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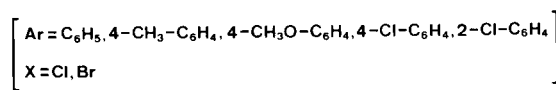
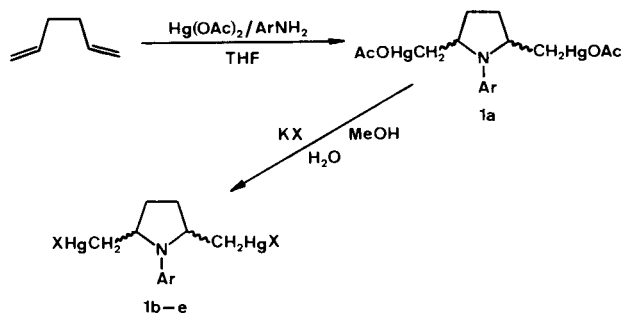
The aminomercuration-demercuration of 1,4- and 1,5-hexadiene yield *cis*- and *trans*-2,5-dimethyl-*N*-arylpyrrolidines *via* one-pot process. The intermolecular cyclization reaction goes through the corresponding mercurated pyrrolidines; these intermediates were isolated and characterized when the mercuration reaction was completed. The high stereoselectivity observed allows an easy way of synthesis for *N*-substituted *trans*-2,5-dimethylpyrrolidines.

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In preceding papers we have reported the synthesis of six membered nitrogenated saturated heterocycles through a double aminomercuration-demercuration process with intermolecular cyclization of suitable unsaturated systems. By this reaction substituted piperidines (1a), morpholines (1b) and piperazines (1c,d) were obtained. This observation prompted us to investigate the synthesis of five membered nitrogenated heterocycles by this method, the results of which were already reported (2). On the other hand, substituted 2,5-dialkylpyrrolidines are interesting because of their physiological activity (3).

The mercuration of 1,5-hexadiene with mercury (II) acetate in the presence of primary aromatic amines (4) leads to mercurated 2,5-disubstituted *cis* and *trans*-*N*-arylpyrrolidines **1**, which were isolated and characterized as acetoxy- or halomercuriomethyl derivatives (Equation 1 and Table I).

2,5-Dimethyl-*N*-arylpyrrolidines **2** were isolated as a mixture of *cis*- and *trans*-isomers (6) (Equation 2 and Table II), in a one-pot synthesis, by *in situ* reduction of the corresponding mercurated derivatives with sodium borohydride in alkaline media.



(Eq. 1)

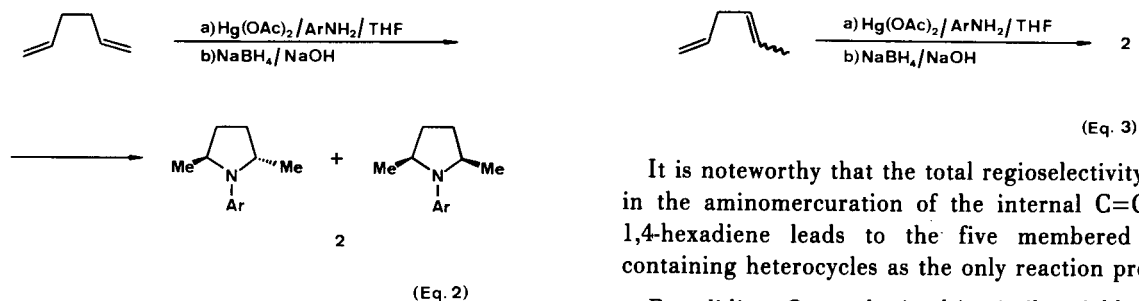
Pyrrolidines **2** were obtained in high yields somewhat impure in some experiments from compounds resulting from a mono and/or double deaminomercuration process (7). Heterocycles **2** were easily separated in both cases by distillation.

