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LETTERS TO THE EDITOR

Unexpected Reaction of Secondary Phosphine Chalcogenides with Acridine

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Abstract—Secondary phosphine chalcogenides reacted with acridine under mild conditions according to the nucleophilic addition scheme to form 9-chalcogenophosphoryl-9,10-dihydroacridines.

Keywords: acridine, secondary phosphine chalcogenides, nucleophilic addition, 9-chalcogenophosphoryl-9,10-dihydroacridines

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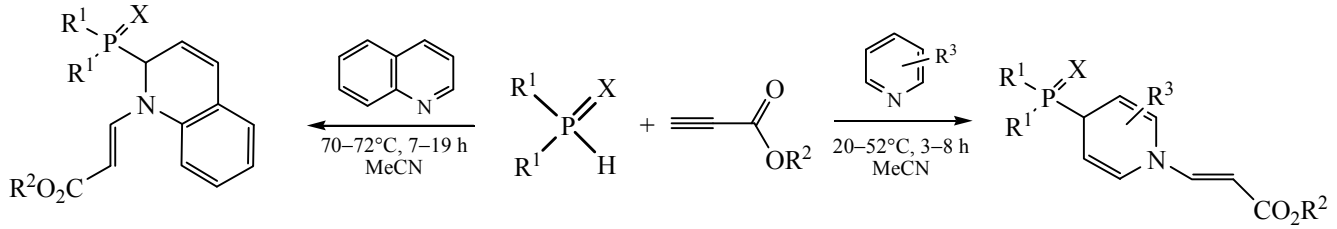
We have recently reported on an original three-component reaction of azines, secondary phosphine chalcogenides, and alkyl propiolates exemplified by pyridines and quinolines [1–3]. The reaction proceeds under mild conditions (20–72°C, 3–19 h, MeCN) with regio- and stereoselective formation of the *C*-phosphorylated (*E*)-*N*-ethenyl-1,4(or 1,2)-dihydropyridines (or quinolines) [1–3] (Scheme 1).

In this study, we attempted to realize that three-component reaction using acridine as the azine. However, heating (50–52°C) of acridine, secondary phosphine chalcogenides **1a**–**1c**, and methyl propiolate in acetonitrile for 4–7 h did not give the expected C^9-phosphorylated *N*-ethenyl-9,10-dihydroacridines (Scheme 2). Under those conditions, methyl propiolate was not involved in the reaction, but 1 : 1 adducts of phosphine chalcogenides with acridine – 9-chalcogenophosphoryl-9,10-dihydroacridines **2a**–**2c** were formed in 60–65% yield. Such addition of secondary phosphine chalcogenides to acridine readily proceeded also in the absence of methyl propiolate, the yield of dihydroacridines **2a**–**2c** being 64–69%. That meant that the electron-deficient acetylene did not participate in the reaction even at the intermediate stages (Scheme 2).

At the same time, according to the reference data, acridine can enter three-component reactions with methyl propiolate [4] or dimethyl acetylenedicarboxylate [5] and some CH- or OH-acids (nitromethane [4] and methanol [5]) to form the corresponding functionalized *N*-ethenyl adducts.

Therefore, phosphorylation of acridine by secondary phosphine chalcogenides easily prepared

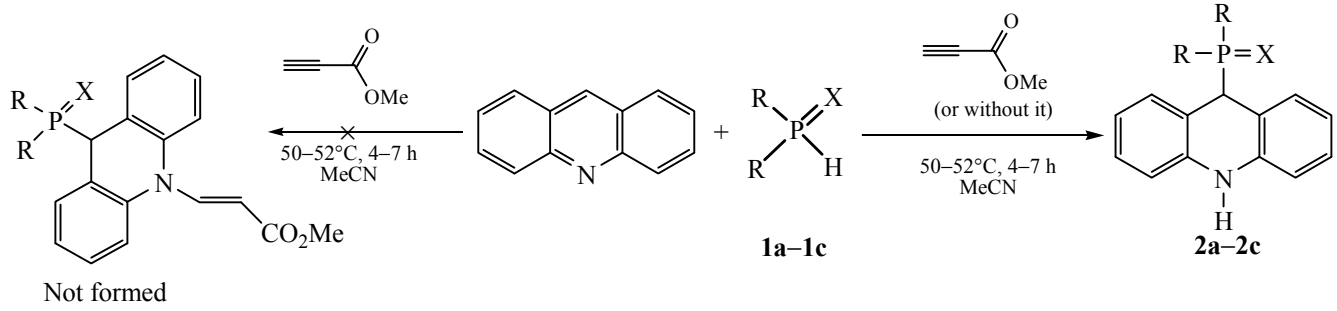
Scheme 1.



35–75% 47–86%

R^1 = Ph, $Ph(CH_2)_2$; R^2 = Me, Et; R^3 = H, Me; X = O, S, Se.

Scheme 2.



