Prediction of esterification rate constants for secondary alkan-2-ols based on one- and two-parameter Taft equations

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Abstract
Equilibrium constants and reaction rate constants for the esterification of secondary alkan-2-ols with acetic acid were measured at 60°C in 1,4-dioxane. Taft coefficients, as single parameter (without inductive effects), and two-parameter correlation (including inductive and steric effects), of the measurements were used for the prediction of esterification rate constants for secondary alkan-2-ols with monocarboxylic acids. For this prediction, previously observed results of linear correlation of rate constants for the esterification of propan-1-ol with monocarboxylic acids measured under identical experimental conditions were applied. Two parameter Taft equations for the correlation of secondary alkan-2-ols and for monocarboxylic acids were combined, resulting in an overall correlation equation usable for the prediction of reaction rates for secondary alkan-2-ols with any monocarboxylic acid. This equation was experimentally verified for the esterification of three randomly chosen alkan-2-ols with three randomly chosen monocarboxylic acids.

Keywords
Esterification, rate constants, secondary alkan-2-ols, Taft equation

Introduction
Esters of secondary alcohols with organic acids, like esters of primary alcohols,¹,² have been applied in industrial production of fragrances and aromas. For example, propan-2-yl acetate is used in the preparation of apple aromas (FEMA 2926), propan-2-yl propionate for plum- or raspberry-type aromas (FEMA 2959), cyclohexyl acetate for raspberry-, banana-, or pineapple-type aromas (FEMA 2349), and cyclohexyl butyrate for pineapple or apple aromas,
or jasmine scents (FEMA 2351). Apart from applications in the food industry, esters of secondary alcohols have various usages. The 2-propyl ester of 4-chloro-2-methylphenoxyacetic acid has been utilized as a herbicide. Propan-2-ol and butan-2-ol esters with fatty acids lower the cloud and pour points of biodiesel by up to $-17^\circ$C in comparison with methyl esters. Esters of propan-2-ol with tetradecanoic (myristic) or 16-methylheptadecanoic (isostearic) acids significantly increase the penetration of various substances through skin. Compounds containing propan-2-yl tetradecanoate are described as carriers of natural antioxidants. Esters of decan-2-ol and tridecan-2-ol are used for the preparation of synthetic oils.

This article is an attempt to determine experimentally a correlation equation of Taft-type for one and two parameters (including coefficients for steric and inductive effects) for the esterification of secondary alkan-2-ols with monocarboxylic organic acids. This equation was combined with previous results leading to an equation according to which it is possible to predict the esterification rate constants of secondary alkan-2-ols with any monocarboxylic acid without experimental measurements. This methodology can be applied in ester synthesis and the food and perfume industries for the calculation of reaction time expenses for the production of these materials.

The esterification of secondary alcohols with organic acids is a well-studied reaction. Its reaction rate depends on temperature, concentrations of reactants and products, concentration of catalyst (hydrogen ions), solvent, and the structures of alcohols and acids. The rate of esterification $v_{overall}$ for secondary alcohols (including alkan-2-ols) is described by the following equation

$$v_{overall} = k_E c_{alcohol} - k_H c_{ester}$$

where $c$ is the molar concentration of the corresponding species. Since the equilibrium constant $K$ is defined as the ratio of the forward (esterification) $k_E$ and reverse (hydrolysis) $k_H$ reaction rate constants

$$K = \frac{k_E}{k_H}$$

equation (1) may be rewritten as follows

$$v_{overall} = k_E c_{alcohol} - \frac{1}{K} c_{ester}$$

The solution of this differential equation was derived under initial conditions $c_{acid} = c_{alcohol} = 1$ mol dm$^{-3}$ and $c_{ester} = c_{water} = 0$ mol dm$^{-3}$ and may be expressed as

$$k_E = \frac{\sqrt{K}}{2t} \ln \left( \frac{\sqrt{K} - 1}{\sqrt{K} + 1} x - \sqrt{K} \right)$$

where $x$ is the degree of conversion as a function of time $t$

**Experimental**

Propan-2-ol, butan-2-ol, pentan-2-ol, hexan-2-ol, 4-methylpentan-2-ol, 1,4-dioxane (Merck, Germany), anhydrous CuSO$_4$, methanol, H$_2$SO$_4$, phenol, acetone, and NaOH (Lachema,
Czech Republic) were of AR purity. Ethanol was used for ultraviolet (UV) spectroscopy in all experiments.

