

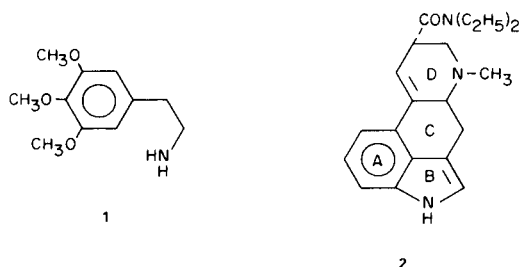
## 1-Arylquinolizidines

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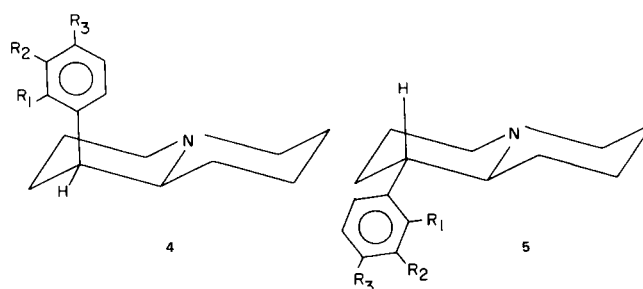
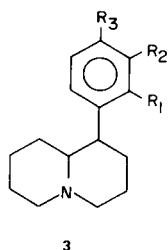
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The reaction of arylmagnesium bromides with 1-ketoquinolizidine provided predominantly 1-(e)-aryl-1(a)-hydroxyquinolizidines. Dehydration of the latter and subsequent hydrogenation yielded 1-arylquinolizidines.

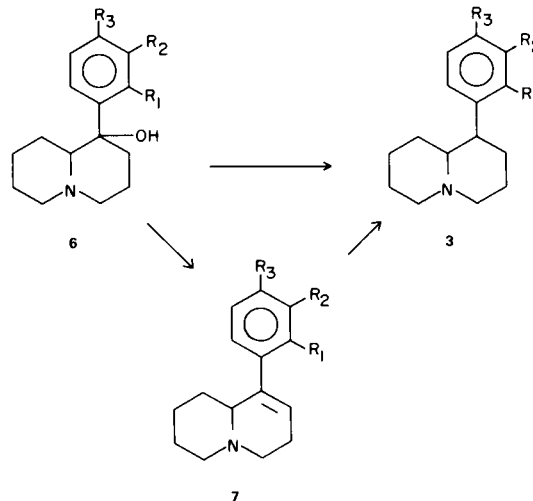
Solomon and Richelson (1) have suggested that psychedelic compounds derived from indole and phenethylamine (mescaline, **1**) all act at the same central receptor by simulating, in part, rings A, B, and C of LSD (**2**). In an attempt to elucidate the stereochemical requirements for hallucinogenic activity, 1-phenylquinolizidines (**3**) were prepared and separated into the corresponding stereoisomers.



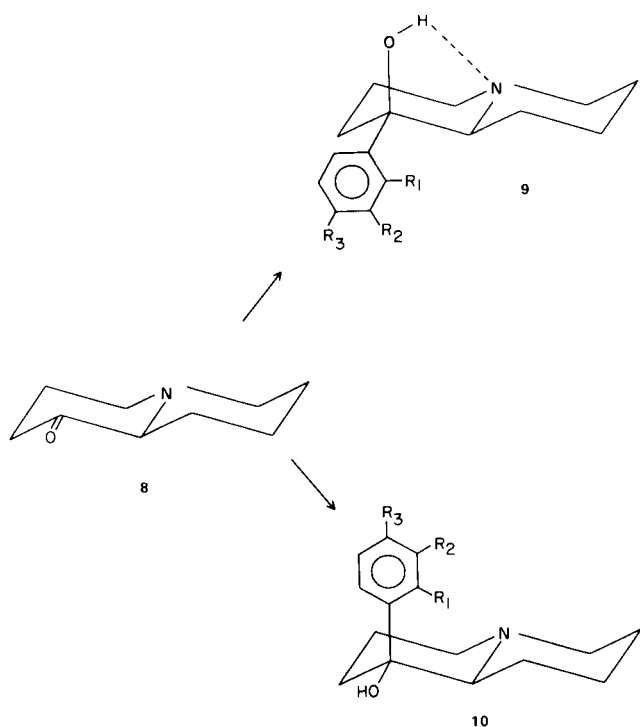
It is apparent that neither **4** nor **5** could closely approximate the nearly planar A-B ring system of LSD (**2**), much less retain the phenyl ring in the vicinity of the nitrogen at the same time. Structure **4**, however, more nearly approaches the planar conformation required by Solomon and Richelson, if only the phenethylamine portion is considered. Although the quinolizidine ring is not a rigid system and could result in a conformation at the receptor which is different than one predicted from theoretical considerations, the biological activity of **4** and **5** should provide some information about the stereochemical requirements of central adrenergic receptors and perhaps about adrenergic receptors in general.



