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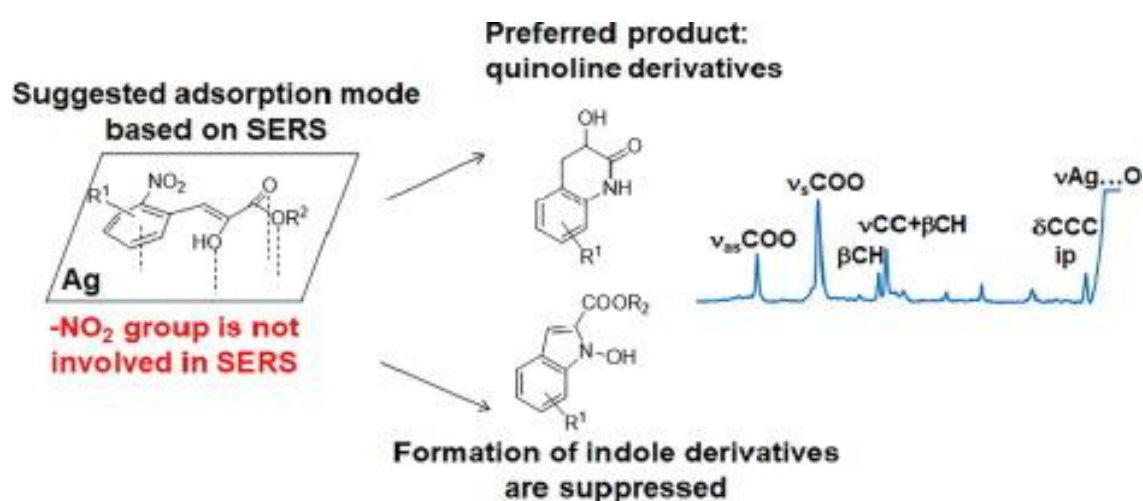
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### Highlights:

- Nitrophenylpyruvates were investigated in heterogeneous catalytic cascade reaction.
- The strength and geometry of their adsorption on Ag surface were studied by SERS.
- The enol form is predominant in solid and methanolic solutions of phenylpyruvates.
- SERS and calculations evidenced the adsorption through oxygen in acidic media.
- NO<sub>2</sub> is not involved in the adsorption: lack of indole formation has been explained.

### Graphical Abstract:



## Surface Enhanced Raman Spectroscopic (SERS) behavior of phenylpyruvates used in heterogeneous catalytic asymmetric cascade reaction

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### Abstract:

The strength and geometry of adsorption of substituted phenylpyruvates on silver surface was studied by means of surface enhanced Raman spectroscopy (SERS) using silver sol. 2'-nitrophenylpyruvates were used as starting materials in a newly developed heterogeneous catalytic asymmetric cascade reaction to produce substituted quinoline derivatives. Substituents on the aromatic ring of the starting materials had significant influence on the yield of the desired quinoline derivatives. Product selectivity of the transformation of nitrophenylpyruvates were enhanced by the acid added. The geometry and the strength of the adsorption are assumed to play an important role in the outcome of this reaction, so we have tried to find correlation between the structure of adsorbed phenylpyruvates and their catalytic performance. Based on the results of our spectroscopic measurements, the enol form is predominant in the series of phenylpyruvates in solid form and methanol solutions. Stronger adsorption of phenylpyruvates in acidic media through oxygen atoms was indicated by the increased enhancement in the SERS spectrum. The nitro group of 2'-nitrophenylpyruvates has no direct role in the adsorption on Ag surface. This observation has explained why the hydrogenation of the keto group (presumably via the enol form) occurs preferentially and why the formation of the undesired indole derivatives requiring reduction of the nitro group is suppressed. The SERS behavior has helped to get a closer look on the first step of adsorption of starting materials contributing to a better understanding of the cascade reaction studied, thus providing a better flexibility in catalyst design.

Keywords: SERS; 2'-nitrophenylpyruvates; ethyl 3-phenylpyruvate; *p*-nitrothiophenol; *p*-nitrophenol; adsorption geometry

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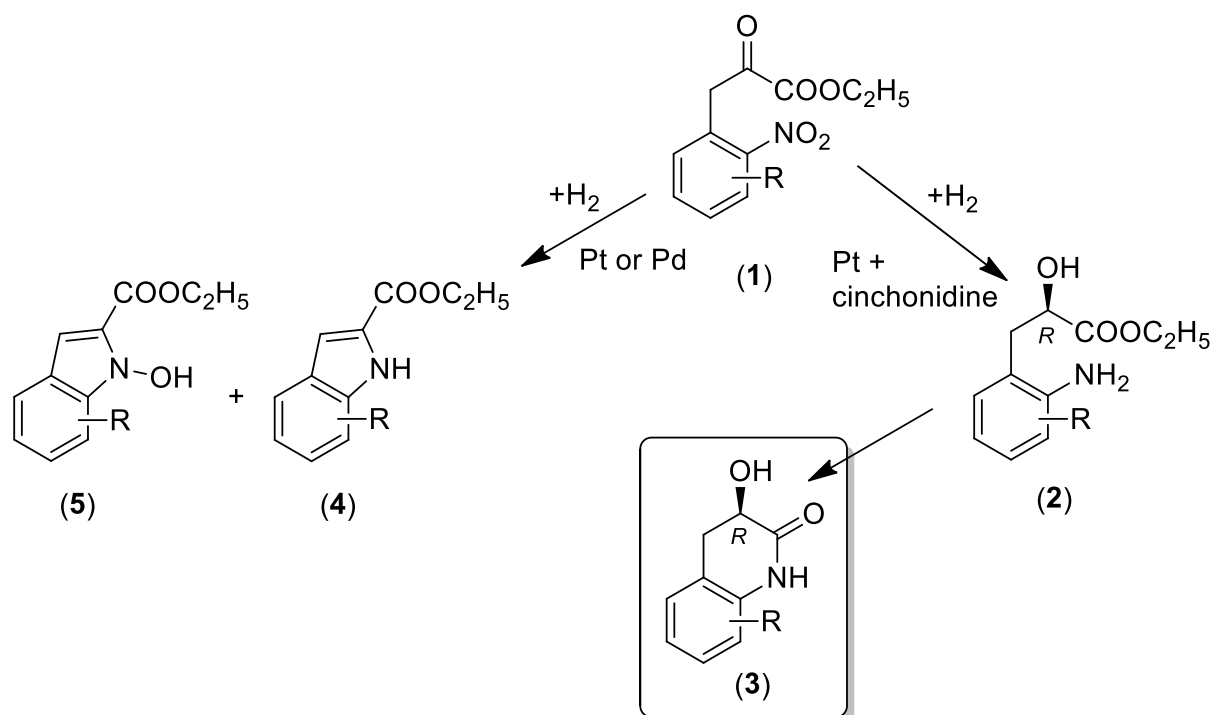
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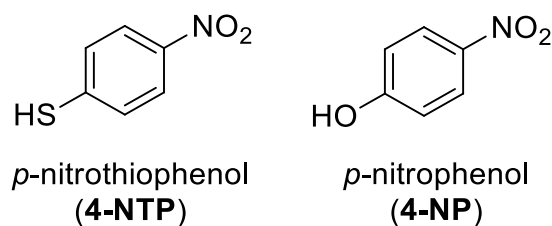
## 1. Introduction

Optically pure partially saturated quinoline derivatives are important intermediates in the preparation of natural products and pharmaceuticals [1]. Recently, optically enriched 3-hydroxy-3,4-dihydroquinolin-2(1*H*)-one derivatives have been successfully prepared by a newly developed heterogeneous catalytic asymmetric cascade reaction over supported Pt catalysts in the presence of H<sub>2</sub> and cinchona alkaloid chiral modifiers (Fig.1) [2,3]. Cascade reactions, also known as domino reactions or tandem reactions, are chemical processes in which at least two consecutive steps occur, therefore, incorporate multiple bond-forming events carried out in one-pot manner. Furthermore, isolation of intermediates is not required in cascade reactions, as each reaction composing the sequence occurs spontaneously. The starting materials of our cascade reaction are the 2'-nitrophenylpyruvates. The transformation of nitrophenylpyruvates follows two different pathways: one with formation of indole derivatives, another with formation of the desired quinoline derivatives [3]. The composition of the product mixture strongly depends on the reaction conditions as type and amount of catalyst and cinchona alkaloid chiral template, reaction temperature, H<sub>2</sub> pressure, pH of the solvent, etc. [3]. Substituents on the aromatic ring of the starting material also have significant influence on the yield of the desired quinoline derivative [3]. Obviously, the substituents can guide the geometry and the strength of the adsorption of these phenylpyruvates. Despite the fact that the geometry and the strength of the adsorption are believed to play important role in the outcome of this heterogeneous catalytic reaction, these have not been studied in details.

