Short Note

Not peer-reviewed version

4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione

Dmitry Tatarinov * , Elisa Bajnazarova , Mohsin Ali , Alexey Dovzhenko , Rustem Zairov * , Vladimir Mironov , Asiya Mustafina

Posted Date: 8 December 2023

doi: 10.20944/preprints202312.0553.v1

Keywords: phosphine oxides; ligands; lanthanides; triketones; keto-enolic tautomerism

Short Note

4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione

Dmitry Tatarinov [1,2,*], Elisa Bajnazarova [2], Mohsin Ali [2,3], Alexey Dovzhenko [1,2],
Rustem Zairov [1,2,*], Vladimir F. Mironov [1] and Asiya Mustafina [1]

[1] Arbuzov Institute of Organic and Physical Chemistry, FRC Kazan Scientific Center, Russian Academy of Sciences, 8 Arbuzov Street, 420088 Kazan, Russia; aleksej_dovghenko@mail.ru (A.D.); mironov@iopc.ru (V.F.M.); asiya@iopc.ru (A.M.)

[2] Kazan (Volga Region) Federal University, 18 Kremlyovskaya Street, 420008 Kazan, Russia; elizabajnazarova@gmail.com

[3] Department of Chemistry, University of Karachi, Karachi-75270, Pakistan; mohsin.ali@uok.edu.pk

* Correspondence: datint@iopc.ru (D.T.); rustem@iopc.ru (R.Z.).

Abstract: Novel 4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione was synthesized by the reaction of diketone enamine with diphenylchloro phosphine followed by oxidation and hydrolysis of the enamine phosphine formed. Tautomeric transformation of the diketone moiety of phosphine oxide was investigated by ^{1}H NMR. Three out of five possible tautomers were observed in the 4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione solution. The major tautomer was the form with a diketone fragment.

Keywords: phosphine oxides; ligands; lanthanides; triketones; keto-enolic tautomerism

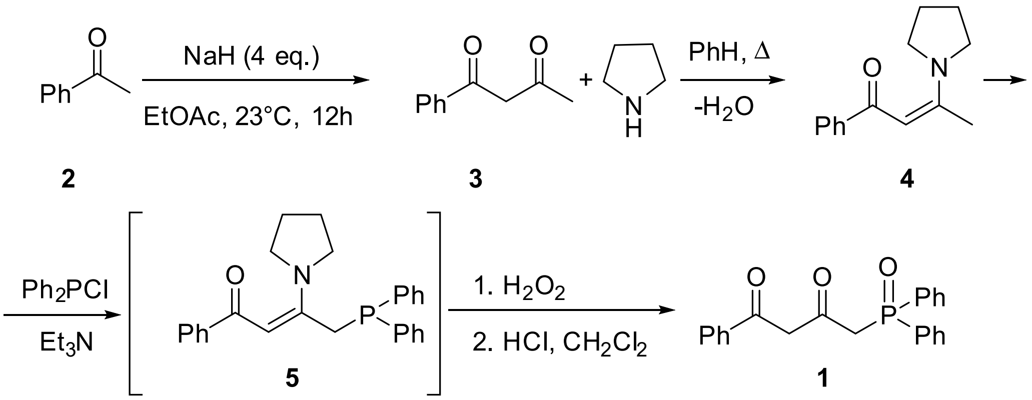
1. Introduction

Phosphine oxides with an additional functional group are effective ligands for preparing complexes with lanthanides [1] with promising photophysical properties for fabricating OLEDs [2–4] or detecting various compounds [5]. Another class of well-studied ligands for complex synthesis with lanthanides are β-diketones [6]. Their functionalization with more coordination groups of various nature leads to more complex ligands with interesting and perspective coordination properties [7,8]. Moreover, both phosphine oxides and β-diketones are used as co-ligands for obtaining various luminescent complexes with lanthanides [9,10] for biomedical application [11]

We report here the synthesis and keto-enolic tautomerism of 4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione.

