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Retention of a six-membered ring in the reaction of 2-dialkylaminobenzo[*e*]-1,3,2-dioxaphosphinin-4-ones with pentafluorobenzaldehyde: O,N-exchange at phosphorus

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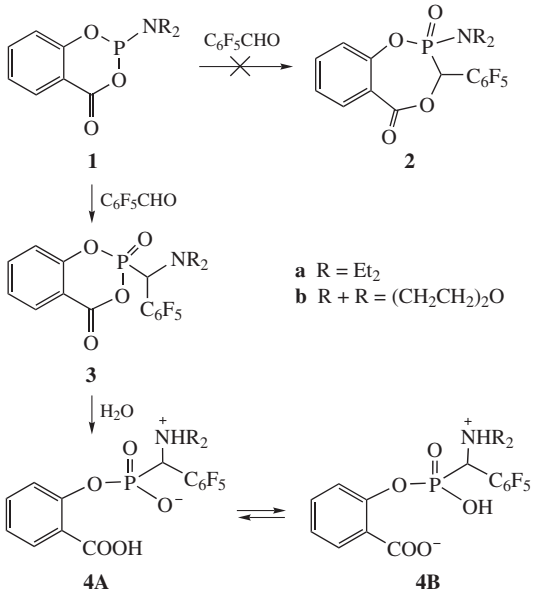
The title reaction leads to the formation of diastereoisomeric 2-[(dialkylamino)(pentafluorophenyl)methyl]benzo[*e*]-1,3,2-dioxaphosphinine-2,4-diones in a ratio of 70 : 30. The configuration of chiral centres for the preferable diastereoisomer was determined by single crystal X-ray diffraction analysis.

2-Alkylbenzo[*d*]-1,3,2-dioxaphosphinin-4-ones containing the reactive fragment P–O–C(O) readily interact with carbonyl compounds and imines containing acceptor substituents with the formation of tetracoordinated phosphorus derivatives – benzo[*e*]-1,3,2(1,4,2)-dioxa(oxaza)phosphepines, seven-membered phosphorus heterocycles.[1–7] Among them are the isosteres of 1,4-benzodiazepine-2,5-diones, which exhibit high biological activity.[8] The method is simple; the process is highly stereoselective, and the starting compounds are available. In some cases, for example, with the use of ethyl trifluoropyruvate and diethyl mesoxalate, spirophosphoranes are formed, and the fragment P–O–C(O) remains unaffected.[9,10]

We found that, unlike chloral,[1,2] ethyl trifluoropyruvate and diethyl mesoxalate, pentafluorobenzaldehyde forms 1,3,2-dioxaphosphinane derivatives **3**† instead of expected benzo[*e*]-1,4,2-dioxaphosphepines **2** in reactions with 2-NR_2-benzo[*d*]-1,3,2-dioxaphosphinin-4-ones **1** (Scheme 1).† In this case, the starting heterocycle remains unchanged, and an unusual O,N-exchange process[11–16] occurs in the course of reaction under mild conditions to afford a P–C bond and a phosphoryl group. The reaction stereoselectivity is ~70%.



Scheme 1

The ^{31}P NMR spectra (CH_2Cl_2) of compounds **3** exhibit characteristic signals with δ_P 11–13 ppm (d, $^2J_{PCH}$ 28.0–29.0 Hz), which corresponds to a P^{IV} derivative containing a P–C bond. Their IR spectra exhibit a characteristic band at 1773–1775 cm^{-1},