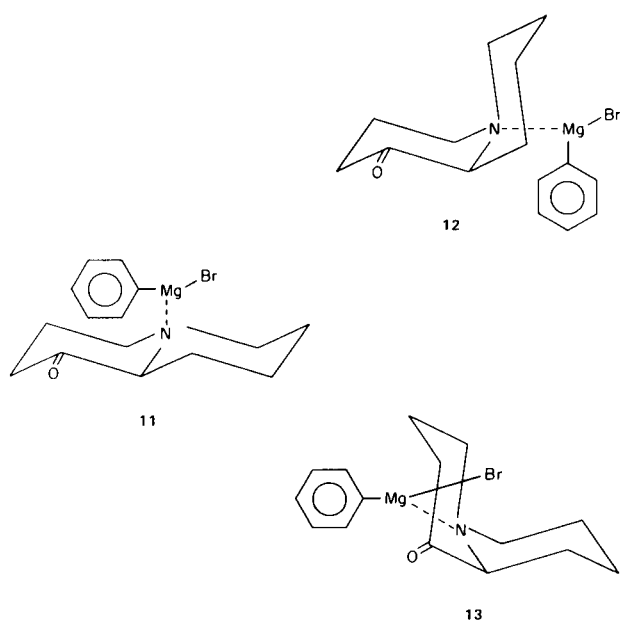
The compounds were prepared from their respective alcohols (**6**) either by hydrogenolysis or by dehydration and reduction.



1-Hydroxy-1-arylquinolizidines (**6**) were prepared according to the method described by England and Sam (3) by the reaction of the appropriate arylmagnesium bromide with 1-ketoquinolizidine (**8**). Ether was found not to be a suitable solvent for the preparation of methoxyphenylmagnesium halides even when entrainment procedures with ethylene bromide were used. However, the use of tetrahydrofuran circumvented these difficulties.



An examination of **8** would not immediately suggest that either epimer (**9,10**) would predominate in the Grignard reaction; however, it has been observed in this and in previous work (3,4) that axial alcohols predominate. Grignard reagents readily coordinate with unshared electrons, and indeed coordination with the unshared carbonyl oxygen electrons most probably is a necessary component of the mechanism of the Grignard reaction (5). The aryl-magnesium bromide also should coordinate readily with the lone pair on the nitrogen. With the nitrogen com-



plexed with a large group such as seen in **11**, the two *cis*-conformers should be present in significant amounts. An examination of **11**, **12**, and **13** reveals that the preferred direction of attack of all three compounds by phenylmagnesium bromide would be from the bottom side resulting in the formation of an excess of the axial alcohol (**9**). This is in agreement with the analysis of the epimeric content of the actual reaction mixture.

As may be seen from Table I, the greatest relative amounts of equatorial aryl epimers were obtained with 3-methoxy and 3,4-dimethoxyphenylmagnesium bromides (**10c** was not obtained), indicating that stereochemical factors are maximum when a methoxy group on the attacking Grignard reagent occupies the 3 position.

Epimers **9a-e** showed broad hydroxyl absorption with maxima occurring at variable wave numbers ( $3360\text{ cm}^{-1}$  -  $3480\text{ cm}^{-1}$ ) in the infrared spectra (Table II). This is in good agreement with the position of intramolecularly hydrogen bonded O-H stretch reported by others (6,7).

Infrared dilution studies in chloroform of epimers **10a, d, e**, show both strong intermolecularly hydrogen bonded hydroxyl absorption (variable  $\text{cm}^{-1}$ ) and weak free hydroxyl absorption at  $3620\text{ cm}^{-1}$ . Both **9** and **10** exhibit Bohlmann bands (8) in the  $2700\text{-}2800\text{ cm}^{-1}$  region indicative of the *trans*-fused conformation. Bohlmann bands, however, do not necessarily mean that **9** and **10** do not exist in equilibrium with an appreciable amount of their respective *cis*-conformers (**14, 15, 16, 17**) (9). The infrared spectrum of **10b** was quite unusual in that there was a single, strong, extremely sharp hydroxyl absorption at  $3520\text{ cm}^{-1}$ . The band remained unchanged when determined in Nujol or in dilute chloroform (2-5%). The  $3520\text{ cm}^{-1}$  band of **10b** was within the range suggested by Bellamy (7) ( $3570\text{-}3450\text{ cm}^{-1}$ ) for intramolecular hydrogen bonding, but occurred at a higher wave number than that usually observed for these compounds ( $\text{OH} \cdots \text{H}$ ) and was much sharper (Figure 1).

