

Acyl Iodides in Organic Synthesis: XI.* Unusual N–C Bond Cleavage in Tertiary Amines

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Abstract—Acyl iodides reacted with excess primary and secondary amines in a way similar to acyl chlorides, yielding the corresponding carboxylic acid amide and initial amine hydroiodide. Reactions of tertiary amines with acyl iodides were accompanied by cleavage of the N–C bond with formation of the corresponding *N,N*-di(hydrocarbyl)carboxamide and alkyl iodide. In the presence of excess tertiary amine the latter was converted into quaternary tetra(hydrocarbyl)ammonium iodide.

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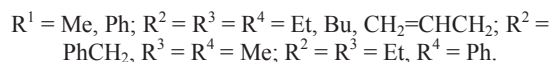
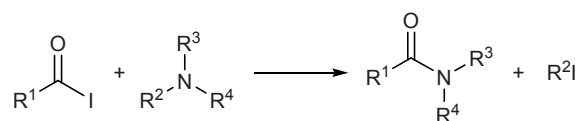
It is known [2] that acyl chlorides react with primary and secondary amines in the presence of hydrogen chloride acceptor (inorganic or organic base or excess initial amine) to give the corresponding carboxamides. While studying analogous reactions of acetyl and benzoyl iodides with primary and secondary amines, such as aniline, *N*-ethylaniline, etc., we have found that they follow the same pattern: the products are the corresponding amides, but the reactions are considerably more facile.

Acyl chlorides are known [2] to react with tertiary amines to produce either the corresponding quaternary ammonium chlorides or ketenes (as a result of dehydrochlorination of the initial acyl chloride). Nevertheless, as noted in [3], prolonged heating of benzoyl chloride with *N,N*-dimethyl- or *N,N*-diethylaniline at 190–200°C resulted in cleavage of one N–C_{Alk} bond with formation of *N*-alkyl-*N*-phenylbenzamide. Likewise, elimination of one methyl group from the initial amine was observed in the reactions of benzoyl chloride with *N,N*-dimethylnaphthalen-1- and -2-amines under severe conditions (170–190°C).

We have found that acyl iodides react with tertiary aliphatic and arylaliphatic amines even at room temperature and that the reaction is accompanied by cleavage of the N–C bond with formation of the corresponding *N,N*-di(hydrocarbyl)carboxamide and alkyl

iodide (Scheme 1). Cleavage of the N–C bond in tertiary amines by the action of acyl iodides is strongly facilitated if one of the substituents on the nitrogen atom is a benzyl, allyl, or alkyl group. No N–C_{arom} bond cleavage was observed under the given conditions. In the presence of excess tertiary amine, alkyl or allyl iodide formed in the first step reacts further with the other amine molecule to give the corresponding quaternary tetra(hydrocarbyl)ammonium iodide.

Scheme 1.



In all cases, benzoyl iodide was more reactive than acetyl iodide toward tertiary amines. For example, we succeeded in obtaining *N,N*-dibutyl- and *N,N*-diallylbenzamides in 85 and 62% yield, respectively. In the reactions with acetyl iodide, the yields of *N,N*-di(hydrocarbyl)acetamides were much lower (16–37%), presumably as a result of concurrent dehydroiodination of acetyl iodide with formation of ketene.

The selectivity and ease of N–C bond cleavage in the reactions of benzoyl iodide with tertiary amines prompted us to optimize the conditions for reactions of tertiary amines with acyl iodides having no hydrogen

* For communication X, see [1].

atom in the α -position, i.e., those incapable of undergoing dehydroiodination and generating ketene. In some cases, specifically when elimination of hydrogen iodide and its binding by appropriate HI acceptor are undesirable, such a procedure for the synthesis of *N,N*-disubstituted carboxylic acid amides attracts interest from both preparative and analytical viewpoints.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400.13 MHz for ^1H and 100.58 MHz for ^{13}C using CDCl_3 as solvent and tetramethylsilane or cyclohexane as internal reference. The reaction mixtures were analyzed, and the purity of products was checked, by GLC on a Tsvet-500 chromatograph equipped with a thermal conductivity detector and a 3-m \times 4-mm glass column packed with 10% of PSM-1000 on Inerton-Super (0.125–0.150 mm); carrier gas helium.

