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(E)- γ -Substituted Allylic Alcohols and α -Substituted Homoallylic Alcohols via Acidic Treatment of the Acetonides Derived from γ -Substituted Vinyl Diols

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(E)- Y-SUBSTITUTED ALLYLIC ALCOHOLS AND α-SUBSTITUTED HOMOALLYLIC ALCOHOLS VIA ACIDIC TREATMENT OF THE ACETONIDES DERIVED FROM Y-SUBSTITUTED VINYL DIOLS

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ABSTRACT: Treatment of the acetonides of γ -substituted vinyl diols under acidic deprotection conditions afforded γ -substituted allylic alcohols and α -substituted homoallylic alcohols.

Deprotection of diol acetonides to diols under acidic conditions are common transformations in organic synthesis.¹ We have observed unexpected substitutions of the acetonides 1 derived from γ -substituted vinyl diols in the deprotection conditions to afford γ -substituted allylic alcohols 3^2 and α -substituted homoallylic alcohols 4 (eq 1), which might be used as chiral synthons in organic synthesis.

The acetonides of vinyl diols, la and lb was prepared from 4-0benzyl 2,3-0-isopropylidene-L-threose³ by Wittig olefination reation with isopropylidenetriphenylphosphorane and ethylidenetriphenylphosphorane, respectively. When the acetonide la was subjected to deprotection condition with Dowex 50W x 8 resin in methanol, the (E)- γ -substituted allylic alcohol 3a (40%), the thermodynamically more stable α -substituted homoallylic alcohol 4a (54%, α : $\beta = 2:1^4$), was obtained (entry 1 in Table 1). The (E)-stereochemistry of 3a was judged by ¹H NMR (300 MHz) analysis. It is presumed that deprotection of the acetonide la followed by allylic rearrangement gave the α - or γ -substituted alcohols 3a and 4a. As an indirect evidence, treatment of 2a with Dowex 50W x 8 resin in methanol also gave a mixture of 3a

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Entry	Substrate	Reaction Conditions	Product (Yield %)*
1	la	Dowex 50 W x 8 resin, MeOH, rt, 24 h	3a (40%), 4a (54%)
2	la	70 % ageous HoAc, rt, 24 h	2a (38%), 3b (54%)
3	la	1N HCl, THF, rt, 12h	2a (70%), 3b (10%)
4	1b	Dowex 50 W x 8 resin, MeOH, rt, 12 h	2b (79%)
5	16	Dowex 50 W x 8 resin, MeOH, reflux, 12 h	3c (48%), 4c (21%)
6	la	Dowex 50 W x 8 resin, PhSH, rt, 24 h	3d (20%), 4d (36%)

Table 1. Acidic Treatment of the Acetonides la and lb

* The yields are isolated yields after separation by column chromatography.



and 4a in the same ratio. Alternatively, treatment of the acetonide 1a with 70% ageous acetic acid afforded the allylic alcohol 3b, the S_N2' type substitution product, as the major product (54%) along with the deprotected diol 2a (38%) (entry 2). On the other hand, deprotection reaction of the acetonide 1a with 1 N HCl in THF at room temperature provided the deprotected 2a as the major product (70%) and the allylic alcohol 3b as a minor product (10%) (entry 3). Deprotection was also carried out with Dowex 50W x 8 resin in methanol with the acetonide of γ -monosubstituted

vinyl diol 1b. In contrast to 1a, the reaction of 1b with Dowex 50W x 8 resin in methanol at room temperature for 12 h gave a clean product 2b (entry 4). However, treatment of 1b with Dowex 50W x 8 resin in methanol at reflux for 12 h afforded the α -substituted alcohol 3c (48%, $\alpha:\beta = 1:1$), the thermodynamically controlled product, and γ -substituted alcohol 4c (21%) (entry 5). This kind of reaction was applied to 1a with Dowex 50W x 8 resin in thiophenol. On treatment of 1a with Dowex 50 W x 8 resin in thiophenol, the γ -substituted alcohol 3d (20%) and the γ -substituted alcohol 4d (36%, $\alpha:\beta = 2:3$) was obtained (entry 6). The results are summarized in Table 1.

It is notable that treatment of 5 with Dowex $50W \times 8$ resin in methanol at room temperature for 24 h or reflux for 24 h also afforded **6** without allylic rearrangement.



