

Regio- and Stereoselective [2+2] Photodimerization of 3-Substituted 2-Alkoxy-2-oxo-2H-1,2-benzoxaphosphorines

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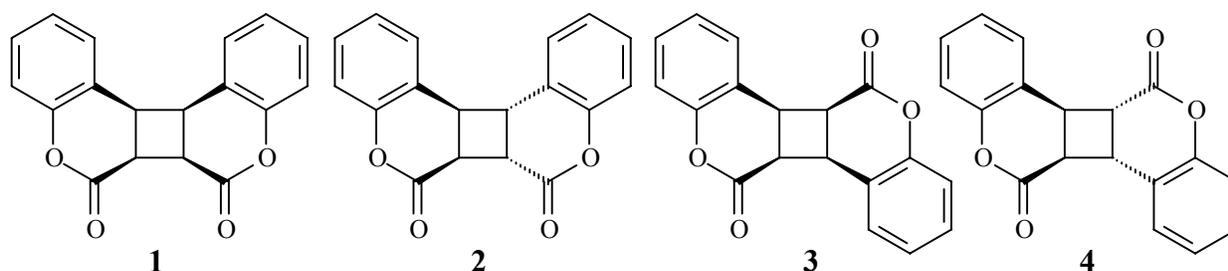
Abstract: Diethyl 1,2-benzoxaphosphorine-3-carboxylates **5** undergo a regio- and stereoselective [2+2] photodimerization reaction in methanol solution under the action of sunlight, giving in all cases the corresponding *anti* head-to-tail dimers **6** and **7**. Concerning the stereogenic P atom, the photodimerization is also stereoselective, and the centrosymmetric stereoisomer **6** predominates over the non symmetric P-epimer **7**.

Keywords: 2-Oxo-2-alkoxy-1,2-benzoxaphosphorines, [2+2]photocycloaddition, benzoxaphosphorine dimers

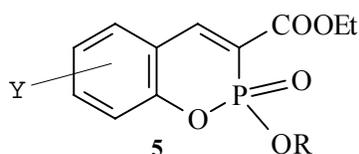
Introduction

The photochemical [2+2] dimerization of 2-oxo-2H-1-benzopyrans (coumarins) is well known [1-7]. Over the last few years there has been a growing interest in some coumarin photodimers due to their applications in organic synthesis [8-10], in medicine [11-13] and in other modern technologies [14-16]. All four possible regio and stereoisomers, i.e. *syn* head-to-head **1**, *anti* head-to-head **2**, *syn* head-to-tail **3**, and *anti* head-to-tail **4** have been isolated from the [2+2] photodimerization of coumarins. The published yields of the isolated isomers were shown to depend on the substitution of the starting coumarins [5-7,15-16], as well as on the reaction conditions, i.e. the solvent used [17-21],

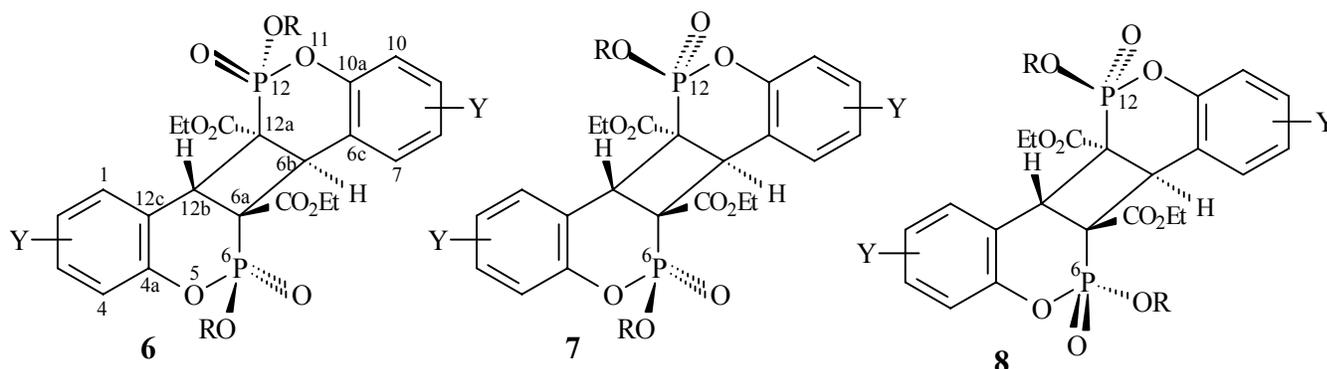
the concentration of the starting compounds [18,19] or the presence in the photoreaction of a sensitizer [4,17,18].



Recently, while working on the synthesis of the 2-alkoxy-2-oxo-2*H*-1,2-benzoxaphosphorine coumarin analogues **5a-d**, it was found that these coumarin analogues were not stable in solution, undergoing dimerization under the action of sunlight and during their workup to give small amounts of the corresponding [2+2] cycloaddition dimers. The isolated dimers were shown to have a centrosymmetric *anti* head-to-tail structure **6**, whereas in one case the unsymmetrical P12 epimer **7** (R=C₂H₅, Y=H) was isolated [22].



