SYNTHESIS OF ACETYLTRIALKYLPYRROLES FROM 2,4-PENTANEDIONES

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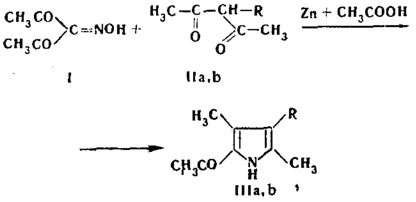
The condensation of isonitrosoacetylacetone with 3-alkyl-2,4-pentanediones and reduction with zinc in acetic acid gives α-acetyltrialkylpyrroles. The analogous condensation of 3-alkyl-3-nitroso-2,4-pentanediones with acetylacetone leads to β-acetyltrialkylpyrroles, and condensation with acetoacetic ester leads to β-ethoxycarbonyltrialkylpyrroles. When the α- and β-acetyltrialkylpyrroles undergo salt formation, the oxygen of the carbonyl group is protonated.

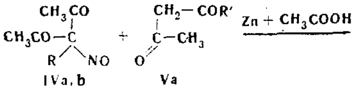
In studying salt formation in acylpyrroles [1, 2], we found it necessary to prepare acetyltrialkylpyrroles. α-Acetyltrialkylpyrroles have been obtained previously by introducing acetyl groups into α-unsaturated trialkylpyrroles [3, 4]. It was more promising to obtain these compounds in one stage by a reaction of the Knorr condensation type. The use in this condensation of isonitrosomalonic and isonitrosocyanoacetic esters [5] has broadened the range of application of the reaction and made it possible to obtain α-ethoxycarbonyl- and α-cyanotrialkylpyrroles in a simple manner. The use of isonitrosoacetoacetic ester in place of isonitrosomalonic ester in condensation with substituted β-diketones [6] has simplified the method of obtaining α-ethoxycarbonyltrialkylpyrroles.

We have used an analogous condensation to obtain α-acetyltrialkylpyrroles. When a mixture of isonitrosoacetylacetone (I) with a 3-alkyl-2,4-pentanedione (II) was reduced with zinc in acetic acid, the corresponding α-acetylpyrrole (III) was obtained with a yield of the order of 30%, which is characteristic for a condensation of this type. Thus, in this reaction, and also in the reaction with isonitrosoacetoacetic and isonitrosomalonic esters, on cyclization the acyl residue readily splits out.



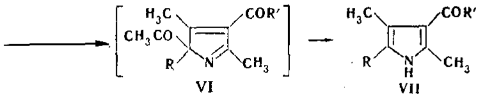
a R = CH_3, b R = C_2H_5

In order to obtain β-acetyltrialkylpyrroles, we studied the condensation of 3-nitroso-3-alkyl-2,4-pentanediones (IV) with acetylacetone (Va) under the conditions of the Knorr reaction.



IVa R=CH_3
IVb R=C_2H_5

Va R′=CH_3
Vb R′=OC_2H_5



VIIa R=R′=CH_3
VIIb R=C_2H_5, R′=CH_3
VIIc R=CH_3, R′=OC_2H_5
VIId R=C_2H_5, R′=OC_2H_5

An interesting feature of this condensation is that in the hypothetical intermediate pyrrolenine VI there are not two acyl groups on the α-carbon atom, as in the reactions of the first type, but an acyl and an alkyl group, in consequence of which the splitting off of the acyl group must be hindered. However, in this case, also, the only reaction products were the corresponding β-acetylpyrroles VIIa and VIIb.

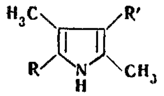
The similar condensation of IV with acetoacetic ester (Vb) leads to the β-ethoxycarbonyltrialkylpyrroles VIIc and VIId.

When the condensation was carried out by the usual method without the isolation of the nitroso compound from the reaction mixture, the yield of product was 15–30%; however, the previous isolation of IV enabled the yield to be raised to 50%.

The hydrochlorides of the acetyltrialkylpyrroles are fairly unstable compounds rapidly losing hydrogen chloride (low chlorine content in comparison with the calculated figure; rapid appearance of a carbonyl band in the IR spectrum of the salt). When the salts are treated with water, the base is regenerated quantitatively. In the IR spectra of the acetyltrialkylpyrroles, salt formation causes the changes characteristic for such compounds [1, 2]: disappearance of the N—H absorption bands; disappearance of the C=O absorption band at ~1630 cm^{-1}, and appearance of absorption bands of a β-pyrrolene ring in the β-acetylpyrroles at ~1570 cm^{-1}; and a slight shift in the band at ~1630 cm^{-1} in the α-acetylpyrroles (vibrations of the α-pyrrolene ring). A difference from the compounds described previously [1, 2] is the absence from the IR spectra of the salts of the acetyltrialkylpyrroles of the "immonium" bands at ~1800 to 2000 cm^{-1}. However, there is a broad "immonium" band at 2200–2400 cm^{-1}. This permits an O-protonated structure to be ascribed to the trialkylacetylpyrrole salts.