EXPERIMENTAL

(2*R*,3*E*)-1-Benzyloxy-5-methoxy-5-methyl-3-hexen-2-ol (3a) and (2*R*)-1-Benzyloxy-3-methoxy-5-methyl-4-hexen-2-ol (4a). To a stirred solution of 1a (3.81 g, 1.38×10^{-2} mol) in dry methanol (25 ml) was added Dowex 50W x 8 resin (0.30 g) and then stirred at room temperature for 24 h. The reaction mixture was filtered and methanol was evaporated *in vacuo*. The crude product was separated by column chromatography using EtOAc/hexanes (1:2) as eluent to afford 3a (1.38 g, 40%) and 4a (1.86 g, 54%). 3a : TLC; SiO₂, EtOAc/hexanes 1:2, $R_r = 0.31$, $[\alpha]_D^{-25}$ -3.64° (*c* 0.55, CHCl₃). IR (neat): 3400 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.26 (s, 6 H), 3.14 (s, 3 H), 3.37 (dd, 1 H, *J* = 8.4, 8.1 Hz), 3.40 (dd, 1 H, *J* = 3.3, 2.7 Hz), 4.38 (m, 1 H), 4.59 (s, 2 H), 5.58 (dd, 1 H, *J* = 15.5, 3.0 Hz), 5.76 (dd, 1 H, *J* = 15.5, 0.9 Hz), 7.35 (s, 5 H). Anal. Calcd for C₁₅H₂₂O₃: C, 71.97 ; H, 8.86. Found: C, 71.80 ; H, 8.75. 4a : TLC; SiO₂, EtOAc/hexanes 1:2, $R_r = 0.47$. IR (neat): 3400 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.70, 1.77 (two singlets, 6 H), 3.26, 3.28 (two singlets, 3 H), 3.43 (m, 1 H), 3.54 (m, 1 H), 3.87 (m, 1 H), 3.97 (m,

1 H), 4.55 (2s, 2 H), 5.00, 5.14 (two singlets, 1 H), 7.33 (s, 5 H). Anal. Calcd for $C_{15}H_{22}O_3$; C, 71.97; H, 8.86. Found: C, 71.84 ; H, 8.98.

(2R,3E)-1-Benzyloxy-5-methyl-3-hexen-2,5-diol (3b) and (2S,3S)-1-Benzyloxy -5-methyl-4-hexen-2,3-diol (2a). To a stirred solution of la (3.24 g, 1.18 x 10⁻² mol) was added 70% ageous acetic acid (25 ml) and then stirred at room temperature for 24 h. To this reaction mixture was added saturated sodium bicarbonate solution (15 ml) and stirred for 30 min, and then extracted with ether (50 ml). The ether layer was washed with saturated sodium bicarbonate solution, brine and then dried over anhydrous magnesium sulfate. The ether layer was concentrated and in vacuo and the crude product was separated by column chromatography using EtOAc/ hexanes (1:1) as eluent to afford 1.05 g (38%) of 2a and 1.50 g (54%) of 3b. Data of 3b : TLC; SiO₂, EtOAc/hexanes 1:1, $R_f = 0.19$, $[\alpha]_n^{25}$ -8.94 ° (c 0.35, CHCl₁) IR (neat): 3350 cm⁻¹. ¹H NMR (300 MHz, CDCl₁) δ 1.32 (s, 6 H), 1.85 (bs, 1 H), 2.72 (bs, 1 H), 3.38 (dd, 1 H, J = 9.6, 8.1 Hz), 3.54 (dd, 1 H, J = 9.6, 3.3 Hz), 4.36 (m, 1 H), 4.58 (s, 2 H), 5.65 (dd, 1 H, J= 15.6, 6Hz), 5.95 (dd, 1 H, J = 15.6, 1.5 Hz), 7.32-7.38 (m, 5 H). Anal. Calcd for C14H20O3 : C, 71.16; H, 8.53. Found: C, 70.88; H, 8.67. Data of 2a : TLC; SiO₂, EtOAc/hexanes 1:1, $R_f = 0.34$. IR (neat) : 3400 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.67 (s, 3 H), 1.72 (2s, 3 H), 2.70 (bs, 2 H), 3.46 (m, 1 H), 3.62 (m, 2 H), 4.37 (m, 1 H), 4.53 (s, 2 H), 5.17 (d, 1 H), 7.33 (s, 5 H). Anal. Calcd for C₁₄H₂₀O₃: C, 71.16; H, 8.53. Found: C, 70.92; H, 8.77.

