PALLADIUM-CATALYZED 1,4-DISILYLATION OF α, β-UNSATURATED KETONES WITH 1,1-DICHLORO-1-PHENYL-2,2,2-TRIMETHYLDISILANE

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Summary: 1,4-Disilylation of α , β -unsaturated ketones proceeded with 1,1-dichloro-1-phenyl-2,2,2-trimethyldisilane in the presence of a phosphine-palladium catalyst in benzene. Treatment of the disilylation products with an excess of methyllithium generated β -silyl lithium enolates, of which hydrolysis and alkylation gave β -(phenyldimethylsilyl) ketones and anti β silyl α -alkyl ketones, respectively.

Fleming and coworkers have reported¹ that conjugate addition of a silyl group to α,β unsaturated carbonyl compounds is effected by use of a silyl cuprate reagent and the resulting β -silyl carbonyl compounds are useful synthetic intermediates convertible, for example, into β -hydroxy ketones. Here we wish to describe a new conjugate silylation of α,β -unsaturated ketones which has been achieved by palladium-catalyzed 1,4-disilylation² with an unsymmetrically substituted disilane.

We examined a variety of disilanes and catalysts for the silylation of (\underline{E}) -4-phenyl-3buten-2-one (la), and found that tetrakis(triphenylphosphine)palladium(0) effectively catalyzes the addition of 1,1-dichloro-1-phenyl-2,2,2-trimethyldisilane (Cl₂PhSiSiMe₃)³ in refluxing benzene, with phenyldichlorosilyl group and trimethylsilyl group attacking at β -carbon and



carbonyl oxygen, respectively. Treatment of the disilylation product 2a with an excess of methyllithium in ether, which should generate β -(phenyldimethylsilyl) lithium enolate **3a**, followed by hydrolysis with dil. hydrochloric acid gave 4-phenyl-4-(phenyldimethylsilyl)butan-2-one (4a) in 78% yield (Scheme 1) (entry 1 in Table 1). The disilylation with Cl₂PhSiSiMe₃ proceeded at lower temperature, though it requires longer reaction time to obtain reasonable yield (entry 2). Other palladium complexes that contain tertiary phosphines as ligands were also effective giving the disilylation product in good yields (entries 3-5), but the disilylation did not occur with palladium complexes lacking phosphine ligands (entries 6 and 7), or with other transition metal complexes such as NiCl₂L₂, PtCl₂L₂, RhClL₂, and RuCl₂L₃ (L = PPh₃). Disilane Cl₃SiSiMe₃ could be also used for the disilylation of la, which gave 39% yield (at 25 °C for 20 h) of 4-phenyl-4-(trimethylsilyl)butan-2-one after the methylation and acidic hydrolysis. The disilylation was not observed with other disilanes (MeO)₃SiSiMe₃, X_2 MeSiSiMe₃ (X = C1, F), or symmetrically substituted disilanes such as XMe₂SiSiMe₂X (X = F, Cl, Ph). The disilylation product 2a formed in the reaction of la with Cl₂PhSiSiMe₃ can be also isolated as 4-phenyl-4-(phenyldiethoxysilyl)butan-2-one (5a) by treatment of the reaction mixture with ethanol and triethylamine (entry 8).

 α,β -Unsaturated ketones 1b-1d, which have analogous structure to 1a, underwent the 1,4disilylation with Cl₂PhSiSiMe₃ in the presence of Pd(PPh₃)₄ to give β -(phenyldimethylsilyl) ketones 4b-4d or β -(phenyldiethoxysilyl) ketones 5b-5d in high yields (entries 10, 11, 14, 15, 17, and 18). Disilylation was also observed with cyclohexenone (1e), though in lower yield due to side reactions (entry 19). Disilylation did not take place with β,β -disubstituted enones such as 4-phenyl-3-penten-2-one while α,β -disubstituted enone 1f underwent the disilylation in a high yield (entry 20).

The β -(phenyldimethylsilyl) ketones 4 were readily converted into β -hydroxy ketones by fluorodephenylation (HBF₄·Et₂O/CH₂Cl₂)⁴ on the silyl group followed by oxidation of the silicon-carbon bond (H₂O₂/KF/KHCO₃/MeOH/THF) according to the procedure reported by Tamao.⁵ Phenyldiethoxysilyl group on 5 could be directly substituted with hydroxy group by the oxidation with H₂O₂.⁵

Methylation of β -silyl lithium enolate **3a**, generated by treatment of the disilylation product **2**a with methyllithium in ether, with methyl iodide in THF introduced methyl group anti selectively (>20/1)⁶ at α -position to give 58% yield of 4-phenyl-4-(phenyldimethylsilyl)-3methylbutan-2-one **6a** (entry 9). Anti selective alkylation was also observed in the reaction of lithium enolates **3b** and **3c** with methyl iodide or benzyl bromide in THF (entries 12, 13, and 16). The oxidation of carbon-silicon bond in anti β -silyl ketones **6** proceeded with retention of configuration to give anti β -hydroxy ketones.

