

Reactivity of primary and secondary alcohols in nucleophilic addition to a triple bond: the vinylation of butane-1,3-diol

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Acetylene adds to butane-1,3-diol in the presence of KOH to give, along with the corresponding divinyl ether and 2,4-dimethyl-1,3-dioxane, 4-vinyloxybutan-2-ol and its structural isomer 3-vinyloxybutan-1-ol, the ratio between the latter two products, (5–8) : 1, depending on the reaction conditions.

Key words: butane-1,3-diol, vinylation, 4-vinyloxybutan-2-ol, 3-vinyloxybutan-1-ol, IR spectroscopy, ^1H NMR spectroscopy.

Base-catalyzed vinylation of primary alcohols with acetylene occurs only severalfold faster than that of secondary alcohols, which is explained by electrophilic assistance from the more "acidic" primary hydroxy group and more favorable steric factors.¹ It is surprising, therefore, that monovinyl ethers involving only primary hydroxy groups have been obtained so far upon vinylation of primary–secondary diols,^{2,3} in which case a much larger difference between the corresponding reaction rates is implied. It seemed as if the reactivity of the secondary hydroxy group with respect to the triple bond in nucleophilic processes is completely blocked in the presence of the primary one. When reactions are carried out at higher temperatures or in superbasic media,⁴ complete vinylation occurs to give the corresponding divinyl ethers.

To elucidate this matter related to a fundamental problem of organic chemistry, namely, to the mechanism of nucleophilic addition to a triple bond, we performed a detailed analysis of products of the base-catalyzed vinylation of butane-1,3-diol with acetylene under pressure. Based on the literature data, one could expect the predominant formation of 4-vinyloxybutan-2-ol (**1**), 1,3-divinyloxybutane (**2**), and 2,4-dimethyl-1,3-dioxane (**3**),¹ a product of cyclization of monovinyl ether **1**. The yields of these products would depend on the concentration of the catalyst, the reagent ratio, the reaction temperature, and the reaction time. GLC analysis of the reaction mixture confirmed the formation of products **1**–**3**. It turned out that an isomeric monovinyl ether, viz., 3-vinyloxybutan-1-ol (**4**), was also formed in up to 10% yield.

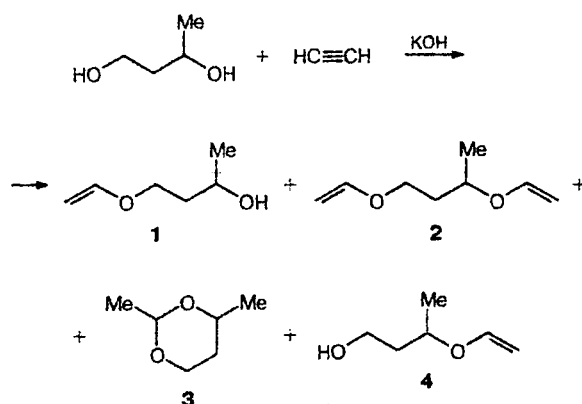
Pure monovinyl ethers **1** and **4** were isolated by preparative GLC. The IR spectra of both compounds contain intense bands at 1615–1640 cm^{-1} ($\nu(\text{C}=\text{C})$) and 3350 cm^{-1} ($\nu(\text{OH})$). The ^1H NMR spectra of

compounds **1** and **4** exhibited signals with virtually the same chemical shifts and multiplicities.

In the two-dimensional NOE spectrum (NOESY) of 4-vinyloxybutan-2-ol (**1**), a signal for the C(2)H proton (δ 3.93) has cross-peaks with OH, C(1)H, and C(3)H protons, which attests to the fact that the vinyloxy group is in position 4. Moreover, the spectrum shows an intense cross-peak for the *trans*-proton of the vinyl group at δ 4.16 with C(4)H protons, which suggests *syn*-spatial orientation of the vinyl group with respect to the alkyl group, as was shown earlier.² For vinyl ether **4**, a signal for the C(3)H proton has cross-peaks with C(4)H and C(2)H protons, while the OH proton gives a cross-peak with C(1)H protons.