Table I

Mercurated Substituted Pyrrolidines **1** (a)

Compound No.	Ar	X	Yield % (b)	Mp °C (c)	Molecular Formula (d)	Analyses %	
						Calcd./Found	Hg N
1a	4-CH ₃ -C ₆ H ₄	-	91	154-156 (benzene)	C ₁₇ H ₂₃ Hg ₂ NO ₄ (706.6)	56.78 56.70	1.98 1.97
1b	C ₆ H ₅	Br	100	137-138 (dec, dioxan)	C ₁₂ H ₁₅ Br ₂ Hg ₂ N (734.3)	54.64 54.52	1.91 1.89
1c	4-CH ₃ -O-C ₆ H ₄	Br	80	70-2 (dec)(e)	C ₁₃ H ₁₇ Br ₂ Hg ₂ NO (764.3)	52.49 52.38	1.83 1.80
1d	4-Cl-C ₆ H ₄	Cl	97	114-115 (dec, dioxan)	C ₁₂ H ₁₄ Cl ₃ Hg ₂ N (679.8)	59.02 58.89	2.06 2.03
1e	2-Cl-C ₆ H ₄	Br	90	126-128 (dec, tetrahydrofuran)	C ₁₂ H ₁₄ Br ₂ ClHg ₂ N (768.7)	52.19 52.10	1.82 1.83

(a) From 1,5-hexadiene; for mercuration time see Table II. (b) Based on starting 1,5-hexadiene, (c) Uncorrected. (d) Ir spectra were consistent with the proposed structures. (e) Could not be recrystallized.



The same pyrrolidines **2** were also obtained from a mixture of *cis* and *trans*-1,4-hexadiene as the starting diene. So, their mercuration with mercury(II) acetate and primary aromatic amines and *in situ* reduction with sodium borohydride-sodium hydroxide leads to the expected heterocycles **2** (Equation 3 and Table III).

It is noteworthy that the total regioselectivity observed in the aminomercuration of the internal C=C bond of 1,4-hexadiene leads to the five membered nitrogen-containing heterocycles as the only reaction product.

Pyrrolidines **2** are obtained in similar yields from both 1,4- and 1,5-dienes. The *trans* isomer is always the major product (see Table II) and 1,4 hexadiene behaves in general as the most selective diene towards the addition. These results are in good agreement with those reported by Brown for the oxymercuration-demercuration reaction of 1,5-hexadiene (8). In this case the *trans*-tetrahydrofuran

Table II
cis and *trans*-2,5-Dimethyl-*N*-arylpyrrolidines **2**

Compound No.	Ar	Hexadiene	Mercuration Time	Reduction	Yield % (a)		Isomer Ratio (b) <i>cis/trans</i>
					Hg(O)	2	
2a	4-CH ₃ -C ₆ H ₄	1,5	4 hours	1 hour	95	93	8/92
		1,4	8 hours	1 day	80	70	6/94
2b	C ₆ H ₅	1,5	30 minutes	2 hours	99	99	2/98
		1,4	1 hour	2 days	99	99	6/94
2c	4-CH ₃ O-C ₆ H ₄	1,5	18 hours	1 day	88	23	32/68
		1,4	18 hours	2 days	95	25	10/90
2d	4-Cl-C ₆ H ₄	1,5	1 hour	30 minutes	88	83	1/99
		1,4	1.5 hours	2 days	85	80	6/94
2e	2-Cl-C ₆ H ₄	1,5	1 hour	2 days	91	75	6/94
		1,4	1 hour	2 hours	90	76	1/99

(a) Based on starting diene. (b) From glc analysis.

Table III
Physical, Analytical and spectral Data for Compounds **2**

Compound No.	Bp Range °C/torr	Molecular Formula (a)	Analyses %				¹ H-NMR (Carbon Tetrachloride) δ Multiplicity (b)				
			Calcd.	Found							
			C	H	N	CH ₃ (c)	CH ₂	CH	Ar	Other	
2a	80-85/0.1	C ₁₃ H ₁₉ N (189.3)	82.48	10.12	7.40	1.05 d	1.4-2.3 m	3.65 m	6.3-7.1 m	2.25 s	
			82.36	9.98	7.41	1.25 d		3.9 m			
2b	70-75/0.5 (d)	C ₁₂ H ₁₇ N (175.3)	82.23	9.78	7.99	1.05 d	1.4-2.4 m	3.6 m	6.4-7.3 m	—	
			82.06	9.72	7.96	1.2 d		3.95 m			
2c	90-93/0.1	C ₁₃ H ₁₉ NO (205.3)	76.06	9.28	6.82	1.1 d	1.4-2.1 m	3.3 m	6.5 m	3.65 s	
			75.89	9.28	6.80	1.2 d		3.65 m			
2d	82-85/0.01 (e)	C ₁₂ H ₁₆ ClN (209.7)	68.73	7.69	6.68	1.0 d	1.4-2.3 m	3.6 m	6.3 m	—	
			68.60	7.70	6.66	1.2 d		3.9 m	7.0 m		
2e	80-83/0.1	C ₁₂ H ₁₆ ClN (209.7)	68.73	7.69	6.68	0.95 d	1.3-2.2 m	3.1 m	7.0 m	—	
			68.58	7.65	6.65	1.2 d		3.3 m			

