Unusual cyclopropanol formation from a β-silyl aldehyde

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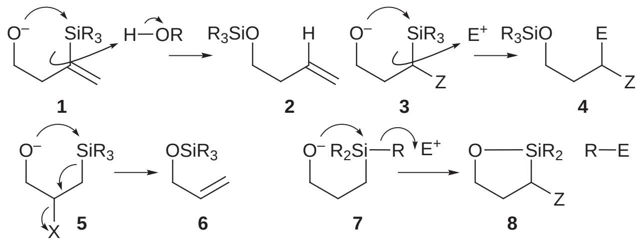
The hemiacetals 15 and 18 gave cyclopropanols 17 and 20 when treated with NaH in DMSO, showing that the silyl group has enhanced electrofugal powers because of the participation of the oxyanion.

The well known electrofugal power of a silyl group attached to carbon is enhanced when a nucleophilic atom coordinates to it. This unexceptionable statement is supported by much circumstantial evidence (Scheme 1). A silyl group can be removed more easily (**1** → **2**) by protodesilylation from a vinyl, or even an alkyl, carbon when an oxyanion is poised five atoms away.[1] More generally, a variety of electrophiles can be made to react with the incipient or actual carbanion nucleophile (**3** → **4**) if the carbon carrying the silyl group has an anion-stabilising group on it.[2] An oxyanion can also remove a silyl group in a 5-*endo-tet* sense to create a double bond (**5** → **6**).[3] And an oxyanion can push one of the other ligands off a silyl group in the sense (**7** → **8**) to make the R group into a carbon nucleophile.[4] We now report a case where the presence of an oxyanion makes a silyl group behave more like a stannyl group, in a reaction with precedent only with a 1,2-Brook rearrangement from an α-oxyanion rather than a γ-oxyanion.[5]



Scheme 1

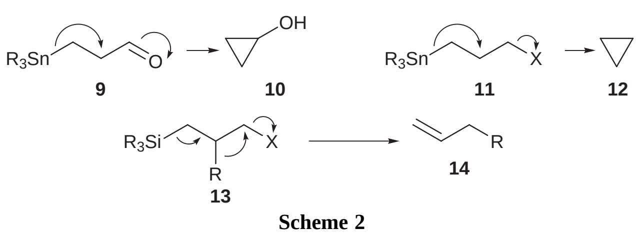
β-Stannyl aldehydes and ketones[6] form cyclopropanols on treatment with Lewis acids (**9** → **10**) (Scheme 2), but β-silyl aldehydes and ketones are remarkably robust to acid and base, often being carried through many steps before being used as masked α,β-unsaturated carbonyl compounds,[7] or as masked β-hydroxy carbonyl compounds.[8] When they do react with Lewis or protic acids, they undergo rearrangements,[9] or intramolecular transfer of ligand from the silicon to the carbonyl group,[10] and we know of only one example where a cyclopropanol-forming pathway has been suggested.[11] In parallel with these observations, cyclopropane formation (**11** → **12**) is normal with γ stannyl carbocations and their precursors,[12] but is unusual with the corresponding silyl compounds,[13] for which rearrangement (**13** → **14**) is the normal pathway.[14]

The reaction we have now discovered occurred originally when we had been trying to carry out a Wittig reaction on the racemic hemiacetal **15**, prepared by DIBAL-H reduction of the corresponding lactone.[15] When we treated the hemiacetal **15** with NaH in DMSO at room temperature for 3 h, with or without methyltriphenylphosphonium iodide, we obtained only the cyclopropanol **17** (Scheme 3). We see this tin-like behaviour as having taken place because of the presence in the intermediate aldehyde of an oxyanion, which can coordinate to the silicon **16** (arrows), and make the pentacovalent silyl anion into a better electrofugal group. We were not able to assign the stereochemistry of the cyclopropanol **17** reliably from the ^{1}H NMR spectrum, it is assigned here by analogy, so we repeated the reaction with a marginally more simple analogue **18**, which similarly gave the cyclopropanol **20** (Scheme 3). COSY and NOE difference experiments on this compound allowed us to confirm the stereochemistry, which corresponds to inversion of configuration at the silicon-bearing carbon, exactly analogous to the inversion seen in reactions of the type **11** → **12** in the tin series. The stereochemistry at the C–OH carbon corresponds to that expected if the carbonyl group more or less eclipses the neighbouring hydrogen atom at the time of cyclopropane formation, which seems reasonable.

