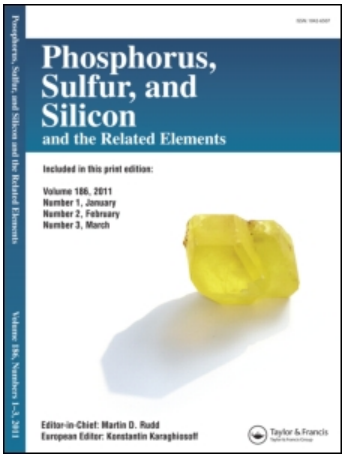

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PHOTOCHEMISTRY OF PESTICIDES, 7[1]. REGIOSELECTIVE PHOTODIMERIZATION OF *o,o*-DIETHYL-*o*-(3-CHLORO-4-METHYLCOUMARIN-7-YL)-THIOPHOSPHATE (COUMAPHOS)

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PHOTOCHEMISTRY OF PESTICIDES, 7[1]. REGIOSELECTIVE PHOTODIMERIZATION OF *o,o*-DIETHYL-*o*-(3-CHLORO-4-METHYLCOUMARIN-7-YL)-THIOPHOSPHATE (COUMAPHOS)

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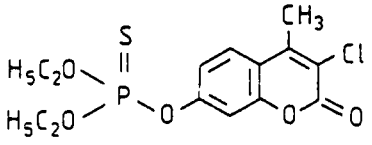
UV-irradiation ($\lambda > 313$ nm) of *o,o*-diethyl-*o*-(3-chloro-4-methyl-coumarin-7-yl)-thiophosphate (Coumaphos; **1**) in chloroform results in an regioselective dimerization reaction to afford the head-to-tail anti-dimer **2**. The structure of **2** is established by single crystal x-ray diffraction. Singlet oxygen does not affect the formation of **2**.

INTRODUCTION

o,o-Diethyl-*o*-(3-chloro-4-methylcoumarin-7-yl)-thiophosphate (Coumphos; **1**),[2] marketed under the trade names Bayer 21/199, Asuntol®, Resitox®, and Muscatox®, is a valuable insecticide for the control of ectoparasites of domestic animals.[3] Because of its low toxicity for fish, it acts as an agent for the control of mosquito larvae.[3b,4] Moreover, compound 1 shows marked acaricidal,[5] anthelmintic,[6] and nematocidal[7] activities. In coumaphos **1**, both the coumarin nucleus[8] and the thiophosphate moiety[9] are photoreactive and expected to undergo transformations of particular interest both from chemical and biological point of view. This, and our increasing interest in the photochemistry of pesticides,[10] has prompted us to study the photochemistry of **1**, and additionally the influence of singlet oxygen on **1**.



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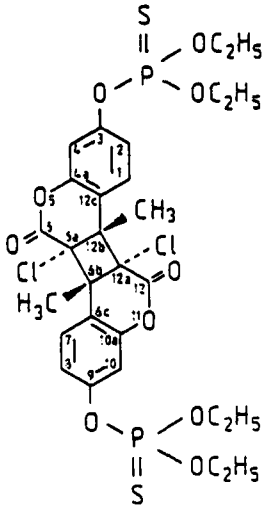
RESULTS AND DISCUSSION

A solution of coumaphos **1**, in chloroform was irradiated in a Pyrex reactor ($\lambda > 313$ nm). After 250 hr, column chromatography gave a fraction from which a colourless crystalline substance was isolated and assigned from the elemental analysis to be the dimeric structure **2**. The spectroscopic data support this structure, as follows: (a) The ^{31}P NMR shift (δ + 62.35 ppm) is compatible with thiophosphate shifts.[11] (b) The singlet that appeared at δ 2.62 ppm in the ^1H NMR spectrum of **1** (4-CH_3) underwent upfield shift (δ 1.66 ppm) in the spectrum of **2**. The latter shift is in best agreement with a methyl group attached to a bridgehead carbon.[12] (c) The IR spectrum of **2** showed strong absorption bands at 1760 cm^{-1} (saturated lactone carbonyl) and at 1035 cm^{-1} (P—OC_2H_5).[12] The same groups absorb at 1735 and 1030 cm^{-1}, respectively, in the IR-spectrum of **1**. (d) In MS, the m/z-peak of **2** has indicated a molecular formula of $C_{14}H_{16}ClO_6PS$ [m/z 362 (364)] which is assignable for the monomeric form **1**. Thus, **2** undergoes primarily thermolysis to afford coumaphos **1** before ionization under electron impact. Such behaviour is well known for many other dimerization products.[13] That **2**, however, possesses the assigned dimeric structure $C_{28}H_{32}Cl_2O_{12}P_2S_2$ is absolutely and unambigously confirmed on the basis of single crystal x-ray analysis as shown in Figure 1 and by the data compiled in Tables 1 and 2.* Upon irradiation (Pyrex; $\lambda > 313$ nm) of **1** in the presence of singlet oxygen no influence on the dimerization process **1** → **2** has been observed, and no additional oxidation products could be detected.



