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Reaction of 1-Alkyl(aryl)-5-alkyl(aryl)amino-2-oxo-2,3-dihydro-1*H*-imidazole-4-carbonitriles with Lawesson's Reagent

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Abstract—The reaction of substituted 2-oxo-2,3-dihydro-1*H*-imidazole-4-carbonitriles with Lawesson's reagent gave new compounds of the fused imidazo[4,5-*d*][1,3,2]diazaphosphinine system.

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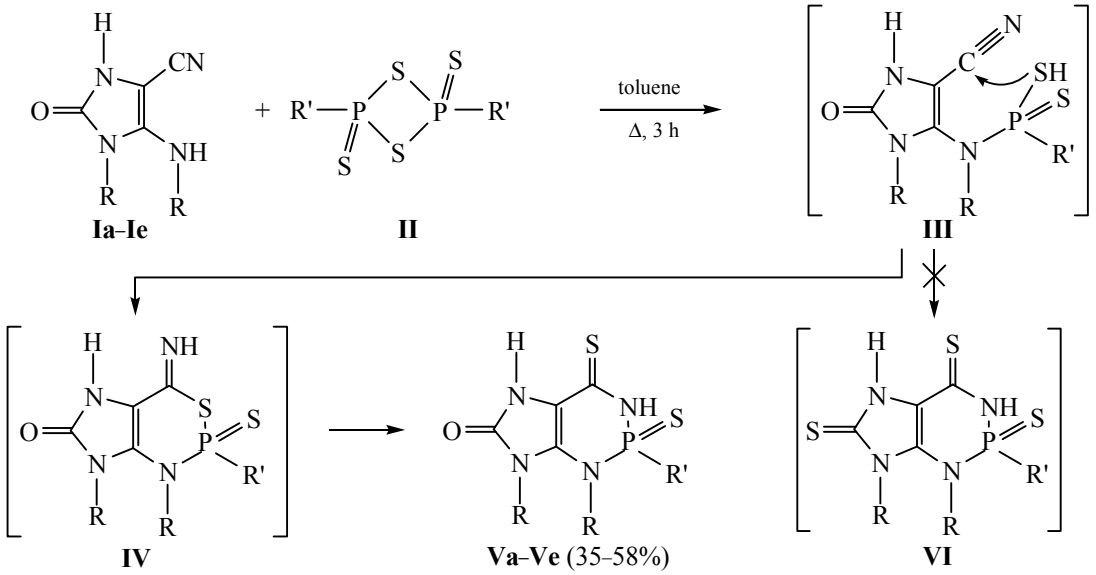
We previously described a simple and convenient procedure for the synthesis of 1-alkyl(aryl)-5-alkyl-(aryl)amino-2-oxo-2,3-dihydro-1*H*-imidazole-4-carbonitriles **I** [1] on the basis of accessible acrylonitrile derivatives [2]. These compounds have already found wide application in the syntheses of many other heterocyclic systems [3–10]. In the present work we studied the reaction of substituted imidazol-2-ones **I** with Lawesson's reagent (**II**) which is known as mild and efficient sulfurizing agent. We found that heating of compounds **I** and **II** in toluene over a period of 3 h yields imidazodiazaphosphinines **V** rather than their thio derivatives **VI** (Scheme 1).

It should be noted that even fourfold excess of Lawesson's reagent very slowly replaces the oxo group in the imidazole fragment by thioxo. After prolonged (~10 h) heating of the reaction mixture, we succeeded in detecting only ~4% of thioxo analog **VI** by GC–MS. Several examples of sulfurization of imidazolones and their analogs with Lawesson's reagent have been reported [11–13]; on the other hand, in same cases the

Scheme 1.



Ia–**Ie** **II** **III** **IV** **Va**–**Ve** (35–58%) **VI**

I, V: R = $PhCH_2$ (**a**), $PhCH_2CH_2$ (**b**), Ph (**c**),4-MeC_6H_4 (**d**), 4-$MeOC_6H_4$ (**e**); R' = 4-$MeOC_6H_4$.

