



Figure 3. Initial observed rate constants vs. volume fraction (ϕ) of chloroform for the acylation of phthalic anhydride by morpholine (●) and diethylamine (○) in mixed chloroform-cyclohexane solvent systems.

of $1.05 M^{-1}$ and $0.29 M^{-2}$, respectively. The stability constant for complexation between an aliphatic amine such as diethylamine with chloroform is likely to have a value of about $0.2 M^{-1}$ at 25° .⁵ In the presence of excess chloroform relative to the amine concentration, as in the present case, the activity of morpholine may be drastically lowered through complexation without compensatory solvation of the transition state. Thus, the reaction rate is reduced with increasing content of chloroform in the reaction medium. In the case of the reaction involving diethylamine, the comparatively weaker solvation of the amine reactant by chloroform may be adequately counterbalanced by solvation of the transition state involved. Thus, inhibition by chloroform is not observed.

Experimental Section

Reagents. Unless otherwise specified, all reagents were of reagent grade. Diethyl ether (ACS) was dried over LiAlH_4 and distilled. Chloroform (AR) was washed with distilled water five to six times, dried over CaCl_2 overnight, then distilled over phosphorus pentoxide, and used immediately. Cyclohexane (AR) was distilled over phosphorus pentoxide. Tetrahydrofuran (AR) was dried by LiAlH_4 and distilled. All purified solvents were stored over molecular sieve (Linde 4A). Morpholine was refluxed with KOH pellets for 1 hr, fractionally distilled, and then again fractionally distilled over sodium. Diethylamine was refluxed with KOH pellets for 1 hr and then distilled. The middle fractions were collected and stored over KOH pellets. Piperidine was fractionally distilled over KOH pellets under nitrogen. The amines were stored under nitrogen in closed containers in a refrigerator. Their purity was checked by titration with standard acid. Phthalic anhydride was recrystallized from a chloroform-cyclohexane mixture; mp $129\text{--}130^\circ$ (lit. mp 131.5°). *N,N*-Diethylphthalamic acid was prepared according to

Maxim;⁶ mp $151\text{--}152^\circ$ (lit. mp 153°). Glacial acetic acid was used without purification.

Kinetic Procedure. Rates and rate constants for the acylation reactions were calculated from changes in ultraviolet absorbance at a wavelength where phthalic anhydride was the main absorbing species. Measurements were made using Cary 14, Cary 16, and Durrum stop-flow spectrophotometers. In the cases when the reactions were first order or pseudo first order (in the presence of excess amine), rate constants were calculated from plots of $\log(A - A_\infty)$ against time. Initial rates were calculated from the slope of the absorbance against time plot at a point as close to zero time as possible. In these studies an accurate amount (0.01–0.1 ml) of a concentrated solution of the amine in the solvent to be studied was placed in a 1 cm absorption cell. Three milliliters of phthalic anhydride solution in the same solvent was injected into the cell through a hypodermic syringe. The instrument recorder was turned on after insertion of the needle through the cell compartment cover but before injection of the anhydride solution. For the studies of effects of acetic acid on the reaction, the proper amount of acetic acid was added to the amine before mixing with anhydride. The uv spectra of the products of the reaction, when different acids were used as catalysts, were identical. All kinetic studies were done at 25° .

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Registry No.—Phthalic anhydride, 85-44-9; diethylamine, 109-89-7; cyclohexane, 110-82-7; diethyl ether, 60-29-7; chloroform, 67-66-3; THF, 109-99-9; morpholine, 110-91-8; *N,N*-diethylphthalamide, 53336-79-1; succinic acid, 110-15-6; benzoic acid, 65-85-0; trifluoroacetic acid, 76-05-1; acetic acid, 64-19-7.

Supplementary Material Available. Fuller kinetic details will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105×148 mm, $24\times$ reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for \$5.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-75-378.

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Solvolysis Problems in Chlorinations in Sulfuric Acid

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Recently several papers have reported chlorinations in 50–96% sulfuric acid. Kollonitsch and coworkers used Cl_2 to chlorinate α -amino acids in 100% H_2SO_4 ¹ and 50% H_2SO_4 ,² amines in 100% H_2SO_4 ,³ and carboxylic acids in $\text{H}_2\text{SO}_4\text{--HF}$.³ Minisci and coworkers published a number of papers on chlorination of esters, amines, and 1-chloroalkanes using *N*-chloro- and *N*-bromoammonium ions in 85–96% H_2SO_4 .⁴ Our own group has studied Cl_2 and R_2NHCl^+ chlorinations of carboxylic acids in 85–96%

Table I
Half-Lives for Solvolyses^a of the Seven Isomeric Chlorooctanoic Acids in 84, 90, and 96% H₂SO₄ at 25°

Registry no.	Position of Cl	Half-life (hr) at		
		84% H ₂ SO ₄	90% H ₂ SO ₄	96% H ₂ SO ₄
53431-81-5	2	>10 ³	>10 ³	>10 ³
53431-82-6	3	>10 ³	>10 ³	>10 ³
53431-83-7	4		2 × 10 ²	4 × 10
53466-52-7	5	2 × 10 ²	11	1.5
53431-84-8	6	70	5.2	1.0
53431-85-9	7	50	5.5	0.9
1795-62-6	8	>10 ³	>10 ³	>10 ³

^a The inertness of the 2-Cl and 8-Cl acids was demonstrated by nmr monitoring. Using these as standards, disappearance rates were determined by periodic dilution of aliquots with ice, ether extraction of the acids, esterification with diazomethane, and gc of the methyl esters as described in ref 6 and 13.

