

# Distinction of Some Dialkyl Amides of Lysergic and *iso*-Lysergic Acids from LSD

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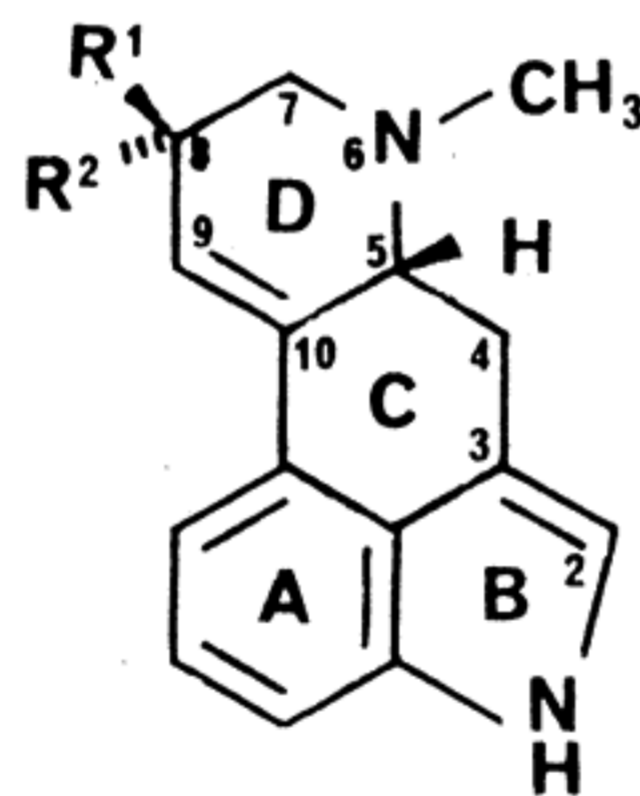
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The 10 lysergic and *iso*-lysergic acid amides described are *N,N*-dimethyl-, *N,N*-diethyl-, *N*-methyl-*N*-propyl-, *N*-ethyl-*N*-propyl-, and *N,N*-dipropyl-. Their ultraviolet spectra are insufficiently different for distinction. Mass spectra do not readily differentiate between isomers. Proton magnetic resonance spectra are distinct and provide a positive structural identification of the amide. Their infrared spectra are similar, but suitable for distinguishing these compounds from LSD. Various reference spectra are provided. Thin layer and gas-liquid chromatographic systems suitable for distinguishing these compounds from LSD are described.

*D*-Lysergic acid diethylamide (LSD, III) is the most potent hallucinogen known and one of the most widely abused. An unambiguous identification is imperative in courts of law. Chromatographic techniques have been used extensively (1), although they are regarded as not completely specific, and infrared (IR) spectroscopy has therefore been recommended (2). Mass spectrometry has been suggested (3) and was claimed (4) to provide an unequivocal method for establishing the presence of LSD. However, as reported below, the mass spectra of the *N*-methyl-*N*-propyl amides of lysergic and *iso*-lysergic acids are similar to those of LSD (3, 4) and *iso*-LSD (IV), and confusion could arise. Previously, spectral and chromatographic comparisons between LSD, other ergot alkaloids, and structurally dissimilar compounds (e.g., tryptamines, amphetamines, etc.) have been made. This report describes the mass spectra, ultraviolet (UV), proton magnetic resonance (PMR), and IR spectra of simple dialkylamides of *D*-lysergic acid and *D*-*iso*-lysergic acid: *N,N*-dimethyl (I and II); *N,N*-diethyl (III and IV); *N*-methyl-*N*-propyl (V and VI); *N*-ethyl-*N*-propyl (VII and VIII); and *N,N*-dipropyl (IX and X). The spectroscopic properties were expected to resemble those of LSD more than for compounds previously re-

ported. Some systems which distinguish these compounds from LSD by thin layer chromatography (TLC) and gas-liquid chromatography (GLC) are evaluated.

- I  $R^1 = \text{CON}(\text{CH}_3)_2, R^2 = \text{H}$
- II  $R^1 = \text{H}, R^2 = \text{CON}(\text{CH}_3)_2$
- III  $R^1 = \text{CON}(\text{C}_2\text{H}_5)_2, R^2 = \text{H}$
- IV  $R^1 = \text{H}, R^2 = \text{CON}(\text{C}_2\text{H}_5)_2$
- V  $R^1 = \text{CON}(\text{CH}_3)\text{C}_3\text{H}_7, R^2 = \text{H}$
- VI  $R^1 = \text{H}, R^2 = \text{CON}(\text{CH}_3)\text{C}_3\text{H}_7$
- VII  $R^1 = \text{CON}(\text{C}_2\text{H}_5)\text{C}_3\text{H}_7, R^2 = \text{H}$
- VIII  $R^1 = \text{H}, R^2 = \text{CON}(\text{C}_2\text{H}_5)\text{C}_3\text{H}_7$
- IX  $R^1 = \text{CON}(\text{C}_3\text{H}_7)_2, R^2 = \text{H}$
- X  $R^1 = \text{H}, R^2 = \text{CON}(\text{C}_3\text{H}_7)_2$



## Experimental

The amides were prepared from *D*-lysergic acid by suitably adapting a published method (5). An authentic sample of LSD was available from these laboratories. Column chromatography on alumina (6) was used for separation, purification, and preliminary identification of isomers. Confirmation that the second eluted isomer belonged to the *iso* series (6) came from PMR spectra<sup>1</sup> (see *Results*). Melting points were as follows: recrystallized VI, 172–173° (lit. (7) 180–181°); IX, 192–195° (lit. (6) 195°); LSD, 87–92° (lit. (8) 80–85°); and *iso*-LSD, 176–178° (lit. (8) 182°); all were subject to decomposition. The amides I and II were initially isolated as solids, but

attempts to recrystallize them were unsuccessful. Compound II has a reported melting point of 146° (6).

All of the amides are unstable in light and air. Infrared spectra were determined as soon as possible after column chromatography. The central fraction of series indicated by TLC to contain only one component was examined. PMR spectra were determined at 60 MHz in these laboratories by H. W. Avdovitch, using a Varian A-60A; at 100 MHz on a Varian XL-100 through the courtesy of G. Buchanan, Carleton University, Ottawa; and at 220 MHz on a Varian HR-220 by A. Grey, Ontario Research Foundation, Sheridan Park, Ontario. Mass spectra were measured in these laboratories by W. Miles, using a Hitachi Perkin-Elmer RMS-4 operated at 80 eV with a probe temperature of about 170 and source at 250°. TLC was carried out on layers (ca 250  $\mu\text{m}$ ) deposited on glass from slurries of silica gel G with water or ("Basic") with 0.5*N* NaOH, and of aluminum oxide G from water. The plates were dried by heating at 110° for 1 hr within 1/2 hr of preparation and then stored for equilibration at 24°C, relative humidity 40–45%, for 24 hr before use. Precoated plates and precoated sheets were used as received.

In the case of Solvents E, F, and G (Table 1), the plates were developed for their full length (20 cm) in the solvent system, and the solvent was allowed to evaporate from the plate for 45 min in a fume-hood before spotting. Spots of a mixture (ca 1+1) of each isomeric pair (e.g., I + II) and also mixtures of III/IV and V/VI were applied to each plate, and the chromatogram was developed for 15 cm. The plate was examined under 254 nm UV light and sprayed with a 1% solution of *p*-dimethylaminobenzaldehyde in 90% ethanolic sulfuric acid, which produces long-lasting blue-violet spots with all of these amides. GLC was carried out with an all-glass system. Bis(trimethylsilyl) acetamide was used for silylation (9).

## Results and Discussion

### Ultraviolet Spectra

All of the amides of lysergic acid in ethanol exhibit absorption maxima at about 311 nm and a shoulder or inflexion at 235–240 nm. The *iso*-lysergamides have maxima at about 306 nm (ca 311 nm for IX), and inflexions at 235–240 nm. The spectra are characteristic of such indole derivatives, and are not suitable for distinction from LSD (3, 9).

### Mass Spectra

Normalized spectra of compounds I, V, VII and IX are presented in Figs. 1–4, respectively. The spectra of the *iso*-lysergamides very closely resemble those shown for their corresponding isomers, and distinction is not considered satisfactory. Further, the mass spectra of IV, V, and VI are very similar to those recorded for LSD (3, 4). Since the molecular ion is generally the base peak of these spectra, the presence of LSD or one of its isomers is immediately determined. The breakdown of the molecular ions exactly parallels that reported for LSD (3, 4).

### Proton Magnetic Resonance Spectra

Present PMR techniques require comparatively large amounts of material (i.e., several milligrams) and are not likely to be used by forensic analysts, who are often limited to microgram quantities. In deuteriochloroform, several clear signals (singlets or finely split multiplets) are observed at 60 or 100 MHz, and sample identification is possible by examining the integrated PMR spectra. Thus, average chemical shifts (ppm downfield of internal TMS) for the lysergamides are 2.58 (N-CH<sub>3</sub>), 6.35 (=CH), 6.85 (ring 1

Table 1. Solvent systems for thin layer chromatography

No.	System
A <sup>a</sup>	1,1,1-trichloroethane:methyl ethyl ketone:methanol (7:2:1)
B <sup>a</sup>	hexane:ethyl acetate:methanol (7:13:15)
C <sup>a</sup>	toluene:nitromethane:methanol (8:10:2)
D <sup>a</sup>	chloroform:methanol (9:1)
E	benzene: <i>N,N</i> -dimethylformamide (9:1)
F <sup>b</sup>	benzene: <i>N,N</i> -dimethylformamide (13:2)
G <sup>b</sup>	ethyl acetate: <i>N,N</i> -dimethylformamide:ethanol (13:1.9:0.1)
H <sup>b</sup>	chloroform:ether:water (organic phase) (3:1:1)
J <sup>c</sup>	chloroform saturated with aqueous ammonia:methanol (18:1)
K <sup>d</sup>	chloroform:acetone (1:2)

<sup>a</sup> Beckstead, H. D., & French, W. N. (1971) *Some Analytical Methods for Drugs Subject to Abuse*, Department of National Health and Welfare, Ottawa, Canada.

<sup>b</sup> McLaughlin, J. L., Goyan, J. E., & Paul, A. G. (1964) *J. Pharm. Sci.* **53**, 306.

<sup>c</sup> Sperling, A., private communication.

<sup>d</sup> Davis, J. S., private communication, Food and Drug Administration, 1966.

<sup>1</sup> G. A. Neville, Research Laboratories, kindly furnished an authenticated PMR spectrum of LSD.

