

SPECTRAL DISTINCTION BETWEEN *CIS*- AND *TRANS*-4-METHYLAMINOXEX

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Summary

The recent identification of the anorectic agent 4-methylaminorex (2-amino-4-methyl-5-phenyl-2-oxazoline) as a police exhibit in Canada led to the need to synthesize a reference standard specimen. Since this substance can occur as *cis*- and *trans*- isomers, both had to be prepared and characterized spectrally. *Cis*-methylaminorex was made from the *erythro* amino alcohol norephedrine (phenylpropanolamine), while the *trans* compound was made from the *threo* diastereoisomer norpseudoephedrine, in both cases by the treatment of the substrate with cyanogen bromide in a methanolic solution of sodium acetate. In this paper, the ^{13}C - and ^1H -NMR, infrared (IR), mass (MS) and ultraviolet (UV) spectra are reported, together with a commentary on the distinguishing features noted between the sets of spectra.

Key words: Methylaminorex; Isomers; Spectral distinction

Introduction

Several samples of 4-methylaminorex were received in gram quantities as police exhibits in our laboratory during 1987. The substance was also reported in the United States [1], where it was described as a potent central nervous system stimulant. Scheduling action was taken in both Canada and the U.S., since the substance had not previously been controlled. Although originally synthesized as a potential anorectic agent [2], it was later investigated for its hypertensive and central nervous system stimulating activities [3,4]. 4-Methylaminorex can occur in both a *cis*- and a *trans*- form (Fig. 1) and it is important to be able to characterise these. Both isomers have therefore been synthesized and their spectroscopic properties measured.

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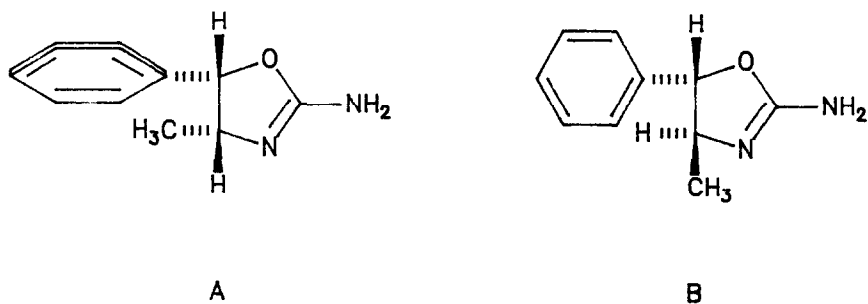


Fig. 1. The structure of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.

Experimental

Both specimens used in this study were synthesized according to the procedure of Poos et al. [2], with yields and melting points as reported.

Spectra were obtained on the following instruments: (1) ^{13}C and ^1H -NMR on a Bruker WP-80 transform spectrometer at 20.1 and 80 MHz respectively, in CDCl_3 using Me_4Si as internal standard (Figs. 2 and 3). (2) IR spectra were obtained on a Nicolet model 60SX Fourier transform spectrometer, as KBr dispersions (Fig. 4). (3) Mass spectra were obtained on a Finnigan Mat model 4610B instrument (Fig. 5). (4) UV spectra were obtained on a Varian DMS-90 UV-VIS spectrometer (Fig. 6.).

Discussion

NMR

The main differences in chemical shifts between the *cis* and *trans* isomers (Table 1) are due to the steric interactions between the methyl and phenyl groups in the *cis* compound. Thus, in the ^{13}C spectra, the chemical shifts for C1', C4, C5 and the CH_3 are all $\sim 3-5$ ppm to higher field in the *cis* isomer. In the ^1H spectra, H5 for the *cis* isomer is 0.7 ppm to lower field while the CH_3 is 0.6 ppm to higher field. The *cis* methyl protons are shifted to higher field because they are in the shielding region of the phenyl ring.

IR

As expected, there are significant differences in the fingerprint region of the respective IR spectra. In addition, both isomers show a strong, narrow band at 3442 cm^{-1} (*trans*) and 3423 cm^{-1} (*cis*) due to the NH_2 vibration.