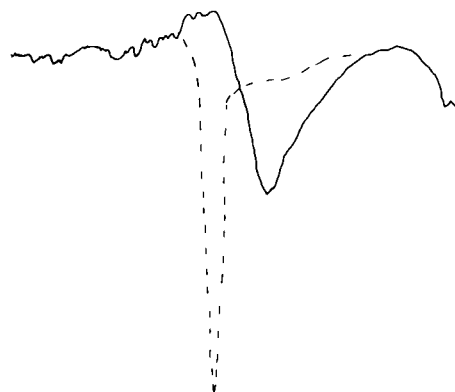
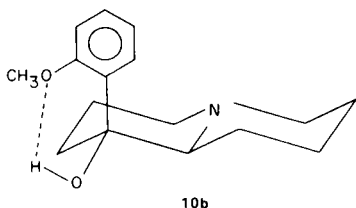
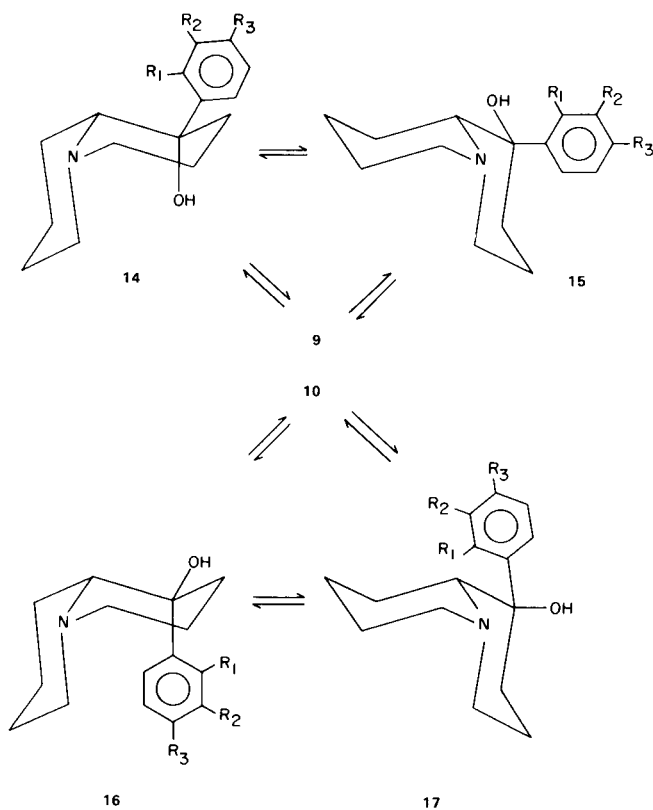


Figure 1. Infrared spectra (Nujol Mull) of **10a** ( $3360\text{ cm}^{-1}$ , solid line) and **10b** ( $3520\text{ cm}^{-1}$ , broken line) in the O-H stretch region.



Although two *cis*-conformers are possible for compounds **9**, (**14**, **15**) and **10** (**16**, **17**), it is doubtful that a significant amount of **14** and **15** would exist in equilibrium with **9** due to the additional stability imparted to **9** by the intramolecular hydrogen bond (an additional 0.5 Kcal/mole (10)). An examination of the two *cis*-conformers (**16**, **17**) of **10**, however, indicates that **17** is able to hydrogen bond intramolecularly. Moreover, the phenyl group in **17** occupies the more favored equatorial position. These two observations predicate the existence of a significant amount of **17** in solution, particularly in dilute solutions where intermolecular hydrogen bonding is not a factor. Infrared spectra of relatively dilute solutions of **10a** in chloroform do not show any bands which could be attributed to intramolecular hydrogen bonding; however, very dilute solutions (10) of **10a** (0.002 *M* carbon tetrachloride, 2 cm. cell path length) show strong intramolecularly hydrogen bonded hydroxy absorption at 3475  $\text{cm}^{-1}$  in addition to free hydroxyl stretch at 3609  $\text{cm}^{-1}$ .



Integrational analysis of these bands by Aaron (10) indicated the presence of the equilibrium **10** (60%)  $\rightleftharpoons$  **17** (40%). High dilution studies of **10d** and **10c** have not been carried out; however, results similar to those obtained for **10a** would be expected.

