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Improved Method for the Synthesis of β-Carbonyl Silyl-1,3-Dithianes by the Double Conjugate Addition of 1,3-Dithiol to Propargylic Carbonyl Compounds

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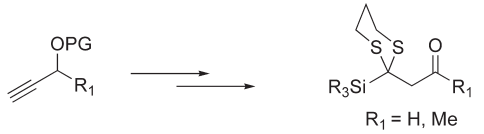
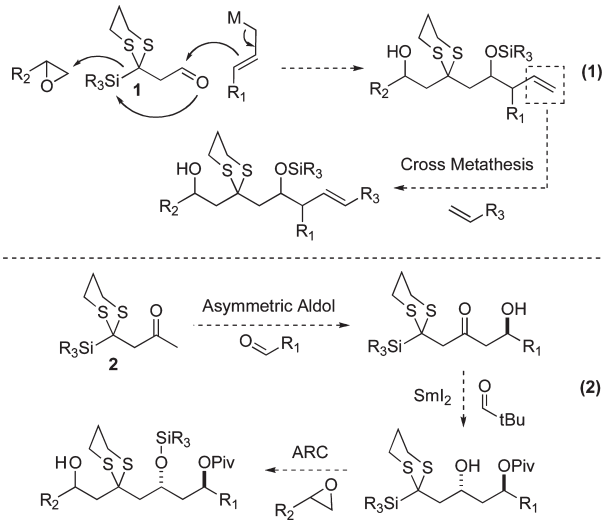


R_3Si = Me_3Si, Et_3Si, (^{t}Bu)Me_2Si, (Allyl)Me_2Si,(Vinyl)Ph_2Si, (Vinyl)Me_2Si, (Benzyl)Me_2Si, (Me)Ph_2Si

Base-mediated double conjugate addition of 1,3-propane dithiol to various silylated propargylic aldehydes and ketones allows for an efficient and scalable synthesis of β-carbonyl silyl-1,3-dithianes.

Polyketide-based natural products show a tremendous variety of biological activity and structural diversity, and thus the development of new synthetic methods for their efficient syntheses has been a highly pursued goal in organic chemistry.[1] Most general and effective methods for the construction of typical polyketide motifs include an aldol reaction between enolates and aldehydes,[2] asymmetric allylation and crotylation of aldehydes,[3] and opening of epoxides with 2-lithiodithianes.[4] In our plan to develop a modular approach for the construction of polyketides, we desired to take advantage of the capacity of olefin metathesis.[5] Thus, allylation or a crotylation product derived from bifunctional aldehyde **1** can be directly joined with another polyketide motif without any functional group manipulation. Also, it was envisioned that these processes could be further streamlined by a tandem allylation (crotylation)−epoxide opening via 1,4-Brook rearrangement, further improving the economy of polyketide synthesis (eq 1). Such a streamlined synthesis can also be envisaged for the corresponding ketones **2** via an asymmetric aldol,[6] Evans−Tishchenko reduction[7] and anion relay chemistry (ARC)[4] sequence (eq 2).



The effectiveness of this concept was amply demonstrated in our recent formal synthesis of cochleamycin A (Scheme 1),[8] where triethylsilyldithiane aldehyde **1b** was converted to the β-hydroxy dithiane by Leighton's asymmetric allylation.[9] A subsequent alkylation with bromoacetaldehyde dimethylacetal under basic conditions in the presence of HMPA afforded a product, which later takes part in a tandem enyne RCM to afford an advanced intermediate in the formal synthesis of cochleamycin A.

(1) (a) Shang, S.; Tan, D. S. *Curr. Opin. Chem. Biol.* **2005**, *9*, 248. (b) Shang, S.; Iwadare, H.; Macks, D. E.; Ambrosini, L. M.; Tan, D. S. *Org. Lett.* **2007**, *9*, 1895.

(2) (a) Yeung, K.-S.; Paterson, I. *Chem. Rev.* **2005**, *105*, 4237. (b) Schetter, B.; Mahrwald, R. *Angew. Chem., Int. Ed.* **2006**, *45*, 7506. (c) Brodmann, T.; Lorenz, M.; Schackel, R.; Simsek, S.; Kalesse, M. *Synlett* **2009**, 174.

