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THE LUMINESCENCE SPECTRA OF TROPINE DRUGS

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Summary

Fluorescence and phosphorescence spectra were determined on solutions of atropine, cocaine, hyoscine (scopolamine) and some related drugs. The emission parameters of the excited states involved are discussed in relation to the structure and configuration of the respective tropines. The data obtained provide a basis for the microanalytical determination of these drugs.

1. Introduction

The tropine drugs atropine (hyoscyamine), hyoscine (scopolamine) and cocaine have acquired considerable importance in the medical and forensic fields. The requirement for the detection and estimation of traces of these drugs in biological extracts presents difficulties inherent in the limited sensitivity of conventional analytical techniques. In line with earlier work on the luminescence of drugs [1], we have therefore undertaken a study of the emission spectra of relevant tropine derivatives (Fig. 1) with the object of providing a firm basis for their analysis by luminescence spectroscopy. This investigation was also designed to provide some insight into the nature of the excited states involved in relation to the molecular structure and the stereochemistry of the tropine system.

2. Experimental details

The techniques, spectroscopic equipment and spectral corrections employed have been described earlier [2].

3. Quantum yield determinations and procedure

The spectral quantum yields of fluorescence at 298 K were determined by the comparative method adopted in our earlier work [2]. These were

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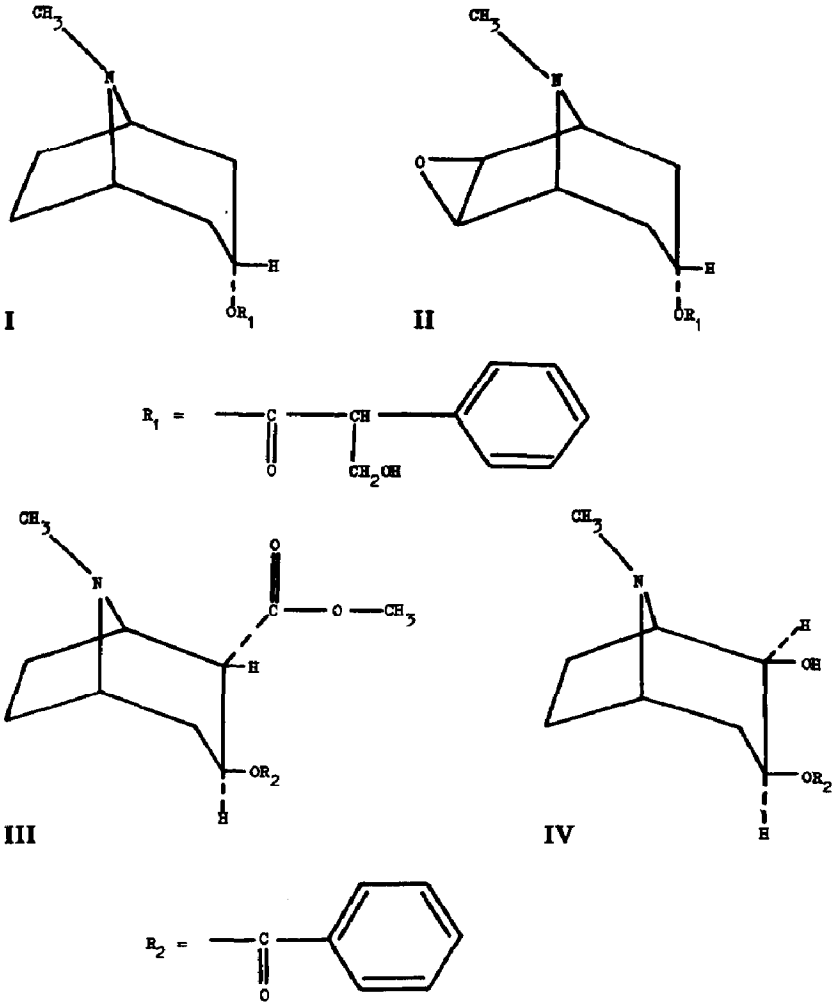

Fig. 1. Chemical structures of tropine derivatives: **I**, atropine; **II**, hyoscine; **III**, cocaine; **IV**, cocaine analogue.

then used to estimate the relative values of quantum yields for luminescence at 77 K.

