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Catalytic Hydrolysis of Phosphate Esters in Microemulsions. 3. Analysis of the Hydrolysis Products of *p*-Nitrophenyl Diphenyl Phosphate via ^{31}P NMR

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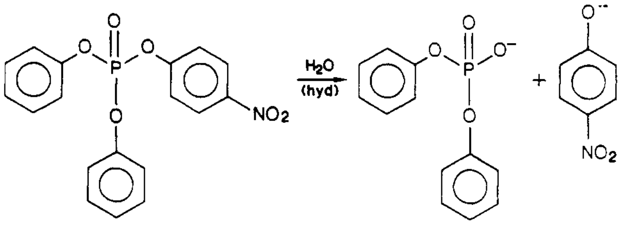
An analysis of the hydrolysis products of *p*-nitrophenyl diphenyl phosphate (PNDP) in three different microemulsions via ^{31}P NMR has proven that diphenyl phosphate is the major product and that *p*-nitrophenyl phenyl phosphate is the second most abundant product in each of the three media. For the media containing butanol, butyl diphenyl phosphate is observed as a third primary product. Numerous secondary products result from the hydrolysis of butyl diphenyl phosphate.

Introduction

Many mechanistic studies have involved the model substrate *p*-nitrophenyl diphenyl phosphate (PNDP), which upon hydrolysis was implicitly assumed to produce only two organic products, the diphenyl phosphate anion (DPP) and *p*-nitrophenoxide:[1-5]



Based on this assumption we have recently reported a kinetic investigation of the 2-iodosobenzoate (IBA) catalyzed hydrolysis of PNDP in a cetyltrimethylammonium bromide (CTAB) microemulsion.[6]

Mackay and Hermansky[7] studied the hydroxide- and fluoride-assisted hydrolysis of PNDP and suggested that the sole phosphate product of the hydrolysis of PNDP in a microemulsion composed of hexadecane in water, stabilized by CTAB and *n*-butanol, is *n*-butyl diphenyl phosphate.[7] Gellman, Petter, and Breslow[8] reported that diphenyl phosphate was the major product but that *p*-nitrophenyl phenyl phosphate (PNPP) was also produced upon zinc complex catalyzed hydrolysis of PNDP in aqueous acetonitrile and in Brij 35 micellar solution; the molar ratio of DPP to PNPP varied from 3.8 to 8.6, depending on the conditions.

We[9] reported that diphenyl phosphate anion (DPP) and *p*-nitrophenyl phenyl anion (PNPP) are major hydrolysis products of PNDP in a CTAB microemulsion. Since the reported results are contradictory and surprising, we decided to reinvestigate the problem using a less ambiguous technique, i.e., ^{31}P FT NMR.

Experimental Procedures

The hydrolysis products of *p*-nitrophenyl diphenyl phosphate (PNDP) were investigated in three microemulsion media at 25 °C (see Table I), where CTAB and CTAC are cetyltrimethylammonium bromide and chloride, respectively, and Adogen 464 is trialkyl(C_8–C_{10})methylammonium chloride; the number 1.1 after CTAC refers to the surfactant to cosurfactant mass ratio).

The ^{31}P NMR spectra were recorded with a Varian XL-200 superconducting FT NMR system operating at 81 MHz in an unlocked mode. In all cases, spectra were obtained at probe temperature ($\sim$21 °C), and phosphoric acid (85%) was used as the external reference. The uncertainties in the chemical shifts are less than ±0.1 ppm; a negative chemical shift value indicates that the resonance is upfield with respect to the reference.

For each sample analyzed, data were accumulated during a period of 2 to 18 h, depending on the signal-to-noise level desired. All spectra were obtained with a pulse width of 3 μs (33°), a sweep width of 20 KHz, an acquisition time of 1.6 s, and a pulse delay of 2.5 to 3.0 s. Gated decoupling was used to eliminate any nuclear Overhauser effects, and quantitative data were obtained by digital integration of the peak areas.

