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Chiral discrimination of 2,3-butanediols by laser spectroscopy

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The resonance enhanced two-photon ionization time-of-flight (R2PI-TOF) excitation spectra of supersonically expanded complexes of isomeric 2,3-butanediols with a suitable chromophore, *i.e.* *R*-(+)-1-phenyl-1-propanol, represent powerful means for structurally discriminating the diol moiety and for investigating the nature of the intra- and intermolecular interactions involved in the complexes.

Many biologically active chiral compounds have the partial structure of secondary alcohols. Most of the methods applied to chiral discrimination of compounds carrying hydroxy groups are based on the stability and reactivity of the diastereomeric complexes with chiral selectors (chiral shifts reagents, chiral stationary phases, *etc.*). However, the study of the interactions involved in these diastereomeric contact pairs is often complicated by the presence of the solvent which may level off the difference in their physicochemical properties. A way to eliminate undesired solvent effects and to evaluate the intrinsic factors governing enantioselective complexation is to study diastereomeric aggregates in a supersonic beam by mass resolved resonant two-photon ionization (R2PI-TOF) spectroscopy.[1–3] Gas-phase studies have the advantage that the results can be directly compared to theoretical estimates of the structure and stability of the complexes under investigation.[4–8]

Structural discrimination of all the isomers—diastereomers and enantiomers—of 2,3-butanediol has been recently achieved by mass spectrometry using Cooks' kinetic method.[9] By this procedure, some information is obtained about the relative stability of their *charged* complexes with suitable acceptors. This communication reports on an one-color R2PI-TOF (1cR2PI-TOF) spectroscopic study of the forces intervening in the supersonically expanded *neutral* diastereomeric complexes of isomeric 2,3-butanediols with a suitable chromophore and of their sensitivity to the configuration and conformation of the diol moiety.

The complexes have been obtained from the association of a chiral chromophore, *i.e.* *R*-(+)-1-phenyl-1-propanol (**R**), with each member of the 2,3-butanediol family, *i.e.* (2*R*,3*R*)-(−)-2,3-butanediol (**rr**), (2*S*,3*S*)-(+)-2,3-butanediol (**ss**) enantiomers, and the *meso* form (2*R*,3*S*)-2,3-butanediol (**rs**). The corresponding isomeric contact pairs, *i.e.* [**R·rr**], [**R·ss**], and [**R·rs**], are formed in supersonic expansion of Ar seeded with the chromophore **R** mixed with the diol in *ca.* 1 : 2 ratio. The inlet system is heated to 100 °C. The beam is skimmed into a TOF mass spectrometer, where it is resonantly ionized by laser light absorption. The laser system consists of a Nd:YAG (Quantel model 781) doubled in frequency (λ = 532 nm) which pumps a dye laser. The dye frequencies are doubled and mixed with residual 1064 nm radiation. Neutral compounds in the supersonic beam are excited to the S_1 state by absorption of one photon of energy $h\nu_1$ and then ionized by absorption of a second photon with the same energy (1cR2PI). The ions formed are mass discriminated and detected in a TOF mass spectrometer.

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Fig. 1(a) illustrates the excitation spectra of the bare **R**, taken around the 0_0^0 electronic $S_0 \leftarrow S_1$ origin. The band origin region of the spectrum displays a peak at 37577 cm^{-1} (peak A) and two other major peaks at 37618 cm^{-1} (peak B) and at 37624 cm^{-1} (peak C). This triplet of bands have been assigned to the 0_0^0 electronic $S_0 \leftarrow S_1$ origin of three stable conformers of **R**.[4] The 1cR2PI excitation spectra of the isomeric [**R·ss**], [**R·rs**], and [**R·rr**] complexes are illustrated in Fig. 1(b), (c) and (d), respectively. Their spectral patterns are characterized by an ensemble of bands red-shifted relative to the 0_0^0 electronic $S_0 \leftarrow S_1$ origin of the bare chromophore **R** at 37618 cm^{-1} (peak B). The most intense band of each ensemble is red-shifted relative to the peak B of the chromophore by the $\Delta\nu$ values reported in Fig. 1. As pointed out in related papers,[4] these red shifts are due to the increase of attractive interactions in the complex in going from the S_0 ground state to the S_1 excited state. According to the $\Delta\nu$ values of Fig. 1(b)–(d), this strengthening decreases in the order: [**R·rr**] > [**R·rs**] > [**R·ss**].

