PHẢN ỨNG ĐÓNG VÒNG BẤT NGỜ TẠO THÀNH CÁC DẪN XUẤT 1-AZA-5,7-DIOXATRICYCLO [4.3.1.0^{4,8}]DECANE TỪ 1-(2-OXOALKYL) 4-PIPERIDONE

UNEXPECTED FORMATION OF 1-AZA-5,7-DIOXATRICYCLO- [4.3.1.0^{4,8}]DECANE DERIVATIVES THROUGH INTRAMOLECULAR CYCLIZATION OF 1-(2-OXOALKYL) 4-PIPERIDONES

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ABSTRACT

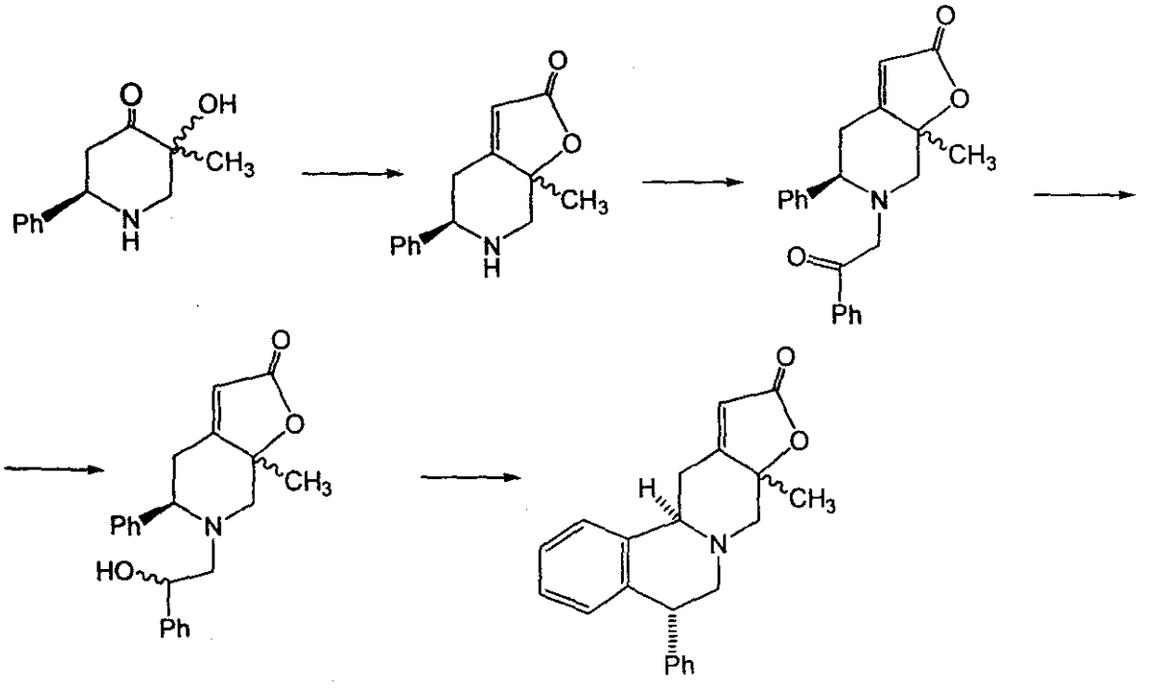
1-Aza-5,7-dioxatricyclo [4.3.1.0 ^{4,8}]decane derivatives were prepared from 1-(2-oxoalkyl)-4-piperidones. The structures of the decane derivatives were confirmed by elemental analysis and spectral data. The mechanism of the transformation was proposed.

I. INTRODUCTION

Benzo [a] quinolizine-2-ones are key intermediates in synthetic routes of biologically active natural compounds and their analogs [1]. It was reported that N-acetonyl (phenacyl) substituted 2-arylpiridines are cyclized in acid medium with the formation of benzo [a] quinolizinium salts [2]. However, an attempt to cyclize 1-(2-oxoalkyl)-3e-hydroxy-6e-phenyl-4-piperidones into benzo [a] quinolizines was unsuccessful. Instead, products of semiketal cyclization were unexpectedly formed.

