

Phosphorus Derivatives of Fatty Acids. II. Diethyl Acyloxyethylphosphonates²

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Diethyl acyloxyethylphosphonates derived from acetic, caproic, lauric, myristic, palmitic, stearic and oleic acids were prepared by the reaction of the 2-bromoethyl esters with triethyl phosphite. Various physical properties of these compounds are reported. The free phosphonic acids could not be obtained from the esters by the usual means; hydrolysis even under the mildest acidic conditions liberated the parent fatty acid. A more detailed study of the hydrolysis led to the following conclusions: (1) hydrolysis of the carboxyl ester occurs much more rapidly than that of the phosphonic esters, (2) rate of hydrolysis is not affected by length of acyl chain or size of phosphonic ester groups, and (3) rate of hydrolysis is approximately the same as that of the ethyl ester of the corresponding fatty acid.

In the first paper of this series,⁴ alkylphosphonates were shown to be much more resistant to hydrolysis than acylphosphonates of the same molecular weight. Diethyl lauroxyethylphosphonate, $\text{CH}_3(\text{CH}_2)_{10}\text{COOCH}_2\text{CH}_2\text{P}(\text{O})(\text{OCH}_2\text{CH}_3)_2$, was used in the hydrolysis experiments as an example of an alkylphosphonate derived from a fatty acid. Because of the greater stability of this type of compound, it was thought that a study of the acyloxyethylphosphonates would be of practical and theoretical interest. An examination of the literature revealed no examples of this specific type of phosphorus derivative.

This paper describes the preparation and properties of diethyl acyloxyethylphosphonates derived from acetic, caproic, lauric, myristic, palmitic, stearic and oleic acids. The diethyl esters were chosen in order to achieve structural consistency with the compounds described previously. In addition, di-*n*-butyl and di-*n*-hexyl lauroxyethylphosphonate were prepared for the purpose of comparison.

The dialkyl acyloxyethylphosphonates were prepared by heating the 2-bromoethyl ester of the appropriate fatty acid with an excess of the trialkyl phosphite at elevated temperature for several hours. After the unused trialkyl phosphite was removed, the residue was distilled under high vacuum with the desired product being obtained in a yield varying from 53 to 85%.

The phosphonates derived from acetic, caproic, lauric and oleic acids are colorless liquids at room temperature while those from myristic,⁵ palmitic⁵ and stearic acids are white crystalline solids. Physical properties of these compounds are listed in Table I.

The relative hydrolytic stability of the diethyl acyloxyethylphosphonates previously noted⁴ was the basis for attempts to obtain the free phosphonic acid by acidic hydrolysis. However, even under mildly acidic conditions, the only crystalline prod-

uct obtainable was the parent fatty acid. This unexpected result prompted a more detailed study of the hydrolysis of these compounds under acid conditions.

The study of the rate and extent of hydrolysis included ethyl laurate and diethyl myristoylphosphonate in addition to alkylphosphonates of various molecular weights. The samples were hydrolyzed in 20% aqueous-acetone solution which was 0.1 *N* with respect to hydrochloric acid. To compensate for differences in molecular weight of the samples the results were calculated on the basis of equivalents of acid produced per mole. The results are shown in Fig. 1.

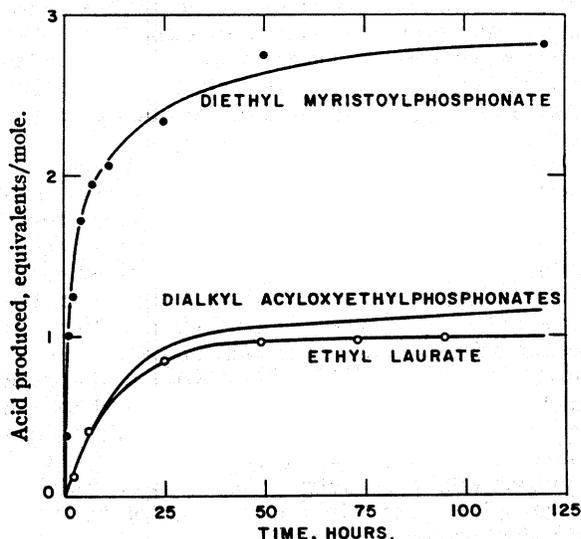


Fig. 1.—Rates of hydrolysis of diethyl myristoylphosphonate, dialkyl acyloxyethylphosphonates and ethyl laurate at 61° in aqueous acetone 0.1 *N* with respect to HCl.