4. Results and discussion

Spectral measurements were made on ethanolic solutions of atropine (I, $R_1 \equiv$ —CO·CH(CH_2OH)Ph), hyoscine (II, $R_1 \equiv$ —CO·CH(CH_2OH)Ph), homatropine (I, $R_1 \equiv$ —CO·CH(OH)Ph), cocaine (III, $R_2 \equiv$ —CO·Ph) and the cocaine analogue (IV, $R_2 \equiv$ —CO·Ph). In addition we examined the spectra of cinnamoyl tropine (I, $R_1 \equiv$ —CO·CH=CH·Ph) on account of the current forensic interest in the structurally related cinnamoyl cocaine (III, $R_2 \equiv$ —CO·CH=CH·Ph).

4.1. Stereochemistry

The stereochemical *trans*-piperidine (chair) ring conformation is a characteristic common structural feature of all the tropine derivatives studied here [3]. The esterified hydroxyl group has the α (axial) configuration in atropine, hyoscine and homatropine, but it adopts the β (equatorial) configuration in the cocaines. In all cases, however, the *trans* (chair) conformation of the piperidine ring sets the phenyl chromophore at a distance from the vicinity of the *N*-methyl group. The *trans* configuration about the double bond in the cinnamoyl tropine was confirmed from the proton magnetic resonance spectrum.

4.2. Absorption spectra

All the tropine derivatives displayed absorption spectra arising from the common single phenyl chromophore in the ester side chain. The absorption spectrum of atropine (Fig. 2, curve A) is characteristic. The well-defined low intensity UV absorption peaks (λ_{max} = 253 nm, ϵ = 155; λ_{max} = 259, ϵ = 198; λ_{max} = 265 nm, ϵ = 150) arise from the familiar π,π^* transition of the isolated phenyl group which is represented by the structured low frequency secondary ^1L_b band. The absorption spectrum of tropic acid was virtually identical with that of atropine.

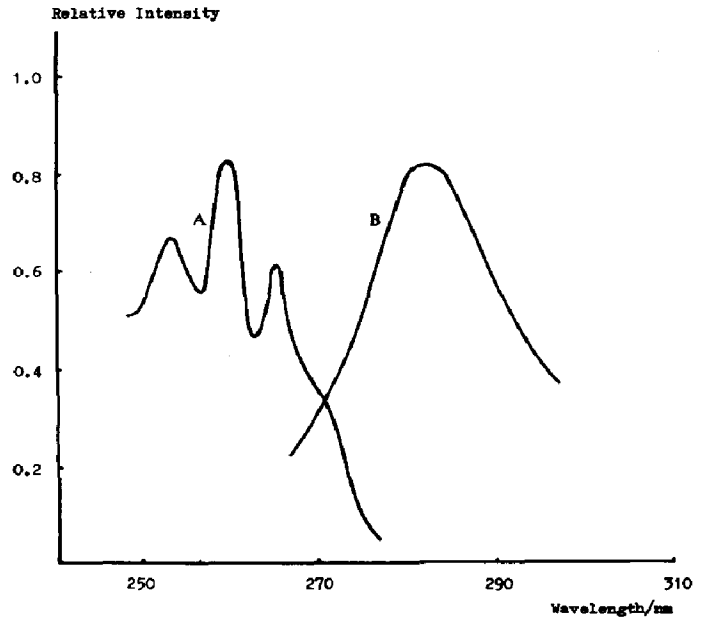

Fig. 2. Absorption (curve A) and fluorescence (curve B) spectra of atropine in 95% aqueous ethanol at 298 K.

