Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 149 (2015) 75–82

Contents lists available at ScienceDirect

Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy

journal homepage: www.elsevier.com/locate/saa

Charge-transfer complexes of 2,3-dichloro-5,6-dicyano-1, 4-benzoquinone with amino molecules in polar solvents

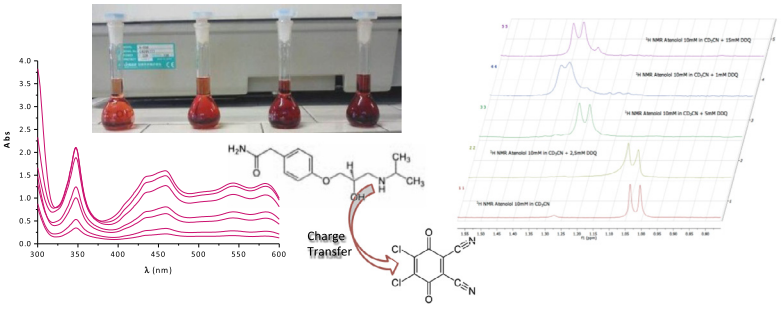
Silvia Berto [a], Enrico Chiavazza [a,*], Valentina Ribotta [a], Pier Giuseppe Daniele [a], Claudia Barolo [a,b], Agnese Giacomino [c], Davide Vione [a], Mery Malandrino [a]

[a] Dept. of Chemistry, University of Torino, Via P. Giuria 7, 10125 Turin, Italy
[b] INSTM and NIS Centre, University of Torino, Via Quarello 15A, 10135 Turin, Italy
[c] Dept. of Drug Science and Technology, University of Torino, Via Giuria 9, 10125 Turin, Italy

HIGHLIGHTS

- The stability of the DDQ–atenolol complex was determined in acetonitrile and ethanol.
- The stability of the DDQ–procaine complex was determined in ethanol.
- The association constants were determined by HypSpec® software.
- Only the aliphatic amino groups are involved in the charge transfer complex formation.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 4 December 2014
Received in revised form 1 April 2015
Accepted 16 April 2015
Available online 25 April 2015

Keywords:
CT complexes
DDQ
Procaine
Atenolol
Spectrophotometry
NMR

ABSTRACT

The charge-transfer complexes have scientific relevance because this type of molecular interaction is at the basis of the activity of pharmacological compounds and because the absorption bands of the complexes can be used for the quantification of electron donor molecules. This work aims to assess the stability of the charge-transfer complexes between the electron acceptor 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and two drugs, procaine and atenolol, in acetonitrile and ethanol. The stability of DDQ in solution and the time required to obtain the maximum complex formation were evaluated. The stoichiometry and the stability of the complexes were determined, respectively, by Job's plot method and by the elaboration of UV–vis titrations data. The latter task was carried out by using the non-linear global analysis approach to determine the equilibrium constants. This approach to data elaboration allowed us to overcome the disadvantages of the classical linear-regression method, to obtain reliable values of the association constants and to calculate the entire spectra of the complexes. NMR spectra were recorded to identify the portion of the donor molecule that was involved in the interaction. The data support the participation of the aliphatic amino groups in complex formation and exclude the involvement of the aromatic amine present in the procaine molecule.

Introduction

The charge-transfer (CT) complexes formed from the reaction of electron acceptors with donors containing heteroatoms, such as nitrogen, sulfur or oxygen, have seen a growing importance in recent years. Some studies on acceptor–donor systems were performed to characterize the nature, the kinetic and the stability of the complexes in different organic solvents

* Corresponding author at: Via P. Giuria, 5, 10125 Torino, Italy. Tel.: +39 011 6705259.
E-mail address: enrico.chiavazza@unito.it (E. Chiavazza).

http://dx.doi.org/10.1016/j.saa.2015.04.044
1386-1425/

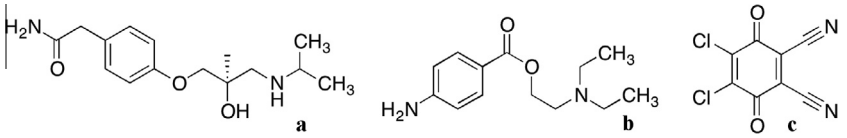


Fig. 1. Donor molecules studied: (a) atenolol, (b) procaine, (c) 2,3-dichloro-5,6-diciano-1,4-benzoquinone (DDQ).

[3,4,6,7,11,13,15–19,22]. Other works report the application of this type of interaction for the quantitative determination of the donor molecules, including the quantification of pharmaceutical products [1,2,8,9,19,21,24]. The peculiarity of the CT complexes is their elevated absorption in the visible range, where donor and acceptor usually do not absorb. Therefore, the absorbance values at the wavelengths of maximum absorption are used for the quantification of the drugs in pharmaceutical formulates. Typical electron acceptors are the 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), 2,3-dibromo-5,6-dicyano-1,4-benzoquinone (DBQ), tetracyanoquinodimethane (TCNQ), tetracyanoethylene (TCNE), 2,3,5,6-tetrabromo-1,4-benzoquinone (bromanil), 2,3,5,6-tetrachloro-1,4-benzoquinone (chloranil), dinitrobenzene (DNB) [20]. The donors are usually molecules with nitrogen or sulfur atoms, having free electron pairs or electron-rich aromatic rings.