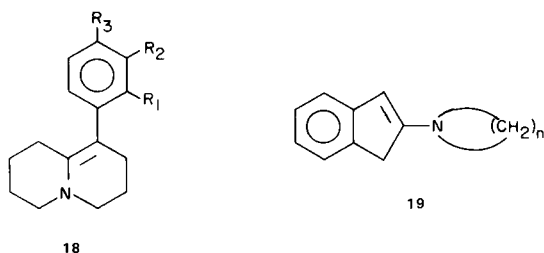
The NMR spectrum of **10a** does not indicate the presence of **17** at normal working concentrations. The aromatic signal is split into two families of signals occurring at 7.23  $\delta$  and 7.75  $\delta$  which integrate to 3 and 2 protons, respectively. Compound **9a** shows only one family of signals at 7.40  $\delta$  which integrates to 5 protons (3). The presence of two families of signals in the NMR spectrum of **10a** can be attributed to the anisotropy of the lone pair of electrons on the nitrogen (11). The NMR spectra (Table 2) of **10b**, **d**, **e** are similarly different from those of **9b**, **d**, **e**.

Strong bands appear in the region 1000-650  $\text{cm}^{-1}$  in the infrared spectra of aromatic compounds due to out-of-plane deformation vibrations of free, ring hydrogen atoms. Their position is determined primarily by their relative positions on the benzene ring rather than by the nature of the ring substituents. The bands that result from various combinations of substituents have been tabulated by Bellamy (7). A close examination of various arylquinolizidines prepared revealed that these aromatic out-of-plane deformation vibrations appear at higher wave numbers for axial phenylquinolizidines than for the corresponding equatorial compounds. These absorptions appear as two bands for monosubstituted phenyl compounds (5 adjacent free hydrogen atoms) and as a single band for 1 single or 2, 3, and 4 adjacent free hydrogen atoms. Substitution patterns which possess more than one such combination give rise to more than one band. It was observed that in the infrared spectra of phenylquinolizidines (Table 3) which showed more than one of these bands, that only the band at the higher wave number was shifted in the spectra of axial phenyl compounds. Compound **9a** showed aromatic C-H out-of-plane deformations (5 adjacent free hydrogen atoms) at 740  $\text{cm}^{-1}$  and 704  $\text{cm}^{-1}$ . The corresponding axial phenyl compound **10a** showed these absorptions at 760  $\text{cm}^{-1}$  and 697  $\text{cm}^{-1}$ .

The unsaturated compounds (**7a-d**) were prepared in 30-85% yield from their respective alcohols (**6**) using the procedure of Leonard (12). Compound **7e** was obtained in 85% yield by dehydration of **10e** with 50% sulfuric acid solution. The compounds were generally obtained as unstable oils and were usually hydrogenated immediately upon purification.

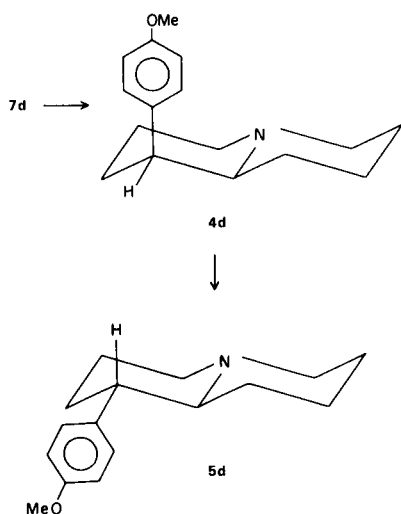
Ultraviolet (UV) and NMR spectral data demonstrated that the  $\Delta^{1,2}$  compounds were preferentially formed upon acid catalyzed dehydration of **6**. The infrared spectra were of little use other than to note the disappearance of the hydroxyl absorption upon dehydration. A band was

not seen in the infrared for the olefinic C—H stretch, but bands were present for olefinic C—H out-of-plane deformation; however, these bands were limited in their usefulness by overlap with aromatic C—H out-of-plane deformation bands. The NMR spectra showed an olefinic proton near 5.8  $\delta$ . The UV spectra (single absorption maxima near 250  $m\mu$ ) of **7a-7c** offer excellent supportive evidence that the alternate enamine system (**18**) was not formed. Blomquist and Moriconi (13) have shown that various enamines (**19**) display two maxima, a broad band at 224-227  $m\mu$  and another broad band of greater intensity at longer wave-length (291-303  $m\mu$ ).



The phenylquinolizidines (Table 4) were prepared from either **6** or **7**. The hydrogenolysis (14) of **6** was not affected by active grades ( $W_2$ ) of Raney nickel in boiling ethanol after prolonged periods of time. In most instances the catalytic hydrogenations of **7** with palladium/carbon, however, proceeded smoothly and were readily followed with UV (near 250  $m\mu$ ).

For structural elucidation infrared aromatic C—H out-of-plane deformation absorptions (Table III) were useful. The aromatic region of the NMR spectra also was helpful since the aromatic signals of each arylquinolizidine (Table III) were very similar to that of its corresponding parent alcohol (Table II). Usually only one product was isolated; however, the hydrogenation of **7d** gave both epimers



(**4d**, **5d**). Also, it was found that the stereochemistry of all of the products was not the same. This somewhat confusing situation was partially cleared up by the observation that **7d** gave only one isomer (**5d**) upon prolonged

hydrogenation, indicating that the axial isomer (**4d**) is initially and rapidly formed (kinetic product) and is then slowly isomerized by the palladium catalyst to the equatorial isomer (**5d**, thermodynamic product).

