An Improved Acid Chloride Preparation via Phase Transfer Catalysis

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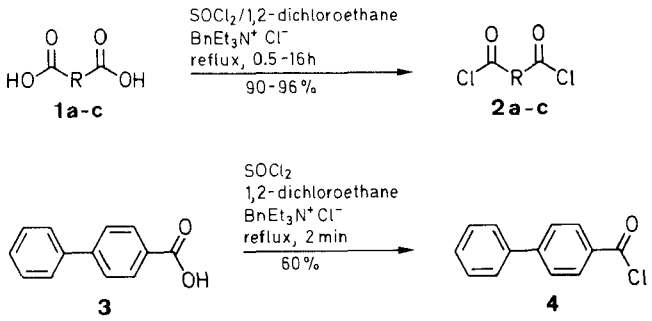
Phase transfer catalysis has been found to be effective for the rapid conversion of carboxylic acids in high yield to the corresponding acid chlorides. The procedure is well suited for acids that exhibit low solubilities in normal organic solvents.

One of the main thrusts of polymer science over the last five years has been toward high performance engineering thermoplastics, which are generally characterized by very high heat distortion temperatures and glass transition temperatures (Tg's). One route to these materials is via the syntesis of new rigid rod type monomers. While the polymers are generally difficult to work with due to their low solubility and high melting temperatures, the rigid rod monomers may be equally difficult to manipulate for the same reasons and pose unique synthetic problems. The lack of solubility of 4,4'-biphenyldicarboxylic acid (**1a**) during conversion to the diacid dichloride with thionyl chloride prompted the use of a phase transfer catalyst to overcome the low solubility. The solubility of **1a** is < 0.03 wt% in refluxing 1,2-dichloroethane and a standard acid chloride preparation yielded $< 5\%$ product and 95% recovered starting material after 48 hours at reflux. In the presence of catalytic quantities of benzyltriethylammonium chloride ($BnEt_3NCl$), the reaction was complete in 16–24 hours with a yield in excess of 90%. This remarkable rate increase was observed for each of the products listed in the Table. A significant rate increase was observed even in the case of 4-biphenylcarboxylic acid, which exhibited much higher solubility than the other acids.



1–2	R
a	4,4'-biphenyldiyl
b	*trans*-1,4-cyclohexanediyl
c	2,6-naphthalenediyl

It was envisioned that the use of a large organic quaternary ammonium ion to form a salt with the carboxylic acid would impart some organic solubility to the acid. Quaternary salt formation with carboxylic acids has been utilized during the extractive alkylation technique described by Brändström.[5] Yanagida[6] prepared acyl fluorides directly by reacting an organic acid, base and a fluoride source in the presence of a phase transfer catalyst.

Both Brändström and Holmberg[7] utilized neutralization of the preformed sodium carboxylate anion with a tertiary amine to form the quaternary carboxylate to achieve phase transfer catalyzed alkylations. Esterifications have also been achieved with powdered potassium hydroxide and Aliquat® 336,[8] again using the carboxylate salt.[9] However, no mention was made of the reaction of the quaternary salt and the protonated acid to form a quaternary ammonium carboxylate with loss of hydrogen halide. It is well known that quaternary salts decompose[10] at moderate temperatures to generate the free trialkyl amine, and either an olefin or an alkyl halide derived from one of the alkyl groups on the quaternary ammonium salt. The free amine could react with the protonated acid to form the proposed ammonium salt. However, attempts to isolate the ammonium carboxylate salt directly from a reaction of **1a** and benzyltriethylammonium chloride with no thionyl chloride led only to the isolation of the bis(2-chloroethyl) ester of the diacid, in 42% yield, presumably via alkylation by the solvent. Formation of this diester was in line with the phase transfer catalyzed alkylation of carboxylic acids as described by Brändström. Just refluxing benzyltriethylammonium chloride and the solvent for a number of hours returned it unchanged, indicating that a significant amount of decomposition of the phase transfer catalyst or alkyl exchange with the solvent was not taking place during reaction. Further evidence for a phase transfer catalyzed mechanism was derived from the reactions catalyzed by methyltriphenylphosphonium bromide or (carboxymethyl)trimethylammonium hydroxide inner salt (Betaine). These two phase transfer catalysts have much higher thermal stabilities than benzyltriethylammonium chloride and would be expected to yield even less trialkyl amine via thermal decomposition.

It has been found that the phase transfer catalyst could be present in truly catalytic amounts with no substantial increase in reaction rate or change in yield accompanying larger amounts of catalyst. In the conversion of **1b** to **2b** a tenfold increase in the catalyst concentration decreased the reaction time by only a factor of two, with essentially the same yield. This indicated the rate determining step was not involved with phase transfer, and the amount of proposed alkylammonium carboxylate salt present during the reaction may have been below the detection limits of these experiments.

