LACTAM ACETALS

V.* SYNTHESIS AND SOME CHEMICAL PROPERTIES OF THE DIETHYL ACETAL OF N-METHYLPIPERIDIN-2-ONE

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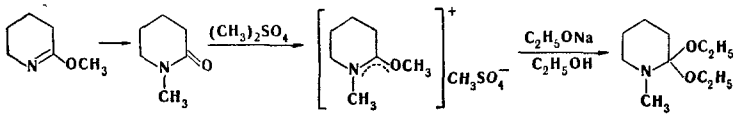
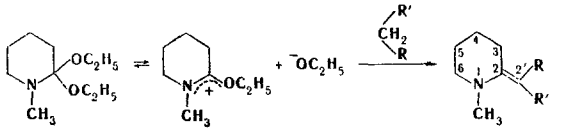
The diethyl acetal of N-methylpiperidin-2-one has been synthesized and its reactions with compounds having active CH_2 and CH_3 groups have been studied. In the reaction of diethyl acetal of N-methylpiperidin-2-one with malonic ester, in addition to the condensation product, ethylmalonic ester is formed. The reaction of the acetal with benzoic acid leads to O-alkylation and the formation of ethyl benzoate.

It has been shown previously that the diethyl acetal of N-methylcaprolactam readily reacts with various nucleophilic [1] and electrophilic [2] reagents, and is also capable of acting as an alkylating agent in O- and C-alkylation reactions [3]. The present work was devoted to a study of the synthesis and some chemical properties of the diethyl acetal of N-methylpiperidin-2-one (I). The synthesis of the initial lactam – N-methylpiperidin-2-one (II) – was effected by a method not previously described for this compound – by heating O-methylvalerolactim [4] in benzene in the presence of catalytic amounts of dimethyl sulfate by the method proposed for preparing N-methylcaprolactam [5]. The alkylation of (II) with dimethyl sulfate and subsequent treatment of the resulting methosulfate complex with sodium ethoxide gave (I):



II I

The reaction of (I) with compounds having active methylene or methyl groups yielded a number of enamines – 1-methyl-2-(R,R'-methylene)piperidines (IIIa-k):



I Ia IIIa-k

III a R=H, R'=NO_2; b R=CN, R'=$CONH_2$; c R=H, R'=C_6H_5CO; d R=H, R'=p-$NO_2C_6H_4CO$; e R=H, R'=m-$NO_2C_6H_4CO$; f R=CN, R'=$CONHCH_2CH_2N(C_2H_5)_2$; g R=R'=CN; h R=C_6H_5, R'=CN; i R=H, R'=p-$MeOC_6H_4CO$; j R=R'=$COOC_2H_5$; k R=H, R'=CN.

The readiness with which (I) takes part in nucleophilic substitution reactions permits the assumption that, as for the acetal of N-methylcaprolactam [6], the equilibrium (I) ⇌ (Ia) also exists in this case. The

*For communication IV, see [2].

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TABLE 1. Conditions for the Synthesis and Properties of the 1-Methyl-2-(R,R'-methylene)piperidines (IIIa-k)