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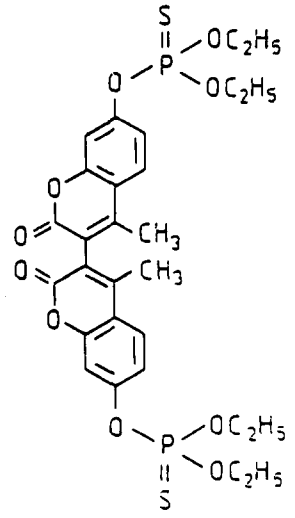

3 *(MS)*

*For details of this x-ray investigation cf. Fachinformationszentrum Energie, Physik, Mathematik, D-7514 Eggenstein-Leopoldshafen 2, FRG, referring to the code No. CSD 51766, the author's name, and the citation of this work.

CONCLUSION

From this preliminary investigation, it is evident that the coumarin ring in coumaphos **1** is the most photoreactive part of the molecule. This type of photoinduced [2 + 2]photodimerization is widely known for numerous other coumarin derivatives.[8] However, several mechanistic studies have revealed that dependent on the solvent used the predominant dimerization products possess *syn* and *anti head-to-head* cyclobutane stereochemistry,[14] where the *syn* isomer proceeds through the intermediacy of coumarine singlet excimers, and the *anti* isomer is a product of the

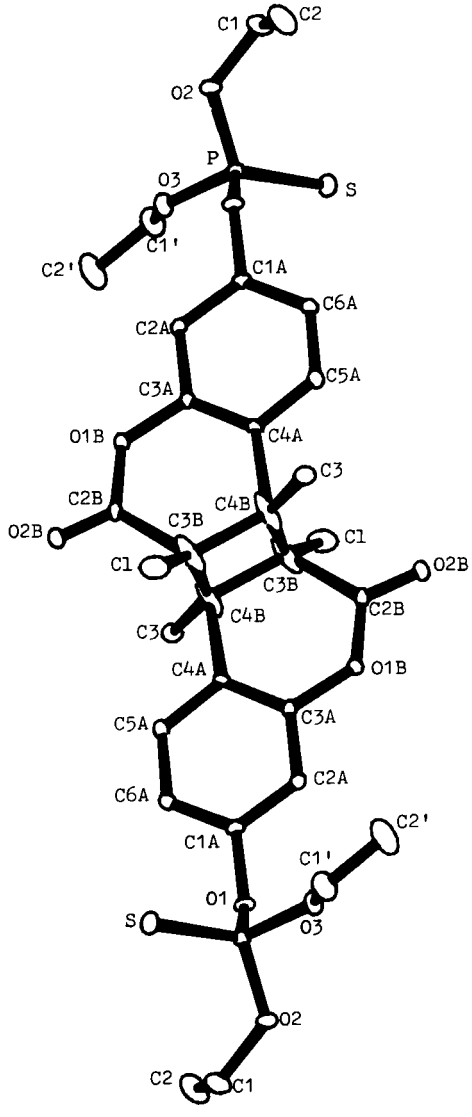

FIGURE 1 ORTEP view of **2** (numbering not according to IUPAC-rules).

TABLE I

Final Atomic Parameters for **2**
(Standard Deviations in Parentheses)