First, 1-chloropropan-2-ol was prepared by the rectification of a mixture of 1-chloropropan-2-ol and 2-chloropropan-1-ol (ratio 3:1), which was prepared by the reaction of propene with hypochlorous acid (supplied by CHZ Nováky, Slovakia) using a column with an efficiency of 80 TP at a pressure of 4 kPa. From this precursor (1-chloropropan-2-ol), 1-methoxypropan-2-ol, and 1-phenoxypropan-2-ol were synthesized by condensation with sodium methoxide or sodium phenoxide, respectively, in anhydrous methanol and then purified using the same distillation column. Physical properties related to the synthesized alkan-2-ols are presented in Table 1.

A static method was used for the determination of the esterification equilibrium constants. Solutions containing equimolar amounts of the relevant alkan-2-ol and acetic acid at a concentration of 1 mol dm$^{-3}$, 1,4-dioxane (dried using CuSO$_4$), and catalyst (H$_2$SO$_4$, 0.01 mol dm$^{-3}$) were sealed in glass vials and heated to 90°C for 3 h and then left for 3 months at room temperature. Subsequently, vials were placed into a thermostatically controlled device, keeping the temperature at 60 ± 0.1°C for 7 days. The acetic acid content was determined titrimetrically, and equilibrium constants were calculated according to equation (6).

A discontinuous isothermal reactor, immersed in a bath at 60 ± 0.1°C, equipped with an electromagnetic stirrer, and closed by a cap, was used for the measurements related to esterification reaction kinetics of secondary alkan-2-ols. Samples for analysis, carried out by titration, were taken at selected intervals using a syringe.

Titration was carried out using phenolphthalein indicator in the NaOH titration solution. The purity of synthesized alkan-2-ols was assessed using an Abbe refractometer, a pycnometer, and capillary gas chromatography.

**Results and discussion**

The esterification rate of secondary alcohols is an order of magnitude slower in comparison with primary alcohols; therefore, a larger amount of catalyst has been used for measuring rate constants. The esterification rate constant depends linearly on the hydrogen ion concentration according to equation (5)

$$k_E = k_E^0[H^+]$$  \hspace{1cm} (5)
where $k_0^E$ is the esterification rate constant at the concentration of hydrogen ions equal to unity. This relationship for the esterification of propan-2-ol (isopropanol) with acetic acid was verified experimentally and the results are summarized in Table 2.

Measured values, $x_N$, of conversion at equilibrium (degree of conversion $x$ for $t = t_N$) for the secondary alkan-2-ols are presented in Table 3.

Then, concentration equilibrium constants were calculated according to the following equation

$$K_c = \frac{x_N^2}{(1 - x_N)^2}$$

(6)

The kinetics of esterification for secondary alkan-2-ols with acetic acid at 60°C were measured as in our previous paper.\textsuperscript{1} The equilibrium constants $K_c$ (given in Table 3) were used for the calculation of the rate constants $k_E$ (refer to equation (4)). The results acquired are shown in Table 4.