5	R	Y
a	CH ₃	H
b	C ₂ H ₅	H
c	C ₂ H ₅	6-Br
d	C ₂ H ₅	6-Cl
e	C ₂ H ₅	7-N(C ₂ H ₅) ₂
f	C ₂ H ₅	7-NHC ₂ H ₅



The structural similarity of compounds **5** to coumarins and the fact that only one out of the four possible regio- and stereoisomers was isolated, prompted us to undertake a more systematic study of this [2+2] photochemical cyclodimerization.

Result and Discussion

Photodimerization of compounds **5a-d** was carried out by the action of sunlight in 0.1M methanol solution and the results are given in Table 1. In order to explore the influence of the experimental conditions on the reaction products, photodimerization of the bromo derivative **5c** was also performed in solvents with different polarities, (Methods A-D), and the corresponding results are given in Table 2.

Table 1. Photochemical dimerization of 3-substituted 2-oxo-2*H*-1,2-benzoxaphosphorines **5a-d**

5	R	X	Reaction time	Yields, %				6:7
				Unreacted starting compd.	Overall	6	7	
a	CH ₃	H	40 days	24	45	56	44	1.3:1
			90 days	20	44	68	32	2.1:1
b	C ₂ H ₅	H	90 days	7	71	72	28	2.6:1
c	C ₂ H ₅	6-Br	42 days	-	89	56	44	1.3:1
d	C ₂ H ₅	6-Cl	20 days	51	26	68	32	2.1 :1
			50 days	-	92	60	40	1.5 :1
e	C ₂ H ₅	7-N(C ₂ H ₅) ₂	90 days	72	*	-	-	-

* No dimer was detected. Instead the 6-ethylaminoderivative **5f** was isolated in 9% yield.

Table 2. Photochemical dimerization of ethyl 6-bromo-2-ethoxy-2-oxo-2*H*-1,2-benzoxaphosphorine-3-carboxylate **5c** in various solvents.

Method	Reaction conditions	Yields, %			6c : 7c
		Overall	6c	7c	
A	5 mL spectr. grade CH ₃ OH, 42 days	89	56	44	1.3:1
B	2 mL dry benzene, 55 days	83	64	36	1.8:1
C	1.5 mL glacial CH ₃ COOH, 4 days	94	76	24	3.2:1
D	suspension in 1.5 mL water, 14 days	83	72	28	2.6:1

As it is seen from Tables 1 and 2, in all cases the photodimerization reaction proceeds with complete regio- and stereoselectivity, giving only the *anti head-to-tail* isomers **6** or **7**. However, with regards to the phosphorous stereogenic centre, both diastereomers **6** and **7** were isolated. The

symmetric *exo,exo*-6,12-diethoxyderivatives **6** prevailed in all cases over the non symmetric *exo,endo*-6,12-diethoxyderivatives **7**, with the **6/7** ratio being between 1.3:1 to 3.2:1 (Tables 1 and 2). The separation of the diastereomers and their cleanup was carried out by multi-stage column chromatography. Here it should be noted that the alternative centrosymmetric diastereomer, i.e. *endo,endo*-6,12-diethoxyderivative **8** was not detected among the reaction products.

In almost all experiments some amount of the starting material was isolated (see Table 1). The higher overall yields of dimers were obtained from the reaction of the halogenated 6-bromo and 6-chloro derivatives **5c** and **5d** (89% and 92%), respectively (Table 1), whereas the higher yields and reaction rates of dimerization for the 6-bromoderivative **5c** were observed in the polar solvents, e.g. in acetic acid (94% of dimer in 4 days, Method C), versus those in benzene (83% of dimer in 55 days, Method B) (Table 2).