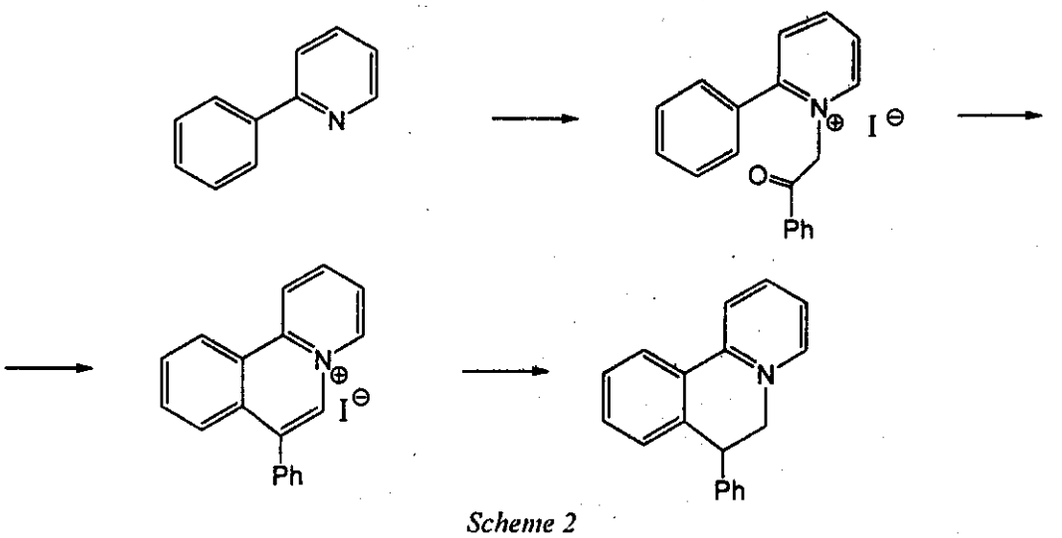
II. RESULTS AND DISCUSSION

It was proposed that 3-hydroxy-4-piperidones can be used in syntheses of 3-hydroxybenzo [a] quinolizine-2-ones according to a scheme AC → ABC similarly to syntheses of 2-oxobenzo [a] furo [2,3-g] quinolizines [3] (Scheme 1)