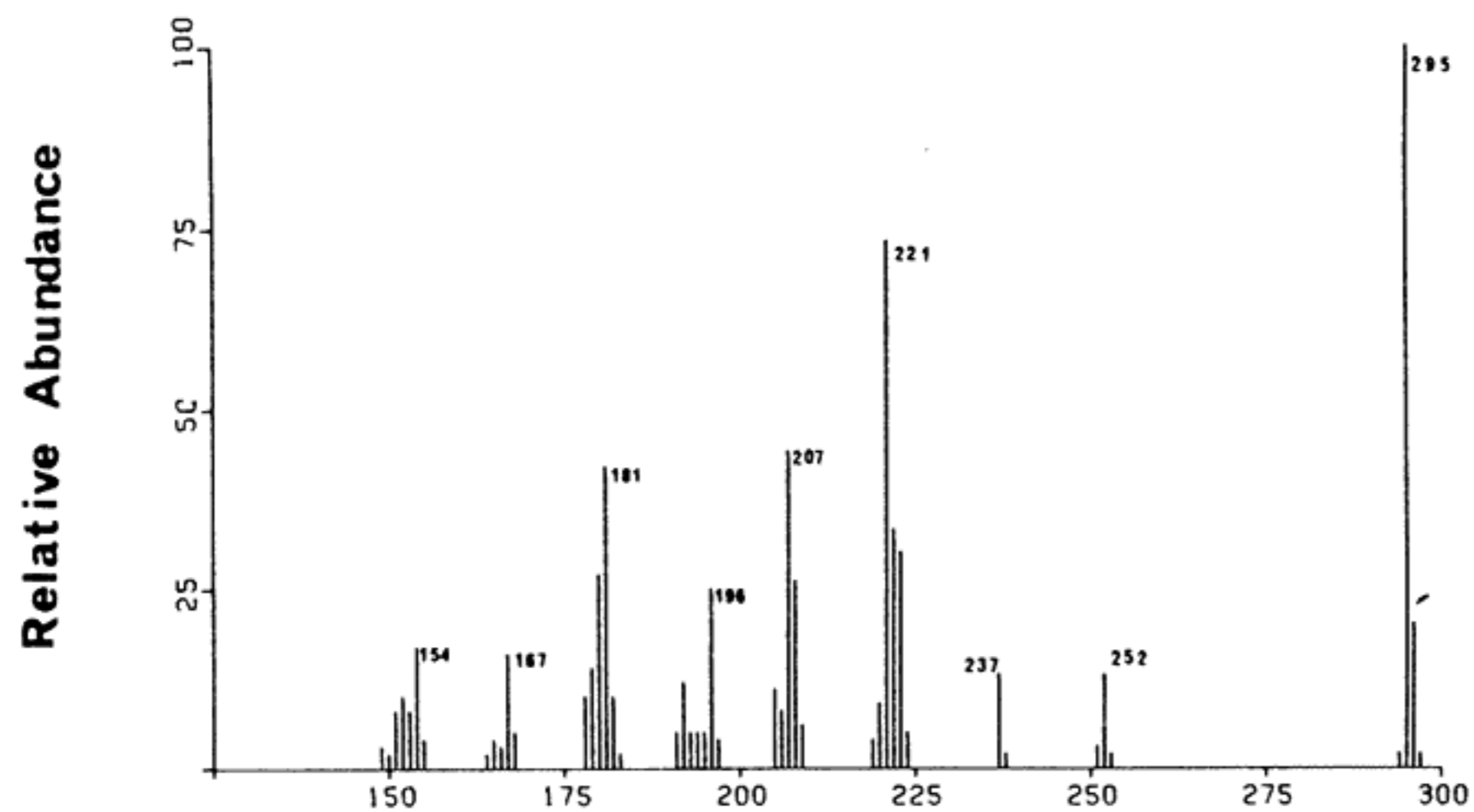


FIG. 1—Normalized mass spectrum of lysergic acid dimethylamide I.

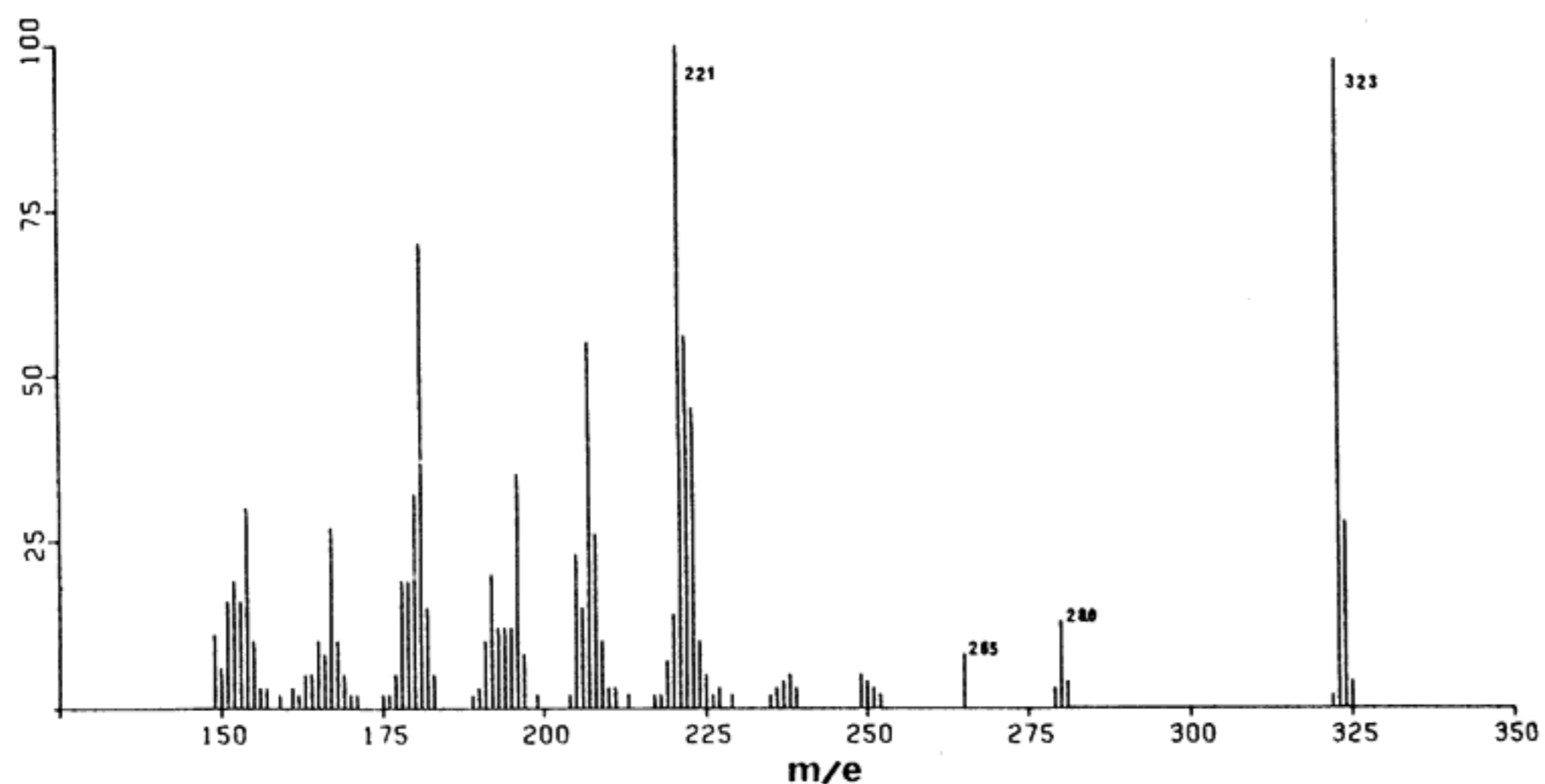


FIG. 2—Normalized mass spectrum of lysergic acid methylpropylamide V.

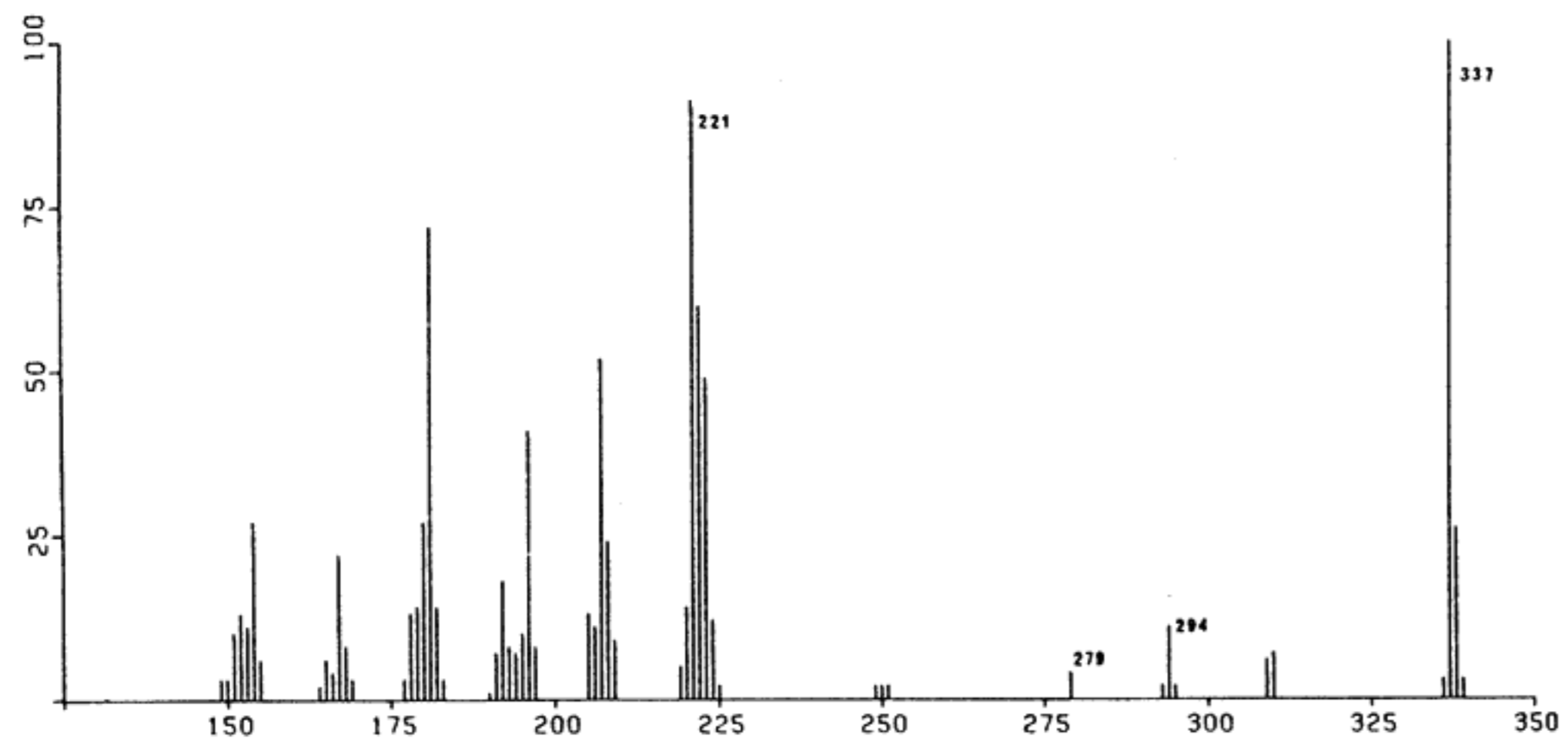


FIG. 3—Normalized mass spectrum of lysergic acid ethylpropylamide VII.

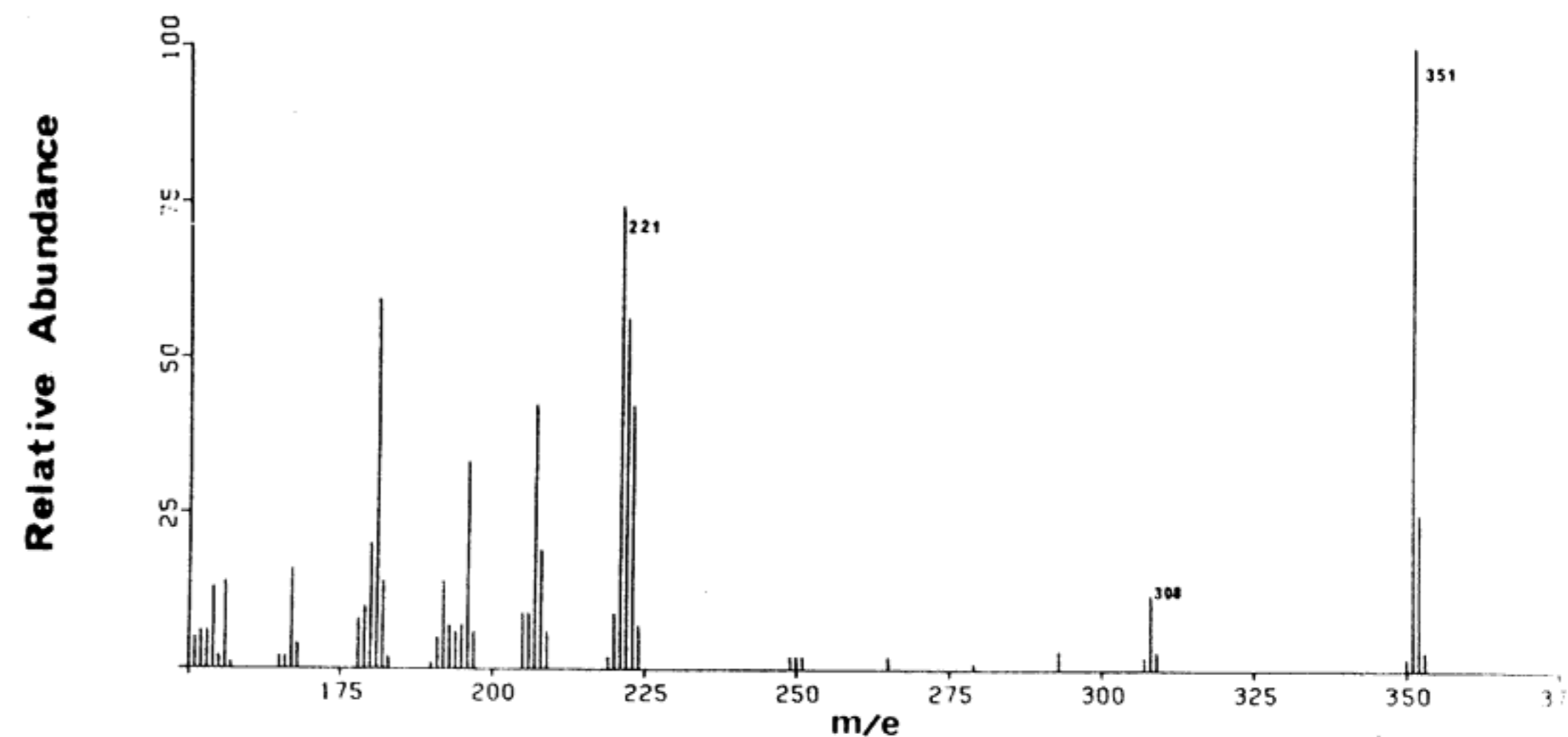


FIG. 4—Normalized mass spectrum of lysergic acid dipropylamide IX.