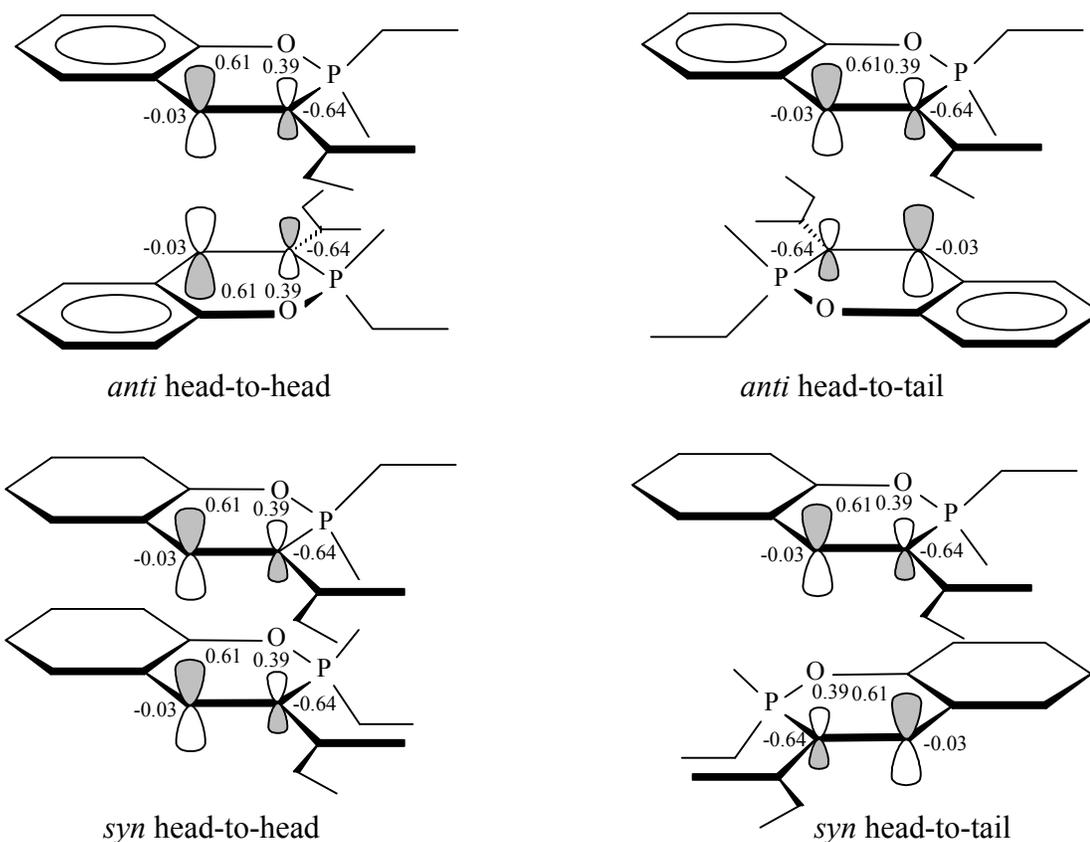
It was also found that ethyl 7-N,N-diethylamino-2-ethoxy-2-oxo-2*H*-1,2-benzoxaphosphorine-3-carboxylate **5e** is very stable towards sunlight irradiation in methanol solution. In this case the starting compound **5e** (72%) and a small amount (9%) of the 6-ethylaminoderivative **5f** (as a result of dealkylation of the starting compound **5e**) were isolated from the reaction mixture after 90 days. Such dealkylations have been described earlier [23,24] in irradiation of 7-N,N-diethylaminocoumarins.

From the experimental data given above it is obvious that the studied photodimerization of the esters of 2-alkoxy-2-oxo-2*H*-1,2-benzoxaphosphorine-3-carboxylic acid **5a-d**, contrary to the corresponding coumarin reactions, proceeds with high regioselectivity to the formation of the head-to-tail dimers. Moreover, the [2+2]-photodimerization of **5a-d** is also a stereoselective reaction and leads to the formation of the *anti* head-to-tail, but not *syn* head-to-tail, dimer. The stereoselectivity of the above photodimerization is also apparent in respect to the stereogenic P2-atom of compounds **5**. Of the corresponding three possible diastereomers, i.e. **6**, **7** and **8**, the formation of the symmetric **6** predominated (Tables 1 and 2) whereas the symmetric **8**, with the two alkoxy groups directed over the cyclobutane ring, were not detected in the reaction products.

It is not possible to give any strong evidence supporting a particular mechanism for the above [2+2] photodimerization. According to the classical mechanism [25], the synchronous [2+2] photodimerization takes place through interaction of the empty LUMO orbital of a molecule in the ground state and a HOMO orbital of a molecule in excited state (that originates from the same LUMO of the ground state). MO calculations performed for the methyl benzoxaphosphorin-3-carboxylate **5a**, have shown that the p_z -orbital coefficients of the C3-C4 double bond have values of 0.39 and 0.61 respectively and the same values show also the corresponding coefficients in the HOMO orbital of the excited state (Figure 1). Therefore, it would be expected that if a synchronous reaction takes place, by interaction of the lobes with the same sign and according to the maximum overlapping principle (see Figure 1), then the head-to-head regioisomers (with structures analogous to **1** or **2**) would predominate in the reaction products of compounds **5**. In the studied reactions however only the head-to-tail regioisomers, **6** or **7**, have been isolated and this fact implies that a synchronous mechanism of this reaction should be excluded. It is therefore obvious that the [2+2] photodimerization of compounds **5** is a multistep reaction that proceeds through a triplet excited state of the molecule of oxaphosphorine **5** or