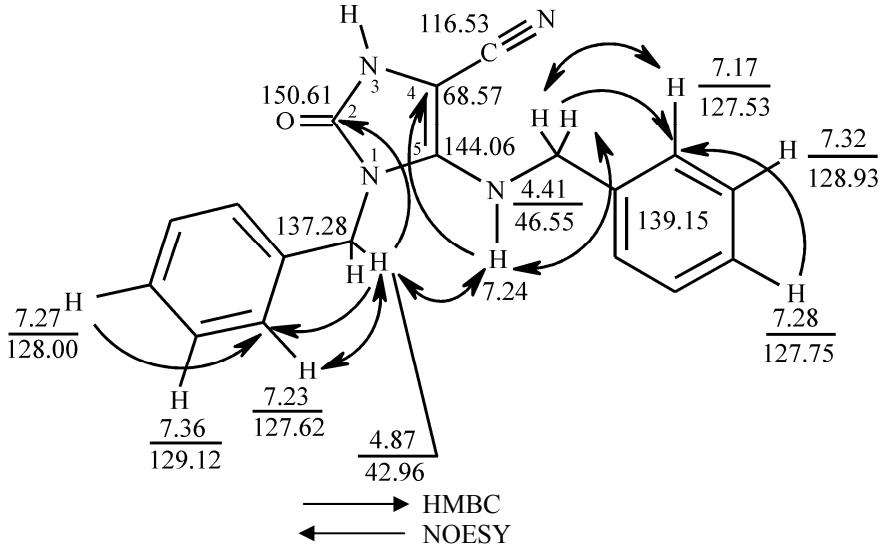


Fig. 1. Principal correlations (shown with arrows) and signal assignment (δ, δ_C, ppm) in the ^{1}H and ^{13}C NMR spectra of compound **Ia**.

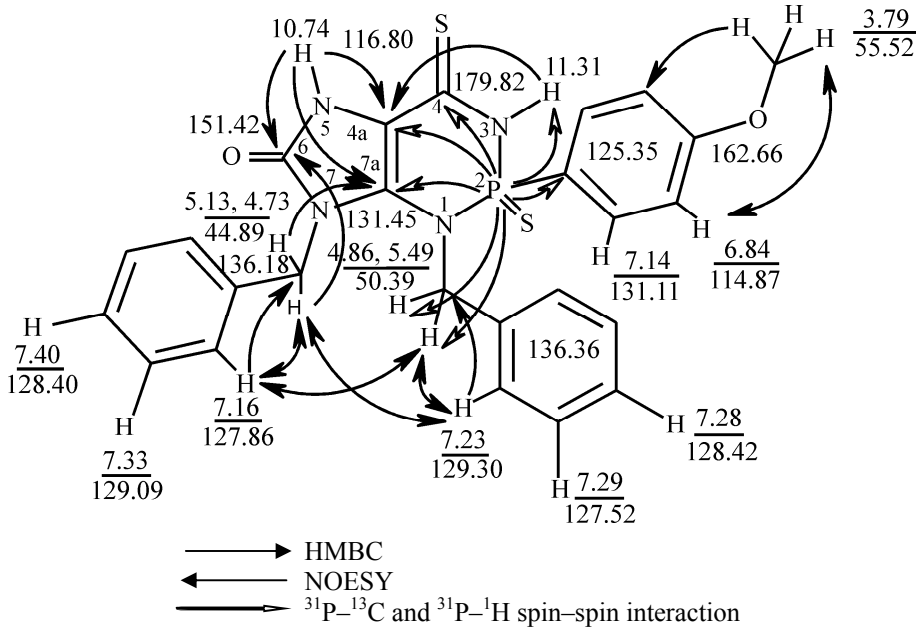


Fig. 2. Principal correlations (shown with arrows) and signal assignment (δ, δ_C, ppm) in the ^{1}H and ^{13}C NMR spectra of compound **Va**.

carbonyl group was resistant to that reagent [14–17]. The use of a more potent sulfurizing agent, phosphorus pentasulfide, in the reaction with imidazolones **I** resulted in the formation of a complex mixture of products which we failed to isolate and identify.

Compounds **Va**–**Ve** are new representatives of already known imidazodiazaphosphinine system [18, 19]. By analogy with the data of [20], where the formation of diazaphosphinine ring from β-aminonitrile fragment and Lawesson's reagent was described, compounds **Va**–**Ve** are likely to be formed via phosphorylation of the nitrogen atom to give derivative **III** and its subsequent cyclization as a result of addition of the HS fragment at the cyano group. Intermediates **IV** thus formed undergo fast rearrangement into final products **V**.

The structure of **Va**–**Ve** was confirmed by their elemental compositions and mass, IR, and NMR spectra. In the IR spectra of **Va**–**Ve**, as well as in the spectra of initial compounds **Ia**–**Ie**, we observed strong carbonyl absorption in the region 1715–1724 cm^{-1}.