(3) (a) Arefolov, A.; Panek, J. S. *J. Am. Chem. Soc.* **2005**, *127*, 5596. (b) Wang, X.; Meng, W.; Perl, N. R.; Xu, Y.; Leighton, J. L. *J. Am. Chem. Soc.* **2005**, *127*, 12806. (c) Hu, T.; Takenaka, N.; Panek, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 12806. (d) Zacuto, M. J.; O'Malley, S. J.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7890. (e) de Lemos, E.; Poree, F.-H.; Bourin, A.; Agouridas, E.; Lannou, M.-I.; Commercon, A.; Betzer, J.-F.; Pancrazi, A.; Ardisson, J. *Chem.—Eur. J.* **2008**, *14*, 11092. (f) Herber, C.; Breit, B. *Chem.—Eur. J.* **2006**, *12*, 6684. (g) Nicolaou, K. C.; Kim, D. W.; Baati, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 3701. (h) Bouzbouz, S.; Cossy, J. *Org. Lett.* **2003**, *5*, 3029. (i) Allais, F.; Cossy, J. *Org. Lett.* **2006**, *8*, 3655. (j) Ferrié, L.; Reymond, S.; Capdevielle, P.; Cossy, J. *Org. Lett.* **2007**, *9*, 2461.

(4) (a) Smith, A. B. III; Xian, M. *J. Am. Chem. Soc.* **2006**, *128*, 66. (b) Smith, A. B. III; Adams, C. M. *Acc. Chem. Res.* **2004**, *37*, 365. (c) Smith, A. B. III; Boldi, A. M. *J. Am. Chem. Soc.* **1997**, *119*, 6925. (d) Smith, A. B. III; Wuest, W. M. *Chem. Commun.* **2008**, *45*, 5883. (e) Smith, A. B. III; Kim, D.-S. *Org. Lett.* **2007**, *9*, 3311. (f) Smith, A. B. III; Cox, J. M.; Furuichi, N.; Kenesky, C. S.; Zheng, J.; Atasoylu, O.; Wuest, W. M. *Org. Lett.* **2008**, *10*, 5501.

(5) For reviews on alkene metathesis, see: (a) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117. (b) *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003. (c) Schrock, R. R.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4592. (d) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (e) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012. (f) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413. (g) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371. (h) Schusterand, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2037. (i) Schmalz, H. G. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1833. (j) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995**, *28*, 446.

(6) (a) Evans, D. A.; Cee, V. J.; Siska, S. J. *J. Am. Chem. Soc.* **2006**, *128*, 9433. (b) Evans, D. A.; Côté, B.; Coleman, P. J.; Connell, B. T. *J. Am. Chem. Soc.* **2003**, *125*, 10893. (c) Paterson, I.; Di Francesco, M. E.; Kuehn, T. *Org. Lett.* **2003**, *5*, 599. (d) Evans, D. A.; Coleman, P. J.; Côté, B. *J. Org. Chem.* **1997**, *62*, 788. (e) Paterson, I.; Gibson, K. R.; Oballa, R. M. *Tetrahedron Lett.* **1996**, *37*, 8585. (f) Paterson, I.; Yeung, K. S.; Ward, R. A.; Smith, J. D.; Cumming, J. G.; Lamboley, S. *Tetrahedron* **1995**, *51*, 9467. (g) Evans, D. A.; Calter, M. A. *Tetrahedron Lett.* **1993**, *34*, 6871. (h) Duplantier, A. J.; Hantz, M. H.; Roberts, J. C.; Short, R. P.; Somfai, P.; Masamune, S. *Tetrahedron Lett.* **1989**, *30*, 7357. (i) Blanchette, M. A.; Malamas, M. S.; Nantz, M. H.; Roberts, J. C.; Somfai, P.; Whritenour, D. C.; Masamune, S.; Kageyama, M.; Tamura, T. *J. Org. Chem.* **1989**, *54*, 2817.

(7) Evans, D. A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1990**, *112*, 6447.

