the aminomethylated polystyrene resin (0.3 g, 3.46 mequiv of NH_2/g) suspended in dry THF was added a THF solution of L-leucine NCA (5.7 g, 36.3 mmol), and the solution was stirred at room temperature for 40 h. The resulting polymer beads were filtered and washed with THF and methanol. After drying in vacuo at 40 °C for 24 h, 4.20 g of polymer was obtained. Nitrogen analysis indicated an average degree of polymerization (n) of poly(L-leucine) corresponding to 33.

Preparation of α,β-Unsaturated Ketones. All α,β-unsaturated ketones were synthesized according to the literature.[13]

(*E*)-1,3-Diphenyl-2-propen-1-one: mp 57–58 °C (lit.[13a] mp 57–58 °C).

(*E*)-1-(4-Methoxyphenyl)-3-phenyl-2-propen-1-one: mp 99–102 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.70; H, 5.85.

(*E*)-3-(4-Nitrophenyl)-1-phenyl-2-propen-1-one: mp 163–165 °C (lit.[13b] mp 165 °C).

(*E*)-3-(2-Methoxyphenyl)-1-phenyl-2-propen-1-one: mp 59–61 °C (lit.[13c] mp 58–59 °C).

(*E*)-3-(2-Ethoxyphenyl)-1-phenyl-2-propen-1-one: oil. Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39 Found: C, 80.85; H, 6.30.

(*E*)-3-(4-Chlorophenyl)-1-phenyl-2-propen-1-one: mp 114–116 °C (lit.[13b] mp 115 °C).

(*E*)-3-(4-Methoxyphenyl)-1-phenyl-2-propen-1-one: mp 69–71 °C. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.60; H, 5.95.

(*E*)-1-(4-Chlorophenyl)-1-phenyl-2-propen-1-one: mp 94–95 °C. Anal. Calcd for $C_{15}H_{11}ClO$: C, 74.23; H, 4.57; Cl, 14.61. Found: C, 74.29; H, 4.60; Cl, 14.65.

Asymmetric Epoxidation of Benzalacetophenone. The following procedure is representative of these reactions. To a stirred solution of 1.0 g of benzalacetophenone (4.8 mmol) in toluene (12 mL) was added 3.98 g of PL2 (1.0 mequiv of poly(L-leucine). Then 4.4 mL of H_2O_2 (30 wt % solution in water) and 0.35 g of NaOH in water (2 mL) were added at 0 °C. The mixture was stirred at room temperature for 2 days. The reaction was monitored by TLC. The polymeric catalyst was filtered off and toluene layer was washed with water and dried over $MgSO_4$, and the solvent was evaporated. The residue was subjected to silica gel column chromatography using toluene as eluent to obtain a white solid (0.99 g, 92%): mp 64–65 °C; $[\alpha]^{25}_{577}$ −255° (*c* 2.15, CH_2Cl_2) [lit.[8b] mp 63–65 °C; lit.[8b] $[\alpha]^{20}_{578}$ −214° (*c* 1, CH_2Cl_2)]; TLC R_f = 0.3 in toluene. The enantiomeric excess was determined by using chiral-phase HPLC to give 99% ee. The ^1H NMR and IR spectra of (−)-(2*R*,3*S*)-epoxy-1,3-diphenyl-1-propanone were essentially identical with those reported in the literature.[8b]

Epoxidations of other olefins were performed in the same manner as described above.

(−)-2,3-Epoxy-3-(4-methoxyphenyl)-1-phenyl-1-propanone: mp 60–63 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.60; H, 5.53.

(−)-2,3-Epoxy-3-(4-nitrophenyl)-1-phenyl-1-propanone: mp 140–142 °C (lit.[8b] mp 139–141.5 °C). Anal. Calcd for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 66.93; H, 4.16; N, 5.18.

(−)-2,3-Epoxy-3-(2-methoxyphenyl)-1-phenyl-1-propanone: mp 90–91 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.62; H, 5.57.