† *Synthesis of 2-dialkylaminobenzo[e]-1,2-dioxaphosphinin-4-ones* **1**. Trimethylsilylamine (0.1 mol) was added dropwise to a solution of 0.1 mol of 2-chlorobenzo[*e*]-1,3,2-dioxaphosphinin-4-one in 50 ml of CH_2Cl_2 with bubbling of argon (10 °C). Upon completion of the addition, the solvent and the resulting trimethylchlorosilane were removed *in vacuo*. A mixture of 10 ml of CH_2Cl_2 and 20 ml of pentane was added to the resulting mass, and the mixture was kept at –10 °C for one to three days for the freezing of an amine hydrochloride impurity, which was filtered off in an argon atmosphere. The residue as a viscous yellowish oily substance of 2-R-amino-4-oxobenzo[*e*]-1,2-dioxaphosphinin-4-ones **1** was used without additional purification. ^{31}P NMR spectrum (161.0 MHz, CH_2Cl_2) δ: 137.7 (s, quint., $^3J_{HCNP}$ 10.8 Hz) for **1a**, 133.5 (s, quint., $^3J_{HCNP}$ 7.3 Hz) for **1b**.

Reaction of compound **1a** *with pentafluorobenzaldehyde*. A solution of pentafluorobenzaldehyde (8.48 g, 0.043 mol) in 5 ml of CH_2Cl_2 was added dropwise to a solution of compound **1a** (10.34 g, 0.043 mol) in 10 ml of CH_2Cl_2. After three days, a portion of the solvent was removed, and the residue was kept at 0 °C for a day. The resulting crystals of 2-[(diethylamino)(pentafluorophenyl)methyl]benzo[*e*]-1,3,2-dioxaphosphinine-2,4-dione **3a** were washed with dry diethyl ether and dried; yield, 95%; mp 146–147 °C (main diastereoisomer). IR (Vaseline oil, ν/cm^{-1}): 1775, 1700, 1650, 1605, 1580, 1525, 1500, 1460, 1380, 1305, 1290, 1240, 1200, 1155, 1110, 1060, 1010, 990, 975, 940, 920. ^{31}P NMR (121.4 MHz, CH_2Cl_2) δ: 13.0 (br. d, $^2J_{PCH}$ 28.0 Hz). MS, *m/z*: 435 $[M]^{\bullet+}$. Found (%): C, 51.28; H, 4.04; P, 7.49. Calc. for $C_{18}H_{15}F_5NO_4P$ (%): C, 51.23; H, 3.57; P, 7.39.

Compound **3a** was ground in wet acetone; in this case, the immediate formation of a snow-white precipitate occurred. This precipitate was filtered off, washed with diethyl ether and dried *in vacuo*. The yield of 2-carboxyphenyl[(diethylammonio)(pentafluorophenyl)methyl]phosphonate **4a** was 95%; mp 192–193 °C (DMF). IR (Vaseline oil, ν/cm^{-1}): 3400, 2660–2680, 2450–2550, 1680, 1600, 1510, 1455, 1330, 1300, 1280, 1262, 1220–1230, 1162, 1100, 1090, 1070, 1010, 953, 918, 784, 766, 643, 610, 520. ^1H NMR (400 MHz, DMSO-d_6) δ: 1.22 (t, Me, 6H, $^3J_{HH}$ 7.2 Hz), 3.46 (m, 4H, NCH_2, $^3J_{HH}$ 6.4 Hz), 3.13 (br. m, 1H, NH), 4.97 (d, 1H, PCH, $^2J_{PCH}$ 17.3 Hz), 7.14 [ddd, 1H, H(6), $^3J_{HH}$ 8.1 and 6.2 Hz, $^4J_{HH}$ 2.3 Hz], 7.46 [m, H(7), H(8)], 7.70 [br. d, 1H, H(5), $^3J_{HH}$ 7.4 Hz], 11.41 (ws, 1H, COOH). ^{31}P NMR (161.9 MHz, DMSO-d_6) δ: 3.0 (d, $^2J_{HCP}$ 20.0 Hz). Found (%): C, 47.54; H, 3.87; P, 6.72. Calc. for $C_{18}H_{17}F_5NO_5P$ (%): C, 47.68; H, 3.75; P, 6.84. For ^{13}C NMR spectrum of compound **4a**, see Online Supplementary Materials.