Hydrogenation of **7e** gave 1(a)-(3',4'-dimethoxyphenyl)-quinolizidine (**4e**). Hydrogenolysis of **9e** with palladium hydroxide on carbon in ethanol at 40° and 40 psi was unsuccessful. The addition of concentrated hydrochloric acid to the reaction mixture followed by hydrogenation at room temperature for 53 hours, however, yielded a mixture of decomposition products, starting material, and the equatorial epimer (**5e**).

## EXPERIMENTAL

### 1-Aryl-1-hydroxyquinolizidines (Table I).

The general procedure described by England and Sam (3) was utilized. A solution of 0.02 mole of 1-ketoquinolizidine in 150 ml. of dry tetrahydrofuran was added dropwise with stirring over a 1 hour period to a 300 ml. tetrahydrofuran solution of Grignard reagent (prepared from 7.78 g. (0.320 mole) of magnesium and 0.315 mole of appropriate aryl bromide). The mixture was stirred at reflux for 24 hours and then at room temperature for an additional 24 hours. The Grignard complex was decomposed by the dropwise addition of 150 ml. of 10% potassium hydroxide solution and thereafter extracted with ether. The extract was dried over anhydrous magnesium sulfate and then evaporated to yield an oil which darkened upon standing.

The oil was dissolved in a small amount of ether and placed on a 54 x 2.7 cm. column containing 300 g. of Woelm Grade I neutral alumina. The material was eluted with ether-petroleum ether (1:1) at a flow rate of 5 ml. per minute. The early fractions contained starting materials, followed by the axial hydroxy epimer (**9**) and then the equatorial hydroxy epimer (**10**). Infrared and NMR spectra were utilized to identify the fractions. The epimers, where possible, were crystallized, recrystallized and converted to a picrate in the usual manner.

### 3,4,6,7,8,9-Hexahydro-1-aryl-9aH-quinolizines (**7**).

#### Method A.

The procedure of Leonard (12) was essentially followed. The appropriate 1-aryl-1-hydroxyquinolizidine (0.022 mole) was slowly added to a mixture of 10 g. of phosphorus pentoxide and 40 ml. of phosphoric acid. The mixture was slowly heated to 170° (1 hour) and maintained there for an additional 1 hour with stirring. The dark mass was cooled in an ice bath and then treated slowly with 25 ml. of water. The solution was saturated with sodium carbonate and then extracted with three 100-ml. portions of ether. The ether extract was dried over anhydrous magnesium sulfate and then evaporated to yield a light yellow oil. The infrared spectrum (liquid film) of the oil showed no hydroxyl absorption; the UV spectrum showed a single  $\lambda$  max (ethanol) near 250  $m\mu$ , indicative of structure **7**. The NMR spectrum (deuteriochloroform) showed an olefinic proton signal near 5.80  $\delta$ .

TABLE I  
Arylhydroxyquinolizidines

	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	M.p. °C (Recrystallization solvent) (a)	% Yield	Picrate, M.p. °C (Recrystallization solvent) (a)	Molecular Formula	Calcd. C H N	Analysis C H N	Found C H N
<b>9a</b>	H	H	H	oil	73	188.5-189.5 (E)	C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>8</sub> (b)	---	---	---
<b>10a</b>	H	H	H	114-115 (PE)	9	239-240 (E)	C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>8</sub> (b)	---	---	---
<b>9b</b>	OCH <sub>3</sub>	H	H	104-105 (PE)	24	---	C <sub>16</sub> H <sub>23</sub> NO <sub>2</sub>	73.53	8.87	5.36
<b>10b</b>	OCH <sub>3</sub>	H	H	143-144 (PE)	8	218-220 (E)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>9</sub>	53.87	5.34	11.42
<b>9c</b>	H	OCH <sub>3</sub>	H	oil	78	150-152 (E)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>9</sub>	53.87	5.34	11.42
<b>10c</b>	H	OCH <sub>3</sub>	H	-(c)						
<b>9d</b>	H	H	OCH <sub>3</sub>	107-108 (PE)	7	213-214 (E)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>9</sub>	53.87	5.34	11.42
<b>10d</b>	H	H	OCH <sub>3</sub>	78-89 (Et)	4	196-198 (E)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>9</sub>	53.87	5.34	11.42
<b>9e</b>	H	OCH <sub>3</sub>	OCH <sub>3</sub>	oil	95	208-299 (E)	C <sub>23</sub> H <sub>28</sub> N <sub>4</sub> O <sub>10</sub>	53.07	5.42	10.76
<b>10e</b>	H	OCH <sub>3</sub>	OCH <sub>3</sub>	oil	<1	---	C <sub>17</sub> H <sub>25</sub> NO <sub>2</sub> (d)	---	---	---

(a) E = ethanol, PE = petroleum ether (30-60°), Et = ether. (b) Ref. 3. (c) Not isolated. (d) Sample too small for elemental analysis.

