Acyl Iodides in Organic Synthesis: XIII.* Reaction of Acyl Iodides with Nitrogen-Containing Heteroaromatic Compounds

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Abstract—Reactions of acetyl iodide with pyridine at room temperature and with quinoline both at $20-25^{\circ}$ C and on cooling to -50° C involve dehydrohalogenation of acetyl iodide with formation of ketene and pyridinium or quinolinium iodides. The reaction of acetyl iodide with pyridine at -5 to -50° C led to the formation of *N*-acetylpyridinium iodide. Benzoyl iodide reacted with both pyridine and quinoline at both -50° C and at $20-25^{\circ}$ C to form stable *N*-benzoylpyridinium and *N*-benzoylquinolinium iodides. The reaction of pyrrole with acetyl iodide under analogous conditions was accompanied by polymerization.

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Published data on reactions of acyl iodides RCOI (R = Me, Ph, etc.) with nitrogen-containing heterocyclic compounds are very few in number. The synthesis of 2-iodo- and 2,4-diiodopyridines by exchange reaction of the corresponding chloro- and bromo-substituted pyridines with acetyl iodide (generated in situ from acetyl chloride and sodium iodide) was reported. The reaction involved intermediate formation of 1-acetyl-2-chloropyridinium iodide [2]. Likewise, acetyl iodide reacted with 2-chloroquinoline to produce 2-iodoquinoline [2]. Attempts to replace in such a way the chlorine atoms in 2,6-dichloropyridine by iodine were unsuccessful, which was attributed to steric hindrances to the formation of intermediate 1-acetyl-2,6dichloropyridinium iodide [2]. The above scanty data cannot represent the reactivity of acyl iodides toward nitrogen-containing heteroaromatic compounds.

In continuation of our systematic studies on acyl iodides as reagents and synthons in organic and organometallic synthesis [2], in the present work we examined reactions of acetyl and benzoyl iodides (RCOI; R = Me, Ph) with pyridine (I), quinoline (II), and pyrrole (III). The reactions were carried out using equimolar amounts of the reactants both at room (20– 25°C) and reduced temperature (down to –50°C).

It is known that acetyl chloride reacts with tertiary amines along two pathways. The first of these leads to the formation of quaternary ammonium salts, and the second is dehydrochlorination of MeCOCl with formation of ketene [3]. A number of attempts to obtain products of the reaction of acetyl chloride with pyridine were unsuccessful [4, 5]. *N*-Acetylpyridinium chloride was synthesized by direct reaction of acetyl chloride with pyridine in toluene, and the product was used as analytical reagent for the determination of alcohols and phenols [6]. By contrast, *N*-benzoylpyridinium chloride was readily obtained by reaction of pyridine (I) with benzoyl chloride and used as reagent for the synthesis of benzoic anhydride as early as in the end of the XIXth century [3].

We found that the reaction of acetyl iodide with pyridine (I) at 20°C was accompanied by considerable evolution of heat (the temperature rose from 20–24 to 125° C). By analogy with acetyl chloride, the process occurred as dehydrohalogenation of acetyl iodide with formation of ketene and pyridine hydroiodide (IV) (Scheme 1), the latter being isolated as a solid insol-



^{*} For communication XII, see [1].

uble in organic solvents. Ketene was identified as methyl acetate.

The IR spectrum of hydroiodide IV lacked absorption band typical of C=O stretching vibrations, and absorption bands due to vibrations of the pyridine ring were displaced toward higher frequencies (1640–1480 cm⁻¹ against 1590–1430 cm⁻¹ in the IR spectrum of initial pyridine).

We succeeded in synthesizing previously unknown *N*-acetylpyridinium iodide (**V**) by reaction of acetyl iodide with pyridine (**I**) at -10 to -5° C under solvent-free conditions or in hexane at -50° C; the yields of **V** were 89 and 84%, respectively (Scheme 2).