Results

An Examination of Authentic Samples. Microemulsions containing authentic samples of various phosphate esters suspected as products were prepared according to the procedure above, to give a final concentration of 4 mg/mL in the microemulsions. The resonance line positions for these compounds are shown in Table II. We also observe additional peaks due to phosphate species in the spectra at −5.5 ppm, −4.2 ppm, and +1.0 ppm that we assign to dibutyl phenyl phosphate (DBPP), butyl phenyl phosphate anion (BPP), and dibutyl phosphate anion (DBP), respectively. Authentic samples of the phosphate esters in microemulsion media give sharp resonance peaks, all of which are shifted slightly upfield in the CTAC 1.1 microemulsion relative to the CTAB microemulsions. The resonance signals produced by the authentic compounds in uncatalyzed microemulsion, except for BDPP, were stable, even after a period of 3 months. A more thorough discussion of BDPP appears below.

Product Analysis for Reactions Occurring in Uncatalyzed Microemulsions. In all the uncatalyzed mi-

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Table I. Microemulsion Media Used in NMR Product Analysis

name	surfactant	cosurfactant	hexadecane, %	aqueous
CTAB pH 9	18% CTAB	18% *n*-butanol	4	60% 0.03 M Na borate buffer pH 9.2
CTAB pH 12	18% CTAB	18% *n*-butanol	4	60% pH 12.6 NaOH
CTAC 1.1	15.5% CTAC	14% Adogen 464	9	61.5% 0.03 M Na borate buffer, pH 9.2

Table II. ^{31}P NMR Chemical Shifts for Various Phosphates

phosphate ester	CTAB pH 9	CTAB pH 12	CTAC 1.1
1. PNDP[a]	−17.6		
2. BDPP[a]	−11.0		−11.0
3. PNPP 11.0	−10.9	−10.9	
4. DPP[a] 10.0	−9.9		
5. DBPP[b]	−5.5	−5.5	
6. BPP[b,c]	−4.2	−4.2	
7. TBP[a]	−0.2		
8. PP[a] +0.56	+0.6		
9. DBP[b]	+1.0		

[a] Authentic samples. [b] Suspected products of hydrolysis. Authentic samples not available. [c] ^{1}H–^{31}P coupled spectrum gies a well-defined triplet. PP was never detected, nor was any other dianion.

Table III. Observed Percent Yields of PNDP Hydrolysis Products in Uncatalyzed Microemulsion Media

	BPP (−4.2 ppm)	DPP (−9.9)	PNPP (−10.9)	BDPP (−11.0)	PNDP (−17.6) substr
		CTAB pH 9			
17 days ($t \sim \infty$)	0	75	13	10	0
		CTAB pH 12			
1 day	6.5	77	12	4	0
14 days	10	77	12	0	0
		CTAC 1.1			
10 days ($t \sim \infty$)		90	10		0

Table IV. Observed Percent Yields of BDPP Hydrolysis Products in Uncatalyzed CTAB Microemusions

	DBP (+1.0 ppm)	TBP (−0.2)	BPP (−4.2)	DBPP (−5.5)	DPP (−10.0)	BDPP (−11.0) substr
		CTAB pH 9				
1 day	0.0	0.0	0.0	0.0	0.0	100.0
3 months	0.0	0.0	26.9	0.0	12.7	60.4

croemulsion media (containing no IBA), the major product of the hydrolysis of PNDP is DPP observed at a 75% yield in CTAB pH 9, 77% in CTAB pH 12, and 90% in CTAC 1.1 (see Table III). PNPP is observed to be the next most abundant product at yields of 13%, 12%, and 10% for CTAB pH 9, CTAB pH 12, and CTAC 1.1, respectively.

Scheme I

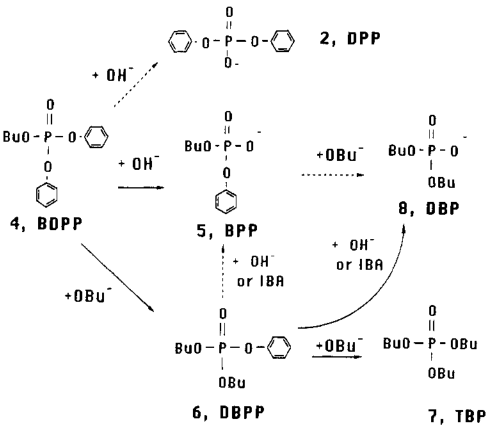


Table V. Observed Percent Yields of PNDP Hydrolysis Products in Catalyzed Microemulsion Media at $t \sim$ 17 Days

	BPP (−4.2 ppm)	DPP (−9.9)	PNPP (−10.9)	BDPP (−11.0)	PNDP (−17.6) substr
CTAB pH 9	0	90.5	7	2	0
CTAB pH 12	8	81	11	0	0
CTAC 1.1		94	6		0