The absorption spectrum of cocaine (Fig. 3, curve A), somewhat modified and red shifted by the conjugation in the benzoyl side chain, displays more intense peaks (λ_{max} = 276 nm, ϵ = 1040; λ_{max} = 283 nm, ϵ = 834). A virtually identical absorption spectrum was found for the cocaine analogue

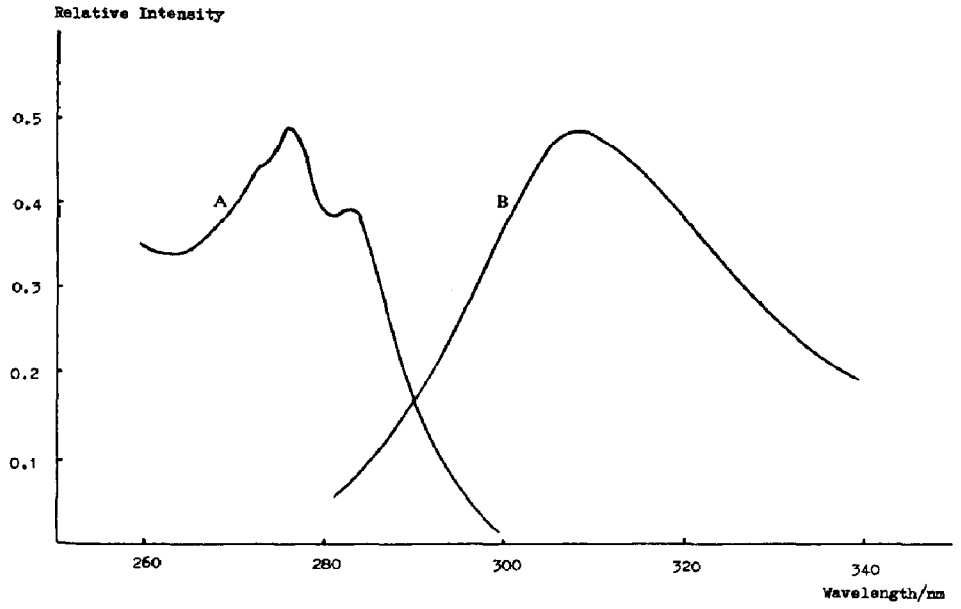

Fig. 3. Absorption (curve A) and fluorescence (curve B) spectra of cocaine hydrochloride in 95% aqueous ethanol at 298 K.

IV. These spectra show the expected close similarity to the spectrum of benzoic acid. Cinnamoyl tropine, which possesses the same conjugated chromophore as cinnamoyl cocaine, reveals an absorption spectrum which is further intensified and displaced to the red by the conjugated double bond (λ_{max} = 282 nm; ϵ = 20 890). These spectra are not affected by protonation of the basic nitrogen in solutions of the base hydrochlorides.

4.3. Emission spectra

The fluorescence spectra of atropine, homatropine and hyoscine, measured at 298 nm (Table 1), show very similar features. The spectrum of atropine (Fig. 2, curve B) is characteristic. The fluorescence emission takes the form of a single smooth peak (λ_{max} = 282 nm) of low intensity (ϕ_f = 2.6×10^{-2}). The spectrum, measured at 77 K (Fig. 4, curve A), gave a marked increase in intensity (ϕ_f = 0.28) with a very small blue shift (λ_{max} = 279 nm, $\Delta\lambda$ = 382 cm^{-1}).

The phosphorescence spectra of atropine, homatropine and hyoscine (Table 1) also closely resembled each other. The phosphorescence spectrum of atropine (Fig. 4, curve B) typically displayed well-defined peaks (λ_{max} = 343, 362 and 377 nm) of greater intensity than the fluorescence emission (ϕ_p = 0.37). Phosphorescence lifetime measurements gave τ_p = 5.25 s. The long lifetime of this triplet emission and the large singlet–triplet split (8936 cm^{-1}) are consistent with the π,π^* nature of this state, associated as it is with the isolated phenyl group in the side chain of the parent molecule.