N-Acetylpyridinium iodide (**V**) was isolated as a yellow crystalline substance which was insoluble in most organic solvents. Compound **V** at room temperature slowly decomposed into ketene and pyridine hydroiodide (**IV**). Iodide **V** characteristically displayed in the IR spectrum an absorption band at 1700 cm⁻¹ due to stretching vibrations of the carbonyl group. *N*-Acetylpyridinium iodide (**V**) vigorously reacted with alcohols (methanol and ethanol) to give pyridine, methyl or ethyl acetate, and HI (Scheme 3).



Iodide V readily reacted with dimethyl sulfoxide. The products were pyridine, acetic acid, and thioacetaldehyde (Scheme 4). This process may be regarded as a version of Pummerer rearrangement [7]. Intermediate methyl iodomethyl sulfide **B** loses HI, yielding thiirane [8, 9], and the latter undergoes isomerization to thioacetaldehyde [9].

Elimination of hydrogen iodide from benzoyl iodide is improbable; therefore, it reacted with pyridine (I) both at -10 to -5° C and at room temperature (20–





25°C) to give stable *N*-benzoylpyridinium iodide (VI) (Scheme 5). The reaction of pyridine with benzoyl chloride follows a similar pattern [3].



We failed to obtain *N*-acetylquinolinium iodide by reaction of acetyl iodide with quinoline (II). The latter is less basic than pyridine, and in all cases (both at room and at reduced temperature) the reaction of compound II with acetyl iodide involved elimination of HI with formation of ketene and quinoline hydroiodide (VII) (Scheme 6), a yellow amorphous hygroscopic substance insoluble in organic solvents. The reaction at room temperature was accompanied by heat evolution but was not so exothermic as with pyridine (the mixture warmed up to 50–55°C). In the IR spectrum of hydroiodide VII we observed no carbonyl absorption band in the region of 1700 cm⁻¹, but absorption bands corresponding to stretching vibrations of the quinoline ring changed their position relative to those typical of initial quinoline (1620, 1580, 1540, and 1470 cm⁻¹



against 1600, 1590, 1570, and 1490 cm^{-1} in the spectrum of **II**).

As might be expected, benzoyl iodide reacted with quinoline both at room and reduced temperature to give *N*-benzoylquinolinium iodide (**VIII**) (Scheme 7).



The reaction of pyrrole **III** with acetyl iodide both at 20–25°C and at –10 to –5°C in the absence of solvent resulted in polymerization of the heterocyclic substrate (Scheme 8), as in its reactions with other acidic reagents [10]. The resulting polymers were black powder-like substances with an approximate composition of $[C_4H_5NI]_n$ (**IX**). We presumed that these reactions involved hydroiodination of pyrrole, followed by polymerization of the hydroiodide thus formed.



Benzoyl iodide reacted with pyrrole very vigorously both at room temperature and on cooling to -10 to -5° C; the reaction mixtures spontaneously warmed up to 70–115°C. In all cases, the products were black powder-like polymers which were insoluble in water and organic solvents. Their elemental composition was estimated at C₉₋₁₁H₈₋₁₀NI_{1-1.5}, which corresponds to polymerization of initially formed N-benzoylpyrrolium iodide $C_4H_4N^+HCOC_6H_5I^-$. This process is likely to be accompanied by iodination of pyrrole, and the iodination products also undergo polymerization. The contribution of the iodination process is larger in the reaction carried out at room temperature. The elemental composition of the polymer obtained from pyrrole and benzoyl iodide at -10°C almost coincided with that of *N*-benzoylpyrrole hydroiodide, $C_4H_4N^+HCOC_6H_5I^-$.

EXPERIMENTAL

The IR spectra were recorded from thin films on a UR-20 spectrometer. The ¹H and ¹³C NMR spectra were measured on a Bruker DPX-400 spectrometer (400 MHz for ¹H) from solutions in CDCl₃ using tetramethylsilane or hexamethyldisiloxane as internal reference. Chromatographic analysis was performed on an HP-5890 instrument equipped with a thermal conductivity detector and an Ultra-2 column, 2 m×4 mm; injector temperature 250°C, oven temperature programming from 70 to 280°C; carrier gas helium.

