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INFRARED IDENTIFICATION OF N-1,3-DITHIOLAN-2-YLIDENE-4-HEXYL-BENZENAMINE BY THE ABSORBANCE RATIO METHOD

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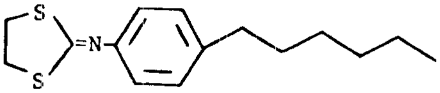
ABSTRACT

A simple infrared procedure for identifying N-1,3-dithiolan-2-ylidene-4-hexyl-benzenamine based on an absorbance ratio technique is described. It is demonstrated that the combination of band specifications and absorbance ratios can provide a specific method for the differentiation of a pharmaceutical raw material from isomeric substances and homologues.

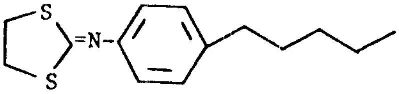
INTRODUCTION

Identification of a bulk drug substance is often established on the basis of an infrared spectrum. However, the infrared characteristics of the drug substance must be specific, allowing differentiation of close analogues. In the case of N-1,3-dithiolan-2-ylidene-4-hexyl-benzenamine, specificity requires the

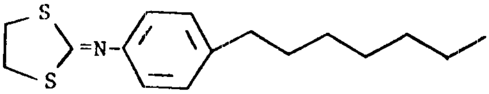
N-1,3-Dithiolan-2-ylidine -4-hexyl benzenamine



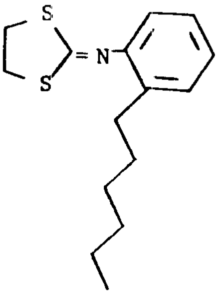
Pentyl homologue



Heptyl homologue



Ortho isomer



Meta isomer

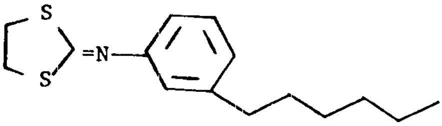


FIGURE 1

STRUCTURE FOR N-1,3-DITHIOLAN-2-YLIDINE-4-HEXYL-BENZENAMINE AND RELATED COMPOUNDS ability to differentiate homologues as well as positional isomers, Figure 1. The homologues present a problem in that the n-pentyl, n-hexyl and n-heptyl derivatives display identical infrared absorbance spectra. The meta substituted benzenamine has been identified as an impurity so the infrared must also provide specificity with respect to ring substitution.

The infrared ratio method has been used to quantitate carboxyl groups in rubbers, and to study methylene group absorptivities (1,2). The quantitative work with rubber suggested that chain-length could be differentiated on the basis of an absorbance ratio. Ring substitution was specified on the basis of differential band position to compensate for instrumental variations, especially in view of the proximity of the two absorptions, 1509 for the para isomer and 1485 for the meta isomers. The combination of a ratio in conjunction with differential band position to specify a pharmaceutical raw material represents a technique which has not, to our knowledge, been reported previously.

EXPERIMENTAL

Spectra were obtained in the absorbance mode with a Perkin Elmer Model 180 Spectrophotometer set up for a nominal resolution of 4 cm^{-1}. All samples were run as tetrachloroethylene solutions with concentrations of approximately 2% (w/w).

The absorbance ratio was calculated using the band at 1509 cm^{-1} and the band at 2926 cm^{-1}. Wavenumber differences were calculated for the band at 1509 cm^{-1} and the solvent band at 910 cm^{-1}.

RESULTS AND DISCUSSION

The infrared spectrum for N-1,3-dithiolan-2-ylidine-4-hexyl-benzenamine recorded neat along with the spectrum recorded as a 2% solution in tetrachloroethylene is presented in Figure 2.

The band at 2926 cm^{-1} reflecting chain length and the band at 1509 cm^{-1} specifying a para aromatic substitution were chosen to calculate the absorbance ratio. The spectra for the ortho and the meta isomers are presented in Figure 3. There is an absence in both spectra of the band at 1509 cm^{-1}. Instead, a band of lower intensity occurs in the neighborhood of 1485 cm^{-1}.