MS

The two mass spectra (Figs 4A and 4B) are virtually indistinguishable, as expected. The base peak in each case is at m/z 70, and there is a prominent molecular ion at m/z 176.

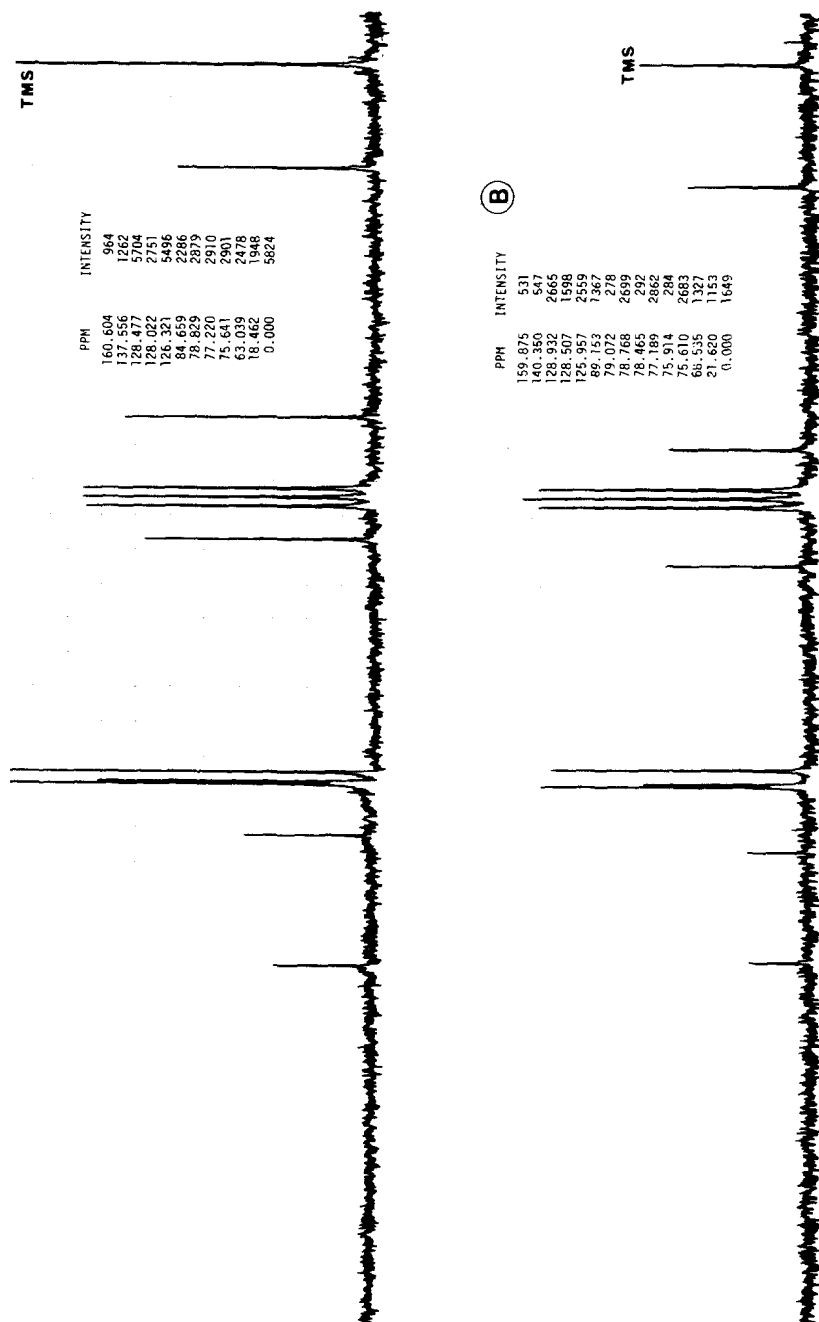
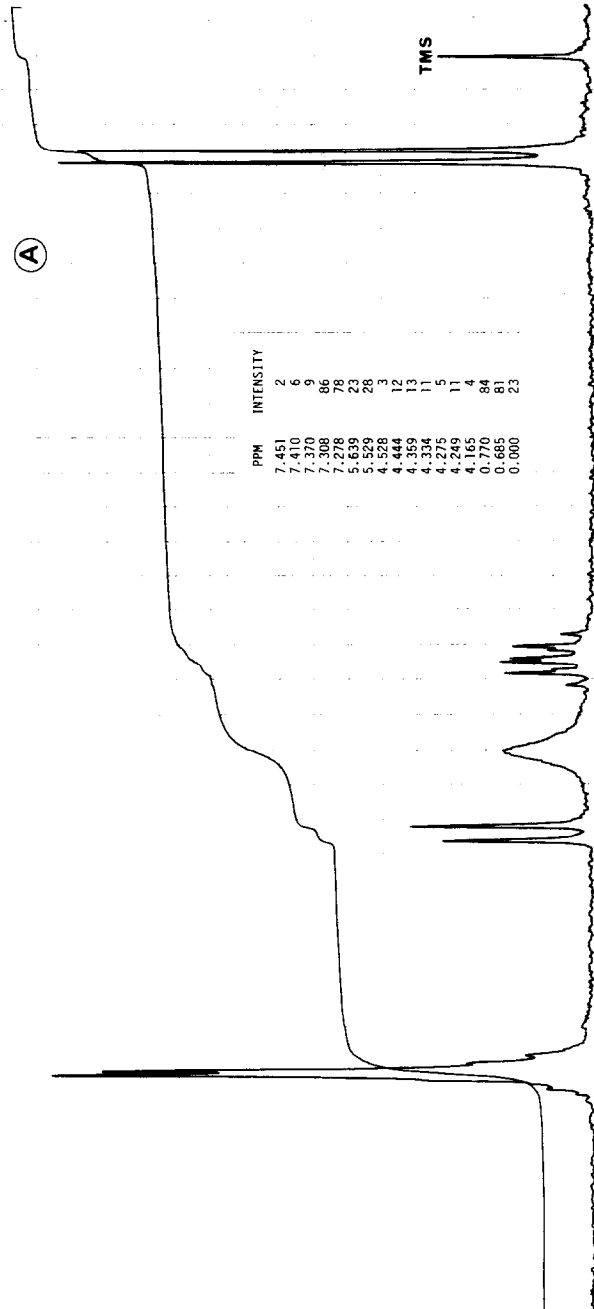