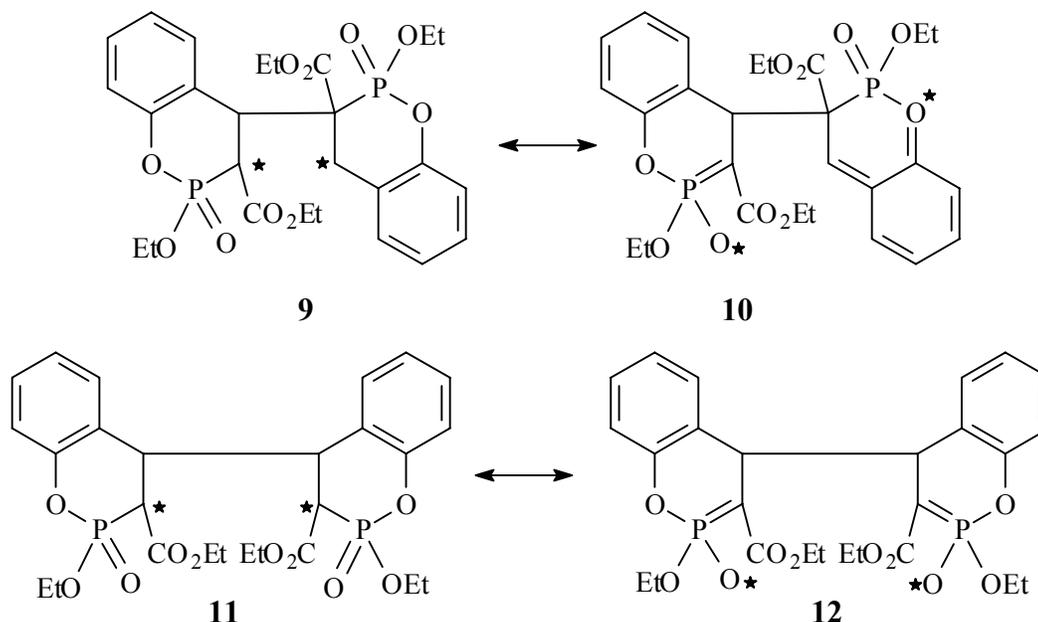
through the formation of a bimolecular triplet transition state as it is shown for coumarin photodimerization [17-19, 26]. This assumption is in accordance also with the known results [26,27], that in the presence of a "heavy" atom in the molecule of the starting compound or in the solvent the transition from a basic singlet into excited triplet condition is taking place directly.

Figure 1. Orbital interactions for synchronous anti- and syn-HH and anti- and syn-HT photo-dimerization of methyl ester 2-methoxy-2-oxo-2H-1,2-benzoxaphosphorine-3-carboxylic acid. The calculated AO coefficients and charges of C3 and C4 carbon atoms obtained by NBO analysis are shown



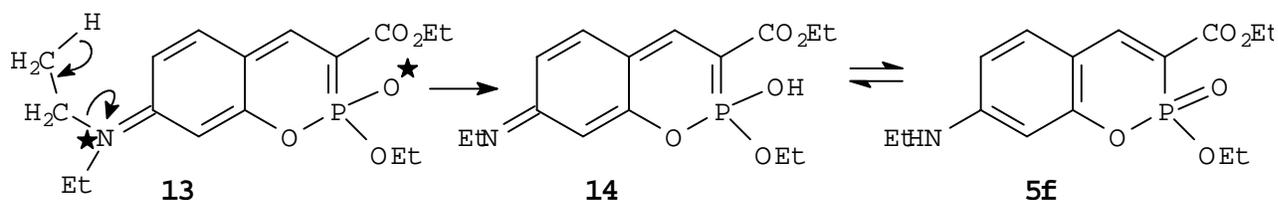
The regioselectivity of the reaction could be explained by a diradical or dipolar intermediate, **9** and **10**, which is formed by a C3, C4' interaction of two molecules of **5**. This one would be much more stabilized by electron or charge delocalisation than the alternatives, e.g. that would be formed by a C3,C3' or C4,C4' attachment, **11** and **12**, where such a delocalisation is much more restricted. A C3, C4' interaction could be also considered as favoured by the charges (obtained by NBO analysis) of the C3 and C4 atoms, where C3 bears a negative charge with a high value of -0.64 e, whereas C4 appears with essentially no charge. Hence, while formation of a head-to-head product through e.g. a C3, C3' interaction is highly disfavoured, a C3, C4' interaction leading to head-to-tail products appears more likely to occur.

Scheme 1. Possible C3-C4' and C4-C4' diradical or dipolar intermediates leading in HH or HT stereoisomers respectively, of the cyclophotodimerization of compounds **5**. * Denotes radical or ion.



The dipolar or diradical mechanism is supported by the above mentioned behaviour of the 7-dimethylamino-derivative **5e**. Thus the formation of the dealkylation product **5f** could be explained by assuming a dipolar or diradical intermediate, **13**, stabilized by the localization of the charge or radical on the 7-nitrogen atom, giving finally instead of dimerization the dealkylation product **5c**, as depicted in Scheme 2.

Scheme 2. Possible diradical or dipolar intermediate leading to the dealkylation product **5f**.



The formation of a dipolar intermediate is also supported by the higher dimerization rates of **5c** observed in polar solvents [25], e.g. 4 days of sunlight irradiation in acetic acid versus 55 days in benzene (Table 2). The stereoselectivity of the reaction, i.e. the formation of only the *anti* isomer as well as the predominance of the centrosymmetric stereoisomer **6** over the non symmetric **7** and the absence of **8** in the reaction products, is most probably the result of steric interactions caused by the oxo and alkoxy groups at P2 atom of the oxaphosphorine ring.