(+)-2,3-Epoxy-3-(2-ethoxyphenyl)-1-phenyl-1-propanone: mp 92–93 °C. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01. Found: C, 76.14; H, 5.99.

(−)-3-(4-Chlorophenyl)-2,3-epoxy-1-phenyl-1-propanone: mp 69–70 °C (lit.[8b] mp 68 °C).

(−)-2,3-Epoxy-1-(4-methoxyphenyl)-3-phenyl-1-propanone: mp 60–62 °C. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.62; H, 5.53.

(−)-1-(4-Chlorophenyl)-2,3-epoxy-3-phenyl-1-propanone: mp 90–91 °C. Anal. Calcd for $C_{15}H_{11}ClO_2$: C, 69.64; H, 4.29; Cl, 13.70. Found: C, 69.67; H, 4.30; Cl, 13.73.

Supplementary Material Available: ^1H NMR spectra of α,β-unsaturated ketones and epoxy ketones (16 pages). Ordering information is given on any current masthead page.

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Hydrolysis of 4-Nitrophenyl Phenyl(trichloromethyl)phosphinate: Predominance of a P–C vs P–O Bond Cleavage Reaction†

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Results of kinetic and product distribution studies in the hydrolysis of 4-nitrophenyl phenyl(trichloromethyl)-phosphinate, at pH values ranging from 1.3 to 10.2, are described. P–C (vs P–O) bond cleavage predominates at all pH levels and represents the first report of P–CCl_3 bond scission under either acidic or neutral conditions for a trichloromethyl phosphorus ester.

The carbon–phosphorus bond in dialkyl (trichloromethyl)phosphonates [$(RO)_2P(O)X$, where X = CCl_3] and other trichloromethyl-containing organophosphorus compounds undergoes P–C bond cleavage, but significant chemoselectivity results depending on the reaction conditions employed. The trichloromethyl–phosphorus bond is cleaved under strongly basic aqueous conditions;[1] following treatment with ethanolic potassium hydroxide,[2] fluoride ion,[3] strong base, sodium ethoxide, and potassium *tert*-butoxide;[4] by sodium methoxide in anhydrous methanol;[5] and photochemically.[6] In contrast, under milder conditions, the P–C bond in these same (and other) trichloromethyl-containing organophosphorus compounds is stable. Thus, treatment with dilute base or with various amines;[7] exposure to dilute acid, ethanol, or recrystallization from water;[1c,4] treatment with strong hydrochloric acid,[8] with refluxing ethanol;[9] during transesterification of aliphatic and aromatic carboxylic acids;[10] and even exposure to 0.1 N aqueous $Ba(OH)_2$(room temperature, 20 hr) of nucleoside 5′-trichloromethyl)phosphonates[4] leads to no P–C bond cleavage. Of particular note is the stability of the P–CCl_3 bond under even strongly acidic (18% aqueous HCl) conditions.

During investigations into the inhibition of cholinesterases by a variety of organophosphinates,[11] Lieske et al.[12] obtained unexpected results during characterization of one of these compounds. Routine alkaline hydrolysis studies carried out to assess the reactivity of 4-nitrophenyl phenyl(trichloromethyl)phosphinate (1) produced only 4% of the stoichiometric amount of 4-nitrophenol at pH 9.10 and 25.0 °C.[13] Evidence for the identity of 1 was conclusive, i.e., elemental analysis, IR spectrum, ^{31}P and proton NMR. Thus, it appeared possible that one or more competing, parallel reactions could be occurring during the hydrolysis to account for the low production of 4-nitrophenol. Hydrolysis of 1 to produce 4-nitrophenol is illustrated by reaction sequence a shown in Scheme I. In accord with published results for strong base cleavage of the analogous phenyl trichloromethyl chloridate,[4] P–CCL_3 cleavage during base-mediated hydrolysis of 1 might occur via pathway b.