Fig. 2. ^{13}C -NMR spectra of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.



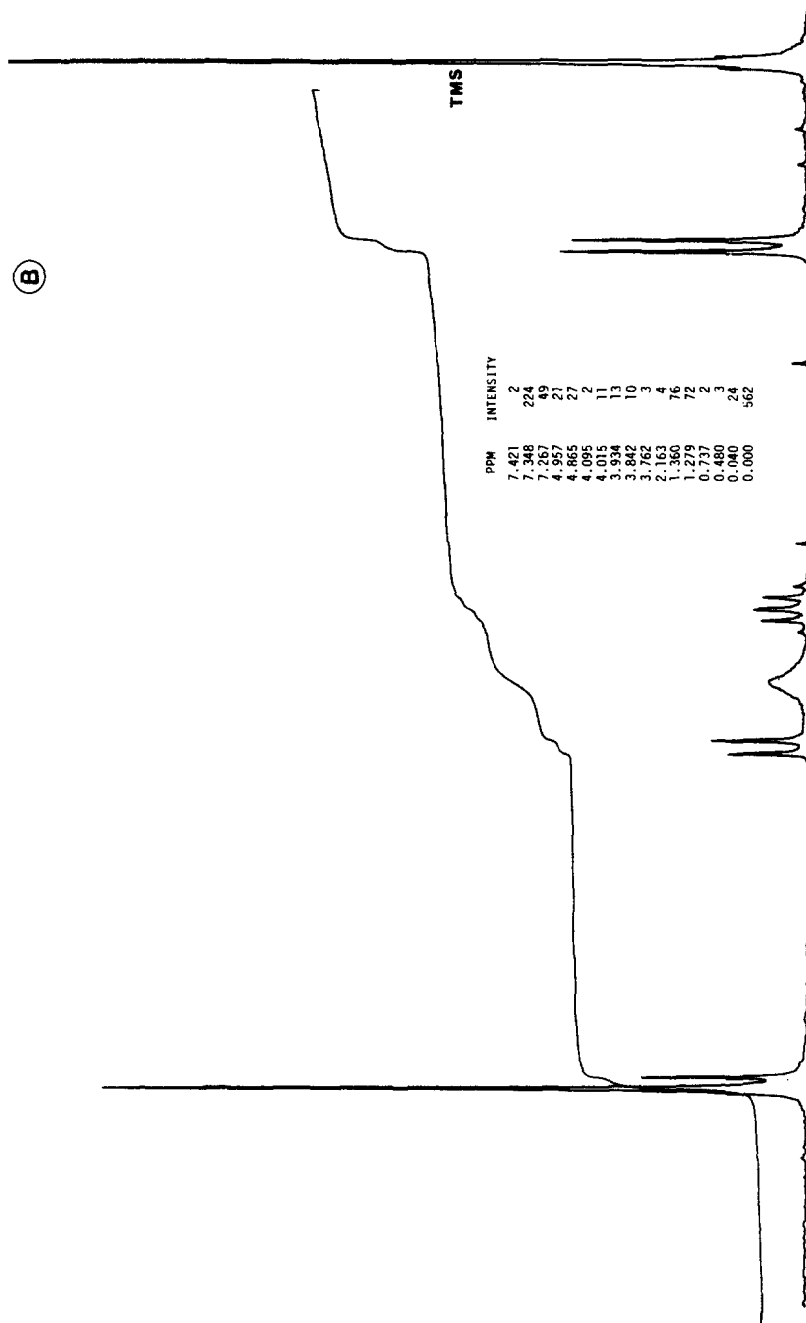


Fig. 3. $^1\text{H-NMR}$ spectra of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.