2. Results and Discussion

The synthesis was performed based on acetophenone **1** by the technique described for enamines of acetoacetic acid (Scheme 1). [12]. By condensing **1** with ethyl acetate, diketone **2** was obtained [13]. Then diketone **2** was transformed in enamine **3** at the reaction with pyrrolidine [14]. The subsequent reaction with diphenylchlorophosphine intermediately forming phosphine **5** followed by oxidation and hydrolysis have led to the target phosphine oxide with a 50% yield. Synthesis of compound **1** at the reaction of 1-(diphenylphosphoryl)propan-2-one with methyl benzoate over lithium diisopropylamide is mentioned in the recent study of [15] as an intermediate. However, phosphine oxide **1** was not isolated, and its spectral characteristics were not defined either. Moreover, the synthetic route presented herein is distinguished by using simpler techniques and readily available reagents.



Scheme 1. Synthesis of 4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione.

Structure of compound **1** was studied by ^{1}H NMR and ^{13}C spectroscopy (Figure 1).

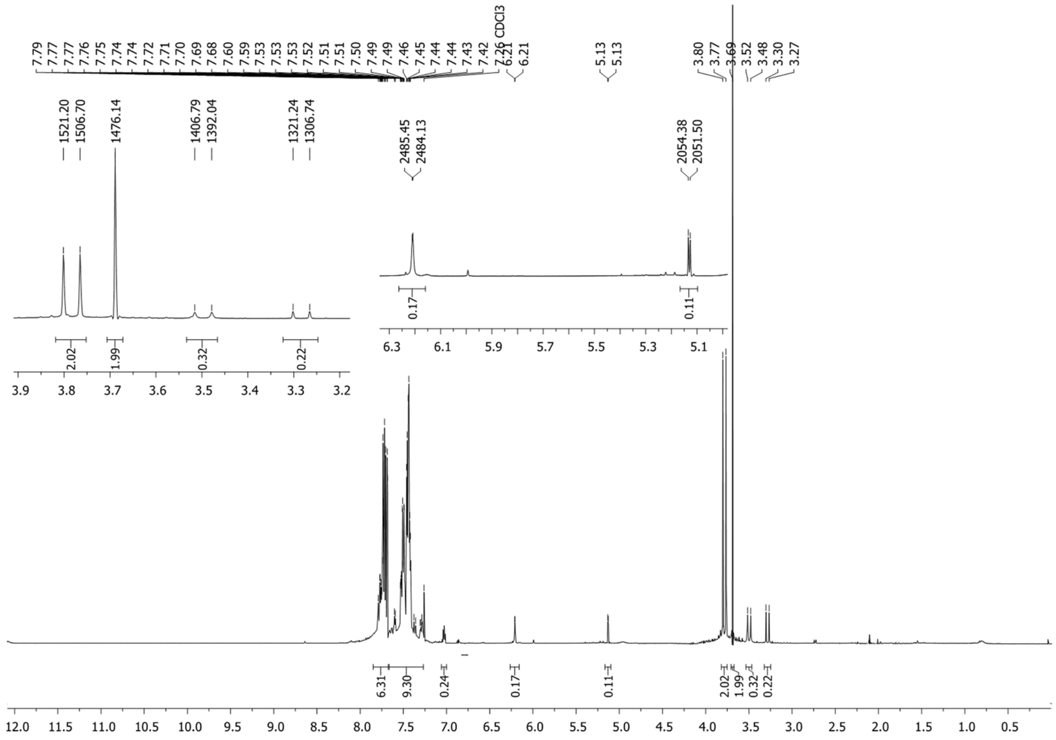
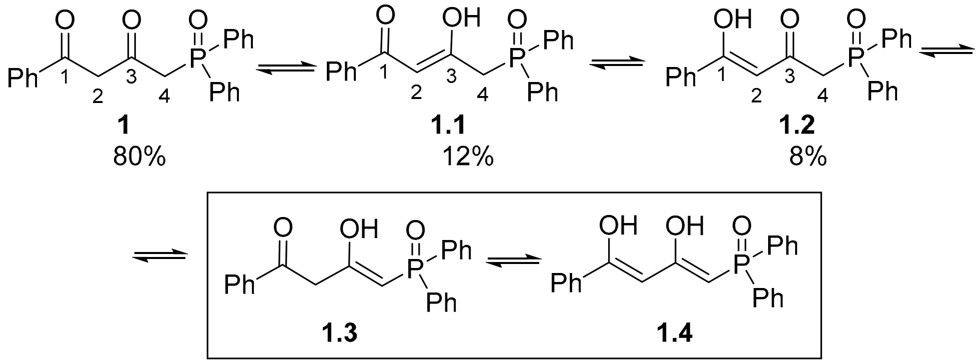


