Ortho Lithiation of 2-Hydroxymethyl-1,4,5,6,8-pentamethoxynaphthalene, a Supplement[1)]

Yasuhiro TANOUE* and Akira TERADA*,†
Department of Food Science and Technology, Shimonoseki University of Fisheries, Nagatahonmachi, Shimonoseki, Yamaguchi 759-65
† Department of Chemistry, Kyushu Institute of Technology, Tobata, Kitakyushu, Fukuoka 804
(Received August 9, 1990)

Synopsis. The structures of the products in our previous report "One-Pot Ortho Hydroxylations of 2-(1-Hydroxyalkyl)-naphthalenes and (1-Hydroxyalkyl)benzenes"[2)] were reexamined by ^{13}C NMR spectra and part of our previous interpretation will be corrected here. The lithiations of 2-(1-hydroxyalkyl)-1,4,5,6,8-pentamethoxynaphthalenes occurred at the 7-position, and not at the 3-position as we reported.

During our synthetic study of fusarubin (**1**)[3)] (see Scheme 1), we found an error in our previous report titled "One-Pot Ortho Hydroxylations of 2-(1-Hydroxyalkyl)-naphthalenes and (1-Hydroxyalkyl)benzenes" published in this Journal.[2)] We therefore used ^{13}C NMR spectroscopy to reexamin the hydroxylation products in further detail.

In this paper, we wish to correct part of our previous explanation.

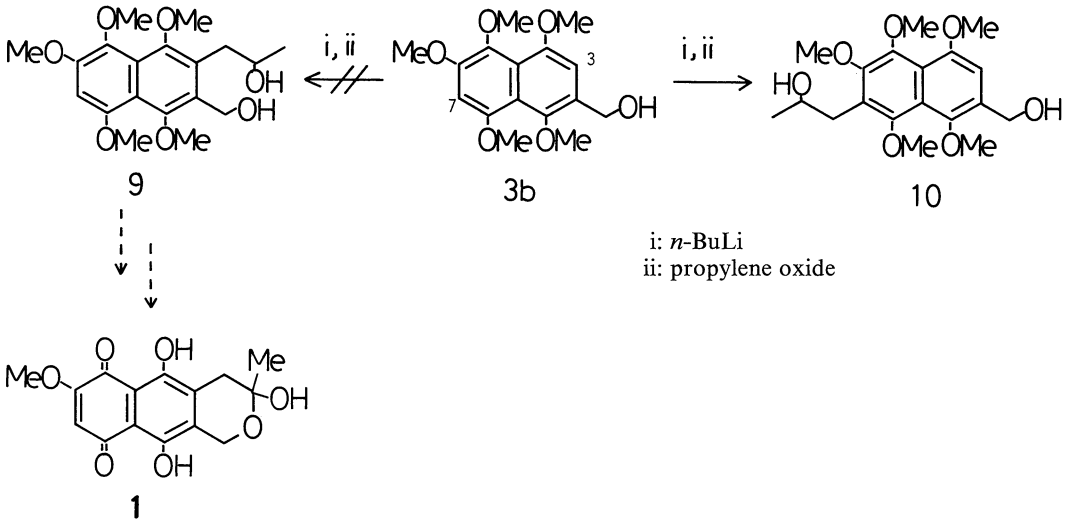
Results and Discussion

We have already reported that the lithiation of 2-hydroxymethyl-1,4,5,6,8-pentamethoxynaphthalene (**3b**) with butyllithium and subsequent oxidation by oxygen gave 3-hydroxymethyl-1,4,5,7,8-pentamethoxy-2-naphthol (**2b**).[2)] However, a question during our synthetic study of fusarubin led us to reexamine the structure of the product. The ^{13}C NMR spectrum of **3b** showed the C-2,3, and 7-signals at δ=128.30, 108.20, and 98.91, respectively. If the structure of our product was **2b**, the 6-position carbon would be slightly affected by the hydroxyl group and the C-6 signal would have been found near δ=96 (i.e., shifted upfield by 2—3 ppm relative to that (δ=98.91) of **3b**). However, the aromatic carbon signal bearing no substituent in our product was found at δ=104.38, not near δ=96. If we presume the formation of 7-hydroxymethyl-1,3,4,5,8-pentamethoxy-2-naphthol (**2B**) instead of **2b**, these ^{13}C NMR results could be reasonably interpreted. That is to say, the C-6 signal (δ=104.38) in **2B** was shifted upfield by 3.8 ppm relative to that (δ=108.20) of **3b** by the introduction of a hydroxyl group (see Chart 1).