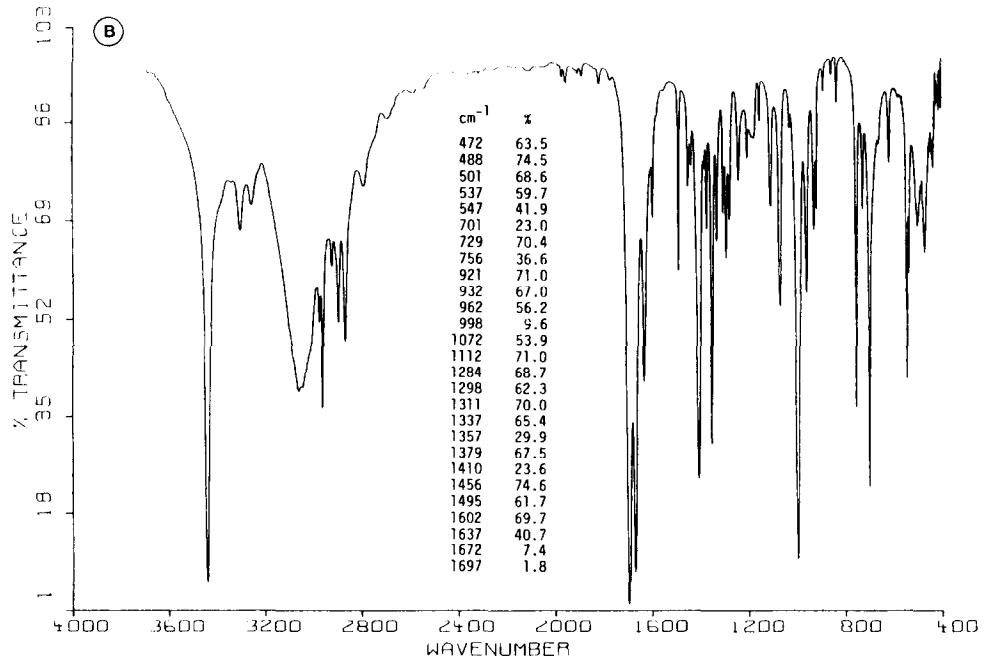
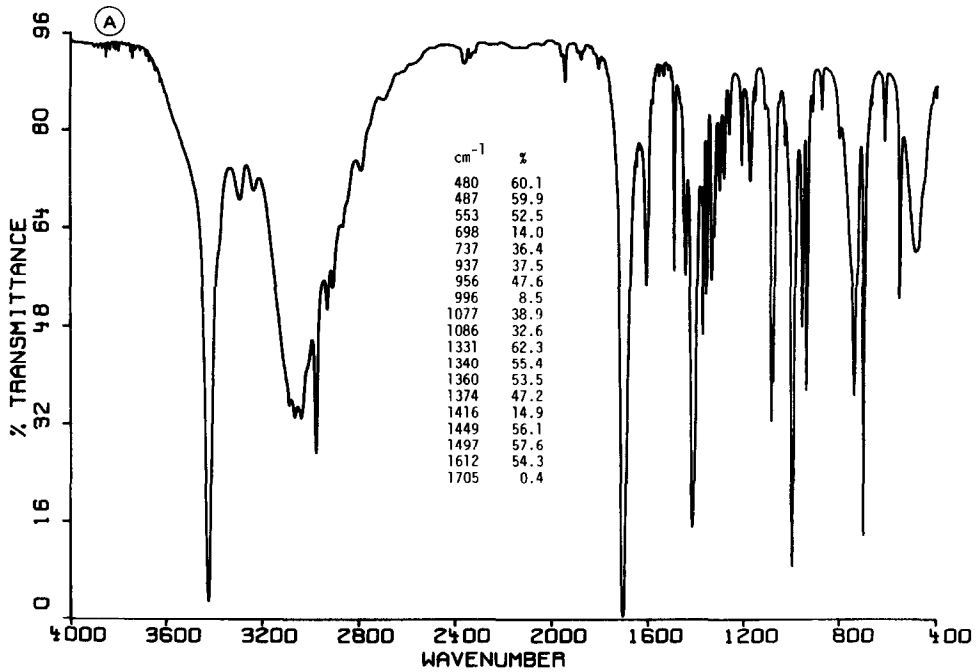


Fig. 4. IR spectra of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.