The esterification rate constants were correlated in two ways. The first correlation was restricted to the secondary alkan-2-ols with nearly zero inductive effects. The esterification rate of these alkan-2-ols is controlled just by the steric effects. The correlation equation with Taft coefficients for the second case was calculated as follows
log \( k_E \) = \log k_E^0 + 0.77E_S \quad (7)

where \( k_E \) is the esterification rate constant related to the relevant alkan-2-ols with CH₃COOH, \( k_E^0 \) is the esterification rate constant of propan-2-ol with CH₃COOH as a reference secondary alcohol, and \( E_S \) is the Taft coefficient for the steric effect of the relevant alkan-2-ol. The fit of equation (7) \( (R^2 = 0.986) \) is presented in Figure 1 and Table 5.

Subsequently, the rate constants of all measured secondary alkan-2-ols were correlated using the following two-parameter Taft equation:

### Table 4. Experimental and calculated esterification rate constants for secondary alkan-2-ols with acetic acid at 60°C in 1,4-dioxane.

| Alcohol          | \( k_E \times 10^6 \) (\( c(H^+) = 0.1 \text{ mol dm}^{-3} \)) | \( k_E \times 10^7 \) (calc.) (\( c(H^+) = 0.01 \text{ mol dm}^{-3} \)) | \log k_E |
|------------------|---------------------------------------------------------------|---------------------------------------------------------------|--------|
| Ethanol          | 218.0                                                         | 218.0                                                         | -4.661 |
| Propan-2-ol      | 22.4                                                          | 22.4                                                          | -5.650 |
| Butan-2-ol       | 16.5                                                          | 16.5                                                          | -5.783 |
| Pentan-2-ol      | 11.5                                                          | 11.5                                                          | -5.940 |
| 4-Methylpentan-2-ol | 5.6                                                          | 5.6                                                          | -6.251 |
| Hexan-2-ol       | 10.6                                                          | 10.6                                                          | -5.975 |
| Octan-2-ol       | 10.3                                                          | 10.3                                                          | -5.987 |
| 1-Chloropropan-2-ol | 3.2                                                          | 3.2                                                          | -6.495 |
| 1-Methoxypropan-2-ol | 9.7                                                          | 9.7                                                          | -5.013 |
| 1-Phenoxypropan-2-ol | 5.4                                                          | 5.4                                                          | -5.268 |

**Figure 1.** Dependence of ratio \( \log \frac{k_E(\text{experimental})}{k_E^0(\text{experimental})} \) on steric coefficient \( E_S \) for secondary alkan-2-ols without inductive effect, where \( k_E^0(\text{experimental}) \) is the esterification rate constant for propan-2-ol with acetic acid.
where \( k_E \), \( k_E^0 \), and \( E_S \) have the same meaning as in equation (7) and \( \sigma_1 \) is the Taft coefficient for the inductive effect of the relevant alkan-2-ol. The relationship between the experimental and calculated rate constants of the secondary alkan-2-ols was obtained by the fitting of equation (8) as given in Table 6 and Figure 2 (\( R^2 = 0.972 \)). It may be said that the correlation of rate constants for the esterification of secondary alkan-2-ols using the Taft coefficients is feasible, but investigation of a larger number of alcohols is required. However, the present selection of secondary alcohols, where one alkyl is always methyl, provides a straightforward basis for their correlation using the Taft coefficients.

It is interesting to note that the esterification equilibrium constants with acetic acid for the secondary alkan-2-ols lacking inductive effects are practically constant (\( K_C \rightarrow 2 \)). This finding confirms the general conclusion\(^9,10\) where \( K_C \) of different acids (\( K_C \rightarrow 4 \)) was found in the esterification with propanol. As mentioned above, the esterification rate of the secondary alkan-2-ols (see Table 2) is approximately an order of magnitude slower than the esterification of primary alcohols.\(^1\) This may be caused by higher steric shielding of the

Table 5. Relationship between the esterification rate constants of secondary alkan-2-ols and Taft coefficients for the steric effect.