Butyl diphenyl phosphate (BDPP) can be observed in the CTAB pH 9 and the CTAB pH 12 microemulsions. In CTAB pH 12, the BDPP resonance signal (−11.0 ppm) appears, diminishes, and goes to zero in 14 days. Concommitantly, a new peak characteristic of butyl phenyl phosphate (BPP) appears and grows in at −4.2 ppm. Hence, the BPP forms from the BDPP. The BPP is not detected in CTAB pH 9 probably because the process at pH 9 is much slower. The results of a study of the hydrolysis of an authentic sample of BDPP, shown in Table IV, bear this out. After 3 months in CTAB pH 9 microemulsion, yields of 26.9% BPP (−4.2 ppm) and 12.7% DPP (−9.9 ppm) were observed, while 60% of the substrate remained. The hydrolysis of BDPP in CTAB pH 12 yields a more complex mixture, containing at least five species. However, BPP remains the major product. Scheme I succinctly presents a series of reactions which could lead to the product distribution given in Table IV for the CTAB pH 12 microemulsion. We propose that the complexity of the reaction mixture is due primarily to the BDPP which forms from PNDP by butoxide (OBu⁻) attack. BDPP (**4**) is subject to nucleophilic attack by either OH⁻ or OBu⁻ to form DPP (**2**), BPP (**5**), and DBPP (**6**), as shown in Scheme I. However, the formation of DPP (**2**) by OH⁻ attack on **4** is not favorable, and therefore DPP is formed predominantly from PNDP. Only **6** was found to undergo further nucleophilic attack, potentially forming BPP (**5**), TBP (**7**), or DBP (**8**), but since formation of **5** involves loss of OBu⁻, this pathway is not favorable.

We observed compounds **2**, **5**, and **7** to remain stable to any further hydrolysis since no decreases in their resonance peaks occur. Therefore, **6** is the most likely precursor to **7** and **8**. Other pathways to **8** are included but they involve improbable anion–anion attack or release of OBu⁻; these improbable processes are indicated with a dashed arrow. It should be noted that we did not detect the presence of di- or trianions in these reaction mixtures.

Product Analysis for the Hydrolysis of PNDP in Catalyzed Microemulsions. When PNDP is incubated in an IBA-catalyzed CTAB pH 9 microemulsion for 17 days we find a high yield, 90.5%, of DPP, 7% PNPP, 2% BDPP, and no BPP (see Table V). This suggests that the conversion of BDPP into BPP is strongly dependent on OH⁻ since the yield of BPP in CTAB pH 12 is 8% and BDPP is absent after 17 days. Since the CTAC 1.1 microemulsion contains no *n*-butanol, the product distribution is quite simple: 94% DPP and 6% PNPP.

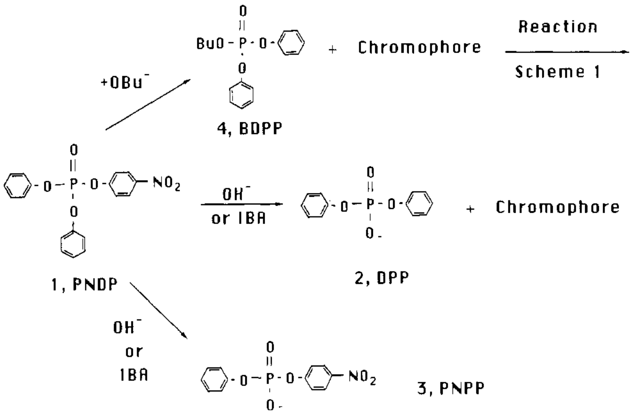
Product Analysis for the Hydrolysis of BDPP in Catalyzed CTAB Microemulsions. The results of a study of the hydrolysis of an authentic sample of BDPP

Table VI. Observed Percent Yields of BDPP Hydrolysis Products in Catalyzed CTAB Microemulsions

	DBP (+1.0 ppm)	TBP (−0.2)	BPP (−4.2)	DBPP (−5.5)	DPP (−10.0	BDPP (−11.0) substr
		CTAB pH 9				
13 days	0.0	0.0	4.0	0.0	2.3	93.6
		CTAB pH 12				
1 day	0.0	0.0	80.0	10.0	0.0	10.0
26 days[a]	6.1	0.5	88.5	3.8	0.7	0.0

[a] An uncharacterized product, 0.4%, appears at −3.2 ppm.