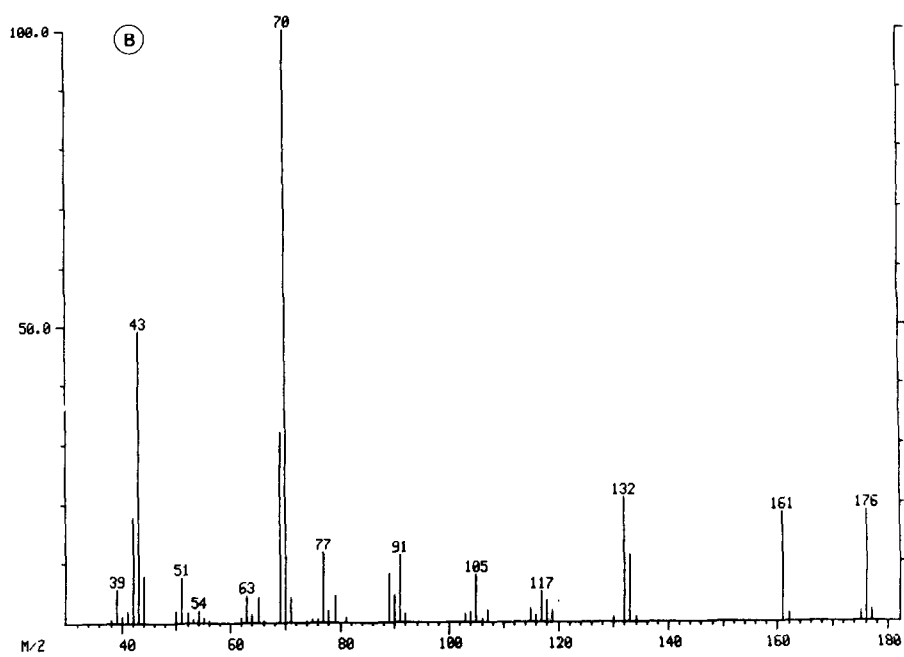
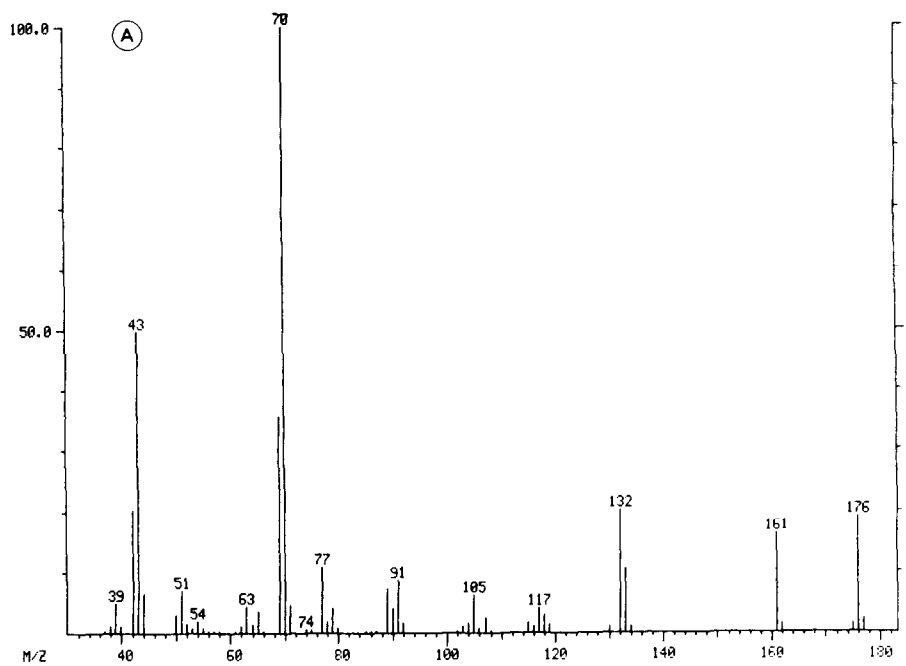


Fig. 5. Mass spectra of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.