The fluorescence and phosphorescence spectral characteristics of the foregoing tropines are virtually identical with those of free tropic acid. The

TABLE 1

Fluorescence and phosphorescence emission characteristics of tropines in ethanol

Compound	*Fluorescence (298 K)*		*Fluorescence (77 K)*		*Phosphorescence (77 K)*		
	λ_{max} (nm)	ϕ_f	λ_{max} (nm)	ϕ_f	λ_{max} (nm)	ϕ_p	τ_p (s)
Atropine	282	2.6×10^{-2}	279	2.8×10^{-1}	343, 362, 377	0.37	5.3
Hyoscine (hydrobromide)	281	2.3×10^{-2}	279	2.5×10^{-1}	343, 361, 377	0.34	6.3
Homatropine	280	3.4×10^{-2}	280		345, 365, 380		3.5
Tropic acid	282	3.7×10^{-2}	279	2.4×10^{-1}	345, 363, 377	0.27	6.3
Cocaine (hydrochloride)	307	2.1×10^{-3}	297	4.7×10^{-2}	368, 393, 405	0.30	2.6
Cocaine analogue (IV)	306	2.3×10^{-3}	297	8.4×10^{-2}	370, 393, 405	0.56	3.0

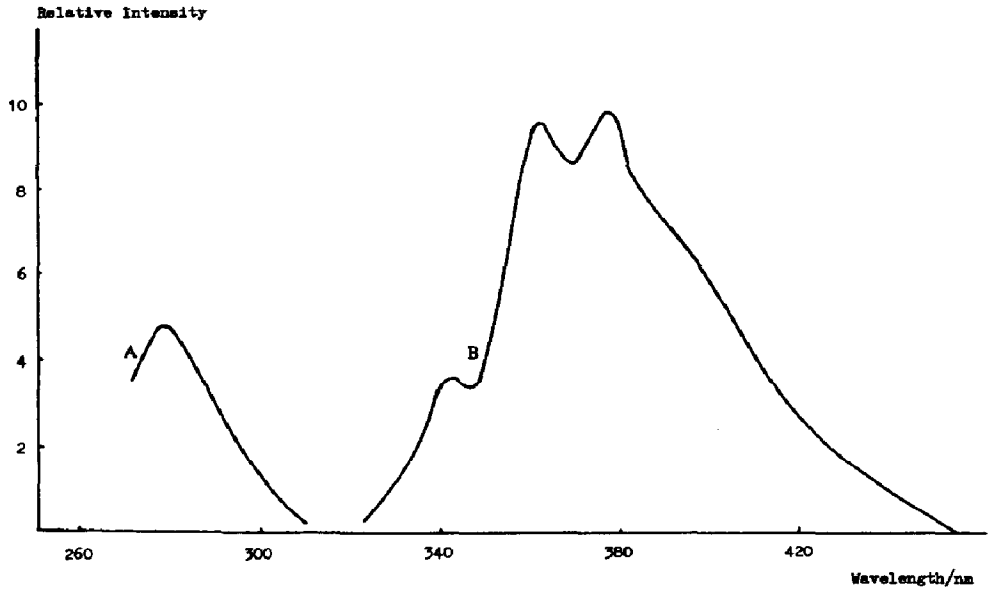

Fig. 4. Fluorescence (curve A) and phosphorescence (curve B) spectra of atropine in 95% aqueous ethanol at 77 K.

emission parameters of the latter are in fact very similar to those recorded for the isoelectronic molecule of phenylalanine [4, 5].