This explanation was also supported by the following reaction result. The lithiation of **3b** with butyllithium and subsequent treatment with propylene oxide gave 2-hydroxymethyl-7-(2-hydroxypropyl)-1,4,5,6,8-pentamethoxynaphthalene (**10**) in 62% yield, and no 2-hydroxymethyl-3-(2-hydroxypropyl)-1,4,5,6,8-pentamethoxynaphthalene (**9**) (Scheme 1). The ^{13}C NMR spectrum of **10** is shown in Chart 1.

In the cases of **3d** and **3f**, the hydroxyl group was also introduced at the 7-position between two methoxyl groups. We have concluded, therefore, that the lithiation of **3b**, **3d**, and **3f** with butyllithium occurred at the 7-position.

A similar hydroxylation of 3-methoxybenzylalcohol (**6c**) gave a mixture of 2-hydroxy-3-methoxybenzylalcohol (**7c**) and 4-hydroxy-3-methoxybenzylalcohol (**8C**). The product mixture could be separated by silica gel column chromatography. The ^{13}C NMR spectra of these products are shown in Chart 1. The IR and ^{1}H NMR spectra of **7c** and **8C** agreed with those of the authentic samples obtained by reduction of *o*-vanillin and vanillin, respectively.



Scheme 1.

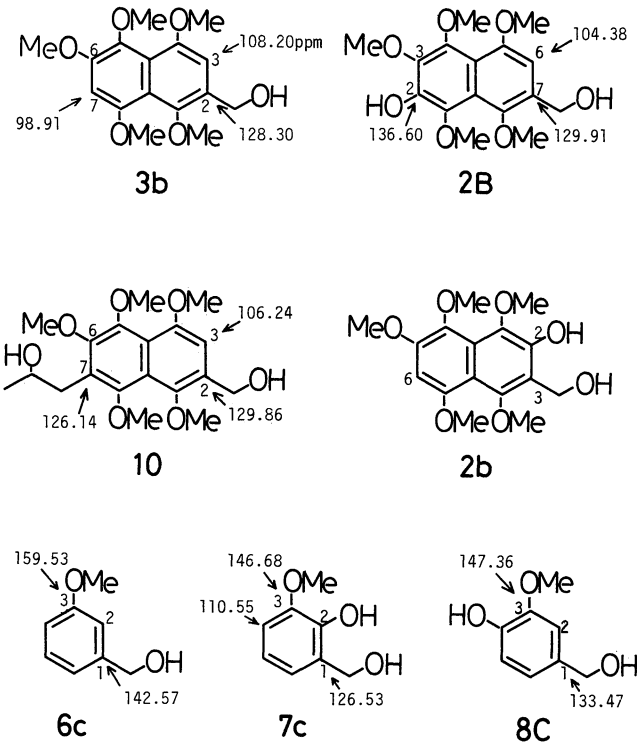
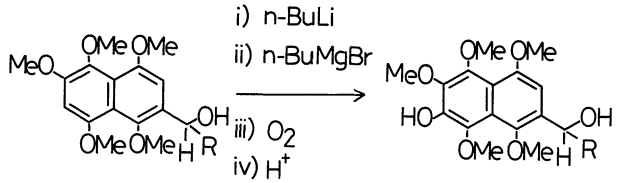
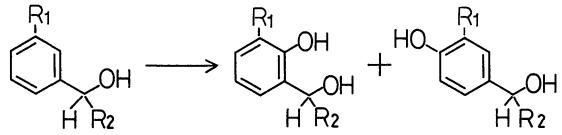


Chart 1.

Table 1. Hydroxylation of 2-(1-Hydroxyalkyl)-1,4,5,6,8-pentamethoxynaphthalene and (1-Hydroxyalkyl)-3-methoxybenzene

Substrate	Product and Yield/%
	
3b: R=H	**2B**, 59[98][a]
3d: R=C_4H_9	**2D**, 73
3f: R=$CH_2CH{=}CH_2$	**2F**, 78
	
6c: R_1=OMe, R_2=H	**7c**, 12[23]	**8C**, 21[40]
6d: R_1=OMe, R_2=C_4H_9	**7d**, 23[37]	**8D**, 35[56]
6e: R_1=R_2=H	**7e**, 26[66]	
6f: R_1=H, R_2=C_4H_9	**7f**, 19[93]	

a) Conversion yield.