In most literature reports, the evaluation of the stability of the complexes has been performed with linear regression methods, such as the Benesi–Hildebrand or Scott equation. However, it has long been known [10,23] that these methods: (i) may be affected by lack of linearity; (ii) can give negative intercepts that hinder the calculations; (iii) are limited by the assumption of the formation of a single complex in 1:1 stoichiometric ratio; (iv) have to respect the conditions $C_A \gg C_D$ (C_A = concentration of the acceptor, C_D = concentration of the donor), or $C_A \ll C_D$, on which the development of the entire equation is based.

In this work, we studied the interaction of the acceptor DDQ with molecules containing nitrogen atoms in acetonitrile and ethanol. The stoichiometry and the stability of the complexes were determined, respectively, by Job's plot method and by the elaboration of UV–vis titrations data. The data collection was achieved by applying the same approach used in the evaluation of the association constants in supramolecular chemistry [23]. This approach is directly derived from the chemical equilibrium theory, and the data elaboration was performed by a software, HypSpec®, dedicated to the determination of equilibrium constants from spectrophotometric data. The software can process the entire UV–vis spectrum and it calculates the stability constants with an iterative method. The single requirement is that the spectral intensity of each chemical species should be proportional to the concentration of that species in solution.

Because preliminary experiments suggested that DDQ preferentially interacts with non-aromatic amines, we chose to study the interaction of DDQ with two pharmaceuticals that contain aliphatic amino groups: a β-adrenergic blocker (atenolol) and a synthetic local anesthetic drug (procaine; see Fig. 1 for their molecular structures). Both molecules have nitrogen functions that could interact with DDQ: procaine has an aliphatic and an aromatic amine, while atenolol has an amino and an amidic nitrogen. NMR spectra were recorded to identify the portion of the donor molecule that is involved in the interaction. Optimal working conditions were assessed, evaluating the stability of DDQ in solution and the time required to obtain the maximum complex formation.

Experimental

Chemicals

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (purity 98%), atenolol (purity ⩾ 98%); procaine hydrochloride (purity 99.9%), tetrabutylammonium hydroxide solution (0.1 mol L^{-1} in organic solvent, which is a mixture of 2-propanol and methanol), ethanol (⩾99.8%) and acetonitrile (99.9%) were Sigma Aldrich products. Ethanol-d_6 (anhydrous, ⩾99%) and acetonitrile-d_3 (⩾99.8%) were Euriso-top products.

The solutions of the donors were prepared by dissolving the drugs in the solvent and were stored at 4 °C. The solutions of the acceptor molecule (DDQ) were always freshly prepared.

Procaine does not interact with DDQ if it is protonated, which is the case for the commercial (hydrochloride) form. Therefore, we used the commercial solution of tetrabutylammonium hydroxide to neutralize the procaine solutions, immediately before mixing them with DDQ.

Spectroscopic measurements

The UV–visible molecular absorption spectra (300–600 nm) of the donor–acceptor systems were recorded with a V-550 Jasco spectrophotometer, equipped with 1.000 cm or 5.00 cm quartz cells (Hellma), and working with a 200 nm/min scanning speed and 1.0 nm band width.

^{1}H NMR measurements at variable temperature were performed on a Jeol EX 400 spectrometer (B_0 = 9.4 T, work frequency ^{1}H = 399.78 MHz), in common 5 mm NMR tubes, while titrations were performed on a Bruker Avance 200 (B_0 = 4.7 T, work frequency ^{1}H = 399.78 MHz) spectrometer. In titration experiments, the drugs concentration was kept constant at 10 mmol L^{-1} while the DDQ concentration was varied from zero to 15 mmol L^{-1}.

Optimization of working conditions

In order to obtain stable and coherent results, we evaluated preliminarily the stability of the DDQ absorption spectra in the two polar solvents and the time necessary to reach the maximum complex formation. As far as the first issue is concerned, DDQ spectra change over time and show an increase of the absorbance values in the same range of the CT-complexes (400–550 nm). The spectral features are in agreement with those reported for the $DDQ^{\cdot-}$ radical ion [14].

In order to assess the sensitivity of DDQ to atmospheric exposure, we recorded the time trend of the absorbance of 5×10^{-3} mol L^{-1} DDQ in ethanol and acetonitrile under environmental atmospheric conditions, or by bubbling nitrogen into the solvent before use and in the solution after preparation. The absorbance was recorded at 460 nm, where absorption by the CT-complexes under study is maximum. To assess the complex development, the spectra of equimolar solutions of DDQ/drug were recorded during time and the absorbance at 460 nm was monitored. Both solvents were used for subsequent studies.

Job's plot method

The Job's plot method was used to evaluate the stoichiometry of the CT-complexes in the two solvents. The drug and the DDQ stock solutions (all 5×10^{-3} mol L^{-1}) were prepared in acetonitrile or ethanol. Then, for each solvent, 9 donor–acceptor solutions were prepared in 10 mL volumetric flasks. In each case, the content of acceptor and donor was chosen so as to vary their molar fractions