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REACTION OF α-α'-DICHLORO-SUBSTITUTED 1,5-DIKETONES WITH AMMONIA AND AMMONIUM ACETATE

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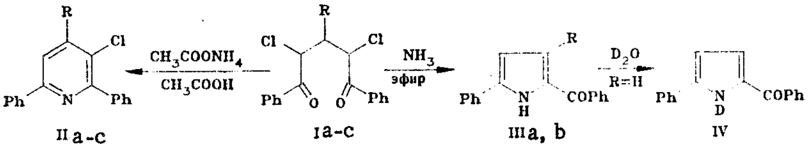
Under the influence of ammonia or ammonium acetate, α-α'-dichloro-substituted 1,5-diketones undergo heterocyclization to give β-chloropyridines or 2-benzoylpyrrole derivatives. The structure of the final product depends on the reagent and the character of the substituent in the 3 position of the starting dichloro diketones.

Products of the pyridine series are formed in the reaction of acyclic 1,5-diketones with ammonia and ammonium acetate [1]. The literature does not contain any information relative to the utilization of chloro-substituted 1,5-diketones in the indicated reaction, inasmuch as the latter, prior to our research, were unknown and were recently obtained by the reaction of acyclic diketones with chlorine [2]. A new active center, which probably opens up new aspects of the chemistry of this class of compounds, develops when a chlorine atom is introduced into the 1,5-diketone structure.

In the present research we studied the reactions of α-α'dichloro-substituted 1,5-diketones Ia-c with ammonia and ammonium acetate in order to ascertain the effect of the chlorine atom on the direction of the transformation. We found that the character of the products of the reaction of chloro-substituted diketones Ia-c with nucleophilic reagents is determined by the competitive reactivities of the active centers:



I—III a R=H; b $R=CH_3$; c R=Ph

The Chichibabin reaction of diketones Ia-c with ammonium acetate (by heating in acetic acid at 60-80°C) proceeds most smoothly and unambiguously. In this case the attack of the nucleophilic reagent, as assumed, is realized at the C=O groups and leads to the formation of β-chloropyridines IIa-c in up to 90% yields. The structure of the β-chloropyridines is confirmed by the presence in the IR spectra of absorption bands of a pyridine ring at 1540 cm^{-1}. In the PMR spectrum of IIa (Fig. 1) the signal of the 4-H proton is found at weak field at 7.83 ppm in the form of doublet (J = 8.5 Hz). The splitting of the signal is the result of coupling with the 5-H proton, the signal of which also appears in the form of a doublet at 7.46 ppm. In the spectra of IIb and IIc, which have substituents in the 4 position, the signal of the 5-H proton is present in the form of a singlet at 7.53 and 7.63 ppm, respectively.

The reaction of dichloro-substituted 1,5-diketones Ia-c with ammonia in ether at room temperature proceeds ambiguously, and the structures of the final products depend on substituent R in the 3 position of the starting diketones. Thus, as in the case of ammonium acetate, 2,4,6-triphenyl-3-chloropyridine (IIc) is formed in the reaction of Ic with ammonia. Under the same conditions, unsubstituted diketone Ia gives 2-benzoyl-5-phenylpyrrole (IIIa) in 80% yield, whereas in the case of 3-methyl-1,5-diphenyl-2,4-dichloropentanedione (Ib) we obtained a mixture of the corresponding β-chloropyridine IIb and 2-benzoyl-3-methyl-5-phenylpyrrole (IIIb). The formation of pyrrole derivatives IIIa,b can be represented by the scheme

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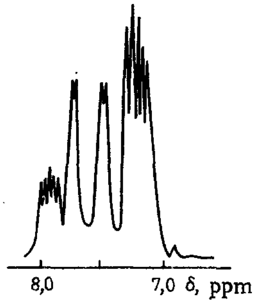
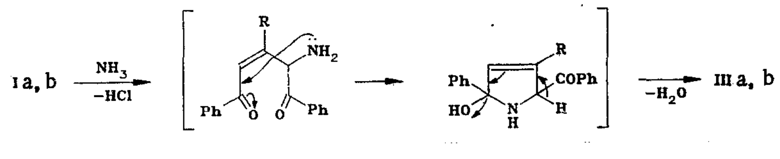


Fig. 1. PMR spectrum of β-chloropyridine IIa.



Nucleophilic substitution of the chlorine atom in the case of 3-phenyl-substituted diketone Ic is probably hindered as a consequence of steric factors, as a result of which, in this case and with ammonia, the reaction is realized at the C=O groups to give only β-chloropyridine IIc.

The structures of IIIa,b were established on the basis of IR and PMR spectroscopic data. The IR spectrum of IIIb contains absorption bands at 1660 (C=O) and 3300 cm^{-1} (heteroring NH). In the spectrum of IIIa the absorption of the NH bond shows up at 3300-3320 cm^{-1}, and a shift of the absorption of the carbonyl group to the low-frequency region (1640 cm^{-1}) is observed. In the IR spectrum of deuterated product IV the absorptions of the C=O and ND bonds appear at 1650 and 3260 cm^{-1}, respectively. A broad signal of the NH proton of the pyrrole ring at 9.47 ppm is present in the PMR spectrum of IIIb at weak field; the signal of the 4-H proton shows up in the form of a doublet at 6.42 ppm. A characteristic feature of the PMR spectrum of IIIa is splitting of the signals of the 3-H and 4-H protons of the heteroring, which exist in the form of double doublets at 6.62 and 6.93 ppm, respectively. The indicated splitting is probably a consequence of coupling of the 3-H and 4-H protons with one another and with the NH proton of the pyrrole ring, upon which the latter reacts to give a broad signal at 10.18 ppm [3]. In fact, in the PMR spectrum of deuterated product IV the signal of the NH proton vanishes, and the signals of the 3-H and 4-H protons are present in the form of doublets at 6.64 and 6.90 ppm, respectively.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil and hexachlorobutadiene were recorded with a UR-20 spectrometer. The PMR spectra of solutions in $CDCl_3$ were obtained with a Varian Fi-80 spectrometer with hexamethyldisiloxane (HMDS) as the internal standard.