There was little difference in the rates of hydrolysis of the various dialkyl acyloxyethylphosphonates. A single curve representing five series of closely coinciding points was drawn for these compounds. Variation in the acyl chain length included the C₆, C₁₂ and C₁₈ compounds. The ethyl, *n*-butyl and *n*-hexyl groups comprised the variation in the phosphonic esters. Neither of these variations had any appreciable effect on the rate of hydrolysis. The extent of hydrolysis increased

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(4) B. Ackerman, T. A. Jordan, C. R. Eddy and D. Swern, THIS JOURNAL, 78, 4444 (1956).

(5) Diethyl myristoxy- and palmitoxyethylphosphonate were very slow to crystallize at room temperature.

TABLE I

CHARACTERIZATION OF DIALKYL ACYLOXYETHYLPHOSPHONATES, $R_1COOCH_2CH_2P(O)(OR_2)_2$										
R_1COO- ($R_2 = \text{ethyl}$)	M.p., °C.	B.p. °C.	Mm.	n_D^{20}	d_4^{20}	Phosphorus, %		[M.R.]		Yield, %
						Calcd.	Found	Calcd.	Found	
Acetoxy	...	162	20.0	1.4282	1.1161	13.82	13.57	51.68	51.70	79
Caproöxy	...	103-105	0.1	1.4340	1.0382	11.05	11.16	70.16	70.31	70
Lauroxy	20-21	164	.2	1.4419	0.9837	8.50	8.63	97.88	97.92	57
Myristoxy	31-32	157-159	.1	1.4440	.9703	7.89	8.03	107.12	107.32	66
Palmitoxy	40-41	169-172	.1	1.4452	.9607	7.37	7.37	116.36	116.58	75
Stearoxy	46	185-191	.1	1.4411 ^a	.9391 ^a	6.91	6.73	125.60	125.92	64
Oleoxy	...	184	.1	1.4542	.9680	6.94	6.60	125.13	124.94	53
Di- <i>n</i> -butyl lauroxyethylphosphonate	...	164-172	.1	1.4440	.9587	7.37	7.22	116.36	116.51	85
Di- <i>n</i> -hexyl lauroxyethylphosphonate	...	193-197	.1	1.4459	.9409	6.50	6.54	134.84	135.06	59

^a Taken at 50°.

relatively rapidly to about one equivalent of acid produced, and only slowly afterward, indicating that one of the three possible linkages was being preferentially attacked. The parent fatty acid was isolated and identified from the residual solutions; thus it is apparent that hydrolysis proceeded for the most part at the carboxylic ester.

On the other hand it is unlikely that the hydrolysis curve for the acyloxyethylphosphonates from 0 to 30 hours represents *only* the cleavage of the carboxylic ester. It is probable that some small amount of phosphonic ester is hydrolyzed before hydrolysis of the carboxylic ester is complete. This would account for the deviation of the acyloxyethylphosphonate curve from that of ethyl laurate. If the contribution made by the phosphonic ester groups is taken into account, the two curves would coincide more closely. This indicates that the presence of the phosphonate group has little or no effect on the hydrolytic stability of the carboxylic ester.

In contrast to the acyloxyethylphosphonates, diethyl acylphosphonates hydrolyze to give three equivalents of acid per mole in neutral solution, as reported previously,⁴ and under the present conditions. It is likely that the hydrolysis of acylphosphonates in mild acid solution proceeds in the same order as in neutral solution, *i.e.*, the acyl carbon-phosphorus bond is cleaved first. The resulting fragment, $HPO(OCH_2CH_3)_2$, is therefore much less stable to further hydrolysis than the fragment $HOCH_2CH_2PO(OCH_2CH_3)_2$ which is obtained initially from the hydrolysis of the diethyl acyloxyethylphosphonates. The greater stability of the latter is due to the presence of the *alkyl* carbon-phosphorus bond.

Infrared spectra were obtained on the diethyl acyloxyethylphosphonates having 2, 12 and 18 carbon atoms in the acyl groups, and also on diethyl oleoxyethylphosphonate. A spectrum for diethyl lauroxyethylphosphonate is typical.⁶ The absorption bands which may be associated with the phosphorus-containing part of the molecule are at positions similar to those of the diethyl acylphosphonates,⁴ as shown in Table II. In this table, the

(6) This spectrum has been deposited as Document No. 4977 with the American Documentation Institute Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. Either a photoprint or a 35-mm. microfilm copy may be secured for \$1.25, payable in advance by check or money order payable to: Chief, Photoduplication Service, Library of Congress.

assignments are those of Bellamy⁷ and of Meyrick and Thompson.⁸

TABLE II
ASSIGNMENT OF INFRARED BANDS OF DIETHYL
ACYLOXYETHYLPHOSPHONATES

791-792 cm. ⁻¹	P-O-C
962-963	P-O (pentavalent phosphorus)
1028-1030	P-O-C (aliphatic)
1163-1167	P-O-Ethyl
1256 ^a	P → O
1740-1741	C=O

^a This band occurs at 1237 cm.⁻¹ in diethyl acetoxyethylphosphonate.