The fluorescence spectrum of cocaine measured at 298 K (Fig. 3, curve B) displayed a single smooth peak of low intensity ($\lambda_{max\,f}$ = 307 nm; $\phi_f = 2.1 \times 10^{-3}$). At 77 K the fluorescence emission is increased ($\phi_f = 4.7 \times 10^{-2}$) but it remains very weak (Fig. 5, curve A). At the same time a relatively intense phosphorescence emission is observed ($\lambda_{max\,p}$ = 368, 393 and 405 nm) (Fig. 5, curve B) with a quantum yield ϕ_p of 0.30, a lifetime τ_p of 2.63 s and a singlet–triplet split of 7882 cm. These data lie close to corresponding values recorded for the phosphorescence of benzoic acid [6], and they are accordingly assigned to the lowest π,π^* triplet state of the benzoyl group. The significantly shorter triplet radiative lifetime of cocaine in comparison with atropine is ascribed to a coupling of charge transfer states within the benzoate moiety [6]. The cocaine analogue IV revealed very similar emission characteristics to cocaine itself. Cinnamoyl tropine, in contrast, which was selected as an analogue of cinnamoyl cocaine, emitted no detectable fluorescence or phosphorescence in our experiments.

4.4. Analytical results

A linear plot of the effective fluorescence intensity ($\lambda_{max\,f}$ = 282 nm) against the molar concentration in 95% ethanol (Fig. 6) shows that atropine can be determined by this technique down to a level of 5×10^{-5} mol dm^{-3} (14 μg cm^{-3}). In a similar manner fluorescence intensity–concentration plots were obtained for cocaine hydrochloride in aqueous solution (Fig. 7). The data, based on $\lambda_{max\,f}$ = 315 nm (in water), demonstrate that cocaine can

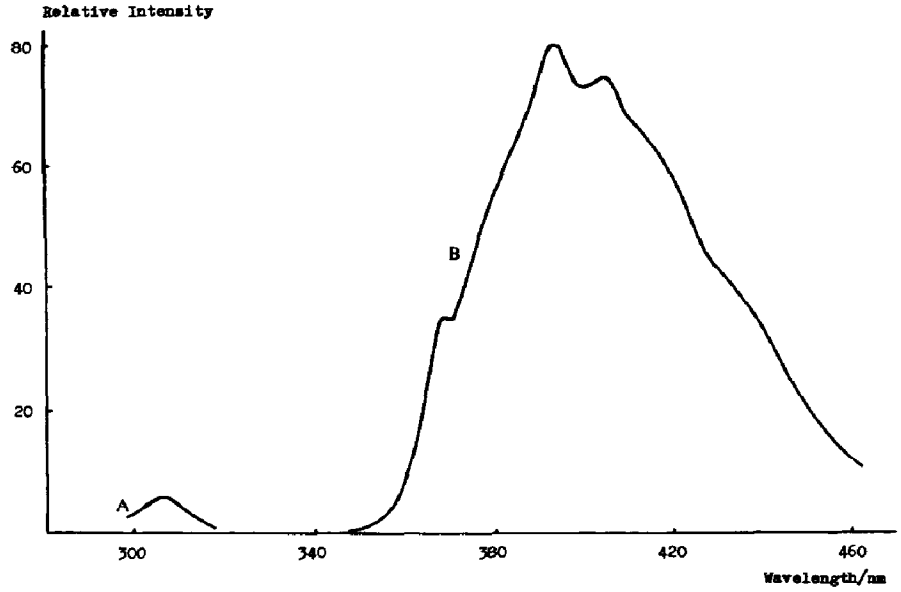

Fig. 5. Fluorescence (curve A) and phosphorescence (curve B) spectra of cocaine hydrochloride in 95% aqueous ethanol at 77 K.

