The Reactions of 3-Chloro- and 3-Bromo-2,4-pentanedione with Malonitrile and with Ethyl Cyanoacetate

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2-Amino-3-cyano-4-acetyl-5-methylfuran (I a), 2-amino-3-ethoxy-carbonyl-4-acetyl-5-methylfuran (I b) and 2-amino-3-ethoxycarbonyl-4,4,5-triacetyl-6-methylpyran (II) have been prepared.

When the sodium salt of 3-chloro-2,4-pentanedione reacts with malonitrile or ethyl cyanoacetate in ethanol-water solution, cyclization of the primarily formed III a, b occurs with formation of the neutral compounds, 2-amino-3-cyano-4-acetyl-5-methylfuran (I a) or 2-amino-3-ethoxycarbonyl-4-acetyl-5-methylfuran (I b).

RCH₂CN + (CH₃CO)₂CClNa → RCH(CN)-CH(COCH₃)₂ + NaCl

a. R=CN

b. $R = COOC_2H_5$

I a and b are stable (cf. unsubstituted 2-aminofuran which is very unstable), probably on account of the resonance possibilities offered by the 3-cyanoor the 3-ethoxycarbonyl groups, e.g.

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The IR absorption curve of I a (in KBr and in nujol) has one single nitrile band at 2 175 cm⁻¹. This means a displacement of about 75 cm⁻¹ from the unconjugated nitrile band at 2 250 \pm 10 cm⁻¹, indicating a strong resonance effect on the nitrile group ¹. A nujol suspension of the product shows absorption at 3 100 and 3 250 cm⁻¹, which is within the region characteristic of associated amino groups. After equilibration with D₂O, ND₂-bands at 2 330 and 2 500 cm⁻¹ were obtained. Thus I a β is probably the main structure of the product formed. With o-nitrobenzaldehyde a Schiff's base can be prepared from I a, and with 2,4-dinitrophenylhydrazine a 2,4-dinitrophenylhydrazone.

The IR spectrum of I b in potassium bromide has no nitrile band and

shows the expected NH₂-bands at 3 200 and 3 390 cm⁻¹.

The basic character of the amino group of I a, b is so weak that the products cannot be titrated with perchloric acid in glacial acetic acid. Excess of alkali dissolves I a and b with opening of their furan rings. On acidification ring closure with reformation of I a and I b takes place, but only in low yields because of alkaline hydrolysis of the nitrile and carbethoxy groups.

The reaction of the sodium salt of 3-bromo-2,4-pentanedione with malonitrile is analogous to the reaction described above of the corresponding chloro compound, I a being formed though in lower yield. The reactions of ethyl cyanoacetate with 3-bromo-2,4-pentanedione and with 3-chloro-2,4-pentanedione, however, are essentially different. With the bromo compound a pyran derivative, II, is formed evidently according to the equations:

$$\begin{array}{c} \text{CN} \\ \text{CH}_{3} \\ \text{COCEt} \\ \text{COCEt} \\ \text{COCEt} \\ \text{COCEt} \\ \text{CH}_{3}\text{CO})_{2}\text{CBrNa} \rightarrow (\text{CH}_{3}\text{CO})_{2}\text{C} = \text{C}(\text{COCH}_{3})_{2} \\ \rightarrow \text{CH}(\text{CN})_{2}\text{C} - \text{CH}(\text{COCH}_{3})_{2} \\ \rightarrow \text{CH}(\text{CN})\text{COOEt} \\ \text{H}_{3}\text{CCO} \\ \text{COCH}_{3} \\ \text{H}_{3}\text{CCO} \\ \text{COCH}_{3} \\ \text{H}_{3}\text{CCO} \\ \text{COCH}_{3} \\ \rightarrow \text{EtOOC-CH} \\ \text{C} - \text{COCH}_{3} \\ \rightarrow \text{C} - \text{CH}_{3} \\ \text{H}_{2}\text{N} - \text{C} \\ \text{C} - \text{CH}_{3} \\ \text{H}_{2}\text{N} - \text{C} \\ \text{C} - \text{CH}_{3} \\ \text{C} - \text{CH}_{4} \\ \text{C} - \text{CH}$$

The IR absorption curve of the product (in KBr) has no nitrile band but NH₂ stretching bands at 3 225 and 3 325 cm⁻¹. The amino group is basic enough to be titrated with perchloric acid in glacial acetic acid, though not very sharply.