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Experimental

General

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded with a Specord IR 71 or IR 75 spectrophotometers. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were obtained with a Bruker WM 250 (at 250 MHz and 62,9 MHz respectively) or a Bruker AM 300 (at 300 MHz and 75,4 MHz respectively) instruments. All NMR spectra were obtained by using TMS as internal standard in CDCl_3 and are reported in δ units. E.I. mass spectra were obtained at 70 eV a VG TS-250 spectrometer. Elemental analyses of C, H, P, N and Cl were carried out in the Laboratory of Elemental Analysis at the Department of Organic Chemistry of University of Sofia. Column chromatography was carried out on silica gel (Merck or Fluka 0.063-0.2 mm) using n-hexane/EtOAc or n-hexane/chloroform mixtures of increasing polarity as eluents.

Preparation of the Starting Materials.

The 2-oxo-2H-1-benzoxaphosphorines **5a-e** were prepared by means of the Knoevenagel reaction as described in the literature [22]. The UV absorption spectra of the starting oxaphosphorins **5a-e** were as follows (MeOH), nm (log ϵ): **5a** (MeOH): nm (log ϵ) = 285 (3.92), 322 (3.38); **5b** (MeOH): nm (log ϵ) = 287 (4.10), 322 (3.56); **5c** (MeOH): nm (log ϵ) = 285 (4.03), 333 (3.34); **5d** (MeOH): nm (log ϵ) = 282 (4.02), 328 (3.36); **5e** (MeOH): nm (log ϵ) = 263 (3.25), 403 (4.11).

Photochemical dimerization of the 3-substituted 2-oxo-2H-1-benzoxa-phosphorines **5**. General Procedure:

Depending of the reaction conditions (solvent and reaction time) the following methods are distinguished:

Method A. The solution of corresponding benzoxaphosphorines **1** (0,5 mmoles) in methanol (spectroscopy grade, 5 mL) was left in direct sunlight and monitored by tlc. After evaporation of the solvent, the residue was chromatographed on a silica gel column with n-hexane - chloroform of increasing polarity as eluent. In the case the reaction was not finished, the unreacted starting compound was removed on a silica gel column with n-hexane - ethyl acetate (of increasing polarity) as eluent.

Method B. The same as in method A, but with dry benzene (2 mL) as solvent.

Method C. As in method A, but glacial acetic acid (1.5 mL) was used as solvent.

Method D. As in A, but the reaction was performed in a water suspension (1.5 mL).

Diethyl 16a,6b,12a,12b-tetrahydro-exo,exo-6,12-dimethoxy-endo,endo-6,12-di-oxo-6H,12H-cyclobuta-[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (6a).

Yield: 0.04g (30%), when the reaction was carried out for 90 days and 0.034g (25%) when the reaction was carried out for 40 days, m.p. = 235-237 °C (ether). Lit. [22] m.p. 235-237 °C.

Diethyl 6a,6b,12a,12b-tetrahydro-exo,endo-6,12-dimethoxy-endo,exo-6,12-di-oxo-6H,12H-cyclobuta-[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (7a).

Yield: 0.02g (14%), when the reaction was carried out for 90 days and 0.028g (20%), when the reaction was carried out for 40 days, M.p. = 211-213 °C (ether); IR (CHCl₃): ν = 1735, 1620, 1580, 1485, 1260, 1190, 1040 cm⁻¹; ¹H-NMR (CDCl₃) (300 MHz): δ = 0.85 (t, J=7.1 Hz; 3H, CH₃), 0.913 (t, J=7.1 Hz; 3H, CH₃), 3.65 (dd, J=7.1 and 10.7 Hz; 1H, CH_AHO), 3.71 (d, J=12.2 Hz; 3H, OCH₃), 3.72-3.88 (m, 2H, CH₂), 3.96 (dd, J=7.1 and 10.7 Hz; 1H, CH_BHO), 4.08 (d, J=11.1 Hz; 3H, OCH₃), 5.32 (dd as t, J=21.5 Hz; 1H) and 5.46 (dd, J=16.8 and 22.3 Hz; 1H) (6b/12b-H), 7.09 (two d as t, 2H), 7.17 (dd as t, J=7.6 Hz; 1H), 7.20 (dd as t, J=7.8 Hz; 1H), 7.28-7.36 (m, 3H), 7.48 (dd, J=1.4 and 7.6 Hz; 1H); ¹³C-NMR (CDCl₃) (75.4 MHz): δ = 13.51, 13.54 (CH₃), 42.75 (t, ²J_{CCP}=4.7 Hz) and 43.85 (t, ²J_{CCP}=6.3 Hz) (C-6b/C-12b), 51.24 (dd, ¹J_{CP}=136.8 Hz; ³J_{CCCP}=6.6 Hz) and 51.35 (dd, ¹J_{CP}=134.2 Hz; ³J_{CCCP}=4.2 Hz), (C-6a/C-12a), 53.53 (d, ²J_{COP}=7.7 Hz) and 55.40 (d, ²J_{COP}=5.1 Hz) (CH₃OP), 63.43/62.54 (CH₂O), 119.65 (d, ³J_{CCCP}=4.8 Hz) and 120.29 (d, ³J_{CCCP}=4.7 Hz) (C-4/C-10), 122.77 (dd, ³J_{CCCP}=13.9 and 5.7 Hz) and 123.57 (dd, ³J_{CCCP}=13.6 and 3.9 Hz) (C-6c/C-12c), 124.16, 125.26 (C-2/C-8), 130.38 (C-3/C-9), 131.09 (d, ⁴J_{CCCP}=1.7 Hz) and 132.10 (d, ⁴J_{CCCP}=1.5 Hz) (C-1/C-7), 151.64 (d, ²J_{COP}=5.2 Hz) and 151.69 (d, ²J_{COP}=8.7 Hz) (C-4a/C-10a), 166.14 (d, ³J_{CCCP}=1.9 Hz) and 166.64 (d, ³J_{CCCP}≈1.0 Hz) (C=O). – MS: m/z (%) = 537 (8), 536 (M⁺, 16), 463 (25), 462 (17), 418 (9), 417 (24), 391 (11), 390 (22), 389 (31), 312 (13), 269 (42), 268 (38), 267 (38), 254 (15), 240 (37), 234 (18), 224 (33), 223 (74), 222 (15), 209 (59), 196 (73), 182 (56), 166 (49), 146 (62), 118 (75), 115 (73), 101 (43), 89 (72), 77 (62), 29 (100); Analysis, calcd. for C₂₄H₂₆O₁₀P₂ (536.40): C, 53.74; H, 4.89; found: C, 53.46; H, 5.09.

