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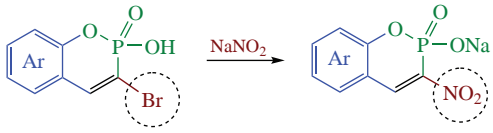
Synthesis and structure of nitro-substituted phosphacoumarins

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The reaction of 3-bromo-2-hydroxy-2-phosphacoumarin 2-oxides with sodium nitrite proceeds as the replacement of bromine atom by the nitro group, which affords the corresponding 3-nitro derivatives as sodium salts. X-ray diffraction study for the two representatives demonstrates that their structures can be classified as coordination polymers.



Keywords: coumarins, phosphacoumarins, organophosphorus compounds, phosphonates, nitro compounds, coordination polymers.

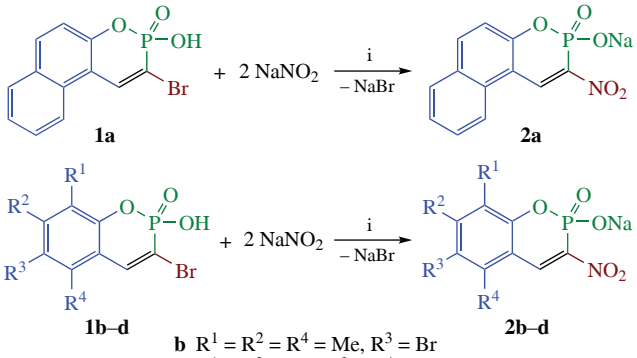
Organic nitro compounds find application in the creation of energy materials, agrochemicals, dyes, organic electronics,[1–5] as well as new chemicals for fine organic synthesis.[6,7] Growing interest in the chemistry of organic nitro compounds has led to the publication of a large number of relevant thematic reviews over the past 5 years.[8–14] The unique properties of the nitro group not only play a decisive role in the activation of electrophiles and the stabilization of nucleophiles, but also influence the interaction with biological targets, thereby facilitating the emergence of a certain type of biological activity.[15] A special place is occupied by heterocyclic compounds containing a nitro group, which are widely used as drugs of various types: antibacterial,[16,17] antitumor,[18,19] as well as tranquilizers and fungicides.[15]

The presence of the nitro group in a heterocyclic compound, linked to an exocyclic double bond, enables the formation of polycyclic complex structures, which are of interest for the creation of new drugs with different types of therapeutic action.[20] Thus, further development of methods for the synthesis of new types of heterocyclic compounds containing an endocyclic double bond linked to a nitro group is a significant and pressing task in organic chemistry.

One of the important classes of heterocyclic compounds is phosphacoumarins (belonging to cyclic phosphonate family), isosteres of coumarins, whose chemistry is actively developing due to their high and diverse biological activity. These compounds can act as cholesterol esterase inhibitors,[21] and exhibit antibacterial[22] or antitumor[23,24] activities. We have previously begun work on the synthesis of functional derivatives of phosphacoumarin containing an aldehyde group in the aromatic ring,[25] as well as a bromine atom[26] at the endocyclic carbon–carbon double bond.

In this work, we introduced a nitro group at the endocyclic double bond of some phosphacoumarins. The synthesis (Scheme 1) was achieved by reacting sodium nitrite with a series of bromo phosphacoumarins **1a–d**, which we described previously.[26] After optimizing the experimental conditions, we selected DMSO as the solvent, which allows the reaction to be carried out at high temperatures and completely dissolves bromo phosphacoumaric acid. The stoichiometric ratio of the reactants was determined by previously measured high pK_a value (0.2 to –1.3) for phosphacoumaric acids.[27] Taking this property into account, we used a fourfold excess of sodium nitrite. The treatment of bromo phosphacoumarins **1a–d** with sodium nitrite in DMSO at 135 °C for 12–36 h ($^{31}P\{^1H\}$ NMR monitoring), depending on the nature of the starting phosphacoumarin, led to the target nitro derivatives **2a–d** in yields of 83–94% (see Scheme 1). It should be noted that *ipso*-substitution of the bromine atom with a nitro group at the carbon–carbon double bond in aromatic and heterocyclic compounds is catalyzed by metal salts or organic catalysts;[28] in our case, all reactions occur without any catalyst. The reaction mechanism has not been studied in detail. Probably, the reaction proceeds either by an addition–elimination mechanism or as a redox process.

