piers, E.; Nagakura, I.; Morton, H. E. *J. Org. Chem.* **1978**, *43*, 3630. Piers, E.; Lau, C. K. *Synth. Commun.* **1977**, *7*, 495. Danishefsky, S.; Singh, R. K. *J. Am. Chem. Soc.* **1975**, *97*, 3239. Miller, R. D.; McKean, D. R. *Tetrahedron Lett.* **1979**, 583, 587. Halazy, S.; Lucchetti, J.; Krief, A. *Ibid.* **1978**, 3971. Harms, R.; Schollkopf, U.; Muramatsu, M. *Justus Liebigs Ann. Chem.* **1978**, 1194. Marino, J. P.; Browne, L. J. *Tetrahedron Lett.* **1976**, 3241. Marino, J. P.; Ferro, M. P. *J. Org. Chem.* **1981**, *46*, 1828.

(2) This compound has been characterized by IR, NMR, and mass spectroscopy and elemental composition established by combustion analysis and/or high-resolution mass spectroscopy.

(3) 1: IR ($CDCl_3$) 3640, 3380, 1590, 1485 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–7.4 (m, 5 H), 3.70 (dd, J = 11, 6 Hz, 1 H), 3.51 (dd, J = 11, 7 Hz, 1 H), 2.13 (dt, J = 8, 5 Hz, 1 H), 1.41 (m, 1 H), 1.01 (dt, J = 8, 5 Hz, 1 H), 0.91 (dt, J = 9, 5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 139.3, 129.2, 126.9, 125.3, 64.2, 25.7, 17.1, 13.0. 3: IR ($CDCl_3$) 3590, 3410, 1580, 1480 cm^{-1}; NMR ($CDCl_3$) δ 7.0–7.6 (m, 5 H), 5.30 (d, J = 4 Hz, 1 H), 4.12 (dd, J = 8, 3 Hz, 1 H), 3.81 (d, J = 7 Hz, 1 H), 3.74 (d, J = 8 Hz, 1 H), 1.95 (td, J = 7, 3 Hz, 1 H), 1.14 (d, J = 7 Hz, 2 H).

(4) Trost, B. M.; Keeley, D. E.; Arndt, H. C.; Rigby, J. H.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1977**, *99*, 3080.

(5) For other (1-phenylthiocyclopropyl)lithium reagents, see ref 1 and 4 and the following: Trost, B. M.; Keeley, D. E.; Arndt, H. C.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1977**, *99*, 3088. Cohen, T.; Daniewski, W. M.; Weisenfeld, R. B. *Tetrahedron Lett.* **1978**, 4665. Cohen, T.; Matz, J. R. *Synth. Commun.* **1980**, *10*, 311. Tanaka, K.; Uneme, H.; Matsui, S.; Tanikaga, R.; Kaji, A. *Chem. Lett.* **1980**, 287.

(6) For a similar independent observation in a different series, see Klumpp, G. W.; Kool, M.; Schakel, M.; Schmitz, R. F.; Boutkan, C. *J. Am. Chem. Soc.* **1979**, *101*, 7065.

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