Atom	x/a	y/b	z/c
Cl	1.7975(3)	0.9399(3)	0.5566(3)
S	0.6945(2)	0.5285(2)	0.7180(2)
P	0.8387(2)	0.4705(2)	0.8336(2)
01	1.0434(5)	0.4625(4)	0.7773(4)
02	0.8242(5)	0.3152(4)	0.9149(4)
03	0.8206(6)	0.5663(5)	0.9307(4)
01B	1.3603(5)	0.8566(4)	0.7631(4)
02B	1.5355(6)	1.0035(5)	0.7791(4)
C1A	1.1316(7)	0.5826(6)	0.7075(6)
C2A	1.1953(8)	0.6688(6)	0.7668(5)
C3A	1.2983(8)	0.7765(7)	0.6961(5)
C4A	1.3377(9)	0.7991(7)	0.5717(6)
C5A	1.266(1)	0.7110(9)	0.5177(6)
C6A	1.1646(9)	0.6051(7)	0.5840(6)
C2B	1.479(1)	0.9533(8)	0.7143(6)
C3B	1.587(1)	0.9805(9)	0.5545(9)
C3	1.6307(4)	0.7751(4)	0.4087(3)
C4B	1.514(1)	0.9019(9)	0.4727(8)
C1	0.787(1)	0.1903(8)	0.8783(9)
C2	0.939(1)	0.118(1)	0.8128(9)
C1′	0.666(1)	0.659(1)	0.9728(9)
C2′	0.702(1)	0.762(1)	1.033(1)
H2A	1.181(6)	0.656(5)	0.852(4)
H5A	1.290(8)	0.722(7)	0.438(6)
H6A	1.135(7)	0.545(6)	0.549(5)
H1	0.71(1)	0.255(8)	0.824(7)
H2	0.780(9)	0.098(8)	0.955(7)
H3	0.918(8)	0.028(7)	0.804(6)
H4	0.97(1)	0.21(1)	0.74(1)
H5	0.97(1)	0.056(9)	0.887(8)
H1′	0.64(2)	0.60(1)	1.05(1)
H2′	0.65(2)	0.73(1)	0.88(1)
H3′	0.636(9)	0.841(7)	1.037(7)
H4′	0.77(1)	0.752(9)	1.063(8)
H5′	0.77(1)	0.744(9)	0.916(8)

coumarin triplet state. *Syn head-to-tail* isomers have been found only scarcely, and then only in traces;[14,15] they have been obtained directly only by straight synthetic approaches.[16]

As the x-ray analysis reveals, surprisingly, in our case the opposite trend is observed leading in a regioselective photodimerization only to one isolable product with a definite *anti head-to-tail* cyclobutane stereochemistry. Most obviously, steric and electronic effects, e.g. by the thiophosphate rest and the 3- and 4-substituents (Cl, CH_3), respectively, seem to govern the cycloaddition mode exclusively to an *anti head-to-tail* fusion.

The present investigation also shows that the thiophosphoryl group in **1** seems to possess relative stability towards UV-irradiation and oxidation under the prevailing experimental conditions.

It is also worthy to note that the MS analysis of a crude sample of the singlet oxygen photolysate of **1** has indicated the potential formation of a dehalodimeriza-

TABLE II

Bond Distances [Å] and Angles (deg.) of **2**
(Standard Deviations in Parentheses)

Cl –C3B	1.673(8)	C1A–C6A	1.349(9)
S –P	1.905(2)	C2A–C3A	1.379(8)
P –01	1.599(4)	C3A–C4A	1.358(9)
P –02	1.554(4)	C4A–C5A	1.385(9)
P –03	1.546(5)	C4A–C4B	1.818(14)
01 –C1A	1.400(6)	C5A–C6A	1.346(9)
02 –C1	1.418(9)	C2B–C3B	1.803(15)
03 –C1′	1.453(11)	C3B–C4B	1.567(10)
01B –C3A	1.393(7)	C3 –C4B	1.603(8)
01B –C2B	1.337(7)	C1 –C2	1.433(14)
02B –C2B	1.162(7)	C1′ –C2′	1.40(2)
C1A–C2A	1.376(8)		

S –P –01	115.8(2)	C3A–C4A–C5A	116.9(6)
S –P –02	117.6(2)	C3A–C4A–C4B	125.1(6)
S –P –03	117.5(2)	C5A–C4A–C4B	116.2(6)
01 –P –02	99.8(2)	C4A–C5A–C6A	122.4(7)
01 –P –03	101.6(2)	C1A–C6A–C5A	119.3(7)
02 –P –03	101.5(3)	01B –C2B–02B	119.1(6)
P –01 –C1A	123.9(4)	01B –C2B–C3B	122.1(6)
P –02 –C1	125.4(6)	02B –C2B–C3B	117.5(6)
P –03 –C1′	125.0(5)	Cl –C3B–C2B	104.0(7)
C3A–01B –C2B	124.3(5)	Cl –C3B–C4B	116.6(7)
01 –C1A–C2A	118.8(5)	C2B–C3B–C4B	115.6(9)
01 –C1A–C6A	119.8(6)	C4A–C4B–C3B	107.6(9)
C2A–C1A–C6A	121.1(6)	C4A–C4B–C3	100.2(7)
C1A–C2A–C3A	118.0(6)	C3B–C4B–C3	120.5(7)
01B –C3A–C2A	114.3(5)	02 –C1 –C2	112.5(9)
01B –C3A–C4A	123.5(5)	C3 –C1′ –C2′	112.(1)
C2A–C3A–C4A	122.2(6)		

tion product, such as **3** (m/z 654). However, verification of this argument is beyond the scope of the present study and will be discussed in a forthcoming communication.