Initial acyl iodides were prepared by reaction of the corresponding acyl chlorides with anhydrous sodium iodide according to the procedure described in [11].

Reaction of acetyl iodide with pyridine. a. Pyridine, 7.9 g (0.1 mol), was added dropwise at room temperature (22–24°C) to 17.0 g (0.1 mol) of acetyl iodide. The mixture spontaneously warmed up to 125°C, and evolution of ketene (a greenish gas) was observed; the latter was trapped with methanol. The resulting methyl acetate was identified by GLC using an authentic sample. When the reaction was complete, the crystals were filtered off, washed with chloroform, and evacuated under a residual pressure of 2-5 mm to remove traces of the solvent. We isolated 16.0 g (78%) of pyridine hydroiodide (IV). IR spectrum, v, cm^{-1} : 3080-3050 (C-H); 1640, 1600, 1520, 1470 (pyridine ring); 1220, 1150, 990, 730, 670 (δCH). Found, %: C 27.57; H 2.81; I 64.27; N 6.46. C₅H₆IN. Calculated, %: C 28.98; H 2.89; I 61.36; N 6.76.

b. Pyridine, 7.9 g (0.1 mol), was added to 17.0 g (0.1 mol) of acetyl iodide cooled to -10 to -5° C (using a dry ice–acetone bath). The mixture spontaneously warmed up to 5–10°C. The solid product was washed with chloroform and evacuated at 20–30 mm to remove traces of the solvent. We isolated 19.2 g of *N*-acetylpyridinium iodide (**V**) as a yellowish amorphous solid with mp 170–180°C. IR spectrum, v, cm⁻¹: 1700 (C=O); 1610, 1590, 1520, 1470 (pyridine ring); 1140, 1010, 730, 670 (δ CH). Found, %: C 31.54; H 2.78; I 54.22; N 5.92. C₇H₈INO. Calculated, %: C 33.73; H 3.21; I 51.00; N 5.62.

c. A solution of 8.5 g (0.05 mol) of acetyl iodide in 10 ml of hexane was cooled to -60 to -50° C, and 3.9 g (0.05 mol) of pyridine was added. Removal of the solvent from the reaction mixture gave 10.5 g (84%) of *N*-acetyl-pyridinium iodide (**V**).

Reaction of *N*-acetylpyridinium iodide (V) with dimethyl sulfoxide. *N*-Acetylpyridinium iodide (V),

7.0 g (0.03 mol) was mixed with 2.2 g (0.03 mol) of dimethyl sulfoxide, and the mixture spontaneously warmed up to 65°C. Distillation under atmospheric pressure gave volatile thioacetaldehyde, bp 34–36°C; published data [12]: bp 36.9°C. IR spectrum: v 1000 cm⁻¹ (C=S). ¹H NMR spectrum, δ , ppm: 1.96–1.98 d (3H, CH₃), 8.5–8.9 (1H, CH=S). ¹³C NMR spectrum, δ_C , ppm: 16.5–16.9 (CH₃), 149.5 (CH=S). The residue obtained after separation of thioacetaldehyde contained pyridine and acetic acid which were identified by GLC using authentic samples.

Reaction of acetyl iodide with quinoline. *a*. Quinoline, 3.23 g (0.025 mol), was added dropwise at room temperature to 4.25 g (0.025 mol) of acetyl iodide. The mixture spontaneously warmed up to 50°C, and a dark red crystalline solid separated. The precipitate was washed with chloroform and evacuated at 20–30 mm without heating to remove residual chloroform. We isolated 5.1 g (80%) of quinoline hydroiodide (VII) as a dark yellow amorphous solid insoluble in organic solvents. IR spectrum, v, cm⁻¹: 1620, 1580, 1540, 1470 (quinoline ring); 1200, 1110, 790, 730 (δ CH). Found, %: H 2.62; I 49.73; N 4.26. C₉H₈IN. Calculated, %: H 3.11; I 49.39; N 5.44.

b. The same amounts of the reactants were mixed at -10° C. Yield of **VII** 5.3 g (83%).