These results point to a significant effect of the configuration of the diol moiety on the intracomplex forces involved in the

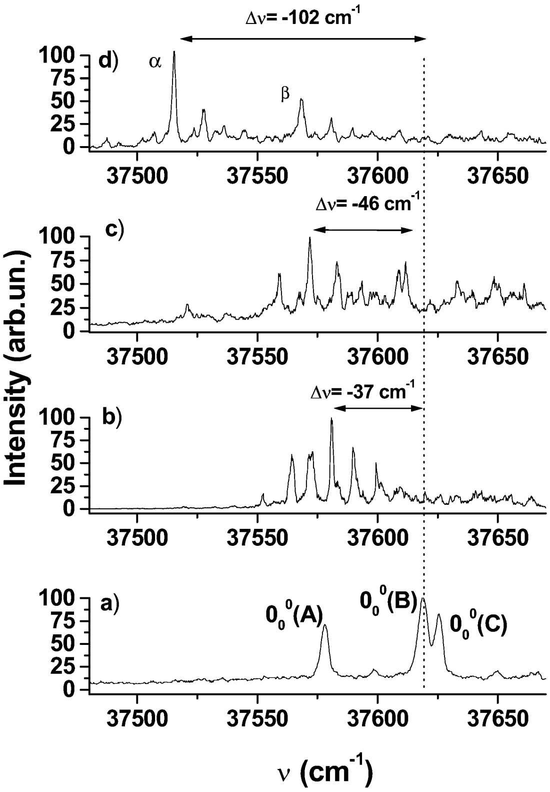

Fig. 1 Mass resolved 1cR2PI excitation spectrum of: (a) the bare (*R*)-(+)-1-phenyl-1-propanol (**R**); (b) the [**R·ss**] cluster; (c) the [**R·rs**] cluster; (d) the [**R·rr**] cluster (total stagnation pressure = 2 × 10^5 Pa).

isomeric [**R**·**rr**], [**R**·**ss**] and [**R**·**rs**] adducts. It is well established[10] that $O_{\mathbf{R}}$–H···O hydrogen bonding between **R** (acting as the proton donor ($O_{\mathbf{R}}$–H)) and an alcohol molecule (acting as the proton acceptor) is responsible for the bathochromic shifts observed in the corresponding spectra. Different spectral shifts for diastereomeric complexes are often due to the superimposing effects of attractive dispersive (polarization) and repulsive (steric) interactions.[4]

When the chromophore is bound to a bifunctional solvent molecule, such as vicinal amino alcohols, the IR/UV double resonance spectra of the gaseous complexes exhibit spectral features due to structures involving not only the expected intermolecular hydrogen bonding, but also extensive intramolecular O–H···N hydrogen bonding.[8] It is conceivable that similar intramolecular interactions are present in the isomeric [**R**·**rr**], [**R**·**ss**] and [**R**·**rs**] adducts. They are expected to increase the electron density at the oxygen of the chromophore and, therefore, to enhance the H-bonding contribution to the bathochromic shift.

The [**R**·**ss**] adduct exhibits the same mass fragmentation patterns at all its excitation frequencies. A similar situation is met with the [**R**·**rs**] adduct. In contrast, the homochiral [**R**·**rr**] isomer shows a different fragmentation pattern at the excitation frequencies marked α and β in Fig. 1(d).