Table 1. Correlations found in the COSY, NOESY, HSQC, and HMBC spectra of compound **Ia**[a]

^{1}H, δ, ppm	^{1}H, δ, ppm		^{13}C, δ_C, ppm	
	COSY	NOESY	HSQC	HMBC
7.23	7.36	7.36, 4.87	127.62	128.00, 127.62, 42.96
7.36	7.23, 7.27	7.23, 7.27	129.12	129.12, 137.28
7.27	7.36	7.36	128.00	127.62
4.87	–	7.23, 7.24	42.96	137.28, 127.62, 150.61, 144.06
4.41	7.24	7.24, 7.17	46.55	139.15, 127.53, 144.06
7.24	4.41	4.41, 4.87	–	68.57
7.17	7.32	7.32, 4.41	127.53	127.53, 127.75, 46.55
7.32	7.17, 7.28	7.17, 7.28	128.93	128.93, 139.15
7.28	7.32	7.32	127.75	127.53

[a] For signal assignment, see Fig. 1.

Table 2. Correlations found in the COSY, NOESY, HSQC, and HMBC spectra of compound **Va**[a]

^{1}H, δ, ppm	^{1}H, δ, ppm		^{13}C, δ_C, ppm	
	COSY	NOESY	HSQC	HMBC
10.74	–	–	–	116.80, 131.45, 151.42
11.31	–	–	–	116.80
5.13	4.73	4.73, 7.16	44.89	151.42, 136.18, 131.45, 127.86
4.73	5.13	5.13, 7.16, 7.23	44.89	151.42, 136.18, 127.86
5.49	4.86	4.86, 7.23	50.39	–
4.86	5.49	5.49, 7.16, 7.23	50.39	–
7.14	6.84	6.84	131.11	131.11, 162.66
6.84	7.14	7.14	114.87	114.87, 125.35
3.79	–	6.84	55.52	114.87
7.23	7.29	7.29, 4.86, 4.73	129.30	129.30, 50.39, 128.42
7.29	7.23, 7.28	7.23, 7.28	127.52	127.52
7.28	7.29	7.29	128.42	129.30
7.16	7.33	7.33, 4.86, 4.73	127.86	127.86, 128.40, 44.89
7.33	7.16, 7.40	7.16, 7.40	129.09	129.09
7.40	7.33	7.33	128.40	127.86

[a] For signal assignment, see Fig. 2.

Their ^{13}C NMR spectra characteristically displayed a signal at δ_c 150.73–151.42 ppm (cf. δ_C 150.61 for **Ia**; Figs. 1, 2; see Experimental). These findings indicate that the imidazolone fragment does not change during the transformation. The formation of diazaphosphinine ring follows from the ^{1}H NMR spectra. The N^{3}H signal in the spectra of **Va**–**Ve** is split due to coupling with the phosphorus nucleus ($^2J_{HP}$ = 14.0–15.0 Hz), and protons in the methylene group on N^1 in compounds **Va** and **Vb** appear as multiplets due to additional coupling with the phosphorus nucleus. However, the formation of imidazodiazaphosphinine system was unambiguously proved by two-dimensional homo- and heteronuclear (NOESY, COSY, HSQC, HMBC) NMR experiments performed for compounds **Ia** and **Va**. The principal correlations and assignments of ^{1}H and ^{13}C

signals are shown in Figs. 1 and 2, and their complete list is presented in Tables 1 and 2, respectively. The presence of the following cross peaks in the HMBC spectrum of **Va** (Fig. 2) casts no doubts on the assumed structure (δ, δ_C, ppm): N^5H (10.74)–C^{4a} (116.80), N^3H (11.31)–C^{4a} (116.80), N^7CH_2 (5.13, 4.73)–C^6 (151.42), N^7CH_2 (5.13, 4.73)–C^{7a} (131.45), N^5H (10.74)–C^{7a} (131.45). The information obtained from the two-dimensional spectra is supplemented by the ^{31}P–^{13}C spin–spin coupling constants: (S)C^4 J = 7.0 Hz; C^{4a}, J = 8.7 Hz; C^{7a}, J 5.0 Hz.

EXPERIMENTAL

The IR spectra were recorded in KBr on a Bruker Vertex 70 spectrometer. The ^1H, ^{13}C, and ^{31}P NMR spectra were measured on a Bruker Avance DRX-500 instrument at 500.07, 125.76, and 202.43 MHz, respectively, from solutions in DMSO-d_6; the chemical shifts are given relative to tetramethylsilane (^1H, ^{13}C, internal reference) or 85% phosphoric acid (external reference). The mass spectra were run on an Agilent 1100 Series high-performance liquid chromatograph (diode array) coupled with an Agilent LC\MSD SL mass-selective detector [4.6×15-mm Zorbax SB-C18 column, grain size 1.8 μm, PN 821975–932; liquid phases: acetonitrile–water (95:5 + 0.1% of trifluoroacetic acid (A), 0.1% aqueous trifluoroacetic acid (B); flow rate 3 ml/min; injection volume 1 μl; UV detectors, λ 215, 254, 285 nm; atmospheric pressure chemical ionization, amu range 80–1000]. The melting points were determined on a Fisher–Johns melting point apparatus.