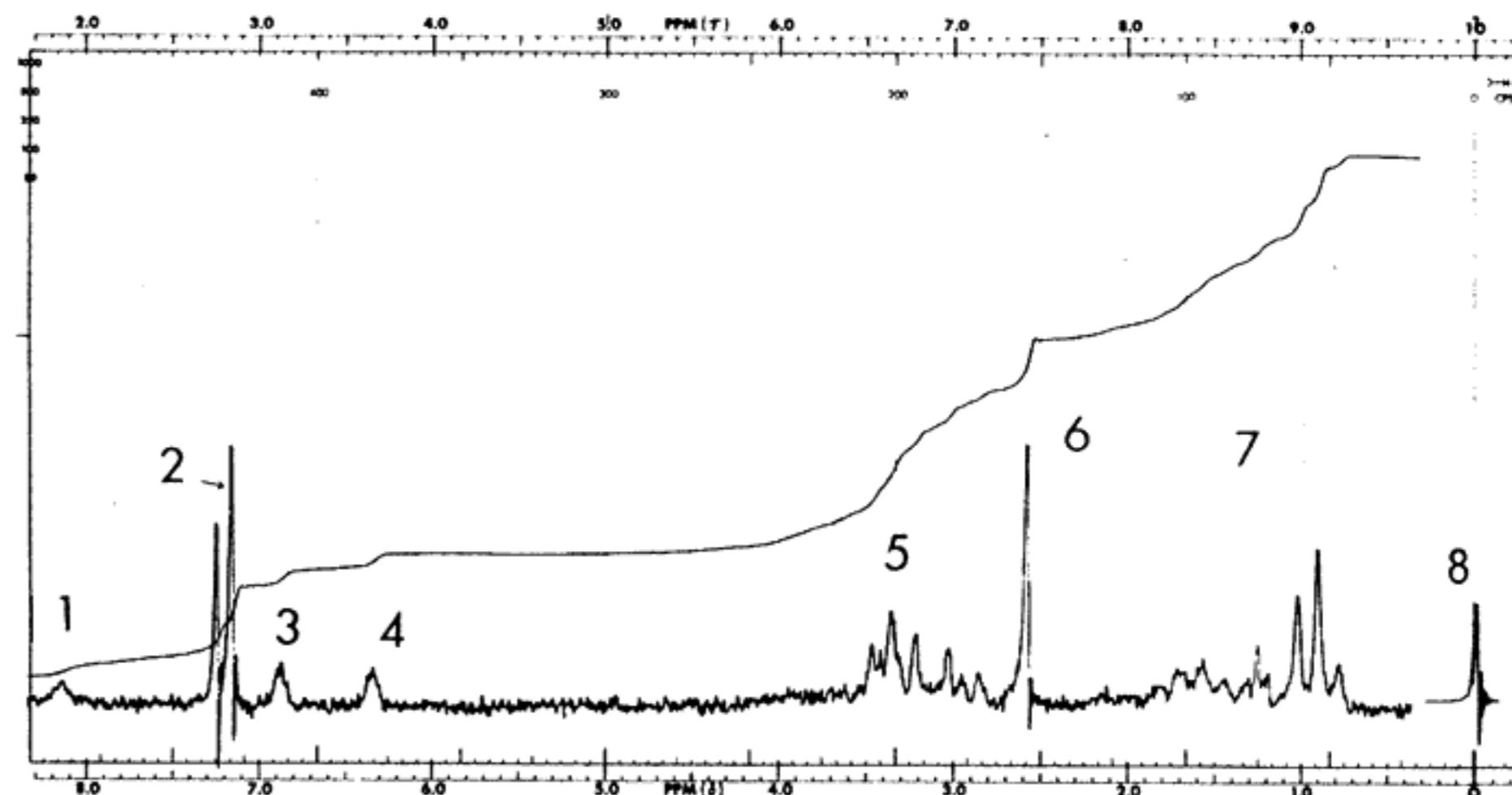
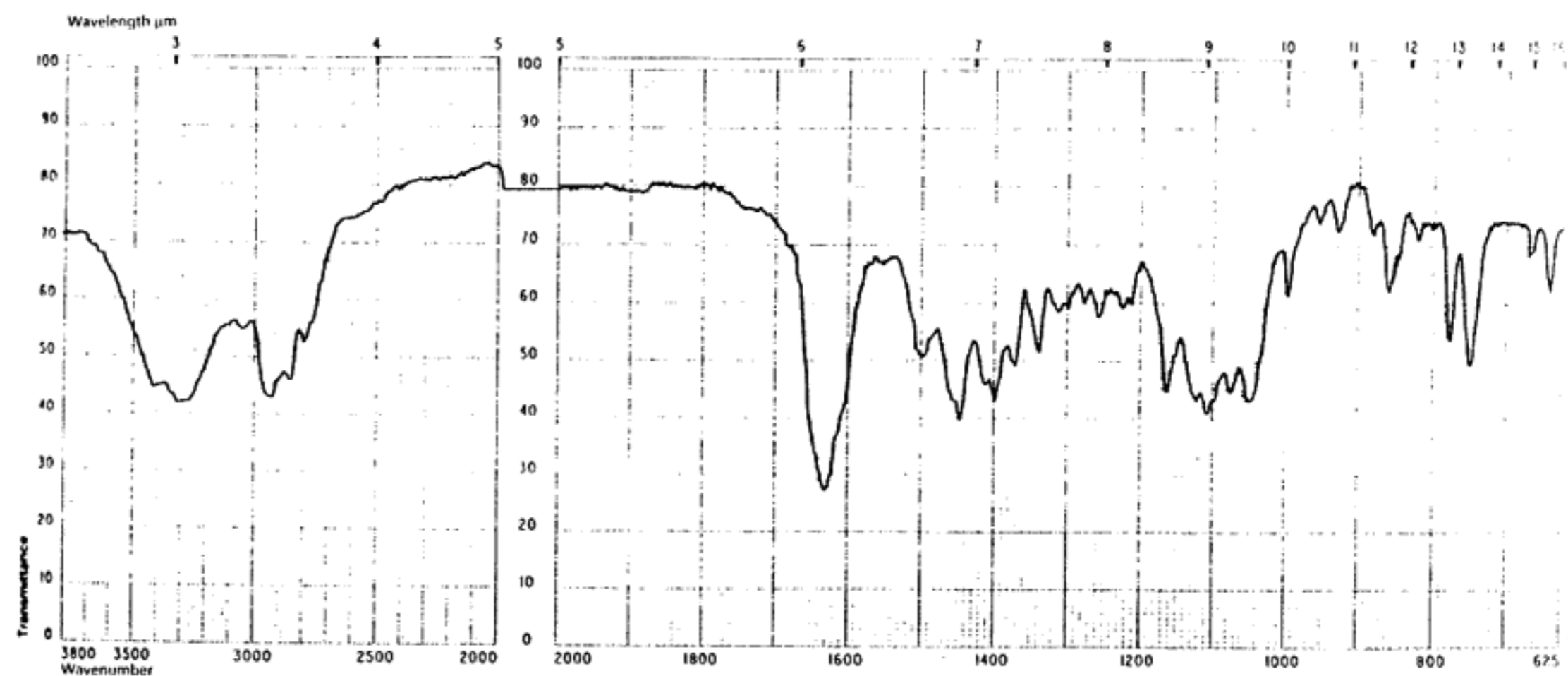
FIG. 5—60 MHz PMR spectrum of lysergic acid dipropylamide IX in  $\text{CDCl}_3$ . 1, N—H. 2, Ring A protons. 3, Ring proton. 4, Olefinic proton. 5,  $\text{CON}(\text{CH}_2)_2$ , alicyclic protons. 6, N— $\text{CH}_3$ . 7,  $(-\text{CH}_2\text{CH}_3)_2$  protons. 8, Internal TM

FIG. 6—Infrared spectrum of lysergic acid dimethylamide; KBr window.



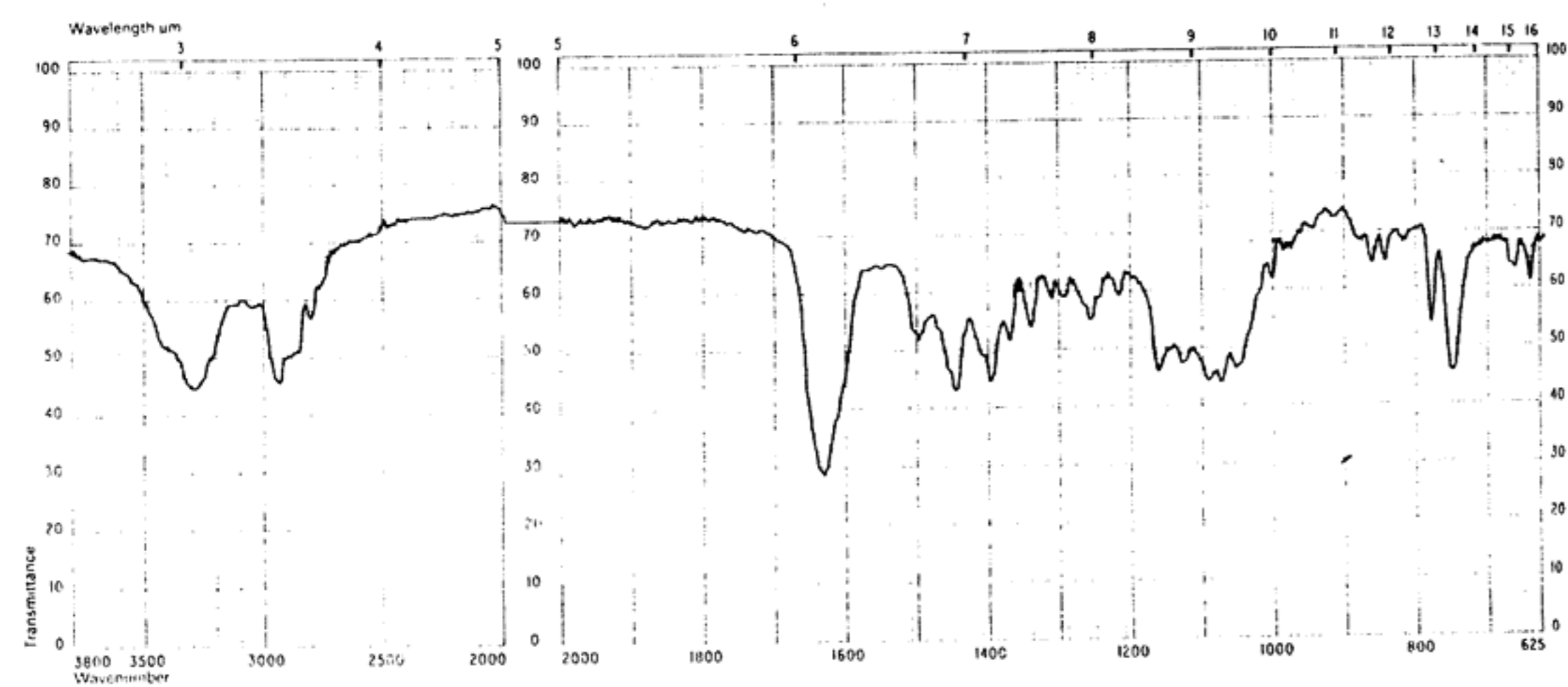


FIG. 7—Infrared spectrum of *iso*-lysergic acid dimethylamide; KBr window.

