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AN AMIDINE MOIETY AS AN N-NUCLEOPHILIC EXO GROUP FOR CONSTRUCTING CONDENSED PHOSPHORUS-CONTAINING HETEROCYCLIC SYSTEMS

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The use of an amidine group to construct condensed phosphorus-containing benzazaphosphole [1] and pyrazolodiazaphosphinine [2] systems was demonstrated earlier. In the first case, heterocyclization occurs through a step involving phosphorylation of the formamidine carbon atom; in the second case, annelation was the result of nucleophilic substitution at the formamidine carbon atom. It was also suggested earlier that N-phosphorylated arylamidines might be used for synthesis of a benzodiazaphosphinine system, but this hypothesis was not rigorously confirmed experimentally [3]. In this work, we have studied the possibility of constructing a condensed phosphorus-containing heterocyclic system using the NH of the amidine functional group. In this case, phosphorylation occurs at the imino group of the isoindole moiety and then at the C-nucleophilic center of the benzene ring, which is consistent with the properties of unsubstituted N,N-dimethylaniline with respect to phosphorus(III) halides [4]. Reaction of the object of investigation **1** with phosphorus(III) chlorides in pyridine medium in the presence of triethylamine leads to formation of a novel type of condensed phosphorus-containing heterocyclic system, 5,11-dihydroisoindolo[1,2-*c*][2,4,1]benzodiaza-phosphinine (Scheme 1).

As a result of reaction with $PhPCl_2$, we obtained compound **2**, which is stable in air. Upon reaction with PCl_3, the cyclic acid chloride **3** is formed; this was not isolated because of its low thermal stability, but its formation was confirmed by conversion to phosphorus(V) derivatives **4** and **5** which are stable in air. We could not carry out analogous transformations with PBr_3; this is probably connected with interaction of the highly reactive phosphorylating agent with the acidic CH_2 group of the dihydroisoindole.

The structure of compounds **2**, **4**, and **5** were confirmed by ^{31}P and ^{1}H NMR spectroscopy; the structure of compound **5** was also confirmed by ^{13}C NMR and mass spectroscopy. The most characteristic evidence for ring formation in the ^{1}H NMR spectrum is the disappearance of the signal from the proton in the 4 position in the dimethylaniline ring at 6.81 ppm and the signal from the NH group at 6.74 ppm, as well as splitting of the signal from carbon atom 4a in compound **5** with constant J_{CP} = 116.8 Hz.

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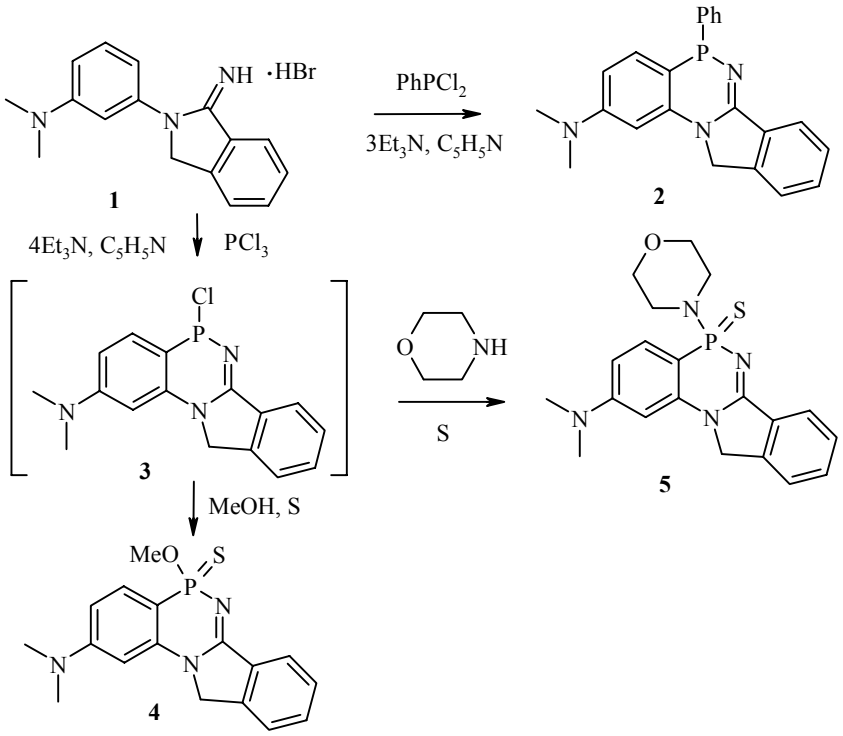
Scheme 1



2-[3-(N,N-Dimethylamino)phenyl]-1-imino-2,3-dihydro-2H-isoindole Hydrobromide (1). Obtained according to the familiar procedure in [5]; mp 223°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.03 (6H, s, CH_3); 5.27 (2H, s, CH_2); 6.66 (1H, d, CH); 6.68 (1H, d, CH); 6.74 (1H, s, NH); 6.81 (1H, dd, CH); 7.40 (1H, t, CH); 7.55 (1H, t, CH); 7.65-7.73 (2H, m, CH); 9.10 (1H, d, CH); 11.32 (1H, s, HBr).

