Reactivity of cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids with diazodiphenylmethane in aprotic solvents

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Rate constants for the reaction of diazodiphenylmethane with cyclohex-1-enyl-carboxylic acid and 2-methylcyclohex-1-enylcarboxylic acid were determined in nine aprotic solvents, as well as in seven protic solvents, at 30 ºC using the appropriate UV-spectroscopic method. In protic solvents the unsubsituted acid displayed higher reaction rates than the methyl-substituted one. The results in aprotic solvents showed quite the opposite, and the reaction rates were considerably lower. In order to explain the obtained results through solvent effects, reaction rate constants (k) of the examined acids were correlated using the total solvatochromic equation of the form: $\log k = \log k_0 + s\pi^* + a\alpha + b\beta$, where π^* is the measure of the solvent polarity, α represents the scale of the solvent hydrogen bond donor acidities (HBD) and β represents the scale of the solvent hydrogen bond acceptor basicities (HBA). The correlation of the kinetic data were carried out by means of multiple linear regression analysis and the opposite effects of aprotic solvents, as well as the difference in the influence of protic and aprotic solvents on the reaction of the two examined acids with DDM were discussed. The results presented in this paper for cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids were compared with the kinetic data for benzoic acid obtained in the same chemical reaction, under the same experimental conditions.

Keywords: cyclohex-1-enylcarboxylic acid, 2-methylcyclohex-1-enylcarboxylic acid, diazodiphenyulmethane, kinetic measurements, protic and aprotic solvents.

INTRODUCTION

The connection that exists between the carboxylic acids structure and their reactivity with diazodiphenylmethane (DDM) has been studied by many authors,[1,2] with a particular regard to solvent influence. The main advantage that makes this esterification convenient for studying solvent effects is the absence of a catalyst. The reaction between carboxylic acids and DDM may vary in rate, but takes place without any additional support and in aprotic solvents it follows the second order kinetics.[3,4]

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Our previous investigations[5,6] of the reactivity of cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acid with DDM in protic solvents have shown that the unsubstituted acid displays higher reaction rates than the methyl-substituted one. In the present work the rate constants of cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids reaction with diazodiphenylmethane were recorded in nine aprotic solvents, as well as in seven protic solvents for comparison. The effects of solvent polarity and hydrogen bonding on the rate constant were interpreted by means of the linear solvation energy relationships (LSER) concept, developed by Kamlet and Taft[7] using a general solvatochromic equation of the form:

$$\log k = \log k_0 + s\pi^* + b\beta + a\alpha \qquad (1)$$

where α, β and π^* are solvatochromic parameters and s, a and b are solvatochromic coefficients.

In Eq. (1) π^* is the index of the solvent dipolarity/polarizability, which is a measure of the ability of a solvent to stabilize a charge or a dipole by its own dielectric effects. The π^* scale was selected to run from 0.00 for cyclohexanone to 1.00 for dimethyl sulfoxide. The α coefficient represents the solvent hydrogen bond donor (HBD) acidity, in other words it describes the ability of a solvent to donate a proton in a solvent-to-solute hydrogen bond. The α scale extends from 0.00 for non-HBD solvents to about 1.00 for methanol. The β coefficient is a measure of a solvent hydrogen bond acceptor (HBA) basicity, and describes the ability of a solvent to accept a proton in a solute-to-solvent hydrogen bond. The β scale was selected to extend from 0.00 for non-HBA solvents to about 1.00 for hexamethylphosphoric acid triamide.

RESULTS AND DISCUSSION

In order to explain the difference in the influence of protic and aprotic solvents on cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids reaction with DDM, the rate constants in a range of both solvent types were determined, as well as those of benzoic acid, for comparison. The rate constants are given in Table I and Table II.