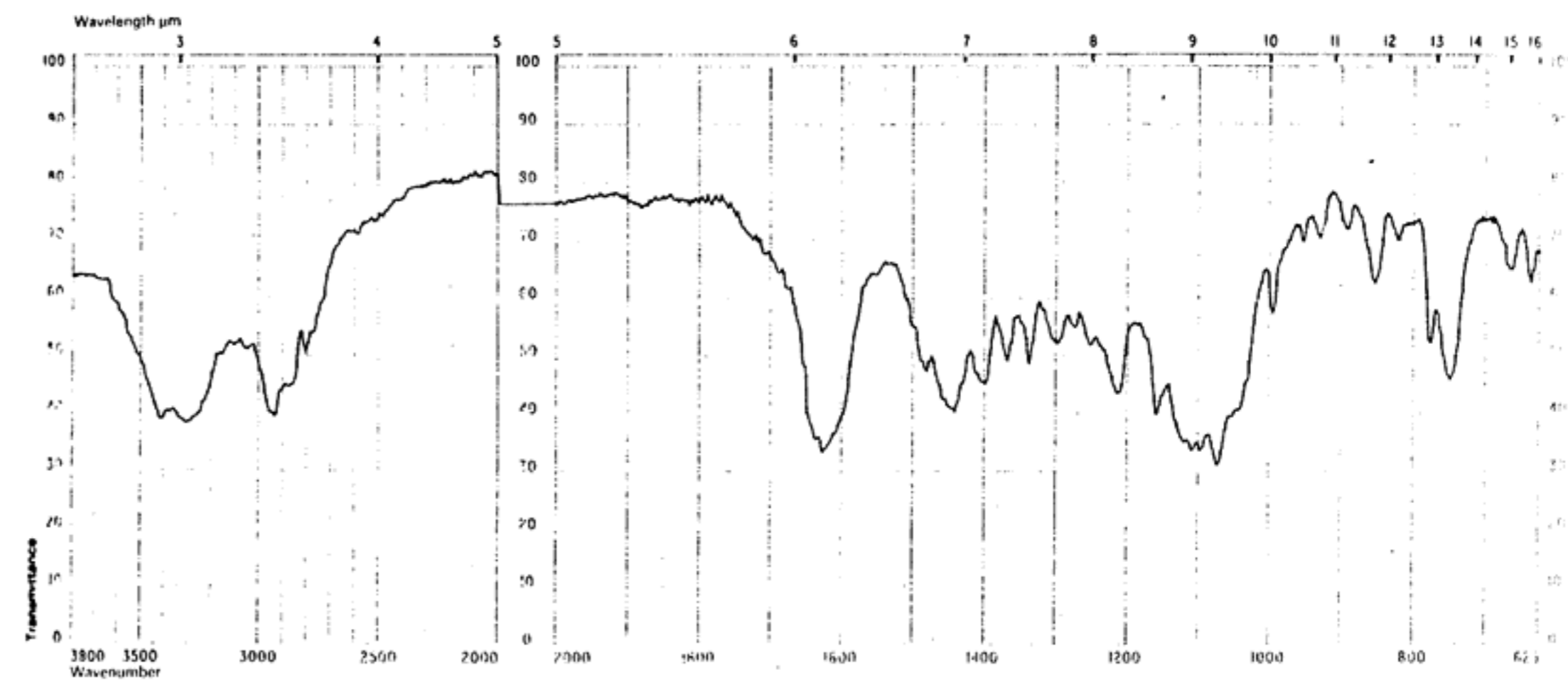


FIG. 10—Infrared spectrum of lysergic acid *N*-methyl-*N*-propylamide; KBr window.

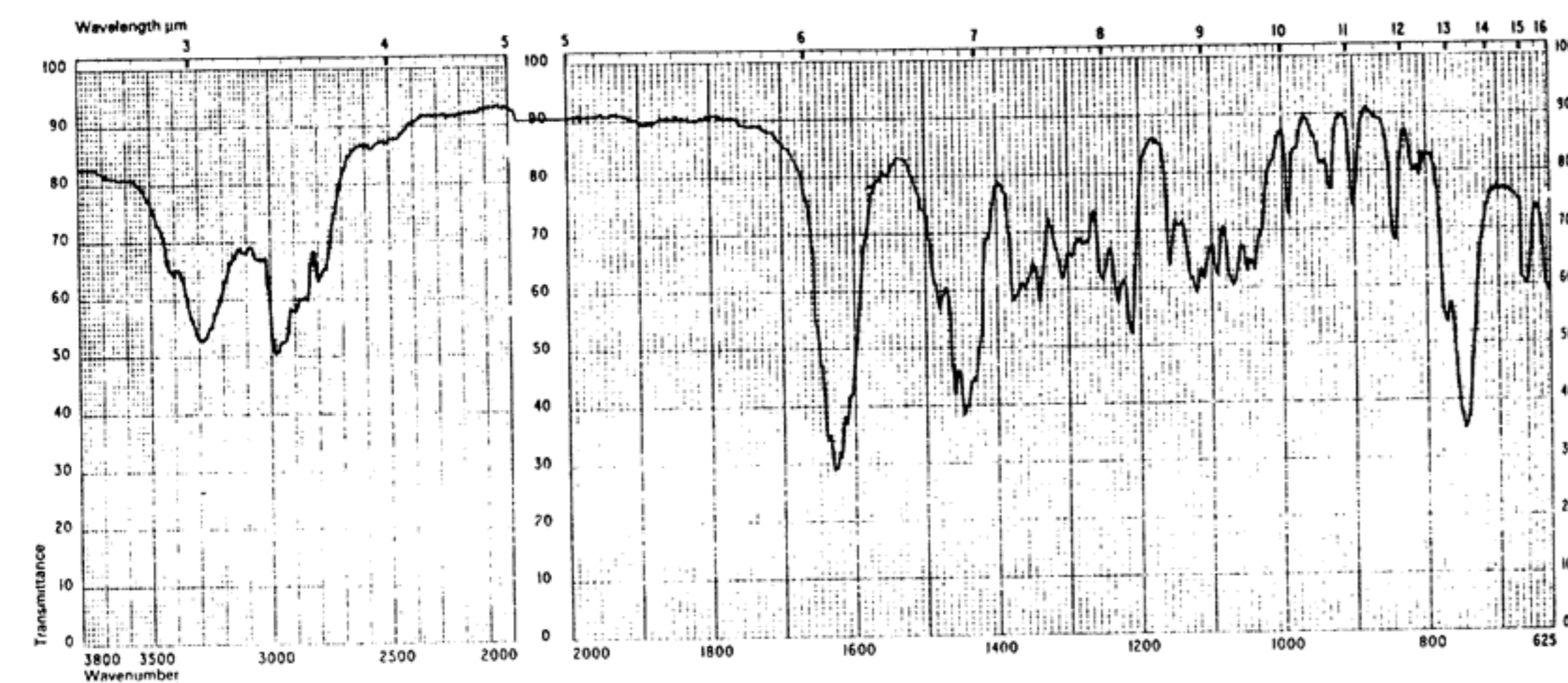


FIG. 8—Infrared spectrum of "amorphous" LSD; NaCl window.

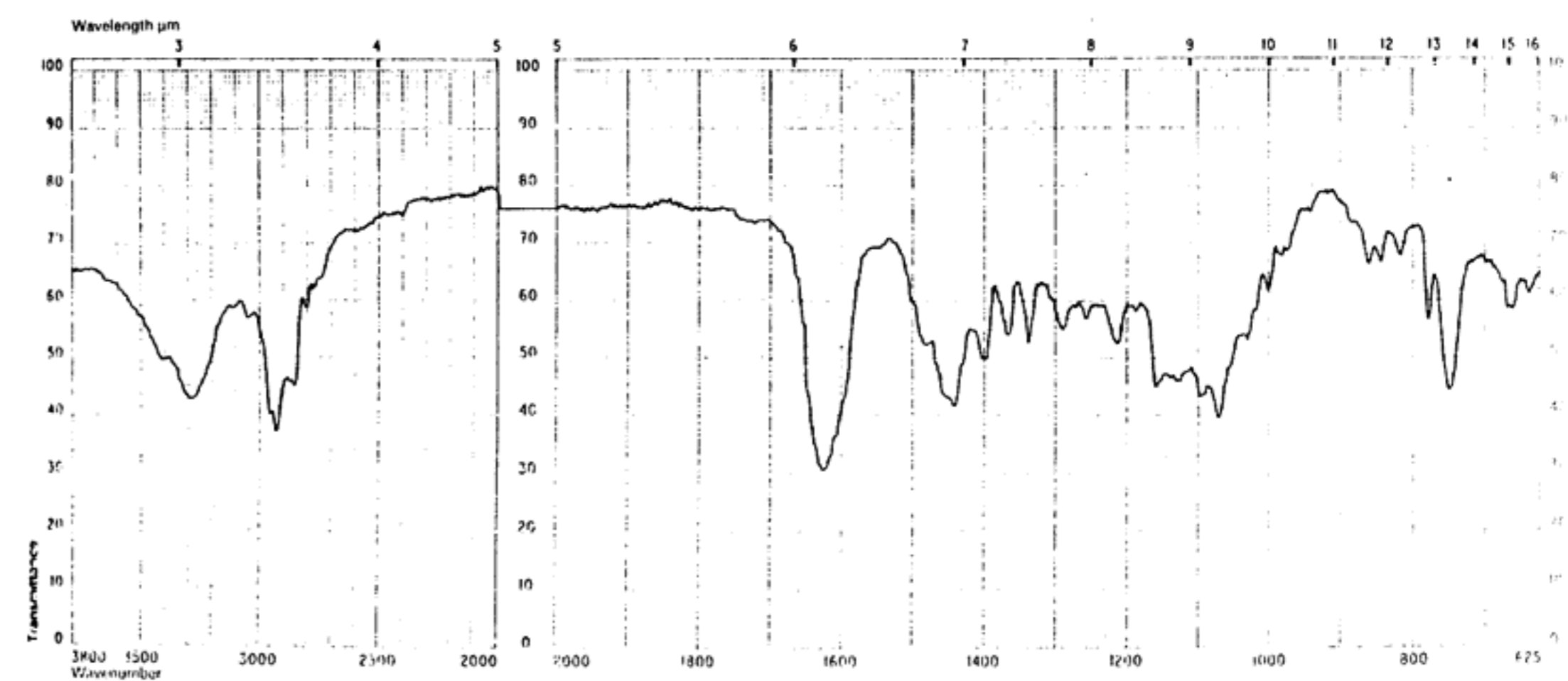


FIG. 11—Infrared spectrum of *iso*-lysergic acid *N*-methyl-*N*-propylamide; KBr window.