Initial acetyl and benzoyl iodides were prepared by reaction of the corresponding acyl chloride with anhydrous sodium iodide [4].

***N*-Phenylacetamide.** Acetyl iodide, 2.04 g (12 mmol), was added dropwise under stirring to a solution of 2.2 g (24 mmol) of aniline in 10 ml of benzene, and the mixture was stirred for 3 h at room temperature. The precipitate of phenylammonium iodide, 2.09 g (79%), was filtered off, and the product was isolated by removal of the solvent from the filtrate. Yield 0.96 g (59%), mp 113–115°C; published data [5]: mp 114°C. ^1H NMR spectrum, δ , ppm: 2.14 s (3H, CH_3), 7.70 m (1H, NH), 7.05–7.48 m (5H, Ph). ^{13}C NMR spectrum, δ_{C} , ppm: 24.38 (CH_3), 119.9–138.09 (Ph), 168.17 (C=O). Mass spectrum, m/z (I_{rel} , %): 135 (20) [M] $^+$, 93 (100), 77 (5), 66 (25), 51 (10), 43 (45).

***N*-Phenylbenzamide.** Benzoyl iodide, 2.8 g (12 mmol), was added dropwise under stirring to a solution of 2.2 g (24 mmol) of aniline in 10 ml of benzene, and the mixture was stirred for 8 h at 78°C. The precipitate was filtered off, and the solvent was distilled off from the filtrate. Yield 0.9 g (39%), mp 160–164°C; published data [6]: mp 161°C. ^1H NMR spectrum, δ , ppm: 8.94 s (1H, NH), 7.10–7.85 m (10H, Ph). ^{13}C NMR spectrum, δ_{C} , ppm: 119.6–137.5 (C_{arom}), 164.9 (C=O). Found, %: C 72.07; H 5.73; N 7.40. $\text{C}_{13}\text{H}_{11}\text{NO}$. Calculated, %: C 72.21; H 5.60; N 7.10.

***N*-Ethyl-*N*-phenylacetamide.** *a.* Acetyl iodide, 2.04 g (12 mmol), was added dropwise under stirring to a solution of 2.9 g (24 mmol) of *N*-ethylaniline in

10 ml of benzene, and the mixture was stirred for 3 h at room temperature. The precipitate of *N*-ethylaniline hydroiodide, 2.7 g (91%), was filtered off, and the solvent was distilled off from the filtrate. Yield 0.54 g, mp 49–50°C; published data [7]: mp 50°C. Mass spectrum, m/z (I_{rel} , %): 163 (15) [M] $^+$, 148 (3), 135 (10), 106 (75), 77 (15), 51 (10).

b. Acetyl iodide, 4.43 g (26 mmol), was added dropwise under stirring to 7.78 g (52 mmol) of *N,N*-diethylaniline, and the mixture was stirred for 3 h at room temperature. The precipitate of *N,N*-diethylaniline hydroiodide was filtered off, and 4.72 g of unreacted *N,N*-diethylaniline (conversion 39%) was distilled off from the filtrate to isolate the target amide. Yield 0.38 g (23% on the reacted *N,N*-diethylaniline), mp 50–52°C. Mass spectrum, m/z (I_{rel} , %): 162 (5) [M] $^+$, 149 (35), 134 (90), 106 (65), 77 (40), 51 (25).

***N*-Ethyl-*N*-phenylbenzamide.** *a.* Benzoyl iodide, 2.78 g (12 mmol), was added dropwise under stirring to a solution of 2.9 g (24 mmol) of *N*-ethylaniline in 10 ml of benzene, and the mixture was stirred for 8 h at 78°C. The precipitate of *N*-ethylaniline hydroiodide was filtered off, and the solvent was distilled off from the filtrate. Yield 2.49 g (92%), mp 56–58°C; published data [7]: mp 58°C. ^1H NMR spectrum, δ , ppm: 1.12 t (3H, CH_3), 3.25 q (2H, CH_2), 6.98–7.87 m (10H, Ph). ^{13}C NMR spectrum, δ_{C} , ppm: 12.49 (CH_3), 44.86 (CH_2), 127.1–142.9 (C_{arom}), 169.28 (C=O).