Fig. 2 reports the optimized [**R**·**rr**], [**R**·**ss**] and [**R**·**rs**] structures, calculated at the MM3 force-field level of theory.[11]

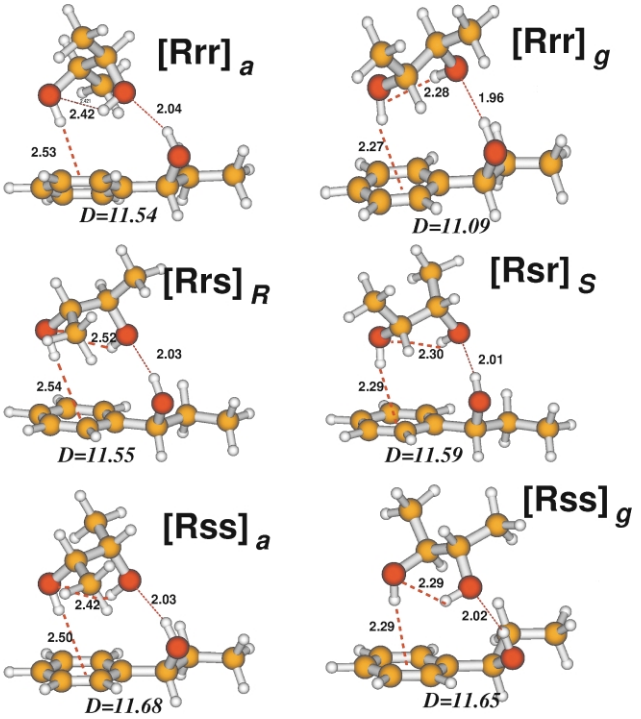

Fig. 2 H-Bond distances (in Å) and dissociation energies (*D*, in kcal mol^{-1}) of the isomeric [**R**·**rr**], [**R**·**ss**] and [**R**·**rs**] structures.

For [**R**·**rr**] and [**R**·**ss**], two different stable structures, involving intramolecular O–H···O–H hydrogen bonding, were found, characterized by the diol moiety in a *gauche* ([**R**·**rr**]$_g$ and [**R**·**ss**]$_g$ in Fig. 2) or the *anti* conformation ([**R**·**rr**]$_a$ and [**R**·**ss**]$_a$ in Fig. 2). Two different structures have been identified for the [**R**·**rs**] isomer as well, one with the $O_{\mathbf{R}}$–H···O(H)–$C_{(R)}$ intermolecular arrangement ([**R**·**rs**]$_R$ in Fig. 2) and the other with the $O_{\mathbf{R}}$–H···O(H)–$C_{(S)}$ one ([**R**·**sr**]$_S$ in Fig. 2).

According to the *D* values and the $O_{\mathbf{R}}$–H···O–H···O–H interaction distances of the structures of Fig. 2, it is reasonable to assign the α band of [**R**·**rr**], which displays the largest red shift, to the tightest structure [**R**·**rr**]$_g$. The smaller red shift associated with band β is attributed to the comparatively loose conformer [**R**·**rr**]$_a$, characterized by longer $O_{\mathbf{R}}$–H···O–H···O–H interaction distances. The appreciable structural and energetic differences in the [**R**·**rr**]$_g$/[**R**·**rr**]$_a$ pair become much less evident in the [**R**·**ss**]$_g$/[**R**·**ss**]$_a$ and ([**R**·**rs**]$_R$/[**R**·**rs**]$_S$ ones (Fig. 2). In particular, irrespective of the specific conformation and orientation of the diol moiety, the $O_{\mathbf{R}}$–H···O–H distance in these latter structures ranges around 2.01–2.03 Å and are much closer to that of [**R**·**rr**]$_a$ (2.04 Å) than of [**R**·**rr**]$_g$ (1.96 Å). This analogy may explain the similar red shifts observed between [**R**·**rr**]$_a$ and the conformers of [**R**·**rs**] and [**R**·**ss**].

In conclusion, the R2PI/TOF technique has been applied for the first time to structurally differentiate the neutral 2,3-butanediol isomers by complexation with the chiral selector **R** in a supersonic molecular beam. It has been shown that the forces involved in the solvation of **R** by isomeric 2,3-butanediols critically depend upon conformation and the configuration of the solvent molecule.

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