R = Ph, X = O (**a**); R = Ph$(CH_2)_2$, X = S (**b**), X = Se (**c**).

from elemental phosphorus, styrene, and chalcogens [6] opens a convenient way to the earlier unknown phosphorylated dihydroacridines, promising precursors for the design of drugs [7–9], reagents for preparation of innovative materials [10, 11], ligands for the synthesis of metal complexes [12–14], and building blocks for organic and organoelement synthesis [15–17].

The mentioned experiments were performed under inert atmosphere (argon). The reactions were monitored by ^{31}P NMR spectroscopy.

Nucleophilic addition of secondary phosphine chalcogenides 1a–1c to acridine. 1.0 mmol of acridine was added to a solution of secondary phosphine chalcogenide **1a–1c** (1.0 mmol) in 3 mL of acetonitrile. The reaction mixture was stirred at 50–52°C during 4 h (in the case of phosphine chalcogenide **1c**) or 7 h (in the cases of phosphine chalcogenides **1a**, **1b**) until disappearance of the signal of the starting phosphine chalcogenide (2–23 ppm) in the ^{31}P NMR spectrum and appearance of the signal of compounds **2a**–**2c** at 30–60 ppm. The solvent was removed under reduced pressure, the residue was washed with Et_2O (5×1 mL) via decantation (in the case of dihydroacridine **2a**) or resedimented from acetone to hexane (in the cases of dihydroacridines **2b**, **2c**).

9-(Diphenylphosphoryl)-9,10-dihydroacridine (2a). Yield 263 mg (69%), white powder, mp 218–219°C. IR spectrum (KBr), ν, cm^{-1}: 3391, 3055, 2903, 1631, 1473, 1435, 1301, 1252, 1181, 1106, 1031, 752, 697, 560, 533. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.40 d (1H, CHP, $^2J_{PH}$ = 11.3 Hz); 6.46 d. d [2H, $H_{2,7}$, $^3J_{2(7)\text{-}1(8)} \approx {}^3J_{2(7)\text{-}3(6)}$ = 7.2 Hz]; 6.62 d [2H, $H_{1,8}$, $^3J_{1(8)\text{-}2(7)}$ = 7.2 Hz]; 6.68 d [2H, $H_{4,5}$, $^3J_{4(5)\text{-}3(6)}$ = 8.2 Hz]; 6.98 d. d [2H, $H_{3,6}$, $^3J_{3(6)\text{-}4(5)} \approx {}^3J_{3(6)\text{-}2(7)}$ = 7.5 Hz]; 7.41 m (4H, H_m); 7.54 m (2H, H_p); 7.72 m (4H, H_o); 8.56 s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 45.7 d (CHP, $^1J_{CP}$ = 64.0 Hz); 113.6 d ($C_{4,5}$, $^4J_{CP}$ = 2.1 Hz); 114.2 d (C_{8a}, $^2J_{CP}$ = 5.6 Hz); 119.0 d ($C_{2,7}$, $^4J_{CP}$ = 2.3 Hz); 127.6 d ($C_{3,6}$, $^5J_{CP}$ = 2.7 Hz); 128.1 d (C_m, $^3J_{CP}$ = 10.7 Hz); 129.9 d ($C_{1,8}$, $^3J_{CP}$ = 3.8 Hz); 131.5 d (C_{ipso}, $^1J_{CP}$ = 91.5 Hz); 131.6 d (C_p, $^4J_{CP}$ = 2.7 Hz); 131.9 d (C_o, $^2J_{CP}$ = 8.7 Hz); 141.8 d (C_{4a}, $^3J_{CP}$ = 3.4 Hz). ^{15}N NMR spectrum (DMSO-d_6), δ_N: –279.6 ppm. ^{31}P NMR spectrum (DMSO-d_6), δ_P: 30.3 ppm. Found, %: C 78.89; H 5.43; N 3.75; P 7.93. $C_{25}H_{20}NOP$. Calculated, %: C 78.73; H 5.29; N 3.67; P 8.12.