The carbonyl band is at 1740-1741 cm.⁻¹ in the acyloxyethylphosphonates, whereas it is found at 1697-1698 cm.⁻¹ in the acylphosphonates. The former frequency is normal for an ester, which is to be expected since the C=O and P→O groups are too far apart to conjugate in the acyloxyethylphosphonates.

The 1300-1500 cm.⁻¹ region of the acyloxyethylphosphonates is richer in absorption bands than in the case of acylphosphonates, alkylphosphonates, or ethyl esters of fatty acids, the latter two of which may be considered to make up the molecule of the acyloxyethylphosphonates. Besides the usual bands due to methylene at 1458-1468 cm.⁻¹ and methyl at 1369 cm.⁻¹, the long-chain acyloxyethylphosphonates also have bands at 1357, 1392 and 1420 cm.⁻¹. A band near 1392 cm.⁻¹ is found in the acylphosphonates and several phosphate and phosphite esters, but the 1357 and 1420 cm.⁻¹ bands are not found in these other phosphorus compounds. A band near 1410 cm.⁻¹ has been attributed to a methylene adjacent to an ester group⁹⁻¹¹ consistent with the presence of this type of methylene in the acyloxyethylphosphonates. It is interesting to note, however, that no band near 1420 cm.⁻¹ appears in the acylphosphonates, which also have a methylene adjacent to the carbonyl group. No attempt is made to account for the band at 1357 cm.⁻¹; its frequency is too low to fit

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, p. 257.

(8) C. I. Meyrick and H. W. Thompson, *J. Chem. Soc.*, 225 (1950).

(9) S. A. Francis, *J. Chem. Phys.*, **19**, 942 (1951).

(10) R. G. Sinclair, A. F. McKay and R. Norman Jones, *THIS JOURNAL*, **74**, 2570 (1952).

(11) R. G. Sinclair, A. F. McKay, G. S. Myers and R. Norman Jones, *ibid.*, **74**, 2578 (1952).

the usual explanations for displaced C-H deformation vibrations. It is not present in diethyl acetoxyethylphosphonate.

Experimental

2-Bromoethyl Esters.—These were prepared by the reaction of the highly purified fatty acid with 2-bromoethanol (Eastman Organic Chemical), followed by vacuum distillation as described in the previous publication,⁴ with the exception of 2-bromoethyl palmitate and stearate. These esters were purified by recrystallization from acetone at 0 to 5°. The boiling point (or melting point), n_D^{20} and yield of the 2-bromoethyl esters are: caproate, 116–118° (20 mm.), 1.4505, 74%; laurate, 114–119° (0.5 mm.), 1.4564, 84%; myristate, 157–160° (0.9 mm.), 1.4539, 59%; palmitate, 43.0–43.5°, 1.4507 (55°), 81%; stearate, 49–50°, 1.4500 (55°), 84%; oleate, 185–186° (0.6 mm.) 1.4669, 74%. 2-Bromoethyl acetate, b.p. 160–161°, was an Eastman Organic Chemical.

Dialkyl Acyloxyethylphosphonates.—The preparation of diethyl lauroxyethylphosphonate has been described in a previous publication.⁴ The preparation of the other diethyl acyloxyethylphosphonates followed this procedure with only minor variations. Dry nitrogen was passed through the reaction mixture which was refluxed from 4 to 5 hours at 155–165°. Diethyl acetoxyethylphosphonate was distilled through a short packed column to achieve good separation from the unused triethyl phosphite. Di-*n*-butyl-

and di-*n*-hexyl lauroxyethylphosphonate were prepared by heating 2-bromoethyl laurate with the appropriate trialkyl phosphite in 33% excess for 5 to 6 hours at 180 to 200°. Properties of these compounds are shown in Table I.

Hydrolysis Experiments.—The medium for hydrolysis was freshly prepared for each run by adding 1 volume of 0.5 *N* HCl solution to 4 volumes of acetone. The resulting solution was thus 0.1 *N* with respect to the HCl and contained 20% water by volume.

Two to three grams of the sample was weighed accurately into a 100-ml. volumetric flask. The hot hydrolysis solution was added to the mark and the contents of the flask thoroughly mixed. The solution was transferred to a reaction flask where it was maintained at reflux temperature (61°). Ten-ml. aliquots were removed periodically, added to 60–70 ml. of 95% ethanol and the solution was titrated with 0.1 *N* NaOH. A blank consisting of the hydrolysis solution containing no sample was treated in exactly the same way. The sample titration minus the blank titration indicated the degree of hydrolysis of the sample.

Infrared Absorption Spectra.—The procedure and instrument used to obtain the infrared spectra were the same as previously reported.⁴

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