The structure of compounds **2a–d** was confirmed by ^{31}P, ^1H, ^{13}C NMR and IR spectroscopy, as well as mass spectrometry and elemental analysis. Their ^{31}P NMR spectra contain one singlet in the region of –11.8 to –13.5 ppm, which is typical of compounds with tetracoordinated phosphorus atoms in phosphacoumarin derivatives. In the ^1H NMR spectra, the proton at the carbon–carbon double bond resonates as a doublet. Signals characteristic



b $R^1 = R^2 = R^4 = Me$, $R^3 = Br$
c $R^1 = R^3 = Bu^t$, $R^2 = R^4 = H$
d $R^1 = R^4 = H$, $R^2 + R^3 = OCH_2O$

Scheme 1 *Reagents and conditions*: i, DMSO, 135 °C, 12–36 h.

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of compound **2b** in the ^{1}H NMR spectrum are as follows: 2.23 (3H, s, CH_3), 2.42 (3H, s, CH_3), 2.55 (3H, s, CH_3), 8.15 (1H, d, J_{HP} 20.2 Hz, P–CH=CH).

Recrystallization of compounds **2a**,**b** from glacial acetic acid affords good crystals suitable for X-ray diffraction (Figure 1).† Compound **2a** crystallizes in the monoclinic space group $P2_1/c$ while **2b** gives crystals of triclinic space group $P\bar{1}$. The asymmetric part of the unit cell of both compounds is represented by a single molecule ($Z' = 1$).

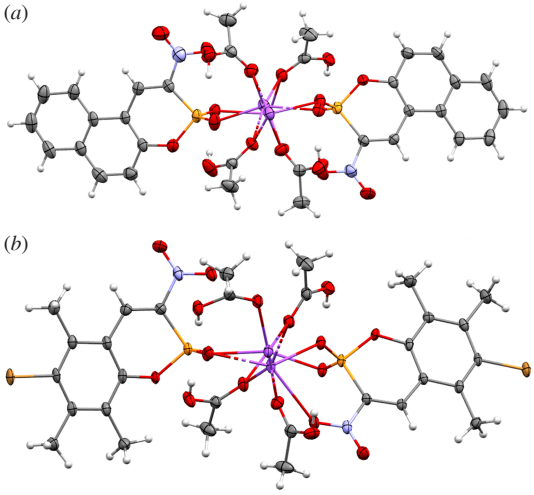


Figure 1 Molecular geometry (*a*) in crystal of **2a** and (*b*) in crystal of **2b** (solvates with AcOH).

† *Crystal data for* **2a**. $C_{32}H_{30}N_2Na_2O_{18}P_2$ [M = 838.50 for $(\mathbf{2a})_2 \cdot (CH_3CO_2H)_4$], monoclinic, space group $P2_1/n$ (no. 14), a = 17.5371(6), b = 7.4728(2) and c = 29.7694(9) Å, α = 90°, β = 106.2400(10)°, γ = 90°, V = 3745.6(2) Å^3, Z = 4, Z' = 1, d_{calc} = 1.487 g cm^{-3}, μ(Mo Kα) = 0.220 mm^{-1}, F(000) = 1728. Total of 108418 reflections were measured, and 8182 independent reflections (R_{int} = 0.0701) were used in the further refinement. Final indices R_1 = 0.0913, wR_2 = 0.2087 [$I > 2\sigma(I)$], goodness-on-fit on F^2 = 1.147, largest difference in peak and hole (0.708 and –0.396 e Å^{-3}), data completeness 99.8%.

Crystal data for **2b**. $C_{30}H_{36}Br_2N_2Na_2O_{18}P_2$ [M = 980.35 for $(\mathbf{2b})_2 \cdot (CH_3CO_2H)_4$], triclinic, space group $P\bar{1}$ (no. 2), a = 7.9354(5), b = 13.9329(9) and c = 18.5815(13) Å, α = 73.392(2)°, β = 89.626(2)°, γ = 78.530(2)°, V = 1926.6(2) Å^3, Z = 2, Z' = 1, d_{calc} = 1.690 g cm^{-3}, μ(Mo Kα) = 2.288 mm^{-1}, F(000) = 992. Total of 39073 reflections were measured, and 8347 independent reflections (R_{int} = 0.0821) were used in the further refinement. Final indices R_1 = 0.0416, wR_2 = 0.1006 [$I > 2\sigma(I)$], goodness-on-fit on F^2 = 1.023, largest difference in peak and hole (1.065 and –0.810 e Å^{-3}), data completeness 99.2%.