The Surface Enhanced Raman Spectroscopy (SERS) is a useful tool to get the fingerprint of the studied compounds [4,5], to obtain information about the orientation of adsorbed molecules [6-10], the changes in their chemical bonds [11,12], and the formation of new chemical bonds between the adsorbed molecules and the metal surface [13,14]. Our aim was to get information about the adsorption geometry (tilted or flat) of a series of phenylpyruvates by means of SERS method using silver sol. As the product selectivity of the transformation of nitrophenylpyruvates depends strongly on the added acid [3] we tried to figure it out how the acidic pH influences the behavior of our probe molecules. We made attempt to find correlation between the structure of adsorbed phenylpyruvates and their catalytic performance. In this study, *p*-nitrothiophenol (4-NTP) and *p*-nitrophenol (4-NP) (Fig.2) were used as reference probe molecules. Molecular modelling was used to facilitate the interpretation of the results obtained.



**Figure 1:** Possible pathways in the heterogeneous asymmetric cascade reaction of 2'-nitrophenylpyruvates. (1) substituted 2'-nitrophenylpyruvate (starting material); (2) substituted 2'-aminophenyl-hydroxyester (intermediar); (3) 3-hydroxy-3,4-dihydroquinolin-2(1H)-one (desired product); (4,5) indole derivatives (side products)

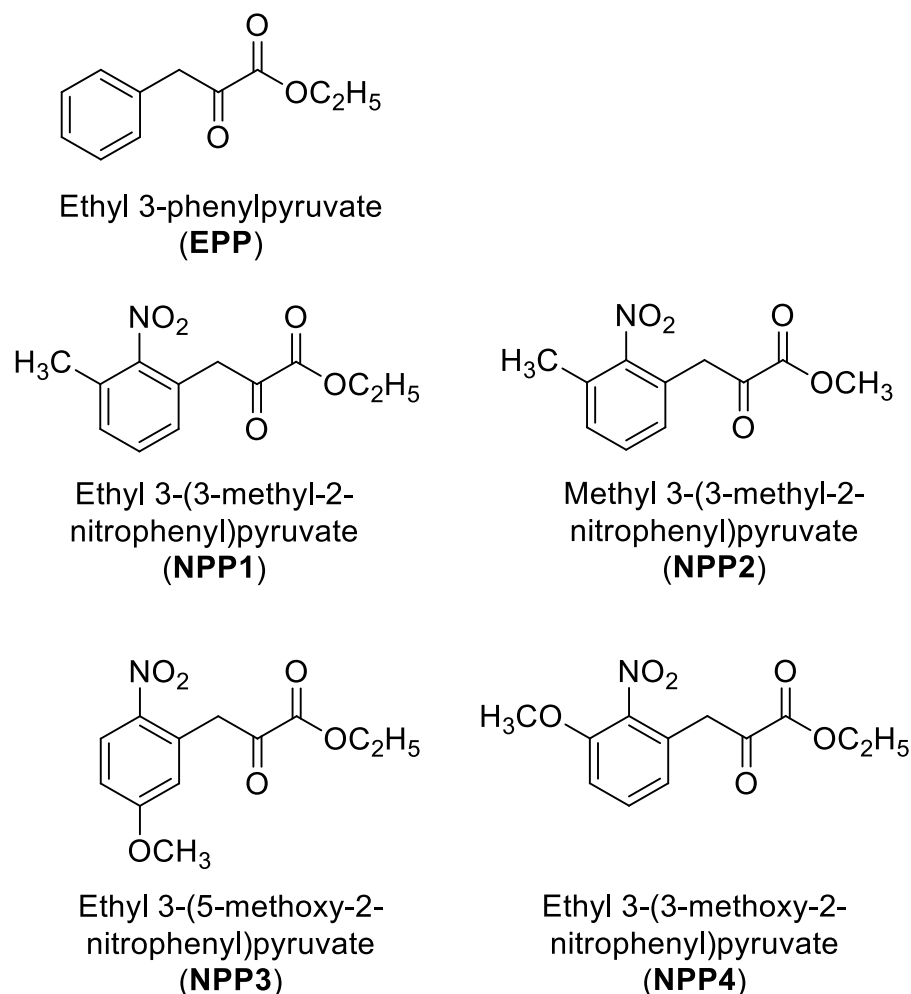


**Figure 2:** Probe molecules as references

## 2. Experimental

### 2.1 Materials

NaNO<sub>3</sub> (Reanal), *p*-nitrothiophenol (4-NTP), *p*-nitrophenol (4-NP) (Merck) were used as received. Ethyl 3-phenylpyruvate was prepared by esterification of phenylpyruvic acid (Sigma-Aldrich) as described previously [2]. 2'-nitrophenylpyruvic acid, 2-nitrotoluene derivatives, diethyl oxalate and potassium *tert*-butoxide used for the preparation of ethyl 2'-nitrophenylpyruvates substituted in various positions were purchased from Sigma-Aldrich. The substituted 2'-nitrophenylpyruvates were prepared according to literature [15]. Phenylpyruvates studied in this work and their abbreviations are shown in Fig.3.



**Figure 3:** Phenylpyruvates and their abbreviations

The Ag nanoparticles were prepared by using Lee and Meisel's method [16] often used in SERS investigations to synthesize silver substrates [17-19]. Briefly, 0.09 g AgNO<sub>3</sub> was dissolved in 500 cm<sup>3</sup> double distilled water, the solution was boiled and 10 ml 1% trisodium-citrate aqueous solution was added dropwise into the boiling solution accompanied by vigorous stirring. Boiling was continued for 10 more minutes. Finally, a greenish slightly grey solution was obtained. The silver sol was used after a week of ageing time.

Detailed characterization by UV-Vis spectroscopy and transmission electron microscopy (TEM) of the as-prepared silver sol is described in our previous paper [10]. In short, polydisperse silver particles with cca. 10 nm diameter are formed, exhibiting surface plasmon resonance (SPR) absorbance peak at 430 nm. By addition of NaNO<sub>3</sub>, the intensity of SPR absorbance decreases and a new shoulder at 720 nm appears indicating a partial aggregation of the colloid (corroborated also by TEM picture).

## 2.2 Spectroscopic measurements

Raman and SERS spectra were recorded with a Bio-Rad (Digilab) dedicated FT-Raman spectrometer equipped with a Spectra-Physics Nd-YAG-laser (1064 nm) and high sensitivity liquid-N<sub>2</sub> cooled Ge detector. The laser power used was about 400 mW at the samples. The resolution of the Raman instrument was ca. 4 cm<sup>-1</sup> and a backscattered geometry was used. For each spectrum 256 individual spectra were averaged.

SERS spectra of reference probe molecules and phenylpyruvates were recorded in both, methanol and acidified methanol solution. The methanol solutions of probe molecules were

acidified by 37% HCl solution to achieve acid concentration approximately 2M. Concentration of probe molecules was  $4 \times 10^{-2}$  M, the final concentration in colloidal solution was  $9 \times 10^{-3}$  M. Similarly to the method of Sanchez et al. [20], in the preparation of SERS sample 200  $\mu$ l solution of phenylpyruvates was added to 600  $\mu$ l silver colloid, then 80  $\mu$ l of aqueous solution of  $\text{NaNO}_3$  ( $5 \times 10^{-1}$  M) was added into the mixture, SERS spectra were recorded after 5 min standing time.

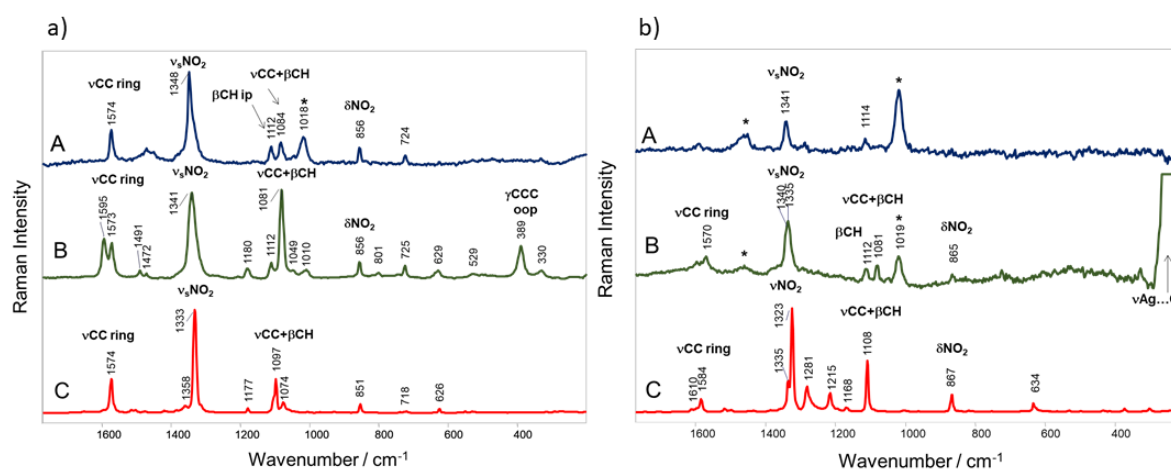
### 2.3 Computational method

We have performed a goal oriented computer simulation to estimate the equilibrium geometries of EPP molecule and its derivatives using the Spartan'06 [21] and the Gaussian [22] software package for *ab initio* (density functional (DFT)) calculations. Equilibrium geometries, energies, as well as frequencies (to model Raman spectra) for keto and enol form of phenylpyruvates was estimated using the B3LYP/6-31+G(d,p) level of theory [21,23]. For simulated Raman spectra scaling equations [24] were used. To model SERS spectra, DFT spectra relative to molecule - Ag complex and molecule - Ag surface models were also calculated. For the latter, SDD basis set with pseudopotential was applied.

