433. *Reactions in Carboxylic Acid–Thionyl Chloride Systems.*

By W. GERRARD and A. M. THRUSH.

The rate of formation of acid chlorides from acids and thionyl chloride depends on the nature of the acid.

In the presence of pyridine, another reaction occurs concurrently with some acids, the acid chloride reacting with unchanged acid to give the anhydride.

RELATIVE merits of different procedures for the preparation of acyl chlorides (R·COCl) have been discussed in several papers (*e.g.*, McMaster and Ahmann, *J. Amer. Chem. Soc.*, 1928, **50**, 145; Clark and Bell, *Trans. Roy. Canad. Soc.*, 1933, **27**, 97; Bauer, *Oil and Soap*, 1946, **23**, 1), but little information has been given from which the probable sequence of reactions can be deduced. From a mixture of acetic acid (1 mol.) and thionyl chloride (1 mol.) at 20°, sulphur dioxide and hydrogen chloride were evolved from the beginning, and reaction was nearly complete after 1 hr.; *iso*butyric acid required 5 and benzoic acid 50 hr. for close approach to the end-point. After 5 days diphenylacetic acid had reacted to the extent of 38%; trichloroacetic acid did not react during 9 days, and even after 12 hr.' heating at 85°, the acid was recovered.

If the mechanism entails the formation of an intermediate chlorosulphinate, R·CO·O·SOCl, which readily decomposes to acyl chloride and sulphur dioxide, the former has but transitory existence.

Carré and Libermann (*Compt. rend.*, 1934, **199**, 1422) observed that pyridine facilitates formation of trichloroacetyl chloride. We now show that when trichloroacetic acid (1 mol.) and pyridine (1 mol.) are mixed in ether, the pyridinium salt is precipitated. During the addition of thionyl chloride (1 mol.) to this, acyl chloride and probably the salt $C_5H_5N,SO(OH)Cl$ are readily formed. With certain other acids, however, another reaction occurs concurrently; *e.g.*, with acetic, *iso*butyric, *iso*valeric, heptanoic, phenylacetic, diphenylacetic, and benzoic acids the anhydride is formed by the time 0·5 mol. of thionyl chloride has been added (cf. Gerrard and Thrush, *J.*, 1952, 741) :

$$\tfrac{1}{2}R\cdot CO_2^{-}\ {}^{+}HNC_5H_5 + \tfrac{1}{2}SOCl_2 \longrightarrow \tfrac{1}{2}R\cdot COCl + \tfrac{1}{2}C_5H_5N,SO(OH)Cl$$
$$\tfrac{1}{2}R\cdot CO_2^{-}\ {}^{+}HNC_5H_5 + \tfrac{1}{2}R\cdot COCl \longrightarrow \tfrac{1}{2}(R\cdot CO)_2O + \tfrac{1}{2}C_5H_5N,HCl$$

The second reaction has been shown to be rapid at −78°, whereas formation of the acyl chloride–pyridine complex (cf. *Org. Synth.*, 1946, **26**, 1) is very slow, and when formed, the substance does not react very quickly with an acid to give the anhydride. In the systems now described we do not believe that the acid chloride–pyridine complex is a necessary intermediate.

Trichloroacetate anion does not react with trichloroacetyl chloride, but it does so with acetyl chloride; and the acetate anion reacts with trichloroacetyl chloride. However, diphenylacetyl chloride reacts with the diphenylacetate anion to give the anhydride.

If the structure $R\cdot CO_2SO\cdot$ can be formed at all it should be during the addition of *n*-butyl chlorosulphinate (1 mol.) to the acid (1 mol.) and pyridine (1 mol.) in ether at −10°. The products, however, were in accordance with the formation of the acyl chloride by a mechanism not entailing that structure.

EXPERIMENTAL

Carboxylic Acids and Thionyl Chloride in the Absence of Pyridine.—The acid (1 mol.) and thionyl chloride (1 mol.) were mixed, and the effluent gases trapped by sodium hydroxide in a U-tube attached to the mechanically shaken apparatus kept at 20°. Thionyl chloride alone (blank) gave no significant amount of effluent. Amounts of sulphur dioxide and chloride ion present in the U-tube after different time intervals were determined. The following results are selected from the whole range.