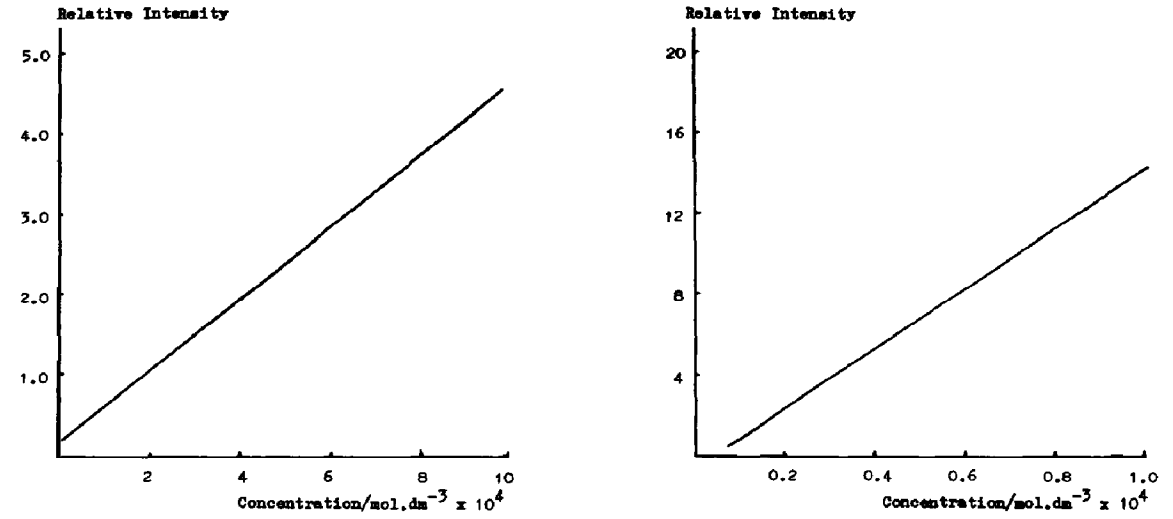

Fig. 6. Fluorescence intensity of atropine *vs.* concentration in 95% aqueous ethanol at 298 K.

Fig. 7. Fluorescence intensity of cocaine hydrochloride *vs.* concentration in water at 298 K.

be determined fluorometrically down to a level of 5×10^{-6} mol dm^{-3} (1.7 μg cm^{-3}).

The absence of luminescence emission from cinnamoyl tropine indicates that luminescence spectroscopy cannot be employed for the direct determination of cinnamoyl cocaine [7].

5. Conclusion

The foregoing results demonstrate that tropine drugs possessing aromatic ester side chains, in particular atropine and cocaine, can be determined by fluorescence spectroscopy techniques in solution down to concentrations of the order of a few micrograms per centimetre cubed. The employment of phosphorescence spectroscopy would increase this sensitivity by almost one order of magnitude, if the inconvenience of working with glassy matrixes at liquid nitrogen temperatures were acceptable.

The emission spectral parameters determined for the tropine derivatives studied show no significant difference from those of the corresponding aromatic carboxylic acids. It is evident that the *trans* conformation of the *N*-methyl piperidine ring permits no perturbing interaction between the basic nitrogen atom and the π electron system of the phenyl group, regardless of whether the ester side chain is axial or equatorial in configuration.

References

1 B. Savory and J. H. Turnbull, *J. Photochem.*, *17* (1981) 93.
E. P. Gibson and J. H. Turnbull, *Analyst (London)*, *104* (1979) 582.
A. Bowd, J. B. Hudson and J. H. Turnbull, *J. Chem. Soc., Perkin Trans. II*, (1973) 1312.
J. D. Winefordner and M. Tin, *Anal. Chim. Acta*, *32* (1965) 64.
S. P. Singh, D. Kaufman and V. I. Stenberg, *J. Heterocycl. Chem.*, *16* (1979) 625.
2 E. P. Gibson and J. H. Turnbull, *J. Photochem.*, *11* (1979) 313.
3 R. L. Clarke, *Alkaloids (N. Y.)*, *16* (1977) 157.
4 V. Shore and A. Pardee, *Arch. Biochem. Biophys.*, *60* (1956) 100.
5 J. Nag-Chanduri and L. Augenstein, *Biopolym. Symp.*, *1* (1964) 440.
6 H. J. Maria and S. P. McGlynn, *J. Chem. Phys.*, *52* (1970) 3399.
D. S. McClure, *J. Chem. Phys.*, *17* (1949) 905.
7 M. Yousseefi, R. G. Cooks and J. L. McLaughlin, *J. Am. Chem. Soc.*, *101* (1979) 3401.