Diethyl 6a,6b,12a,12b-Tetrahydro-exo,exo-6,12-diethoxy-endo,endo-6,12-di-oxo-6H,12H-cyclobuta-[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (6b).

Yield: 0.03g (20%), M.p. = 251-253 °C (ether). Lit. [22] m.p. 251-253 °C.

Diethyl 6a,6b,12a,12b-tetrahydro-exo,endo-6,12-diethoxy-endo,exo-6,12-di-oxo-6H,12H-cyclobuta[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (**7b**).

Yield: 0.07g (51%), M.p. = 217-219 °C (ether). Lit. [22] m.p. 217-219 °C.

Diethyl 6a,6b,12a,12b-tetrahydro-2,9-dibromo-exo,exo-6,12-diethoxy-endo,endo-6,12-dioxo-6H,12H-cyclobuta[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (**6c**).

Yields: Method A: 0.09g (50%), Method B: 0.1g (53%), Method C: 0.13g (72%), Method D: 0.11g (60%), M.p. = 272-274 °C (ether). Lit. [22] m.p. 272-274 °C; UV (CH₃OH): *nm* (log ϵ) = 270 (s, 3.32), 278 (3.53), 287 (3.60), 303 (s, 3.20).

Diethyl 6a,6b,12a,12b-tetrahydro-2,9-dibromo-exo,endo-6,12-diethoxy-endo,exo-6,12-dioxo-6H,12H-cyclobuta[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (**7c**).

