

Dedicated to Full Member of the Russian Academy of Sciences
B.A. Trofimov on the 65th Anniversary of His Birth

Acyl Iodides in Organic Synthesis: IV.* Reaction of Acetyl Iodide with Carboxylic Acids

M. G. Voronkov, L. I. Belousova, A. A. Trukhina, and N. N. Vlasova

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences,
ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: voronkov@irioch.irk.ru

Received May 6, 2003

Abstract—In contrast to acyl chlorides, reactions of acetyl iodide with monocarboxylic acids follow the exchange pattern to give the corresponding acyl iodides and acetic acid. The reaction attracts interest from the preparative viewpoint as a simple and convenient route to acyl iodides. Acetyl iodide reacts with phthalic acid, yielding acetic acid and phthalic anhydride, while the reaction of acetyl iodide with oxalic acid leads to formation of acetic acid, carbon(II) oxide, and molecular iodine.

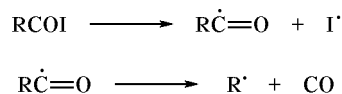
It was found previously that trialkyliodosilanes readily cleave C–O–C, C–O–Si, and Si–O–Si moieties in the absence of a catalyst [4–6]. In 1975, the possibility of using trimethyliodosilane in organic synthesis was demonstrated for the first time [5–9]. We have recently started a search for organic reagents which can be regarded as synthetic equivalents of trimethyliodosilane or alternative to it. Acyl iodides RCOI turned out to be excellent iodinating, deoxygenating, and acylating agents capable of reacting according to both homolytic and heterolytic patterns and often yielding unexpected products [1–3, 10].

As compared to other acyl halides RCOX (X = F, Cl, Br), acyl iodides remain poorly studied, presumably because of their instability. For example, only a few publications on acyl iodides were cited in the monograph [11] dealing with acyl halides.

Unlike readily accessible acyl chlorides, some reactions of which with aprotic compounds require severe conditions and/or the presence of a catalyst (usually Lewis acids), acyl iodides exhibit a high reactivity. This is explained by strong polarization of the C–I bond which readily dissociates according to both hetero- and homolytic mechanisms. The energy of dissociation of the C–I bond in acetyl iodide is 46.0 kcal/mol, i.e., it is considerably lower than the energies of dissociation of the C–X bonds in acetyl

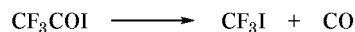
halides MeCOX, where X = F, Cl, Br: 110.0, 76.7, and 62.0 kcal/mol, respectively [12]. Therefore, acyl iodides readily dissociate with formation of radicals (Scheme 1).

Scheme 1.



In particular, the energy of formation of acetyl radical was estimated at 5.8 ± 0.4 kcal/mol [13]. It is interesting that homolytic (thermal) decomposition of trifluoroacetyl iodide [14] yields carbon(II) oxide and trifluoroiodomethane (Scheme 2).

Scheme 2.

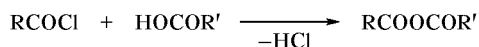


The above data suggest wide prospects in using acyl iodides in organic and organometallic synthesis [10]. We previously studied reactions of acyl iodides with alcohols [1, 2] and acyclic and cyclic ethers [3]. In continuation of these studies, in the present work we examined reactions of acetyl iodide with mono- and dibasic saturated, unsaturated, and aromatic acids, namely trifluoroacetic, trichloroacetic, butyric, isobutyric, acrylic, benzoic, oxalic, and phthalic.

* For preceding communications, see [1–3].

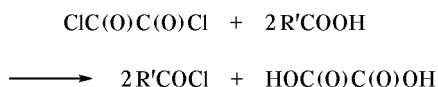
Aliphatic acyl chlorides react with carboxylic acids with liberation of hydrogen chloride both in the absence and in the presence of catalysts; these reactions usually lead to formation of the corresponding anhydrides [15] (Scheme 3).

Scheme 3.