Acetic acid			*iso*Butyric acid.			Benzoic acid		
Time, min.	SO_2, mol.	Cl^-, equiv.	Time, min.	SO_2, mol.	Cl^-, equiv.	Time, hr.	SO_2, mol.	Cl^-, equiv.
3	0·26	0·51	22	0·27	0·43	1·3	0·04	0·08
11	0·56	0·91	73	0·54	0·75	5·9	0·28	0·41
51	0·76	1·12	199	0·71	0·88	30·0	0·76	0·83

Trichloroacetic acid (10·9 g.) and thionyl chloride (7·94 g.) after 9 days at 20° afforded but a trace of effluent. After being at 85° for 12 hr., the acid (10·3 g.), b. p. 95°/12 mm. (Found : Cl, 65·0. Calc. : Cl, 65·1%), and thionyl chloride (6·8 g.), b. p. 75—80°, were recovered.

When diphenylacetic acid (10·6 g.) and thionyl chloride (5·99 g.) were mixed at 20° the evolution of gas was slow; after 5 days the absorption tube contained SO_2, 0·21 mol., and Cl^-, 0·38 equiv. However, when the acid was heated at 85° for 4 hr. with more thionyl chloride (16 g.), diphenylacetyl chloride (10·6 g., 92%), m. p. 55—56° (Found : Cl, 15·4. Calc. for $C_{14}H_{11}OCl$: Cl, 15·4%), was obtained.

Monochloroacetic acid (18·9 g., 1 mol.) and thionyl chloride (23·8 g., 1 mol.) reacted very slowly at 20°; but after being at 90° for 6 hr. the mixture gave the acyl chloride (19·0 g., 86%), b. p. 106—107° (Found : Cl, 62·0. Calc. for $C_2H_2OCl_2$: Cl, 62·8%).

Carboxylic Acid–Thionyl Chloride–Pyridine System.—By the method previously described (*J.*, 1952, 741), dropwise addition of thionyl chloride (0·5 mol.) to a cooled ethereal solution of acid (1 mol.) and pyridine (1 mol.), phenylacetic anhydride (6·1 g., 96%), m. p. 72° (Found : equiv., 127·5. Calc. : equiv., 127·0), was obtained.

When pyridine (1 mol.) was added to a cooled ethereal solution of diphenylacetic acid (1 mol.) the white pyridine salt crystallised (Found : C_5H_5N, 27·1. Calc. : C_5H_5N, 27·1%). Addition of thionyl chloride (2·98 g., 0·5 mol.) to an ethereal suspension of the salt (14·55 g., 1 mol.) afforded diphenylacetic anhydride (9·7 g., 96%), m. p. 96—97° (Found : equiv., 202. Calc. : equiv., 203).

Trichloroacetic acid formed with pyridine a salt insoluble in ether (Found : C_5H_5N, 32·7;

Cl, 42·8. Calc.: C_5H_5N, 32·6; Cl, 43·9%). When thionyl chloride (11·8 g., 0·5 mol.) was added to a cooled suspension of this salt (48·5 g., 1 mol.), and the mixture kept for 12 hr., the ethereal filtrate afforded trichloroacetyl chloride (14·1 g., 0·39 mol.), b. p. 118° [Found: Cl (water-hydrolysable), 19·4. Calc. for C_2OCl_4: Cl (water-hydrolysable), 19·5%], and trichloroacetic acid (5·4 g.), m. p. 58° (Found: Cl, 65·3. Calc. for $C_2HO_2Cl_3$: Cl, 65·1%). Similar results were obtained from the reaction at −78°, and the separated solid was kept in a vacuum until constant in weight (sulphur dioxide having been removed) (33·4 g.) (Found: Cl^-, 0·525 mol., 11·1%; C_5H_5N, 0·94 mol., 44·1%. Calc. for an equimolecular mixture of C_5H_5N,HCl and $C_5H_5N,CCl_3{\cdot}CO_2H$: Cl^-, 9·9; C_5H_5N, 44·2%).

