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A Novel Fused Phosphorus Heterocycle: 4-(1′, 2′, 3′, 4′-Tetrahydro-1, 3, 2-benzodiazaphosphorin-2′-sulfide)-3, 4b, 4a-thiazphosphaphenanthridine Derivative

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Abstract: The first example of fused phosphorus heterocyclic 4-[1′-(*b*-bromoethyl)-4′-oxo-3′-propyl-1′, 2′, 3′, 4′-tetrahydro-1, 3, 2-benzodiazaphosphorin-2′-sulfide]-1, 2, 3, 4, 4a, 4b, 5, 6-octahydro-6-oxo-5-propyl-3, 4b, 4a-thiazphosphaphenanthridine 4a, 2′-dioxide was synthesized in excellent yield by refluxing a mixture of 1-(2-bromoethyl)-2, 3-dihydro-3-propyl-1, 3, 2-benzodiazaphosphorin-4(1*H*)-one 2-oxide with carbon disulfide in benzene in the presence of triethylamine.

Keywords: Synthesis, [3, 4b, 4a] thiazphosphaphenanthridine.

Organophosphorus compounds are ubiquitous in nature and they have broad applications in the fields of agriculture and medicine[1-4]. There has been a considerably growing interest in heterocyclic compounds due to their pharmaceutical importance and extensive application in organic synthesis, and the application of heterocycles is suggested to enhance the biological activity and/or offer other diverse properties[5-7]. In the previous work[8], we have reported that 11-ethoxycarbonylmethyl-6-oxo-3, 4, 6, 11-tetrahydro-1-thio-[1, 4, 3] thiazaphosphorino [3, 4-b][1, 3, 2] benzodiazaphosphorine 12-oxide **2** was synthesized by the addition and ring-closure reaction of 3-(2-chloroethyl)-2, 3-dihydro-1-ethoxycarbonylmethyl-1, 3, 2-benzodiazaphosphorin-4(1*H*)-one 2-oxide **1** with carbon disulfide in the presence of sodium hydride, as shown in **Scheme 1**, which also afforded 1, 1-bisspiro{11-ethoxycarbonylmethyl-6-oxo-3, 4, 6, 11-tetrahydro-[1, 4, 3] thiazaphosphorino [3, 4-b][1, 3, 2] benzodiazaphosphorine 12-oxide} **3** at the same time in a one-pot procedure, and the mechanism was outlined in **Scheme 2**.

Herein, we wish to report our further investigation on the reaction of 3-alkyl-1-(2-bromoethyl)-2, 3-dihydro-1, 3, 2-benzodiazaphosphorin-4(1*H*)-one 2-oxide **4** with carbon disulfide. Preparation of **4** was readily accomplished in a four-step sequence outlined in **Scheme 3** starting from the cheap and available material *o*-aminobenzoic acid. In the presence of triethylamine, **4a**[9] (R = *n*-Pr) was refluxed with carbon disulfide in benzene, which gave fused phosphorus heterocyclic 4-[1′-(*b*-bromoethyl)-4′-oxo-3′-propyl-1′, 2′, 3′, 4′-tetrahydro-1, 3, 2-benzodiazaphosphorin-2′-sulfide]-1, 2, 3, 4, 4a, 4b, 5, 6-octahydro-6-oxo-5-propyl-3, 4b, 4a-thiazphosphaphenanthridine 4a, 2′-