Since the principal quality of aprotic solvents is the lack of ability to act as a hydrogen bond donor, only classical solvation and hydrogen bond acceptor (HBA) effects are present in a solute-to-solvent hydrogen bond, described by the simplified equation:

$$\log k = \log k_0 + s\pi^* + b\beta \qquad (2)$$

The results of kinetic studies have shown that reaction rates of both cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids with DDM are of second order (confirmed by high correlation coefficients – R runs from 0.991 to 0.998, obtained by calculating rate constants based on experimental data).

It can be noticed from Table I that in all aprotic solvents the relation k_M/k_H exceeds 1, showing that reaction rates for the substituted acid were higher, opposite to the order in alcohols (Table II). In ketons and acetates the applied reaction went rather slowly, in dimethylformamide even more so, while acetonitrile was noted for the high-

est value of the rate constant, enabling faster esterification. For a slow, rate determining step the reaction of carboxylic acids with DDM has the *proton transfer* from the carboxylic group to the DDM molecule (Scheme 1).

TABLE I. Rate constants for the reaction of cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enyl-carboxylic acids with diazodiphenylmethane in aprotic solvents

Solvent	k/dm^3 mol^{-1} min^{-1}		
	Cyclohex-1-enyl-carboxylic acid (k_H)	2-Methylcyclohex-1-enyl-carboxylic acids (k_M)	k_M/k_H
Cyclopentanone	0.0253	0.0535	2.11
Diethylketone	0.0530	0.0640	1.20
Methylacetate	0.0325	0.0930	2.65
Acetonitrile	0.3180	0.4200	1.32
Acetone	0.0480	0.1060	2.20
Ethylacetate	0.0250	0.0580	2.32
Dimethylformamide	0.0019	0.0022	1.15
Nitrobenzene	0.3820	0.9970	2.61
Chlorobenzene	0.1730	0.6040	3.49
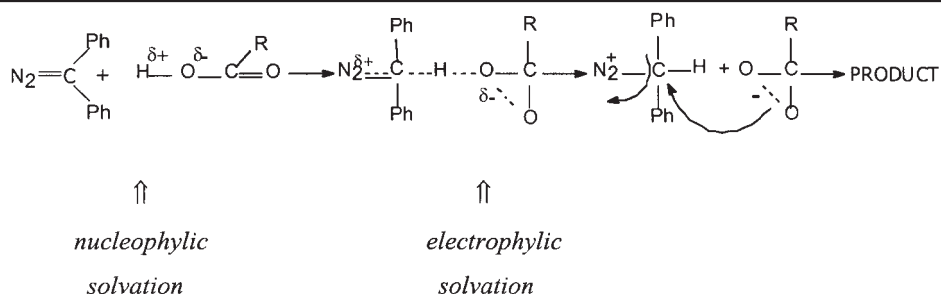
Scheme 1. The mechanism of the reaction of carboxylic acids with DDM.

Results of correlating kinetic parameters with solvent characteristics π* and β for benzoic acid[7] in eleven aprotic solvents are given in Eq. (3):

$$\log k = 0.130 + 3.060\pi^* - 5.630\beta \qquad (3)$$

$$R = 0.989, s = 0.110, n = 11$$

From this equation can be concluded that aprotic solvents influence the benzoic acid – DDM reaction by two reverse effects. The opposite signs of the electrophylic and nucleophylic parameters are in accordance with the described reaction mechanism. Classical solvation effects dominate the transition state and *increase the reaction rate* (positive sign), and proton acceptor effects support the ground state before the reaction starts, *decreasing the rate* (negative sign).

Similar results were obtained (Table I) by correlating kinetic parameters for cyclohex-1-enylcarboxylic and 2-methylcyclohex-1-enylcarboxylic acids, given in Eqs. (4) and (5).