The l,4-disilylation is considered to take place via (phenyldichlorosilyl)(trimethylsilyl)palladium(II) which is formed by oxidative addition of the disilane to a palladium(0). Coordination of the enone 1 to the disilylpalladium followed by selective migration of phenyldichlorosilyl group and trimethylsilyl group to β -position and carbonyl oxygen of the enone, respectively, will form the 1.4-disilylation product. The detailed mechanism of transfer of the two silyl groups from palladium to enone remains to be clarified. Trimethylsilyl enol ether 7 obtained by treatment of lithium enolate 3a with trimethylchlorosilane and triethylamine in THF was found to consist of \underline{Z} and \underline{E} isomers in a ratio of 10 to 1,⁷ indicating that the enone coordinates to palladium mainly in a cisoid conformation.

entry	α,β-unsaturated ketone (1)	catalyst	reaction time (h)	isolation ^b	product ^c	yield (%) <u>d</u>
1	$R^1 = Ph, R^2 = Me (1a)$	Pd(PPh ₃) ₄	5	1) MeLi. 2) H ₃ 0 ⁺	4a	78
2 	la	Pd(PPh ₃) ₄	20	1) MeLi. 2) H ₃ 0 ⁺	4a	60
3	la	PdC1 ₂ (PPh ₃) ₂	29	1) MeLi. 2) H ₃ 0 ⁺	4a	35
4	la	PdC1(C ₃ H ₅) ^{<u>f</u>/dppf}	g 1.5	1) MeLi. 2) H ₃ 0 ⁺	4a	45
5	1a	PdC1(C ₃ H ₅) ^f /dppb	<u>h</u> 4	1) MeLi. 2) H ₃ 0 ⁺	4a	66
6	la	PdC1(C3H5) <u>f</u>	6	1) MeLi. 2) H ₃ 0 ⁺	4a	0
7	la	Pd(OAc) ₂	6	1) MeLi. 2) H ₃ 0 ⁺	4a	0
8	la	Pd(PPh ₃) ₄	5	EtOH/Et ₃ N	5a	65
9	la	Pd(PPh ₃) ₄	5	l) MeLi. 2) MeI	6a <u>i</u>	58
10	$R^1 = Me, R^2 = Ph$ (1b)	Pd(PPh ₃) ₄	1.5	1) MeLi. 2) H ₃ 0 ⁺	4b	68
11	1b	Pd(PPh ₃) ₄	1.5	EtOH/Et ₃ N	5b	78
12	1b	Pd(PPh ₃) ₄	1.5	1) MeLi. 2) MeI	6b <u>i</u>	42
13	1b	Pd(PPh ₃) ₄	1.5	1) MeLi. 2) PhCH ₂ B	r 6b' i	55
14	$R^1 = R^2 = Ph (1c)$	Pd(PPh ₃) ₄	2	1) MeLi. 2) H ₃ 0 ⁺	4c	80
15	lc	Pd(PPh ₃) ₄	2	EtOH/Et ₃ N	5c	78
16	lc	Pd(PPh ₃) ₄	2	1) MeLi. 2) MeI	6c <u>i</u>	49
17	$\mathbb{R}^1 = \mathbb{R}^2 = \operatorname{Me} (\mathbf{1d})$	Pd(PPh ₃) ₄	4	1) MeLi. 2) H ₃ 0 ⁺	4d	64
18	1d	Pd(PPh ₃) ₄	4	EtOH/Et ₃ N	5d	64
19	— 0 (1e)	Pd(PPh ₃) ₄	4	1) MeLi. 2) H ₃ O ⁺	4e	43
20	(\underline{E}) -PhCH=CMeCOMe (1f)	Pd(PPh ₃) ₄	2	1) MeLi. 2) H ₃ 0 ⁺	6a.İ	70

Table 1. Palladium-Catalyzed 1,4-Disilylation of α,β -Unsaturated Ketones with 1-Pheny1-1,1-dichloro-2,2,2-trimethyldisilane.²

^a To a mixture of a palladium catalyst (0.01 mmol) and 0.55 g (2.2 mmol) of $Cl_2PhSiSiMe_3$ in 2.0 mL of benzene was added 2.0 mmol of enone 1, and the mixture was heated to reflux for a given period. ^b The 1,4-disilylation products were isolated as 4, 5, or 6 after one of the following procedures. 4: Ether (2.0 mL) was added, the mixture was cooled to -70 °C, and 6.2 mL (12 mmol) of 1.9 M methyllithium in ether was added. The mixture was stirred at -70 °C for 10 min and then quenched with dil. hydrochloric acid. Workup in a usual manner followed by preparative TLC on silica gel gave 5. 6: To the lithium enolate generated in the same procedure as above, was added at -70 °C 10 mL of THF and 10 mmol of an alkyl halide. The mixture was slowly warmed up to room temperature and quenched with dil. hydrochloric acid. 5: At 0 °C, 20 mL of ether, 0.76 mL (12 mmol) of ethanol, and 1.86 mL (12 mmol) of triethylamine were added successively, and the reaction mixture was stirred at room temperature for 1 h. Ammonium salts were filtered off, and bubb-to-bub distillation of the filtrate gave 5. $c \ 1 \ H \ NMR$ spectra of the products are shown in footnote 8. $d \ Isolated yield$. $e \ Reaction at 40 °C$. $f \ Di-\mu-chlorobis(\pi-allyl)dipalladium. <math>f \ 1,1'-Bis(diphenylphosphino)ferrocene$. $h \ 1,4-Bis(diphenylphosphino)butane$. $i \ Anti/syn = >20/1$. $i \ Anti/syn = 4/6$.