b. Benzoyl iodide, 6.62 g (28.5 mmol), was added dropwise under stirring to 8.51 g (57 mmol) of *N,N*-diethylaniline, and the mixture was stirred for 21 h at 78°C. Distillation gave 3.1 g of unreacted *N,N*-diethylaniline (conversion 64%). Yield of *N*-ethyl-*N*-phenylbenzamide 1.22 g (30%, calculated on the reacted *N,N*-diethylaniline), mp 57–59°C. Mass spectrum, m/z (I_{rel} , %): 225 (10) [M] $^+$, 207 (5), 197 (3), 147 (2), 132 (2), 120 (3), 105 (75), 77 (55), 51 (22), 36 (18).

***N,N*-Diethylacetamide.** Acetyl iodide, 15.63 g (92 mmol), was added dropwise under stirring to 28.34 g (280 mmol) of triethylamine, and the mixture was stirred for 5 h at room temperature. The precipitate of triethylamine hydroiodide, 6 g (25%), was filtered off, and the filtrate was subjected to vacuum distillation to isolate 1.57 g (15%) of *N,N*-diethylacetamide, bp 57°C (7 mm), $n_{\text{D}}^{20} = 1.4353$; published data [8]: bp 185–186°C, $n_{\text{D}}^{20} = 1.4374$. Mass spectrum, m/z (I_{rel} , %): 115 (72) [M] $^+$, 100 (10), 86 (5), 72 (26), 58 (100), 44 (27), 30 (9).

***N,N*-Diethylbenzamide.** Benzoyl iodide, 2.51 g (11 mmol), was added dropwise under stirring to 2.32 g (23 mmol) of triethylamine, and the mixture

was stirred for 5 h at room temperature. The precipitate was filtered off, and the filtrate was subjected to vacuum distillation. Yield 1.15 g (59%), bp 89°C (1 mm), $n_D^{20} = 1.4370$; published data [9]: bp 280–282°C, $n_D^{20} = 1.4374$. Mass spectrum, m/z (I_{rel} , %): 177 (31) $[M]^+$, 162 (2), 148 (5), 105 (100), 77 (50), 44 (27), 51 (20).

***N,N*-Dibutylacetamide.** Acetyl iodide, 1.7 g (10 mmol), was added dropwise under stirring to a solution of 1.85 g (10 mmol) of tributylamine in 5 ml of methylene chloride, and the mixture was stirred for 10 h at 40°C. Distillation gave 0.38 g (21%) of butyl iodide, bp 130°C, and 0.35 g (16%) of *N,N*-dibutylacetamide, bp 110°C (8 mm); published data [10]: bp 110–112°C (8 mm). ^1H NMR spectrum, δ , ppm: 0.84–0.89 t (6H, CH_3), 1.25–1.40 m (4H, CH_2), 1.99 s (3H, MeCO), 2.72–3.46 m (4H, CH_2N). ^{13}C NMR spectrum, δ_C , ppm: 13.62 (CH_3), 20.27 (C_2H_5), 30.93 (CH_2CH_2), 45.33 (CH_2N), 48.46 (CH_2N), 21.39 (MeCO), 169.85 (C=O).

***N,N*-Dibutylbenzamide.** Benzoyl iodide, 2.32 g (10 mmol), was added dropwise under stirring to a solution of 1.85 g (10 mmol) of tributylamine in 5 ml of methylene chloride, and the mixture was stirred for 10 h at 40°C. Distillation gave 0.46 g (25%) of butyl iodide, bp 130°C (identified by GLC), and 1.97 g (85%) of *N,N*-dibutylbenzamide, bp 95°C (2 mm); published data [11]: bp 122–125°C (7 mm). ^1H NMR spectrum, δ , ppm: 0.92–0.94 t (6H, CH_3); 1.36–1.44 m (4H, CH_2); 3.16–3.46 m (4H, CH_2N); 7.27 m, 7.33 m, 7.49 m, 8.12 m (5H, H_{arom}). Mass spectrum, m/z (I_{rel} , %): 233 (2) $[M]^+$, 218 (2), 204 (5), 190 (3), 176 (5), 160 (2), 105 (60), 77 (85), 41 (100).