Figure 1. ^{1}H NMR spectra of tautomeric mixture of compound **1** ($CDCl_3$, 400 MHz).

It is common knowledge that keto-enol tautomerism is characteristic of β-diketones and enol tautomer is often preferable in non-hydrogen bonding solvents [6–8,16]. In contrast, phosphine oxide **1** was isolated as a mixture of tautomers with prevailing diketo-form, the content of which as about 80% (Scheme 2). Mono-enol tautomers 1.1 and 1.2 made 8 and 12 %, respectively. Doublet H^4 at 3.64 ppm ($^2J_{PH}$ = 14.5 Hz) and the H^2 proton singlet at 3.55 ppm confirm the presence of tautomer **1** as the main one in the mixture. At the same time, the H^4 protons of minor tautomers **1.1** and **1.2**, as well, show as doublets in the ^{1}H NMR spectrum (3.36 ppm, $^2J_{PH}$ = 14.7 Hz and 3.14 ppm, $^2J_{PH}$ = 14.5 Hz). Presence of the H^4 proton doublets in alpha-position relative to phosphorus points clearly to the absence of any prototropism involving them. Signals of the H^2 protons located in tautomers **1.1** and **1.2** at the sp^2-hybrid carbon atom manifest themselves in weaker fields (6.07 ppm, $^4J_{PH}$ = 1.7 Hz, and 4.99 ppm, $^4J_{PH}$ = 2.9 Hz). Protons of the hydroxy groups of enols **1.1** and **1.2** were not registered in the spectra, probably due to low intensity or deuterium exchange with $CDCl_3$ (For full ^{1}H NMR spectrum

(0-18.2 ppm), please see ESI). Tautomers **1.3** and **1.4** were not registered spectrally. Thus, three of five possible tautomers are realized for compound **1**.



Scheme 2. Tautomeric transformations of 4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione in solution.

4. Materials and Methods

All reagents were used as purchased from Sigma-Aldrich or Acros Chemicals without further purification. Solvents were purified by standard procedures before use. All reactions were run under an argon atmosphere unless in aqueous media.

NMR experiments were carried out with 400 MHz [400 MHz (^{1}H), 162 MHz (^{31}P)] or 600 MHz [600 MHz (^{1}H), 243 MHz (^{31}P),] spectrometers equipped with a pulsed gradient unit capable of producing magnetic field pulse gradients in the z-direction of 53.5 G cm^{-1}. All spectra were acquired in a 5 mm gradient inverse broadband probe head. Chemical shifts (d) are expressed in parts per million, relative to the residual ^{1}H signal of $CDCl_3$, and the signals are designated as follows: s, singlet; d, doublet; t, triplet; m, multiplet. Coupling constants (J) are in hertz (Hz). The ESI MS measurements were performed using an AmazonX ion trap mass spectrometer (Bruker Daltonic GmbH, Germany) in the positive or negative mode in the mass range of 70–3000. IR spectra were recorded with a Bruker Tensor-27 instrument for the samples in KBr pellets. The elemental analysis was carried out on a CHNS analyzer EuroEA3028-HT-OM (Eurovector SpA, Italy). The samples were weighed on Sartorius CP2P (Germany) microbalances in tin capsules. Callidus 4.1 software was used to perform quantitative measurements and evaluate the data received.