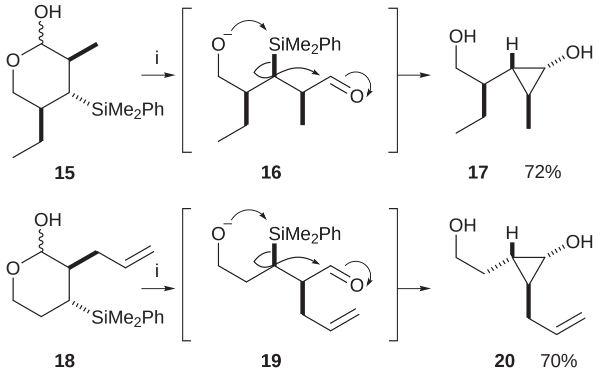
If we left the hemiacetal **18** and NaH/DMSO at room temperature for 10 h instead of 3 h, we obtained a mixture of four hemiacetals, which gave a mixture of two lactones **21** and **22** on oxidation (Scheme 4). The hemiacetal precursor of the lactone **21** looks as though the original hemiacetal **18** had merely undergone a somewhat implausible protodesilylation, but the true pathway, by way of the cyclopropanol **20**, is revealed by the presence of the minor lactone **22**.

This observation may explain our failure to achieve cyclopropanol formation from the even more simple hemiacetal **23**, which gave only the product **24** of protodesilylation (Scheme 5), possibly directly in this case, but also possibly by way of a cyclopropanolate, which can be expected to open regioselectively by way of the benzyl anion.

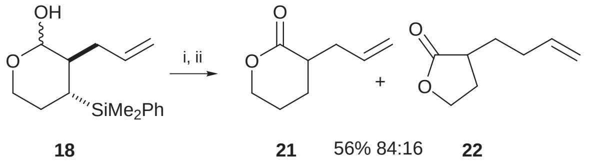
The cyclopropanol formation is not a general reaction, for we found that the 2-methyl and 2-allyl groups in **15** and **18** appear to be necessary, not only for the determination of the stereochemistry of the reaction, but also for it to take place at all. The hemiacetal **25** gave no sign of a cyclopropanol, but gave instead a diene **26**, which we suggest has taken the course illustrated in Scheme 6, with the possibility that the final elimination step is actually preceded by a Mislow rearrangement.



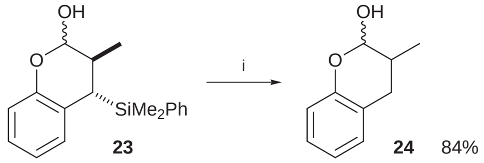
Scheme 2



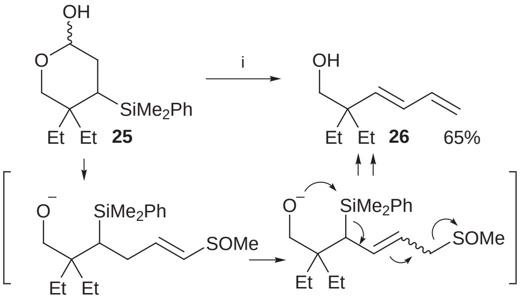
Scheme 3 *Reagents and conditions*: i, NaH, DMSO, rt, 3 h.



Scheme 4 *Reagents and conditions*: i, NaH, DMSO, rt, 10 h; ii, PCC, CH_2Cl_2, rt, 2 h.

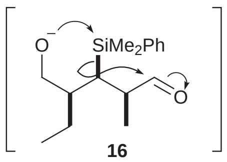


Scheme 5 *Reagents and conditions*: i, NaH, DMSO, rt, 3 h.



Scheme 6 *Reagents and conditions*: i, NaH, DMSO, rt, 3 h.

Perhaps most intriguing is the contrast between the reaction described here, *pushed* forward by nucleophilic activation **16**, and the reaction on a closely similar system **27** *pulled* forward by electrophilic activation.[10] In both cases, our plans for a synthesis of ebelactone-a were thwarted.



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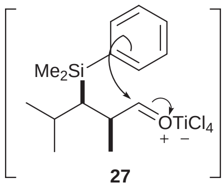

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Notes and references

1 S. Murata and I. Matsuda, *Synthesis*, 1978, 221; M. Isobe, M. Kitamura and T. Goto, *Tetrahedron Lett.*, 1980, 4727; A. G. Brook and J. J. Chrusciel, *Organometallics*, 1984, **3**, 1317; K. Yamamoto, T. Kimura and Y. Tomo, *Tetrahedron Lett.*, 1985, **26**, 4505; A. D. Kaye, G. Pattenden and S. M. Roberts, *Tetrahedron Lett.*, 1986, **27**, 2033; P. F. Hudrlik, P. E. Holmes and A. M. Hudrlik, *Tetrahedron Lett.*, 1988, **29**, 6395; E. Schaumann, A. Kirschning and F. Narjes, *J. Org. Chem.*, 1991, **56**, 717.