9-[Bis(2-phenylethyl)phosphorothioyl]-9,10-dihydroacridine (2b). Yield 290 mg (64%), yellow powder, mp 133–135°C. IR spectrum (film), ν, cm^{-1}: 3388, 3289, 3204, 3057, 3029, 2921, 1602, 1484, 1450, 1406, 1301, 1214, 1072, 1033, 906, 835, 737, 703, 646, 603, 470. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.86, 2.10 m (4H, CH_2P); 2.76 m (4H, C$\underline{H_2}$Ph); 4.60 d (1H, CHP, $^2J_{PH}$ = 15.1 Hz); 6.14 s (1H, NH); 6.75 d [2H, $H_{4,5}$, $^3J_{4(5)\text{-}3(6)}$ = 7.8 Hz]; 7.04 d. d [2H, $H_{2,7}$, $^3J_{2(7)\text{-}1(8)} \approx {}^3J_{2(7)\text{-}3(6)}$ = 7.3 Hz]; 7.15 m (4H, H_o); 7.21 m (2H, $H_{3,6}$); 7.24 m (2H, H_p); 7.29 m (4H, H_m); 7.37 d [(2H, $H_{1,8}$, $^3J_{1(8)\text{-}2(7)}$ = 7.3 Hz]. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 28.7 d ($\underline{C}H_2$Ph, $^2J_{CP}$ = 2.9 Hz); 29.2 d (CH_2P, $^1J_{CP}$ = 43.3 Hz); 49.9 d (CHP, $^1J_{CP}$ = 42.2 Hz); 114.3 ($C_{4,5}$); 115.4 d (C_{8a}, $^2J_{CP}$ = 3.6 Hz); 121.0 ($C_{2,7}$); 126.4 (C_p); 128.2 (C_o); 128.7 (C_m); 128.9 d ($C_{3,6}$, $^5J_{CP}$ = 3.4 Hz); 130.6 d ($C_{1,8}$, $^3J_{CP}$ = 3.2 Hz); 140.0 d (C_{4a}, $^3J_{CP}$ = 3.1 Hz); 141.3 d (C_{ipso}, $^3J_{CP}$ = 14.6 Hz). ^{15}N NMR spectrum ($CDCl_3$), δ_N: –284.1 ppm. ^{31}P NMR spectrum ($CDCl_3$), δ_P: 59.3 ppm. Found, %: C 76.53; H 6.39; N 3.24; P 6.62; S 6.79. $C_{29}H_{28}NPS$. Calculated, %: C 76.79; H 6.22; N 3.09; P 6.83; S 7.07.

9-[Bis(2-phenylethyl)phosphoroselenoyl]-9,10-dihydroacridine (2c). Yield 330 mg (66%), beige powder, mp 128–131°C. IR spectrum (film), ν, cm^{-1}: 3392, 3264, 3188, 3058, 3027, 2928, 1607, 1480, 1455, 1405, 1304, 1211, 1069, 1031, 909, 853, 742, 702, 651, 485. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm:

1.95, 2.19 m (4H, CH_2P); 2.76 m (4H, $C\underline{H}_2Ph$); 4.74 d (1H, CHP, $^2J_{PH}$ = 13.9 Hz); 6.09 br. s (1H, NH); 6.76 d [2H, $H_{4,5}$, $^3J_{4(5)-3(6)}$ = 7.7 Hz]; 6.97 d. d [(2H, $H_{2,7}$, $^3J_{2(7)-1(8)} \approx {}^3J_{2(7)-3(6)}$ = 7.3 Hz]; 7.09 m (4H, H_o); 7.15 m (4H, Ph, Ar); 7.21 m (4H, Ph, Ar); 7.44 br. d [2H, $H_{1,8}$, $^3J_{1(8)-2(7)}$ = 7.3 Hz]. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 29.0 d (CH_2P, $^1J_{CP}$ = 36.0 Hz); 29.7 d (d, $\underline{C}H_2Ph$, $^2J_{CP}$ = 2.1 Hz); 49.6 d (CHP, $^1J_{CP}$ = 34.7 Hz); 114.2 d ($C_{4,5}$, $^4J_{CP}$ = 2.8 Hz); 115.4 d (C_{8a}, $^2J_{CP}$ = 4.1 Hz); 121.7 d ($C_{2,7}$, $^4J_{CP}$ = 2.8 Hz); 126.1 (C_p); 128.0 (C_o); 128.3 (C_m); 128.7 d ($C_{3,6}$, $^5J_{CP}$ = 2.8 Hz); 130.7 d ($C_{1,8}$, $^3J_{CP}$ = 3.4 Hz); 140.1 d (C_{4a}, $^3J_{CP}$ = 3.4 Hz); 141.3 d (C_{ipso}, $^3J_{CP}$ = 15.3 Hz). ^{15}N NMR spectrum ($CDCl_3$), δ_N: –283.1 ppm. ^{31}P NMR spectrum ($CDCl_3$), δ_P: 53.5 ppm (+d-satellites, $^1J_{PSe}$ = 709.8 Hz). ^{77}Se NMR spectrum ($CDCl_3$), δ_{Se}: –379.9 ppm, d ($^1J_{PSe}$ = 709.8 Hz). Found, %: C 69.43; H 5.82; N 2.64; P 6.04; Se 15.56. $C_{29}H_{28}NPSe$. Calculated, %: C 69.60; H 5.64; N 2.80; P 6.19; Se 15.78.

IR spectra were recorded using a Varian 3100 FT-IR spectrometer (KBr pellet or thin layer). ^1H, ^{13}C, ^{15}N, ^{31}P, and ^{77}Se NMR spectra were recorded using Bruker DPX-400 and Bruker AV-400 spectrometers (400.13, 10.62, 40.56, 161.98 and 76.31 MHz, respectively) in $CDCl_3$ or DMSO-d_6, with the following internal [HMDS (^1H, ^{13}C), $MeNO_2$ (^{15}N), Me_2Se (^{77}Se)] or external [85% H_3PO_4 (^{31}P)] references. The signals in the proton spectra were assigned using 2D homonuclear correlation method COSY. The ^{13}C signals were assigned basing on the analysis of the 2D heteronuclear correlation spectra HSQC and HMBC.

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CONFLICT OF INTEREST

No conflict of interest was declared by authors.

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