To examine whether 1 was hydrolyzed in part via pathway b, the reaction mixture was assayed for the pro-

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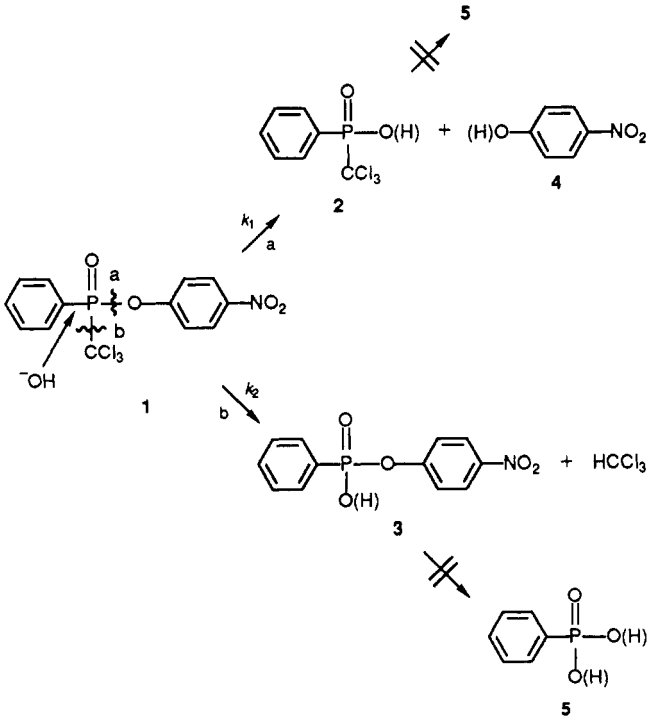
† **Note.** The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting views of the Department of the Army or the Department of Defense.

Table I. First-Order Rate Constants and Product Distributions for Parallel Reactions of 4-Nitrophenyl Phenyl(trichloromethyl)phosphinate (1) under Various pH Conditions[a]

pH[b]	extraction efficiency[c]	% $CHCl_3$ from compd 1[d]	% 4-nitrophenol from compd 1[e]	k_1,[f] min^{-1}	k_2, min^{-1}
10.2	95.1 (2.1)	106.3 (2.8)	0.0–0.4	–	–
9.2	98.7 (2.3)	100.2 (3.2)	2.83 (0.74)	0.162 (0.03)	5.62
9.1	>99	≈92	3.98 (0.31)	0.131 (0.01)	3.15
7.0	98.4 (5.3)	97.9 (4.8)	–	–	–
4.9	98.6 (2.9)	>90[g]	–	–	0.0117 (0.002) 0.0115[h]
1.3	90.4 (4.2)	91.4[i]	8.6	4.8×10^{-5}	5.1×10^{-4}

[a] Numbers in parentheses are standard deviations for the parameter measured and have the same dimensions. [b] All buffers were prepared using double distilled water as follows: pH 10.2, 0.06 M in sodium carbonate and 0.04 M in sodium bicarbonate; pH 9.2 Bicine buffer, 0.132 M in *N,N*-bis(2-hydroxyethyl)glycine, 6.68 mM in $MgCl_2$, 0.013% (w/v) bovine serum albumin, and 4.1 mM sodium azide; pH 9.1 Bicine buffer, 0.10 M in *N,N*-bis(2-hydroxyethyl)glycine, 0.01 M in $MgCl_2$, 0.01% (w/v) bovine serum albumin, and 0.002% sodium azide; pH 7.2 phosphate buffer, 0.134 M in both K_2HPO_4 and KH_2PO_4, 0.0001 M $MgCl_2$ and 0.04% in sodium azide; pH 4.9, 0.1 M in dibasic sodium succinate adjusted to the final pH using 1 N HCl; pH 1.3 HCl was prepared by dilution of concentrated HCl. [c] Percent $CHCl_3$ extraction efficiencies determined for each buffer. [d] Percentage of reaction proceeding by pathway b, as evidenced by actual vs theoretical amount of $CHCl_3$ produced at completion. In all cases, the % $CHCl_3$ produced were corrected for the observed $CHCl_3$ extraction efficiency of the controls. Determined experimentally except as noted. [e] Reactions at pH ≥9.1 were followed spectrophotometrically at 400 nm; at pH 1.3, the value for 4-nitrophenol produced during hydrolysis of 1 was derived from the predicted % $CHCl_3$. [f] Kinetic constants k_1 and k_2 for hydrolysis of 1 were determined by following the production of 4-nitrophenol or $CHCl_3$ over time. The second kinetic constant was then calculated from the relationship for two parallel first-order reactions discussed in the text. [g] Percentage $CHCl_3$ produced was greater than 90% of the theoretical amount following 120-min reaction. [h] Rate constant based on formation of 3, followed spectrophotometrically. [i] $CHCl_3$ produced at infinity derived from exponential fit of data to first-order kinetic model.