| Alcohol          | \( k_E \text{ (exper.)} \times 10^7 \) (dm\(^3\) mol\(^{-1}\) s\(^{-1}\)) | \( \log k_E \text{ (exper.)} \) | \( \log k_E^0 \text{ (exper.)} \) | \( E_S \) |
|------------------|---------------------------------------------------------------------------------|-------------------------------|---------------------------------|---------|
| Ethanol          | 218.0                                                                            | -4.661                        | 0.988                           | 1.24    |
| Propan-2-ol      | 22.4                                                                             | -5.650                        | 0.000                           | 0.00    |
| Butan-2-ol       | 16.5                                                                             | -5.783                        | -0.133                          | -0.07   |
| Pentan-2-ol      | 11.5                                                                             | -5.940                        | -0.290                          | -0.36   |
| 4-Methylpentan-2-ol | 5.6                                                                            | -6.252                        | -0.602                          | -0.93   |
| Hexan-2-ol       | 10.6                                                                             | -5.975                        | -0.325                          | -0.39   |
| Octan-2-ol       | 10.3                                                                             | -5.987                        | -0.337                          | -0.40   |

Table 6. Comparison of the experimentally acquired and calculated values of the esterification rate constants of secondary alcohols.

| Alcohol          | \( k_E \text{ (exper.)} \times 10^7 \) (dm\(^3\) mol\(^{-1}\) s\(^{-1}\)) | \( \log k_E \text{ (exper.)} \) | \( \log k_E^0 \text{ (exper.)} \) | \( \log k_E \text{ (calc.)} \) | \( k_E \text{ (calc.)} \times 10^7 \) (dm\(^3\) mol\(^{-1}\) s\(^{-1}\)) | \( \% \) |
|------------------|---------------------------------------------------------------------------------|-------------------------------|---------------------------------|---------------------------------|--------------------------------------------------------------------------------|------|
| Ethanol          | 218.0                                                                            | 0.988                         | 0.932                           | 191.8                           | 0.932                                                                              | +12.0|
| Propan-2-ol      | 22.4                                                                             | 0.000                         | 0.000                           | 22.4                            | 0.000                                                                              | 0.0  |
| Butan-2-ol       | 16.5                                                                             | -0.133                        | -0.043                          | 20.3                            | -0.043                                                                              | -23.0|
| Pentan-2-ol      | 11.5                                                                             | -0.289                        | -0.267                          | 12.1                            | -0.267                                                                              | -5.2 |
| 4-Methylpentan-2-ol | 5.6                                                                            | -0.602                        | -0.704                          | 4.4                             | -0.704                                                                              | +21.4|
| Hexan-2-ol       | 10.6                                                                             | -0.325                        | -0.289                          | 11.5                            | -0.289                                                                              | -8.5 |
| Octan-2-ol       | 10.3                                                                             | -0.337                        | -0.297                          | 11.3                            | -0.297                                                                              | -9.7 |
| 1-Chloropropan-2-ol | 3.2                                                                            | -0.844                        | -0.707                          | 4.4                             | -0.707                                                                              | -37.5|
| 1-Methoxypropan-2-ol | 9.7                                                                           | -0.363                        | -0.481                          | 7.4                             | -0.481                                                                              | +23.4|
| 1-Phenoxypropan-2-ol | 5.4                                                                            | -0.617                        | -0.697                          | 4.5                             | -0.697                                                                              | +16.7|

\[
\log k_E = \log k_E^0 + 0.77E_S - 1.11\sigma_1 \tag{8}
\]
secondary alcohol by two alkyl groups. Hence, a 10 times higher catalyst concentration \( c(H^+) = 0.05 \text{ mol dm}^{-3} \) was used for the measurement of the esterification rate constants to effect the esterification at an appropriate rate. Subsequently, the acquired esterification rate constants were divided by five because equation (3) is valid within the range of catalyst concentrations used as experimentally demonstrated (see Table 2), so that the correlation equation used previously for organic acids is applicable

\[
\log k_E = \log k_E^0 - 0.0034 + 0.98E_S + 0.22\sigma_1
\]  