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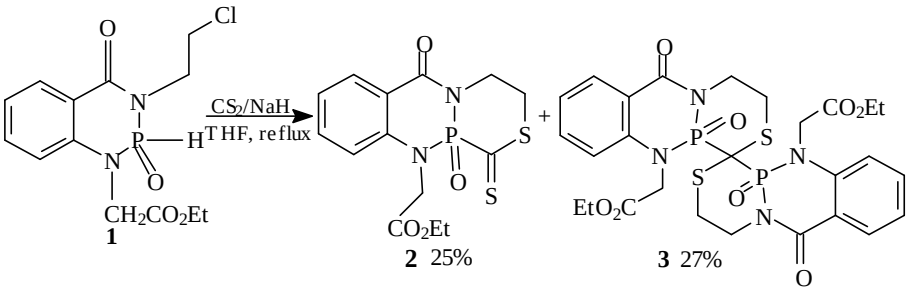
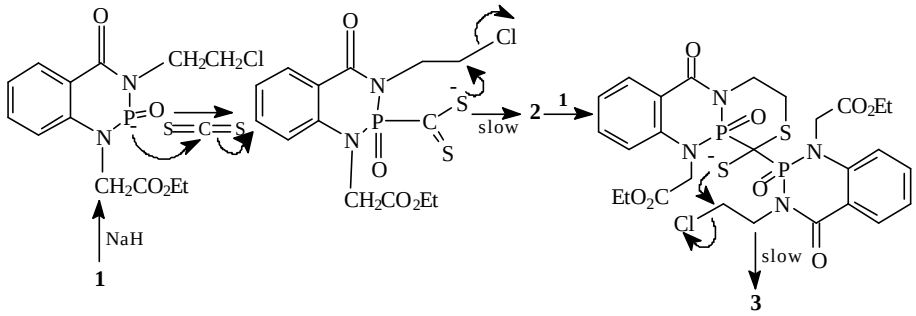
dioxide **5a**[10] in 89% yield, as shown in **Scheme 4**. This is the first example for such a reaction.

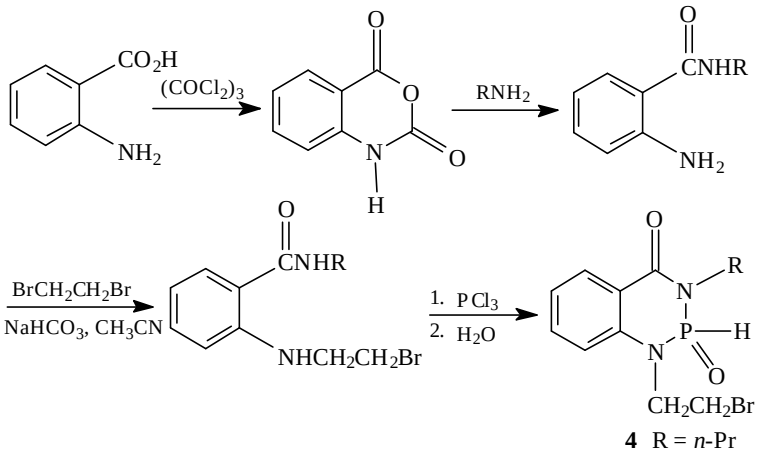
Scheme 1



Scheme 2



Scheme 3



4 R = *n*-Pr

Scheme 4

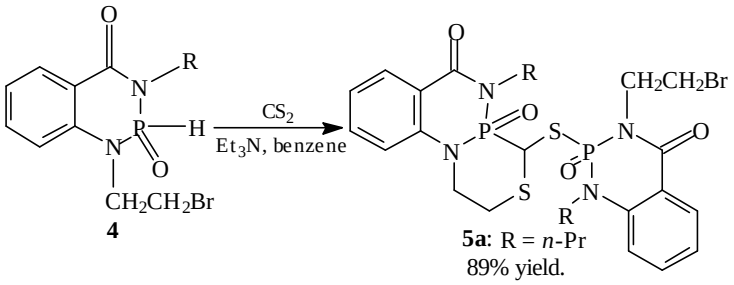
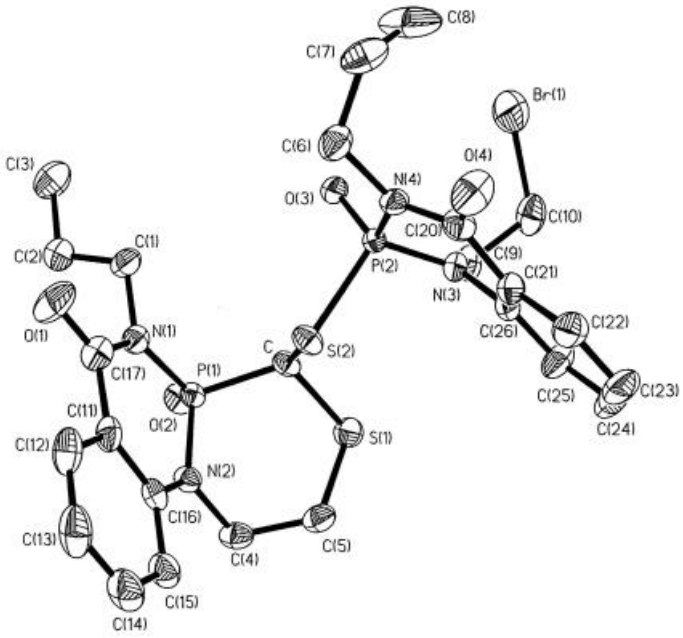