Cyclohex-1-enylcarboxylic acid:

$$\log k = 0.428 + (1.465 \pm 0.321)\, \pi^* - (6.252 \pm 1.816)\, \beta \qquad (4)$$

$$R = 0.980,\ s = 0.160,\ n = 7$$
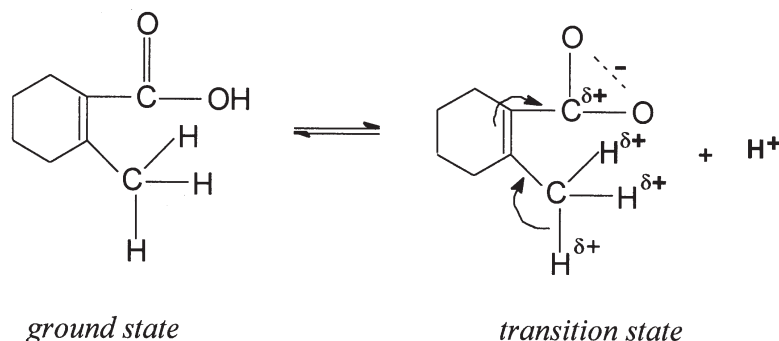
2-Methylcyclohex-1-enylcarboxylic acid:

$$\log k = 1.381 + (0.230 \pm 0.064)\, \pi^* - (5.889 \pm 1.640)\, \beta \qquad (5)$$

$$R = 0.962,\ s = 0.231,\ n = 7$$

In the two opposite effects which influence the rate constant ('+' in front of classical solvation and '–' in front of the HBA effects, as it is shown in the Eqs. (3), (4) and (5)) reason can be found for the low rates of the reaction which does not have the complete support of the medium. As the 'slowing' HBA effects are more expressed than the solvation ones, the aprotic solvents influence on the reaction rate is, generally considered, negative.

The proton acceptor effects of the solvent more expressed in the ground state ('–') for both cyclohexenic acids, are stronger for the unsubstituted one, which brings about the additional decrease of its rate constant even in comparison with the same parameter's value for the methyl-substituted acid. The noted fact could be the consequence of the substituted acid structure – the presence of methyl group in the *ortho*-position possibly causes the distortion of the carboxylic group from the planar part of the molecule round the double bond, making it more accessible for the other reactant, namely DDM. As it is proved by coefficients in Eqs. (4) and (5) the interactions between the solvent and the methyl- substituted acid are weaker than those for the unsubstituted one, for which the mentioned steric effects could be responsible. However, an exceptionally low value of the solvation parameter coefficient (*s*) of the methyl-substituted acid points to an additional effect which causes the absence of solvation. As steric effects alone do not have an influence strong enough to bring about such drastic effects (six times lower solvation than the one for unsubstituted acid), it can be suppored that there is a contribution from secondary interactions which steric effects have coused themselves. Protons of the neighbouring methyl group can stabilize the transition state, slightly acidic near the double bond and the carboxylic group, where the hyperconjugation is possible – π electrons are drawn to the partly positively charged carboxylic C atom, which also affects the methyl group, a weak electron donor, as shown on Scheme 2.

As a result of the described effect, the methyl group protons can interact with partly negative oxygen atoms (δ^- in between two oxygen atoms in the transition state), so that the stabilizing influence of the solvent is practically unnecessary. This effect at the same time brings about the increase of the substituted acid's reaction rate in comparison to the reaction rate of the unsubstituted one, particularly expressed in aprotic solvents which strongly attract the methyl group protons due to their pronounced HBA effect.

ground state   *transition state*

Scheme 2. The ground and the transition state of 2-methylcyclohex-1-enylcarboxylic acid in the reaction with DDM.

The influence of aprotic solvents is stronger on cyclohex-1-enylcarboxylic acid, more accessible to their effects, which can also be noted in absorption spectra correlation,[8] as well at the DDM reaction constants ones. The accordance of the two researches confirms that the mentioned type of solvent is responsible for low reaction rates. 2-Methylcyclohex-1-enylcarboxylic acid, less solvated in aprotic solvents, they also 'slow down' less higher than in aprotic solvents. The unsubstituted acid displays somewhat higher rate constants than the methyl-substituted one in alcohols, as it is shown in Table II.