EXPERIMENTAL

General Data. All melting points are uncorrected. Technical coumaphos **1** was supplied by the Bayer AG, D-5090 Leverkusen, and was recrystallized from methanol before use (mp 94°C[3,17] of a pure sample). -IR (KBr): Perkin-Elmer 157-G. -^{1}H NMR ($CDCl_3$) and ^{31}P NMR ($CDCl_3$, vs 85% H_3PO_4): Bruker WH-90. -MS (70 eV): MS-50 of Kratos (A.E.I.). -Microanalysis: Mikroanalytisches Laboratorium Pascher, Bonn.

o,o-Diethyl 6a,12a-dichloro-6a,6b,12a,12b-tetrahydro-6b,12b-dimethyl-6,12(6H, 12H)-dioxocyclobuta[1,2-c: 3,4-c′]bis[1]benzopyran-3,9-di-o-thiophosphate. A solution of coumaphos **1** (2.5 g, 6.9 mmol) in $CHCl_3$ (250 ml) was irradiated in a Pyrex reactor ($\lambda > 313$ nm) with a Hg-high pressure lamp (Philips HPK 125). After 250 hr, coumaphos **1** could be still identified (TLC) in the reaction mixture. Then the solvent was evaporated to dryness in the presence of silica gel (7 g) then introduced to a column charged with silica gel (Kieselgel 60, particle size 0.2–0.5 mm; E. Merck, Darmstadt) and packed with light petroleum (b.r. 40–60°C). After elution with toluene (300 ml), the eluent was evaporated in vacuo. The residual substance (500 mg; 20%) was recrystallized from methanol to give dimer **2** as colourless needles of mp 124°C. -IR 3100, 1760, 1500–1610, 1035, 810 cm^{-1}; ^{1}H NMR δ 1.30 (t, 12H), 1.66 (s, 6H), 4.25 (q, 8H), 7.30 (m, 6H); MS m/z 362 (100%), 364 (33%), 334 (base peak-CO);

Anal. Calcd. for $C_{28}H_{32}Cl_2O_{10}P_2S_2$ (725.6): C, 46.35; H, 4.44; Cl, 9.77. Found: C, 46.42; H, 4.55; Cl, 9.67.

Elution with toluene-ethylacetate (9.5 : 0.5, v/v) gave a fraction from which coumaphos **1** (1.2 g) was obtained and identified (mp, mixed mp, and comparative IR spectra).

Similar results have been obtained, when coumaphos **1** was irradiated (Pyrex; $\lambda > 313$ nm) with a Hg-high pressure lamp in the presence of singlet oxygen (the solution contained 30 mg methylene blue, and oxygen was steadily bubbled into the mixture with a moderate rate).

X-Ray data collection and structure solution. Adduct **2**, $C_{28}H_{32}Cl_2O_{10}P_2S_2$, crystallizes from ethanol in the triclinic space group $P\bar{1}$ with a = 7.969 (2), b = 9.401 (2), c = 11.456 (3) Å, α = 77.45 (2), β = 75.92 (2), γ = 82.15°, V = 809.47 Å^3, Z = 1, D_{calc} = 1.488 g · cm^{-3}. One crystal with dimensions of 0.18 × 0.10 × 0.63 mm was used for data collection on an Enraf-Nonius CAD 4 diffractometer using graphite-monochromated CuK_α radiation (λ = 1.5418 Å). 2537 intensities were measured up to θ = 60° by $\omega/2\theta$ scan technique and corrected for Lorentz/polarization effects. Empirical absorption correction [$\mu(CuK_\alpha)$ = 44.4 cm^{-1}] was made according to *North*, *Phillips* and *Mathews*[18]. The structure was solved by direct methods using MULTAN 80[19] and the difference Fourier techniques. Hydrogen atoms were included in the refinement with isotropic thermal parameters. Non-hydrogen atoms were assigned anisotropic thermal parameters. C3 was weighted with 1.8 and Cl with 0.85, as approximately 15% of Cl and Me groups are exchanged. 1617 unique reflections with $\sin\theta/\lambda \leq 0.5$ Å and $F > 3\sigma(F)$ were retained for the refinement of the structure. The final R_1 factor with 252 variables was 0.063.

An ORTEP view of the molecule is shown in Figure 1. A centre of symmetry of the space group is located in the middle of the molecule. Atom coordinates, bond lengths and bond angles have been summarized in Tables I and II.

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