The IR spectra of vinyl ethers **1** and **4** exhibit two components of the C=C stretching vibrations. In the case of 4-vinyloxybutan-2-ol (**1**), a low-frequency band at 1616 cm^{-1} corresponding to a planar conformation is

Scheme 1



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Table 1. Effect of the reaction conditions in the vinylation of butane-1,3-diol on the yields of the reaction products

Entry	Reaction conditions				Degree of conversion of butane-1,3-diol (%)	Reaction products yields (%)			
	m_{diol} /mol	C_{KOH} /mol. %	$T/^{\circ}\text{C}$	t/h		1	2	3	4
1	0.2	3	139–141	2	72	52.7	5.9	1.7	6.7
2	0.26	5	138–140	3	83	50.4	7.4	6.0	9.3
3	0.3	5	136–140	3	90	56.7	10.2	3.5	10.1
4	0.5	5	140–144	3	75	47.9	7.3	2.2	8.7
5	0.2	7	150–155	1	92	31.7	24.5	6.0	1.5
6	0.2	10	148–150	1	100	37.7	34.4	6.8	0.6

more intense, while for vinyl ether **4** the pattern is opposite, which correlates with the dependence of the conformation on the extent of C_{α} -branching in the alkyl radical.^{2,5}

The content of vinyl ether **4** in the reaction mixture depends on the vinylation conditions and amounts to ~1–10%. Under conditions favorable for partial vinylation, viz., at relatively low concentrations of the catalyst (KOH, 3–5 mol.%, Table 1, entries 1–3) and deficiency of acetylene with respect to the diol (see Table 1, entries 3 and 4), the yields of both monovinyl ethers **1** and **4** are increased. The main reaction product is 4-vinylxybutan-2-ol (**1**) (yield up to 60%, the degree of conversion of the diol is 80–90%). An excess of acetylene with respect to the diol as well as an increase in the concentration of KOH to 7–10 mol.% and in the reaction temperature to 150 °C (see Table 1, entries 5 and 6) favor higher yields of divinyl ether **2** and cyclic acetal, thus decreasing the yields of monovinyl ethers **1** and **4**. Moreover, comparison of entries 5 and 6 shows that the more drastic the conditions and the higher the yield of divinyl ether **2** the higher the ratio of ether **1** to **4**, because the vinylation rate of compound **1** containing the secondary hydroxy group is an order of magnitude lower than that of ether **4**.

Thus, based on a simple model and concepts of the method of competitive reactions, one can conclude that the primary hydroxy group is more reactive in nucleophilic addition to acetylene than the secondary one by a factor of 5–15 when they are both present in a diol molecule.

Experimental

IR spectra were recorded on a JFS-25 spectrometer (thin film) in the range 400–4000 cm^{-1} . ^1H NMR spectra were recorded at ~20 °C on a Bruker DPX-250 instrument (250 MHz) in CDCl_3 with HMDS as the internal standard. Reaction mixtures were analyzed and the purity of the compounds obtained was checked by GLC on an LKhM-80 instrument (katharometer, helium as the carrier gas (flow rate 2 L h^{-1}), column 3000×3 mm, polyethylene glycol (PEG) 20,000 as the liquid phase, 1% on NaCl (0.16–0.25 mm)). Retention times of compounds **3**, **2**, **1**, and **4** were 1, 2, 8, and 11 min, respectively (isothermal regime, column temperature 120 °C).

Preparative separation of the compounds was carried out on a PAKhV-07 preparative chromatograph (column 1000 mm, 1% PEG on NaCl, column temperature 85 °C).