## 3. Results and discussion

### 3.1 Spectroscopic behavior of the reference probe molecules

The Raman spectra of solid 4-NTP (Fig.4a) are in accordance with the literature data [25]. The strongest band at  $1333 \text{ cm}^{-1}$  can be attributed to the symmetric stretching vibration of the  $\text{NO}_2$  group, as well as the medium intensity bands at  $1574$  and  $1097 \text{ cm}^{-1}$  are assigned to ring C-C stretching and to C-C stretching coupled with CH in-plane deformation vibrations, respectively.



**Figure 4:** Spectroscopic behavior of a) 4-nitrothiophenol (4-NTP) and b) 4-nitrophenol (4-NP) reference probe molecules: (A) SERS spectrum in methanol; (B) SERS spectrum in acidified methanol; (C) Raman spectrum of solid. Bands denoted with \* belong to methanol

The SERS spectrum of 4-NTP/methanol (Fig.4a) exhibits a decent correlation with its normal Raman spectrum. The bands related to benzene ring mode appear nearly at the same position. The S-H stretching band (observed at  $2553 \text{ cm}^{-1}$  in normal Raman spectrum of solid 4-NTP, not shown) is absent as a consequence of the strong adsorption of 4-NTP as thiolate [26,27] assuming a strong charge transfer (CT) enhancement between the probe molecule and Ag surface. The enhancement of the in-plane deformation,  $\beta\text{CH}$  (14b) at  $1112 \text{ cm}^{-1}$  determines a mainly perpendicular orientation of the benzene ring towards Ag surface. However, the shift of  $\nu_s\text{NO}_2$  upon adsorption from  $1333$  to  $1348 \text{ cm}^{-1}$  implies that the charge transfer (CT) expands

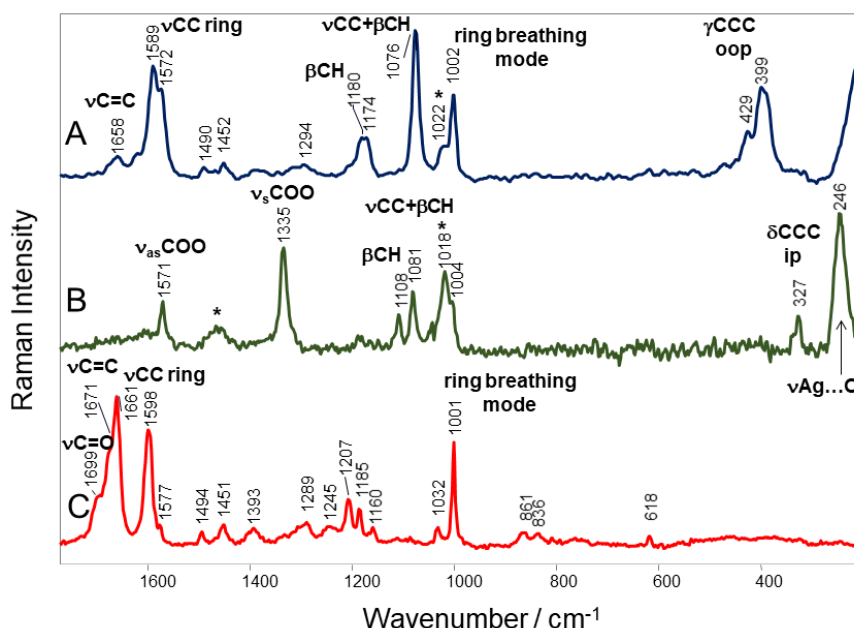
through the benzene involving the nitro group in para substitution, too. If the methanol solution of 4-NTP is acidified (Fig.4) a strong enhancement of the band at  $1081\text{ cm}^{-1}$  belonging to the breathing mode of benzene ring ( $\nu_{\text{CCX}}$  (18a)) coupled with  $\nu_{\text{CS}}$  suggests a strong CT between Ag surface and probe molecule with a perpendicular positioning of the latter. However, some additional bands appear at  $1595$ ,  $1180$ ,  $801$ ,  $629$  and  $389\text{ cm}^{-1}$  which can be assigned to benzene ring vibrations as ring stretching,  $\nu_{\text{CC}}$  (8a); in-plane CH deformation,  $\beta_{\text{CH}}$  (9b); out-of-plane CH deformation,  $\gamma_{\text{CH}}$  (11); in-plane ring deformation,  $\delta_{\text{CCC}}$  (6b) and out-of-plane ring deformation,  $\gamma_{\text{CCC}}$  (16a), respectively. (The Whiffen notation [28] of benzene ring modes was used and the assignments of vibrational forms ( $\nu$ ,  $\beta$ ,  $\delta$  and  $\gamma$ ) are taken from Ref. [29,30]). Since the out-of-plane deformations, especially the ring skeleton  $\gamma_{\text{CCC}}$  are well enhanced, we can conclude that there is strong  $\pi$ - coordination between the benzene ring and Ag surface with a parallel orientation [10]. Additionally, the weak band at  $529\text{ cm}^{-1}$  can be assigned to  $\nu_{\text{S-S}}$  indicating the formation of disulfide bond [31]. It seems plausible that under acidic conditions part of 4-NTP are dimerized, forming disulfides. Presumably, these dimers lay parallel to the Ag surface producing EM-enhanced SERS spectrum. However, since the S-S stretching is usually a very strong band in Raman spectrum, probably a small fragment of 4-NTP is dimerized only.

Due to the formation of the disulfide bond in acidic media in case of 4-NTP, the 4-NP seems to be a more adequate probe molecule (Fig.4b). Using methanolic solution of 4-NP, however, only very weak enhancement was observed with bands at  $1341\text{ cm}^{-1}$  ( $\nu_{\text{s}}\text{NO}_2$ ) and  $1114\text{ cm}^{-1}$  ( $\beta_{\text{CH}}$ , i.p.), the latter suggests a perpendicularly oriented benzene ring on the Ag surface. For acidified methanol solution, a stronger coordination by the  $-\text{OH}$  group was observed. The enhanced ring vibrations ( $\nu_{\text{CC}}$ ,  $\beta_{\text{CH}}$  and  $\nu_{\text{CC}}+\beta_{\text{CH}}$  at  $1570$ ,  $1112$  and  $1081\text{ cm}^{-1}$ , respectively) indicate a perpendicular arrangement of 4-NP. The very strong and broad band around  $230\text{ cm}^{-1}$ , which may be due to the strongly enhanced  $\nu_{\text{Ag}\cdots\text{O}}$  stretching vibration [32,33] is challenging.

### 3.2 Spectroscopic behavior of phenylpyruvates

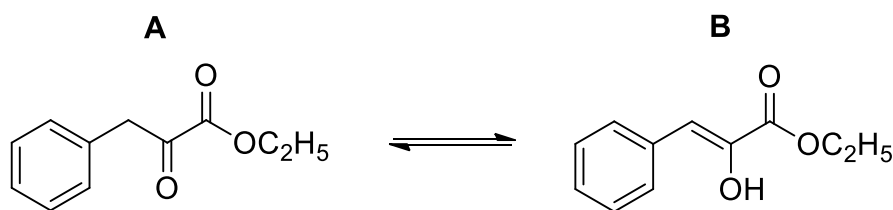
#### 3.2.1 Ethyl 3-phenylpyruvate

EPP can be considered as a skeleton of 2-nitrophenylpyruvate derivatives, so studying its spectroscopic behavior is useful. The Raman spectrum of solid EPP (Fig.5) exhibits strong bands at  $1598$  and  $1001\text{ cm}^{-1}$  corresponding to the phenyl ring vibration modes (ring  $\nu_{\text{C-C}}$  and ring breathing mode, respectively). The strongest band at  $1661\text{ cm}^{-1}$  can be assigned to the  $\text{C}=\text{C}$  stretching band.