Compound	Mp, °C	Solvent for recrystallization	Empirical formula	Found, %			Calc., %			UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-3}$)	IR spectrum, cm^{-1}				Conditions of synthesis		
				C	H	N	C	H	N		ν_{CO}	$\nu_{C=C}$	$\nu_{C=N}$	ν_{NH}	temp., °C	time, h	yield, %
IIIa	92—93	Heptane	$C_7H_{12}N_2O_2$	54,2	7,7	18,1	53,9	7,6	17,9	219 (4,8), 244 (2,8) — shoulder 352 (26,7)	—	1570	—	—	20	0,5	85
IIIb	180—181	Water	$C_9H_{13}N_3O$	60,1	7,4	23,3	60,4	7,3	23,5	302 (16)	1630	1565	2180	3180, 3440	20	0,5	84
IIIc*	73—74	Heptane	$C_{14}H_{17}NO$	77,8	7,7	6,6	78,1	7,9	6,5	245 (10), 338 (25,7)	—	—	—	— —	150	3	48
IIId*	146—146,5	Methanol	$C_{14}H_{16}N_2O_3$	64,4	6,0	10,5	64,6	6,2	10,8	291 (17), 372 (14)	—	—	—	— —	150	3	64
IIIe*	94—96	Heptane	$C_{14}H_{16}N_2O_3$	64,8	6,1	10,8	64,6	6,2	10,8	227 (17), 250 (11,2) shoulder, 340 (21,6)	—	—	—	— —	150	3	69
IIIf	67—68	Heptane	$C_{15}H_{26}N_4O$	64,6	8,9	20,0	64,8	9,4	20,1	302 (17,4)	1625	1570	2180	3330	80‡	2	71
IIIg	57—58	Petrol. ether	$C_9H_{11}N_3$	66,7	6,7	25,8	67,1	6,8	26,1	286 (18,6)	—	1590	2200	—	80‡	1	62
IIIh	82—83	Hexane	$C_{14}H_{16}N_2$	78,9	7,7	13,2	79,3	7,6	13,2	270 (6,8) - shoulder 309 (14,4)	—	1565	2180	—	120	6	82
IIIi*	110—111	Hexane	$C_{15}H_{19}NO_2$	73,5	8,0	6,2	73,5	7,8	5,7	219 (10,4), 270 (8), 341 (30,3)*	—	—	—	—	150	3	71
IIIj	56—60	Petrol. ether	$C_{13}H_{21}NO_4$	60,8	8,2	5,6	61,2	8,2	5,5	251 (7,4), 310 (12,6)	1650	1550	—	—	130	3	52
IIIk	130—131† (1 mm)		$C_8H_{12}N_2$	70,3	9,0	20,1	70,6	8,8	20,6	272 (14,7)	—	1580	2200	—	120	1	22

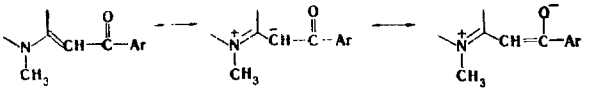
*The IR spectrum has absorption bands at 1530-1605 cm^{-1} which are characteristic for an enamino ketonic fragment.

†Boiling point.

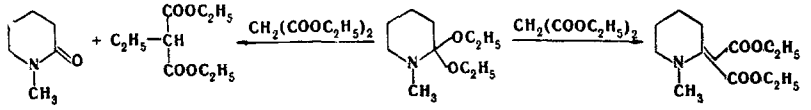
‡Boiling in ethanol.

reaction for the preparation of the enamines (IIIa-k) is apparently similar to the condensation of ketones with compounds having active methylene groups in the presence of bases, the role of the base in this case being played by the alkoxide anion present together with the cation (Ia) in equilibrium with the acetal (I). The enamines (IIIa-k) absorb strongly in the ultraviolet region of the spectrum, their long-wave absorption maxima being somewhat shifted in the direction of smaller wavelengths as compared with the corresponding compounds of the hexahydroazepine series [1]. In the IR spectra of the compounds obtained there are absorption bands of the C=C bond in the 1570-cm^{-1} region, and absorption bands of groupings (CO, C≡N. etc.) conjugated with the multiple bond that are shifted in the low-frequency direction. In the spectra of (IIIc-e, i) there are no absorption bands of a nonconjugated carbonyl (in the 1690-cm^{-1} region), and a series of bands is found in the 1530-1605-cm^{-1} region which are assigned to the $\rangle N-\underset{|}{C}=CH-CO-$. It must be mentioned that it has been shown previously that such a considerable shift in the absorption band of the carbonyl in the low-frequency direction is due not only to conjugation but also the presence of a hydrogen bond between the C=O group and the enamine NH group:

In the case of compounds (IIIa-k) the appearance of such a bond is impossible, and the observed shift of the carbonyl band is due to an exceptional lowering of the multiplicity of the C=O bond through conjugation:



The existence of the equilibrium (I) ⇌ (Ia) must be expressed not only in the capacity of (I) for reacting readily with nucleophilic reagents, but also in its capacity for acting as an alkylating agent. In actual fact, when equimolecular amounts of (I) and benzoic acid were boiled in benzene, ethyl benzoate was obtained in high yield. In view of this, the reaction of (I) with malonic ester was studied in detail. After equimolecular amounts of the reactants had been heated in the absence of a solvent at 130°C, the reaction mixture was analyzed with the aid of a gas-liquid chromatograph. The analysis showed that among the reaction products, in addition to the initial malonic ester and (IIIj), there were (II) and ethylmalonic ester, the ratio of these products being 4.16 : 12.3 : 2.9 : 1, and their relative retention time 1, 14.6, 3.24, and 1.97, respectively. Thus, it has been shown that the reaction of (I) with malonic ester takes place in two directions: with the formation of the enamine (IIIj) and by the C-alkylation of the malonic ester to ethylmalonic ester:



II I IIIj

EXPERIMENTAL

The IR spectra of the substances were taken in paraffin oil on a UR-10 spectrophotometer. The UV spectra of alcoholic solutions of the substances (~10^{-4} M) were taken on an EPS-3 recording spectrophotometer (layer thickness 1 cm). Gas-chromatographic analysis was performed as described previously [2] but at T_{init} 80°C (1 min), T_{final} 200°C (15 min), rate of heating 6°C per min.

1-Methylpiperidin-2-one (II). To a solution of 11.3 g of O-methylvalerolactim in 25 ml of benzene was added 5 ml of dimethyl sulfate, and the mixture was boiled for 6 h and cooled, 12 ml of 50% potassium carbonate solution was added to pH ~8, the benzene layer was separated off, the aqueous layer was extracted with chloroform, the combined organic phases were dried with anhydrous Na_2SO_4 and filtered, the solvent was evaporated off in vacuum, and the residue was distilled to give (II) with a yield of 76%, bp 95-98°C (12 mm), n_D^{20} 1.4795 [8].

Diethyl Acetal of N-Methylpiperidin-2-one (I). A mixture of 22.6 g of (II) and 25.2 g of dimethyl sulfate was heated at 80°C for 3 h and cooled, 15 ml of dry ether was added, and the mixture was stirred. Then the ethereal layer was decanted off and the operation was repeated twice, after whith the ether residues were evaporated in vacuum and the residue was added dropwise to a solution of sodium ethoxide (from 5.5 g of Na and 100 ml of absolute ethanol) at 50-60°C, the mixture was kept for 3 h at this tempera-

ture and was filtered, the ethanol was distilled off in vacuum, 25 ml of absolute ether was added, the mixture was filtered, the ether was evaporated off, and the residue was distilled to give (I), yield 55.6%, bp 69-70°C (12 mm), n_D^{20} 1.4541. Found, %: C 64.4; H 11.4; N 7.6. $C_{10}H_{21}NO_2$. Calculated, %: C 64.2; H 11.2; N 7.5.

2,4-Dinitrophenylhydrazone of N-Methylpiperidin-2-one. This was obtained by boiling equimolecular amounts of the acetal (I) and of 2,4-dinitrophenylhydrazine in ethanol for 1 h. Mp 183.5-184°C (ethyl acetate, 1:30). Found, %: C 49.0; H 4.9, N 23.9. $C_{12}H_{15}N_5O_4$. Calculated, %: C 49.2; H 5.1; N 23.9.

1-Methyl-2-(nitromethylene)piperidine (IIIa). To 3.5 g of (I) was added 1.14 g of nitromethane (exothermic reaction), the mixture was kept for 30 min at 20°C, and was then cooled and the (IIIa) was filtered off. The other compounds (III) were obtained similarly (Table 1).

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