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-2H-1,2-benzoxaphosphorine couramin 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].
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-2H-1,2-benzoxaphosphorines 5a-d

| 5 | R | X | Reaction time | Yields, % | 6 : 7 |
|---|---|---|---------------|----------|------|
|   |   |   |               | Unreacted starting compd. | Overall | 6 | 7 | |
| a | CH₃ | H | 40 days | 24 | 45 | 56 | 44 | 1.3:1 |
|   |   | H | 90 days | 20 | 44 | 68 | 32 | 2.1:1 |
| b | C₂H₅ | H | 90 days | 7 | 71 | 72 | 28 | 2.6:1 |
| c | C₂H₅ | 6-Br | 42 days | - | 89 | 56 | 44 | 1.3:1 |
| d | C₂H₅ | 6-Cl | 20 days | 51 | 26 | 68 | 32 | 2.1:1 |
| e | C₂H₅ | 7-N(C₂H₅)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-2H-1,2-benzoxaphosphorine-3-carboxylate 5c in various solvents.

| Method | Reaction conditions | Yields, % | 6c : 7c |
|--------|---------------------|-----------|---------|
|        | Overall | 6c | 7c |               |
| A      | 5 mL spectr. grade CH₃OH, 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 CH₃COOH, 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 \textit{exo,exo}-6,12-dioxyderivatives 6 prevailed in all cases over the non symmetric \textit{exo,endo}-6,12-dioxyderivatives 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. \textit{endo,endo}-6,12-dioxyderivative 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-dietylamino-2-ethoxy-2-oxo-2\texttextit{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\texttextit{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 \textit{anti} head-to-tail, but not \textit{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\texttextit{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. $^1$H-NMR and $^{13}$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 $\delta$ 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-2$H$-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 $\varepsilon$): 5a (MeOH): nm (log $\varepsilon$) = 285 (3.92), 322 (3.38); 5b (MeOH): nm (log $\varepsilon$) = 287 (4.10), 322 (3.56); 5c (MeOH): nm (log $\varepsilon$) = 285 (4.03), 333 (3.34); 5d (MeOH): nm (log $\varepsilon$) = 282 (4.02), 328 (3.36); 5e (MeOH): nm (log $\varepsilon$) = 263 (3.25), 403 (4.11).

Photochemical dimerization of the 3-substituted 2-oxo-2$H$-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: 0.04 g (30%), when the reaction was carried out for 90 days and 0.034 g (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: 0.02 g (14%), when the reaction was carried out for 90 days and 0.028 g (20%), when the reaction was carried out for 40 days, M.p. = 211-213 °C (ether); IR (CHCl₃): v = 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, CHH₂O), 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, CHₙₐHO), 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, ¹₁_CCP=136.8 Hz; ³J_CCCP=6.6 Hz) and 51.35 (dd, ¹₁_CCP=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_CCCCCP=1.7 Hz) and 132.10 (d, ⁴J_CCCCCP=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: 0.03 g (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.