Scheme I



duction of chloroform. *n*-Heptane extraction of 0.01 M, pH 9.10 Bicine buffer spiked with known amounts of chloroform gave approximately 99% recovery, with assays carried out by gas chromatography. Addition of an aliquot of 1 to pH 9.10 Bicine buffer followed by extraction after a 15-min reaction period gave ca. 92% of the theoretical yield of chloroform.[12-13] Within the experimental error for these numbers, this was in reasonable agreement with the 96% expected based on 4-nitrophenol production. For two parallel first-order reactions, such as a and b in Scheme I, it may be shown that the product ratio is related to the first-order rate constants by the equation k_1/k_2 = [4-nitrophenol]/[$CHCl_3$].[14] Based on the observed rate constant (k_1 = 0.131 min^{-1}) for the production of 4-nitrophenol, from the relationship just cited for two parallel first-order reactions the rate constant (k_2) for the hydrolysis of 1 to (4-nitrophenyl)phenylphosphonic acid (3) and chloroform was calculated to be 3.15 min^{-1}.

To better understand the atypical reactivity of 1, we examined its hydrolysis under various conditions. First-order rate constants were evaluated [15] using linearized forms of the data, by following either production of $CHCl_3$ or 4-nitrophenol. Except as noted in Table I, final amounts of $CHCl_3$ produced during a reaction were determined in each case. Data from hydrolysis studies at pH 1.3 were analyzed using a nonlinear exponential regression program to calculate a first-order rate constant for P–C bond cleavage and an infinity value for chloroform production.[16] This reaction was allowed to proceed to greater than 90% completion for this determination. All results are summarized in Table I.

Due to the small amount of 4-nitrophenol produced at pH 10.2 for the hydrolysis of 1 by pathway a, no estimate

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(16) Nonlinear regression program written by John R. Lowe, copyright 1984. Lieske, C. N.; Clark, J. H.; Lowe, J. R.; Horton, G. L.; Jewell, D. K.; Daasch, L. W. Edgewood Arsenal Technical Report EB-TR-76113, 1976, Aberdeen Proving Ground, MD, 21010. DTIC AD#A035231.

for the rate constants k_1 and k_2 could be made. No attempt was made to evaluate the rate constants k_1 and k_2 for hydrolysis of 1 at pH 7.0. However, the product ratio for $CHCl_3$/4-nitrophenol of 98:2 indicates that k_2 remains approximately 49-fold greater than k_1 for hydrolysis of 1 at this pH. For hydrolysis of 1 at pH 4.9, k_2 was determined both by following production of $CHCl_3$ and by following formation of (4-nitrophenyl)phenylphosphonic acid, 3, at 307 nm.

The validity of these kinetic results and the final concentration values for reaction products from both pathways for the hydrolysis of 1 depends on the stability of the reaction products produced by both paths. Thus, phenyl(trichloromethyl)phosphinic acid (2), 3, and $CHCl_3$ must be stable under the reaction conditions and the time periods studied. We have found this to be true under the reaction conditions employed.