2,6-Diphenyl-3-chloropyridine (IIa). A solution of 6 mmoles of diketone Ia and 10 mmoles of ammonium acetate in 50 ml of acetic acid was heated at 60-80°C for 3 h, after which the mixture was diluted with ether. The ether solution was washed with water, dried, and evaporated to give IIa (80%) with mp 136-138°C (alcohol). IR spectrum: 1540 cm^{-1}. PRM spectrum: 7.46 (1H, d, J = 8.5 Hz, 5-H), 7.83 (1H, d, J = 8.5 Hz, 4-H), and 7.37-7.91 ppm (10H, m, C_6H_5). Found: C 77.6; H 4.5; Cl 13.2; N 5.1%. $C_{17}H_{12}ClN$. Calculated: C 77.8; H 4.5; Cl 13.4; N 5.3%.

4-Methyl-2,6-diphenyl-3-chloropyridine (IIb). This compound, with mp 112-113°C (alcohol), was similarly obtained in 80% yield. IR spectrum: 1545 cm^{-1}. PMR spectrum: 2.46 (3H, s, CH_3), 7.53 (1H, s, 5-H), and 7.35-7.87 ppm (10H, m, two C_6H_5). Found: C 77.6; H 5.1; Cl 12.5; N 4.7%. $C_{18}H_{14}ClN$. Calculated: C 77.3; H 5.0; Cl 12.7; N 5.0%.

2,4,6-Triphenyl-3-chloropyridine (IIc). This compound, with mp 153-154°C (alcohol), was obtained in 92% yield by a method similar to that used to obtain IIa. IR spectrum: 1540 cm^{-1}. PMR spectrum: 7.63 (1H, s, 5-H) and 7.35-7.85 ppm (15H, m, three C_6H_5). Found: C 81.0; H 4.5; Cl 10.6; N 4.0%. $C_{23}H_{16}ClN$. Calculated: C 81.0; H 4.6; Cl 10.3; N 4.1%.

2-Phenyl-5-benzoylpyrrole (IIIa). A solution of 6 mmole of diketone Ia in 50 ml of absolute ether was saturated with ammonia in the course of 5-10 min, after which the mixture was allowed to stand at room temperature for 5-10 h. It was then washed with water, and the ether solution was dried and evaporated to give IIIa (80%) with mp 164-165°C (chloroform). IR spectrum: 1640 (CO) and 3300-3320 cm^{-1} (NH). PMR spectrum: 6.62 (1H, dd, J = 4 Hz, 3-H), 6.93 (1H, dd, J = 4 Hz, 4-H), 7.21-7.97 (10H, m, two C_6H_5), and 10.18 ppm (1H, s, NH). Found: C 82.5; H 5.5; N 5.6%. $C_{17}H_{13}NO$. Calculated: C 82.4; H 5.6; N 5.7%.

Under similar conditions, from diketone Ib, after removal of the ether by distillation and fractional crystallization from alcohol, we obtained 4-methyl-2,6-diphenyl-3-chloropyridine (IIb) (35% yield; identical to the product obtained by the reaction of diketone Ib with ammonium acetate) and 2-phenyl-3-methyl-5-benzoylpyrrole (IIIb) [40% yield, mp 160-161°C (chloroform]. IR spectrum: 1660 (CO) and 3300 cm^{-1} (NH). PMR spectrum: 2.0 (3H, s, CH_3), 6.42 (1H, d, J = 0.5 Hz, 3-H), 7.24-7.74 (10H, m, two C_6H_5), and 9.47 ppm (1H, s, NH). Found: C 82.5; H 6.0; N 5.7%. $C_{18}H_{15}NO$. Calculated: C 82.7; H 5.7; N 5.3%.

Under similar conditions, from diketone Ic we obtained only 2,4,6-triphenyl-3-chloropyridine (IIc) in 90% yield; this product was identical to the product obtained by the reaction of diketone Ic with ammonium acetate.

ND-2-Phenyl-5-benzoylpyrrole (IV). A 4-ml sample of D_2O, previously treated with sodium to pH 10, was added to a solution of 0.45 g of 2-phenyl-5-benzoylpyrrole (IIIa) in 5 ml of absolute dioxane. The reaction was carried out in an inert atmosphere by boiling in an ampul on a water bath for 30 h. Workup gave 0.35 g (80%) of IV with mp 163-165°C (dioxane). IR spectrum: 1650 (CO) and 3260 cm^{-1} (ND). PMR spectrum: 6.64 (1H, d, J = 1 Hz, 3-H), 6.90 (1H, d, J = 1 Hz, 4-H), and 7.22-7.95 ppm (10H, m, two C_6H_5).

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