When thionyl chloride (29·7 g., 1 mol.) was added to an ethereal suspension of pyridinium trichloroacetate (60·2 g., 1 mol.) at −10° the solid contained Cl^-, C_5H_5N, and SO_2 in molar ratios 0·96, 0·95, and 0·64, whilst the filtrate afforded trichloroacetyl chloride (42·3 g., 93%), b. p. 117—118° [Found: Cl (water-hydrolysable), 19·5%].

Thionyl chloride (5·9 g., 0·5 mol.), added to an ethereal solution of benzoic acid (12·2 g., 1 mol.) and pyridine (7·9 g., 1 mol.) at −10°, immediately gave a precipitate (Cl^-, 0·96 equiv.; C_5H_5N, 0·96 mol.; SO_2, 0·39 mol.) whilst the filtrate afforded benzoic anhydride (11·0 g., 98%), m. p. 42° (Found: equiv., 113·0. Calc.: equiv., 113·0).

Reactions in which thionyl bromide was used instead of thionyl chloride gave similar results. Yields of anhydride obtained were: acetic, 94%; *n*-heptanoic, 95%; benzoic, 99%.

n-*Butyl Chlorosulphinate–Carboxylic Acid–Pyridine*.—The chlorosulphinate (15·65 g., 1 mol.) was used instead of thionyl chloride. Added to a well-shaken ethereal solution of acetic acid (6·0 g., 1 mol.) and pyridine (7·9 g., 1 mol.) at −10°, it immediately afforded a precipitate (Cl^-, 0·97 equiv.; C_5H_5N, 0·94 mol.; SO_2, 0·44 mol.), acetic anhydride (4·71 g., 0·46 mol.), b. p. 136—138°, $n_D^{18·5}$ 1·3930 (Found: equiv., 51·7. Calc.: equiv., 51·0), and di-*n*-butyl sulphite (9·7 g., 0·50 mol.), b. p. 109—110°/15 mm., n_D^{18} 1·4325. Similarly, the chlorosulphinate (20 g., 1 mol.), *n*-heptanoic acid (16·6 g.), and pyridine (10·1 g.) gave a precipitate (Cl^-, 0·97 equiv.; C_5H_5N, 0·97 mol.; SO_2, 0·3 mol.), di-*n*-butyl sulphite (12·9 g., 0·5 mol.), b. p. 104°/11 mm., n_D^{20} 1·4318 (Found: S, 16·3. Calc. for $C_8H_{18}O_3S$: S, 16·4%), and *n*-heptanoic anhydride (14·8 g., 0·48 mol.), b. p. 106—108°/0·2 mm., n_D^{20} 1·4330 (Found: equiv., 121·0. Calc.: equiv., 121·0). The chlorosulphinate (15·65 g., 1 mol.), benzoic acid (12·2 g.), and pyridine (7·9 g.) afforded a precipitate (Cl^-, 0·898 equiv.; C_5H_5N, 0·880 mol.; SO_2, 0·014 mol.), impure di-*n*-butyl sulphite (7·4 g.), b. p. 70—80°/0·05 mm. (Found: S, 14·7%), benzoic anhydride (7·9 g.), b. p. 135—140°/0·05 mm. (Found: equiv., 113·4. Calc.: equiv., 113·0), and a black residue (3·0 g.).

