SYNTHESIS OF 5H-1,2-DIHYDRO-2,5-DIOXOCHROMENO[2,3-b]PYRIDINES

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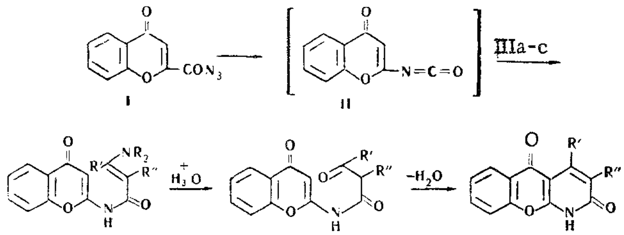
Some representative 5H-1,2-dihydro-2,5-dioxochromeno[2,3-b]pyridines have been prepared by condensation of 2-isocyanatochromone (obtained by Curtius rearrangement of the azide of chromone-2-carboxylic acid) with enamines, followed by cyclization.

We have previously [1] used 2-isocyanatochromone (II), which is obtained by the Curtius rearrangement of the azide of chromone-2-carboxylic acid (I), for the preparation of 2-acylaminochromones. This paper deals with the condensation of the isocyanate II with the enamines 1-piperidino-1-cyclohexene (IIIa), 1-morpholino-1-cyclopentene (IIIb), and 1-piperidino-1-butene (IIIc). The reaction proceeds normally [2] with the formation of the aminocarbonyl compounds (IVa-c), one of which (IVa) was isolated and characterized. Compounds IVa-c were hydrolyzed by dilute mineral acids with loss of the amino group to give the β-dicarbonyl compounds (Va-c). The cyclopentanone derivative Vb was obtained in the free state.



IVa-c Va-c VIa-c

IVa, IVc R_2N-piperidino
IVb R_2N-morpholino
IVa Va, VIa $R'+R''=(CH_2)_4$
IVb, Vb, VIb $R'+R''=(CH_2)_3$
IVc, Vc, VIc $R'=H$, $R''=C_2H_5$

The ketones Va-c cyclized fairly readily and smoothly under the influence of 10% hydrochloric acid to give 1,2-dihydro-2,5-dioxochromeno-[2,3-b]pyridines (VIa-c). The hydrolysis of IV and the cyclization of V into VI may be combined in a single stage. The representatives of the new type of heterocyclic system synthesized in this way (VIa-c) are high-melting compounds with a comparatively acidic character (they react with aqueous sodium bicarbonate). They may be considered as derivatives of α-pyridone and 2-acylaminochromone. Each of these systems accordingly increases the acidity of the NH group. Compounds VI give no coloration with ferric chloride, in contrast to the intermediates V, which are related to amides of acetoacetic acid. The IVa molecule contains two β-aminovinylcarbonyl fragments, and this compound does not give a color reaction with ferric chloride, but it dissolves in caustic alkalies due to the presence of the acidic hydrogen atom on the nitrogen, and in dilute hydrochloric piperidine is split off almost instantaneously. Compound IVa has the same mp as VIa (a mixed mp gave a depression), probably because IVa, on heating, cyclizes to VIa. The NMR spectrum (100 MHz instrument, solvent dimethyl sulfoxide) of IVa shows in the 4-9 ppm region, apart from four signals due to the protons of the benzene ring

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(δ 7.86 ppm, quartet with $J_1 \approx 8$ and $J_2 \approx 1$ Hz, proton at C_5; 7.69 ppm, sextet with $J_1 \approx 8$ and $J_2 \approx 1$ Hz, apparently $C_{(6)}H$; 7.24-7.49 ppm, combined signal due to the two protons at C_7 and C_8), a narrow singlet at 6.77 ppm due to the vinyl proton $C_{(3)}H$ of the chromone ring. The spectrum of VIa similarly shows the protons of the benzene ring, but the signal of the vinyl proton is absent.

The chemical properties of compounds of the type VI, including their possible tautomerism, will be studied further.