It was expected that the absorbance of the band at 2926 cm^{-1} would increase with increasing chain length and that the ratio of absorbances would provide a constant, indicative of chain length. The baseline method was used to obtain absorbance measurements. Ratios were obtained

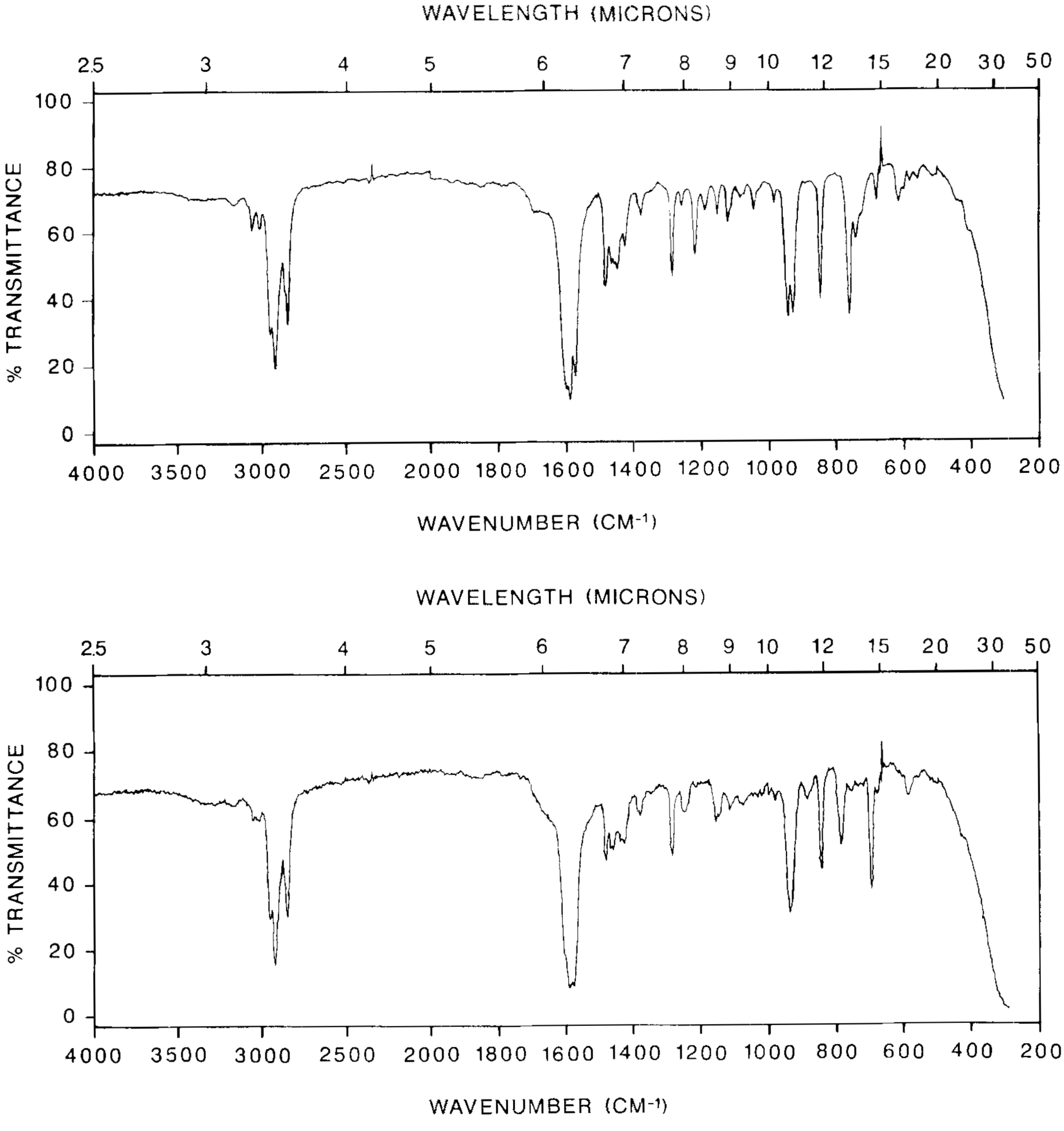


FIGURE 2

INFRARED SPECTRA FOR N-1, 3-DITHIOLAN-2-YLIDENE-4-HEXYLBENZENAMINE