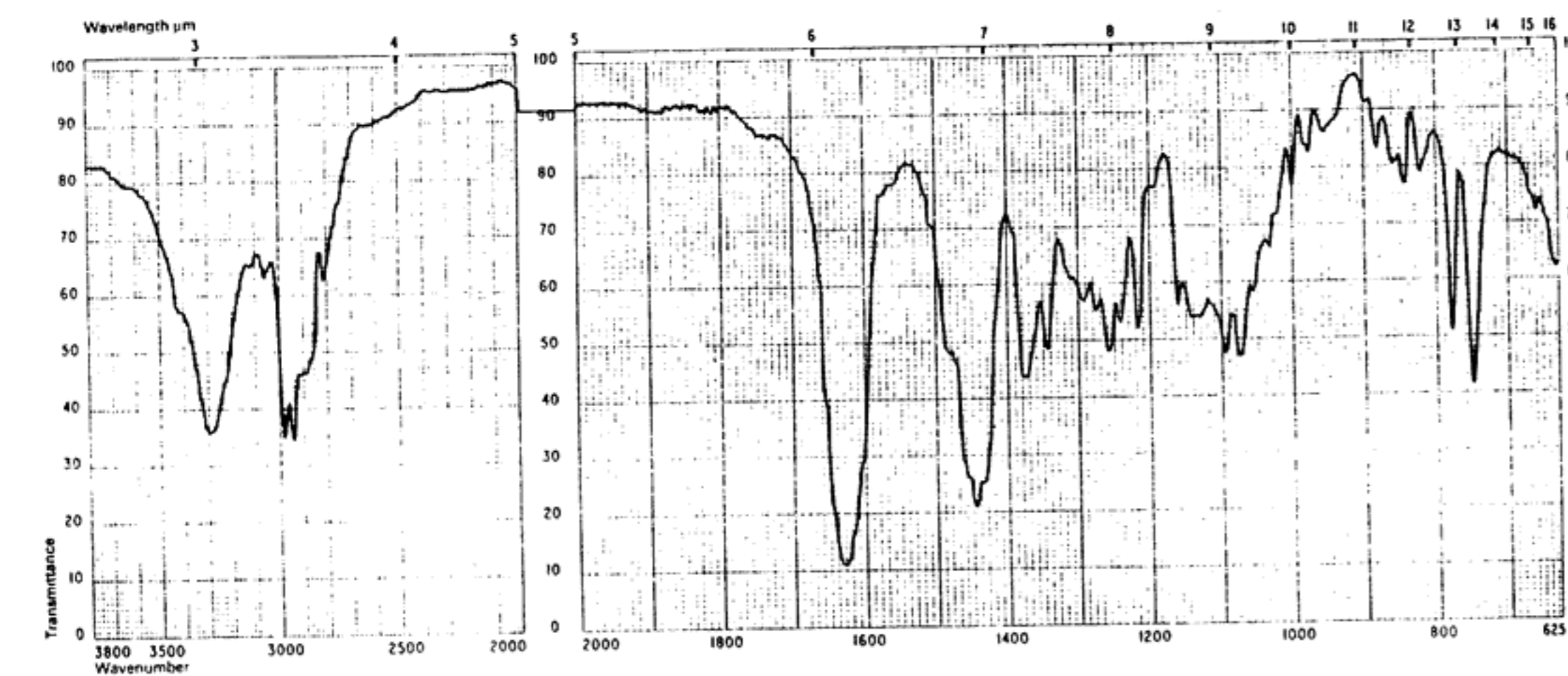


FIG. 9—Infrared spectrum of "amorphous" *iso*-LSD; film, NaCl plates.

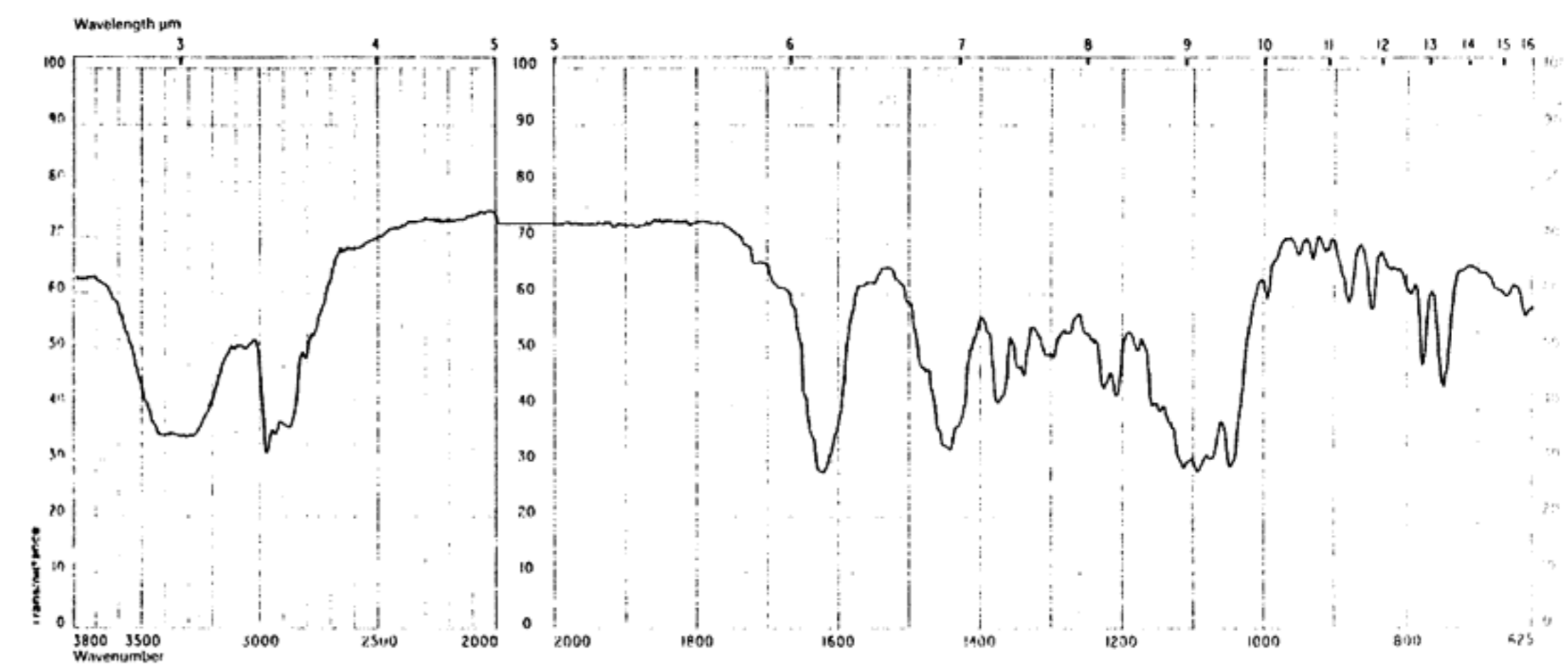


FIG. 12—Infrared spectrum of lysergic acid *N*-ethyl-*N*-propylamide; KBr window.



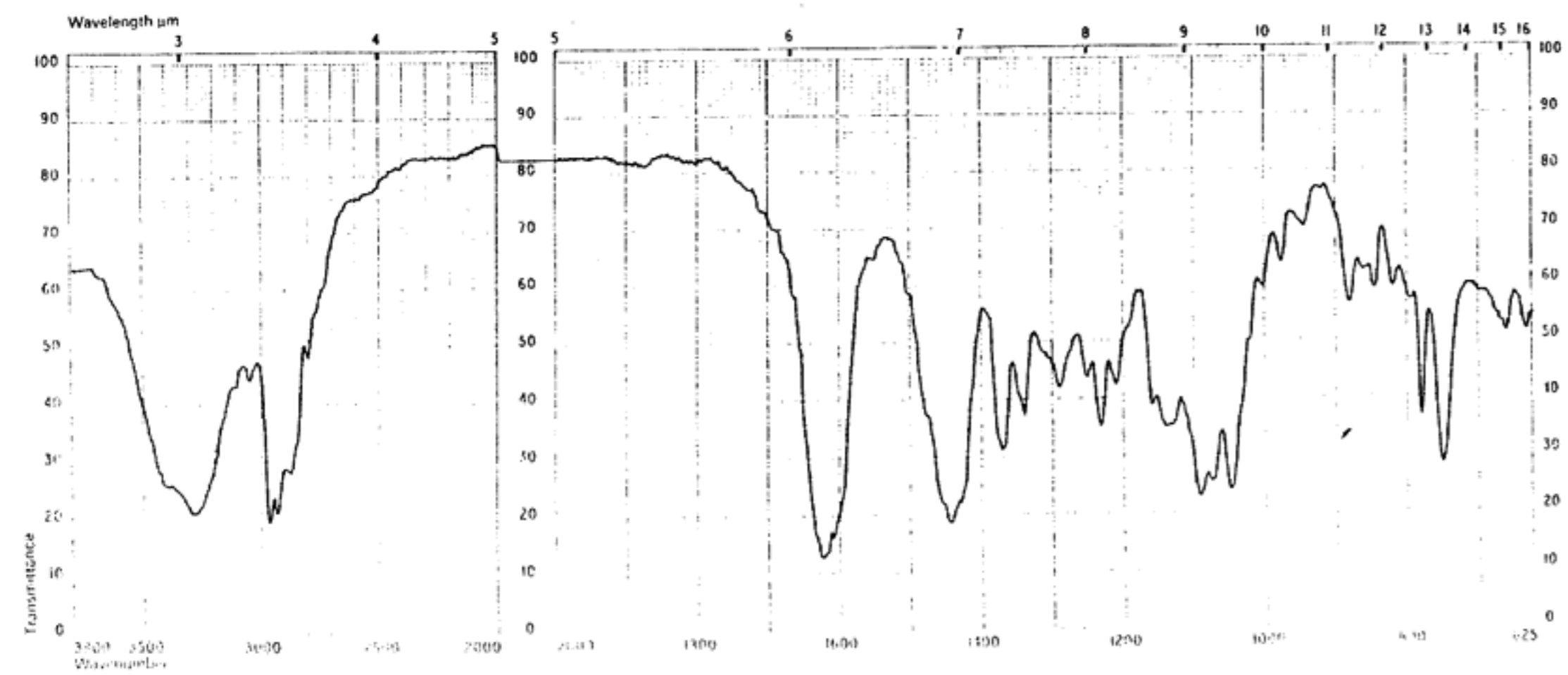


FIG. 13—Infrared spectrum of *iso*-lysergic acid *N*-ethyl-*N*-propylamide; KBr window.

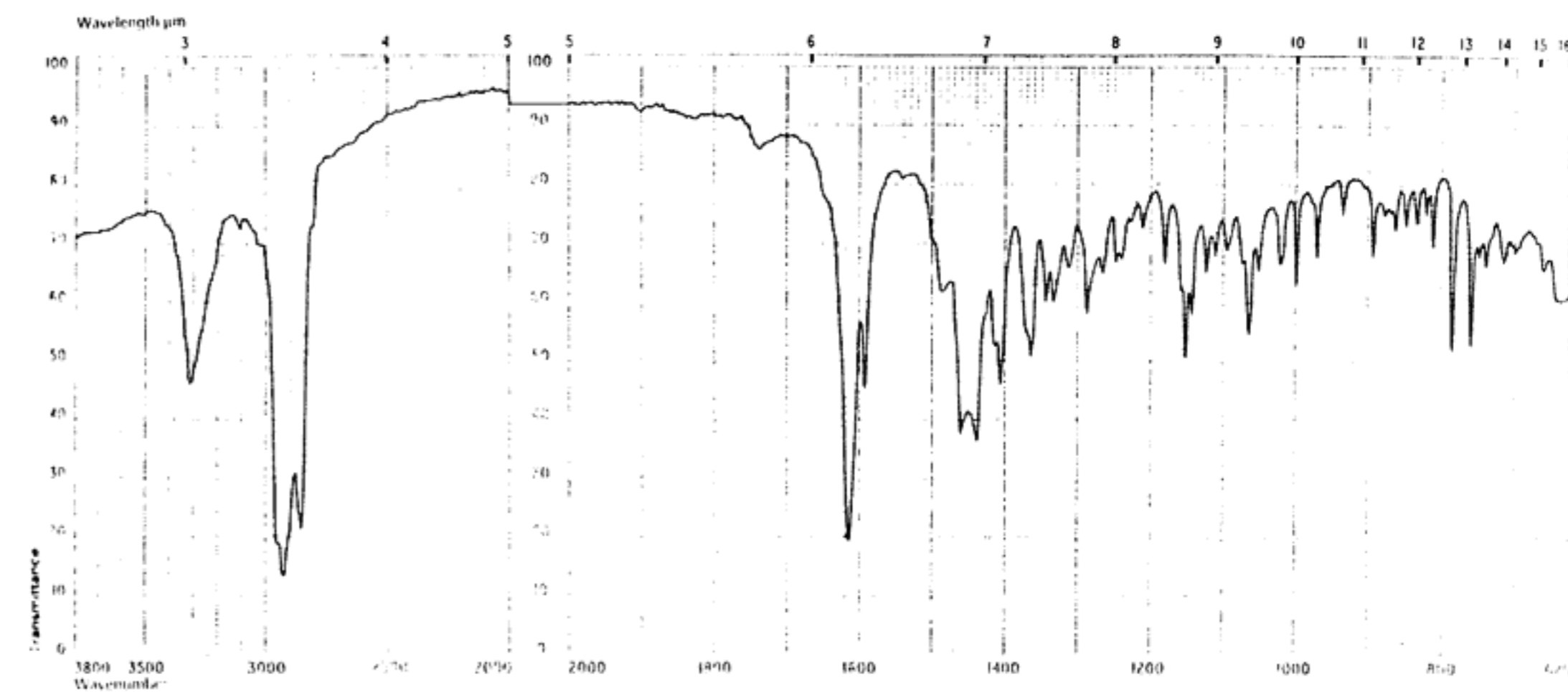


FIG. 16—Infrared spectrum of *iso*-lysergic acid *N*-methyl-*N*-propylamide, mp 172–173°; Nujol mull, NaCl plates.