1-Alkyl(aryl)-5-alkyl(aryl)amino-2-oxo-2,3-dihydro-1*H*-imidazole-4-carbonitriles **Ia–Id** were reported previously [1].

1-(4-Methoxyphenyl)-5-(4-methoxyphenylamino)-2-oxo-2,3-dihydro-1*H*-imidazole-4-carbonitrile (Ie) was synthesized as described in [1] for compounds **Ia–Id**. Yield 72%, mp 205–207°C (from benzene). IR spectrum, ν, cm^{-1}: 1711 (C=O), 2209 (CN), 3264–3325 (NH). ^1H NMR spectrum, δ, ppm: 3.69 s (3H, CH_3), 3.77 s (3H, CH_3), 6.79 d and 6.92 d (2H each, H_{arom}, $^3J_{HH}$ = 8.5 Hz), 7.00 d and 7.28 d (2H each, C_6H_4, $^3J_{HH}$ = 8.5 Hz), 7.91 s (1H, NH), 10.61 s (1H, NH). Found, %: C 64.11; H 4.61; N 16.78. *m*/*z* 335, 337 $[M]^+$. $C_{18}H_{16}N_4O_3$. Calculated, %: C 64.28; H 4.79; N 16.66. *M* 336.

1,7-Dialkyl(diaryl)-4-thioxo-2-(4-methoxyphenyl)-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*][1,3,2λ^5]-diazaphosphinin-6-one 2-sulfides Va–Ve (*general procedure***).** Compound **Ia–Ie**, 10 mmol, was dispersed in 50 ml of toluene, 7 mmol of Lawesson's reagent was added, and the mixture was heated for 3 h under reflux. The mixture was cooled, the solvent was removed under reduced pressure, the residue was treated with 10 ml of ethyl acetate, and the precipitate was filtered off, washed first with ethyl acetate (2×10 ml) and then with diethyl ether (20 ml), and recrystallized from ethyl acetate.

1,7-Dibenzyl-2-(4-methoxyphenyl)-4-thioxo-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*][1,3,2λ^5]-diazaphosphinin-6-one 2-sulfide (Va). Yield 55%, mp 127–129°C. IR spectrum, ν, cm^{-1}: 1722 (C=O), 3226 (NH). The ^1H and ^{13}C NMR data are given in Table 2. ^{31}P NMR spectrum: δ_P 58.5 ppm. Found, %: C 59.14; H 4.72; N 11.17; P 6.00; S 12.84. *m*/*z* 505, 507 $[M]^+$. $C_{25}H_{23}N_4O_2PS_2$. Calculated, %: C 59.27; H 4.58; N 11.06; P 6.11; S 12.66. *M* 506.

2-(4-Methoxyphenyl)-4-thioxo-1,7-bis(2-phenylethyl)-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*]-[1,3,2λ^5]diazaphosphinin-6-one 2-sulfide (Vb). Yield 38%, mp 185–187°C. IR spectrum, ν, cm^{-1}: 1719 (C=O), 3269 (NH). ^1H NMR spectrum, δ, ppm: 2.61–2.64 m (1H, CH_2), 2.90–2.93 m (1H, CH_2), 2.97 m (2H, CH_2), 3.71 m (1H, CH_2), 3.77 s (3H, CH_3), 3.88–3.94 m (1H, CH_2), 4.02 m (1H, CH_2), 4.45 m (1H, CH_2), 6.86 m (2H, H_{arom}), 7.03–7.29 m (10H, H_{arom}), 7.60 m (2H, H_{arom}), 10.51 s (1H, NH), 11.09 d (1H, NH, $^2J_{HP}$ = 15.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 34.09, 36.41, 43.06, 49.01, 55.96, 114.89, 115.01, 116.28, 116.35, 125.12, 126.22, 126.96, 127.10, 128.81, 128.94, 129.00, 129.08, 131.51, 131.63, 131.72, 131.76, 137.94, 137.96, 150.97, 162.95, 162.98, 179.63, 179.73. ^{31}P NMR spectrum: δ_P 56.3 ppm. Found, %: C 60.48; H 5.01; N 10.62; P 5.89; S.78. *m*/*z* 533, 535 $[M]^+$. $C_{27}H_{27}N_4O_2PS_2$. Calculated, %: C 60.66; H 5.09; N 10.48; P 5.79; S.99. *M* 534.