Figure 1 The molecular structure of compound **5a** by single crystals X-ray-analysis



General Procedure for the Preparation of **5**: A mixture of 3.0 mmol of **4**, 3.2 mmol of carbon disulfide and 6.0 mmol of dry triethylamine in 20 mL of anhydrous benzene was heated at reflux till the spot of **4** disappeared on silica gel TLC developed with the solvent of ethyl acetate/petroleum ether (2:1), then the produced triethylamine hydrobromide was filtered off. The solvent from the filtrate was removed under reduced pressure and the residue was chromatographed on a column of silica gel using a mixture of 60% ethyl acetate/petroleum ether (60-90°C) to elute the products **5** in excellent yield. The single crystals of **5a** suitable X-ray analysis were obtained by recrystallization from mixture solvent of ethyl acetate and petroleum ether (90 - 120°C).

The structure of the compound **5a** was determined by X-ray crystallography and is shown in **Figure 1**. The fused phosphorus heterocyclic **5** has a (O)P-S-C-P(O) bond structure with special consideration given to the biological activity[7,11], in which the

phosphoryl group is of fundamental significance in many of important molecules that control molecular replication, cell biochemistry and metabolic processes in all living species[12]. The synthesis of further examples of this ring system and study of their chemistry is in progress.

Acknowledgments

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References and Notes

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9. **4a**: R = *n*-Pr, mp 82 - 84°C. ^{1}H NMR ($CDCl_3$, 200 MHz, δ_{ppm}): 0.96 (t, 3H, $NCH_2CH_2C\mathbf{H}_3$, $^3J_{HH}$ = 7.4 Hz), 1.77 (m, 2H, $NCH_2C\mathbf{H}_2CH_3$), 3.55 - 4.12 (m, 6H, $PNC\mathbf{H}_2CH_2CH_3$ + $PNC\mathbf{H}_2C\mathbf{H}_2Br$), 6.90 - 8.26 (m, 4H, $C_6\mathbf{H}_4$), 7.86 (d, 1H, P (O)**H**, $^1J_{PH}$ = 645.9 Hz). ^{31}P NMR ($CDCl_3$, 80.96 MHz, δ_{ppm}): 5.95 (s). Anal. calcd. for $C_{12}H_{16}BrN_2O_2P$: C 43.52, H 4.87, N 8.46; found: C 43.68, H 5.05, N 8.66.
10. **5a**: R = *n*-Pr, 89% yield, mp 192°C (dec.). ^{1}H NMR ($CDCl_3$, 200 MHz, δ_{ppm}): 0.96 (m, 6H, 2×$NCH_2CH_2C\mathbf{H}_3$), 1.74 (m, 4H, 2×$NCH_2C\mathbf{H}_2CH_3$), 2.47 (dm, 1H, 1/2×$SC\mathbf{H}_2CH_2N$, $^2J_{HH} \approx$ 13 Hz), 3.07 (tm, 1H, 1/2×$SC\mathbf{H}_2CH_2N$, $^2J_{HH} \approx {}^3J_{HH} \approx$ 13 Hz), 3.35 - 4.66 (m, 10H, 2× $NC\mathbf{H}_2CH_2CH_3$ +$SCH_2C\mathbf{H}_2N$+$NC\mathbf{H}_2C\mathbf{H}_2Br$), 4.80 (dd, 1H, C**H**, $^2J_{PH}$ = 17.7 Hz, $^3J_{PH}$ = 14.6 Hz), 6.84 - 8.22 (m, 8H, 2×$C_6\mathbf{H}_4$). ^{31}P NMR ($CDCl_3$, 80.96 MHz, δ_{ppm}): 10.17 (d), 24.45 (d), $^3J_{PP}$ = 31.6 Hz. Anal. calcd. for $C_{25}H_{31}BrN_4O_4P_2S_2$: C 45.67, H 4.75, N 8.52; found: C 45.58, H 4.72, N 8.65.
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