Pure thionyl chloride or phosphorus pentachloride in xylene[11] were also found to work effectively for the preparation of the diacid dichloride, but for ease of workup, cost of reagents, and purity of product, the phase transfer catalyzed reaction with 1,2-dichloroethane and thionyl chloride was superior.

All reagents and solvents were of commercial quality from freshly opened containers. Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. IR spectra were obtained using a Nicolet 5SX FT-IR spectrophoto-

Table. Acid Chlorides Prepared

Product	Catalyst	Molar Ratio Substrate/ Catalyst	Reaction Time (h)	Yield[a] (%)	mp (°C)	Lit. mp (°C)	IR ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ, J (Hz)
2a	none	no catalyst	48	< 5	184	184[1]		
2a	$BnEt_3NCl$	684	24	91	184	184[1]	1778[b]	7.77 (d, 4H, J = 8.7), 8.23 (d, 4H, J = 8.7)
2a	$BnEt_3NCl$	245	16	90	184	184[1]		
2a	Ph_3CH_3PBr	684	16	94	184	184[1]		
2a	(Betaine)	126	17	96	184	184[1]		
2b	$BnEt_3NCl$	132	0.5	96	64–67	67[2]	1790[c]	1.58 (m, 4H), 2.30 (m, 4H), 2.74 (m, 2H)
2b	$BnEt_3NCl$	1176	1.0	93	64–67	67[2]	1790[c]	
2c	$BnEt_3NCl$	1054	12	94	188.5–189.5	187.5–189[3]	1745[c]	8.12 (d, 2H, J = 7.5), 8.26 (d, 2H, J = 7.5), 8.72 (s, 1H)
4	$BnEt_3NCl$	341	0.04	60	109–110	114–115[4]	1770[c]	7.45 (m, 3H), 7.60 (m, 2H), 7.68 (d, 2H, J = 8.6), 8.14 (d, 2H, J = 8.6)

[a] Isolated yield of purified diacid dichloride.
[b] IR in KBr.
[c] IR in $CDCl_3$.

meter. ^{1}H- and ^{13}C-NMR spectra were obtained using a Varian Gemini 300 MHz spectrometer. Mass spectra were taken using a Finnigan-Mat model 4600 spectrometer with DEI ionization.

4,4′-Biphenyldicarbonyl Dichloride 2a; Typical Procedure:
To a dry, three-neck, magnetically stirred, 2 L round-bottom flask, equipped with a gas bubbler is added 4,4′-biphenyldicarboxylic acid (200 g, 0.826 mol), 1,2-dichloroethane (1.512 L) and $BnEt_3NCl$ (0.275 g, 1.2 mmol). The slurry is brought to reflux and $SOCl_2$ (127 mL, 1.75 mol) is added all at once. Reflux is maintained for 16 h. The mixture is pressure filtered hot to remove a small amount of intractable solid, and allowed to crystallize. The mass is filtered, washed with Et_2O and dried to give white crystals; yield: 210.4 g (91%); mp 184–185°C; (Lit.[1] mp 184°C).

IR (KBr): ν = 863 (s), 876 (s), 1202 (s), 1778 cm^{-1} (COCl).

^{13}C-NMR ($CDCl_3$/TMS): δ = 127.9, 132.1, 133.3, 145.7, 167.8.

Bis(2-chloroethyl) 4,4′-Biphenyldicarboxylate:
To a dry 15 mL round-bottom flask is charged **1a** (0.5 g, 2.1 mmol), 1,2-dichloroethane (7 mL) and $BnEt_3NCl$ (0.38 g, 1.7 mmol). The suspension is refluxed for 16 h, filtered hot and concentrated to give a white solid; yield: 0.32 g (42%). The solid is chromatographed on a slurry packed silica gel column (1.3 cm × 20 cm; Merck 35–70 Mesh) with toluene as the eluent. The main component was located in the 2nd and 3rd 50 mL fractions. The white solid is recrystallized from hexane/THF (10:1) to give colorless needles; mp 101–102°C.

$C_{18}H_{16}Cl_2O_4$	calc.	C 58.89	H 4.36	Cl 19.30
(366.8)	found	58.70	4.37	20.00

MS (70 eV): m/z = 370 (M^+ + 4, 10), 368 (M^+ + 2, 64), 366 (M^+, 100).

IR ($CHCl_3$): ν = 1110 (m), 1200 (s), 1270 (s), 1710 cm^{-1} (s).

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.85 (t, 2H, J = 5.5 Hz, CH_2O), 4.61 (t, 2H, J = 5.5 Hz, CH_2Cl), 7.71 (d, 2H, J = 8.2 Hz), 8.17 (d, 2H, J = 8.2 Hz).

^{13}C-NMR ($CDCl_3$/TMS): δ = 41.8, 64.8, 127.8, 129.7, 130.9, 145.2, 166.5.

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