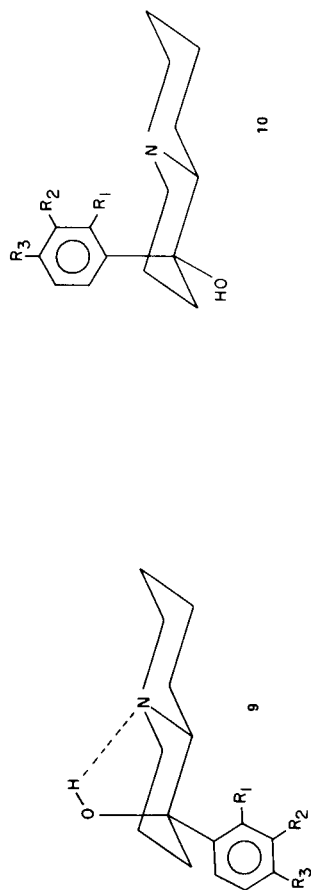
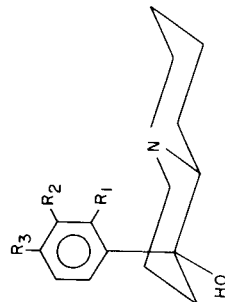


TABLE II

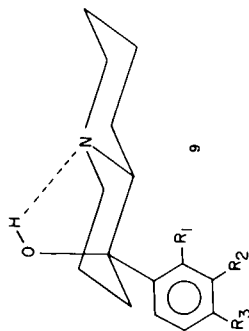
Infrared ( $\text{cm}^{-1}$ ) (a) and NMR ( $\delta$ ) (b) Spectra of Arylquinolizidinols

No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Intramolecular		Free O—H	Aromatic C—H Out-of-Plane Deformation Vibrations (c)	Chemical Shifts of Aromatic Protons					
				H—Bonding	Intermolecular H—Bonding			H <sub>2</sub>	H <sub>3</sub>	H <sub>4</sub>	H <sub>5</sub>	H <sub>6</sub>	
<b>9a</b>	H	H	H	3480 (vs) (d)	---	---	740 (e), 704 (e)	7.23 (f)	7.23 (f)	7.23 (f)	7.23 (f)	7.23 (f)	7.75 (f)
<b>10a</b>	H	H	H	3475 (m) (g)	3438 (vs) (h)	3620 (w) (i)	760 (e), 697 (e)	7.40 (f)	7.40 (f)	7.40 (f)	7.40 (f)	7.40 (f)	7.40 (f)
<b>9b</b>	CH <sub>3</sub> O	H	H	3360 (vs) (d)	---	---	752 (j)	6.88 (f)	7.12 (f)	7.34 (f)	7.34 (f)	7.34 (f)	7.80 (f)
<b>10b</b>	CH <sub>3</sub> O	H	H	3520 (vs) (d)	---	---	767 (j)	6.82	7.36 (k)	7.36 (k)	7.36 (k)	7.36 (k)	8.18 (l)
<b>9c</b>	H	CH <sub>3</sub> O	H	3360 (vs) (d)	---	---	847 (m), 784 (n)	6.62-7.30 (k)	6.62	6.62	6.62	6.62	7.30 (k)
<b>9d</b>	H	H	CH <sub>3</sub> O	3460 (vs) (d)	---	---	820 (o)	6.82 (p)	6.82 (p)	6.82 (p)	6.82 (p)	6.82 (p)	7.38 (p)
<b>10d</b>	H	H	CH <sub>3</sub> O	---	3380 (vs) (h)	3620 (w) (i)	830 (o)	6.82 (p)	6.82 (p)	6.82 (p)	6.82 (p)	6.82 (p)	7.75 (p)
<b>9e</b>	H	CH <sub>3</sub> O	CH <sub>3</sub> O	3470 (vs) (d)	---	---	872 (m), 810 (o)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)
<b>10e</b>	H	CH <sub>3</sub> O	CH <sub>3</sub> O	---	3368 (vs) (h)	3620 (w) (i)	882 (m), 815 (o)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)	6.78 (q)
								7.32 (p)	7.32 (p)	7.32 (p)	7.32 (p)	7.32 (p)	7.50 (l)

