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INCREASED STABILITY OF PHOSPHITE OZONIDES DERIVED FROM 4-HYDROXYMETHYL-1-PHOSPHA-2,6,7-TRIOXABICYCLO[2.2.2]OCTANE†

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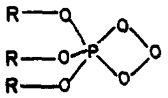
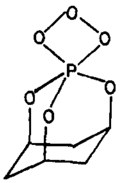
Abstract: Substituent changes at the hydroxyl group in the title compound affect the stability of the corresponding phosphite ozonides generated at the remote phosphorous atom. The benzoyl derivative was found to have a half-life > 100 minutes at 18°C and is at least 10 times more stable at that temperature than 1-phospha-2,8,9-trioxaadamantane ozonide.

Singlet oxygen ($^{1}O_2$) is a versatile oxidant[1,2] and its usefulness in organic and biological systems encourages continued investigation for new and improved sources of this reagent.[3] Numerous chemical sources are available for $^{1}O_2$ generation in aqueous and non-aqueous media.[3] Reagents compatible with the latter system include 9,10-diphenylanthracene [4] and tetraphenyl rubrene[5] peroxides which generate $^{1}O_2$ at elevated temperature (~80°C) and phosphite ozonides[6] which afford $^{1}O_2$ at low temperature (~ -78°C). Though trialkyl phosphite ozonides 1 and 2 show limited stability even at -78°C,[6,7,11] triphenyl phosphite ozonide (3) affords $^{1}O_2$ in the -30°C to -15°C range.[8]



1 R=Me; 2 R=Et; 3 R=ϕ



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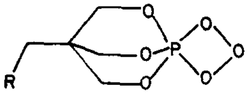

5 R=CH_3

Because of their utility phosphite ozonides have generated a great deal of interest in recent years both mechanistically and practically. Schaap and coworkers[9] demonstrated that 1-phospha-2,8,9-trioxaadamantane ozonide (4) is 106 times more stable than 3 at -5°C and 1.4 times more stable than 4-ethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane ozonide (5).[10,11] In fact, ozonide 4 has a half-life of 10 min (k_1=1.07x10^{-3}sec^{-1}) at 18°C. The barrier to pseudorotation around the phosphorous atom, set up by the rigid bicyclic structures in 4 and 5,[10,11] appears to contribute to the stability of these compounds relative to 1,2 and 3. We undertook a study to determine whether substituents, appended to the hydroxyl group in bicyclic phosphite 6, would

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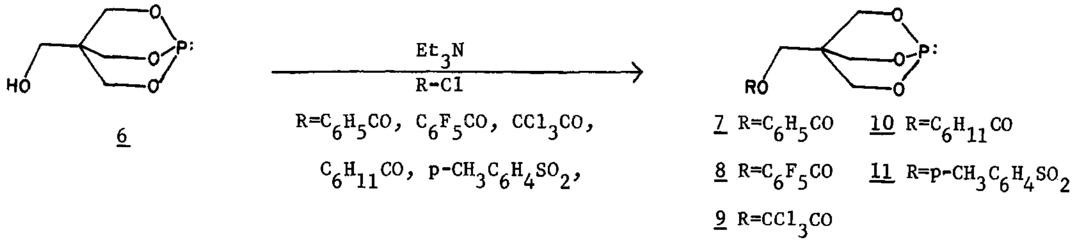
† Dedicated to Professor Harry H. Wasserman on the occasion of his 65th birthday. Congratulations to a respected mentor. Best wishes for continued physical and intellectual strength.

have any effect on the stability of the corresponding ozonides, and herein report our preliminary findings.

Scheme I shows the sequence used to prepare the substituted phosphites. Hydroxymethyl phosphite 6 was synthesized by the method of Wadsworth and Emmons[12] and was converted to substituted phosphites 7-11 by treatment with base and the appropriate electrophile. For example, phosphite 10 was prepared in the following manner. Hydroxymethyl phosphite 6 (3.92 g, 23.8 mmol) was added with stirring and under N_2 to a cold (0°C) solution of dry CH_2Cl_2 (200 ml). Cyclohexanecarboxylic acid chloride (3.96 g, 27.0 mmol) was then added followed by the dropwise addition of triethylamine (2.63 g, 26.0 mmol). After 1 hr the solution was concentrated and the ammonium salt filtered off. After evaporation of the filtrate the residue was crystallized (methylene chloride/cyclohexane) affording phosphite 10 (3.22 g, 49%; mp 82°).[13]