(8) Mukherjee, S.; Lee, D. *Org. Lett.* **2009**, *11*, 2916.

(9) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920.

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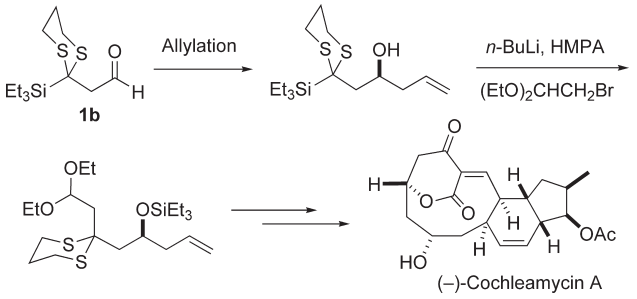
SCHEME 1



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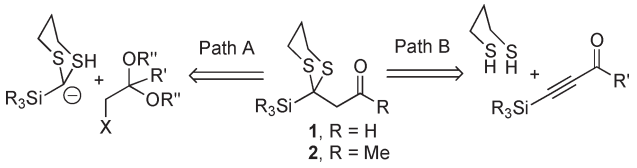
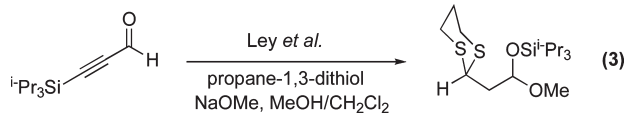
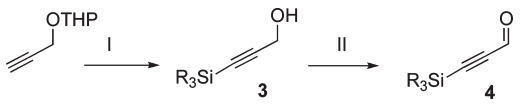


Through this streamlined sequence, various polyketide motifs are expected to be synthesized in an unusually effective manner, which, however, is contingent upon a secure supply of carbonyl compounds **1** and **2** (Scheme 2) containing γ-1,3-dithiane and trialkylsilyl moieties. Conceptually, two general approaches (Paths A and B) to these compounds are envisioned, and along these lines, several procedures[10−13] were already reported in the literature. From the standpoint of substrate scope and functional group tolerance,[11,12] the latter involving a double Michael addition of 1,3-propanedithiol to α,β-acetylenic aldehydes and ketones seems to be most attractive. However, the isolation of a silylated hemiacetal by Ley and co-workers under their base-mediated conjugate addition to silyl-substituted propargylic aldehydes (eq 3) calls for an alternative procedure for silyl-substituted acetylenic aldehydes. Herein, we report the development of a general, efficient, and scalable method for the synthesis of β-carbonyl silyl-1,3-dithianes (**1** and **2**) carrying various silyl groups.



(3)

TABLE 1. Synthesis of Silyl-Substituted Propargylic Aldehydes[a]



entry	R_3Si		yield (%)[b]	yield (%)[b]
1	Me_3Si	**a**	100	71
2[c]	Et_3Si	**b**	[d]	78
3	(^{t}Bu)Me_2Si	**c**	98	89
4	(allyl)Me_2Si	**d**	94	74
5	(vinyl)Ph_2Si	**e**	52	100
6	(vinyl)Me_2Si	**f**	55	72
7	(benzyl)Me_2Si	**g**	61	66
8	(Me)Ph_2Si	**h**	77	65
9	(^{t}Bu)Ph_2Si	**i**	72	100
10	^{i}Pr$_3$Si	**j**	74	68
11	(H)^{t}Bu$_2$Si	**k**	65	85

[a]Reagents and conditions: (I) (i) *n*-BuLi, THF, −78 °C, 1 h; (ii) R_3Si−Cl, −78 °C to rt; (iii) PPTS, MeOH; (II) IBX, DMSO. [b]Isolated yields after column chromatography. [c]Aldehyde was synthesized by formylation with DMF of the lithium acetylide generated with *n*-BuLi. [d]Not applicable.