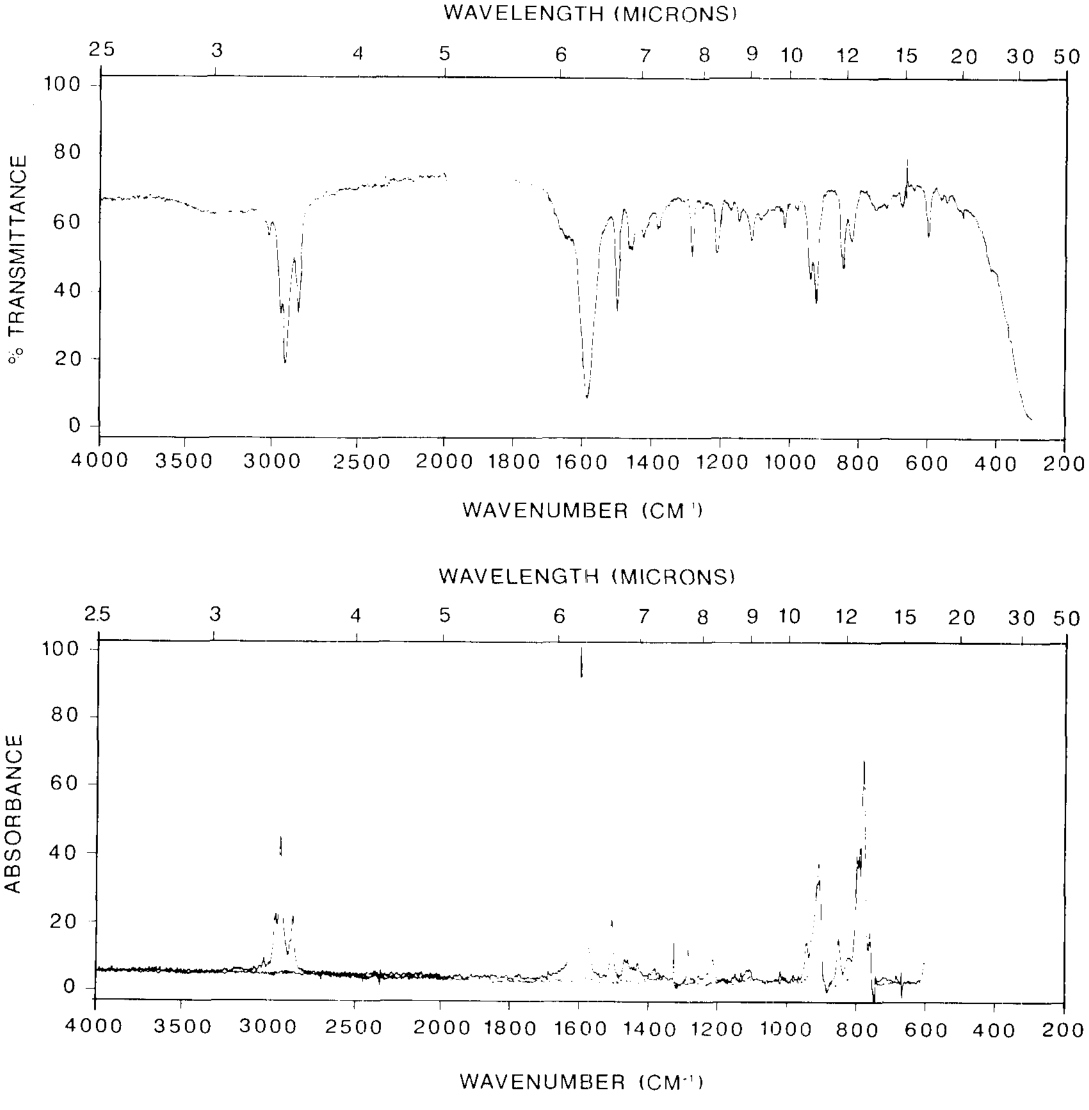


FIGURE 3

INFRARED SPECTRA FOR THE POSITION ISOMERS

TABLE 1

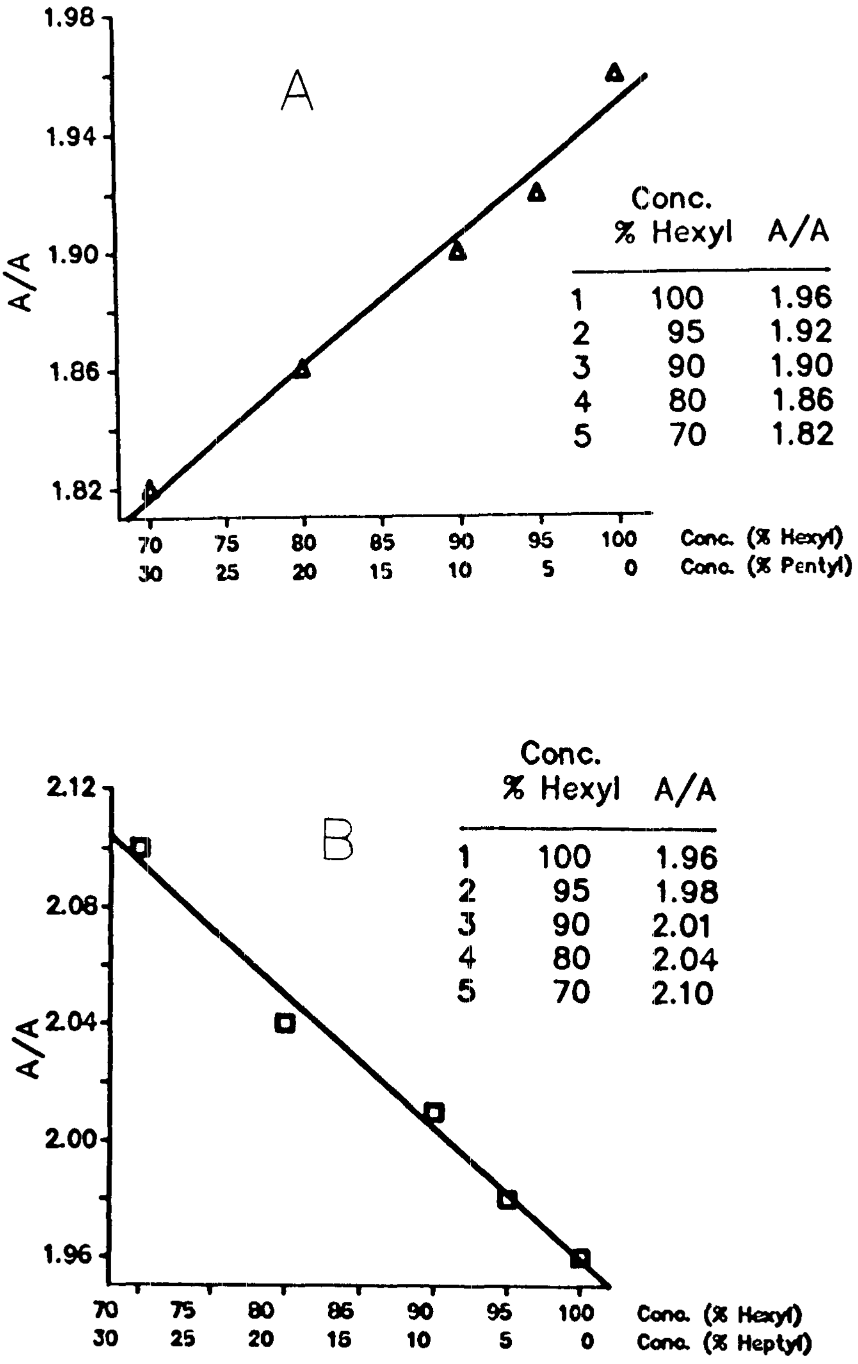
Infrared Absorbance Ratios For A Series Of Authentic Samples Of The N-Hexyl Homologue

