PREPARATION OF 3-SUBSTITUTED 5-ACETYL-N-(β-HYDROXYETHYL) PYRROLIDONES

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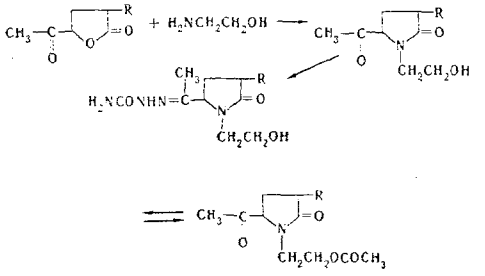
Previously unknown 5-acetyl-3-alkyl-N-(β-hydroxyethyl)pyrrolidones have been synthesized by the reaction of γ-acetyl-α-alkylbutyrolactones with ethanolamine, and their semicarbazones and acetyl derivatives have been obtained.

In recent years, investigations have been carried out in the field of N-(β-hydroxyalkyl) derivatives of the simplest lactams—in particular, pyrrolidone. The latter can be obtained by the reaction of pyrrolidone with olefin oxides, but the yields do not exceed 44% [1,2]. N-(β-Hydroxyalkyl)pyrrolidones are formed in higher yields (72–88%) by the condensation of butyrolactone with alkanolamines [1,3]. We have made use of this method to synthesize 3-substituted 5-acetyl-N-(β-hydroxyethyl)pyrrolidones from α-substituted γ-acetylbutyrolactones [4]. The experiments showed that at high temperatures (70–200° C), and also on prolonged heating, resinification takes place and the condensation product is not obtained. When a mixture of a lactone and ethanolamine was stirred at 50–60° C for 3 hr, condensation yielded 3-substituted 5-acetyl-N-(β-hydroxyethyl)pyrrolidones with yields of 60–64% (calculated on the lactone taken).

The best yields (80–84.4%) of the 3-substituted 5-acetyl-N-(β-hydroxyethyl)pyrrolidones are obtained when the condensation of the lactone with ethanolamine is carried out at a ratio of 1 : 1.6 at a residual pressure of 150–160 mm for 1–1.5 hr. The resulting 3-substituted 5-acetyl-N-(β-hydroxyethyl)pyrrolidones are steadily soluble in chloroform, ethanol, acetone, water, hot benzene, and concentrated hydrochloric acid and are insoluble in alkalis, and they give the iodoform reaction, form semicarbazones, and undergo acetylation with the formation of 3-substituted 5-acetyl-N-(β-acetoxyethyl)pyrrolidones, the saponification of which with alcoholic caustic potash restores the initial pyrrolidones in quantitative yield. The yields, elementary analyses, and some physicochemical constants of the compounds obtained are given in Tables 1–3.



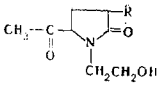
EXPERIMENTAL

5-Acetyl-3-alkyl-N-(β-hydroxyethyl)pyrrolidones (Table 1). A Claisen flask was charged with 0.027 mole of a γ-acetyl-α-alkylbutyrolactone and 0.045 mole of monoethanolamine and was quickly attached to a water pump, and the mixture was kept under a residual pressure of 150–160 mm for 1–1.5 hr. The reaction was exothermic, and as a result of this, the temperature of the reaction mixture immediately rose considerably with the evolution of steam, which condensed on the walls of the upper part of the flask. Then the water and the excess of monoethanolamine were driven off at 15–30 mm and the residue was distilled.

N-(β-Acetoxyethyl)-5-acetyl-3-alkylpyrrolidones (Table 2). With stirring and cooling (~0°C), 0.03 mole of freshly-distilled acetyl chloride was added over 10–15 min to 0.03 mole of a 5-acetyl-3-alkyl-N-(β-hydroxyethyl)pyrrolidone in 0.03 mole of dry pyridine. The reaction mixture was stirred at room temperature for 3 hr, and the resulting mass was treated with 2% HCl. The solution was extracted with ether. The ethereal extracts were washed with sodium carbonate solution and with water and were dried with sodium sulfate. After the solvent had been driven off, the residue was distilled in vacuum.