Reaction of acetyl iodide with pyrrole. *a*. Acetyl iodide, 6.8 g (0.04 mol), was added dropwise at room temperature to 2.68 g (0.04 mol) of pyrrole, and the mixture spontaneously warmed up from 24 to 51°C. The product was a black powder insoluble in water and organic solvents. Found, %: C 22.86; H 3.10; I 66.30; N 6.74. C_4H_5IN . Calculated, %: C 24.74; H 2.57; I 65.46; N 7.21.

b. Acetyl iodide, 6.8 g (0.04 mol), was added dropwise to 2.68 g (0.04 mol) of pyrrole cooled to -10° C, and the mixture warmed up to 10°C. The resulting dark red polymeric substance did not melt and was insoluble in hexane, diethyl ether, and chloroform. Found, %: C 23.70; H 2.76; I 66.73. C₄N₆IN. Calculated, %: C 24.74; H 2.57; I 65.46.

Reaction of benzoyl iodide with pyridine. Benzoyl iodide, 23.2 g (0.1 mol), was added dropwise to 7.91 g (0.1 mol) of pyridine cooled to -10° C. The mixture warmed up to 4°C, and the resulting solid was washed with chloroform and evacuated to remove residual solvent. We isolated 26.5 g (85%) of *N*-benzoyl-pyridinium iodide (**VI**) as an amorphous solid which decomposed on heating and was insoluble in organic solvents. IR spectrum, v, cm⁻¹: 1750 (C=O); 1600,

1590, 1510, 1470, 1430 (aromatic rings); 1220, 1100, 1000, 900, 700, 670 (δCH). Found, %: C 45.77; H 3.11; I 41.28; N 4.56. C₁₂H₁₀INO. Calculated, %: C 46.30; H 3.22; I 40.84; N 4.50.

Reaction of benzoyl iodide with quinoline. Quinoline, 3.87 g (0.03 mol), was added dropwise to 6.96 g (0.03 mol) of benzoyl iodide cooled to -10° C. The temperature of the reaction mixture did not change. The resulting solid was washed with chloroform and evacuated at 20–30 mm without heating. We isolated 8.8 g (81%) of *N*-benzoylquinolinium iodide (**VIII**) as an amorphous substance with mp 200°C, which was insoluble in organic solvents. IR spectrum, v, cm⁻¹: 1710 (C=O); 1620, 1580, 1540, 1440, 1400 (aromatic rings); 1200, 1160, 1020, 1000, 980, 800, 690 (δ CH). Found, %: C 52.29; H 3.52; I 39.28; N 4.16. C₁₆H₁₂INO. Calculated, %: C 53.18; H 3.32; I 35.18; N 3.88.

Reaction of benzoyl iodide with pyrrole. *a*. Benzoyl iodide, 4.15 g (0.018 mol), was added dropwise at room temperature to 1.20 g (0.018 mol) of pyrrole, and the mixture warmed up from 20 to 70°C. The resulting polymeric solid was washed with chloroform and evacuated to remove residual solvent. Found, %: C 43.16; H 2.80, I 47.10; N 5.08. C₁₁H₁₀INO. Calculated, %: C 44.12; H 3.34; I 42.47; N 4.68.

b. Benzoyl iodide, 5.8 g (0.025 mol), was added to 1.68 g (0.025 mol) of pyrrole cooled to -10° C, and the mixture warmed up to 115°C. The precipitate was dissolved in chloroform and the product was precipitated with diethyl ether. The black powder-like solid was evacuated to remove traces of diethyl ether. We isolated 4.4 g (60%) of a polymer with an approximate composition of C₁₁H₁₀INO. Found, %: C 43.70; H 3.10; I 43.49; N 5.10. C₁₁H₁₀INO. Calculated, %: C 44.12; H 3.34; I 42.47; N 4.68.

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