(a) Determined on a Perkin-Elmer Model 257 infrared spectrophotometer. (b) Determined in deuteriochloroform on a Varian Model A-60A spectrometer. (c) Observed in Nujol. (d) Observed in all chloroform dilutions. (e) 5-Adjacent free hydrogens. (f) Multiplet. (g) 0.002 M carbon tetrachloride, 2 cm. cell path length. (h) Observed in 5-20% chloroform. (i) Observed in chloroform concentrations less than 5%. (j) 4-Adjacent free hydrogens. (k) The arrow indicates a broad multiplet between the indicated values. (l) Doublet of doublets. (m) 1-Single free hydrogen atom. (n) 3-Adjacent free hydrogen atoms. (o) 2-Adjacent free hydrogen atoms. (p) Doublet. (q) Singlet with a small signal on each side.



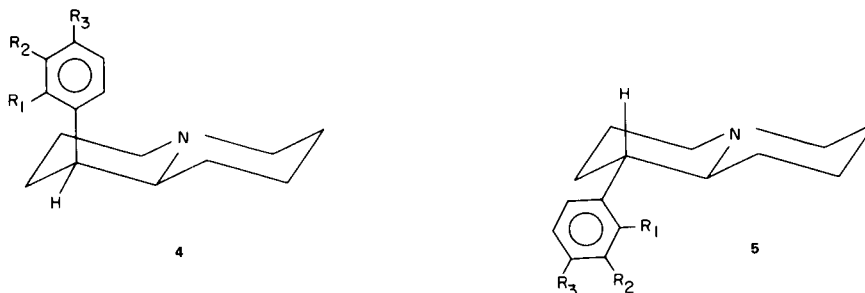
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TABLE III

Infrared (a) and NMR (b) Data of Arylquinolizidines



No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Aromatic C-H Out-of-Plane Deformation Vibrations (cm <sup>-1</sup> )	Chemical Shift of Aromatic Protons (δ)					
					H <sub>2</sub>	H <sub>3</sub>	H <sub>4</sub>	H <sub>5</sub>	H <sub>6</sub>	
4a	H	H	H	764 (c), 700 (c)	7.42-7.67 (d)	7.00	—————→		7.30 (e)	7.42-7.67 (d)
5a (f)	H	H	H							
4b	CH <sub>3</sub> O	H	H	763 (g)	---	6.83		7.40 (e)		8.35 (h)
5b (f)	CH <sub>3</sub> O	H	H							
4c (f)	H	CH <sub>3</sub> O	H							
5c	H	CH <sub>3</sub> O	H	905 (i), 785 (j)	6.65-7.50 (e)	---	6.65	—————→		7.50 (e)
5d	H	H	CH <sub>3</sub> O	820 (k)	7.20 (h)	6.82 (h)	---	6.82 (h)		7.20 (h)
4d	H	H	CH <sub>3</sub> O	830 (k)	---	---	---	---		---
4e	H	CH <sub>3</sub> O	CH <sub>3</sub> O	878 (i), 810 (k)	7.05 (h)	---	---	6.80 (l)		7.30 (l)
5e	H	CH <sub>3</sub> O	CH <sub>3</sub> O	873 (i), 810 (k)	6.91 (m)	---	---	6.91 (m)		6.91 (m)

(a) Determined in Nujol on a Perkin-Elmer Model 257 infrared spectrophotometer. (b) Determined in deuteriochloroform on a Varian Model A-60A spectrometer. (c) 5-Adjacent free hydrogen atoms. (d) Multiplet. (e) Broad multiplet inclusive of protons indicated. (f) Not isolated. (g) 4-Adjacent free hydrogen atoms. (h) Doublet. (i) 1-Single hydrogen atom. (j) 3-Adjacent free hydrogen atoms. (k) 2-Adjacent free hydrogen atoms. (l) Doublet of doublets. (m) Singlet with a small signal on either side.

The oils, because of their lability, were immediately hydrogenated to the quinolizidines (**3**).

#### Method B.

A mixture of 0.014 mole of 1(a)-aryl-1(e)-hydroxyquinolizidine and 20 ml. of 50% sulfuric acid was heated slowly to 125° and maintained at 125-130° for approximately 1 hour. The mixture was cooled in an ice bath, treated with an excess of 20% sodium hydroxide, and extracted with ether. The extract was dried over anhydrous sodium sulfate and thereafter chromatographed on 40 g. of Woelm Grade I neutral alumina. Evaporation of the ether eluant provided product which was immediately hydrogenated to the quinolizidines.