Acyl Chloride–Carboxylic Acid–Pyridine.—Addition of *n*-heptanoyl chloride (8·49 g., 1 mol.) to an ethereal solution of *n*-heptanoic acid (7·43 g., 1 mol.) and pyridine (4·52 g., 1 mol.) at −10° immediately afforded pyridine hydrochloride (6·3 g., 96%) (Found: Cl, 30·7; C_5H_5N, 68·0. Calc. for C_5H_5N,HCl: Cl, 30·7; C_5H_5N, 68·4%). The filtrate afforded *n*-heptanoic anhydride (13·4 g., 97%), b. p. 112—114°/0·3 mm., d_0^{15} 0·9240, n_D^{20} 1·4321 (Found: equiv., 120·8. Calc.: equiv., 121·0). This reaction was shown to be almost instantaneous at −78°. Addition of the acid to a cooled ethereal solution of the acid chloride and pyridine readily gave the anhydride in 95% yield. To form the complex, pyridine (7·9 g., 1 mol.) was added to an ethereal solution of *n*-heptanoyl chloride (14·86 g., 1 mol.). No immediate precipitation occurred, but the *n*-heptanoyl chloride–pyridine complex (11·4 g., 50% after 3 days) separated slowly (Found: Cl, 16·3; C_5H_5N, 34·1. Calc. for $C_{12}H_{18}ONCl$: Cl, 15·6; C_5H_5N, 34·7%). Addition of *n*-heptanoic acid (4·52 g., 1 mol.) to an ethereal suspension of this complex (7·92 g., 1 mol.) at −10° afforded, after 15 min., impure pyridine hydrochloride (3·77 g., 94%) (Found: Cl, 28·7; C_5H_5N, 60·9%) and *n*-heptanoic anhydride (7·1 g., 84%), b. p. 110—115°/0·5 mm., n_D^{20} 1·4326 (Found: equiv., 122·0. Calc.: equiv., 121·0). It was shown that trichloroacetyl chloride did not react with an ethereal suspension (or chloroform solution) of pyridinium trichloroacetate even on prolonged shaking at room temperature. However, acetyl chloride (3·93 g., 1 mol.) when shaken with an ethereal suspension of pyridinium trichloroacetate for 20 hr. afforded acetic trichloroacetic anhydride (1·5 g., 14·6%), b. p. 90—92°/14 mm., n_D^{15} 1·4580 (Found: equiv., 105; Cl, 52·0. Calc.: equiv., 103; Cl, 51·8%).

Trichloroacetyl chloride (9·1 g., 1 mol.) when added dropwise to an ethereal solution of acetic acid (3·0 g., 1 mol.) and pyridine (3·95 g., 1 mol.) at −10° afforded a precipitate (8·95 g.) of an equimolecular mixture of pyridinium trichloroacetate and pyridine hydrochloride (Found: Cl^-, 9·8; C_5H_5N, 43·7. Calc.: Cl^-, 9·9; C_5H_5N, 44·1%) and an inseparable mixture of trichloroacetyl chloride and acetic anhydride. Addition of trichloroacetyl chloride (4·55 g., 0·5 mol.) to the same quantities of acetic acid and pyridine afforded a precipitate (8·4 g.) with the same composition as before and acetic anhydride (2·5 g., 93%), b. p. 138°, n_D^{20} 1·3992 (Found: equiv., 52·0. Calc.: equiv., 51·0).

Dropwise addition of trichloroacetyl chloride (9·1 g., 1 mol.) to an ethereal solution of *n*-butyl alcohol (3·7 g., 1 mol.) and pyridine (3·95 g., 1 mol.) afforded an immediate precipitate of impure pyridine hydrochloride (5·79 g., 101%) (Found: Cl, 29·1%), and the filtrate afforded *n*-butyl trichloroacetate (9·8 g., 90%), b. p. 84°/10 mm., n_D^{20} 1·4530, d_4^{20} 1·276 (Found: Cl, 48·2. Calc. for $C_6H_9O_2Cl_3$: Cl, 48·5%). When pyridine (2·42 g., 1 mol.) was added to a solution of trichloroacetyl chloride (5·58 g., 1 mol.) in light petroleum no precipitate separated even on long standing, and after the unchanged reactants had been removed at 40°/20 mm. only a small residue (0·1 g.) remained.

Dropwise addition of diphenylacetyl chloride (4·1 g., 1 mol.) to an ethereal suspension of pyridinium diphenylacetate at −10° afforded pyridine hydrochloride (1·93 g., 93%) and diphenylacetic anhydride (7·15 g., 98%), m. p. 96—97° (Found: equiv., 202·0. Calc.: equiv., 203·0).

THE NORTHERN POLYTECHNIC, LONDON, N.7.

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