(a) IR spectra were consistent with the proposed structures. (b) The proton assignment was supported by a dnmr experiment. (c) J = 6 Hz. (d) Literature (13) bp 80-86°/0.6 torr. (e) Mp 71-73° (hexane), >99% *trans*-isomer (glc).

derivative was the main product, in accordance with the higher stability of cyclic mercurated compounds bearing the CH_2HgX groups occupying positions as far as possible (1).

The isomeric ratio was obtained by glc analysis on the basis of the shorter retention time for the *cis* isomer (9,10) for heterocyclic systems of this type, as well as by the different ^1H -nmr chemical shifts for methyne and methyl groups. For the *trans* isomers the CH group appears at lower field than for the *cis* isomers (11,12). On the other hand, CH_3 groups show resonances at higher field for the *trans* than for the *cis* isomers.

EXPERIMENTAL

All melting points were taken on a Büchi-Tottoli capillary melting point apparatus and are uncorrected. Glc analysis were performed in a Varian Aerograph 2800 instrument equipped with a OV-101 Chromosorb column. Infrared spectra were determined with a Pye-Unicam Sp-1000 spectrometer, ^1H -nmr spectra were obtained with a Varian EM-390 spectrometer (TMS as internal reference) and the proton assignment was supported by a dnmr experiment. Elemental analysis of **2** were carried out with a Perkin-Elmer 240-Elemental Analyzer. Nitrogen in **1** was determined by Kjeldahl's method (14) and mercury was determined by gravimetric analysis (14).

1,4- and 1,5-Hexadiene are commercially available (Aldrich).

General Procedure for the Preparation of Organomercurials **1**.

To a solution of 1,5-hexadiene (1.2 ml, 10 mmoles) and arylamine (100 mmoles) in tetrahydrofuran (100 ml) mercury(II) acetate (6.4 g, 20 mmoles) was added and the mixture stirred until the reaction was completed (5). The solvents were evaporated *in vacuo* and the resulting oil was dissolved in a mixture of methanol/water (4/1). Addition of potassium chloride or bromide (30 mmoles) led to the precipitation of the halomercurio derivatives (**1b-e**) which were washed with water, methanol and ether, dried and recrystallized.

The acetoxymercurio derivative **1a** was filtered (G-3) after the mercuriation process, washed with ether, dried and recrystallized. *Cis*- and *trans*-2,5-Dimethyl-*N*-arylprrrolidines **2**.

General Procedure.

An aqueous solution of 0.5*N* sodium hydroxide (100 ml) and then sodium borohydride (0.38 g, 10 mmoles) in 2.5*N* aqueous sodium hydroxide (10 ml) were added to the mercuriation mixture after completion of

the mercuriation process. The reaction was continued until no further precipitation of mercury(0) was noticeable. The reaction mixture was extracted with ether, the ethereal layer was washed with water, dried over anhydrous sodium sulfate and a vaporated *in vacuo*. The residue was distilled under reduced pressure to give the product.

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- (4) Primary aliphatic amines afforded amine-mercury (II) acetate complexes instead of the products of addition to the double bond: J. Barluenga, C. Nájera and M. Yus, *An. Quim.*, **75**, 341 (1979).
- (5) Reactions were continued until no yellow precipitate of mercury(II) oxide was observed by treatment with 3*N* potassium hydroxide.
- (6) The mercuriation with primary aliphatic amines and mercury(II) nitrate (15) followed by reduction with sodium borohydride leads to the corresponding δ -unsaturated amines and starting products resulting from a simple or double deaminomercuriation reaction respectively.
- (7) When the reduction was carried out without organic solvents, unsaturated amines resulted as major products in a single deaminomercuriation process (1b,16).
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