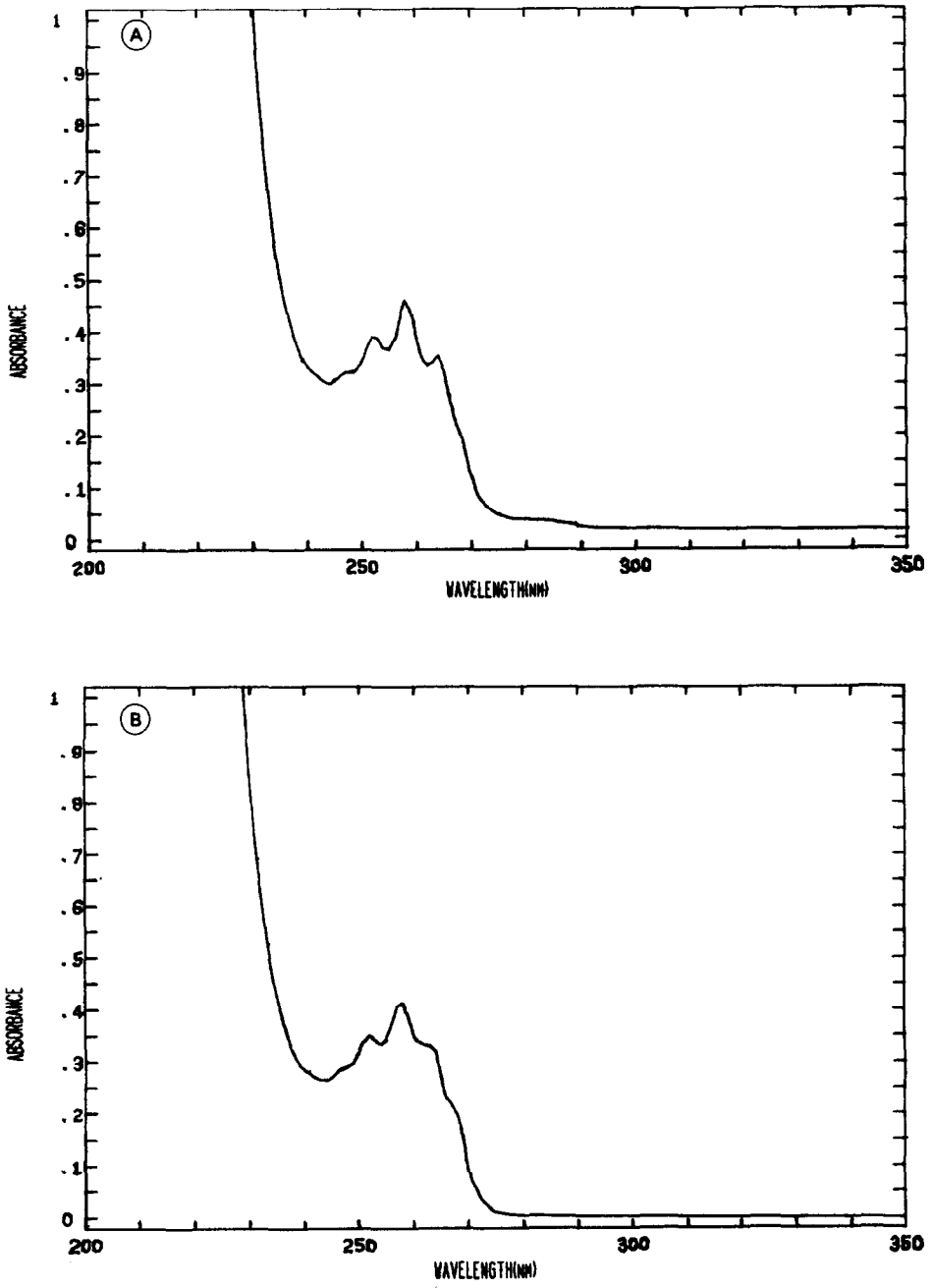


Fig. 6. UV spectra of (A) *cis*-methylaminorex and (B) *trans*-methylaminorex.

TABLE 1

OBSERVED CHEMICAL SHIFTS IN THE NMR SPECTRA OF *CIS* AND *TRANS* 4-METHYLAMINOUREX AND THEIR ASSIGNMENTS

<i>Cis</i>		<i>Trans</i>	
$\delta^{13}C$ (ppm)	<i>C</i> no. ^a	$\delta^{13}C$ (ppm)	<i>C</i> no.
160.6	2	159.9	2
137.6	1'	140.4	1'
128.5	(3')	128.9	(3')
128.0	4'	128.5	4'
126.3	(2')	126.0	(2')
84.7	5	89.2	5
63.0	4	68.5	4
18.5	CH ₃	21.6	CH ₃
δ^1H (ppm) ^b	<i>H</i>	δ^1H (ppm)	<i>H</i>
7.4 (m)	2', 3', 4'	7.3 (m)	2', 3', 4'
5.6 (d, $J_{4,5} = 8.8$)	5	4.9 (d, $J_{4,5} = 7.3$)	5
5.0 (s, broad)	NH ₂	4.4 (s, broad)	NH ₂
4.3 (m, $J_{4,CH_3} = 7.0$)	4	4.0 (m, $J_{4,CH_3} = 6.5$)	4
0.7 (d)	CH ₃	1.3 (d)	CH ₃

^aValues in brackets may be reversed.^bs, singlet; d, doublet; m, multiplet.

UV

The two UV spectra (Figs. 5A and B) are superimposable, with a maximum at 258 nm, and an $E_{1\text{ cm}}^{1\%}$ of 11.6

From an examination of the spectra published in this report, it is clear that neither the MS nor the UV data could be used to assist in making a spectral distinction between the two compounds.

A comparison of spectra obtained from the two synthesized standards with those from the sample seized by the police showed that the seized material was the *cis*-isomer.

References

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