2 I. Fleming and C. D. Floyd, *J. Chem. Soc., Perkin Trans. 1*, 1981, 969; T. Takeda, K. Ando and T. Fujiwara, *Chem. Lett.*, 1983, 1285; E. Block, J.-A. Laffitte and V. Eswarakrishnan, *J. Org. Chem.*, 1986, **51**, 3428; P. L. Coe, A. S. Jones, A. Kumar and R. T. Walker, *Tetrahedron Lett.*, 1988, **29**, 835; E. Schaumann and C. Friese, *Tetrahedron Lett.*, 1989, **30**, 7033; T. Michel, A. Kirschning, C. Beier, N. Bräuer, E. Schaumann and G. Adiwidjaja, *Liebigs Ann. Chem.*, 1996, 1811; H. Shinokubo, K. Miura, K. Oshima and K. Utimoto, *Tetrahedron*, 1996, **52**, 503.

3 M. Ochiai, K. Sumi and E. Fujita, *Chem. Pharm. Bull, Jpn.*, 1984, **32**, 3686; M. Tsukamoto, H. Iio and T. Tokoroyama, *Tetrahedron Lett.*, 1987, **28**, 4561; H. Iio, A. Fujii, M. Ishii and T. Tokoroyama, *J. Chem. Soc., Chem. Commun.*, 1991, 1390; M. Franciotti, A. Mann and M. Taddei, *Tetrahedron Lett.*, 1991, **32**, 6783; A. Fujii, Y. Usuki, H. Iio and T. Tokoroyama, *Synlett*, 1994, 725.

4 C. Eaborn and F. M. S. Mahmoud, *J. Organomet. Chem.*, 1981, **209**, 13; W. Kirmse and F. Söllenböhmer, *J. Chem. Soc., Chem. Commun.*, 1989, 774; C. Eaborn and P. B. Hitchcock, *J. Chem. Soc., Perkin Trans. 2*, 1991, 1137; T. Harada, S. Imamaka, Y. Ohyama, Y. Matsuda and A. Oku, *Tetrahedron Lett.*, 1992, **33**, 5807; P. F. Hudrlik, Y. M. Abdallah and A. M. Hudrlik, *Tetrahedron Lett.*, 1992, **33**, 6743 and 6747; K. Takaku, H. Shinokubo and K. Oshima, *Tetrahedron Lett.*, 1998, **39**, 2575; Y. M. Hijii, P. F. Hudrlik and A. M. Hudrlik, *Chem. Commun.*, 1998, 1213. See also N. D. Hone, S. G. Davies, N. J. Devereux, S. L. Taylor and A. D. Baxter, *Tetrahedron Lett.*, 1998, **39**, 897.

5 K. Takeda, J. Nakatani, H. Nakamura, K. Sako, E. Yoshii and K. Yamaguchi, *Synlett*, 1993, 841.

6 T. Sato, M. Watanabe and E. Murayama, *Tetrahedron Lett.*, 1986, **27**, 1621; T. Sato, M. Watanabe, T. Watanabe, Y. Onoda and E. Murayama, *J. Org. Chem.*, 1988, **53**, 1894; T. Sato, T. Watanabe, T. Hayata and T. Tsukui, *J. Chem. Soc., Chem. Commun.*, 1989, 153; T. Sato, M. Hayashi and T. Hayata, *Tetrahedron*, 1992, **48**, 4099; J. Fujiwara, T. Yamamoto and T. Sato, *Chem. Lett.*, 1992, 1775; J. Fujiwara and T. Sato, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 1258; M. Yamamoto, M. Nakazawa, K. Kishikawa and S. Kohmoto, *Chem. Commun.*, 1996, 2353.

7 I. Fleming and J. Goldhill, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1493; I. Fleming and D. A. Perry, *Tetrahedron*, 1981, **37**, 4027; several papers from the Asaoka group reviewed in I. Fleming, A. Barbero and D. Walter, *Chem. Rev.*, 1997, **97**, 2063.

8 I. Fleming, *Chemtracts*: *Org. Chem.*, 1996, **9**, 1; G. R. Jones and Y. Landais, *Tetrahedron*, 1996, **37**, 7599; K. Tamao, *Adv. Silicon Chem.*, **3**, 1.