It was expected that the aldehyde **4** and ketone **6** could be garnered via formylation[14] or acylation[15] of the corresponding silyl acetylides. However, this route gave poor yields when lithium acetylide and silyl chlorides were employed.[16] An alternative approach involves the silylation of the lithium acetylide of the commercially available THP-protected propargyl alcohol, deprotection of the THP group generating alcohols **3a**−**k** with PPTS, and their oxidation with IBX. This three-step sequence afforded aldehydes **4a**−**k** in good to excellent overall yields (Table 1).[17] Other oxidation protocols such as Swern,[18] Parikh−Doering,[19] or PCC oxidation led to much lower yields. Since triethylsilylacetylene is readily available at low price, the corresponding aldehyde **4b** (entry 2) was synthesized according to our initial plan involving formylation of the lithium acetylide.

Silyl-substituted methyl propargylic ketones **6a**−**j** were also obtained in good to excellent yields by the silylation of commercially available TMS-protected 3-butyn-2-ol,[20] followed by desilylation with 1 M HCl and MnO_2 oxidation[21] of the precursor allylic alcohols **5a**−**j** (Table 2).

With these aldehydes and ketones **4** and **6** in hand, we attempted the addition of 1,3-propane dithiol using NaOMe as the base according to Ley's conditions.[11c,12] As shown in Table 3, the desired dithiane aldehydes **1a** and **1b** with a trimethylsilyl (entry 1) and triethylsilyl group (entry 3) were obtained in 61 and 62% yields, respectively, whereas *t*-butyl dimethylsilyl-substituted aldehyde **1c** (entry 2) was generated in only moderate yield (42%). Further, this procedure is unlikely to be amenable to a large-scale synthesis due to the necessity of large amounts (0.05 M) of solvents, which is

(10) (a) Stossel, D.; Chan, T. H. *J. Org. Chem.* **1988**, *53*, 4901. (b) Taylor, E. C.; LaMattina, J. L. *Tetrahedron Lett.* **1977**, 2077. (c) Hatanaka, K.; Tanimoto, S.; Sugimoto, T.; Okano, M. *Tetrahedron Lett.* **1981**, *22*, 3243. (d) Gammill, R. B.; Sobieray, D. M.; Gold, P. M. *J. Org. Chem.* **1981**, *46*, 3555. (e) Choi, B.; Youn, I. K.; Pak, C. S. *Synthesis* **1988**, 792. (f) Woessner, W.; Ellison, R. *Tetrahedron Lett.* **1972**, 3735. (g) Taylor, E.; LaMattina, J. *J. Org. Chem.* **1978**, *43*, 1200.

(11) (a) Ranu, B. C.; Bhar, S.; Chakraborti, R. *J. Org. Chem.* **1992**, *57*, 7349. (b) Kuroda, H.; Tomiro, I.; Endo, T. *Synth. Commun.* **1996**, *26*, 1539. (c) Gaunt, M. J.; Sneddon, H. F.; Hewitt, P. R.; Orsini, P.; Hook, D. F.; Ley, S. V. *Org. Biomol. Chem.* **2003**, *1*, 15. (d) Xu, C.; Bartley, J. K.; Enache, D. I.; Knight, D. W.; Lunn, M.; Lok, M.; Hutchings, G. J. *Tetrahedron Lett.* **2008**, *49*, 2454.

(12) (a) Gaunt, M. J.; Hook, D. F.; Tanner, H. R.; Ley, S. V. *Org. Lett.* **2003**, *5*, 4815. (b) Gaunt, M. J.; Jeissman, A. S.; Orsini, P.; Tanner, H. R.; Hook, D. F.; Ley, S. V. *Org. Lett.* **2003**, *5*, 4819. (c) Sneddon, H. F.; Gaunt, M. J.; Ley, S. V. *Org. Lett.* **2003**, *5*, 1147.

(13) (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*, 434–436. (c) Collins, D. J.; James, A. M. *Aust. J. Chem.* **1989**, *42*, 223–228.

(14) Journet, M; Cai, D; DiMichele, L. M.; Larsen, R. D. *Tetrahedron Lett.* **1998**, *39*, 6427.

(15) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815–3818.

(16) Michael, M. D.; Roy, J. W.; Patrick, P. *Aust. J. Chem.* **1989**, *42*, 1907–1918.