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 (logε) = 270 (s, 3.32), 278 (3.53), 287 (3.60), 303 (s, 3.20).
Diethyl 6a,6b,12a,12b-tetrahydro-2,9-dichloro-exo,exo-6,12-dieothy-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-dieothy-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): $\nu$ = 1740, 1600, 1475, 1270, 1240, 1090, 1020 cm$^{-1}$; $^1$H-NMR (CDCl$_3$) (300 MHz): $\delta$ = 0.93 (t, $J$=7.1 Hz; 3H) / 0.97 (t, $J$=7.1 Hz; 3H) (CH$_3$CH$_2$OCO), 1.18 (t, $J$=7.1 Hz; 3H) and 1.55 (dt, $J$=0.7 and 7.1 Hz; 3H) (CH$_3$CH$_2$OP), 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) (CH$_3$CH$_2$OCO), 4.06-4.27 (m, 2H) / 4.20-4.40 (m, 2H) (CH$_3$CH$_2$OP), 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); $^{13}$C-NMR (CDCl$_3$) (75.4 MHz): $\delta$ = 13.50 / 13.52 (CH$_3$), 16.19 (d, $3^J$CCOP=5.2 Hz) and 16.51 (d, $3^J$CCOP=6.4 Hz) (CH$_3$CH$_2$OP), 42.54 (t, $3^J$CCOP=4.6Hz) and 43.53 (t, $3^J$CCOP=6.3 Hz) (C-6b/C-12b), 50.51 (dd, $1^J$CP=134.8 Hz; $3^J$CCCP=3.7 Hz) and 50.95 (dd, $1^J$CP=136.8 Hz; $3^J$CCCP=6.6 Hz), (C-6a/C-12a), 62.69, 62.78 (CH$_2$O), 64.10 (d, $2^J$CP=8.4 Hz) and 65.88 (d, $2^J$CP=5.6 Hz) (CH$_2$OP), 120.88 (d, $3^J$CCOP=4.6 Hz) and 121.69 (d, $3^J$CCCP=4.6 Hz) (C-4/C-10), 124.22 (dd, $2^J$CCP / $3^J$CCCP=14.1 / 6.0 Hz) and 125.13 (dd, $2^J$CCP / $3^J$CCCP=13.4 / 3.8 Hz) (C-6c/C-12c), 130.24, 130.35 (C-3/C-9), 130.32 (dd, $2^J$CCP=1.7 Hz) and 130.52 (d, $5^J$CCCCP=1.0 Hz) (C-2/C-8), 130.84 (d, $4^J$CCCCP=1.7 Hz) and 131.71 (d, $4^J$CCCCP=1.7 Hz) (C-1/C-7), 149.22 (d, $2^J$CCP=5.4 Hz) and 150.27 (d, $2^J$CCP=8.7 Hz) (C-4a/C-10a), 165.77 (d, $2^J$CCP=2.3 Hz) and 166.32 (dd, $3^J$CCP≈2 and 1.0 Hz) (C=O). – MS: m/z (%) = 636/634/632 (M$^+$, 25), 588/586 (5), 562/561/559 (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, calcld. for C$_{26}$H$_{28}$O$_{10}$Cl$_2$P$_2$ (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 (CHCl$_3$); $\nu$ = 3700, 3480, 1710, 1630, 1595, 15450, 1525, 1250, 1200, 1075, 1040 cm$^{-1}$; $^1$H-NMR (CDCl$_3$) (300 MHz): $\delta$ = 1.27 (t, $J$=7.2 Hz; 3H, CH$_3$), 1.37 (t, $J$=7.1 Hz; 3H) / 1.38 (t, $J$=7.0 Hz; 3H) (CH$_3$CH$_2$OP), 3.20 (m; 2H, CH$_2$NH), 4.21-4.46 (m; 4H, CH$_3$CH$_2$OP), 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); $^{13}$C-NMR (CDCl$_3$) (75.4 MHz): $\delta$ = 14.33 / 14.38 (CH$_3$), 16.42 (d, $1^J$CP=6.6 Hz), 37.75 (CH$_2$NH), (t, $2^J$CCP=4.6Hz) and 43.53 (t) (C-6b/C-12b), 50.51 (d) and 50.95 (dd, $1^J$CP=136.8 Hz; $3^J$CCCP=6.6 Hz), (C-6a/C-12a), 61.29 (CH$_2$O), 64.10 (d, 78).
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2JCOP=6.3 Hz) (CH₂OP), 100.15 (d, 3JCCOP=7.7 Hz) (C-8), 109.10 (d, 1JCp=180.7 Hz) (C-3), 109.20 (C-6), 109.4 (d, 3JCCCP=15.3 Hz) (C-4a), 133.17 (d, 4JCCCCP=1.4 Hz) (C-5), 151.27 (d, 2JCOP=4.9 Hz) (C-4), 153.41 (d, 4JCCCP=1.9 Hz) (C-7), 155.48 (d, 2JCCP=8.2) (C=O), 164.84 (d, 2JCOP=13.7 Hz) (C-8a); Analysis, calcd. for C₁₇H₂₄O₅NP (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 4.0 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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