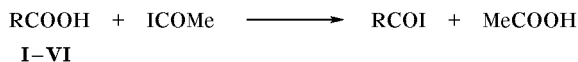
Exchange reaction between aliphatic acyl chlorides and carboxylic acids is an extremely rare case. In particular, such reaction is typical of oxalyl chloride [15] (Scheme 4).

Scheme 4.



We have found no published data on reactions of acyl iodides with carboxylic acids. Using acetyl iodide as an example, we were the first to reveal that, unlike acyl chlorides, acyl iodides react with monocarboxylic acids (trifluoroacetic, trichloroacetic, butyric, isobutyric, acrylic, and benzoic) following exclusively the exchange pattern (Scheme 5).

Scheme 5.

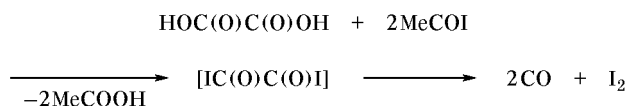


I, R = Pr; II, R = *i*-Pr; III, R = CH₂=CH; IV, R = Ph;
V, R = CF₃; VI, R = CCl₃.

These reactions occur without a solvent in the absence of an HI acceptor. In all cases, except for trihaloacetic acids, the process is accompanied by heat evolution which is especially strong in the reaction with acrylic acid. The reactions of acetyl iodide with alkanolic acids I and II and acrylic acid (III) are almost irreversible, for the initial acetyl iodide is more reactive than the resulting higher acyl iodides. The reaction of acetyl iodide with benzoic acid is reversible, so that a mixture of the initial reactants, acetic acid, and benzoyl iodide is obtained. The reactions with trifluoroacetic and trichloroacetic acids are also reversible. In the latter cases, the equilibrium can be displaced toward the direct reaction by removal from the reaction mixture of the product with a lower boiling point, trifluoroacetyl iodide or acetic acid, respectively.

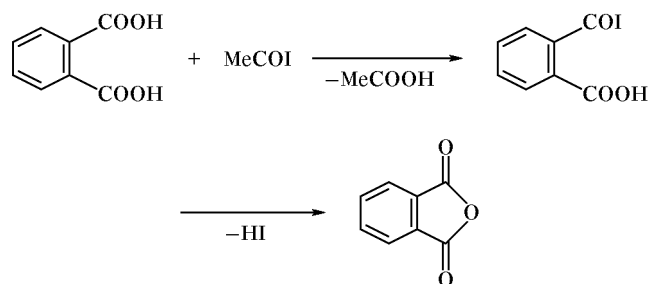
Oxalic acid reacted with acetyl iodide to give acetic acid, carbon(II) oxide, and molecular iodine, indicating the occurrence of exchange process. A probable intermediate, oxalyl iodide, is extremely unstable. It rapidly decomposes according to Scheme 6.

Scheme 6.



Phthalic acid reacts with acetyl iodide in a different way. The products are phthalic anhydride, acetic acid, and hydrogen iodide. This means that the exchange process involves only one carboxylic group. Initially formed *o*-iodoformylbenzoic acid undergoes intramolecular dehydroiodination, yielding phthalic anhydride (Scheme 7).

Scheme 7.



Comparison of the dissociation constants of the examined acids (see table) shows that weak acids with pK_a values within the range from 4 to 5 react with acetyl iodide most readily. Stronger acids, such as trifluoro- and trichloroacetic, react with acetyl iodide at a lower rate. This may be due to considerable electron-acceptor effect of the CX₃ group (X = Cl, F), which increases the acidity and reduces the nucleophilicity of the C=O group. Correspondingly, $\nu(\text{C}=\text{O})$ values in the IR spectra of acids RCOOH where R = Me, CCl₃, CF₃ are 1760, 1780, and 1800 cm⁻¹, respectively. This series indicates increase in the C=O bond order and reduction of the electrophilicity of the carbonyl carbon atom. Presumably, a large difference between pK_1 and pK_2 of phthalic acid (2.95 and 5.41, respectively) is responsible for its specific reaction with acetyl iodide. Insofar as the rates of the reaction of the latter with two carboxylic groups of phthalic acid are different, intramolecular dehydroiodination of labile intermediate monoiodide is faster than formation of the diiodide.