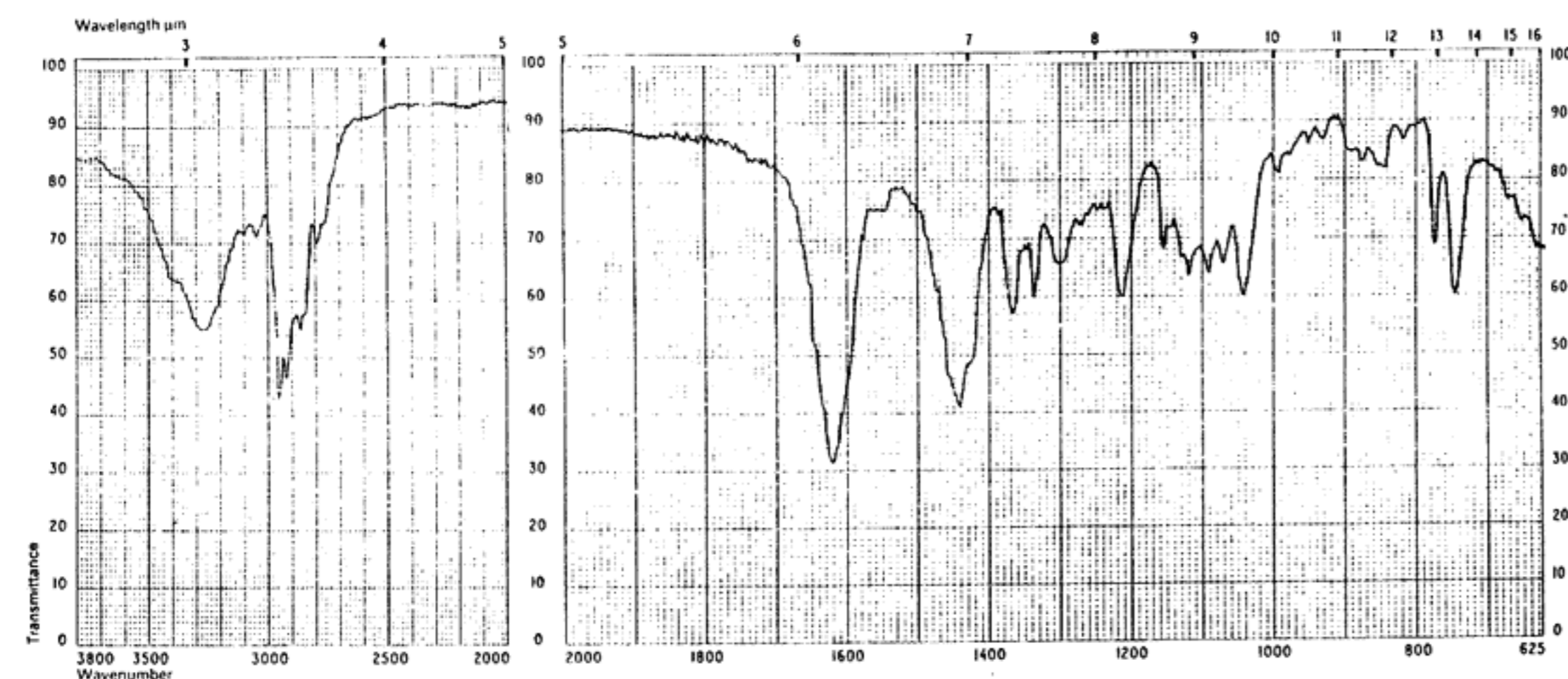


FIG. 14—Infrared spectrum of lysergic acid dipropylamide; film, NaCl plates.

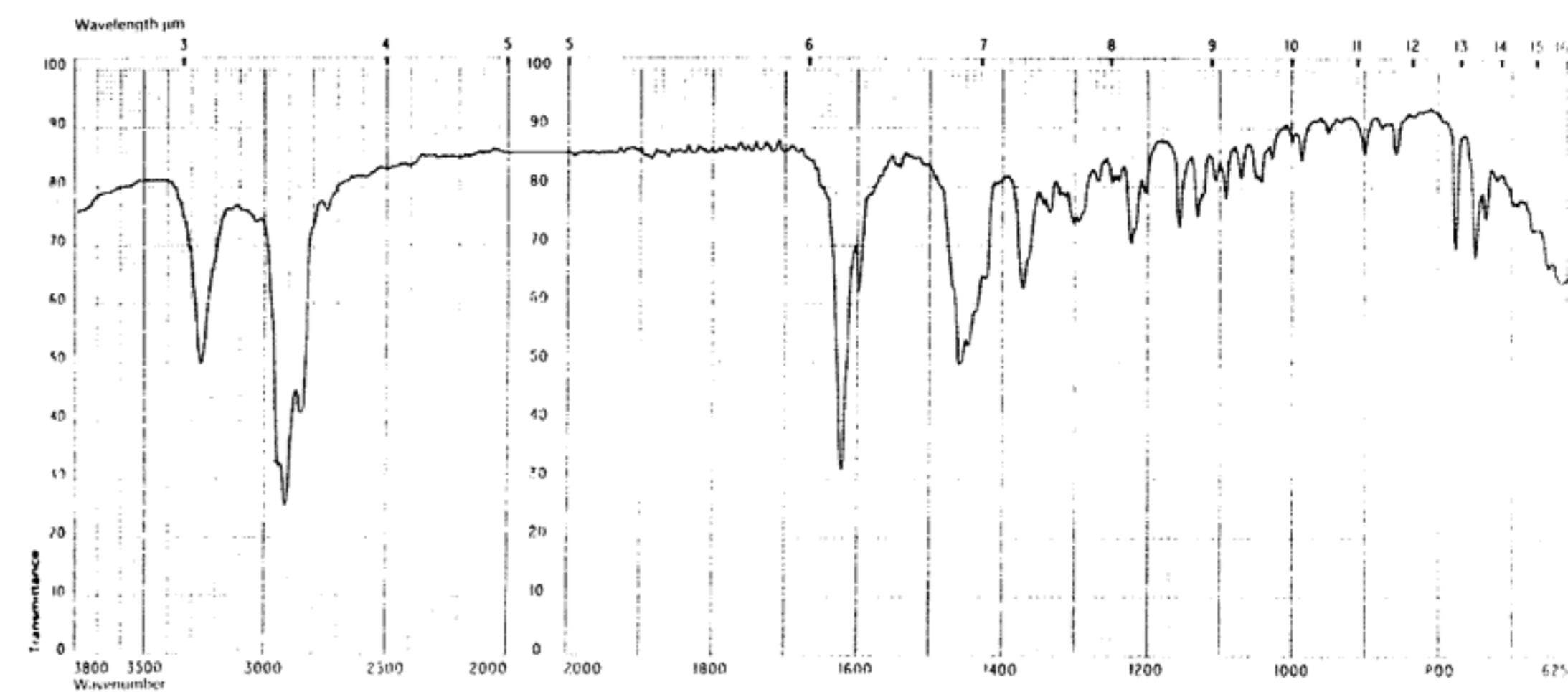


FIG. 17—Infrared spectrum of lysergic acid dipropylamide, mp 190° (dec.); Nujol mull, NaCl plates.

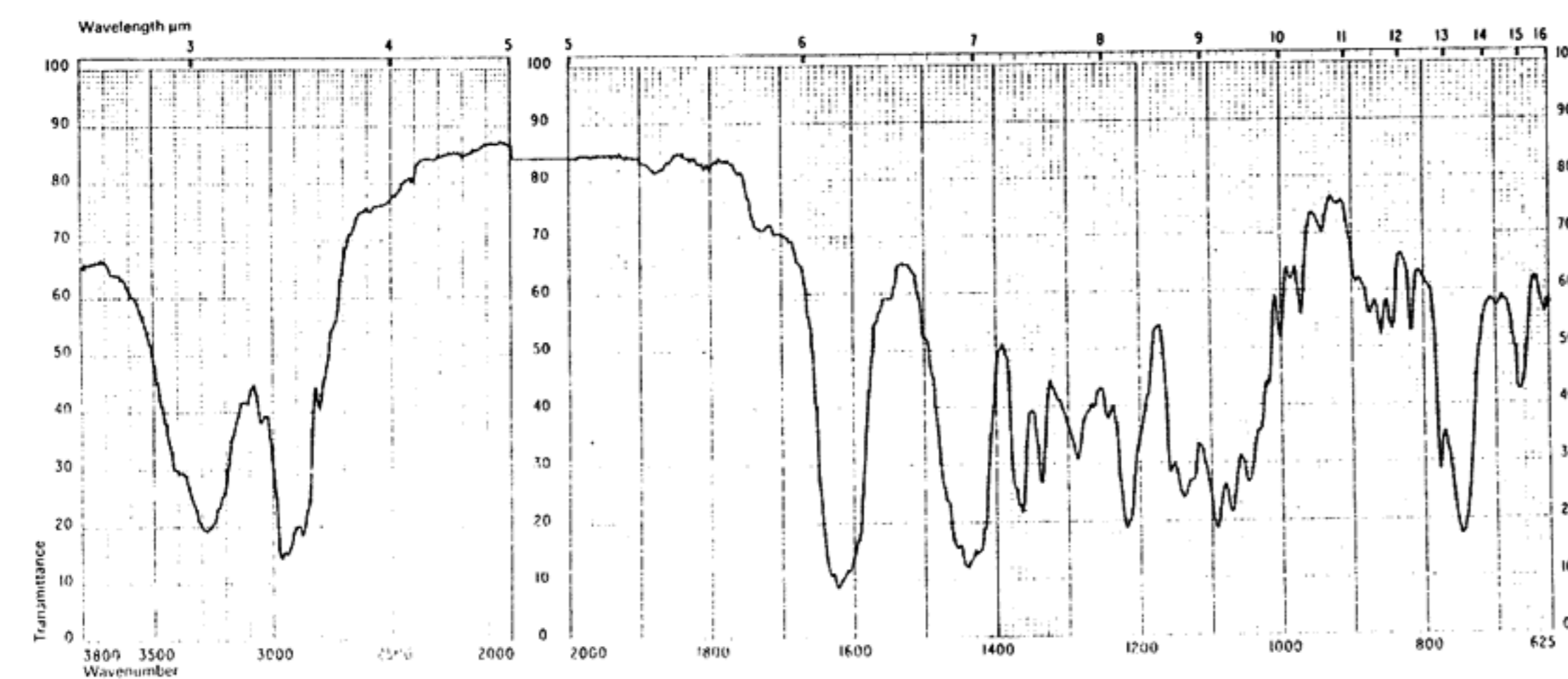


FIG. 15—Infrared spectrum of *iso*-lysergic acid dipropylamide; KBr window.