**Figure 5:** Spectroscopic behavior of ethyl 3-phenylpyruvate (EPP): (A) SERS spectrum in methanol; (B) SERS spectrum in acidified methanol; (C) Raman spectrum of solid. Bands denoted with \* belong to methanol

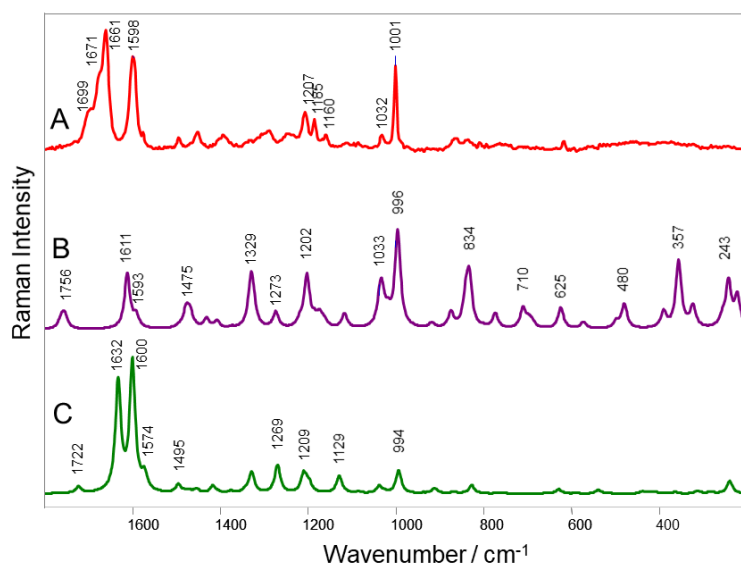
It is known that phenylpyruvates, analogously to pyruvic acid, might exist in keto and enol forms [34], see Fig.6.



**Figure 6:** Possible tautomerism of EPP. A: keto form; B: enol form

Based on  $^1\text{H}$  and  $^{13}\text{C}$  NMR, UV, IR and Raman spectroscopy techniques, the prevalence of enol form in solid state and in organic solutions (e.g. methanol) has been demonstrated [35,36]. In agreement with the study of Hanai et al [36], the band of EPP at  $1661\text{ cm}^{-1}$  indicates the enol form. However, the weak shoulder at  $1699\text{ cm}^{-1}$  might belong to keto  $\text{C}=\text{O}$  indicating the presence of only a trace amount of keto form. The stronger shoulder at  $1671\text{ cm}^{-1}$  can be assigned to the  $\text{C}=\text{O}$  band of ester groups. Comparison with simulated spectra via *ab initio* calculations using density functional theory (DFT) method (B3LYP with 6-31 G(d,p) basis set, along with scaled frequency with quadratic scaling equation) the dominance of enol form in solid EPP is also consolidated (Fig.7).

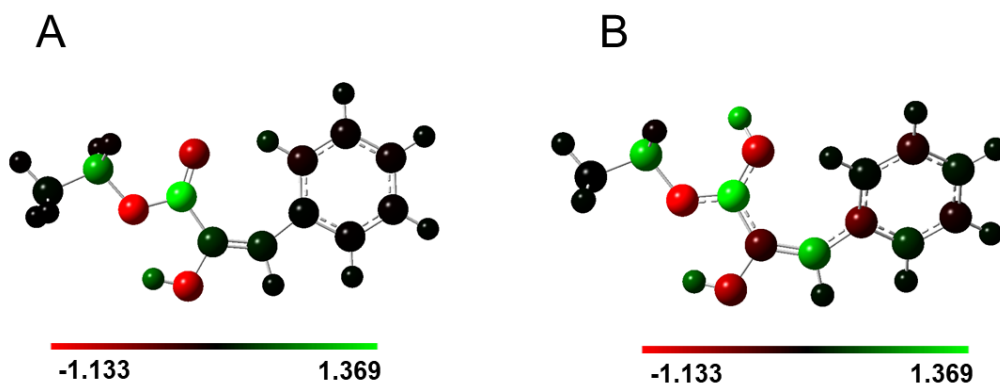




**Figure 7:** Experimental Raman spectrum of solid EPP (A) and calculated Raman spectra of its keto (B) and enol (C) form

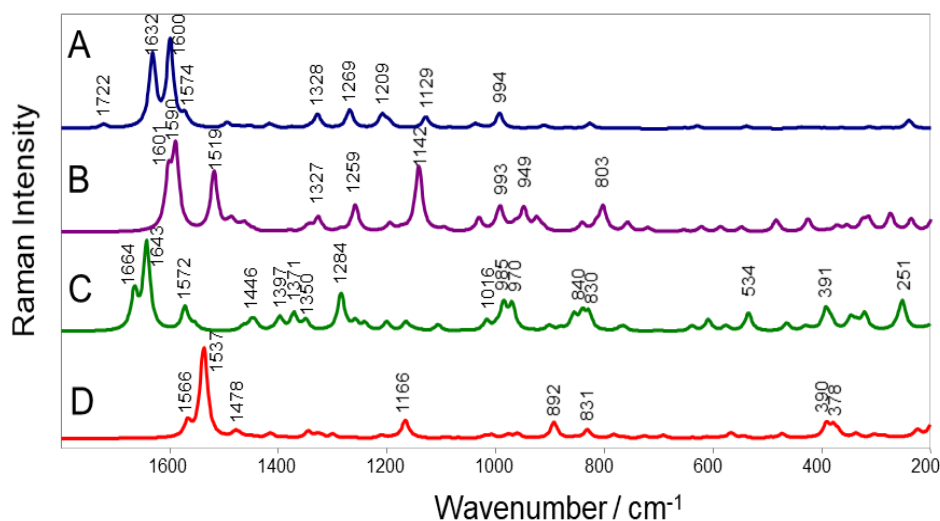
In the SERS spectrum of EPP in methanol (Fig.5) the strong enhancement of ring  $\nu$ CC (8a),  $\nu$ CCX (18a) and  $\beta$ CH (15) bands at 1589, 1076 and 1180  $\text{cm}^{-1}$ , respectively, suggests a perpendicular position of the benzene ring towards the Ag surface, similarly to the 4-NTP reference molecule (Fig.4a). The intense bands at 1002 and 399  $\text{cm}^{-1}$ , however, corresponding to ring breathing mode (1) and to the  $\gamma$ CCC (16a) out-of-plane deformation of the ring skeleton, respectively, indicate a  $\pi$ -coordination between the parallel benzene ring and the Ag surface. The presence of  $\nu$ C=C at 1658  $\text{cm}^{-1}$  in the SERS spectrum suggests that the C=C is also involved in coordination.

By acidification of the methanol solution, however, the SERS feature of the EPP is completely altered (Fig.5). The enhancement of the bands related to the phenyl ring ( $\nu$ CCX, notated as  $\nu$ CC +  $\beta$ CH, also) (18a) at 1081  $\text{cm}^{-1}$  and the ring breathing mode (1) at 1004  $\text{cm}^{-1}$  are suppressed. Simultaneously, new strong bands appear at 1571, 1335 and 246  $\text{cm}^{-1}$ . The latter belongs to the  $\nu$ Ag $\cdots$ O vibration as experienced also in the case of the 4-NP reference molecule under identical experimental conditions. It seems reasonable, that acidification via protonation leads to activation of the enolic -OH group to more susceptible adsorption. More importantly, the new SERS bands at 1571 and 1335  $\text{cm}^{-1}$  can be assigned to antisymmetric and symmetric stretch of -(C=O)O (more exactly COO) moiety [10] confirming the adsorption of EPP on the Ag surface through carboxylic O atoms. Indeed, atomic charge distribution calculated on the base of atomic polar tensors (APT) [37] indicates a strong conjugation of C=C double bond with the enol-keto moiety including also the etheric oxygen atom (Fig.8). The stronger charge separation for protonated form, due to van der Waals forces, might cause a stronger adsorption towards metal (Ag) surface.



**Figure 8:** Optimal geometry of EPP enol (A) and protonated enol (B) form displaying the atomic polar tensors (APT) based atomic charge distribution by colored atoms. In the protonated EPP a strong 'backbone' conjugation is clearly visible

This strong conjugation alters the spectral feature, too, as revealed by the theoretical Raman spectra (Fig.9, Table 1). Moreover, to model the SERS spectrum, DFT spectra relative to the EPP-Ag complex and EPP-Ag surface model, respectively were also calculated [38, 39]. The Ag surface was approximated by an assembly of 7 Ag atoms. For the latter, SDD basis set with pseudopotential was used.



**Figure 9:** Simulated spectra of EPP molecules without adjusted pH (A), protonated EPP (B) and simulated EPP-Ag complex (C) and EPP-Ag surface model (D)

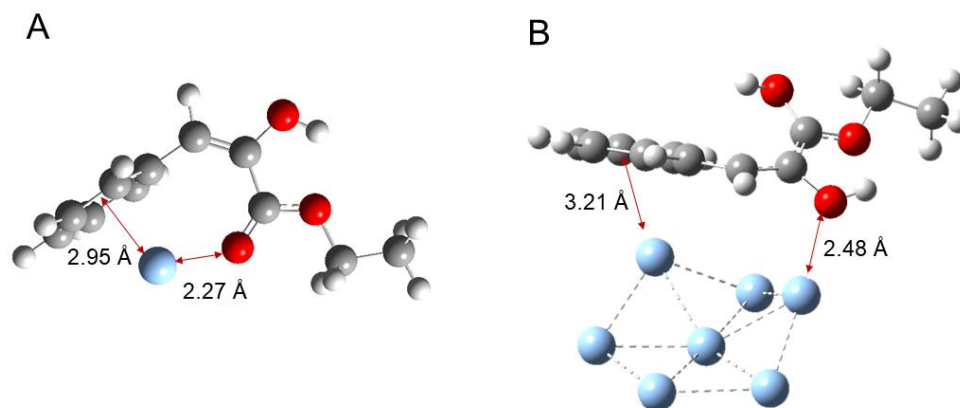
**Table 1** Band positions ( $\text{cm}^{-1}$ ) and possible assignment of simulated Raman spectra without pH adjustment, in protonated form and of simulated EPP-Ag complex. Notations and assignments of benzene ring vibrations are taken from Ref. [29, 40].