EXPERIMENTAL

1-Piperidino-2-(2-chromonylaminoformyl)-1-cyclohexene (IVa). A solution of 4.3 g (0.02 mole) of chromone-2-carboxazide (I) in 100 ml of dry benzene was boiled for 1 hr, and to the resulting solution of the isocyanate (II) was added without cooling 3.32 g (0.024 mole) of the enamine IIIa, and the mixture was kept overnight. The precipitate which separated was filtered off and washed with ether to give 5.3 g (75%) of IVa, mp 271-272° C (from alcohol). Found, %: C 71.3, 71.5; H 6.7, 6.9; N 8.0, 8.0. Calculated for $C_{21}H_{24}N_2O_3$, %: C 71.6; H 6.9; N 8.0. IR spectrum (in Vaseline oil), cm^{-1}: 2200-2700 (several wide bands due to NH, possibly $\geq N^+H$), 1630, 1610, 1575, 1520 (strong bands due to C=O group and C=C bond).

5H-1,2-Dihydro-3,4-tetramethyleno-2,5-dioxochromeno[2,3-b]pyridine (VIa). A suspension of 1.0 g of IVa in 20 ml of 10% HCl was heated for 5 min on a boiling water bath, stirred for 4 hr at ~ 20° C, and then the precipitate was filtered off, washed with water, and dried over P_2O_5 to give 0.7 g (92%) of VIa, mp 271-272° C (from alcohol). Found, %: C 71.9, 71.8; H 5.0, 5.1; N 5.5, 5.3. Calculated for $C_{16}H_{13}NO_3$, %: C 71.9; H 4.9; N 5.2. IR spectrum (in Vaseline oil), cm^{-1}: 2200-2700 (wide band due to NH), 1620 (very wide and intense, unresolved bands due to C=O and C=C), 1550, 1500 (band of medium intensity); in tetrahydrofuran: 1675 (intense, probably the C=O of the pyridone group), 1645 (very intense, probably the C=O of the chromone), 1615 (weak), 1580 (intense).

2-(2-Chromonylaminoformyl)cyclopentanone (Vb). A 2-g (0.0093 mole) quantity of the azide I in 50 ml of dry benzene was boiled for 1 hr, and 1.7 g (0.011 mole) of the enamine IIIb was added to the hot solution. After it had stood overnight, the mixture was filtered to give 1.7 g of the enamine IVb. This compound (1.12 g) was suspended in 20 ml of 10% HCl, and the mixture was heated for 1 hr on a water bath. The precipitate was filtered off, washed with water, and dried over P_2O_5 to give 0.85 g (52.2%) of Vb, mp 229-230° C (decomp, from alcohol). Found, %: C 66.3, 66.0; H 4.8, 4.9; N 5.4, 5.4. Calculated for $C_{15}H_{13}NO_4$, %: C 66.4; H 4.8; N 5.2. IR spectrum (in Vaseline oil), cm^{-1}: 3190-3300 (series of bands due to bound NH), 1740 and 1710 (C=O group of the—NHCOCHCO—fragment), 1610-1630, 1510-1540 (intense, wide, not fully resolved band due to the C=O of the chromone and the C=C bond).

5H-1,2-Dihydro-3,4-trimethyleno-2,5-dioxochromeno[2,3-b]pyridine (VIb). A 2.15-g (0.01 mole) quantity of the azide I in 25 ml of benzene was boiled for 1 hr, and 1.7 g (0.011 mole) of the enamine IIIb was added to the hot solution. The mixture was kept overnight, the residue (2.5 g) of the enamine IVb was suspended in 40 ml of 10% HCl, and the mixture was heated for 30 min at ~ 100° C, stirred at ~ 20° C for an additional 2 hr 30 min, and kept overnight. The precipitate was isolated to give 2 g (78.4%) of VIb, mp 316-317° C (decomp, from acetic acid). Found, %: C 71.2, 71.3; H 4.4, 4.22; N 5.7, 5.8. Calculated for $C_{15}H_{11}NO_3$, %: C 71.2; H 4.4; N 5.5.

5H-1,2-Dihydro-3-ethyl-2,5-dioxochromeno[2,3-b]pyridine (VIc). A 4-g (0.0186 mole) quantity of the azide I and 60 ml of benzene were boiled for 1 hr, 2.7 g (0.0194 mole) of the enamine IIIc added, and the mixture kept overnight. The precipitate was isolated and stirred with 20 ml of 10% HCl for 4 hr at ~ 20° C, then for 30 min at ~ 100° C. The solid was filtered off to give 0.96 g (21.5%) of VIc, mp 239-240° C (from alcohol). Found, %: C 69.7, 69.9; H 4.8, 4.6. Calculated for $C_{14}H_{11}NO_3$, %: C 69.7; H 4.6.

LITERATURE CITED

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