Vinylation of butane-1,3-diol (see Table 1, entry 2). A mixture of butane-1,3-diol (23.4 g, 0.26 mol) and KOH (0.7 g, 0.013 mol) was fed with acetylene at an initial pressure of 10 atm and heated in a rotating 1-L autoclave at 138–140 °C for 3 h, the maximum pressure in the autoclave reaching 15 atm. Distillate of the reaction mixture *in vacuo* gave 1,3-divinylxybutane (**2**) (2.8 g, 7.4%), 2,4-dimethyl-1,3-dioxane (**3**) (1.8 g, 6%) a fraction with b.p. 44–47 °C (2 Torr) (18.0 g) containing 4-vinylxybutan-2-ol (**1**) (84.6%) and 3-vinylxybutan-1-ol (**4**) (15.6%), and the starting butane-1,3-diol (4.0 g) (degree of conversion 83%). The individual monovinyl ethers **1** and **4** were isolated by preparative chromatography.

4-Vinylxybutan-2-ol (1): b.p. 62 °C (12 Torr), n_D^{20} 1.4376 (cf. Ref. 2: b.p. 40 °C (2 Torr), n_D^{20} 1.4377). IR, ν/cm^{-1} : 614, 701, 817, 913, 963, 993, 1044, 1072, 1113, 1137, 1200, 1278, 1321, 1376, 1411, 1461, 1471, 1514, 1553, 1616, 1638, 2879, 2929, 2967, 3063, 3118, 3371. ^1H NMR, δ : 6.41 (dd, 1 H, OCH=); 4.16 and 3.97 (both dd, each 1 H, $\text{CH}_2=$, $J_{\text{cis}} = 6.8$ Hz, $J_{\text{trans}} = 1.4$ Hz, $J_{\text{gem}} = 2.16$ Hz); 3.93 (m, 1 H, C(2)H); 3.79 (m, 2 H, C(4)H_2); 2.38 (br.s, 1 H, OH); 1.75 (m, 2 H, C(3)H_2); 1.17 (d, 3 H, CH_3 , $J_{1,2} = 6.2$ Hz).

1,3-Divinylxybutane (2): b.p. 42 °C (12 Torr), n_D^{20} 1.4343 (cf. Ref. 4: b.p. 58–59 °C (20 Torr), n_D^{20} 1.4363). IR, ν/cm^{-1} : 699, 818, 871, 913, 950, 967, 1019, 1051, 1074, 1113, 1144, 1201, 1231, 1321, 1348, 1380, 1451, 1474, 1616, 1635, 2881, 2932, 2975, 3046, 3073, 3118. ^1H NMR, δ : 6.42 (dd, 1 H, OCH=); 4.16 and 3.97 (both dd, each 1 H, $\text{CH}_2=\text{CH}-\text{O}-$, $J_{\text{cis}} = 6.9$ Hz, $J_{\text{trans}} = 14.4$ Hz, $J_{\text{gem}} = 1.90$ Hz); 6.28 (dd, each 1 H, CH=); 4.26 and 3.97 (both dd, each 1 H, $\text{CH}_2=\text{CH}-\text{O}-\text{C(1)H}_2$, $J_{\text{cis}} = 6.7$ Hz, $J_{\text{trans}} = 14.2$ Hz, $J_{\text{gem}} = 1.28$ Hz); 4.06 (tq, 1 H, C(3)H , $J_{3,4} = 6.3$ Hz, $J_{3,2} = 6.2$ Hz); 3.75 (m, 2 H, C(4)H_2); 1.86 (m, 2 H, C(2)H_2); 1.22 (d, 3 H, CH_3 , $J_{4,3} = 6.3$ Hz).

2,4-Dimethyl-1,3-dioxane (3): b.p. 114 °C, n_D^{20} 1.4130 (cf. Ref. 6: b.p. 46 °C (50 Torr), n_D^{20} 1.4115). IR, ν/cm^{-1} : 650, 809, 844, 865, 893, 952, 1045, 1084, 1100, 1138, 1174, 1224, 1252, 1323, 1379, 1410, 1428, 1444, 1463, 2631, 2721, 2798, 2852, 2941, 2974. ^1H NMR, δ : 4.67 (q, 1 H, C(2a)H , $^3J = 5.1$ Hz); 4.05 (cd, 1 H, C(6e)H , $^2J = 11.3$ Hz, $J_{6e,5a} = 5.0$ Hz, $J_{6e,5c} = 1.2$ Hz); 3.73 (m, 2 H, C(6a)H , C(4a)H); 1.62 (m, 1 H, C(5a)H); 1.41 (two m, 1 H, C(5e)H , $^2J = 13.3$ Hz); 1.29 (d, 3 H, Me C(2) , $^3J = 5.1$ Hz); 1.21 (d, 3 H, Me C(4) , $^3J = 6.3$ Hz).