2-(N,N-Dimethylamino)-5-phenyl-5,11-dihydroisoindolo[1,2-*c*][2,4,1]benzodiazaphosphinine (2). $PhPCl_2$ (0.41 ml, 3.01 mmol) and triethylamine (1.26 ml, 9.03 mmol) were added with stirring to a suspension of compound **1** (1 g, 3.01 mmol) in pyridine (30 ml). After 2 days, the pyridine was evaporated off and the residue was recrystallized from absolute methanol. Yield 0.76 g (71%); mp 263-265°C. ^{31}P NMR spectrum (C_5H_5N), δ, ppm: 7.4 (1P); 13.8 (3P). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.96 s/3.05 s (1:3, 6H, CH_3); 4.99 s/5.27 s (1:3, 2H, CH_2); 6.23-6.71 (2H, m, CH); 7.00-7.93 (10H, m, CH). Most likely, compound **2** exists as a mixture of two diastereomers, which are also detected in the ^{1}H and ^{31}P NMR spectra. Found, %: N 11.6; P 8.7. $C_{22}H_{20}N_3P$. Calculated, %: N 11.7; P 8.7.

2-(N,N-Dimethylamino)-5-methoxy-5,11-dihydro-5λ^5-isoindolo[1,2-*c*][2,4,1]benzodiazaphosphinine-5-thioxide (4). PCl_3 (0.13 ml, 1.51 mmol) and triethylamine (0.84 ml, 6.02 mmol) were added with stirring to a suspension of compound **1** (0.5 g, 1.51 mmol) in pyridine (30 ml); this mixture was allowed to stand for 2 days, then methanol (0.04 ml, 1.51 mmol) and sulfur (0.044 g, 1.51 mmol) were added. This was stirred until the sulfur dissolved. The pyridine was evaporated off and the residue was triturated with water and then recrystallized from acetone. Yield 0.37 g (72%); mp 303°C. ^{31}P NMR spectrum (DMSO), δ, ppm: 60.2. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J*, Hz: 3.06 (6H, s, CH_3); 3.51 (3H, d, J_{POCH} = 13, OCH_3); 5.24 (2H, s, CH_2); 6.34 (1H, d, CH); 6.79 (1H, d, CH): 7.38-7.59 (4H, m, CH); 7.84 (1H, d, CH). Found, %: N 11.7; P 8.6; S 9.5. $C_{17}H_{18}N_3OPS$. Calculated, %: N 12.2; P 9.0; S 9.3.

2-(N,N-Dimethylamino)-5-morpholino-5,11-dihydro-5λ^5-isoindolo[1,2-*c*][2,4,1]benzodiazaphosphinine-5-thioxide (5). PCl_3 (0.13 ml, 1.51 mmol) and triethylamine (0.84 ml, 6.02 mmol) was added with stirring to a suspension of compound **1** (0.5 g, 1.51 mmol) in pyridine (30 ml). This was allowed to stand for 2 days. Then

morpholine (0.13 ml, 1.51 mmol) and sulfur (0.044 g, 1.51 mmol) were added. The mixture was stirred until the sulfur dissolved. The pyridine was evaporated off and the residue was triturated with water, then recrystallized from acetone. Yield 0.35 g (60%); mp 262°C. M^+ 398. ^{31}P NMR spectrum ($CHCl_3$) δ, ppm: 49.5. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 3.02 (6H, s, CH_3); 3.14 (2H, m, CH_2); 3.26 (2H, m, CH_2); 3.60 (4H, t, CH_2); 4.87 (2H, d, CH_2); 6.05 (1H, d, CH); 6.48 (1H, d, CH); 7.47-7.62 (4H, m, CH); 8.00 (1H, d, CH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm, *J*, Hz: 40.12 (s, $N(\underline{C}H_3)_2$); 44.99 (s, $N(\underline{C}H_2CH_2)_2O$); 51.61 (s, 11-C); 67.45 (d, $N(CH_2\underline{C}H_2)_2O$); 94.53 (d, 1-C); 101.21 (d, J_{CP} = 116.8, 4a-C); 109.95 (d, 3-C); 122.41 (s, 7-C); 124.08 (s, 10-C); 128.39 (s, 8-C): 132.00 (s, 9-C); 132.38 (d, 4-C); 134.45 (d, 6b-C); 139.26 (s, 10a-C); 141.21 (d, 12a-C); 152.68 (s, 2-C); 157.52 (d, 6a-C). Found, %: N 13.5; P 7.3; S 8.6. $C_{20}H_{23}N_4OPS$. Calculated, %: N 14.1; P 7.8; S 8.1.

REFERENCES

1. A. A. Tolmachev, A. S. Merkulov, and G. V. Oshovsky, *Khim. Geterotsikl. Soedin.*, 1000 (1997).
2. G. V. Oshovsky, A. M. Pinchuk, and A. A. Tolmachev, *Mendeleev Commun.*, **9**, 4, 161 (1999).
3. G. S. Borovikova, I. S. Tsymbal, E. S. Levchenko, and E. I. Borovik, *Zh. Org. Khim.*, **20**, 1784 (1984).
4. M. Bourneuf, *Bull. Soc. Chim. Fr. Memor.,* Ser. 4, **33**, 808 (1923).
5. F. S. Babichev and V. A. Kovtunenko, *The Chemistry of Isoindole* [in Russian], Nauk. Dumka, Kiev (1983), p. 21.