9 K. Tanino, K. Sato and I. Kuwajima, *Tetrahedron Lett.*, 1989, **30**, 6551.

10 S. C. Archibald and I. Fleming, *Tetrahedron Lett.*, 1993, **34**, 2387.

11 A. R. Katritzky, M. V. Voronkov and D. Toader, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2515.

12 D. D. Davis and H. T. Johnson, *J. Am. Chem. Soc.*, 1974, **96**, 7576; D. D. Davis and R. H. Black, *J. Organomet. Chem.*, 1974, **82**, C—30; S. Teratake, *Chem. Lett.*, 1974, 1123; R. H. Fish and B. M. Broline, *J. Organomet. Chem.*, 1978, **159**, 255; D. C. McWilliam, T. R. Balasubramanian and H. G. Kuivila, *J. Am. Chem. Soc.*, 1978, **100**, 6407; I. Fleming and C. J. Urch, *J. Organomet. Chem.*, 1985, **285**, 173; C. R. Johnson and J. F. Kadow, *J. Org. Chem.*, 1987, **52**, 1493; L. Plamondon and J. D. Wuest, *J. Org. Chem.*, 1991, **56**, 2066 and 2076; T. Sato, T. Kikuchi, H. Tsujita, A. Kaetsu, N. Sootome, K. Nishida and E. Murayama, *Tetrahedron*, 1991, **47**, 3281; T. Sato and S. Nagatsuka, *Synlett*, 1995, 653; R. L. Beddoes, M. L. Lewis, P. Quayle, S. Johal, M. Atwood and D. Hurst, *Tetrahedron Lett.*, 1995, **36**, 471; S. Hanessian, U. Reinhold and S. Ninkovic, *Tetrahedron Lett.*, 1996, **37**, 8976; N. Isono and M. Mori, *J. Org. Chem.*, 1997, **62**, 7867; H. Wakamatsu, N. Isono and M. Mori, *J. Org. Chem.*, 1997, **62**, 8917; A. Krief and L. Provins, *Tetrahedron Lett.*, 1998, **39**, 2017. But for notable exceptions, see G. D. Hartman and T. G. Traylor, *J. Am. Chem. Soc.*, 1975, **97**, 6147; M. J. Goldstein and J. P. Barren *Helv. Chim. Acta*, 1986, **69**, 548.

13 V. J. Shiner, Jr., M. W. Ensinger and R. D. Rutkowske, *J. Am. Chem. Soc.*, 1987, **109**, 804; W. Kirmse and F. Söllenböhmer, *J. Am. Chem. Soc.*, 1989, **111**, 4127; V. J. Shiner, Jr., M. W. Ensinger and J. C. Huffman, *J. Am. Chem. Soc.*, 1989, **111**, 7199; J. Coope and V. J. Shiner, Jr., *J. Org. Chem.*, 1989, **54**, 4270; V. J. Shiner, Jr., M. W. Ensinger, G. S. Kriz and K. A. Halley, *J. Org. Chem.*, 1990, **55**, 653.

14 I. Fleming and J. P. Michael, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1549; J. P. Michael, N. F. Blom and J. C. A. Boeyens, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1739; I. Fleming, S. K. Patel and C. J. Urch, *J. Chem. Soc., Perkin Trans. 1*, 1989, 115; S. R. Wilson and A. Shedrinsky, *J. Org. Chem.*, 1982, **47**, 1983; S. R. Wilson, A. Shedrinsky and M. S. Haque, *Tetrahedron*, 1983, **39**, 895; W. R. Roush and T. E. D'Ambra, *J. Am. Chem. Soc.*, 1983, **105**, 1058; M. Hannaby and S. Warren, *Tetrahedron Lett.*, 1986, **27**, 765; M. Asaoka and H. Takei, *Tetrahedron Lett.*, 1987, **28**, 6343; K. Tanino, Y. Hatanaka and I. Kuwajima, *Chem. Lett.*, 1987, 385; W. Kirmse and F. Söllenböhmer, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 1667; J. Coope, V. J. Shiner, Jr., and M. W. Ensinger, *J. Am. Chem. Soc.*, 1990, **112**, 2834; J. R. Hwu and J. M. Wetzel, *J. Org. Chem.*, 1992, **57**, 922; A. Yamazaki, I. Achiwa, K. Horikawa, M. Tsurubo and K. Achiwa, *Synlett*, 1997, 455; E. J. Corey and B. E. Roberts, *J. Am. Chem. Soc.*, 1997, **119**, 12425; I. Achiwa, A. Yamazaki and K. Achiwa, *Synlett*, 1998, 45; A. Nowak, O. Bolte and E. Schaumann, *Tetrahedron Lett.*, 1998, **39**, 529.

15 I. Fleming, N. L. Reddy, K. Takaki and A. C. Ware, *J. Chem. Soc., Chem. Commun.*, 1987, 1472.

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