

Acyl Iodides in Organic Synthesis: I. Reactions with Alcohols

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Abstract—Reaction of acyl iodides $RC(O)I$ ($R = Me, Ph$) with alcohols $R'OH$ ($R' = Me, Et, i\text{-}Pr, t\text{-}Bu, CH_2=CHCH_2, HC\equiv CCH_2$) provides in the corresponding organyl iodides $R'I$. Unlike that 2-chloroethanol and phenol ($R' = CH_2CH_2Cl, Ph$) react with $RC(O)I$ in the same way as with acyl chlorides yielding esters RCO_2R' . This reaction path occurs partially also with methanol and ethanol.

In 1958 Voronkov and Khudobin [1, 2] demonstrated that trialkylsilylanes easily cleave the bonds C–O–C, C–O–Si, and Si–O–Si. Basing on this fact 17 years later Voronkov and Dubinskaya were the first to introduce Me_3SiI into organic synthesis [3] as they reported at two international conferences [4, 5]. Therewith Me_3SiI was shown to readily produce the rupture of C–O–C bonds in acyclic and cyclic ethers. These studies aroused wide interest, and soon several reviews were published concerning the application of trimethylsilylating reagent [6, 7].

We attempted to develop alternative or equivalent to the trimethylsilylating reagent deoxygenating and iodinating agents that would provide new opportunities in organic and organoelemental synthesis. As such we selected acyl iodides $RCOI$, in particular, their simplest representatives ($R = Me, Ph$). These are easily obtained by treating the corresponding acyl chlorides with sodium iodide [8]. It should be noted therewith that acyl iodides are poorly studied compounds, and even in the book [9] dedicated specially to acyl halides there are only few citations regarding the acyl iodides. Starting the studies in this field we carried out reactions of acyl iodides with aliphatic alcohols $R'OH$ [$R' = Me_nCH_{3-n}$, $n = 0$ (**I**), 1 (**II**), 2 (**III**), 3 (**IV**); $CH_2=CHCH_2$ (**V**); $HC\equiv CCH_2$ (**VI**); $ClCH_2CH_2$ (**VII**)], and phenol **VIII**. The trimethylsilylating reagent reacts with alcohols as a iodinating agent, and this reaction was proposed for synthesis of organyl iodides [10]. Acyl chlorides $RCOCl$ were long ago established to afford with alcohols the corresponding esters $RCOOR'$ [9, 11] [Scheme (1)].



In contrast the acyl iodides under study reacted with aliphatic alcohols similarly to trimethylsilylating reagent [Scheme (2)].



Similar to reaction with Me_3SiI the alkyl iodides formation is a general process for primary (**I**, **II**), secondary (**III**), and tertiary (**IV**) alcohols, and also for unsaturated alcohol both with a double (compound **V**) and a triple (compound **VI**) bond. The reaction of $RCOI$ with these alcohols at equimolar ratio and 60–100°C is completed within 1.5–2 h. The yield of alkyl iodides does not change at excess $RCOI$. No liberation of hydrogen iodide occurred in this process as indicated the absence of products of HI addition to the double bond of the allyl alcohol.

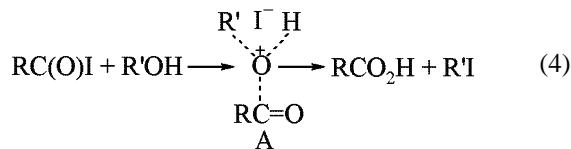
Unlike alcohols **I–VI** 2-chloroethanol (**VII**) and phenol (**VIII**) with $RCOI$ yield the corresponding esters and not organyl iodides [Scheme (3)].



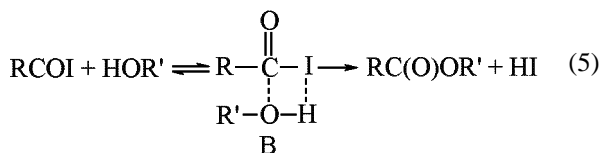
Reaction (3) partially occurred alongside reaction (2) also with methanol and ethanol. As a result alkyl iodides $R'I$ ($R' = Me, Et$) and esters RCO_2R' formed in 1:1 weight ratio. With excess $RC(O)I$ the yield of $R'I$ increased and that of RCO_2R' respectively decreased.

Reaction (3) occurred apparently due to the relatively high acidity of the hydroxy group of 2-chloroethanol (**VII**) and phenol **VIII** and to some extent of methanol (**I**) and ethanol (**II**). It is seen from the acidity constants pK_a of the alcohols **I–IV** under study which amount to 15.1, 15.9, 18.0, and over 19.0 respectively. Therewith the pK_a values for 2-chloroethanol and phenol are respectively 11.2 and 9.9. Thus the acidity of the alcohol switches the mechanism of its reaction with acyl iodides. For instance, the reaction of acyl iodides with the alcohols of low acidity **I–IV** results in substitution of the hydroxy group with the iodine atom. The process

apparently occurs as with Me_3SiI through an intermediate formation of an acylated oxonium ion A followed by its nucleophilic transformation along S_N2 mechanism where iodide anion plays the role of a nucleophile [Scheme (4)].



The esters arise probably through a four-centered intermediate B; the formation of the latter with 2-chloroethanol (VII) and phenol (VIII) and also partially with alcohols I and II is facilitated by the higher polarity of their O-H bonds [Scheme (5)].