Correcting Tables 1 and 3 in our previous report,[2] we present our new results in Table 1 of this text. The C-4 chemical shift of δ=128.83 in the ^{13}C NMR spectrum of 2-hydroxymethylnaphthalene (**4a**) noted in the previous report should be corrected to δ=128.98.

Experimental

Melting points were determined with a Yanagimoto micro-melting point apparatus and were uncorrected. ^1H and ^{13}C NMR spectra were taken on a JEOL JNM-60 in $CDCl_3$ solutions, using Me_4Si and $CDCl_3$ as internal standards, respectively. Mass spectra and IR spectra were obtained with a JEOL DX-300 spectrometer and a Hitachi 260-30 spectrometer, respectively. Column chromatography was carried out on silica gel (Wakogel C-200) eluting with chloroform. The procedure for the hydroxylation of **3b**, **3d**, **3f**, and **6c**—**6f** is described in Ref. 2. The spectra (IR, ^1H NMR, MS, and HRMS) of **2B**, **2D**, and **2F** were the same as those of **2b**, **2d**, and **2f** in the previous report.[2]

2B: Viscous oil; ^{13}C NMR δ=56.47 (CH_2OH), 61.02, 61.46, 62.09, 62.34, and 62.73 (OCH_3), 104.38 (C-6), 116.56 (C-4a), 121.30 (C-8a), 129.91 (C-7), 136.60 (C-2), 141.05, 142.42, 145.45, 145.65, and 152.84 (C–OCH_3).

2D: Viscous oil; ^{13}C NMR δ=14.08 (CH_3), 22.69, 28.41, and 38.23 (CH_2), 56.47, 61.41, 62.09, 62.34, and 62.97(OCH_3), 68.69 (CH), 102.23 (C-6), 116.37 (C-4a), 121.01 (C-8a), 133.52 (C-7), 136.70 (C-2), 140.95, 142.42, 144.47, 145.70, and 152.98 (C–OCH_3).

2F: Viscous oil; ^{13}C NMR δ=43.07 (CH_2), 56.42, 61.36, 62.05, 62.29, and 62.92 (OCH_3), 67.71 (CH), 104.14 (C-6), 116.37 (C-4a), 117.93 (=CH_2), 120.96 (C-8a), 132.54 (C-7), 134.94 (–CH=), 136.65 (C-2), 140.95, 142.38, 144.43, 145.65, and 152.88 (C–OCH_3).

7c: Viscous oil; IR (neat) 3350 (OH), 1615, 1590, 1480, 1270, 1230, 1080, 1035, and 1000 cm^{-1}; ^1H NMR δ=2.40 (broad, 1H, OH), 3.88 (s, 3H, OCH_3), 4.74 (s, 2H, CH_2), 6.83 (s, 4H, OH, ArH); ^{13}C NMR δ=56.08 (OCH_3), 61.65 (CH_2OH), 110.55 (C-4), 119.64 (C-6), 120.81 (C-5), 126.53 (C-1), 143.84(C-2), and 146.68 (C-3); MS *m/z* 154 (M^+), 136, 107, and 65; HRMS, Found: *m/z* 154.0612. Calcd for $C_8H_{10}O_3$: M, 154.0630.

8C: Mp 115—116 °C (hexane)(lit,[4] 115 °C); IR (KBr) 3340 (OH), 3150 (OH), 1610, 1270, 1240, 1038, 998 cm^{-1}; ^1H NMR δ=1.82 (broad, 1H, OH), 3.90 (s, 3H, OCH_3), 4.60 (s, 2H, CH_2), 5.50 (broad, 1H, OH), 6.86(s, 2H, ArH), and 6.91 (s, 1H, ArH); ^{13}C NMR δ=55.59 (OCH_3), 63.07 (CH_2OH), 111.13 (C-2), 115.09 (C-5), 119.15 (C-6), 133.47 (C-1), 145.31 (C-4), and 147.36 (C-3); MS, *m/z* 154 (M^+), 137, 93, and 65. Found: C, 62.37; H, 6.66%. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54%.