1-phenylbutane-1,3-dione (**2**)

Prepared according to the previously described procedure [13]. Yellow oil. Yield 85%. Exists as a mixture of keto/enol tautomers with 1:10 ratio. ^{1}H NMR (400 MHz, $CDCl_3$) (enol tautomer) δ 7.90 – 7.86 (m, 2H), 7.55 – 7.49 (m, 1H), 7.45 (dd, *J* = 8.3, 6.7 Hz, 2H), 6.18 (s, 1H), 2.20 (s, 3H).

1-phenyl-3-(pyrrolidin-1-yl)but-2-en-1-one (**3**)

Prepared by previously described procedure [14] from 1g (6.2 mmol) of **2** and 0.5 ml (0.44 g, 6.2 mmol) of pyrrolidine in 10 ml of benzene. Yiled 1.257g (94 %), brown oil, which solidifies while standing. Spectral data are in consistent with the previously described [17] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.42 – 7.37 (m, 3H), 5.61 (s, 1H), 3.53 (brs, 2H), 3.37 (brs, 2H), 2.68 (s, 3H), 2.00 (brs, 4H). Compound **3** was used in the next step without purification.

4-(diphenylphosphoryl)-1-phenylbutane-1,3-dione (diketo-tautomer)

To a stirred solution of compound **3** (0.65 g, 3 mmol) and triethylamine (4.16 ml, 0.303 g, 3 mmol) in CH_2Cl_2 (5 ml) under an argon atmosphere Ph_2PCl (0.55 ml, 0.661 g, 3 mmol) was added dropwise and stirred at room temperature for 24 h. Then $(NH_2)_2CO{\cdot}H_2O_2$ (0.282 g, 3 mmol) was added in one portion and the mixture stirred for additional 1 h. The reaction mixture was washed with water and 10 ml of 5% HCl solution was added. After 2d the water was separated, and organic phase was dried under Na_2SO_4 and concentrated on rotary evaporator. Crude product was purified by dry-column flash chromatography on Schott's funnel (silica gel 230-400 mesh), using gradient elution (eluent from EtOAc : Hexane 4 :1 to EtOAc). Yield 0.542 g (50%)/ Pale yellow gum. Exists as a mixture of keto/enol tautomers **1, 1.1** and **1.2** with 20:3:2 ratio respectively. IR (thin film) 3434 (s, br), 2924 (w, sh), 1710 (w), 1603 (s, br), 1439 (s), 1224 (w), 1194 (s), 1116 (m), 1101 (m), 720 (m), 692 (s), 521 (s) cm ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.71 (m, 3H, ArH), 7.71 – 7.67 (m, 3H, ArH), 7.55 – 7.47 (m, 3H, ArH), 7.47 – 7.39 (m, 6H, ArH), 6.21 (d, *J* = 1.6 Hz, 1H, H^2 of tautomer **1.1**), 5.13 (d, *J* = 3.0 Hz, 1H, H^2 of tautomer **1.2**), 3.78 (d, *J* = 14.6 Hz, 2H, H^4), 3.69 (s, 2H, H^2), 3.50 (d, *J* = 14.7 Hz, 2H, H^4 of tautomer **1.1**), 3.28 (d, *J* = 14.5 Hz, 2H, H^4 of tautomer **1.1**). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.85 (d, *J* = 5.6 Hz), 167.02, 140.37, 132.48 (overlapped on the next signal), 132.47 (d, *J* = 2.9 Hz), 131.89, 131.38 (d, *J* = 104.0 Hz), 131.12, 130.87 (d, *J* = 10.0 Hz), 128.86 (d, *J* = 12.5 Hz), 128.86 (overlapped on the previous signal) 50.83, 46.88 (d, *J* = 56.5 Hz). ^{31}P NMR (243 MHz, $CDCl_3$) δ 30.41 (**1.1**), 29.30 (**1**), 27.07 (**1.2**). Anal. Calcd for $C_{22}H_{19}O_3P$ (%): C, 72.92; H, 5.29; P, 8.55 . Found (%): C 72.63; H 5.41; P 8.47. ESI-MS *m/z* = 363.17 [M + H]$^+$