Yields: Method A: 0.07g (39%), Method B: 0.06g (30%), Method C: 0.04g (22%), Method D: 0.04g (23%), M.p. = 238-240 °C (methanol); UV (CH₃OH): *nm* (log ϵ) = 270 (s, 3.55), 279 (3.78), 287 (3.79); IR (CHCl₃): ν = 1740, 1610, 1560, 1480, 1260, 1230, 1120, 1020 cm⁻¹; ¹H-NMR (CDCl₃) (300 MHz): δ = 0.952 (t, J=7.2 Hz; 3H) / 0.981 (t, J=7.2 Hz; 3H) (CH₃CH₂OCO), 1.185 (t, J=7.1 Hz; 3H) / 1.55 (t, J=7.1 Hz; 3H) (CH₃CH₂OP), 3.75 (dd, J=7.1 and 10.7 Hz; 1H) / 3.83 (dd, J=7.2 and 10.5 Hz; 1H) / 3.87 (dd, J=7.2 and 10.7 Hz; 1H) / 3.95 (dd, J=7.2 and 10.8 Hz; 1H) (CH₃CH₂OCO), 4.09-4.26 (m, 2H) / 4.30-4.41 (m, 2H) (CH₃CH₂OP), 5.21 (dd as t, J=21.5 Hz; 1H) and 5.34 (dd, J=15.9 and 22.7 Hz; 1H) (6b/12b-H), 6.95 (d, J=8.4 Hz; 1H) / 7.04 (d, J=8.6 Hz; 1H) (H-4/H-10), 7.40-7.48 (m, 3H), 7.61 (d, J=2.2 Hz; 1H); ¹³C-NMR (CDCl₃) (75.4 MHz): δ = 13.54 / 13.59 (CH₃), 16.19 (d, ³J_{CCOP}=5.1 Hz) and 16.50 (d, ³J_{CCOP}=6.5 Hz) (CH₃CH₂OP), 42.49 (t, ²J_{CCP}=4.7 Hz) and 43.47 (t, ²J_{CCP}=6.3 Hz) (C-6b/C-12b), 50.63 (dd, ¹J_{CP}=134.4 Hz; ³J_{CCCP}=3.7 Hz) and 52.09 (dd, ¹J_{CP}=136.7 Hz; ³J_{CCCP}=6.7 Hz), (C-6a/C-12a), 62.71, 62.79 (CH₂O), 64.10 (d, ²J_{COP}=7.5 Hz) and 65.59 (d, ²J_{COP}=5.5 Hz) (CH₂OP), 117.61 (d, ⁵J_{CCCCCP}=1.3 Hz) and 117.93 (d, ⁵J_{CCCCCP}≈1 Hz) (C-2/C-8), 121.24 (d, ³J_{CCOP}=4.6 Hz) and 122.06 (d, ³J_{CCOP}=4.7 Hz) (C-4/C-10), 124.63 (dd, ²J_{CCP} / ³J_{CCCP}=13.9 / 6.0 Hz) and 125.59 (dd, ²J_{CCP} / ³J_{CCCP}=12.2 / 2.6 Hz) (C-6c/C-12c), 124.16, 125.26 (C-2/C-8), 133.18, 133.32 (C-3/C-9), 133.79 (d, ⁴J_{CCCCP}=1.7 Hz) and 135.59 (d, ⁴J_{CCCCP}=1.8 Hz) (C-1/C-7), 149.80 (d, ²J_{COP}=5.4 Hz) and 150.85 (d, ²J_{COP}=8.9 Hz) (C-4a/C-10a), 165.54 (d, ²J_{CCP}=2.1 Hz) and 166.30 (d, ²J_{CCP}≈1.0 Hz) (C=O); MS: *m/z* (%) = 722 (19), 721 (13), 720 (M⁺, 32), 649/647 (26), 576/574 (36), 362/360 (37) 334/332 (38), 317/315 (41), 260 (62), 244/242 (53), 235 (45), 232 (65), 214 (40), 212/210 (37), 195 (29), 179 (30), 154 (20), 145 (46), 79 (100), 77 (62); Analysis, calcd. for C₂₆H₂₈O₁₀Br₂P₂ (722.28): C, 43.24; H, 3.91; found: C, 43.43; H, 4.11.

Diethyl 6a,6b,12a,12b-tetrahydro-2,9-dichloro-exo,exo-6,12-diethoxy-endo,endo-6,12-dioxo-6H,12H-cyclobuta[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (6d).

Yield: 0.09g (55%) when the reaction was carried out for 50 days and 0.04g (18%) when the reaction was carried out for 40 days, M.p. = 256-258 °C (ether). Lit. [22] m.p. 238-240 °C.

Diethyl 6a,6b,12a,12b-tetrahydro-2,9-dichloro-exo,endo-6,12-diethoxy-endo,exo-6,12-dioxo-6H,12H-cyclobuta[1,2-c:3,4-c']bis[1,2]benzoxaphosphorine-trans-6a,12a-dicarboxylate (7d).

Yield: 0.06g (37%) when the reaction was carried out for 50 days and 0.02g (8%) when the reaction was carried out for 20 days, M.p. = 229-230 °C (ether); IR (CHCl₃): ν = 1740, 1600, 1475, 1270, 1240, 1090, 1020 cm⁻¹; ¹H-NMR (CDCl₃) (300 MHz): δ = 0.93 (t, J=7.1 Hz; 3H) / 0.97 (t, J=7.1 Hz; 3H) (CH₃CH₂OCO), 1.18 (t, J=7.1 Hz; 3H) and 1.55 (dt, J=0.7 and 7.1 Hz; 3H) (CH₃CH₂OP), 3.77 (dq, J=10.7 and 7.1 Hz; 1H) / 3.80 (dq, J=10.6 and 7.1 Hz; 1H) / 3.86 (dd, J=10.6 and 7.1 Hz; 1H) / 4.00 (dd, J=10.7 and 7.1 Hz; 1H) (CH₃CH₂OCO), 4.06-4.27 (m, 2H) / 4.20-4.40 (m, 2H) (CH₃CH₂OP), 5.13 (dd as t, J=21.5 Hz; 1H) and 5.44 (dd, J=16.0 and 22.7 Hz; 1H) (6b/12b-H), 7.01 (d, J=9.1 Hz; 1H) / 7.05 (d, J=8.7 Hz; 1H) (H-4/H-10), 7.25-7.32 (m, 3H), 7.48 (d, J=2.5 Hz; 1H); ¹³C-NMR (CDCl₃) (75.4 MHz): δ = 13.50 / 13.52 (CH₃), 16.19 (d, ³J_{CCOP}=5.2 Hz) and 16.51 (d, ³J_{CCOP}=6.4 Hz) (CH₃CH₂OP), 42.54 (t, ²J_{CCP}=4.6Hz) and 43.53 (t, ²J_{CCP}=6.3 Hz) (C-6b/C-12b), 50.51 (dd, ¹J_{CP}=134.8 Hz; ³J_{CCCP}=3.7 Hz) and 50.95 (dd, ¹J_{CP}=136.8 Hz; ³J_{CCCP}=6.6 Hz), (C-6a/C-12a), 62.69, 62.78 (CH₂O), 64.10 (d, ²J_{COP}=8.4 Hz) and 65.58 (d, ²J_{COP}=5.6 Hz) (CH₂OP), 120.88 (d, ³J_{CCOP}=4.6 Hz) and 121.69 (d, ³J_{CCOP}=4.6 Hz) (C-4/C-10), 124.22 (dd, ²J_{CCP} / ³J_{CCCP}=14.1 / 6.0 Hz) and 125.13 (dd, ²J_{CCP} / ³J_{CCCP}=13.4 / 3.8 Hz) (C-6c/C-12c), 130.24, 130.35 (C-3/C-9), 130.22 (d, ⁵J_{CCCCCP}≈-1 Hz) and 130.52 (d, ⁵J_{CCCCCP}=1.0 Hz) (C-2/C-8), 130.84 (d, ⁴J_{CCCCP}=1.7 Hz) and 131.71 (d, ⁴J_{CCCCP}=1.7 Hz) (C-1/C-7), 149.22 (d, ²J_{COP}=5.4 Hz) and 150.27 (d, ²J_{COP}=8.7 Hz) (C-4a/C-10a), 165.77 (d, ²J_{CCP}=2.3 Hz) and 166.32 (dd, ²J_{CCP}≈2 and 1.0 Hz) (C=O). – MS: m/z (%) = 636/634/632 (M⁺, 25), 588/586 (5), 562/561/560/559 (12), 514/512 (10) 318/316 (78), 290/2988 (92), 271 (74), 245 (82), 218/216 (74), 207 (81), 180 (82), 154/152 (78), 115 (21), 111 (19), 89 (78), 75 (54), 63 (83), 39 (100); Analysis, calcd. for C₂₆H₂₈O₁₀Cl₂P₂ (633.36): C, 49.31; H, 4.46; found: C, 49.33; H, 4.39.