where \( k_E \) is the esterification rate constant for the organic acid with propan-1-ol; \( k_E^0 \) is the esterification rate constant for ethanol with acetic acid; and \( E_S \) and \( \sigma_1 \) are the steric and inductive Taft coefficients related to \( CH_3COOH \). Because the correlation of the esterification rate constants for the secondary alkan-2-ols ((equation (8)) and acids ((equation (9))) was carried out under identical conditions (i.e. same temperature, same solvent, same catalyst concentration, and same concentration of reagents), it is possible to combine equations (8) and (9) to extrapolate the esterification rate constants and so predict the rate of esterification for any alkan-2-ol with any monocarboxylic acid, as demonstrated in the study of Vojtko and Tomčík for primary alcohols

\[
\log k_{XY} = \log k_{EA} - 0.9296 - 1.11\sigma_{IY} + 0.77E_{SX} + 0.22\sigma_{IX} + 0.98E_{SY}
\]  

where \( k_{XY} \) is the esterification rate constant of any alkan-2-ol in the absence of mesomeric (resonance) effects with any organic acid also without mesomeric (resonance) effects; \( k_{EA} \) is
the esterification rate constant of ethanol with acetic acid; $\sigma_{IX}$ and $E_{SX}$ are, respectively, the inductive and steric Taft coefficients of secondary alkan-2-ols related to propan-2-ol; and $\sigma_{IY}$ and $E_{SY}$ are, respectively, the inductive and steric Taft coefficients of organic acids related to acetic acid.

For the experimental verification of equation (10), the formation of esters from some relevant alcohols and acids was used by measuring the esterification rate constants relating to the formation of pentan-2-yl butyrate, 1-chloro-2-bromopropylacetate, and 1-methoxypropan-2-yl propionate. Measured rate constants relating to the formation of these esters are given in Table 7.

As can be seen from this table, the measured rate constants are in reasonably good agreement with the values calculated according to equation (10).

Prediction of the esterification rate constants for the secondary alkan-2-ols according to equation (10) is justified up to a point as can be seen from these results. However, the accuracy is lower than with the alkan-1-ols, which is presumably due to the limited number of measured alkan-2-ols.

The methodology could probably be applied also for the secondary alkan-3-ols (one of the constant alkyls would be ethyl). However, this test comes up against the lack of suitable model compounds.

**Conclusion**

Here, we developed a simple and rather reliable tool for the prediction of reaction rates for the esterification of secondary alkan-2-ols. Equilibrium and rate constants for the esterification of chosen, easily accessible alkan-2-ols with acetic acid were measured in 1,4-dioxane as a suitable solvent. The above-mentioned procedure is based on fitting a one parameter Taft equation containing only a Taft steric coefficient and a two-parameter Taft equation containing Taft coefficients for inductive and steric effects. This equation was combined with the two-parameter Taft equation from the study of Vojtko and Tomčík under the same experimental conditions. The results of this combination are a two-parameter equation according to which it is possible to estimate esterification rate constants for any secondary alkan-2-ols with any monocarboxylic acid without experimental measurements under compatible experimental conditions.

**Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

| Ester                        | $k_E(\text{exper.}) \times 10^7$ (dm$^3$ mol$^{-1}$ s$^{-1}$) | $k_E(\text{calc.}) \times 10^7$ (dm$^3$ mol$^{-1}$ s$^{-1}$) | $(k_E(\text{exper.}) - k_E(\text{calc.})) / k_E(\text{exper.}) \times 100$ (%) |
|-----------------------------|-------------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------------|
| Pentan-2-yl butyrate        | 6.35                                                        | 5.86                                                        | +7.7                                                              |
| 1-Chloro-2-bromopropylacetate | 2.85                                                        | 3.47                                                        | -21.7                                                             |
| 1-Methoxypropan-2-yl propionate | 7.37                                                        | 6.90                                                        | +6.4                                                              |
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