It should be mentioned that the reaction of 3-chloro (or bromo)-2,4-pentanedione with cyanoacetamide in alkaline solution ² follows other pathways than the reactions described above, pyridine derivatives being formed according to the equations

$$CH_{2}COCHHalCOCH_{3} + CH_{3}(CN)(CONH_{3}) \rightarrow CH_{3} - C$$

$$C - CH_{3} \neq C$$

$$C - CH_{4} \neq C$$

$$C - CH_{5} \neq$$

EXPERIMENTAL

Preparation of 2-amino-3-cyano-4-acetyl-5-methylfuran (I a). 3-Chloro-2,4-pentane-dione (2.69 g) and malonitrile (1.32 g) were dissolved in ethanol (10 ml), and sodium hydroxide (8.26 ml of 2.42 N solution) was added. Colourless crystals of I a started separating immediately. The next day they were collected by filtration and washed with 50 % ethanol. Yield: 3.05 g, m. p. about 240° (decomp.). The product can be recrystallized from ethanol. (Found: C 58.5; H 4.85; N 17.1; O 19.5. Calc. for $C_8H_8N_2O_2$: C 58.5; H 4.9; N 17.1; O 19.5.)

2,4-Dinitrophenylhydrazone: M.p. $166-168^{\circ}$ (decomp.) (Found: C 48.9; H 3.7; N 24.3; O 23.4. Calc. for $C_{14}H_{12}N_6O_5$: C 48.8; H 3.5; N 24.4; O 23.2.) Schiff's base with o-nitrobenzaldehyde (Found: C 60.6; H 4.0; N 14.0. Calc. for $C_{15}H_{11}N_3O_4$: C 60.6; H 3.7; N 14.1).

Preparation of 2-amino-3-ethoxycarbonyl-4-acetyl-5-methylfuran (I b). 3-Chloro-2,4-pentanedione (2.69 g) and ethyl cyanoacetate (2.26 g) were dissolved in ethanol (7 ml). When sodium hydroxide (8.26 ml of 2.42 N solution) was added, colourless crystals of I b soon started separating. The following day the product was filtered and washed with 50 % ethanol. Yield: 3.30 g; m. p. after recrystallization from ethanol: 136°. (Found: C 57.0; H 6.2; N 6.7; O 30.1. Calc. for C₁₀H₁₈NO₄: C 56.9; H 6.2; N 6.6; O 30.3.)

Preparation of 2-amino-3-ethoxycarbonyl-4,4,5-triacetyl-6-methylpyran (II). Bromine

Preparation of 2-amino-3-ethoxycarbonyl-4,4,5-triacetyl-6-methylpyran (II). Bromine (3.2 g) was added with stirring to a cooled (12°) solution of 2,4-pentanedione (2.0 g) in 8.26 ml of 2.42 N sodium hydroxide solution and 15 ml of ethanol. After cooling the solution to 8°, sodium hydroxide (4.1 ml of 2.42 N solution) was added and — one minute later — ethyl cyanoacetate (1.38 g) and another 5.0 ml of sodium hydroxide solution. After 5 h the precipitate formed was filtered and washed with 50 % ethanol. Yield: 0.56 g; m. p. 166° (decomp.). (Found: C 58.2; H 6.2; N 4.7; O 30.9; mol. wt 320. Calc. for C₁₆H₁₉NO₆: C 58.2; H 6.2; N 4.5; O 31.0; mol. wt 309.)

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The analyses were performed by Mikroanalytisches Laboratorium im Max-Planck-Institut für Kohlenforschung, Mülheim, Germany. Dr. Andreas Rosenberg, University of Uppsala, carried out the IR measurements.

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