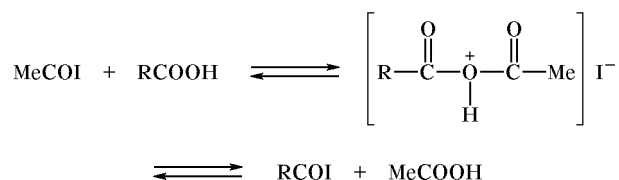
Yields and physical constants of acyl iodides obtained by reaction of carboxylic acids RCOOH with acetyl iodide and pK_a values of the initial acids

R	Yield, %	Reaction time, h	bp °C (<i>p</i> , mm)	n_D^{20}	pK_a (RCOOH)
Pr	79	5	42–43 (11)	–	4.81 [16]
<i>i</i> -Pr	89	5	42–45 (20)	1.3720	4.86 [17]
CH ₂ =CH ^a	86	3	135–140	1.4200	4.26
Ph	78	5	115–118 (15)	1.637	4.18 [16]
CF ₃	9	8	23	–	0.23 [14]
CCl ₃	86	8	55–60 (2–3)	1.4470	0.70 [18]

^a Found I, %: 69.98. C₃H₃IO. Calculated I, %: 69.78.

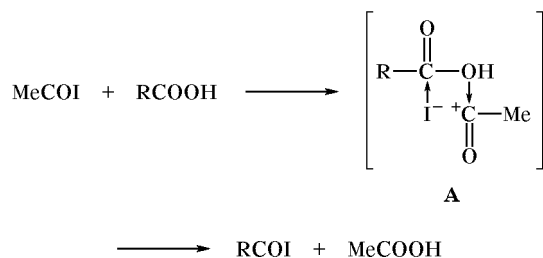
We previously showed that reactions of acyl iodides with acidic alcohols ($pK_a \leq 11$) occur with liberation of HI and that alcohols with $pK_a \geq 18$ give rise to the corresponding iodides RI [1]. By analogy with weakly acidic alcohols, we presume that the reaction of acetyl iodide with carboxylic acids involves intermediate formation of acyloxonium iodide whose subsequent transformation follows S_N2 pattern, as shown in Scheme 8.

Scheme 8.



Alternatively, four-membered activated complex A can be formed as intermediate (Scheme 9).

Scheme 9.



The yields of acyl iodides prepared by reactions of monocarboxylic acids with acetyl iodide and their physical constants (boiling points and refractive indices) are listed in table. The physical constants were consistent with published data; the products were

also identified by GLC using authentic samples. Acryloyl iodide was previously unknown.

The reaction of acetyl iodide, as well of its analogs, with carboxylic acids may be recommended as a simple and convenient preparative route to acyl iodides. The procedure is advantageous, for it requires no preliminary conversion of carboxylic acids into acyl chlorides and subsequent treatment of the latter with sodium iodide.

EXPERIMENTAL

Initial acetyl iodide was prepared by the known procedure, i.e., by reaction of acetyl chloride with anhydrous sodium iodide [19]. Chromatographic analysis was performed on an LKhM-8M instrument equipped with a thermal conductivity detector; carrier gas helium; 2-m × 4-mm column; temperature programming mode.

General procedure for the synthesis of acyl iodides. An equimolar mixture of the corresponding monocarboxylic acid and acetyl iodide was heated at the boiling point until the reaction was complete (according to GLC). The resulting acetic acid and acyl iodide were separated by fractional distillation. High-boiling acyl iodides were distilled under reduced pressure. A typical example is given below.

