

Circular Dichroism Spectra of Nicotine Enantiomers in the Far UV Region



BRITISH AMERICAN
TOBACCO

Peter M. Clayton^{1*}, Carl A. Vas¹, Tam T.T. Bui², Alex F. Drake², Kevin McAdam¹

1. British American Tobacco, Group R&D, Regents Park Road, Southampton, SO15 8TL, UK

2. Applied Photophysics Limited, 21 Mole Business Park, Leatherhead, KT22 7AG, UK

*contact: peter_clayton@bat.com

INTRODUCTION

The stereochemical configuration of the carbon atom at the 2' position of the pyrrolidine ring of the alkaloid nicotine [CAS 54-11-5] has an important effect on biological activity [1]. (S)-(-)-nicotine, Figure 1, is the dominant isomer present in tobacco plants [2] and tobacco smoke [3]. (S)-(-)-nicotine is an agonist at nicotinic acetylcholine receptors, and is six times more potent at muscle-type nicotinic acetylcholine receptors compared to (R)-(+)-nicotine [4].

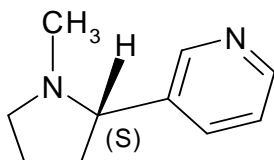


Figure 1: Structure of (S)-(-)-nicotine

In this poster the CD and UV absorption spectra of the enantiomers of nicotine are shown between 300 and 180nm and a number of the electronic transitions are assigned.

EXPERIMENTAL

➤ Simultaneous UV and Circular Dichroism (CD) spectra of (S)-(-)-nicotine and (R)-(+)-nicotine were measured on a Chirascan Plus CD spectrometer (Applied Photophysics Ltd, Leatherhead, UK).

➤ The concentration of (S)-(-)-nicotine was 30.60µg/mL (0.1886mM) and the concentration of the (R)-(+)-nicotine 30.78µg/mL (0.1897mM) in deionised water (18.2MΩ.cm). The pH of the solution was 8.7 (20°C).

➤ The UV absorbance and CD spectra were measured between 300nm - 180nm in a 0.5mm rectangular strain-free cell.

➤ The optical beam of the instrument was continuously flushed with evaporated nitrogen gas which allowed access to low wavelengths.

➤ Spectra were recorded in 0.5nm wavelength steps with 1s measurement time-per-point. The spectral bandwidth was 1nm.

➤ Spectra were water baseline corrected and measured at 20°C.

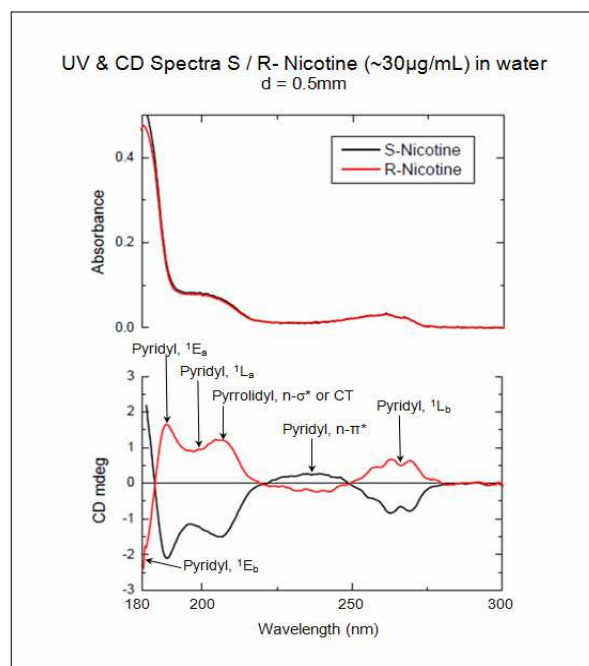
CONCLUSION

The CD and UV absorption spectra of nicotine were previously described down to ~210nm and two transitions at 263 and 237nm were identified [6]. In this poster the aqueous CD and UV spectra are presented between 300 and 180nm and a further four electronic transitions are tentatively assigned to the spectra. Transitions which are sensitive to pH may be of use for determining the ionisation status of nicotine in aqueous solution.

REFERENCES

1. Barlow, RB., Hamilton, JT Br. J. Pharmacol. 1965; 25:206-21
2. Armstrong, DW., Wang, X., Ercal, N Chirality 1998; 10:587-591
3. Perfetti, TA., Coleman, WM Contributions to Tobacco Research International 1998; 18:15-33
4. Rozental, R. et al. J. Pharmacol. Exp. Ther. 1989; 251:395-404
5. Mason, SF. Q. Rev. Chem. Soc. 1961; 15:287-371
6. Testa, B., Jenner, P. Molecular Pharmacol. 1973; 9:10-16
7. Rosini, C. et al. J. Chem. Soc. Chem. Commun. 1983; 287-288

UV and Circular Dichroism Spectra of Nicotine



NICOTINE SPECTRAL ASSIGNMENTS

The CD spectra of the two antipodes of nicotine (Figure 2) are almost exact mirror images of one another which is expected of enantiomers, while the UV spectra are nearly indistinguishable. The general features and spectroscopic assignment of UV spectra of organic chromophores are described in reference [5].

The CD spectra shows a negative cotton effect at around 263 nm for (S)-(-)-nicotine and the positive cotton effect for (R)-(+)-nicotine. This corresponds to the π - π_1^* or 1L_b transition of the pyridine moiety [6]. The transition exhibits vibronic structure which is a result of simultaneous changes involving both electronic and vibrational energies of the aromatic moiety.

The positive CD signal at around 237nm for (S)-(-)-nicotine is associated with the n - π_1^* transition. This transition is a result of the movement of charge from the pyridyl N lone pair to an antibonding molecular orbital (π_1^*); the band vanishes when the nitrogen atom is protonated, ($pK_a \sim 3$, data not shown). The n - π_1^* transition is electric dipole forbidden (very weak absorption, $\epsilon < 100$) but is magnetic dipole allowed ensuring a significant CD.

It is likely that the CD maxima at around 206nm is the result of an n - σ^* transition, but there is also the possibility of charge transfer (CT) from the pyrrolidyl N lone pair to the pyridyl π^* . Both these transitions would be expected to vanish upon protonation of the pyrrolidyl group ($pK_a \sim 8$).

We believe that a π - π_2^* (or 1L_a) transition of the pyridine moiety underlies the CD signal at around 200nm.

The CD maxima at 188nm may be the pyridyl π - π_3^* (1E_a) transition [7].

The lowest wavelength absorption and CD just visible at 180nm ($\lambda_{max} \sim 3$ not observed) may be the π - π_4^* (or 1E_b) transition [7].