H₂SO₄,⁵⁻⁸ ethers⁶⁻⁸ in 85-96% H₂SO₄, alcohols in 20-70% H₂SO₄,⁶⁻⁹ and alkanes in 84% H₂SO₄.¹⁰

A potential hazard in these chlorinations is that the chloro substituent will selectively solvolyze and the product ratios be altered. This paper describes some experiments on the solvolysis of chlorooctanoic acids which show that the solvolysis of chloro substituents is highly sensitive to the H₂SO₄ concentration and to the position of the secondary chloro substituent relative to the carboxyl function.

The rates of solvolysis increase from 84 to 96% H₂SO₄ (Table I). This acid catalysis can be rationalized in terms of acidic species (H₃O⁺, H₂SO₄) pulling off chloride ion. The value of $-d \log k/dH_{R'}$ is ~1.4 for the 5-, 6-, and 7-chlorooctanoic acids.¹¹

The solvolysis rates also increase with an increase in distance between chloro substituent and carboxyl group up to the 6-chloro (rates for 6-Cl and 7-Cl are equal). This is a result of the positive charge that develops on the carbon undergoing substitution. The carboxyl group inhibits the formation of this positive charge and protonation of the carboxyl¹² intensifies this effect.

We regret to state that these results invalidate the conclusion that chlorination of octanoic acid by Cl₂ in 96% H₂SO₄ gives selectivity for 4-Cl and 8-Cl products.¹³ The apparent selectivity was in fact the result of selective destruction of the 5-7 chloro products.

This same problem affects (to a lesser extent) other chlorination studies. Most of Minisci's chlorinations were conducted in 96% H₂SO₄. Selective solvolysis must have been significant in products derived from reactants such as methyl hexanoate and heptanoate so that the selectivity for $\omega - 1$ chlorination is greater than the 70-80% reported. In our own work, octanoic acid was reported to give 80% 7-chlorooctanoic acid in 84% H₂SO₄.⁶ At 84% H₂SO₄, the ratio of RCOOH₂⁺ to RCOOH is about 4 so that higher selectivity for $\omega - 1$ chlorination would be expected in 96% H₂SO₄ where protonation of octanoic acid is more complete. However, this was not found and the selectivity for $\omega - 1$ seemed to be much less. It is now clear that the selectivity was probably greater, but that this was obscured by selective solvolysis. The results of Kollonitsch were on such short chains¹⁻³ that selective solvolysis would be unlikely. However, extrapolation of Kollonitsch's conclusions and methods to longer chains would encounter selective solvolysis problems.

Registry No.—H₂SO₄, 7664-93-9.

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Improved Procedures for Ethynylcarbinol Hydration and Oxime Reduction to Amino Alcohols¹

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Because of a need for 3-amino-2-methyl-2-butanol (**1**) and 1-(1-aminoethyl)cyclohexanol (**2**) in other research, we considered several routes for their synthesis. Early syntheses of **1** involved catalytic reduction of the oxime of 3-hydroxy-3-methyl-2-butanone³ and of 2-methyl-3-nitro-2-butanol⁴ over Raney nickel, whereas **2** has been prepared in several steps starting from cyclohexanone cyanohydrin.⁵⁻⁷ As either the yields or the procedures involved in the earlier syntheses left much to be desired, we have developed improved procedures for **1** and **2**. The chemistry used should be readily adaptable to the preparation of other amino alcohols.

The starting materials were the readily available ethynylcarbinols, R₂C(OH)C≡CH, **3a** and **3b**, prepared by reaction of acetone and of cyclohexanone, respectively, with acetylene.⁸ Although reference to the hydration of acetylenes to ketones is frequently made,⁹ the best yield for the preparation of 1-acetylcyclohexanol by this method that we have located in the literature is 69% in a two-step reaction of ethynylcyclohexanol with mercuric oxide and sulfuric acid.¹⁰ We have obtained a 90% yield by a simplified one-step process. Similarly, 3-hydroxy-3-methyl-2-butanone was obtained from **3a** in 80% yield.

The ketones were then converted into the corresponding oximes which were hydrogenated over 5% rhodium-on-alumina¹¹ to yield the desired **1** and **2** in excellent overall yield. This facile high-yield reduction of hydroxy oximes over a rhodium catalyst is notable in view of our unsuccessful attempts to reduce the same oximes catalytically over platinum or palladium catalysts. In addition, reduction procedures involving sodium in liquid ammonia or LiAlH₄ in ether failed to yield the desired amino alcohols in more than small yield.

Monoacylation of **1** and **2** on nitrogen was effected in over 90% yields by carrying out the acylation with 1 equiv