<b>EPP</b>	<b>protonated EPP</b>	<b>protonated EPP-Ag complex</b>	<b>protonated EPP-Ag surface (Ag<sub>7</sub>)</b>	<b>Band assignment</b>
1722 vw				$\nu\text{C}=\text{O}$
1633 s				$\nu\text{CC}$ ring asym
	1601 s	1592 m		$\nu\text{C}=\text{C}$ asym + $\nu\text{CC}$ ring asym
1600 s	1590 s			$\nu\text{C}=\text{C}$
1574 w		1572 m	1566 m	$\nu\text{CC}$ ring sym+ $\nu\text{C}=\text{C}$
			1537 s	$\nu\text{CC}$ ring asym+ $\nu\text{C}=\text{C}$ + $\nu\text{C}-\text{O}$ <b>conjugated</b>
	1519 s			$\nu\text{CC}$ ring sym+ $\nu\text{C}=\text{C}$ + $\nu\text{C}-\text{O}$ <b>conjugated</b>
			1478 w	$\text{CH}_2, \text{CH}_3$ deform + $\delta\text{C}-\text{O}-\text{H}$
		1446 w		$\text{CH}_2, \text{CH}_3$ deform
1328 w	1327 w			$\nu\text{CC}$ ring + $\delta\text{C}-\text{O}-\text{H}$
		1397 w 1371 w 1350 w		$\delta\text{C}-\text{O}-\text{H}$ + $\delta\text{CH}_2/\text{CH}_3$
1269 m		1284 m		
	1259 m			<b><math>\delta\text{C}-\text{O}-\text{H}</math></b>
1209 m				$\text{CH}_2, \text{CH}_3$ deform
			1166 m	<b><math>\delta\text{C}-\text{O}-\text{H}</math> conjugated</b>
	1142 s			<b><math>\delta\text{C}-\text{O}-\text{C}</math> conjugated</b>
1129 m				
994 m	993 m	1016 w 985 m 970 m		$\delta\text{CH}$ ring o.o.p.
	949 m			$\delta\text{CH}$ o.o.p. sym
			892 m	
		840 m	831 m	$\delta\text{CH}$ o.o.p. asym
	803 m			$\delta\text{C}=\text{C}$ + $\delta\text{CCX}$ conjugated
		534 m		$\delta\text{CCX}$ i.p. ring deformation
		391 m	390 m	$\delta\text{CCC}$ i.p. + $\delta\text{OH}$
			378 m	$\delta\text{CH}$ o.o.p. asym + $\delta\text{OH}$ + $\nu\text{Ag}-\text{O}$
		251 m		<b><math>\nu\text{Ag}-\text{O}</math></b>

Abbreviations:  $\nu$ =stretching vibration;  $\delta$ =deformation vibration; s=strong; m=medium; w=weak; vw=very weak; sym=symmetric; asym=antisymmetric; i.p.=in-plane; o.o.p.=out-of-plane

Comparing the columns in Table 1, the nature of the new bands of protonated EPP can be explained. The medium and strong bands at 1519, 1259 and 1142  $\text{cm}^{-1}$  belong to the  $\nu\text{C-O}$  and  $\delta\text{C-O-H}$  vibrations of the strongly conjugated keto-enol moiety. It seems plausible that this conjugated part is capable to interact with Ag surface leading to a remarkable SERS phenomenon.

In case of simulated EPP-Ag complex, a new band shows up around 251  $\text{cm}^{-1}$ , a further evidence that the strong band around 250  $\text{cm}^{-1}$  in the SERS spectra might origin from the  $\nu\text{Ag}\dots\text{O}$  interaction (Fig.9). It is interesting to note, that optimal geometry obtained by DFT calculations for EPP-Ag complex (Fig.10A) reveals that the EPP suggesting, that both the  $\pi$  system of the aromatic ring and the lone pair electrons of the oxygen has affinity towards the Ag atom, surrounds the Ag atom. Indeed, in the case of a more complex model mimicking Ag surface via assembly of seven Ag atoms the EPP overlies on the Ag surface assuring a preferable adsorption for both phenyl ring and the conjugated keto-enol moiety (Fig.10B). The spectrum of EPP-Ag<sub>7</sub> complex (Fig.9) is dominated by vibrational bands related to oxygen moieties, namely at 1537  $\text{cm}^{-1}$  (conjugated C-O stretchings), 1166  $\text{cm}^{-1}$  (bendings of C-O-H parts) and 378  $\text{cm}^{-1}$  (a mixed band of phenyl CH, OH bendings but with a significant contribution of Ag-O stretching). We have to note, that even for EPP-Ag<sub>7</sub> complex mimicking molecule – surface interaction, the Ag–O distance is 2.48Å. Neutron scattering study on an aqueous solution of silver(I) perchlorate reported on Ag–O bond distance of 2.42Å [41], so the strong enhancement of Ag-O stretching seems plausible in the protonated SERS spectra.

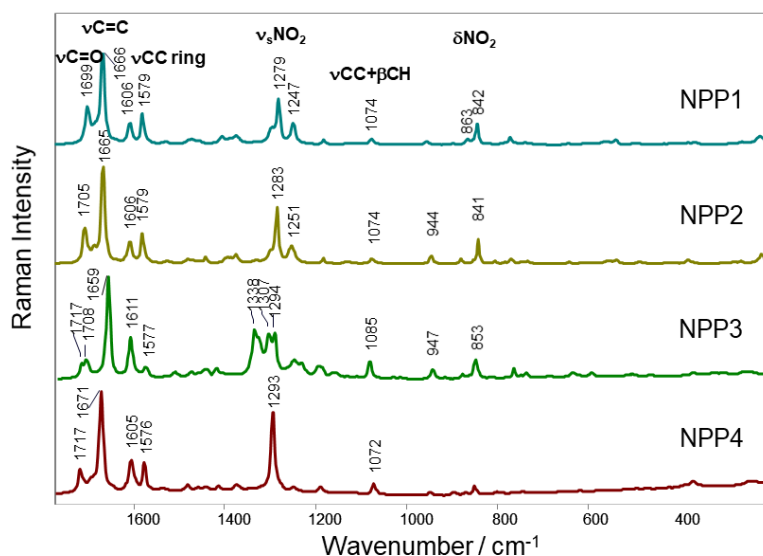


**Figure 10:** Protonated EPP-Ag (A) and protonated EPP-Ag<sub>7</sub> (B) complex optimized structures; colour code: red = oxygen, gray = carbon, white = hydrogen, blue = silver. For EPP-Ag complex Ag was taken with positive charge, while in case of Ag<sub>7</sub> assembly, SDD basis set with pseudopotential was applied

### 3.2.2 Nitro-phenylpyruvates

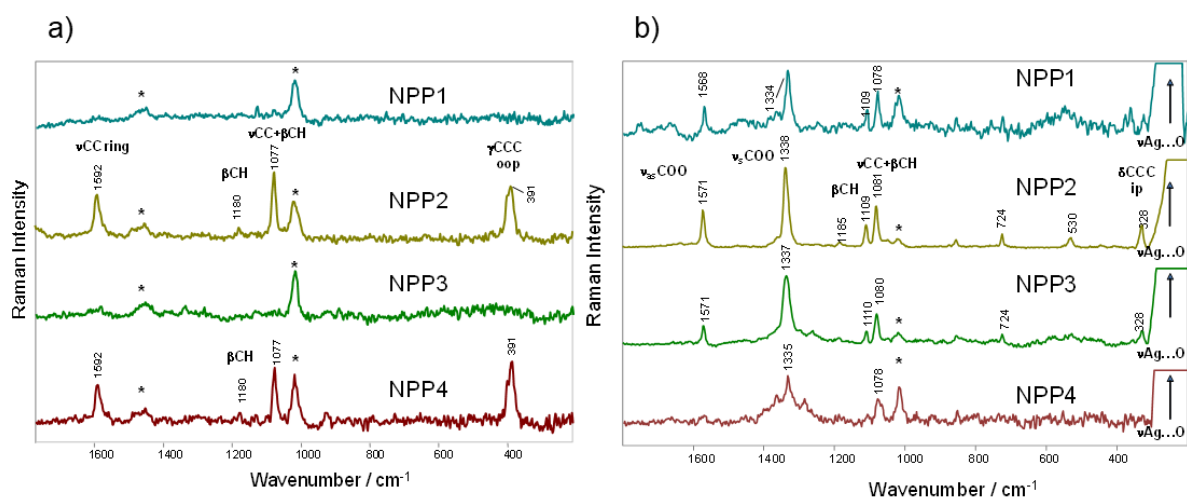
The Raman spectra of the solid NPP samples show typical bands of substituted phenyl ring ( $\nu\text{CC}$  and  $\nu\text{CCX}$ ) around 1606, 1579, and 1074  $\text{cm}^{-1}$ , respectively (Fig.11). The spectra are dominated by the strong  $\nu\text{C=C}$  stretching at 1666  $\text{cm}^{-1}$  confirming the prevalence of the enol form of the 2'-nitrophenylpyruvates. The medium bands between 1720-1699  $\text{cm}^{-1}$  belong to the C=O stretching of ester carbonyl. We have to mention that an overlap with the keto carbonyl band might occur, so the presence of a small amount of keto form cannot be excluded. Medium intense bands of symmetric stretching of  $\text{NO}_2$  around 1280  $\text{cm}^{-1}$  ( $\nu_s\text{NO}_2$ ) and a weak