6

$R=C_6H_5CO$, C_6F_5CO, CCl_3CO, $C_6H_{11}CO$, $p\text{-}CH_3C_6H_4SO_2$,

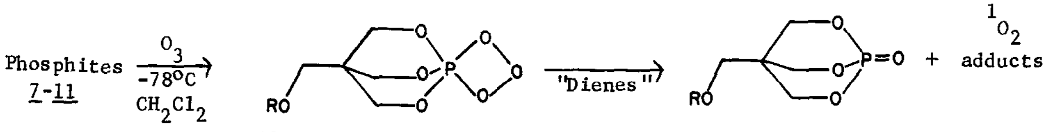
7 $R=C_6H_5CO$ 10 $R=C_6H_{11}CO$

8 $R=C_6F_5CO$ 11 $R=p\text{-}CH_3C_6H_4SO_2$

9 $R=CCl_3CO$

Scheme I

In order to obtain a qualitative determination of the relative stability of the corresponding ozonides, a comparison was made of the temperatures at which the bright orange color of rubrene and/or the deep magenta color of tetraphenylcyclopentadienone (TPCPD) was discharged. The oxidations were carried out in the following manner (Scheme II). Ozone was passed through a cold (-78°C) solution of dry CH_2Cl_2 for 1 hr. The phosphite, dissolved in a minimum of dry CH_2Cl_2, was then added dropwise to the deep blue solution at -78°C. After addition of the phosphite the excess ozone was purged from the cold solution by passing N_2 through the medium. The N_2 purge was continued for 1 hr after the blue color was no longer visible. To this cold solution ca. 0.1-0.2 equivalents of rubrene or TPCPD (relative to the phosphite) was added. The solution was then removed from the cold bath and allowed to warm gradually. The temperature observed, when complete loss of color of the $^1O_2$ acceptors took place, served to indicate the thermal region at which each phosphite ozonide was decomposing at a reasonable rate.[14] After oxygen evolution was



12 $R=C_6H_5CO$ 15 $R=C_6H_{11}CO$

13 $R=C_6F_5CO$ 16 $R=p\text{-}CH_3C_6H_4SO_2$

14 $R=CCl_3CO$

17 $R=C_6H_5CO$ 20 $R=C_6H_{11}CO$

18 $R=C_6F_5CO$ 21 $R=p\text{-}CH_3C_6H_4SO_2$

19 $R=CCl_3CO$

Scheme II

complete the phosphates (17 through 21) were isolated[15] and characterized.[16]

The temperatures at which decoloration was observed are listed in Table 1. It is obvious that a range of stabilities (relative to 5 which decomposes at 0°) are observed for these modified phosphite ozonides. Of the compounds tested the trichloroacetate 14, cyclohexane carboxylate 15 and pentafluorobenzoate 13 showed moderate stability while tosylate 16[17] showed limited stability.[18] Benzoate 12 on the other hand showed substantial stability relative to 4. At 0°C oxygen evolution from 12 was not visible at all while continued oxygen evolution was observed beyond 39°C.

Table 1. Decoloration Temperature (0°C)

Phosphite Ozonides				
12	13	14	15	16
39°	22°	12°	12°	-30°

Table 2. Kinetic Data for Ozonide Decomposition

Compound	Temp °C	$t_{1/2}$	k_1
12	18	>100	1.2×10^{-4}
15	18	> 10	1.2×10^{-3}
4	18.2	10.8	1.07×10^{-3}
	1.1	116	9.94×10^{-5}
3	-17	-	1.58×10^{-3}

Kinetic runs were carried out on phosphite ozonides 12 and 15. The rate of loss of oxygen at 18°C was measured volumetrically as a function of time in CH_2Cl_2. Table 2 summarizes our results, giving the half-lives and first order rate constants, and compares the data with that of compounds 4 and 3. At 18°C the stability of 15 is comparable with that of 4. Phosphite ozonide 12 on the other hand is at least 10 times more stable than 4 and displays approximately the same stability at 18°C as 4 does at 1.1°C.