Sample	$\frac{\text{Absorbance at } 2926\ \text{cm}^{-1}}{\text{Absorbance at } 1509\ \text{cm}^{-1}}$
A	2.1
B	2.1
C	1.9
D	2.0
E	1.9
F	2.0

by dividing the absorbance value for the band at 2926 cm^{-1} by the absorbance of the band at 1509 cm^{-1}. The ratios obtained were; 1.7 for the n-pentyl, 2.0 for the n-hexyl, and 2.2 for the n-heptyl homologue. The ratios calculated from the analysis of six authentic samples of the n-hexyl are presented in Table 1.

The change in the absorbance ratio when the n-hexyl sample was mixed with either the n-heptyl or the n-pentyl homologues was determined. Figure 4 presents plots of the absorbance ratio versus concentration for the mixtures. As expected, the addition of n-pentyl to the n-hexyl homologue lowered the ratio while the addition of the n-heptyl homologue raised the ratio. In each case a linear response was observed.

Isomer differentiation can be achieved by coupling the ratio calculation with a wavenumber difference calculation. The difference value results from subtracting the wavenumber for the solvent band at about 910 cm^{-1} from the wavenumber for the ring breathing band. Wavenumber differences of 577 cm^{-1}, 577 cm^{-1} and 599 cm^{-1}



	Conc. % Hexyl	A/A
1	100	1.96
2	95	1.92
3	90	1.90
4	80	1.86
5	70	1.82

	Conc. % Hexyl	A/A
1	100	1.96
2	95	1.98
3	90	2.01
4	80	2.04
5	70	2.10

FIGURE 4

A) MIXTURE OF PENTYL AND HEXYL COMPOUNDS

B) MIXTURE OF HEPTYL AND HEXYL COMPOUNDS

TABLE 2

WAVENUMBER DIFFERENCE DATA FOR AUTHENTIC SAMPLES OF N-1,3-DITHIOLAN-2-YLIDENE-4-HEXYL-BENZENAMINE

Sample	Band Position cm^{-1}	$\Delta\nu$ cm^{-1}
A	1505	597
B	1509	600
C	1505	603
D	1508	603
E	1505	598
F	1505	596

TABLE 3

WAVENUMBER DIFFERENCE DATA AND ABSORBANCE RATIO DATA FOR SYNTHETIC SAMPLES

Sample Composition	Absorbance Ratio	$\Delta\nu$
para, 80% ortho, 20%	2.33	589 cm^{-1}
para, 75% meta, 25%	2.24	593

were calculated for the ortho, meta, and para isomers, respectively. Data for six authentic samples of the para isomer are presented in Table 2.

The absorbance ratio is sensitive to sample composition. The lack of an absorption band at 1509 cm^{-1} raises the ratio. As a result mixtures of isomers may be detected. Table 3 presents data for synthetic mixtures of the para isomer with the ortho and the meta isomers. In each of the spectra for the synthetic mixtures, a shoulder with a maximum at about 1485 cm^{-1} is observed on the 1509 cm^{-1} band.

SUMMARY AND CONCLUSION

It is demonstrated in this study that the combination of band specification and an absorbance ratio provides a very specific method for the identification of N-1,3-dithiolan-2-ylidene-4-hexylbenzenamine samples. The data document the sensitivity of the measurements to chain length variations as well as to the presence of position isomers.

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