2-(4-Methoxyphenyl)-4-thioxo-1,7-diphenyl-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*][1,3,2λ^5]-diazaphosphinin-6-one 2-sulfide (Vc). Yield 35%, mp 155–157°C. IR spectrum, ν, cm^{-1}: 1715 (C=O, band with a shoulder), 3125 (NH). ^1H NMR spectrum, δ, ppm: 3.84 s (3H, CH_3), 6.89 m (2H, H_{arom}), 7.01 m (5H, H_{arom}), 7.17 m (5H, H_{arom}), 7.81 m (2H, H_{arom}), 10.96 s (1H, NH), 11.25 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 56.05, 114.99, 115.11, 115.40, 115.46, 123.54, 124.64, 127.75, 127.84, 128.58, 128.73, 128.92, 129.15, 131.07, 132.43, 132.56, 132.68, 136.45, 150.73, 163.29, 163.31, 179.26. ^{31}P

NMR spectrum: δ_P 56.4 ppm. Found, %: C 57.65; N 3.87; N 11.84; P 6.62; S 13.55. *m*/*z* 477, 479 $[M]^+$. $S_{23}N_{19}N_4O_2PS_2$. Calculated, %: C 57.73; N 4.00; N 11.71; P 6.47; S 13.40. *M* 478.

2-(4-Methoxyphenyl)-1,7-bis(4-methylphenyl)-4-thioxo-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*]-[1,3,2λ^5]diazaphosphinin-6-one 2-sulfide (Vd). Yield 43%, mp 148–150°C. IR spectrum, ν, cm^{-1}: 1724 (C=O), 3192 (NH). ^{1}H NMR spectrum, δ, ppm: 2.14 s (3H, CH_3), 2.21 s (3H, CH_3), 3.84 s (3H, CH_3), 6.71 d (2H, H_{arom}, $^3J_{HH}$ = 7.5 Hz), 6.83 m (4H, H_{arom}), 6.67 d (2H, H_{arom}, $^3J_{HH}$ = 7.5 Hz), 7.14 m (2H, H_{arom}), 7.78 m (2H, H_{arom}), 10.80 s (1H, NH), 11.10 d (1H, NH, $^2J_{HP}$ = 14.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.25, 21.54, 56.04, 114.94, 115.07, 115.11, 121.14, 121.43, 123.75, 124.84, 125.80, 127.77, 128.69, 129.38, 129.51, 129.94, 131.66, 131.71, 132.53, 132.64, 137.34, 137.83, 138.26, 150.87, 163.25, 163.28, 178.90, 178.96. ^{31}P NMR spectrum: δ_P 56.5 ppm. Found, %: C 59.09; H 4.49; N 11.15; P 6.02; S 12.78. *m*/*z* 505, 507 $[M]^+$. $C_{25}H_{23}N_4O_2PS_2$. Calculated, %: C 59.27; H 4.58; N 11.06; P 6.11; S 12.66. *M* 506.

1,2,7-Tris(4-methoxyphenyl)-4-thioxo-1,2,3,4,5,7-hexahydro-6*H*-imidazo[4,5-*d*][1,3,2λ^5]diazaphosphinin-6-one 2-sulfide (Ve). Yield 58%, mp 230–232° C (decomp.). IR spectrum, ν, cm^{-1}: 1721 (C=O), 3065 (NH). ^{1}H NMR spectrum, δ, ppm: 3.64 s (3H, CH_3), 3.69 s (3H, CH_3), 3.84 s (3H, CH_3), 6.60 d (2H, H_{arom}, $^3J_{HH}$ = 7.5 Hz), 6.74 m (4H, H_{arom}), 6.86 d (2H, H_{arom}, $^3J_{HH}$ = 7.5 Hz), 7.15 m (2H, H_{arom}), 7.78 m (2H, H_{arom}), 10.83 s (1H, NH), 11.12 d (1H, NH, $^2J_{HP}$ = 14.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 55.77, 55.87, 55.99, 114.18, 114.36, 114.43, 114.49, 114.86, 114.99, 115.15, 123.74, 124.84, 125.11, 126.55, 128.72, 129.44, 130.29, 130.33, 132.37, 132.55, 132.66, 151.00, 158.73, 159.30, 159.66, 163.19, 163.21, 178.35, 178.41. ^{31}P NMR spectrum: δ_P 56.9 ppm. Found, %: C 55.65; H 4.49; N 10.27; P 5.61; S 12.09. *m*/*z* 537, 539 $[M]^+$. $C_{25}H_{23}N_4O_4PS_2$. Calculated, %: C 55.75; H 4.30; N 10.40; P 5.75; S 11.91. *M* 538.

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