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- 7 ¹H NMR (δ CDC1₃/TMS) for 7. (<u>Z</u>)-7: 1.82 (d, <u>J</u> = 1.0 Hz, 3H), 3.47 (d, <u>J</u> = 10.9 Hz, 1H), 4.79 (dq, <u>J</u> = 10.9 and 1.0 Hz, 1H). (<u>E</u>)-7: 1.61 (d, <u>J</u> = 1.0 Hz, 3H), 3.06 (d, <u>J</u> = 11.1 Hz, 1H), 5.07 (dq, <u>J</u> = 11.1 and 1.0 Hz, 1H).
- 8 ¹H NMR (δ CC1_λ/TMS) for silyl ketones. **4a**: 0.20 (s, 6H), 1.83 (s, 3H), 2.3-3.0 (m, 3H), 6.7-7.4 (m, 10H). 4b: 0.33 (s, 6H), 0.98 (d, J = 8 Hz, 3H), 1.4-1.8 (m, 1H), 2.56 (dd, J= 16 and 10 Hz, 1H), 2.90 (dd, <u>J</u> = 16 and 4 Hz, 1H), 7.1-7.5, 7.6-7.8 (m, 5H). 4c: 0.22, 0.24 (a pair of s, 6H), 2.9-3.5 (m, 3H), 6.8-7.5, 7.6-7.8 (m, 15H). 4d: 0.29 (s, 6H), 0.91 (d, J = 7 Hz, 3H), 1.3-1.6 (m, 1H), 1.96 (s, 3H), 2.06 (dd, J = 17 and 9 Hz, 1H), 2.35 (dd, J = 17 and 5 Hz, 1H), 7.1-7.5 (m, 5H). 4e: 0.32 (s, 6H), 1.1-2.3 (m, 9H), 7.1-7.5 (m, 5H). 5a: 1.17 (t, <u>J</u> = 7 Hz, 6H), 1.90 (s, 3H), 2.7-3.1 (m, 3H), 3.69, 3.75 (a pair of q, J = 7 Hz, 4H), 6.9-7.5 (m, 10H). 5b: 0.99 (d, J = 7 Hz, 3H), 1.25 (t, J = 7 Hz, 6H), 1.6-2.0 (m, 1H), 2.62 (dd, J = 17 and 9 Hz, 1H), 3.12 (dd, J = 17 and 3 Hz, 1H), 3.85 (q, J = 7 Hz, 4H), 7.2-7.9 (m, 10H). 5c: 1.16, 1.18 (a pair of t, J = 7 Hz, 6H), 3.1-3.5 (m, 3H), 3.75, 3.80 (a pair of q, \underline{J} = 7 Hz, 4H), 6.9-7.6, 7.7-7.9 (m, 15H). 5d: 0.90 (d, J = 8 Hz, 3H), 1.24 (t, J = 7 Hz, 6H), 1.6-1.9 (m, 1H), 2.00 (s, 3H), 2.11 (dd, J= 16 and 10 Hz, 1H), 2.51 (dd, J = 16 and 4 Hz, 1H), 3.79 (q, J = 7 Hz, 4H), 7.1-7.6 (m, 5H). **6a**: 0.07, 0.22 (a pair of s, 6H), 0.86 (d, \underline{J} = 7 Hz, 3H), 1.75 (s, 3H), 2.54 (d, \underline{J} = 11 Hz, 1H), 2.91 (dq, J = 11 and 7 Hz, 1H), 6.7-7.4 (m, 10H). 6b: 0.32, 0.37 (a pair of s, 6H), 0.88 (d, J = 7 Hz, 3H), 1.03 (d, J = 7 Hz, 3H), 1.1-1.5 (m, 1H), 3.2-3.6 (m, 1H), 7.1-7.7 (m, 10H). 6b': 0.39, 0.50 (a pair of s, 6H), 1.01 (d, J = 7 Hz, 3H), 1.0-1.3 (m, 1H), 2.47 (dd, J = 13 and 2 Hz, 1H), 3.22 (dd, J = 13 and 11 Hz, 1H), 3.67 (dt, J = 11 and 2 Hz, 1H), 6.8-7.6 (m, 15H). 6c: 0.04, 0.21 (a pair of s, 6H), 0.97 (d, J = 7 Hz, 3H), 2.91 (d, J = 10 Hz, 1H), 3.86 (dq, J = 10 and 7 Hz, 1H), 6.8-7.5, 7.6-7.9 (m, 15H).

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