

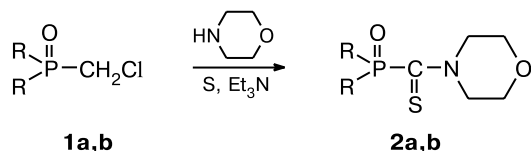
## Functionalization of chloromethylphosphoryl compounds with sulfur in the presence of amines

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It is known<sup>1,2</sup> that a chloromethyl group in tetra-coordinated phosphorus compounds is less reactive than the chloromethyl group in the corresponding carbonyl compounds. However, it turned out that the P-chloromethyl group can be functionalized by treating chloromethylphosphine oxide **1a** or ethyl chloromethylphosphonate **1b** with a previously prepared solution of sulfur, morpholine, and triethylamine in DMF; the above reaction affords morpholides of phosphorylated thioformic acid (**2a,b**). Thus, the chloromethyl fragment at the phosphorus atom was functionalized for the first time with sulfur in the presence of an amine.



R = Ph (**a**), EtO (**b**)

**Diphenylphosphorylthioformic acid morpholide (2a).** A mixture of sulfur (0.55 g, 0.017 mol), triethylamine (1.7 g, 0.017 mol), and morpholine (0.6 g, 0.0068 mol) in 6 mL of DMF was stirred at 20 °C for 30 min, and then chloromethyl(diphenyl)phosphine oxide (**1a**)<sup>1</sup> (1.5 g, 0.0057 mol) was added with stirring. The reaction mixture was kept at 60 °C for 9 h, cooled, and diluted with water (10 mL). The precipitate that formed was filtered off, dried in air, dissolved in 50 mL of acetone, and filtered. The solvent was removed, and the residue was recrystallized from acetone to give compound **2a** (1.2 g, 63%), m.p. 150–151 °C. Found (%): C, 61.38; H, 5.68; N, 4.48; P, 9.62; S, 9.41. C<sub>17</sub>H<sub>18</sub>NO<sub>2</sub>PS. Calculated (%): C, 61.63; H, 5.43; N, 4.23; P, 9.37; S, 9.67. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>), δ: 3.45 (m, 2 H, morpholine ring); 3.70 (m, 2 H, morpholine ring); 4.25 (m, 2 H, morpholine ring); 4.46 (m, 2 H, morpholine ring); 7.50–7.70 (m, 10 H, Ph). <sup>13</sup>C NMR (DMSO-d<sub>6</sub>), δ: 50.53

(s, NCH<sub>2</sub>); 52.90 (s, NCH<sub>2</sub>); 65.96 (s, OCH<sub>2</sub>); 66.16 (s, OCH<sub>2</sub>); 128.61 (d, *o*-C<sub>Ph</sub>, <sup>2</sup>J<sub>31P,13C</sub> = 12.5 Hz); 131.65 (d, *m*-C<sub>Ph</sub>, <sup>3</sup>J<sub>31P,13C</sub> = 9.4 Hz); 131.68 (d, *ipso*-C<sub>Ph</sub>, <sup>1</sup>J<sub>31P,13C</sub> = 109.2 Hz); 132.35 (d, *p*-C<sub>Ph</sub>, <sup>4</sup>J<sub>31P,13C</sub> = 2.2 Hz); 194.71 (d, C=S, <sup>1</sup>J<sub>31P,13C</sub> = 89.95 Hz). <sup>31</sup>P NMR (DMSO-d<sub>6</sub>), δ: 29.85 (P=O). MS, *m/z*: 331 [M]<sup>+</sup>.

**Diethoxyphosphorylthioformic acid morpholide (2b).** A mixture of sulfur (1 g, 0.03 mol), triethylamine (3 g, 0.03 mol), and morpholine (1.05 g, 0.012 mol) in 8 mL of DMF was stirred at 20 °C for 30 min, and then chloromethyl(diethoxy)phosphine oxide (**1b**)<sup>1</sup> (1.86 g, 0.01 mol) was added with stirring. The reaction mixture was kept at 40 °C for 12 h, cooled, and diluted with water (20 mL). The unreacted sulfur was filtered off. The solution was acidified to pH 3, and the product was extracted with chloroform (20 mL). The organic layer was washed with aqueous sodium carbonate and water and dried over Na<sub>2</sub>SO<sub>4</sub>. The product as a thick oil was isolated by column chromatography on silica gel (EtOAc—light petroleum as the eluent with a concentration gradient from 10 to 30% EtOAc). The yield of compound **2b** was 0.3 g (10%). Found (%): C, 40.28; H, 6.34; N, 5.12; P, 11.21; S, 12.46. C<sub>9</sub>H<sub>18</sub>NO<sub>4</sub>PS. Calculated (%): C, 40.45; H, 6.74; N, 5.24; P, 11.61; S, 12.00. <sup>1</sup>H NMR (DMSO-d<sub>6</sub>), δ: 1.30 (t, 6 H, CH<sub>3</sub>, *J* = 7.0 Hz); 3.70 (m, 4 H, morpholine); 4.15 (q, 4 H, CH<sub>2</sub>, *J* = 7.05 Hz); 4.22 (m, 4 H, morpholine). MS, *m/z*: 267 [M]<sup>+</sup>.

### References

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