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BISCHLER-NAPIERALSKI REACTION BY MEANS OF POLYPHOSPHATE ESTERS AND SYNTHESIS OF 5H-2-BENZAZEPINE DERIVATIVES*,**

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The recent report from our laboratory pointed out that polyphosphate esters (PPE) may be useful as an agent for many condensation reactions.[1] This communication describes the Bischler-Napieralski reaction by means of PPE in the synthesis of some dihydroisoquinolines together with the extensive application of this reaction in the synthesis of some 5H-2-benzazepine derivatives which have been rarely encountered in literatures as synthesized by cyclization of this type.[2,3]

PPE was prepared from phosphorous pentoxide and diethyl ether in chloroform solution and used in situ.[1,4,5] Amides of phenethylamine derivatives (Ia-d) were heated with 5 parts of PPE to afford corresponding dihydroisoquinolines (IIa-d) as shown in the Table 1. Amides possessing benzene ring activated by substitution with methoxyl groups (Ia-b) were cyclized under extremely mild conditions. Unsubstituted amides (Ic-d) were also cyclized under moderate conditions in good yields. PPE is thus shown to be a very good agent for conventional Bischler-Napieralski reaction.[6,7]

In a similar manner, amides of γ-(3,4-dimethoxyphenyl)-propylamine (IIIa-c)

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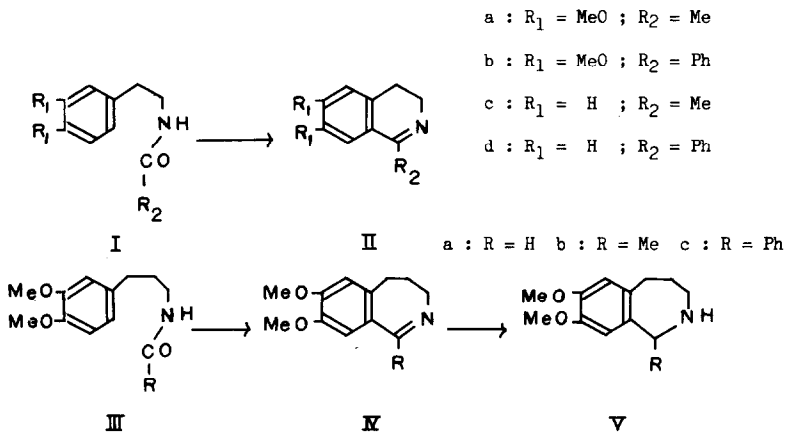

were cyclized to afford corresponding bases (IVa-c) as shown in the Table 1. Subsequent treatment of them with sodium borohydride gave reduced bases (Va-c). Infrared spectra of the bases (IVa-c) showed maxima at 1605 – 1630 cm^{-1} range (C=N), which shifted to 1640 – 1660 cm^{-1} range on salt formation. Ultraviolet spec-

Table 1.

Bischler- Napieralski Reaction

Products	Temp. (°c)*	Time (hr.)	Yields (%)
IIa	in chloroform refl.	0.5	78
IIb	in chloroform refl.	0.5	85
IIc	120	1.5	82
IId	120	1	89
IVa	120	1.5	76
IVb	120	1	63
IVc	120	1	90**

* bath temp.

** crude yield

trum patterns of them and their bathochromic change on protonation are described in the Table 2. These spectroscopic behaviors of the bases are definitely in

Table 2.

Ultraviolet Spectra of the Benzazeipines

	Free Base*		Protonated**	
	mμ	log ε	mμ	log ε
IVa	236	4.19	246	4.05
	273	4.16	326	4.14
	312	3.91	363	4.09
IVb	263	3.78	301	3.77
	297	3.68	346	3.81
IVc	239	4.27	270	4.10
	305	3.67	380	3.80

* in ethanol

** in ethanol containing hydrochloric acid

parallel with those in their 6,7-dimethoxy-3,4-dihydroisoquinoline analogs[8] and confirm the cyclized structures (IVa-c). NMR spectra of the bases (IV and V) indicated the presence of two isolated aromatic protons (3.15 – 3.83 τ range, two singlets) also in good accord with the structural assignment. These results

Table 3.

Properties of Benzazepines*

Compounds	Free Base	Picrate	Perchlorate	Methiodide
IVa	165 – 166	197 – 198	234 (dec.)	182 – 185
IVb	140 – 143 (b.p.3)	183 – 184	190 – 191	190 – 191
IVc	oil	222 (dec.)	246 – 247 (dec.)	206 – 206.5 (dec.)
Va	172 – 173	197 – 198		
Vb	115 – 120 (b.p.3)	163 – 165		
Vc	114 – 115			

* m.p., uncorrected

demonstrate that PPE is a reagent of choice for the synthesis of 3,4-dihydro-5H-2-benzazepine derivatives by the extended Bischler-Napieralski reaction.

Physical properties of 7,8-dimethoxy-3,4-dihydro-5H-2-benzazepines (IV), 7,8-dimethoxy-1,2,3,4-tetrahydro-5H-2-benzazepines (V) and the derivatives are listed in the Table 3. Satisfactory results were obtained for all new compounds on elemental analysis.

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