Semicarbazones of the 5-acetyl-3-alkyl-N-(β-hydroxyethyl)pyrrolidones (Table 3). A solution of 1 g of a pyrrolidone in 15 ml of ethanol was treated with 2 g of semicarbazide hydrochloride and 3 g of potassium acetate in 15 ml of water, and the mixture was shaken, heated on the water bath for 1 hr, and left for 2 days. Then the solution was

Table 1



R	Bp, °C (mm)	d_4^{20}	n_D^{20}	Empirical formula	Found				Calculated				Yield, %
					MR_D	% C	% H	% N	MR_D	% C	% H	% N	
C_2H_5	159—160 (4)	—	1.5300*	$C_{10}H_{17}O_3N$	—	60.20	8.56	7.00	—	60.30	8.54	7.18	80.0
C_3H_7	166—168 (5)	1.1762	1.5280	$C_{11}H_{19}O_3N$	55.73	61.74	9.00	6.9	56.28	61.92	8.92	6.57	80.0
i-C_3H_7	140—141 (2)	1.1753	1.5280	$C_{11}H_{19}O_3N$	55.82	61.84	8.89	6.72	56.28	61.92	8.92	6.57	83.0
C_4H_9	155—158 (2)		1.5270†	$C_{12}H_{21}O_3N$	—	63.23	9.25	5.76	—	63.43	9.29	6.16	81.8
i-C_4H_9	152—154 (2)	1.1501	1.5250	$C_{12}H_{21}O_3N$	60.49	63.10	9.20	6.35	60.90	63.43	9.29	6.16	84.4
i-C_5H_{11}	160—161 (1)	1.1300	1.5220	$C_{13}H_{23}O_3N$	65.05	64.77	9.18	5.95	65.52	64.73	9.54	5.86	80.0

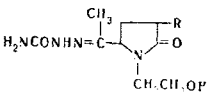
*Mp 30-31° C (petroleum ether)

†Mp 63° C (petroleum ether)

Table 2

R	Bp, °C (mm)	d_4^{20}	n_D^{20}	Empirical formula	Found				Calculated				Yield, %
					MR_D	% C	% H	% N	MR_D	% C	% H	% N	
C_2H_5	129—131 (2)	1.1905	1.5130	$C_{12}H_{19}O_4N$	60.84	59.10	8.00	5.68	61.03	59.33	7.84	5.82	59.2
C_3H_7	132—134 (2)	1.1756	1.5120	$C_{13}H_{21}O_4N$	65.22	61.00	8.28	5.28	65.65	61.17	8.23	5.49	59.1
i-C_3H_7	130—131 (2)	1.1738	1.5111	$C_{13}H_{21}O_4N$	65.30	61.02	8.33	5.32	65.65	61.17	8.23	5.49	60.1
C_4H_9	137—138 (2)	1.1500	1.5080	$C_{14}H_{23}O_4N$	69.72	62.14	8.55	5.30	70.27	62.45	8.54	5.20	60.3
i-C_4H_9	131—132 (0.5)	1.1510	1.5100	$C_{14}H_{23}O_4N$	69.89	62.28	8.60	4.95	70.27	62.45	8.54	5.20	60.00
i-C_5H_{11}	141—143 (3)	1.1365	1.5100	$C_{15}H_{25}O_4N$	74.44	63.40	9.00	4.80	74.88	63.60	8.83	4.94	62.00

Table 3



R	mp °C	Empirical formula	N, %		Yield, %
			found	calculated	
C_2H_5	251—252	$C_{11}H_{20}O_3N_4$	21.50	21.87	75.8
C_3H_7	254	$C_{12}H_{22}O_3N_4$	20.71	20.74	76.4
i-C_3H_7	252	$C_{12}H_{22}O_3N_4$	20.68	20.74	75.6
C_4H_9	255—256	$C_{13}H_{24}O_3N_4$	20.03	19.71	82.5
i-C_4H_9	254—255	$C_{13}H_{24}O_3N_4$	19.40	19.71	78.9
i-C_5H_{11}	256—257	$C_{14}H_{26}O_3N_4$	18.60	18.79	84.7

evaporated to 15 ml and cooled, and the precipitate was filtered off, washed with water, and ethanol, and recrystallized from water.

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