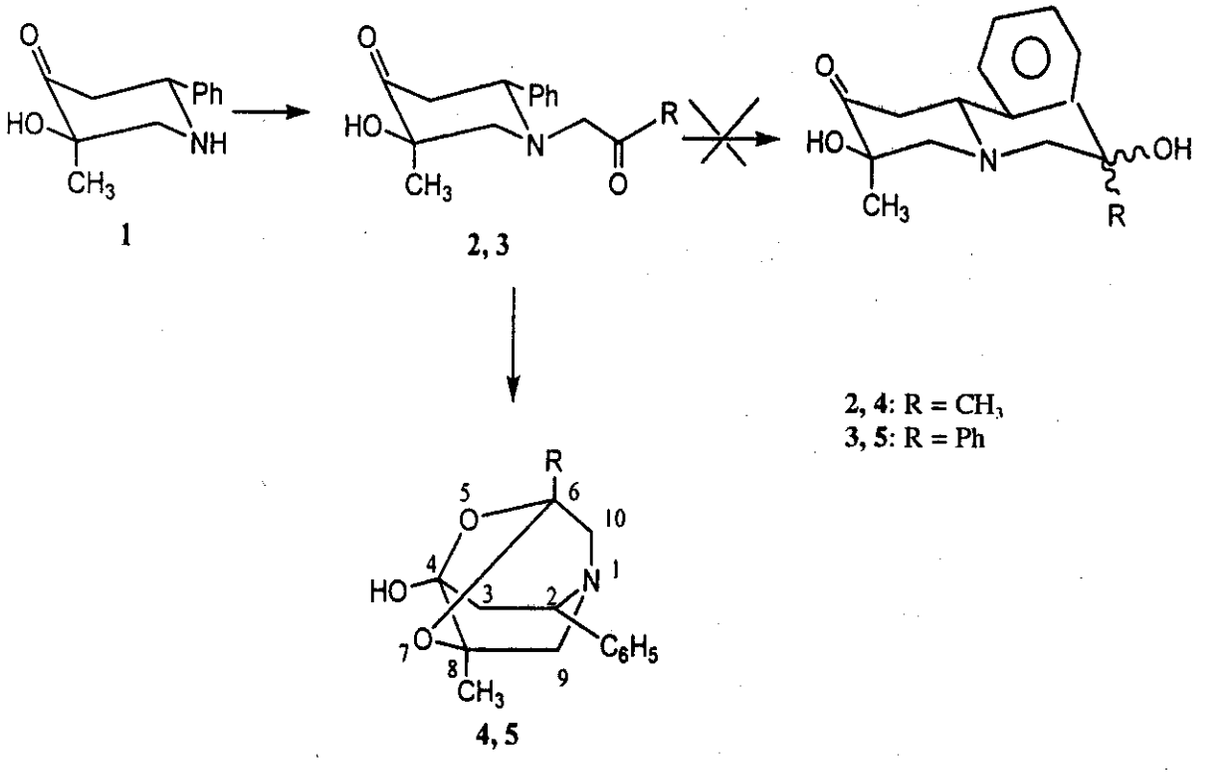
Scheme 1

For this purpose, acetonylpiperidone **2** and phenacylpiperidone **3** were synthesized from piperidone **1**. These intermediates would undergo intramolecular cyclization similarly to a known synthetic scheme of salt benzo [a] quinolizinium [2] (Scheme 2).



Scheme 2

In fact, piperidones **2, 3** being hold in 80% H_2SO_4 acid did not give expected benzo[a]quinolizines. They underwent intramolecular cyclization to form 1-aza-5,7-dioxatricyclo [4.3.1.0 ^{4,8}] decanes (Scheme 3).



Scheme 3

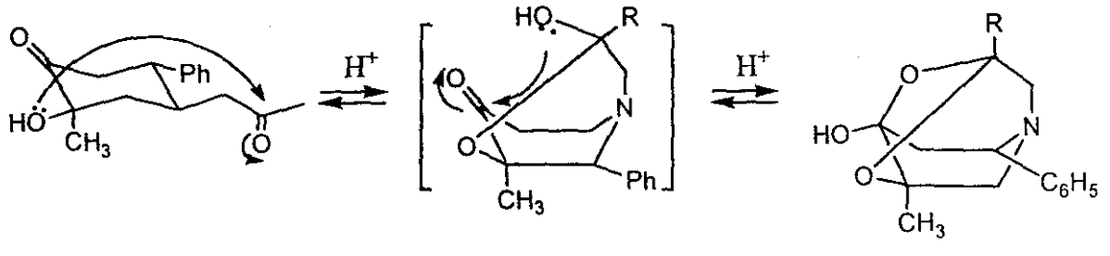
Compound	Yield %	mp,^{0}C	Found % N	Empirical formula	Calculated % N	IR-spectrum ν, cm^{-1}
2	72	89-91	5.3	$C_{15}H_{14}NO_3$	5.5	1680, 1720, 3510
3	62	77-79	4.4	$C_{20}H_{21}NO_3$	4.3	1680, 1715, 3500
4	84	114-116	5.4	$C_{15}H_{14}NO_3$	5.5	3590
5	94	122-123	4.3	$C_{20}H_{21}NO_3$	4.3	3580

Table 1

Compounds **2, 3, 4, 5** are new compounds and have not been reported previously. Their structures were confirmed by elemental analysis and spectral data (table 1). Thus, in the IR-spectra of **2, 3** the presence of two strong bands at 1650-1750 cm^{-1} showed that N-alkylation of **1** with acetonylbromide and phenacylbromide gave **2** and **3**. In the IR-spectra of compounds **2, 3, 4, 5,** the bands at 3500-3600 cm^{-1} region indicated OH-groups with hydrogen bonds. In the ^{1}H-NMR spectra of final products **4, 5** (Table 1), the suggested structure was confirmed by the presence of two AB-systems assigned to the protons at C-10 (J=13.5 Hz) and the protons at C-9 (J=13.8 Hz) . Moreover, the signal of proton at C-2 was shown as a double doublet with coupling constants J = 9.6 Hz and J = 7.8 Hz. This indicated its β-orientation and boat conformation of the piperidine cycle.

