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REGIO- AND STEREO-SELECTIVE ALKYLATION OF 3-TRIMETHYLSILYLMETHYL DIENOLATES. A NOVEL SYNTHESIS OF 3-ALKYLATED 2-METHALLYLSILANES

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Summary: Lithium and copper 3-trimethylsilylmethyl dienolate anions derived from easily available 3-trimethylsilylmethyl-3-butenoic acid and its methyl ester underwent regio- and stereo-selective alkylation. α-Alkylated products were readily transformed to 3-alkylated 2-methallylsilanes by pyrolysis.

We have recently reported a regioselective olefin synthesis using 3-trimethylsilylmethyl(TMSM)-3-butenoic acid 1 and its ester 2 as versatile isoprenoid acid synthons.[1] For synthetic applications of 1 and 2, we have been interested in regio- and stereo-selective alkylation of the 3-TMSM dienolate anions, in which paticular attention has been focused on the stereochemical behavior. We report here novel preparation of 3-alkylated 2-methallylsilanes by pyrolysis of α-alkylated product of 1.

In general, lithium dienolate dianions and monoanions derived from α,β-unsaturated carboxylic acids and their esters, respectively, can be alkylated selectively at the α-positions.[2] Copper(I) dienolate dianions from α,β-unsaturated acids, however, underwent the exclusive γ-alkylation,[3] whereas copper dienolate dianions from their esters showed lower γ-selectivities[4]. In alkylation of dienolate anions, derived from α,β-unsaturated acids and their esters, Kazenellenbogen and Crumrine elabrated regio- and stereo-selectivity for the synthesis of isoprenoid olefins.[3,4]

The regioselectivity in alkylation of lithium or copper dienolate derivatives(5,6,7, and 8) with various alkyl halides is summarized in Table I. Lithium dienolate dianion 5, formed by treatment of 3-TMSM-3-butenoic acid with 2 equiv. of lithium diisopropylamide in THF at - 10 °C, underwent alkylation with methyl iodide, ethyl iodide, n-butyl iodide, benzyl bromide, allyl bromide, and prenyl bromide selectively at the α-position(Entry 1-5). Addition of hexamethylphosphoramide(HMPA) or N,N,N',N'-tetramethylethylenediamine(TMEDA) to the reaction of 5 with methyl iodide did not increase the selectivity of α-alkylation(Entry 6 and 7). Ester-derived lithium dienolate anion 7, also, afforded α-alkylation products in good to excellent yields (Entry 11-15). On the other hand, copper dienolate dianion 6 generated by

addition of 2 equiv. of cuprous iodide to lithium dienolate 5 at - 10 °C gave predominating γ-alkylation(Entry 8-10). But ester-derived copper dienolate 8 decreased γ-selectivity(Entry 16 and 17). In accord with Kazenellenbogen's results[3], are this preference for highly selective γ-alkylation with copper dienolate dianion 6 and the decrease of γ-alkylation with copper dienolate anion 8.

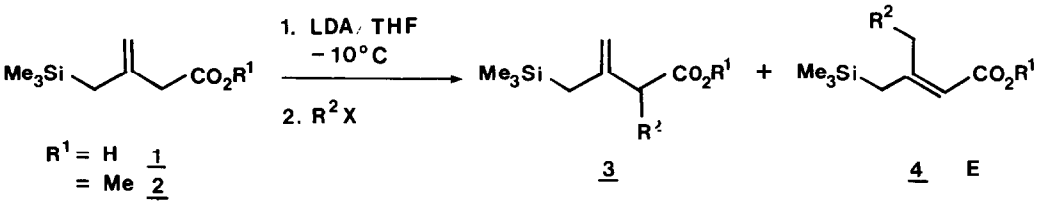
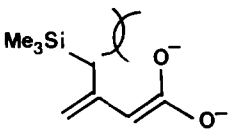


Table I Alkylation of 1 and 2 with alkyl halides.[a]

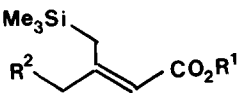
Entry	R^1	R^2X	Additive	3:4(α:γ)[b]	Yield(%)[c]
1	H	MeI	-	83:17	97
2	H	EtI	-	71:29	94
3	H	n-BuI	-	71:29	78
4	H	$PhCH_2Br$	-	62:38	62
5	H		-	68:32	74
6	H	MeI	HMPA	79:21	71
7	H	MeI	TMEDA	77:23	76
8	H	MeI	CuI	14:86	92
9	H		CuI	19:87	93
10	H		CuI	10:90	83
11	Me	MeI	-	87:13	93
12	Me	EtI	-	70:30	94
13	Me	n-BuI	-	66:34	98
14	Me	$PhCH_2Br$	-	89:11	86
15	Me		-	78:22	97
16	Me	MeI	CuI	84:16	99
17	Me		CuI	50:50	99

a. LDA(2.1 equiv. of 1 and 1.1 equiv. of 2), R^2X(1.5 equiv. of 1 and 2), -10°C, 1 hr., CuI(1 equiv. of LDA). b. Determined by ^1H-NMR. c. Isolated.