Scheme II



in catalyzed CTAB microemulsions are summarized in Table VI. In the presence of catalyst, BPP is the major product with a significant amount of BDPP remaining in CTAB pH 12. On the other hand, almost all of the BDPP remains in CTAB pH 9, even after 12 days. Thus, OBu$^-$ is not an effective nucleophile at pH 9 in the CTAB microemulsion medium. In addition, IBA is probably not as effective as a catalyst for BDPP hydrolysis as it is for PNDP.

Discussion

The probable chemical transformations of PNDP are depicted in Scheme II. PNDP (1) is subject to nucleophilic attack by all three available nucleophiles, if present: OH$^-$, OBu$^-$, and IBA. The major product formed in all cases is DPP (2) which, along with the second major product, PNPP (3), are stable to any further attack. BDPP (4), formed only in the CTAB microemulsion, does undergo further hydrolysis which was already discussed.

In view of our product analysis it is clear that the rate of formation of the chromophore, *p*-nitophenoxide, is not equal to the rate of hydrolysis of PNDP. In a CTAB microemulsion the rate of chromophore formation is[6]

$$\text{rate} = [0.145[\text{OH}^-] + 1.22[\text{IBA}]][\text{PNDP}]$$

whereas, in a CTAC 1.1 microemulsion it is[10]

$$\text{rate} = [0.552[\text{OH}^-] + 9.0[\text{IBA}]][\text{PNDP}]$$

But, the rate law for hydrolysis contains two more terms:

$$k_{\text{IBA}}{}^{\text{PNPP}}[\text{IBA}][\text{PNDP}] + k_{\text{OH}}{}^{\text{PNPP}}[\text{OH}][\text{PNDP}]$$

where $k_{\text{IBA}}{}^{\text{PNPP}}$ is the second-order rate constant for the IBA-catalyzed hydrolysis of PNDP to produce PNPP and $k_{\text{OH}}{}^{\text{PNPP}}$ is the second-order rate constant for the OH$^-$ hydrolysis of PNDP to produce PNPP. Assuming that yields of DPP and PNPP are proportional to the appropriate rate constants and neglecting the formation of BDPP we could make an estimate of the rate constants for the formation of PNPP. A more exact estimate of the rate of hydrolysis of phosphate esters could be gained by using a substrate such as *p*-nitrophenyl diethyl phosphate ester, for which a single product, diethyl phosphate anion, would most likely result. Nevertheless, we would find that the rate of hydrolysis of PNDP is approximately 10% to 15% higher than the rate of chromophore formation. Hence, the rate of chromophore formation remains as a good estimate of the rate of hydrolysis.

Registry No. 1, 10359-36-1; 2, 48168-03-2; 3, 113303-25-6; 4, 2752-95-6; 5, 113303-26-7; 6, 2528-36-1; 7, 126-73-8; 8, 32288-01-0; CTAB, 57-09-0; CTAC, 112-02-7; PP, 14057-64-8; *n*-butanol, 71-36-3; hexadecane, 544-76-3.

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A Skeletal Rearrangement of γ-(Acyloxy)-β-keto Phosphonates: Studies on the Formation of 2(3*H*)-Furanones

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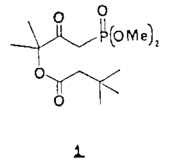
When treated with sodium hydride in dimethoxyethane, some γ-(acyloxy)-β-keto phosphonates react to give 2(3*H*)-furanones via an unexpected rearrangement which proceeds with carbon–carbon bond formation. Several possible mechanisms for this transformation have been tested through crossover experiments, rearrangement of an isotopically labeled substrate, and synthesis of a model intermediate. Results from these experiments allow elimination of several potential reaction pathways from further consideration and suggest a focus for future studies.

We recently reported the preparation of a series of γ-(acyloxy)-β-keto phosphonates for an evaluation of a potential intramolecular Horner–Wadsworth–Emmons route to the 3(2*H*)-furanone ring system.[1,2] During the course of this work, we discovered that treatment of phosphonate 1 with sodium hydride in dimethoxyethane (DME) gave the 2(3*H*)-furanone 2 as the major product, instead of the expected 3(2*H*)-furanone 3. Because this rearrangement



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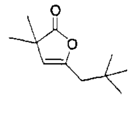

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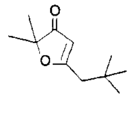

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