(2S,3E)-1-Benzyloxy-5-methoxy-3-hexen-2-ol (3c) and (2S,4Z)-1-Benzyloxy -3-methoxy-4-hexen-2-ol (4c). To a stirred solution of 1b (1.40 g, 5.34 x 10⁻³ mol) in dry methanol (15 ml) was added Dowex 50 W x 8 resin (0.30 g) and then stirred at reflux for 12 h. The reaction mixture was filtered and methanol was evaporated in vacuo. The crude product was separated by column chromatography using EtOAc/hexanes (1:2) as a eluent to afford 3c (0.60 g, 48%) and 4c (0.25 g, 21%). Data of 3c : TLC; SiO₂, EtOAc/ hexanes 1:2, $R_f = 0.20$. IR (neat) : 3400 cm⁻¹. ¹H NMR (300 MHz, CDCl₃) δ 1.23 (d, 3 H), 3.25, 3.27 (2s, 3 H), 3.38 (m, 1 H), 3.53 (m, 1 H), 3.73 (m, 1 H), 4.37 (m, 1 H), 4.58 (s, 2 H), 5.67 (m, 2 H), 7.35 (s, 5 H). Anal. Calcd for C₁₄H₂₀O₃; C, 71.16 ; H, 8.53. Found: C, 71.04 ; H, 8.70. Data of 4c: TLC; SiO₂, EtOAc/hexanes 1 : 2, $R_1 = 0.28$. IR (neat) : 3450 cm⁻¹. ¹H NMR (300 MHz, CDCL) δ 1.71–1.77 (six singlets 3 H), 2.35, 2.75 (two doublets, 3 H), 3.4-3.6 (m, 2 H), 3.61 (m, 1 H), 4.55, 4.56 (2s, 2H), 5.2-5.4 (m, 1 H), 5.7-5.9 (m, 1 H). Anal. Calcd for $C_{14}H_{20}O_3$; C, 71. 16; H, 8.53. Found: C, 71.21; H, 8.74.

(2R, 3E)-1-Benzyloxy-5-methyl-5-phenylthio-3-hexen-2-ol (3d) and (2S)-1-Benzyloxy-5-methyl-3-phenylthio-4-hexen-2-ol (4d). To a stirred solution of 1a $(1.40 \text{ g}, 5.08 \times 10^{-3} \text{ mol})$ in thiophenol (15 ml) was added Dowex 50W x 8 resin (0.20 g) and then stirred at room temperature for 48 h. The reaction mixture was filtered and then thiophenol was evaporated. The crude product was separated by column chromatography using EtOAc /hexanes (1:8) as eluent to afford 3d(0.33 g, 20%) and 4d(0.6 g, 36%). Data of 3d: TLC; SiO₂, EtOAc/hexanes 1:4, $R_f = 0.27$, $[\alpha]_p^{25} - 3.93$ °(c 0.28, CHCl₃), IR (neat): 3350 cm⁻¹. ¹ H NMR (300 MHz, CDCl₂); δ 1.37 (2s, 6 H), 2.32 (bs, 1 H), 3.19 (dd, 1 H, J = 9.6, 8.1 Hz), 3.37 (dd, 1 H), 4.55 (d, 1 H, J = 1.8 Hz), 5.06 (dd, 1 H, J = 15.9, 6.3 Hz), 5.89 (dd, 1 H, J = 15.9, 1.5 Hz), 7.26-7.43 (m, 10 H). MS(m/z) 328 (M⁺), 277, 218, 177, 129, 109, 91 (base peak). Anal. Calcd for $C_{20}H_{24}O_2S$: C, 73.13 ; H, 7.36 ; S, 9.76. Found: C, 73.02; H, 7.53; S, 9.49. Data of 4d. TLC; SiO,, EtOAc/hexanes 1:4, $R_f = 0.35$. IR (neat) : 3400 cm⁻¹. ¹H NMR (300 MHz, CDCl.) & 1.39, 1.51, 1.65, 1.71 (four singlets, 6 H), 3.53, 3.61, 3.74, 3.88, 4.09 (m, 4 H), 4.53 (2s, 2 H), 5.01, 5.23 (2s, 1 H), 7.31, 7.33, 7.45 (m, 10 H). Anal. Calcd for $C_{20}H_{24}O_2S$: C, 73.13 ; H, 7.36 ; S, 9.76. Found: C, 72.89; H, 7.58; S, 9.65.

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