It is important that γ-alkylated products(Entry 1-17) proved to be single products which have E-configuration, 4 exclusively, not to have Z-configuration as 10.[5] This was reasonably interpreted by the expected stability of s-cis and s-trans dienolates(5 and 9). Larger trimethylsilyl group does not permit intermediate s-trans dienolate 9 by steric hindrance, but predominates s-cis dienolate 5 giving E-products.[3,6]

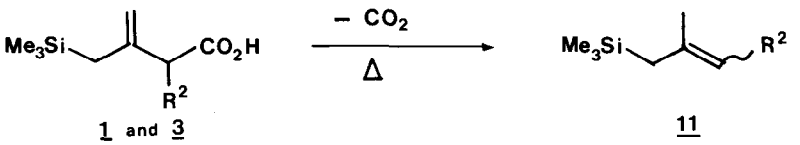


9 s-trans

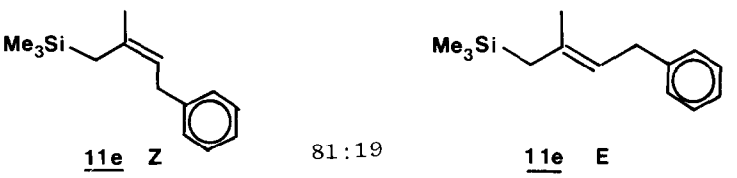


10 7

Hosomi et al have reported many C-C bond formation reactions by means of various allylsilanes,[7] which have generally been prepared with appropriate allyl Grignard reagents[8]. The α-alkylated product 3(R^1= H) was found to be an extremely versatile precursor to 2-methallylsilanes. Pyrolysis of α-alkylated products 3(R^1= H)[9] and 1 gave 3-alkylated 2-methallylsilanes 11 in high yields(64-92 %) as summarized in Table II. Stereochemistry of 11 (Entry 2-6) was determined by ^{1}H-NMR spectra.[10] Z-Configuration products were selectively afforded via a simple intramolecular decarboxylation process.



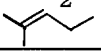
1 and 3 11



11e Z 81:19 11e E

Thus, we have found the regio- and stereo-selective alkylation of easily available 3-TMSM-3-butenoic acid as a potential synthon for construction of isoprenoid or various organic synthesis. Moreover, pyrolysis of α-alkylated products of 1 and 1(β,γ-unsaturated acids) can open a regio- and stereo-selective route for synthesis of new 3-alkylated 2-methallylsilanes.

Table II Pyrolysis of 1 and 3.[a]

Entry	R^2	Temp.(°C)/mmHg	Time(hr)	11 Yield(%)[b]	Z:E[c]
1	H	130-140/760	1	92	-
2	Me	130-150/760	1	92	81:19
3	Et	130-150/760	1	91	83:17
4	n-Bu	140-150/100	1	64	79:21
5	$PhCH_2$	140-145	5	73	81:19
6		140-145	5	68	81:19

a. (Entry 1-4) Neat of 1 or 3 was directly heated to the temperature indicated above and subsequently the product was distilated under described pressure.
(Entry 5 and 6) Heated in xylene. The product was isolated by silica gel column chromatography.
b. Isolated. c. Determined by ^{1}H-NMR spectra.

References and Notes.

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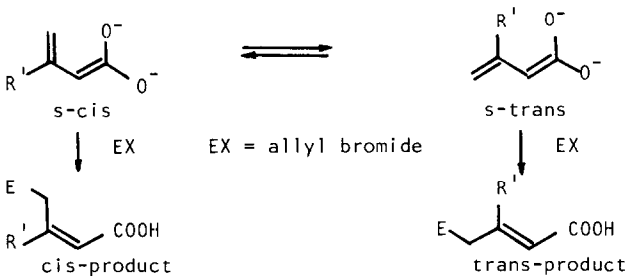
5. ^{1}H-NMR($CDCl_3$, δ ppm) 4(R^1= H, R^2= Me) 1.75(s, 2H, $SiCH_2$), 5.41(bs, 1H, =CH); 4(H, Et) 1.78, 5.45; 4(H, n-Bu) 1.77, 5.43; 4(H, $PhCH_2$) 1.74, 5.48; 4(H, allyl) 1.75, 5.43; 4(H, prenyl) 1.76, 5.42; 4(Me, Me) 1.75, 5.43; 4(Me, Et) 1.76, 5.45; 4(Me, n-Bu) 1.75, 5.46; 4(Me, $PhCH_2$) 1.72, 5.46; 4(Me, allyl) 1.73, 5.46.
6. In Kazenellenbogen's result in γ-alkylation of dienolate with allyl bromide(EX) as the size of substituent R' is increased from H to Me to Pro, the percent of cis-product increases from 0 to 50 to 80%.[3] Larger substituent R' prefers s-cis dienolate to give cis-product rather than s-trans dienolate forming trans-product.



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9. α-Alkylated products were readily purified by $AgNO_3$-silica gel column chromatography as later eluted fraction(ether-benzene).
10. 11e; ^{1}H-NMR($CDCl_3$, δ ppm) (Z), 0.05(s, 9H, Me_3Si), 1.57(s, 2H, $SiCH_2$), 1.73(s,3H, CH_3C=), 3.37(d, 2H, $=CCH_2Ph$), 5.15(t, 1H, =CH), 7.17(s, 5H,Ph), (E), 0.07, 1.65, 1.73, 3.30, 5.20, 7.17.

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