EXPERIMENTAL

3-Methyl-3-nitroso-2,4-pentanedione (IVa). With vigorous stirring, a solution of 16.4 g (0.24 mole) of sodium nitrite in 25 ml of water was added dropwise to a solution of 22.8 g (0.2 mole) of 3-methyl-2,4-pentanedione in 50 ml of acetic acid at a temperature of the reaction mixture of 12–14° C. With the addition of the first portion of the nitrite solution, the mixture became blue-green, and then colorless crystals deposited. It was stirred for 3 hr at 0–5° C and the



Compound	R	R′	Method of Preparation	Mp, °C	R_f[3*]	IR spectrum		Hydrochloride						Yield, %
						ν_{N-H}	$\nu_{C=O}$	Mp, °C	empirical formula	Cl, %		IR spectrum[4*]		
										calculated	found	N^+—H	vibrations of the ring	
IIIa	CH_3CO	CH_3	A	136—137[3]	0.29	3296, 3270	1610	145.5—147	$C_9H_{13}NO \cdot HCl$	18.89	16.42; 16.44	2400 (wide., weak)	1640	29.8
IIIb	CH_3CO	C_2H_5	A	111—112[4]	0.29	3288	1646, 1619	130—132	$C_{10}H_{15}NO \cdot HCl$	17.58	16.11; 16.07	2380	1620	33.2
VIIa	CH_3	CH_3CO	B	208.5—210[7]	0.23	3200	1625, 1600	202—203	$C_9H_{13}NO \cdot HCl$	18.89	16.70; 16.92	2400 (very wide, weak)	1600, 1580	54.0
VIIb	C_2H_5	CH_3CO	B	156.5—157[1*]	0.29	3240, 3190	1623, 1605	127.5—129	$C_{10}H_{15}NO \cdot HCl$	17.58	14.29; 14.40	2380 (wide) 1770 (weak)	1575	58.6
VIIc	CH_3	$CO_2C_2H_5$	B	104—105[2*,8]	0.55	3290 (s), 3200 (w)	1668	—	—	—	—	—	—	48.8
VIId	C_2H_5	$CO_2C_2H_5$	B	106.5—107[2*,8]	0.57	3270 (s), 3200 (w)	1658	—	—	—	—	—	—	47.6

[1*] Found, %: C 72.61; H 9.40; N 8.45. Calculated for $C_{10}H_{15}NO$, %: C 72.68; H 9.15; N 8.48. [2*] From methanol. [3*] On alumina; chloroform — ethanol (100 : 1). [4*] The IR spectra of all the compounds were taken in paraffin oil on a UR-10 spectrophotometer.

precipitate that had deposited was separated off, washed with 100 ml of water and dried. The yield of IVa was 17.0 g (59.4%). Mp 115–116° C (from chloroform). Found, %: C 50.37; H 6.63; N 9.84. Calculated for $C_6H_9NO_3$, %: C 50.35; H 6.34; N 9.79. R_f 0.27 [silica; chloroform–ethanol (100 : 1)]. IR spectrum (in paraffin oil): 1723 cm^{-1} (C=O).

3-Ethyl-3-nitroso-2,4-pentanedione (IVb). The nitrosation of 25.6 g (0.2 mole) of 3-ethyl-2,4-pentanedione in 45 ml of glacial acetic acid was carried out with a solution of 16.4 g (0.24 mole) of sodium nitrite, and the mixture was worked up as described above. Yield 15.5 g of IVb (49.2%). Mp 101–102° C (from chloroform). Found, %: C 53.78; H 7.24; N 8.71. Calculated for $C_7H_{11}NO_3$, %: C 53.50; H 7.05; N 8.91. R_f 0.41. IR spectrum: 1733, 1707 cm^{-1} (C=O).

The acetyl- and ethoxycarbonyltrialkylpyrroles were obtained by one of the following two methods. The yields and constants of the compounds obtained are given in the table.

A. With vigorous stirring, a solution of 3.8 g of sodium nitrite in 4 ml of water added to 0.05 mole of acetylacetone in 40 ml of glacial acetic acid at a temperature of 12–14° C. Stirring was continued for 3 hr, after which the mixture was left for 20 hr. A 0.05 mole quantity of a 3-alkyl-2,4-pentanedione was added, and then, in portions, 12 g of zinc dust at 65–75° C. The mixture was heated for a further hour at 105–110° C, and the hot solution was filtered from unchanged zinc and poured into 500 ml of ice water. The colorless precipitate that deposited was filtered off, washed with water, dried, and crystallized from ethanol.

B. In portion, 12 g of zinc dust was added at 65–70° C to a solution of 0.05 mole of a 3-alkyl-3-nitroso-2,4-pentanedione, 0.05 mole of a β-dicarbonyl compound (Va or Vb), 7.0 g of anhydrous sodium acetate, and 5 ml of acetic acid. The mixture was heated with stirring at 107–112° C for 1 hr, after which it was treated as described in Method A.

The hydrochlorides of the acetylpyrroles (see table) were obtained by adding a solution of dry hydrogen chloride in ether to ethereal solutions of the bases.

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