***N,N*-Diallylacetamide.** Acetyl iodide, 2.07 g (12 mmol), was added dropwise under stirring to 1.67 g (12 mmol) of triallylamine, and the mixture was stirred for 3 h at 40°C. Distillation gave 0.48 g (30%) of allyl iodide, bp 103°C (identified by the ^1H and ^{13}C NMR spectra), and 0.52 g (37%) of *N,N*-diallylacetamide, bp 61°C (2 mm); published data [12]: bp 98–100°C (13 mm). ^1H NMR spectrum, δ , ppm: 2.03 s (CH_3), 3.81 d (2H, CH_2N), 3.92 d (2H, CH_2N), 5.10–5.19 m (4H, $\text{CH}_2=$), 5.68–5.85 m (2H, $\text{CH}=\text{}$). ^{13}C NMR spectrum, δ_C , ppm: 20.89 (CH_3), 47.30 (CH_2N), 49.54 (CH_2N), 129.09 ($\text{CH}_2=$), 123.85 ($\text{CH}_2=$), 170.09 (C=O).

***N,N*-Diallylbenzamide.** Benzoyl iodide, 2.32 g (10 mmol), was added dropwise under stirring to a solution of 1.37 g (10 mmol) of triallylamine in 5 ml of methylene chloride, and the mixture was stirred for 3.5 h at 40°C. Distillation gave 0.15 g (10%) of allyl

iodide (identified by GLC) and 1.17 g (62%) of *N,N*-diallylbenzamide, bp 130°C (1 mm); published data [13]: bp 101°C (0.25 mm). ^1H NMR spectrum, δ , ppm: 3.82 d (2H, CH_2N), 4.07 d (2H, CH_2N), 5.20 m (4H, $\text{CH}_2=$), 5.75 m (2H, $\text{CH}=\text{}$), 7.25–7.30 m (5H, Ph). ^{13}C NMR spectrum, δ_C , ppm: 46.82 and 50.56 (CH_2N); 123.81 ($\text{CH}_2=$); 136.05 ($\text{CH}=\text{}$); 126.39, 128.17, 129.43 (C_{arom}); 171.58 (C=O).

Reaction of acetyl iodide with *N,N*-dimethylphenylmethanamine. Acetyl iodide, 1.7 g (10 mmol), was added dropwise under stirring to a solution of 1.35 g (10 mmol) of *N,N*-dimethylphenylmethanamine in 5 ml of methylene chloride, and the mixture was stirred for 3.5 h at 40°C. The solvent was distilled off, and the solid residue was analyzed by GLC and GC–MS to identify 0.645 g (48%) of unreacted *N,N*-dimethylphenylmethanamine {mass spectrum, m/z (I_{rel} , %): 135 $[M]^+$, 91 (91), 77 (10), 65 (21), 58 (100), 42 (20)}, 0.654 g (30%) of benzyl iodide {mass spectrum, m/z (I_{rel} , %): 218 $[M]^+$, 127 (6), 91 (100), 65 (16)}, and 0.104 g (12%) of *N,N*-dimethylacetamide {mass spectrum, m/z (I_{rel} , %): 87 $[M]^+$, 72 (25), 44 (96), 43 (44), 15 (5)}.

Reaction of benzoyl iodide with *N,N*-dimethylphenylmethanamine. Benzoyl iodide, 2.32 g (10 mmol), was added dropwise under stirring to a solution of 1.35 g (10 mmol) of *N,N*-dimethylphenylmethanamine in 5 ml of methylene chloride, and the mixture was stirred for 3 h at 40°C. The solvent was distilled off, and the residue was analyzed by GLC and GC–MS to identify 0.18 g (13%) of initial *N,N*-dimethylphenylmethanamine {mass spectrum, m/z (I_{rel} , %): 135 $[M]^+$, 91 (100), 77 (10), 58 (100), 42 (20)}, 0.43 g (20%) of benzyl iodide {mass spectrum, m/z (I_{rel} , %): 218 $[M]^+$, 127 (6), 91 (100), 65 (16)}, and 0.77 g (51.4%) of *N,N*-dimethylbenzamide {mass spectrum, m/z (I_{rel} , %): 225 $[M]^+$, 148 (73), 105 (100), 77 (60), 51 (15)}.

The elemental compositions of all isolated products were consistent with the calculated data.

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