3-Vinylxybutan-1-ol (4): n_D^{20} 1.4379. IR, ν/cm^{-1} : 616, 698, 825, 917, 951, 967, 990, 1020, 1056, 1096, 1139, 1180, 1196, 1254, 1321, 1349, 1379, 1450, 1477, 1526, 1620, 1634, 2887, 2935, 2975, 3055, 3117, 3355. ^1H NMR, δ : 6.30 (dd,

1 H, OCH=); 4.31 and 4.05 (both dd, each 1 H, CH₂=, J_{cis} = 6.6 Hz, J_{trans} = 14.1 Hz, J_{gem} = 1.66 Hz); 4.09 (m, 1 H, C(3)H); 3.72 (m, 2 H, C(1)H₂); 2.61 (br.s, 1 H, OH); 1.64–1.84 (m, 2 H, C(2)H₂); 1.24 (d, 3 H, CH₃, $J_{4,3}$ = 6.2 Hz).

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Synthesis of 2-(furazanyl)indolizines

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Heating of *N*-[2-(4-methylfuran-3-yl)-2-oxoethyl]-2-methylpyridinium bromides in *N,N*-dimethylaniline affords indolizine derivatives, whereas in aniline a mixture of indole and indolizine derivatives is formed.

Key words: furazans, indoles, indolizine.

Previously,¹ we showed that pyridinium salts obtained from 3-(2-bromoacetyl)furan² give 3-(*R*-indol-2-yl)furan derivatives upon refluxing in 4-*R*-anilines. The pyridine moiety functioned as a leaving group, while aniline served as a building block for constructing the indole moiety of the molecule that formed.

Under similar conditions, 2-methylpyridinium salts (**1**) react according to both pathway *a* and pathway *b* (Scheme 1) leading to indolizine derivatives **3**, in which the pyridine ring is a structural fragment, and aniline acts as a catalyst.

When the reaction is carried out in *N,N*-dimethylaniline (boiling, 2–3 h), only 2-(furazanyl)-indolizines **3** are formed (yield 67–75%).

Experimental

Melting points were determined on a Kofler stage. ¹H and ¹³C NMR spectra were recorded on Bruker AM-300 (300 and

75 MHz, respectively) and Bruker AM-200 instruments (200 and 50 MHz, respectively). ¹³C signals were assigned with the use of double heteronuclear resonance and selective polarization transfer from H nuclei.

Mass spectra were obtained with Varian MAT CH-6 and Varian MAT CH-111 instruments (70 eV). IR spectra were recorded on a Specord IR-75 spectrometer (KBr).

The course of the reaction was monitored and the purity of reaction products was checked by TLC on Silufol UV-254 plates. Silica gel was used for preparative chromatography.

The starting pyridinium salts **1a–c** were obtained according to the known procedure.¹

2-(4-Methylfuran-3-yl)indolizine (3a). A mixture of *N*-[2-(4-methylfuran-3-yl)-2-oxoethyl]-2-methylpyridinium bromide (**1a**) (2.84 g, 0.01 mol) and aniline (10 mL) was refluxed in an atmosphere of argon for 3.5 h. The reaction mixture was cooled to 20 °C, poured into 5% HCl, and stirred for 0.5 h. Products were extracted with CH₂Cl₂. The extract was dried with MgSO₄ and concentrated. The residue was chromatographed on a column with SiO₂ (pentane–CH₂Cl₂ as the eluent). Eluted first was compound **3a**, yield 35%, m.p. 123–124 °C (from hexane). Found (%): C, 66.43; H, 4.59;

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