TABLE II. Rate constants for the reaction of cyclohex-1-enylacrboxylic and 2-methylcyclohex-1-enylcarboxylic acids with diazodiphenylmethane in protic solvents

Solvent	k/ dm^3 mol^{-1} min^{-1}		k_M/k_H
	Cyclohex-1-enylcarboxylic acid (k_H)	2-Methylcyclohex-1-enylcarboxylic acid (k_M)	
Methanol*	0.818	0.762	0.931
Ethanol*	0.417	0.264	0.633
1-Propanol*	0.503	0.305	0.606
2-Propanol	0.376	0.145	0.385
1-Buthanol	0.478	0.238	0.498
t-Buthanol	0.22	0.0425	0.193
Ethyleneglycol	1.962	1.631	0.831

*Rate constants determined previously.[5]

Results of correlating kinetic parameters (Table II) with protic solvent characteristics π^*, α and β for benzoic acid[5] are given in Eq. (6):

$$\log k = -1.772 + (1.889 \pm 0.518)\, \pi^* - (0.048 \pm 0.008)\, \beta + (1.047 \pm 0.360)\, \alpha \quad (6)$$

$$R = 0.984,\ s = 0.097,\ n = 7$$

Similar results were obtained by correlating kinetic parameters (Table II) for cyclohex-1-enylacrboxylic and 2-methylcyclohex-1-enylcarboxylic acids, given in Eqs. (7) and (8).

Cyclohex-1-enylcarboxylic acid:

$$\log k = -1.553 + (1.288 \pm 0.384)\, \pi^* - (0.063 \pm 0.018)\, \beta + (0.744 \pm 0.210)\, \alpha \quad (7)$$

$$R = 0.971, \; s = 0.093, \; n = 7$$

2-Methylcyclohex-1-enylcarboxylic acid:

$$\log k = -2.996 + (1.997 \pm 0.560)\, \pi^* - (0.212 \pm 0.054)\, \beta + (1.831 \pm 0.457)\, \alpha \quad (8)$$

$$R = 0.977, \; s = 0.151, \; n = 7$$

As it can be seen in the Eq. (6), the classical solvation effects, as well as the HBD effects increase the rate of the benzoic acid – DDM reaction, but the HBA effects slow it down. A similar influence the protic solvents have on cyclohex-1-enylcarboxylic acid, showing that the aromatic structure does not cause any particular difference and the interactions with the solvent are of the approximately same intensity, as shown by the cofficients values in Eqs. (6) and (7).

The interactions with the solvent are stronger with 2-methylcyclohex-1-enylcarboxylic acid (Eq. (8)) than with cyclohex-1-enylcarboxylic acid, opposite to the situation in aprotic solvents. Judging from the coefficient values, the HBA effects have weaker influence than the other two, so *the reaction rate is generally increased by alcohols*, contrary to the aprotic solvents where the HBA effects are dominating and the reaction rates are considerably lower. The substituted acid is generally, though slightly slower than the unsubstituted one, probably due to the steric effects of the methyl group, opposite to the 'speeding up' influence of the classical solvation and the HBD effects. However, the 'slowing down' the HBA effects are stronger on the methyl-substituted acid too, and probably also partly responsible for its lower reaction rates. It can be concluded that the influence of alcohols is completely opposite to the one of aprotic solvents and enables faster esterifcation with DDM.

Taking the investigations in protic and aprotic solvents into consideration together, it can be noticed that the acid with the slower reaction rate is always the one on which the HBA effects are stonger (represented by the higher value of the β parameter coefficient). It can be concluded that the stronger proton acceptor solvent effects are, they are less favourable for the reaction of carboxylic acid with DDM – the reason could lie in the support of the state before the reaction starts by these effects (Scheme 1), which is the same in both solvent types. The proton of the carboxylic group seems to be stabilised by the HBA effects influence, and less likely to leave the molecule, slowing that way the reaction with DDM down.

