

Short Communications

The Influence of Added Ethanol on the Acidities of 4-Hydroxy-3-methoxybenzyl Alcohol and 2,2'-Dihydroxy-5,5'-di(hydroxymethyl)-3,3'-dimethoxybiphenyl in Aqueous Solution

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The acidities of phenols and carboxylic acids are generally lower in ethanol than in water.¹ In connection with work on enzymatic oxidation of phenols related to lignin it was of interest to find out whether the addition of ethanol to the oxidation mixture had a stronger influence on the acidity of *o,o'*-dihydroxybiphenyl structures than on monomeric phenols. The acidity of *o,o'*-dihydroxybiphenyls is strongly influenced by intramolecular hydrogen bond formation² and therefore the effect of solvent polarity on the dissociation constant was expected to be different from that of monomeric phenols.

The model compounds chosen for this study were 3-hydroxy-4-methoxybenzyl alcohol³ (*1*) and 2,2'-dihydroxy-5,5'-di(hydroxymethyl)-3,3'-dimethoxybiphenyl^{3,4} (*2*). The dissociation constants of *1* and *2* in 0.1 M sodium perchlorate were measured spectrophotometrically at 292 and 308 nm, respectively, in a series of ethanol-water mixtures. Buffer solutions for the measurement of *1* were prepared according to Sørensen's method⁵ (0.1 M sodium hydroxide/0.05 M borax) and for the measurement of *2* according to Kolthoff's method⁶ (0.05 M borax/0.1 M potassium dihydrogen phosphate).

The hydrogen ion concentrations of the buffered ethanol-water mixtures were measured

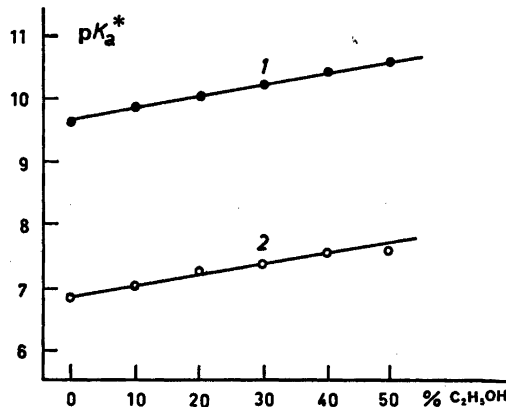
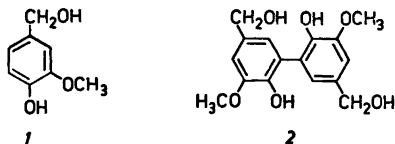


Fig. 1. The acidities of compounds *1* and *2* in ethanol-water mixtures as a function of ethanol concentration in the solvent.

with a glass electrode. Since the response of the glass electrode in aqueous ethanol was not known, it was determined in a separate series of measurements. For each ethanol-water mixture, which was 0.1 M in sodium perchlorate, the electrode was calibrated by addition of known amounts of 0.1 M hydrochloric acid.

The dissociation constants for *1* and *2* in 0.1 M sodium perchlorate at 25 °C in different ethanol-water mixtures are shown in Fig. 1 as a function of the ethanol concentration in the solvent. Each pK_a*-value, the asterisk indicating a solvent mixture, given in the graph is a mean of measurements in three buffer solutions.

In pure aqueous 0.1 M sodium perchlorate solution the constants obtained were 9.59 for the monomeric phenol, and 6.87 for the biphenyl compound. Throughout the measurements individual results from different buffer solutions did not differ more than 0.04 for the monomer and 0.01 for the dimeric compound. To obtain the thermodynamic dissociation constant 0.20 units should be added to the value at ionic strength 0.1. The value 0.20 originates from measurements of the dissociation constant of *1* in pure aqueous solutions of different ionic strength. After the correction for the influence of ionic strength the obtained

values for 1 9.59 and 2 6.87 agree well with those given in the literature, 9.83⁷ and 7.0,⁸ respectively.

When ethanol is added the pK_a -values increase, at 50 % ethanol concentration the value for 1 is 10.54 and for 2 7.57.

The increase over the investigated interval seems to be almost linear, and thus added ethanol does not cause any abrupt change in the mode of dissociation of the two phenols, and the difference in acidity between them remains fairly constant.

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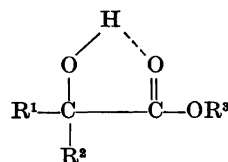
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Investigations of Dithienylglycolic Esters. V. Hydrolytic Stability and Preparation of Some Esters of Glycolic Acids

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The hydrolytic stability of aryl substituted glycolates has received scant attention. Some data for esters of open-chain alkylamino alcohols have been reported by Kuznetsov and Rozinskaya.¹ They found that the rate of hydrolysis of alkylamino esters in an alkaline medium is higher than that of analogs containing no nitrogen. Knowledge of the hydrolytic stability is important for the elucidation of the structure-activity relationships of these atropin-like anticholinergic compounds. We have therefore synthesized and undertaken a study of the hydrolysis of some cyclic amino alcohol glycolates as well as their corresponding methyl esters² with the general structure



	R ¹	R ²	R ³
1	Ph	Ph	-CH ₃
2	3-Th ^a	3-Th	-CH ₃
3	Ph	2-Th	-CH ₃
4	3-Th	2-Th	-CH ₃
5	2-Th	2-Th	-CH ₃
6	Ph	Ph	Q ^b
7	3-Th	3-Th	Q
8	Ph	2-Th	Q
9	2-Th	2-Th	Q
10	2-Th	2-Th	3-Pip ^c
11	2-Th	2-Th	4-Pip ^c

^a Th = thienyl. ^b Q = 3-quinuclidinyl. ^c Pip = piperidyl.

In order to determine the extent to which differences in reaction rates depend upon steric interaction from the alcoholic part of the esters, the intramolecular hydrogen bond between the hydroxyl and the carbonyl groups was studied by IR spectroscopy. The strength of the hydrogen bond will also reflect the various inductive effects within the esters.³ A hydroxyl group hydrogen bonded to a carbonyl group increases the positive charge at the carbonyl