(17) Sharma, A.; Chattopdhyay, S. *J. Org. Chem.* **1998**, *63*, 6128.

(18) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.

(19) Parikh, J. R.; Doering, W. v. E. *J. Am. Chem. Soc.* **1967**, *89*, 5505.

(20) (a) Myers, A. G.; Zheng, B. *Org. Synth.* **1998**, *76*, 178–188. (b) Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **2000**, *65*, 1601.

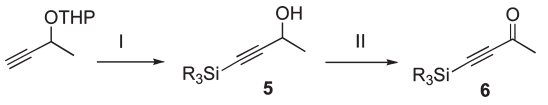
(21) Marshall, J. A.; Eidam, P.; Hillary, S. *Org. Synth.* **2007**, *84*, 120–128.

necessary to prevent the undesired intermolecular processes. Hence, we investigated the heterogeneous conditions employing MgO and basic Al_2O_3 as reported by Knight[11d] and Ranu.[1a] Reactions with MgO purchased from Aldrich were very slow even with 10 equiv at room temperature; only 40% of desired dithiane formed for the triethylsilyl aldehyde after 24 h together with unreacted starting material. On the other hand, with 10 equiv of basic alumina in CH_2Cl_2, dithiane **1b** was obtained in 70% yield after 24 h (entry 7). Optimal yield was observed with 10 equiv of basic Al_2O_3 in THF at 1 M concentration at room temperature. Under these conditions, substrate aldehydes **4b** and **4c** afforded dithianes **1b** and **1c** in 81 and 78% isolated yields, respectively (entries 9 and 10).

Next, an optimization for the formation of 1,3-dithianes via the addition of dithiol to the propargylic ketones was carried out with ketone substrates **6f** and **6g** that contain vinyl dimethylsilyl and benzyldimethylsilyl groups, respectively (Table 4). As expected, the propargylic ketones were much less reactive toward conjugate addition: even the reaction with 30 equiv of Al_2O_3 gave a 1:1 mixture of double and mono conjugate addition product for the benzyldimethylsilyl ketone **6g** after 24 h at room temperature (entry 3). It was found that, for these ketones, homogeneous bases such as NaOMe, NaOEt, and KO^{t}Bu were more efficient (entries 5−9); addition of 0.5 equiv of KO^{t}Bu in ^{t}BuOH at 0 °C, followed by warming to room temperature over 3 h, provided the best ratio of **6**:**2**:**7**.

After establishing these optimized reaction conditions, a range of aldehyde and ketone substrates was further examined (Table 5). Substrate aldehydes **4a**−**h** provided excellent yields of the corresponding products **1a**−**h** in the range of 48−93% yield (entries 1−8) under condition A (10 equiv of Al_2O_3, THF, 1.5 M). Gratifyingly, reactions on 5−6 g scale of triethylsilyl and TBS-propargyl aldehydes (**4b** and **4c**) showed no diminution of yields, demonstrating the utility of these conditions. However, no conversions were observed even with 15 equiv of Al_2O_3 for di-*tert*-butylsilyl- (**4k**),

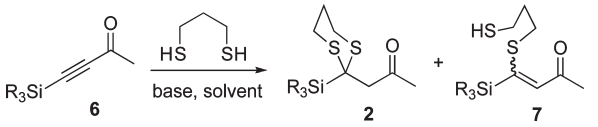
TABLE 2. Synthesis of Silyl-Substituted Propargylic Ketone\s[a]



entry	R_3Si		yield (%)[b]	yield (%)[b]
1	Me_3Si	**a**	72	71
2	Et_3Si	**b**	85	78
3	(^{t}Bu)Me_2Si	**c**	67	92
4	(allyl)Me_2Si	**d**	74	94
5	(vinyl) Ph_2Si	**e**	100	95
6	(vinyl)Me_2Si	**f**	80	65
7	(benzyl)Me_2Si	**g**	82	86
8	(Me)Ph_2Si	**h**	75	85
9	(^{t}Bu)Ph_2Si	**i**	74	83
10	(H)$^i Pr_2Si$	**j**	78	82

[a]Reagents and conditions: (I) (i) *n*-BuLi, THF, −78 °C, 1 h; (ii) R_3Si−Cl, −78 °C to rt; (iii) HCl (1 M); (II) MnO_2, CH_2Cl_2. [b]Isolated yields after column chromatography.