Results presented in this paper point to a rather complex influence of aprotic solvents on the flow and the rate of the reaction between carboxylic acids and DDM, and call for certain reinvestigating of the reaction mechanism in these solvents.

EXPERIMENTAL

Materials

The unsubstituted cyclohex-1-enylcarboxylic acid, b. p. 137 ºC, at 15 mmHg (Ref. 10. b. p. 137 ºC, at 15 mmHg) was synthesised using the Wheeler and Lerner's method,[9] starting from cyclohexanone and sodium cyanide. The obtained cyanohydrine was dehydrated to cyanocyclohex-1-ene. The nitrile was hydrolysed with potassium hydroxide to cyclohex-1-enylcarboxylic acid, using hydrochloric acid to adjust pH.

The same procedure was applied for 2-methylcyclohex-1-enylcarboxylic acid, m. p. 87 ºC (Ref. 10., m. p. 87 ºC), this time using 2-methylcyclohexanone as the starting ketone.

Diazodiphenylmethane was prepared by Smith and Howard's method,[11] stock solutions of 0.06 mol dm^{-3} were stored in a refrigerator and diluted before use.

All applied chemicals were of p.a. purity.

Solvents were purified as described in literature.[12]

Kinetic measurements

Second order rate constant for the reaction of cyclohex-1-enylcarboxylic acid and 2-methylcyclohex-1-enylcarboxylic acid with DDM were determined as prevously reported by the spectroscopic method of Roberts and his co-workers[3] using UV - SHIMATZU 160 A spectrophotometer. Optical density measurements were performed at 525 nm, with 1 cm cells at 30±0.05 ºC.

The second order constants of both examined acids were obtained by dividing the pseudo-first-order rate constants by the acid concentration (the concentration of acid was 0.06 mol dm^{-3} and of DDM 0.006 mol dm^{-3}). Three to five rate determinations were made on each acid and in every case the individual second-order rate constants agreed to within 3 % of the mean.

И З В О Д

РЕАКТИВНОСТ ЦИКЛОХЕКС-1-ЕНИЛКАРБОНСКЕ И 2-МЕТИЛЦИКЛОХЕКС-1-ЕНИЛКАРБОНСКЕ КИСЕЛИНЕ СА ДИАЗОДИФЕНИЛМЕТАНОМ У АПРОТИЧНИМ РАСТВАРАЧИМА

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Константе брзине за реакцију између диазодифенилметана (DDM) и циклохекс-1-енилкарбонске, као и 2-метхилциклохекс-1-енилкарбонске киселине су одређене у девет апротичних и седам протичних растварача, одговарајућом UV-спектрофотометријском методом. У протичним растварачима несупституисана киселина је показала веће реакционе брзине од супституисане. Резултати у апротичним растварачима су показали управо супротно и брзине су знатно мање. Да би се добијени резултати објаснили кроз ефекте растварача, константе брзине реакције (k) су корелисане тоталном солватохромном једначином облика: $\log k = \log k_0 + s\pi^* + a\alpha + b\beta$, где је π^* мера поларности растварача, β представља скалу базности растварача као акцептора протона у водоничној вези, а α представља скалу киселости растварача као донора протона у водоничној вези. Корелација кинетичких података је извршена методом мултипле линеарне регресије и разматрани су супротни ефекти апротичних растварача, као и разлика у утицају протичних и апротичних растварача на реакцију две испитиване киселине и DDM-а. Резултати приказани у овом раду за циклохекс-1-енилкарбонску и 2-метхил-циклохекс-1-енилкарбонску киселину су упоређени са кинетичким подацима

за бензоеву киселину, добијеним у истој хемијској реакцији под истим експеримен-
талним условима.

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