$\text{NO}_2$  deformation (scissoring) around  $860\text{--}840\text{ cm}^{-1}$  ( $\delta\text{NO}_2$ ) are also present in the Raman spectra of the solid probe molecules.



**Figure 11:** Raman spectra of solid 2'-nitrophenylpyruvates

Taking the SERS spectra after adding Ag sol to the methanol dissolved nitrophenylpyruvates, definite SERS enhancements were obtained only in case of NPP2 and NPP4 (Fig.12a).



**Figure 12:** SERS spectra of 2'-nitrophenylpyruvate probe molecules in a) methanol and b) in low pH methanol solution. Bands denoted with \* belong to methanol

In both cases the  $\nu\text{CC}$  ring vibration at  $1592\text{ cm}^{-1}$ , the  $\nu\text{CC}$  coupled with  $\beta\text{CH}$  at  $1077\text{ cm}^{-1}$  and the out-of-plane  $\gamma\text{CCC}$  around  $391\text{ cm}^{-1}$  are enhanced similarly to the EPP reference. Interestingly, indication of  $\text{NO}_2$  enhancement was not observed in case of any nitrophenylpyruvate molecule. The lack of bands belonging to  $\text{NO}_2$  vibrations indicates that the  $\text{NO}_2$  group is not involved in the enhancement. The strong feature of ring out-of-plane deformation around  $391\text{ cm}^{-1}$  in case of NPP2 and NPP4 suggests that the benzene ring is in parallel position to the Ag surface (Fig.12a).

By lowering the pH (adding HCl to methanol solution) higher enhancement was obtained in case of NPP1, NPP2, NPP3 and NPP4 (Fig. 12b) confirmed by the relatively weaker methanol bands (marked with \*).

The SERS spectra, again, is similar to that obtained for EPP under similar conditions. The SERS bands of O-related groups ( $\nu_{as}COO$  at  $1571\text{ cm}^{-1}$  and  $\nu_sCOO$  at  $1334\text{ cm}^{-1}$ ) and the strong  $\nu_{Ag...O}$  (at  $246\text{ cm}^{-1}$ ) confirm the strong adsorption of probe molecules on Ag surface towards O containing moieties. We have to note, that the bands and  $1571\text{ cm}^{-1}$  and  $1334\text{ cm}^{-1}$  were assigned to phenyl ring CC stretching and  $NO_2$  stretching, respectively in Section 3.1. for 4-NTP (Fig.4a). However, the lack of bands related to nitro groups in SERS spectra of EPP (positioned at around  $1300\text{ cm}^{-1}$  for solid NPPs) and the strong resemblance with EPP SERS spectra recorded under same conditions confirm to assign these bands to oxygen-moieties.

SERS bands of NPPs are summarized in Tables 2-3.

**Table 2**

Band positions ( $\text{cm}^{-1}$ ) and their possible assignment in SERS spectra of phenylpyruvates in methanol solutions. Notations and assignments of benzene ring vibrations are taken from Ref. [29,40].

EPP	NPP1	NPP2	NPP3	NPP4	Band assignment
1658 w	-		-		$\nu_{C=C}$
1589 s		1592 m		1592 m	$\nu_{CC}$ ring (8a)
1572 s, sh					
1490 w					$\beta_{CH} + \nu_{CC}$ (19b)
1452 w					$CH_2, CH_3$ deform
1180 m		1180 w		1180 w	$\beta_{CH}$ (15)
1174 m					
1076 s		1077 s		1077 s	$\nu_{CC} + \beta_{CH}$ (18a)
1002 m					ring breathing mode (1)
428 w, sh					$\gamma_{CCC}$ o.o.p.(16b)
399 m		391 s		388 s	$\gamma_{CCC}$ o.o.p. (16a)

Abbreviations:  $\nu$ =stretching vibration;  $\beta$ =bending in-plane vibration;  $\gamma$ =bending out-of-plane vibration

**Table 3**

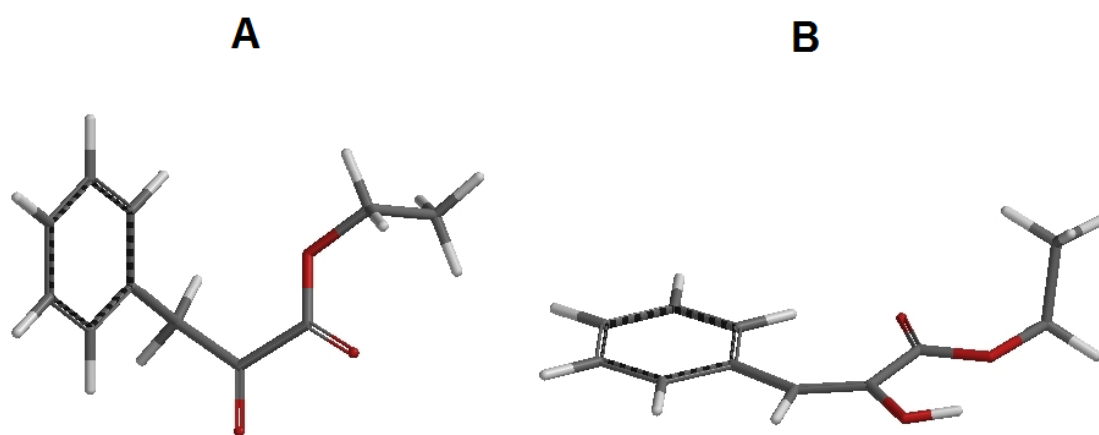
Band positions ( $\text{cm}^{-1}$ ) and their possible assignment in SERS spectra of phenylpyruvates in acidified methanol solutions. Notations and assignments of benzene ring vibrations are taken from Ref. [29,40].

EPP	NPP1	NPP2	NPP3	NPP4	Band assignment
1571 m	1568 w	1571 m	1571 w		$\nu_{\text{as}}\text{COO}$
1335 s	1334 m	1338 s	1337 m	1335 w	$\nu_{\text{s}}\text{COO}$
1108 m	1109 w	1109 m	1110 w		$\beta\text{CH}$
1081 m					$\nu\text{CCX}$
1004 m					ring breathing mode (1)
		855 w			$\gamma\text{CH}$ (11)
		724 w			$\delta\text{CCX}$ (12)
327 m		328 m	328 w		$\delta\text{CCC}$ i.p. (17b)
246 s, br	246 s, br	246 s, br	246 s, br	246 s, br	$\nu\text{Ag}\dots\text{O}$

Abbreviations:  $\nu$ =stretching vibration;  $\delta$ =bending vibration;  $\beta$ =bending in-plane vibration;  $\gamma$ =bending out-of-plane vibration