Though the effect of these remote substituents on the stability of the phosphite ozonides is not understood, it is interesting to point out that a ^{13}C chemical shift difference for the CH_3 unit in phosphite ozonide 5 and its corresponding phosphate is as large as 0.2 ppm even though the CH_3 group is five atoms removed from the phosphorous atom.[8] Perhaps there is a spatial (as opposed to through bond) steric or electronic interaction between the phosphorous-ozonide center and the appended substituents which affect the ozonides stability during or prior to loss of oxygen. In view of these results the possibility of finding a phosphite ozonide which might be stable at ambient temperature and which might be useful as a storable $^1O_2$ reagent is by no means closed. We plan to continue our studies in this area in order to define the effect of remote substitution on the stability of phosphite ozonides.

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13. Yields were not maximized. Most of the phosphites here hygroscopic and they were difficult to purify. However, accurate combustion analyses, for all non-oxygen atoms, were obtained on all the corresponding phosphates. Phosphite (yield %; mp °C):^{1}HNMR:IR:MS. 7 (quant., 157-158):(CDCl$_3$) δ 7.95(m,2H), 7.50(m,3H), 4.15(d,J=1.5Hz,6H), 4.00(s,2H):(KBr)cm^{-1} 1720, 1040:m/e 268,162,132,105; 8(90;-):(CDCl$_3$) δ 4.15(d,J=1.5Hz,6H),4.0(s,2H):(KBr)cm^{-1} 1730, 1040; 9 (15;161-162):(CDCl$_3$) δ 4.18(d,J=1.5Hz,6H), 4.0(s,2H):(KBr)cm^{-1} 1760,1040,850,740; 10 (49;80-82):(CDCl$_3$) δ 4.05(d,J=1.5Hz,6H), 3.70(s,2H), 2.80(m,11H):(KBr)cm^{-1} 1730,1060; 11 (15;143-144):(CDCl$_3$) δ 7.52(AB,J=9Hz,4H), 3.98(d,J=1.5Hz,6H), 3.67(s,2H), 2.45(s,3H):(KBr)cm^{-1} 1364,1195,1180,1100,1060.
14. Oxygen continued to be liberated in all the studies beyond the decoloration point due to the limited amount of acceptor that was added. After effervescence ceased the solution was heated to ca. 45°C to insure complete ozonide decomposition.
15. The phosphates were generally separated from the $^1O_2$ adducts (e.g. cis-dibenzoyl stilbene) by chromatography and crystallized. $^1O_2$ adducts were observed in all runs.
16. Phosphate (yield %; mp °C):^{1}HNMR:IR:MS: 17(88;229.5-230.5):(CDCl$_3$) δ 8.03(m,2H), 7.57(m,3H), 4.80(d,J=6Hz,6H), 4.28(s,2H):(KBr)cm^{-1} 1715,1260,1035:m/e 284,162,132,105,77; 18(95;202-203):(CDCl$_3$) δ 4.80(d,J=6Hz,6H), 4.43(s,2H):(KBr)cm^{-1} 1740,1305,1240,1045:m/e 374; 19(18;215-216):(CDCl$_3$) δ 4.78(d,J=6Hz,6H),4.48(s,2H):(KBr)cm^{-1} 1760,1320,1260,1045,850,690,665:m/e 328,326,324; 20(quant.;162-163):(CDCl$_3$) δ 4.5(d,J=6Hz,6H), 3.90(s,2H), 2.8(m,11H):(KBr)cm^{-1} 1725,1311,1305,1260,1195,1160,1030:m/e 290,207,163,111; 21(quant.;247-249):(acetone-d$_6$) δ 7.60(AB,J=9Hz,4H), 4.50(d,J=6Hz,6H), 3.8(s,2H), 2.5(s,3H):(KBr)cm^{-1} 1364,1330-1310, 1260.
17. Decoloration took place at relatively low temperature unlike the other ozonides (12-15). Solutions of 16 were murky and colloidal indicating the insolubility of the ozonide. Rapid evolution of oxygen, however, was observed for 16 up to 10°C. This ozonide may actually be more stable than indicated.
18. Decoloration temperatures for the phosphite ozonides of 6 with appended α-naphthoyl and benzyl groups were -30°C and 20°C, respectively. The α-naphthoyl phosphite ozonide solution was also murky and colloidal.

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