#### 1(a)-Arylquinolizidines (Table IV).

##### Method A.

A mixture of 0.015 mole of 3,4,6,7,8,9-hexahydro-1-aryl-9aH-quinolizidine (**7**), 125 ml. of absolute ethanol and 0.10 g. of 10% palladium/carbon was hydrogenated on a Parr low-pressure hydrogenator at 40 psi. The reduction, which was completed in 11-36 hours was followed with UV utilizing the 250 mμ absorption band. Gas chromatography (10% Carbowax 20M/Chromosorb W) showed

only one component to be present. The oil was further purified by eluting it from a 50 g. Woelm Grade I neutral alumina column with ether; 52-97% of a light yellow oil was obtained. The picrate was prepared in the usual manner and recrystallized.

##### Method B.

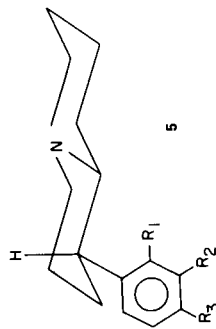
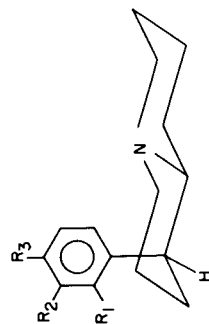
A solution of 3.46 g. (0.012 mole) of 1(a)-hydroxy-1(e)-(3',4'-dimethoxyphenyl)quinolizidine (**9e**) in 100 ml. of absolute ethanol containing 10 ml. of concentrated hydrochloric acid was treated with 10 g. of palladium hydroxide (**15**) and hydrogenated at 40 psi and room temperature on a Parr low-pressure hydrogenator for 53 hours. TLC (Eastman No. 6062 alumina sheets, 50:50 ether:petroleum ether) showed primarily one spot of R<sub>f</sub> value greater than that of the starting alcohol. The catalyst was removed by filtration and washed with 5% hydrochloric acid solution and then with ethanol. The filtrate was evaporated to 20 ml. and then made distinctly basic with 20% sodium hydroxide solution. The mixture was extracted with 150 ml. of ether and then with 150 ml. of chloroform. The extract was dried over anhydrous magnesium sulfate and evaporated to give 1.86 g. (56%) of an orange oil. The infrared spectrum showed strong hydroxyl absorption. The material was dissolved in a minimum amount of absolute ether and placed on a 50 g. Woelm Grade I neutral alumina column.

TABLE IV

## Arylquinolizidines (a)

No.	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Method (Reaction time, Hours)	Yield %	Picrate M.p. °C (Recryst. solvent)(b)	Molecular Formula	Calcd.		Analysis		Found	
								C	H	N	C	H	N
<b>4a</b>	H	H	H	A (11)	85	193-194 (E)	C <sub>21</sub> H <sub>24</sub> N <sub>4</sub> O <sub>7</sub>	56.74	5.44	12.60	57.48	5.85	12.68
<b>5a</b>	H	H	H		-(c)								
<b>4b</b>	CH <sub>3</sub> O	H	H	A (12)	94	205-206 (A)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>8</sub>	55.69	5.52	11.81	55.59	5.94	11.77
<b>5b</b>	CH <sub>3</sub> O	H	H		-(c)								
<b>4c</b>	H	CH <sub>3</sub> O	H	A (30)	52	130-133 (A)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>8</sub>	55.69	5.52	11.81	55.46	5.66	11.55
<b>5c</b>	H	CH <sub>3</sub> O	H		13	165-166 (E)							
<b>4d</b>	H	H	CH <sub>3</sub> O	A (16)(d)	92	168-169 (E)	C <sub>22</sub> H <sub>26</sub> N <sub>4</sub> O <sub>8</sub>	55.69	5.52	11.81	55.55	5.67	11.81
<b>5d</b>	H	H	CH <sub>3</sub> O	A (36)	97	172-174 (E)	C <sub>23</sub> H <sub>27</sub> N <sub>4</sub> O <sub>9</sub>	54.86	5.41	11.13	54.89	5.62	10.98
<b>4e</b>	H	CH <sub>3</sub> O	CH <sub>3</sub> O	A (36)	33	144-146 (E)	C <sub>23</sub> H <sub>27</sub> N <sub>4</sub> O <sub>9</sub>	54.86	5.41	11.13	54.74	5.90	10.59
<b>5e</b>	H	CH <sub>3</sub> O	CH <sub>3</sub> O	B (53)									

(a) Isolated as oils and purified via elution chromatography. (b) A = acetone, E = ethanol. (c) Not isolated. (d) A mixture of **4d** and **5d** was obtained.





The material was eluted with petroleum ether (30-60°) to yield 1.10 g. (33%) of product. A picrate was prepared in the usual manner and recrystallized.

Elution of the column with chloroform yielded 0.45 g. (14%) of starting material.

#### Acknowledgment.

The authors are grateful to the Public Health Service for partial support of this work with Grant No. MH 16973-01.

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Received February 19, 1970

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