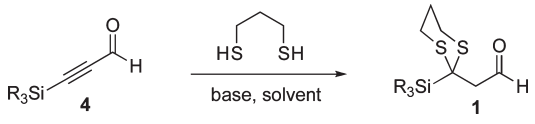
TABLE 4. Optimization of Reaction Conditions for the Addition of Dithiols to Propargylic Ketones[a]



entry		base (equiv)	solvent	time (h)	temp (°C)	**6**:**2**:**7**[b]
1	**6f**	Al_2O_3 (10)	THF	24	rt	0:3:1
2	**6f**	Al_2O_3 (20)	THF	24	rt	0:5:1[c]
3	**6g**	Al_2O_3 (20)	THF	24	rt	0:1:1
4	**6g**	Al_2O_3 (30)	THF	24	rt	0:1:1
5	**6g**	NaOMe (1.5)	THF	3	−10 to rt	0:0:1[d]
6	**6g**	NaOEt (1.5)	THF	3	−10 to rt	4:0:1[d]
7	**6g**	KO^{t}Bu (1.0)	THF	3	−10 to rt	0:1.5:1
8	**6g**	KO^{t}Bu (0.5)	^{t}BuOH	3	0 to rt	0:8:1
9	**6f**	KO^{t}Bu (0.5)	^{t}BuOH	3	0 to rt	0:1:0

[a]All reactions were carried out at a concentration of 0.5 M. SM indicates unreacted starting material. [b]Ratios were determined from ^{1}H NMR spectroscopy of the crude. [c]Obtained significant amounts of unidentified products. [d]Longer reaction times led to a complex mixture as observed on TLC.

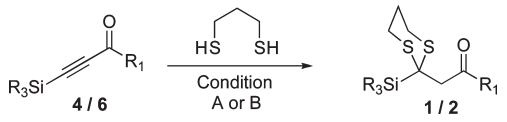
TABLE 3. Optimization of Reaction Conditions for the Addition of Dithiols to Propargylic Aldehydes



entry		base (equiv)	solvent	time (h)	temp (°C)	conc (M)	yield[a] (%)
1	**4a**	NaOMe (1.5)	DCM/MeOH[b]	1	−10	0.05	61
2	**4c**	NaOMe (1.5)	DCM/MeOH	2.5	−10	0.05	42[c]
3	**4b**	NaOMe (1.5)	DCM/MeOH	2	−10	0.05	62
4	**4b**	MgO (4)	THF	10	rt	0.5	20[c]
5	**4b**	MgO (10)	THF	24	rt	0.5	40[c]
6	**4b**	Al_2O_3 (5)[d]	DCM	24	rt	0.5	50[c]
7	**4b**	Al_2O_3 (10)	DCM	24	rt	0.5	70[c]
8	**4b**	Al_2O_3 (10)	THF	10	rt	0.5	80
9	**4b**	Al_2O_3 (10)	THF	3	rt	1	81
10	**4c**	Al_2O_3 (10)	THF	5	rt	1	78
11	**4c**	Al_2O_3 (10)	THF	10	rt	0.5	78

[a]Isolated yields after column chromatography. [b]DCM/MeOH = 4:1. [c]As determined from ^{1}H NMR spectroscopy of the crude. The rest of the mixture was unconverted starting material. [d]Basic alumina.