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Figure S1: ^{1}H NMR spectra of tautomeric mixture of compound **1** ($CDCl_3$, 400 MHz); Figure S2: ^{13}C NMR spectra of tautomeric mixture of compound **1** (101 MHz, $CDCl_3$); Figure S3: ^{13}C NMR (dept) spectra of tautomeric mixture of compound **1** (101 MHz, $CDCl_3$); Figure S4: ^{31}P {^{1}H} NMR spectra of tautomeric mixture of compound **1** (243 MHz, $CDCl_3$).

Author Contributions "Conceptualization, D.T. and R.Z. A.M. and V.M.; methodology, X.X.; validation, and Z.Z.; formal analysis, R.Z.; investigation, E.B.; resources, V.F.; data curation, A.D.; writing—original draft preparation, D.T.; writing—review and editing, A.M.; visualization, D.T.; supervision, V.F. and A.M.; project administration, A.D.; funding acquisition, R.Z. All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

Funding: The authors thank the Russian Science Foundation (grant 22-23-00853) for financial support. The authors are grateful to the staff of the Distributed Spectral-Analytical Center of Shared Facilities for Study of Structure, Composition and Properties of Substances and Materials of Federal Research Center of Kazan Scientific Center of Russian Academy of Sciences» for their research and assistance in discussing the results.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Platt, A.W.G. Lanthanide Phosphine Oxide Complexes. *Coord. Chem. Rev.* **2017**, *340*, 62–78, doi:10.1016/j.ccr.2016.09.012.
2. Aslandukov, A.N.; Utochnikova, V. V.; Goriachiy, D.O.; Vashchenko, A.A.; Tsymbarenko, D.M.; Hoffmann, M.; Pietraszkiewicz, M.; Kuzmina, N.P. The Development of a New Approach toward Lanthanide-Based OLED Fabrication: New Host Materials for Tb-Based Emitters. *Dalt. Trans.* **2018**, *47*, 16350–16357, doi:10.1039/C8DT02911C.
3. Chou, H.-H.; Cheng, C.-H. A Highly Efficient Universal Bipolar Host for Blue, Green, and Red Phosphorescent OLEDs. *Adv. Mater.* **2010**, *22*, 2468–2471, doi:10.1002/adma.201000061.
4. Yang, H.; Liang, Q.; Han, C.; Zhang, J.; Xu, H. A Phosphanthrene Oxide Host with Close Sphere Packing for Ultralow-Voltage-Driven Efficient Blue Thermally Activated Delayed Fluorescence Diodes. *Adv. Mater.* **2017**, *29*, 1700553, doi:10.1002/adma.201700553.
5. R. Zairov, A. Dovzhenko, N. Terekhova, T. Kornev, Y. Zhou, Z. Huang, D. Tatarinov, G. Nizameeva, R.R. Fayzullin, A.T. Gubaidullin, T. Salikhova, F. Enrichi, V.F. Mironov, A. Mustafina, Phosphineoxide-Chelated Europium(III) Nanoparticles for Ceftriaxone Detection, Nanomaterials. 13 (2023). https://doi.org/10.3390/nano13030438.
6. Aromí, G.; Gamez, P.; Reedijk, J. Poly Beta-Diketones: Prime Ligands to Generate Supramolecular Metalloclusters. *Coord. Chem. Rev.* **2008**, *252*, 964–989, doi:10.1016/j.ccr.2007.07.008.
7. Vigato, P.A.; Peruzzo, V.; Tamburini, S. The Evolution of β-Diketone or β-Diketophenol Ligands and Related Complexes. *Coord. Chem. Rev.* **2009**, *253*, 1099–1201, doi:10.1016/j.ccr.2008.07.013.
8. Clegg, J.K.; Li, F.; Lindoy, L.F. Oligo-β-Diketones as Versatile Ligands for Use in Metallo-Supramolecular Chemistry: Recent Progress and Perspectives. *Coord. Chem. Rev.* **2022**, *455*, 214355, doi:10.1016/j.ccr.2021.214355.
9. Xu, H.; Zhu, R.; Zhao, P.; Xie, L.-H.; Huang, W. Photophysical and Electroluminescent Properties of a Series of Monochromatic Red-Emitting Europium-Complexed Nonconjugated Copolymers Based on Diphenylphosphine Oxide Modified Polyvinylcarbazole. *Polymer (Guildf).* **2011**, *52*, 804–813, doi:10.1016/j.polymer.2010.12.016.