### 3.3 Relationships between calculated equilibrium geometries and spectroscopic behaviors

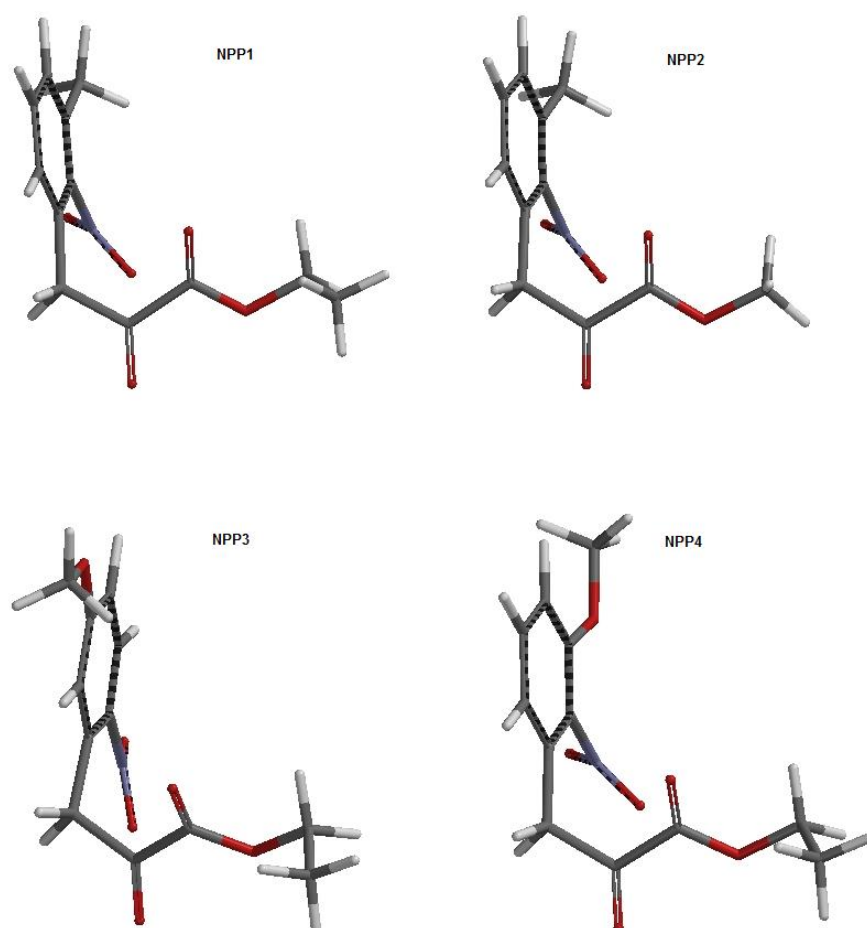
The calculated equilibrium EPP geometries are shown in Fig.13. According to the calculation, the keto form has a rigid U shape, whereas the enol form has a relatively flexible, twisted one. As the double bond and the ring are in one plane, the enol form is able to lay better on the surface than the keto form, and as a consequence, the enol form may provide a stronger adsorption. When the keto form is bonded through oxygen, the phenyl group might be perpendicular to the surface.



**Figure 13:** Equilibrium geometries of EPP calculated at B3LYP/6-31+G(d,p) [21] level of theory. A: keto form; B: enol form

Considering the calculated equilibrium geometries for the keto (Fig.13A) and enol (Fig.13B) form of EPP, it seems plausible that the EPP in enol form with more flexible molecular backbone might contribute to the  $\pi$ -coordination while the more rigid U-shaped keto form will prefer a perpendicularly oriented phenyl ring towards the Ag surface.

In the case of 2'-nitrophenylpyruvates, the equilibrium geometries of the keto form of different samples (Fig.14) are very similar. They have L shape and the benzene ring is almost perpendicular to the plane formed by the ketoester moiety. Despite the similar equilibrium geometries, the spectroscopic behavior of these samples are different. A possible explanation is that the keto form is not dominant although the presence of the keto form in solid state cannot be excluded based on solid Raman measurements. If we suppose, that the SERS enhancement in methanolic solution comes from the keto form, the lack of enhancement in the case of NPP1 might be in line with the steric inhibition of the ethyl group. However, NPP4 gives SERS signal in spite of its ethyl group. Consequently, if we assume the keto form to be dominant in the SERS spectra, nor the ring substituent nor the alcohol part of the ester have influence on it. By this reason we conclude that although the presence of the keto form cannot be ruled out, it is not the source of the SERS signal.



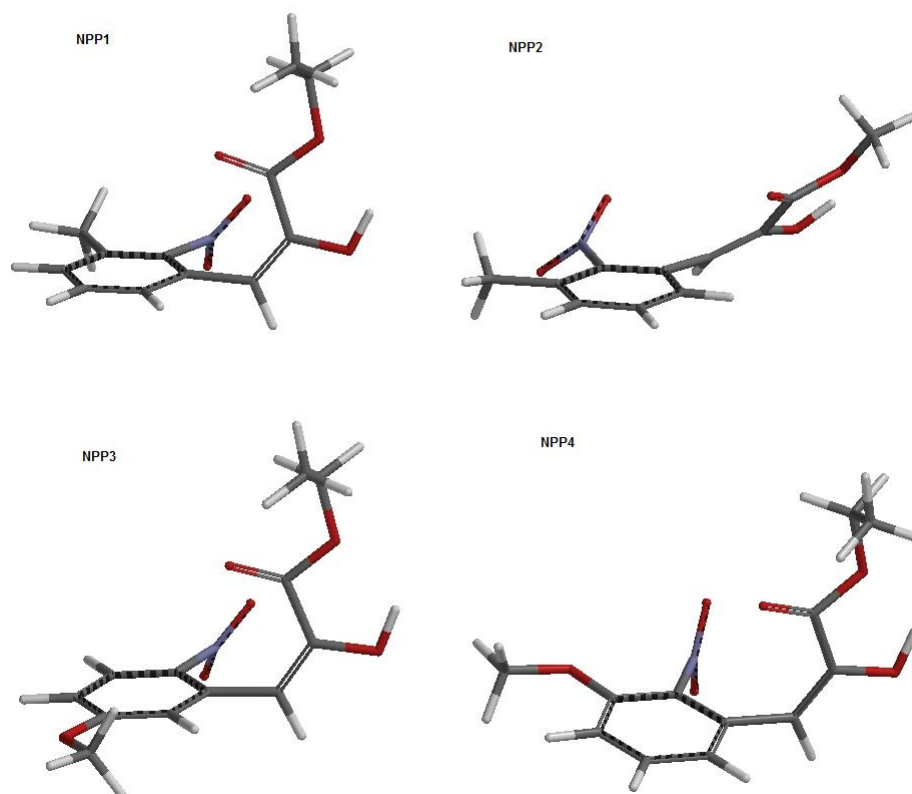
**Figure 14:** Equilibrium geometries of keto forms of 2'-nitrophenylpyruvates calculated at B3LYP/6-31+G(d,p) [21] level of theory

The calculated equilibrium geometries of the enol forms of the 2'-nitrophenylpyruvates seems to be quite different regarding the relative positions of the nitro group, the ester group and the angle between the plane of phenyl ring and plane of double bonds (Fig.15). The NPP2, having similar equilibrium geometry to EPP, was SERS active in methanol solution as the EPP. However, unlike EPP, sign of double bonding could not be observed in the SERS spectra of



NPP2 in methanol solution. As the presence of the nitro group may shift the charge distribution of the benzene ring (see calculated Mulliken charges in Fig.S1 in Supplementary Materials), it seems plausible that the conjugation between the C=C and the benzene ring is changed in NPPs, which may explain the lack of double bonding in the SERS signal. Consequently, the adsorption of ring-substituted phenylpyruvates and their SERS behavior are different from the unsubstituted ones.

At acidic pH values the strong adsorption on Ag surface through O atoms of EPP and NPPs is proved by the SERS bands related to ester carbonyls around 1571, 1333, 1108  $\text{cm}^{-1}$  and the strong band of Ag...O bonding at 246  $\text{cm}^{-1}$ . The bands related to benzene ring are also enhanced suggesting an approximately parallel position to Ag surface.



**Figure 15:** Equilibrium geometries of enol form of 2'-nitrophenylpyruvates calculated at B3LYP/6-31+G(d,p) [21] level of theory

### 3.4 Heterogeneous catalytic asymmetric cascade reaction of nitrophenylpyruvates in relation to our SERS experiments

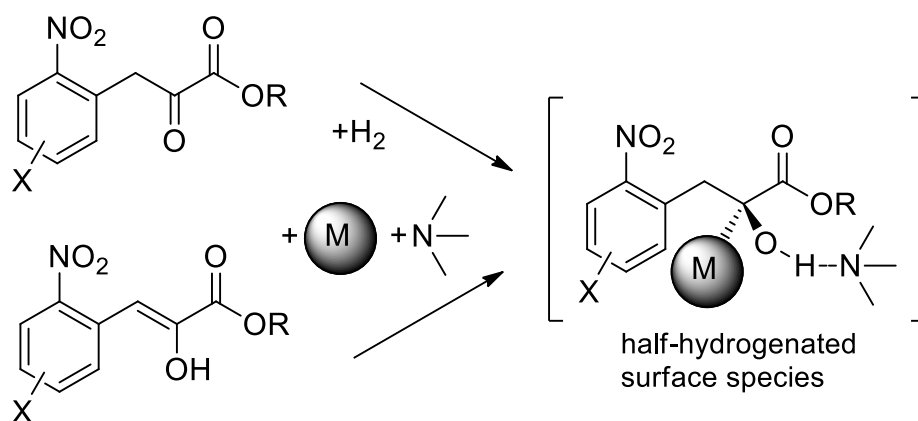
Based on the SERS spectra the strength of adsorption by O containing groups of the derivatives studied are  $\text{NPP2} > \text{NPP3} > \text{NPP1} > \text{NPP4}$ , indicating the effect of size and position of substituents on the phenyl ring on the adsorption strength. Although, at first glimpse these adsorption strengths cannot be correlated with the behavior of the compounds in the cascade reaction, one may observe that the effect of the size of the ester group on the adsorption strength is in accord with the outcome of the catalytic reactions [2].