TABLE 5. Dithiol Additions to Propargylic Aldehydes and Ketones



entry	substrates	R_3Si	R_1	condition[a]	products	yield (%)[b]
1	**4a**	Me_3Si	H	A[c]	**1a**	89
2	**4b**	Et_3Si	H	A	**1b**	81
3	**4c**	(^{t}Bu)Me_2Si	H	A	**1c**	78
4	**4d**	(allyl)Me_2Si	H	A	**1d**	82
5	**4e**	(vinyl)Ph_2Si	H	A	**1e**	48
6	**4f**	(vinyl)Me_2Si	H	A	**1f**	80
7	**4g**	(benzyl)Me_2Si	H	A	**1g**	88
8	**4h**	(Me)Ph_2Si	H	A	**1h**	93
9	**6a**	Me_3Si	Me	B	**2a**	35
10	**6b**	Et_3Si	Me	B	**2b**	64
11	**6c**	(^{t}Bu)Me_2Si	Me	B	**2c**	100
12	**6d**	(allyl)Me_2Si	Me	B	**2d**	100
13	**6e**	(vinyl)Ph_2Si	Me	B	**2e**	100
14	**6f**	(vinyl)Me_2Si	Me	B	**2f**	98
15	**6g**	(benzyl)Me_2Si	Me	B	**2g**	92
16	**6h**	(Me)Ph_2Si	Me	B	**2h**	98
17	**4i**	(^{t}Bu)Ph_2Si	H	A[f]		NR[e]
18	**4j**	$^i Pr_3Si$	H	A[f]		NR[e]
19	**4k**	(H)$^t Bu_2Si$	H	A[d]		NR[e]
20	**6i**	(^{t}Bu)Ph_2Si	Me	B[h]		trace
21	**6j**	(H)$^i Pr_2Si$	Me	B		decomp[g]

[a]Condition: (A) 10 equiv of Al_2O_3, THF (1.5 M); (B) 0.5 equiv of KO^{t}Bu, ^{t}BuOH (0.5 M). [b]Isolated yields after column chromatography. [c]5 equiv of Al_2O_3 was optimum. [d]Reaction was forced with 15 equiv of Al_2O_3. [e]No reaction. [f]Reaction was forced with 30 equiv of Al_2O_3. [g]Decomposed. [h]Reaction was forced with 1.5 equiv of KO^{t}Bu.

tert-butyl diphenylsilyl- (**4i**), and triisopropyl (**4j**)-substituted aldehydes (entries 17−19).

Under condition B, ketones **6a**−**h** afforded the corresponding 1,3-dithiane products **2a**−**h** in good to excellent yields (entries 9−16), except for trimethylsilyl-containing substrate **6a** (entry 9). The poor yield (35%) for **2a** is probably due to the instability of the trimethylsilyl group toward the alkoxide. Similar to the cases with the aldehydes, substrates **6i** and **6j** with sterically bulky silyl substituents showed either decomposition or no reaction (entries 20 and 21).

In conclusion, base-mediated conjugate addition of 1,3-dithiols to silyl propargylic aldehydes and ketones allows for a versatile, efficient, and scalable approach toward the assembly of β-carbonyl silyl-1,3-dithianes.

Experimental Section

General Procedure for Dithiane Aldehydes 1a−h. To a well-stirred solution of propargylic aldehydes (1 equiv) and 1,3-propanedithiol (1 equiv) in THF (1.5 M with respect to aldehyde) was added activated basic alumina (5−10 equiv, standard grade, ~150 mesh, 58 Å) in 10 portions, such that the temperature did not go above room temperature. After completion of the reaction (3−6 h, TLC), the reaction mixture was filtered through a short plug of Celite, followed by washing of the residue with DCM (2 × 50 mL). The filtrate and the washings were evaporated to give the crude product, which was purified by column chromatography (0−5% ethyl acetate in hexanes) to yield the aldehydes **1a**−**h** as a light yellow oil.

General Procedure for Dithiane Ketones 6a−h. To a well-stirred solution of propargylic ketones (1.0 equiv) and 1,3-propanedithiol (1.0 equiv) in ^{t}BuOH (0.5 M with respect to ketone) was added KO^{t}Bu (0.5 equiv) at 0 °C, and the reaction was maintained at that temperature for 1−2 h, following which it was warmed to room temperature and kept there until the reaction was complete (TLC). The reaction was diluted with H_2O and extracted with ether. The combined ether layers were washed with water and brine, dried over $MgSO_4$, filtered, concentrated, and subjected to column chromatography (0−5% ethyl acetate in hexanes) to obtain the ketones **6a**−**h**.

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Supporting Information Available: General procedures and characterization data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.