10. Raj, D.B.A.; Francis, B.; Reddy, M.L.P.; Butorac, R.R.; Lynch, V.M.; Cowley, A.H. Highly Luminescent Poly(methyl Methacrylate)-Incorporated Europium Complex Supported by a Carbazole-Based Fluorinated β-Diketonate Ligand and a 4,5-Bis(diphenylphosphino)-9,9-Dimethylxanthene Oxide Co-Ligand. *Inorg. Chem.* **2010**, *49*, 9055–9063, doi:10.1021/ic1015324.
11. Zairov, R.R.; Dovzhenko, A.P.; Sapunova, A.S.; Voloshina, A.D.; Tatarinov, D.A.; Nizameev, I.R.; Gubaidullin, A.T.; Petrov, K.A.; Enrichi, F.; Vomiero, A.; et al. Dual Red-NIR Luminescent Eu Yb Heterolanthanide Nanoparticles as Promising Basis for Cellular Imaging and Sensing. *Mater. Sci. Eng. C* **2019**, *105*, 110057, doi:10.1016/j.msec.2019.110057.
12. Kostyuk, A.N.; Svyaschenko, Y. V; Volochnyuk, D.M.; Lysenko, N. V; Tolmachev, A.A.; Pinchuk, A.M. Structural Sensitivity in Phosphorylation of Enamines—Derivatives of β-Aminocrotonic Acid with Diphenylchlorophosphine. *Tetrahedron Lett.* **2003**, *44*, 6487–6491, doi:10.1016/S0040-4039(03)01546-6.
13. Inagaki, S.; Saito, K.; Suto, S.; Aihara, H.; Sugawara, A.; Tamura, S.; Kawano, T. Synthesis of 5-Aryl-3(2 H)-Furanones Using Intramolecular Cyclization of Sulfonium Salts. *J. Org. Chem.* **2018**, *83*, 13834–13846, doi:10.1021/acs.joc.8b02153.
14. *A General Synthesis Of 4-Isoxazolecarboxylic Esters: Ethyl 3-Ethyl-5-Methyl-4-Isoxazolecarboxylate. Org. Synth.* ***1973***, *53, 59, doi:10.15227/orgsyn.053.0059.*
15. Maass, J.S.; Wilharm, R.K.; Luck, R.L.; Zeller, M. Photoluminescent Properties of Three Lanthanide Compounds of Formulae LnCl3(diphenyl((5-Phenyl-1H-Pyrazol-3-Yl)methyl)phosphine oxide)2, Ln = Sm, Eu and Tb: X-Ray Structural, Emission and Vibrational Spectroscopies, DFT and Thermogravimetric Studies. *Inorganica Chim. Acta* **2018**, *471*, 481–492, doi:10.1016/j.ica.2017.11.049.
16. Allen, G.; Dwek, R.A. An N.m.r. Study of Keto–enol Tautomerism in β-Diketones. *J. Chem. Soc. B* **1966**, 161–163, doi:10.1039/J29660000161.
17. Zheng, Y.; Liu, Z.-W.; Li, T.; Li, X.; Li, S.-H. KIO 3 -Mediated γ-C(sp 3)–H Sulfenylation of Enaminones. *Org. Lett.* 2022, *24*, 7533–7537, doi:10.1021/acs.orglett.2c02824