Based on the structure of final products, the mechanism of the transformation can be proposed as two consecutive semiketal formations (Scheme 4). It is necessary to mention that the first semiketal attack occurred with probably boat conformation of the piperidine cycle.

The semiketal structures of **4, 5** were confirmed again by the fact that the final products **4, 5** were stable in basic medium, but in acidic water for 10 hours they were converted back to starting piperidones **2, 3** [4].



Scheme 4

III. EXPERIMENTAL

The IR spectra of solutions of the substances in CCl_4 (c=10^{-3} M, l=1cm) were recorded on a Specord-75 spectrometer. The ^{1}H-NMR spectra in $CDCl_3$ were recorded on a Bruker WM-360 spectrometer with TMS as the internal standard. The course of reactions and purity of products were monitored by TLC on Silufol UV-254 plates, developed with iodine vapors. Compound **1** was obtained by the method in [5].

1. Acetonyl and 1-phenacyl-3-hydroxy-3a-methyl-6e-phenyl-4-piperidones (**2, 3**) (Table 1). 0.015 M

piperidone **1** and 0.015 mol acetonyl bromide or phenacyl bromide were dissolved in 30 ml acetonitril. 0.018 Mol diisopropylamine was added to the solution and the mixture was refluxed for 10 min. 100 ml Diethyl ether was added to cooled sodium sulphate and filtered through a fine layer of silica-gel. After solvent evaporation, the product was crystallized from toluen-hexane.

2. 6(β),8(α)-Dimethyl-2(α)-phenyl-1-aza-5,7-dioxatricyclo [43.1.0.^{4,8}] decan-4(α)-ol (**4**) and 8(α)-methyl-2 (α)-6(β)-diphenyl-1-aza-5,7-dioxatricyclo[4.3.1.0 ^{4,8}]decan-4(α)-ol (**5**) (Table 1). 0.03 Mol piperidones **2** or **3** was dissolved in 15 ml 80% sulphuric acid. The mixture was hold at ambient temperature for 48 hours. The reaction mixture was poured into 200 ml distilled water, neutralized with NaOH solution and extracted with diethyl ether. After solvent evaporation, the products were crystallized from toluen-hexane (compound **5**) or ether-hexane (compound **4**).

Compound 4: ^{1}H-NMR (360MHz, $CDCl_3$) δ, ppm: 1.17 (s, 8 - CH_3); 1.41 (s, 6 – CH_3); 1.89 (dd, J=13.4 Hz, 9.6 Hz, 3(α)-H); 2.70 (d, J=13.8 Hz, 9(β) - H); 2.78 (dd, J=13.4 Hz, 7.8 Hz, 3(β) – H; 2.79 (d, J=13.5 Hz, 10(α) - H; 2.94 (d, J=13.5 Hz, 10(β) - H; 3.20 (d, J=13.8 Hz, 9(α) - H); 4.39 (dd, J=9.6 Hz, 7.8 Hz, 2(β) - H); 7.22 – 7.46 (m, 5 Harom).

Compound 5: ^{1}H-NMR (360MHz, $CDCl_3$) δ, ppm: 1.21 (s, 8 – CH_3); 1.96 (dd, J=13.4 Hz, 3(α) - H); 2.74 (d, J=13.8 Hz, 9(β) - H); 2.87 (dd, J=13.4 Hz, 7.8 Hz, 3(β) – H); 2.95 (d, J=13.4 Hz, 10(α) - H); 3.08 (d, J=13.4 Hz, 10(β) - H); 3.34 (d, J=13.8 Hz, 9(α) - H); 4.50 (dd, J=9.6 Hz, 7.8 Hz, 2(β) - H); 7.19-7.56 (m, 10 Harom).

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