X-ray diffraction data were collected on a Bruker D8 QUEST diffractometer with a PHOTON III area detector and an IμS DIAMOND microfocus X-ray tube using MoKα (0.71073 Å) radiation. Data collection and indexing, determination, and refinement of unit cell parameters were carried out using the APEX4 software package. Numerical absorption correction based on the crystal shape, additional spherical absorption correction, and systematic error correction were performed using the SADABS software.[29] Using *Olex*2,[30] the structures were solved by the intrinsic phasing approach using SHELXT[31] and refined by the full-matrix least squares on F^2 using SHELXL.[32] Non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms of methyl groups were found using rotating group refinement with idealized tetrahedral angles. The positions of the H(O) hydrogen atoms were found from Fourier maps, and these atoms were refined isotropically. The other hydrogen atoms were inserted at the calculated positions and refined as riding atoms. Images of the crystal structures were obtained using software program Mercury.[32]

CCDC 2555004 (**2a**) and 2555003 (**2b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk.

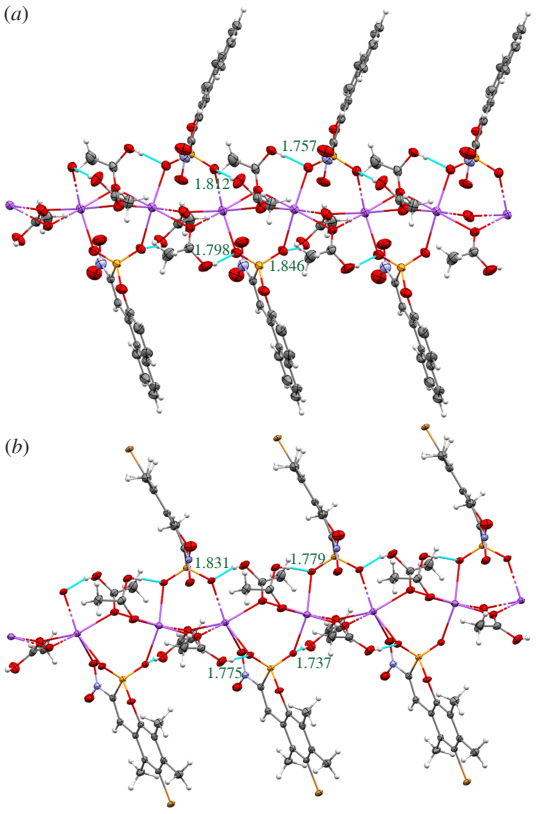


Figure 2 Intermolecular interactions (*a*) in crystals of **2a** and (*b*) in crystals of **2b** (solvates with AcOH).

In both crystals, infinite chains are formed due to O–H···O=P interactions between solvating acetic acid molecules and the base compound (Figure 2). Analysis of X-ray diffraction data for compounds **2a** and **2b** revealed that their main supramolecular motifs are one-dimensional columns of associated molecules due to interactions with a metal cation (Na). The columns are oriented along the shortest parameter 0*b* (**2a**) and 0*a* (**2b**) and are interconnected by weak dispersion interactions, forming a three-dimensional close-packed structure with a Kitaigorodskii index of 69.6% (**2a**) and 72.7% (**2b**). These structures can be classified as coordination polymers. Sodium cations act as linkers forming a molecular framework involving phosphacoumarins and acetic acid.

To conclude, *ipso*-substituting a nitro group for the bromine atom in the reaction of bromo phosphacoumarins with sodium nitrite affords new phosphacoumarins bearing the nitro group at the carbon–carbon double bond. X-ray diffraction data for compounds **2a** and **2b** show that their structures can be classified as coordination polymers. The synthesized phosphacoumarins containing a nitro group at the 3-position can be used to create a large library of new types of annulated polycyclic structures with a broad spectrum of biological activity.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.8136.

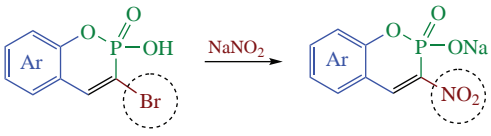
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