We call the attention that the surface and electronic properties of silver nanoparticles differ from that of the real catalyst (e.g.  $\text{Pt}/\text{Al}_2\text{O}_3$ ). Furthermore, the strongly adsorbing cinchona alkaloid chiral template and the hydrogenated molecule co-exist on the surface during the asymmetric hydrogenation. It should also be noted that during the catalytic reaction the acidic medium is provided by the addition of acetic acid while during our SERS measurement hydrochlorid acid was added. Although this may distinct the case, acetic acid could not be used

to adjust the acidity due to bad overlapping in the spectra. In spite of these, certain correlations between the catalytic reactions and the adsorbed forms of starting materials indicated by our SERS study have been found.

The most important findings of the present SERS study are that the adsorption of EPP and its 2'-nitro-substituted derivatives on the metal surface are similar. Furthermore, the nitro group of nitrophenylpyruvates is not directly involved in the adsorption. This with the molecular geometries explain why the hydrogenation of the keto group happens probably via the enolic form, and the formation of the indole derivatives, which requires reduction of the nitro group, is suppressed. Under acidic conditions, the stronger adsorption by oxygen containing groups (demonstrated by SERS) leads to an even more pronounced difference between the two competitive reduction steps, i.e. between C=O hydrogenation and NO<sub>2</sub> group reduction [2]. Regarding the hydrogenation of the enol form, we recall that the asymmetric hydrogenation of the enol esters was successfully performed on Pt-CD and Pd-CD catalyst systems [42]. Moreover, both the enol and keto form may lead to similar half-hydrogenated surface species in the presence of protonated tertiary amine modifiers, such as the cinchona alkaloids, as illustrated in Fig. 16 [43].

The lack of the adsorption of the NO<sub>2</sub> group also implies that during the enantioselective cascade reaction, the higher enantioselectivities obtained in the transformation of the 2'-nitrophenylpyruvates as compared with the phenylpyruvate ester EPP may be rationalized by an additional interaction of this group with the cinchona alkaloid and not with the metal surface. However, the effect of the additional substituents on the adsorption of the 2-nitrophenylpyruvates, as indicated by SERS measurements, cannot be correlated with the enantioselectivities obtained in the reactions of these compounds. Its consequence is that these substituents exert their beneficial/detrimental effects by their (mostly steric) interaction with the adsorbed chiral modifiers. Our future plan is to study these latter interactions on metal surfaces with spectroscopic (SERS, etc.) and computational methods.



**Figure 16.** Possible half-hydrogenated surface species

#### 4. Summary

Based on our spectroscopic measurements, the enol form is predominant in case of all phenylpyruvates in solid forms and methanol solutions. These observations are consistent with the literature. In the case of EPP, a good agreement is found between the calculated geometry and the geometry inferred from the measurement data. Stronger adsorption of phenylpyruvates in acidic media through oxygen atoms is indicated by the increased enhancement in the SERS spectra. As in case of reference probe molecules, the nitro group of 2'-nitrophenylpyruvates has no direct role in the adsorption on Ag surface. This with the molecular geometries explains why the hydrogenation of the keto group (presumably via the enol form) occurs preferentially and why the formation of the indole derivatives requiring reduction of the nitro group is suppressed.

The use of common citrate stabilized Ag colloid, suitable to obtain surface enhancement using IR excitation source, can be a first step to understand SERS behavior of the studied NPPs. These preliminary SERS results help to get a closer look on the first step of adsorption of starting materials contributing to a better understanding of the cascade reactions studied. More complex nanosystems, like Ag@Pt core-shell bimetallic nanoparticles might be further applied for in situ SERS monitoring to provide a better flexibility in designing catalysts.

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# Supplementary Materials

## Surface Enhanced Raman Spectroscopic (SERS) behavior of phenylpyruvates used in heterogeneous catalytic asymmetric cascade reaction

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Abbreviations of the compounds:

EPP: ethyl 3-phenylpyruvate

NPP1: ethyl 3-(3-methyl-2-nitrophenyl)pyruvate

NPP2: methyl 3-(3-methyl-2-nitrophenyl)pyruvate

NPP3: ethyl 3-(5-methoxy-2-nitrophenyl)pyruvate

NPP4: ethyl 3-(3-methoxy-2-nitrophenyl)pyruvate

NPPs: 2'-nitrophenylpyruvates

Mulliken charges (the original definition of partial charges in molecules) were calculated with Spartan'06 package<sup>1</sup>.

Fig. S1 exhibits the Mulliken charges of phenylpyruvates studied. It reveals that the presence of the nitro group slightly shifts the charge distribution of the benzene ring in the NPPs compared to EPP. It seems plausible that the conjugation between the C=C and the benzene ring in the enol form of NPPs is changed compared to EPP which might explain the lack of double bonding in the SERS signal of NPPs while double bonding in the SERS signal of EPP is present.

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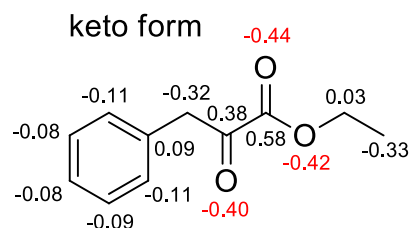
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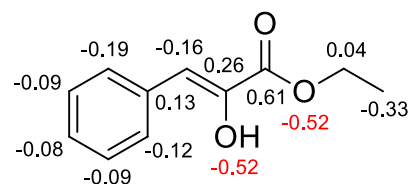


Compound abbreviation

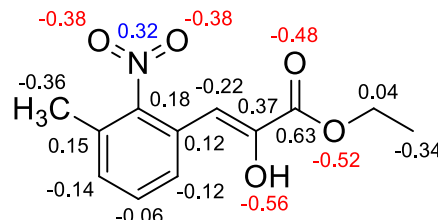
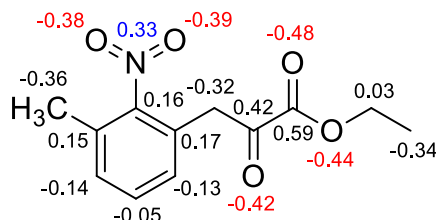
EPP



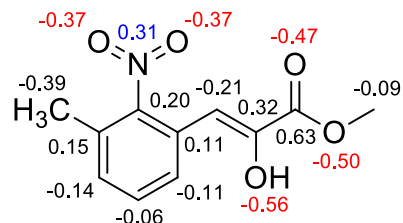
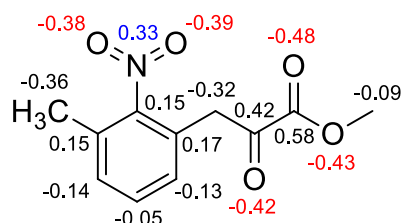
enol form -0.49



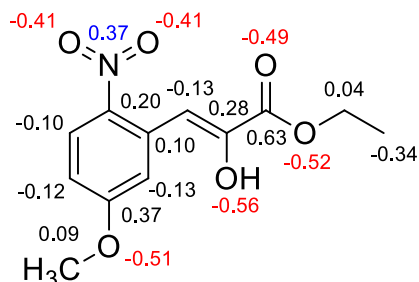
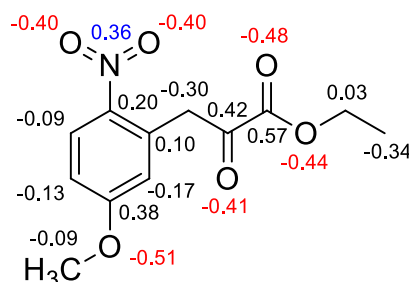
NPP1



NPP2



NPP3



NPP4

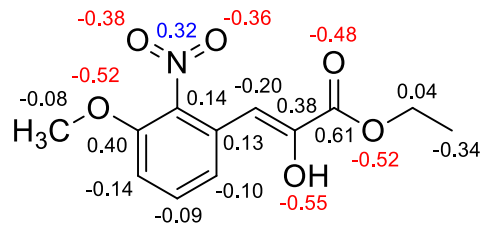
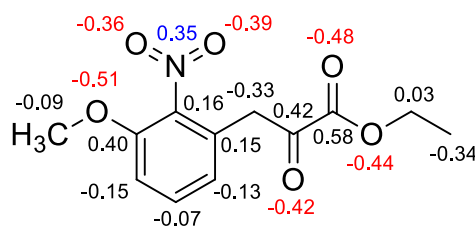


Fig. S1: Mulliken charges of phenylpyruvates studied

Reference:

1. W. J. Hehre, W. W. Huang, P. E. Klunzinger, B. J. Deppmeier, A. J. Driessen, *Spartan '06*. Wavefunction, Inc., 18401 Von Karman Ave., Suite 370, Irvine, CA 92612.