Diethyl 7-N-ethylamino-2-oxo-2H-1-benzoxaphosphorine-3-carboxylate (5f).

Yield: 0.02g (9%), M.p. = 88-89 °C (*n*-hexane/ether); IR (CHCl₃): ν = 3700, 3480, 1710, 1630, 1595, 15450, 1525, 1250, 1200, 1075, 1040 cm⁻¹; ¹H-NMR (CDCl₃) (300 MHz): δ = 1.27 (t, J=7.2 Hz; 3H, CH₃), 1.37 (t, J=7.1 Hz; 3H) / 1.38 (t, J=7.0 Hz; 3H) (CH₃CH₂OP), 3.20 (m; 2H, CH₂NH), 4.21-4.46 (m; 4H, CH₃CH₂OP), 4.64 (bs; 1H, NH), 6.28 (d, J=2.2 Hz; 1H, 8-H), 6.35 (dd, J=2.2 and 8.5 Hz; 1H, 6-H), 7.17 (d, J=8.5 Hz; 1H, 5-H), 8.13 (d, J=37.0 Hz; 1H, 4-H); ¹³C-NMR (CDCl₃) (75.4 MHz): δ = 14.33 / 14.38 (CH₃), 16.42 (d, ³J_{CCOP}=6.6 Hz), 37.75 (CH₂NH), (t, ²J_{CCP}=4.6Hz) and 43.53 () (C-6b/C-12b), 50.51 () and 50.95 (dd, ¹J_{CP}=136.8 Hz; ³J_{CCCP}=6.6 Hz), (C-6a/C-12a), 61.29 (CH₂O), 64.10 (d,

$^2J_{\text{COP}}=6.3$ Hz) (CH_2OP), 100.15 (d, $^3J_{\text{CCOP}}=7.7$ Hz) (C-8), 109.10 (d, $^1J_{\text{CP}}=180.7$ Hz) (C-3), 109.20 (C-6), 109.4 (d, $^3J_{\text{CCCP}}=15.3$ Hz) (C-4a), 133.17 (d, $^4J_{\text{CCCCP}}=1.4$ Hz) (C-5), 151.27 (d, $^2J_{\text{CCP}}=4.9$ Hz) (C-4), 153.41 (d, $^4J_{\text{CCOP}}=1.9$ Hz) (C-7), 155.48 (d, $^2J_{\text{CCP}}=8.2$) (C=O), 164.84 (d, $^2J_{\text{COP}}=13.7$ Hz) (C-8a); Analysis, calcd. for $\text{C}_{17}\text{H}_{24}\text{O}_5\text{NP}$ (353.36): C, 57.79; H, 6.85; N, 3.96; found: C, 57.68; H, 6.84; N, 3.77.

Computational details

The quantum chemical calculations were performed with the NWChem 4.0 package [28]. The geometry of the molecules was optimised at the B3LYP [29] level with TZP basis sets of all atoms. The atomic charges and orbital coefficients were obtained by natural bond orbital analysis using the NBO 4.M program [30] at HF-MP2 level with 6-31+G* basis sets.

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Sample availability: Samples of compounds **6b**, **6c**, **6d** and **7b** are available from MDPI.

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