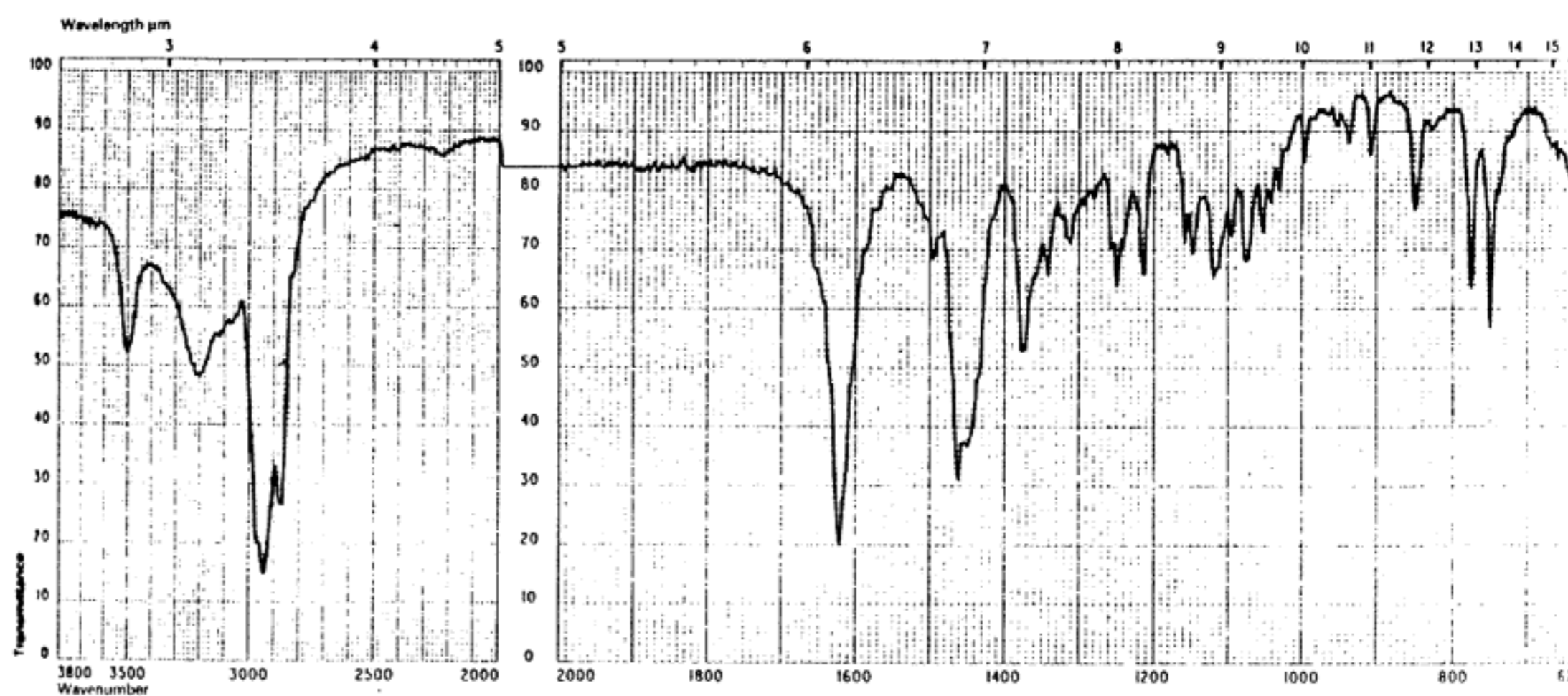


FIG. 18—Infrared spectrum of LSD, mp 87–92°; Nujol mull, NaCl plates.



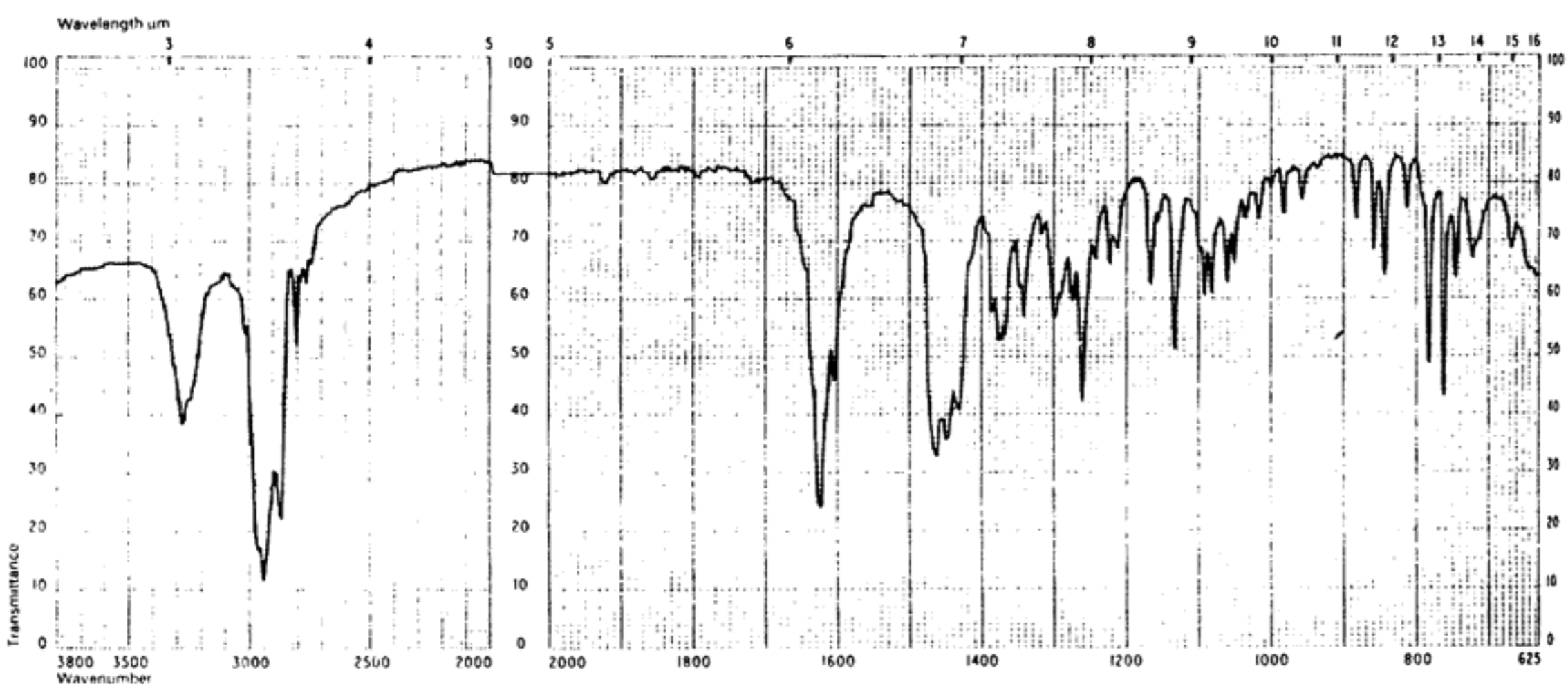


FIG. 19—Infrared spectrum of *iso*-LSD, mp 176–178°; Nujol mull, NaCl plates.

protons), and 7.15 (ring A protons). Signals for individual homologues varied by  $\pm 0.02$  ppm. The corresponding signals for the *iso*-lysergamides appear at 2.59, 6.25, 6.79, and 7.05 ppm ( $\pm 0.03$  ppm). More complex signals result from the other protons, and a conformational analysis of I and II by PMR at 220 MHz has been made (K. Bailey and A. Grey, unpublished results). The spectrum of IX (Fig. 5) is typical of the regular series.

#### Infrared Spectra

Infrared techniques for microgram quantities of LSD are well established and routinely used. The spectra reproduced here (Figs. 6–19) are for the free bases (see *Experimental*). LSD is usually examined in this “amorphous” state, i.e., as the smear obtained on NaCl plates or KBr disks when an ethereal or chloroform solution is evaporated on the disk surface (Fig. 8). The spectra in Figs. 6–15 are for the “amorphous” films. Compounds VI and IX readily crystallized, however, and the spectra of the films changed spontaneously after an hour or so of standing in a desiccator, a second spectrum being almost identical (apart from Nujol peaks) with that obtained for a recrystallized specimen determined in a Nujol mull. Evidently these films had become microcrystalline. The spectra of crystalline VI, IX, LSD (III), and *iso*-LSD (IV) are accordingly recorded (Figs. 16–19) to demonstrate that the compounds need not be confused as a result of these changes of state. The following observations are made: (i) Spectra obtained on either NaCl or KBr disks and measured on any one of 3 machines (produced by 3 manu-

facturers) allowed a positive identification of the samples. (ii) Crystalline state affects the spectra in a reproducible way. (iii) The spectra of isomeric pairs (regular vs. *iso* series) tend to resemble one another more than other isomers or homologues. (iv) Although the resolution of peaks is affected by film thickness, the region 1150–1350  $\text{cm}^{-1}$  consistently distinguishes LSD spectra from those of the homologues presented here. The spectra of I and II are like that of LSD in this region; however, signals at about 1400  $\text{cm}^{-1}$  occur for I and II but not for LSD. (Spectra of the LSD isomers V and VI also have this peak, which is tentatively assigned to the methylamide moiety.) The spectra of LSD and *iso*-LSD reproduced here compare well with those published (2, 9, 10). Spectra of other lysergic and *iso*-lysergic acid derivatives have been published (8).

#### Thin Layer Chromatography

TLC methods for the identification (1) and quantitation (11, 12) of amides of lysergic and *iso*-lysergic acids have been reported in which LSD was compared with structurally unrelated compounds (1) or with derivatives of lysergic acid (1, 11, 13) considerably less like LSD in structure than the homologues and isomers described here. Systems employed are described in Table 1 and the results of  $R_f$  measurement, intended as a guide only (14), in Tables 2–6. The results show that LSD (III) could possibly be confused with only its isomer, lysergic acid *N*-methyl-*N*-propylamide (V). Distinction of III and V was, however, definite in those systems denoted by foot-

Table 2.  $R_f$  and  $R_f'$  values of lysergic and *iso*-lysergic acid amides (silica gel G plates<sup>a</sup>)

Compound	$R_f$ ( $R_f'$ ) in system:									
	A	B	C	D	E	F	G	J	K <sup>b</sup>	
I	0.10 (0.40)	0.33 (0.65)	0.13 (0.52)	0.29 (0.73)	0.14 (0.42)	0.23 (0.51)	0.20 (0.50)	0.39 (0.78)	0.10 (0.40)	
II	0.04 (0.16)	0.15 (0.29)	0.04 (0.16)	0.10 (0.25)	0.09 (0.27)	0.15 (0.33)	0.14 (0.35)	0.25 (0.50)	0.05 (0.16)	
III	0.25 (1.00)	0.51 (1.00)	0.25 (1.00)	0.40 (1.00)	0.33 (1.00)	0.45 (1.00)	0.40 (1.00)	0.50 (1.00)	0.25 (1.00)	
IV	0.08 (0.32)	0.25 (0.49)	0.14 (0.56)	0.12 (0.30)	0.17 (0.52)	0.29 (0.64)	0.25 (0.63)	0.31 (0.62)	0.09 (0.32)	
V	0.24 (0.96)	0.50 (0.98)	0.24 (0.96)	0.39 (0.98)	0.30 (0.91)	0.41 (0.91)	0.38 (0.95)	0.49 (0.98)	0.22 (0.96)	
VI	0.06 (0.24)	0.24 (0.47)	0.13 (0.52)	0.10 (0.25)	0.17 (0.52)	0.28 (0.62)	0.23 (0.58)	0.30 (0.60)	0.08 (0.24)	
VII	0.13 (1.32)	0.58 (1.14)	0.29 (1.16)	0.45 (1.13)	0.40 (1.21)	0.48 (1.07)	0.45 (1.13)	0.53 (1.06)	0.35 (1.13)	
VIII	0.11 (0.44)	0.31 (0.61)	0.14 (0.56)	0.14 (0.35)	0.24 (0.73)	0.35 (0.78)	0.30 (0.75)	0.34 (0.68)	0.13 (0.44)	
IX	0.39 (1.56)	0.62 (1.22)	0.33 (1.32)	0.50 (1.25)	0.48 (1.45)	0.52 (1.16)	0.50 (1.25)	0.55 (1.10)	0.44 (1.56)	
X	0.20 (0.80)	0.42 (0.82)	0.15 (0.60)	0.20 (0.50)	0.33 (1.00)	0.40 (0.89)	0.36 (0.90)	0.38 (0.76)	0.23 (0.80)	

<sup>a</sup> See Experimental.  $R_f' = R_f$  amide/ $R_f$  LSD.

<sup>b</sup> This system distinguished III from V.