7d: Viscous oil; IR (neat) 3400 (OH), 1615, 1595, 1493, 1278, 1080, 1045, and 1010 cm^{-1}; ^1H NMR δ=0.89 (t, *J*=5.0 Hz, 3H, CH_3), 1.1—1.9 (m, 6H, CH_2), 2.20 (broad, 1H, OH), 3.88 (s, 3H, OCH_3), 4.88 (t, *J*=6.7 Hz, 1H, CH), 6.37 (broad, 1H, OH), and 6.81(s, 3H, ArH); ^{13}C NMR δ=14.03 (CH_3), 22.59, 28.06, and 36.96 (CH_2), 55.98 (OCH_3), 72.02 (CH), 109.86 (C-4), 119.15 (C-6), 119.49 (C-5), 129.86 (C-1), 143.25 (C-2), and 146.87 (C-3); MS *m/z* 210 (M^+), 192, 163, 137, 131, and 103; HRMS, Found: *m/z* 210.1227. Calcd for $C_{12}H_{18}O_3$: M, 210.1255.

8D: Mp 79—80 °C (hexane–benzene (10:1)); IR (KBr) 3380 (OH), 1613, 1440, 1270, 1245, 1057, and 1038 cm^{-1}; ^1H NMR δ=0.88 (t, *J*=5.4 Hz, 3H, CH_3), 1.1—1.9 (m, 7H, OH, CH_2), 3.89 (s, 3H, OCH_3), 4.58 (t, *J*=6.9 Hz, 1H, CH), 5.65 (s, 1H, OH), 6.83 (s, 2H, ArH), and 6.87 (s, 1H, ArH), ^{13}C NMR δ=13.98 (CH_3), 22.54, 28.02, and 38.63 (CH_2), 55.84 (OCH_3), 74.51 (CH), 108.54 (C-2), 114.16 (C-5), 118.86 (C-6), 136.90 (C-1), 144.86 (C-4), 146.62 (C-3); MS, *m/z* 210 (M^+), 153, 125, 93. Found: C, 68.61; H, 8.80%. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63%.

2-Hydroxymethyl-7-(2-hydroxypropyl)-1,4,5,6,8-pentamethoxynaphthalene (10). A solution of 2-hydroxymethyl-1,4,5,6,8-pentamethoxynaphthalene **3b**[5] (1.62 g, 5.26 mmol) in

THF (70 ml) was cooled to −10 °C and allowed to react with *n*-BuLi (16.8 ml, 26.3 mmol, 10% (w/v) in hexane) for 1.5 h. Propylene oxide (2.02 ml, 28.9 mmol) in THF (10 ml) was then added to this solution at −10 °C and stirred for 5 h. The reaction mixture was stored in a refrigerator overnight, then quenched with aqueous ammonium chloride, and extracted with chloroform. The chloroform solution was washed with brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on silica gel to give **10** (1.06 g, 62% yield) and **3b** (0.59 g, 36% yield) was recovered.

10: Viscous oil: IR (neat) 3370 (broad, OH), 1610, 1595, 1355, 1045 cm^{-1}; ^1H NMR δ=1.29 (d, J=6.2 Hz, 3H, CH_3), 2.35 (broad, 2H, 2×OH), 3.0 (m, 2H, CH_2), 3.75 (s, 6H, 2×OCH_3), 3.84, 3.98 (each s, 3H, OCH_3), 3.90 (m, 1H, CH), 4.00 (s, 3H, OCH_3), 4.85 (s, 2H, CH_2OH), and 6.85 (s, 1H, ArH); ^{13}C NMR δ=23.71 (CH_3), 33.88 (CH_2), 56.42 (CH_2OH), 60.72, 61.12, 61.56, 62.29, and 62.53 (OCH_3), 69.13 (CH), 106.24 (C-3), 121.11, 121.94, 126.14 (C-7), 129.86 (C-2), 145.26, 145.90, 149.66 (2C), and 152.55 (C–OCH_3); MS, m/z 366 (M^+), 319, and 289. HRMS, Found: m/z 366. 1690. Calcd for $C_{19}H_{26}O_7$: M, 366.1689.

References

1) Paper X, on Synthesis of Naphthoquinone Derivatives. Paper IX, Y. Tanoue, A. Terada, and Y. Matsumoto, *Bull. Chem. Soc. Jpn.*, **62**, 2736 (1989).

2) Y. Tanoue, A. Terada, I. Seto, Y. Umezu, and O. Tsuge, *Bull. Chem. Soc. Jpn.*, **61**, 1221 (1988).

3) R. H. Thomson, "Naturally Occurring Quinones," 2nd ed, Academic Press, London (1971), p. 291.

4) W. H. Carothers and R. Adams, *J. Am. Chem. Soc.*, **46**, 1080 (1924).

5) Y. Tanoue, A. Terada, T. Tsuboi, T. Hayashida, and O. Tsuge, *Bull. Chem. Soc. Jpn.*, **60**, 2927 (1987).