EXPERIMENTAL

The initial acetyl iodide and benzoyl iodide were obtained by the previously described procedure [8].

The chromatographic analysis was carried out on LKhM-8M instrument, detector katharometer, carrier gas helium, column 2000×4 mm (Chromaton N-AW), operation in a programmed mode.

Acetyl iodide reaction with methanol. At mixing 10.6 g of RC(O)I with 2.5 g of MeOH the reaction mixture heated to 40°C . The mixture was stirred for 1.5 h at room temperature. By GLC with standards were identified therein methyl iodide (yield 49%) and methyl acetate (yield 51%). By distillation at atmospheric pressure we isolated 1.56 g (yield 43%) of acetic acid, bp 118°C , n_D^{20} 1.3725 (bp 118°C , n_D^{20} 1.3720 [12]).

Similarly reaction of 10.6 g of MeC(O)I with 1.3 g of MeOH afforded methyl iodide in 64% yield and methyl acetate in 36% yield. The distillation furnished 1.63 g (yield 45%) of acetic acid.

Acetyl iodide reaction with ethanol. A mixture of 10.6 g of MeC(O)I and 2.87 g of anhydrous EtOH was maintained at 70°C for 1.5 h. In the reaction mixture by GLC with standards was detected ethyl

iodide (yield 47%) and ethyl acetate (yield 52%). The distillation of the reaction mixture at 760 mm Hg afforded 1.54 g (yield 42%) of acetic acid.

Similarly reaction of 10.6 g of MeC(O)I with 1.45 g of EtOH afforded ethyl iodide in 52% yield and ethyl acetate in 43% yield. The distillation furnished 1.52 g (yield 42%) of acetic acid.

Benzoyl iodide reaction with ethanol. A mixture of 14.5 g of PhC(O)I and 2.9 g of anhydrous EtOH was maintained at $60\text{--}70^\circ\text{C}$ for 2 h. The distillation of the reaction mixture furnished 2.2 g (20%) of ethyl iodide, bp $72\text{--}73^\circ\text{C}$, n_D^{20} 1.5111 (bp 72°C , n_D^{20} 1.5137 [12]). Sublimation of the residue gave 1.63 g (22%) of benzoic acid, mp 122°C (mp 122°C [12]).

Acetyl iodide reaction with 2-propanol. A mixture of 10.6 g of MeC(O)I and 3.75 g of 2-propanol was maintained at $80\text{--}90^\circ\text{C}$ for 1.5 h. The distillation of the reaction mixture provided 1.6 g (16%) of 2-propyl iodide, bp $89\text{--}90^\circ\text{C}$ (bp 89.5°C [12]). Found, %: C 20.78; H 4.73. $\text{C}_3\text{H}_7\text{I}$. Calculated, %: C 21.20; H 4.15. Besides 2.8 g (78%) of acetic acid was isolated.

Under similar conditions the reaction of 10.6 g of MeC(O)I and 1.9 g of 2-propanol yielded 2.4 g (24%) of 2-propyl iodide and 2.75 g (76%) of acetic acid.

Acetyl iodide reaction with *tert*-butanol. A mixture of 10.6 g of MeC(O)I and 4.6 g of *t*- BuOH was kept for 1 h at $60\text{--}70^\circ\text{C}$; yield of *tert*-butyl iodide identified by GLC with a standard amounted to 90%. The distillation furnished 2.7 g (75%) of acetic acid.

Acetyl iodide reaction with allyl alcohol. A mixture of 10.6 g of MeC(O)I and 3.6 g of allyl alcohol was kept for 1 h at $80\text{--}90^\circ\text{C}$. The distillation of the reaction mixture afforded 6.25 g (62%) of allyl iodide, bp $100\text{--}103^\circ\text{C}$ (bp 103°C [12]). Found, %: C 24.7; H 4.31; I 55.0. $\text{C}_3\text{H}_5\text{I}$. Calculated, %: C 21.42; H 2.98; I 75.55. Besides 2.1 g (58%) of acetic acid was isolated.

Benzoyl iodide reaction with propargyl alcohol. A mixture of 14.5 g of PhC(O)I and 3.5 g of propargyl alcohol was maintained at $90\text{--}100^\circ\text{C}$ for 1 h. The distillation of the reaction mixture afforded 4.98 g (50%) of propargyl iodide, bp $110\text{--}115^\circ\text{C}$ (bp 115°C [12]). Sublimation of the crystalline residue yielded 2.1 g (28%) of benzoic acid.

Acetyl iodide reaction with 2-chloroethanol. To 10.6 g of MeC(O)I was added 5 g of 2-chloroethanol. The mixture self-heated to $40\text{--}50^\circ\text{C}$. Then the mix-

ture was heated to 100°C and kept at this temperature for 1.5 h. The distillation of the reaction mixture furnished 5.9 g (80%) of 2-chloroethyl acetate, bp 135–140°C (bp 145°C [12]). Found Cl, %: 30.66. C₄H₇ClO₂. Calculated Cl, %: 28.98.

Acetyl iodide reaction with phenol. At mixing 10.6 g of MeC(O)I with 5.9 g of PhOH the reaction mixture self-heated. On cooling it was subjected to vacuum distillation to isolate 3.5 g (50%) of phenyl acetate, bp 85–92°C (10 mm Hg) (bp 195.3°C [12]). Found, %: C 70.85; H 5.98. C₈H₈O₂. Calculated, %: C 70.58; H 5.88.

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