Table 3.  $R_f$  and  $R_f'$  values of lysergic and *iso*-lysergic acid amides (“Basic” silica gel G plates<sup>a</sup>)

Compound	$R_f$ ( $R_f'$ ) in system:									
	A	B	C	D	E <sup>b</sup>	F <sup>b</sup>	G <sup>b</sup>	J	K <sup>c</sup>	
I	0.13 (0.52)	0.34 (0.63)	0.14 (0.47)	0.27 (0.68)	0.11 (0.39)	0.23 (0.53)	0.20 (0.56)	0.43 (0.88)	0.31 (0.63)	
II	0.10 (0.40)	0.25 (0.46)	0.09 (0.30)	0.17 (0.43)				0.25 (0.51)	0.18 (0.43)	
III	0.25 (1.00)	0.54 (1.00)	0.30 (1.00)	0.40 (1.00)	0.28 (1.00)	0.43 (1.00)	0.36 (1.00)	0.49 (1.00)	0.39 (1.00)	
IV	0.18 (0.72)	0.44 (0.81)	0.12 (0.40)	0.24 (0.60)				0.26 (0.53)	0.32 (0.72)	
V	0.24 (0.96)	0.52 (0.96)	0.30 (1.00)	0.39 (0.98)	0.27 (0.96)	0.41 (0.95)	0.35 (0.97)	0.50 (1.02)	0.35 (0.96)	
VI	0.18 (0.72)	0.42 (0.78)	0.13 (0.43)	0.24 (0.60)				0.26 (0.53)	0.30 (0.72)	
VII	0.33 (1.32)	0.59 (1.09)	0.34 (1.13)	0.44 (1.10)	0.37 (1.32)	0.53 (1.23)	0.48 (1.33)	0.58 (1.18)	0.45 (1.32)	
VIII	0.24 (0.96)	0.50 (0.93)	0.13 (0.43)	0.27 (0.73)				0.33 (0.67)	0.37 (0.96)	
IX	0.36 (1.44)	0.66 (1.22)	0.37 (1.23)	0.47 (1.18)	0.45 (1.61)	0.59 (1.37)	0.53 (1.47)	0.63 (1.29)	0.53 (1.44)	
X	0.28 (1.12)	0.59 (1.09)	0.17 (0.57)	0.32 (0.80)				0.42 (0.86)	0.45 (1.12)	

<sup>a</sup> See footnote a, Table 2.

<sup>b</sup> This system failed to separate mixtures of the regular and *iso*-amides.

<sup>c</sup> See footnote b, Table 2.

Table 4.  $R_f$  and  $R_f'$  values of lysergic and *iso*-lysergic acid amides (precoated silica gel plates<sup>a</sup>)

Compound	$R_f$ ( $R_f'$ ) in system:							
	A	B	D	E	F	G <sup>b</sup>	J	K
I	0.09 (0.50)	0.30 (0.65)	0.22 (0.63)	0.09 (0.41)	0.16 (0.48)	0.16 (0.48)	0.24 (0.60)	0.06 (0.24)
II	0.02 (0.11)	0.11 (0.24)	0.05 (0.14)	0.04 (0.18)	0.07 (0.21)	0.08 (0.24)	0.16 (0.40)	0.04 (0.11)
III	0.18 (1.00)	0.46 (1.00)	0.35 (1.00)	0.22 (1.00)	0.33 (1.00)	0.33 (1.00)	0.40 (1.00)	0.17 (1.00)
IV	0.04 (0.22)	0.18 (0.39)	0.08 (0.23)	0.07 (0.32)	0.13 (0.39)	0.14 (0.42)	0.20 (0.50)	0.04 (0.22)
V	0.17 (0.94)	0.45 (0.98)	0.34 (0.97)	0.19 (0.86)	0.32 (0.97)	0.29 (0.88)	0.38 (0.95)	0.14 (0.94)
VI	0.04 (0.22)	0.17 (0.37)	0.07 (0.20)	0.06 (0.27)	0.13 (0.39)	0.12 (0.36)	0.19 (0.48)	0.03 (0.22)
VII	0.24 (1.33)	0.55 (1.20)	0.42 (1.20)	0.28 (1.27)	0.42 (1.27)	0.41 (1.24)	0.44 (1.10)	0.23 (1.33)
VIII	0.05 (0.28)	0.24 (0.52)	0.10 (0.29)	0.10 (0.45)	0.16 (0.48)	0.18 (0.55)	0.22 (0.55)	0.04 (0.28)
IX	0.30 (1.67)	0.61 (1.33)	0.45 (1.29)	0.34 (1.55)	0.49 (1.48)	0.48 (1.45)	0.48 (1.20)	0.29 (1.67)
X	0.11 (0.61)	0.33 (0.72)	0.15 (0.43)	0.19 (0.86)	0.25 (0.76)	0.29 (0.88)	0.28 (0.70)	0.10 (0.61)

<sup>a,b</sup> See footnotes to Table 2. The plates were Brinkmann silica gel G. E (3 passes) distinguished III 0.54 (1.00) and V 0.49 (0.90), and K (3 passes) distinguished III 0.33 (1.00) and V 0.27 (0.82).



Table 5.  $R_f$  and  $R_f'$  values of lysergic and iso-lysergic acid amides (precoated silica gel sheets<sup>a</sup>)

Com- pound	$R_f (R_f')$ in system:										
	A	B	C	D	E	F	G	H	J	K	
I	0.23 (0.62)	0.57 (0.81)	0.26 (0.65)	0.49 (0.84)	0.40 (0.62)	0.46 (0.78)	0.62 (0.95)	0.05 (0.50)	0.45 (0.90)	0.21 (0.58)	
II	0.13 (0.35)	0.45 (0.64)	0.11 (0.28)	0.31 (0.53)	0.33 (0.51)	0.42 (0.71)	0.57 (0.88)	0.01 (0.10)	0.35 (0.70)	0.14 (0.39)	
III	0.37 (1.00)	0.70 (1.00)	0.40 (1.00)	0.58 (1.00)	0.65 (1.00)	0.59 (1.00)	0.65 (1.00)	0.10 (1.00)	0.50 (1.00)	0.36 (1.00)	
IV	0.21 (0.57)	0.58 (0.83)	0.13 (0.33)	0.37 (0.64)	0.55 (0.85)	0.53 (0.90)	0.60 (0.92)	0.01 (0.10)	0.38 (0.76)	0.20 (0.56)	
V	0.37 (1.00)	0.70 (1.00)	0.42 (1.05)	0.58 (1.00)	0.62 (0.95)	0.56 (0.95)	0.63 (0.97)	0.09 (0.90)	0.50 (1.00)	0.33 (0.92)	
VI	0.22 (0.59)	0.59 (0.84)	0.15 (0.38)	0.38 (0.66)	0.53 (0.82)	0.51 (0.86)	0.76 (1.17)	0.02 (0.20)	0.38 (0.76)	0.19 (0.53)	
VII	0.43 (1.16)	0.73 (1.04)	0.50 (1.25)	0.62 (1.07)	0.72 (1.11)	0.61 (1.03)	0.87 (1.34)	0.16 (1.60)	0.53 (1.06)	0.44 (1.22)	
VIII	0.26 (0.70)	0.64 (0.91)	0.14 (0.35)	0.44 (0.76)	0.60 (0.92)	0.55 (0.93)	0.81 (1.25)	0.02 (0.20)	0.40 (0.80)	0.27 (0.75)	
IX	0.51 (1.38)	0.75 (1.07)	0.54 (1.35)	0.64 (1.10)	0.76 (1.17)	0.62 (1.05)	0.91 (1.40)	0.22 (2.20)	0.54 (1.08)	0.48 (1.33)	
X	0.36 (0.97)	0.68 (0.97)	0.22 (0.55)	0.50 (0.86)	0.67 (1.03)	0.56 (0.95)	0.87 (1.34)	0.07 (0.70)	0.45 (0.90)	0.35 (0.97)	

<sup>a</sup> See footnote a, Table 2. The sheets were Eastman Chromagram 6060 silica gel. H (3 passes) distinguished III 0.30 (1.00) and V 0.25 (0.83), and K (2 passes) distinguished III 0.63 (1.00) and V 0.58 (0.92).

Table 6.  $R_f$  and  $R_f'$  values of lysergic and iso-lysergic acid amides (alumina plates<sup>a</sup>)

Com- pound	$R_f (R_f')$ in system:										
	A	B <sup>b</sup>	C	D <sup>b</sup>	E	F <sup>b</sup>	G <sup>b</sup>	H	J	K	
I	0.73 (0.94)	0.80 (0.96)	0.76 (0.95)	0.80 (0.94)	0.55 (0.83)	0.63 (0.84)	0.66 (0.85)	0.33 (0.69)	0.60 (0.90)	0.55 (0.82)	
II	0.69 (0.88)		0.70 (0.88)		0.48 (0.73)			0.14 (0.29)	0.41 (0.61)	0.36 (0.54)	
III	0.78 (1.00)	0.83 (1.00)	0.80 (1.00)	0.85 (1.00)	0.66 (1.00)	0.75 (1.00)	0.78 (1.00)	0.48 (1.00)	0.67 (1.00)	0.67 (1.00)	
IV	0.75 (0.96)		0.72 (0.90)		0.61 (0.92)			0.20 (0.42)	0.46 (0.69)	0.55 (0.82)	
V	0.77 (0.99)	0.83 (1.00)	0.80 (1.00)	0.85 (1.00)	0.65 (0.98)	0.75 (1.00)	0.78 (1.00)	0.47 (0.98)	0.68 (1.01)	0.64 (0.96)	
VI	0.74 (0.95)		0.73 (0.91)		0.60 (0.91)			0.19 (0.40)	0.47 (0.70)	0.50 (0.75)	
VII	0.79 (1.01)	0.85 (1.02)	0.82 (1.03)	0.86 (1.01)	0.67 (1.02)	0.79 (1.05)	0.81 (1.04)	0.51 (1.06)	0.71 (1.06)	0.70 (1.04)	
VIII	0.76 (0.97)		0.74 (0.93)		0.62 (0.94)			0.23 (0.48)	0.51 (0.76)	0.59 (0.88)	
IX	0.79 (1.01)	0.85 (1.02)	0.83 (1.04)	0.87 (1.02)	0.68 (1.03)	0.80 (1.07)	0.82 (1.05)	0.58 (1.21)	0.73 (1.09)	0.73 (1.09)	
X	0.76 (0.97)		0.77 (0.96)		0.62 (0.94)			0.34 (0.71)	0.56 (0.84)	0.64 (0.96)	

<sup>a</sup> See footnote a, Table 2.

<sup>b</sup> See footnote b, Table 3.

note b (Tables 2-6), and mixtures of III and V were partially separated in the "best" multipass TLC systems we examined (see footnotes to tables). Systems A-K were examined with each type of plate, and absence from Tables 2-6 indicates that  $R_f$  values were too low to be useful. The preparation of the plates is described in *Experimental*. Results obtained by activation of precoated plates and films by heating at 95° for 15 min were less satisfactory than those obtained by exposing layers for a few hours to laboratory conditions (relative humidity 40-45% at 24°C). The alumina plates gave somewhat elongated spots and their performance was considerably affected by the laboratory conditions, especially the relative humidity.

#### Gas-Liquid Chromatography

As in the case of TLC, LSD has been compared with compounds of somewhat different structures (15). Results obtained (Table 7) demonstrate the easy distinction of LSD from its homologues and from the isomeric pair V and VI by using SE-30. Retention times increase with molecular weight, and isomeric pairs are not separated under these conditions. Some decomposition of the amides and of their silylated derivatives took place in the GLC process (cf. ref. 9).

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Table 7. Retention times (minutes) of lysergic and iso-lysergic acid amides<sup>a</sup>

Compounds	3% SE-30 (225°)	
	3% SE-30 (225°)	3% SE-30 (250°) (silylated compound)
I/II	20.0	11.1
III/IV	24.7	13.6
V/VI	28.9	15.2
VII/VIII	32.3	— <sup>b</sup>
IX/X	35.6	19.4

<sup>a</sup> Columns were of glass, 3' long, with 80-100 mesh Chromosorb W as support; injector at 275°, nitrogen flow 30 ml/min.

<sup>b</sup> This sample completely decomposed.

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