Isobutyryl iodide. A mixture of 8.5 g (0.05 mol) of acetyl iodide and 4.4 g (0.05 mol) of isobutyric acid was heated for 5 h at the boiling point. Distillation of the mixture gave 2.5 g (83%) of acetic acid, bp 117–118°C [20] (identified by GLC), and 8.8 g (89%) of isobutyryl iodide, bp 42–45°C (20 mm) [17].

Reaction of acetyl iodide with oxalic acid. A mixture of 15 g (0.08 mol) of acetyl iodide and 4 g (0.04 mol) of oxalic acid was heated at 60–65°C until carbon(II) oxide no longer evolved. Distillation gave 4.9 g (92%) of acetic acid (GLC).

Reaction of acetyl iodide with phthalic acid.

A mixture of 17 g (0.1 mol) of acetyl iodide and 8.2 g (0.05 mol) of phthalic acid was heated for 5 h at 60–65°C. Distillation gave 2.7 g (92%) of acetic acid and 7.0 g (96%) of phthalic anhydride, mp 130–131°C [20].

REFERENCES

1. Voronkov, M.G., Trukhina, A.A., and Vlasova, N.N., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 1576.
2. Voronkov, M.G. and Shagun, V.A., *Russ. J. Org. Chem.*, 2003, vol. 39, p. 331.
3. Voronkov, M.G., Trukhina, A.A., and Vlasova, N.N., *Russ. J. Org. Chem.*, 2002, vol. 38, p. 1579.
4. Voronkov, M.G. and Khudobin, A.Yu., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1956, p. 713.
5. Voronkov, M.G., Pavlov, S.F., Dubinskaya, E.I., and Puzanova, V.E., Abstracts of Papers, *IV Mezhdunarodnyi simpozium po khimii kremniorganicheskikh soedinenii* (IVth Int. Symp. on the Chemistry of Organosilicon Compounds), Moscow, 1975, vol. 1, p. 184.
6. Voronkov, M.G., Puzanova, V.E., Pavlov, S.F., and Dubinskaya, E.I., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1975, p. 390.
7. Voronkov, M.G., Pavlov, S.F., and Dubinskaya, E.I., *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1975, p. 657.
8. Voronkov, M.G., Dubinskaya, E.I., and Pavlov, S.F., Abstracts of Papers, *VIIth Int. Conf. of Organometallic Chemistry*, Venice, 1975, p. 155.
9. Voronkov, M.G. and Dubinskaya, E.I., *J. Organomet. Chem.*, 1991, vol. 410, p. 1.
10. Voronkov, M.G., Vlasova, N.N., and Trukhina, A.A., *Sovremennyyi organicheskii sintez* (Contemporary Organic Synthesis), Moscow–Ufa: Khimiya–Reaktiv, 2003, p. 9.
11. *The Chemistry of Acyl Halides*, Patai, S., Ed., London: Intersci., 1972, p. 177.
12. Edward, H., O'Neal, H.E., and Benson, S.W., *J. Chem. Phys.*, 1962, vol. 37, p. 540.
13. O'Neal, H.E. and Benson, S.W., *J. Chem. Phys.*, 1962, vol. 37, p. 540.
14. Haszeldine, R.N., *J. Chem. Soc.*, 1951, p. 584.
15. Sonntag, N.O., *Chem. Rev.*, 1953, vol. 52, p. 237.
16. Schmidt, A.H., Russ, M., and Grosse, D., *Synthesis*, 1981, no. 3, p. 216.
17. Hoffman, H.M. and Haase, K., *Synthesis*, 1981, no. 9, p. 715.
18. Gal, I., *C. R. Acad. Sci.*, 1873, p. 1021.
19. Theobald, D.W. and Smith, J.C., *Chem. Ind.*, 1958, p. 1007.
20. *Spravochnik khimika* (Chemist's Handbook), Nikol'skii, B.P., Ed., Moscow: Khimiya, 1963, vol. 2.