In summary, these studies represent the first example of an acid-mediated cleavage of the P–CCl_3 in an organophosphorus ester. Further, these studies represent the first report of kinetic rate studies for P–CCl_3 cleavage in any organophosphorus ester, and for cleavage of both P–O and P–CCl_3 in the same molecule. It is of interest to contrast these present results with the reported results for phenyl(trichloromethyl)phosphinyl chloride, where chloride replaces the 4-nitrophenoxy leaving group. Hydrolysis of that compound in dilute nitric acid gave 2,[1c] with no evidence for P–C bond cleavage. This result is in agreement with our finding that 2 is stable under the reaction conditions employed in the current work.

This novel bond scission could find utility in conventional synthetic organic chemistry and in transformations of sensitive compounds of biological importance. For example, in the preparation of nucleoside 3′,5′-cyclic phosphates. That k_2 remains greater than k_1, as reflected by the product ratios summarized in Table I, over the entire pH range examined is surprising. One would expect that general acid catalysis in pathway a would play a more significant role at the lower pH conditions.

Registry No. 1, 81344-26-5.

Synthesis of C(6)-Carboxylate Analogues of *N*-Acetylmuramic Acid

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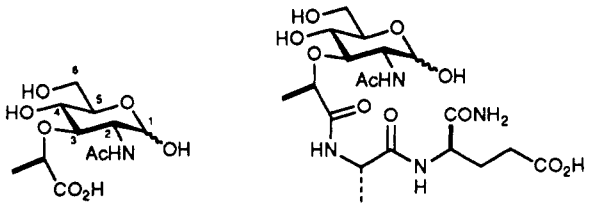
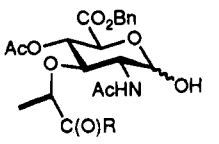
The *N*-acetylmuramic acid unit is an important structural component of the bacterial cell wall.[1] It is also a key structural element in an important class of immunomodulators, represented by muramyl dipeptide (MDP).[2] Our interest in the design and synthesis of agents that inhibit bacterial cell wall biosynthesis prompted our desire to prepare muramic acid cogeners **1a** and **1b**, in which carbon-6 is oxidized to a carboxylate. The preparation of C(6)-carboxylate analogues of *N*-acetylmuramic acid has been reported previously by only one group, that of Zemlyakov and co-workers.[3] We wish to report a new synthesis that utilizes a muramic acid 1′,4-lactone to directly protect the 4-hydroxyl group (Chart I).

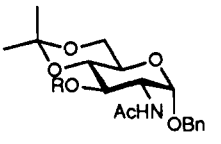
Chart I



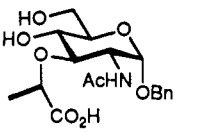
N-acetylmuramic acid MDP



1a: R = NH_2
1b: R = OMe



2: R = H
3: R = (*R*)-CH(Me)CO_2H



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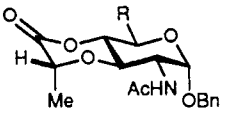
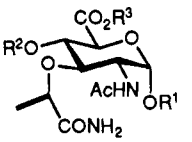
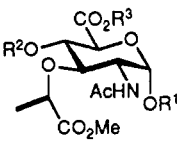


5: R = CH_2OH
6: R = CO_2H



7a: R^1 = CH_2Ph; R^2 = H; R^3 = H
8a: R^1 = CH_2Ph; R^2 = Ac; R^3 = H
9a: R^1 = CH_2Ph; R^2 = H; R^3 = CH_2Ph
10a: R^1 = CH_2Ph; R^2 = Ac; R^3 = CH_2Ph
11a: R^1 = H; R^2 = Ac; R^3 = H



7b: R^1 = CH_2Ph; R^2 = H; R^3 = H
9b: R^1 = CH_2Ph; R^2 = H; R^3 = CH_2Ph
10b: R^1 = CH_2Ph; R^2 = Ac; R^3 = CH_2Ph
11b: R^1 = H; R^2 = Ac; R^3 = H

Alkylation of *N*-acetylglucosamine derivative **2** with (*S*)-2-chloropropionic acid affords carboxylic acid **3**;[4] hydrolysis of the acetonide affords benzyl *N*-acetylmuramic acid (4).[5] In order to allow selective oxidation at C(6), the 4-hydroxyl group of 4 requires protection; this is conven-

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