

REACTIONS OF 2-AMINOBIIPHENYLS WITH ALDEHYDES

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Although many derivatives of phenanthridine have been prepared by the Bischler-Napieralski reaction (1), there is no record of attempts to prepare dihydrophenanthridines by application of the related Pictet-Spengler reaction (2). The experiments herein reported were expected to yield 5,6-dihydrophenanthridines as products of the condensation of 2-aminobiphenyls with aldehydes, but all such attempts were unsuccessful.

Cyclization of 2-aminobiphenyl with formaldehyde in the presence of hydrochloric acid or sodium carbonate apparently failed since only a resin was isolated.

TABLE I
SCHIFF BASES OF 2-AMINO-3',4,4',5-TETRAMETHOXYBIIPHENYL

SCHIFF BASE	YIELD, %	M.P., °C.	FORMULA	ANALYSES ^b					
				Calc'd			Found		
				C	H	N	C	H	N
Benzylidene.....	80	144-145	C ₂₃ H ₂₃ NO ₄	73.19	6.14	3.71	73.09	6.22	3.64
Piperonylidene.....	85	164-165 ^a	C ₂₄ H ₂₃ NO ₆	68.39	5.50	3.33	68.29	5.62	3.20
<i>p</i> -Methoxybenzylidene.....	78	98-99	C ₂₄ H ₂₅ NO ₅	70.75	6.18	3.44	70.71	6.39	3.62
Veratrylidene.....	86	133-134	C ₂₅ H ₂₇ NO ₆	68.63	6.22	3.20	68.64	6.33	3.39
<i>o</i> -Chlorobenzylidene.....	83	125-126	C ₂₃ H ₂₂ ClNO ₄	67.06	5.39	—	67.09	5.36	—

^a Reported m.p. 155°, ref. (9). ^b Analyses by Galbraith Laboratories, P.O. Box 32, Knoxville, Tennessee.

The preparation of tetrahydroisoquinolines by the Pictet-Spengler reaction is greatly facilitated by suitably placed electron-donating groups, and it was thought that 2-aminobiphenyls having groups to activate the 2'-position might be capable of cyclization. 2'-Amino-3,4-dimethoxybiphenyl and 2-amino-3',4,4',5-tetramethoxybiphenyl were prepared for this purpose. Extensive studies on the cyclization of the latter compound with formaldehyde (or paraformaldehyde) and hydrochloric acid or sodium carbonate in aqueous or ethanolic systems were fruitless.

A number of Schiff bases of 2-amino-3',4,4',5-tetramethoxybiphenyl (Table I) were synthesized because it has occasionally been observed (3) that a Schiff base would cyclize to a tetrahydroisoquinoline more easily than a mixture of the amine and the aldehyde. The Schiff bases could not be cyclized with 24% hydrochloric acid, phosphorus pentoxide, a mixture of ethanol and ethereal hydrogen chloride, or an anhydrous solution of hydrogen chloride in benzene. In most cases, 2-amino-3',4,4',5-tetramethoxybiphenyl hydrochloride was recovered, but only tars were isolated when phosphorus pentoxide was used.

EXPERIMENTAL

4-Bromoveratrole (4). Bromine vapors (46 g., 0.29 mole) were introduced by a stream of nitrogen into a solution of 41 g. (0.3 mole) of veratrole in 300 ml. of acetic acid, the process requiring three hours. There was obtained 52 g. (80% yield) of colorless product boiling at 80–82°/4 mm., n_D^{25} 1.5735.

Anal. Calc'd for $C_8H_7BrO_2$: Br, 36.82. Found: Br, 36.55.

2'-Nitro-3,4-dimethoxybiphenyl. The procedure of Tarbell (5) was followed in carrying out the crossed-Ullmann reaction between 4-bromoveratrole and *o*-nitrochlorobenzene. The product was extracted from the cooled melt by hot ethanol which was then concentrated to allow crystallization. The product was highly contaminated with tar and required five recrystallizations (using charcoal) before it was obtained as a light-yellow substance melting at 99° (3% yield).

Anal. Calc'd for $C_{14}H_{13}NO_4$: C, 64.86; H, 5.02; N, 5.41.

Found: C, 64.97; H, 4.90; N, 5.51.

Unsuccessful attempts were made to prepare 2'-nitro-3,4-dimethoxybiphenyl by: condensation of *o*-nitrobenzenediazonium chloride with veratrole by a modified Gomberg reaction (6); condensation of *o*-nitrobenzenediazonium fluoroborate with veratrole in the presence of acetic anhydride and copper (7); decomposition of 1-(*o*-nitrophenyl)-3,3-dimethyltriazene in the presence of veratrole and hydrogen chloride (8).

2'-Amino-3,4-dimethoxybiphenyl. The nitro compound (2.6 g.) was reduced in 20 ml. of ethanol, using Raney nickel, at 750 p.s.i. and 70°. After five hours the bomb was cooled, causing crystallization of the amine. The product crystallized from ethanol as white plates melting at 123–124° (96% yield).

Anal. Calc'd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11.

Found: C, 73.54; H, 6.58; N, 6.17.

2-Amino-3',4,4',5-tetramethoxybiphenyl. This compound was prepared according to the method of Ritchie (9) by iodinating veratrole (62%), condensing the 4-iodoveratrole by the Ullmann reaction to 3,3',4,4'-tetramethoxybiphenyl (51%), nitration (79%), and reduction of the nitro compound (94%). The hydrochloride may be recrystallized from absolute ethanol and diethyl ether, finally melting at 226–228°.

Anal. Calc'd for $C_{18}H_{20}ClNO_4$: C, 58.98; H, 6.19; N, 4.30.

Found: C, 58.94; H, 6.12; N, 4.25.

Schiff bases of 2-amino-3',4,4',5-tetramethoxybiphenyl. Equimolecular amounts of the aldehyde and the amine were heated together on the steam-cone for two hours. The melt was then cooled and recrystallized from ethanol or methanol, the product appearing as yellow needles. The products are described in Table I.

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