Mendeleev
Communications

Mendeleev Commun., 2025, **35**, 420–423

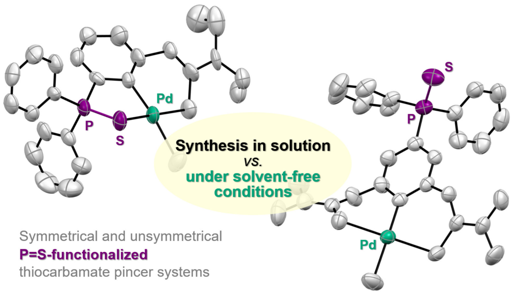
Symmetrical and unsymmetrical thiophosphoryl–thiocarbamate pincer ligands: cyclopalladation in solution and under solvent-free conditions

Vladimir A. Kozlov,[a] Diana V. Aleksanyan,*[a] Yulia V. Nelyubina,[b] Svetlana A. Soloveva,[c,d] Aleksander M. Shakhov[e] and Zinaida S. Klemenkova[a]

[a] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119334 Moscow, Russian Federation. E-mail: aleksanyan.diana@ineos.ac.ru*
[b] *Federal Research Center of Problems of Chemical Physics and Medicinal Chemistry, Russian Academy of Sciences, 142432 Chernogolovka, Moscow Region, Russian Federation*
[c] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation*
[d] *Moscow Center for Advanced Studies, 123592 Moscow, Russian Federation*
[e] *N. N. Semenov Federal Research Center for Chemical Physics, Russian Academy of Sciences, 119991 Moscow, Russian Federation*

DOI: 10.71267/mencom.7705

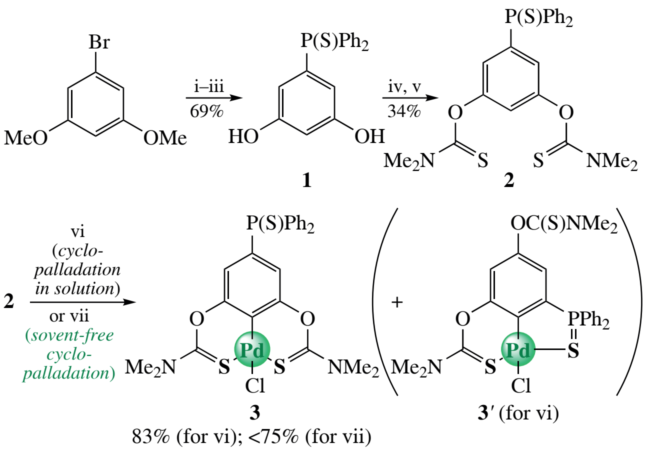
The modern concept of green chemistry calls for the development of more environmentally benign synthetic protocols and a reduction in the use of auxiliary substances, including solvents. In this work the effect of a thiophosphoryl pendant arm on the cyclopalladation features of both symmetrical and unsymmetrical thiocarbamate pincer ligands was explored. The ligands were 1,3-bis(thiocarbamoyloxy)-5-(diphenylthiophosphoryl)- or 1-thiocarbamoyloxy-3-(diphenylthiophosphoryl)benzenes, the palladium source was $(PhCN)_2PdCl_2$.



Keywords: pincer complexes, palladium, cyclometalation, solvent-free reactions, mechanochemistry.

Recent decades have seen a considerable progress in the development of different solvent-free techniques, which are gradually expanding into new areas of chemistry, including the synthesis of metal–organic and organometallic compounds.[1–5] Solvent-free protocols attract growing interest, first of all, owing to their reduced environmental impact. Besides the fundamental importance from the viewpoint of green chemistry principles, reactions in the absence of an added solvent can also address some selectivity, solubility and stability issues, which is especially valuable in organometallic chemistry. The synthesis and reactivity studies of metal-containing compounds under solvent-free conditions are usually performed upon thermal or mechanical activation.[6–17] Our research group has contributed to this field by studying the solid-phase reactivity of tridentate pincer systems towards Pd^{II} ions.[6,7,10,18] The first example of mechanochemical cyclopalladation of a bis(thiocarbamate) ligand paved the way to the synthesis of palladium(II) pincer complexes in a highly efficient and ecologically friendly manner.[19] In this work, the effect of a thiophosphoryl pendant arm on the cyclopalladation of both symmetrical and unsymmetrical thiocarbamate pincer systems was investigated. Particular interest to thiocarbamate pincer systems was caused by their catalytic and anticancer potential.[10,20,21]

At first, it seemed interesting to evaluate the effect of supplementing two thiocarbamate flanking units with an additional thione donor center. A convenient precursor for such a symmetrical bis(thiocarbamate) pincer ligand appeared to be (3,5-dimethoxyphenyl)diphenylphosphine, readily derived from dimethoxy-substituted bromobenzene upon sequential treatment with Mg and Ph_2PCl.[22] The demethylation of the key precursor with HBr followed by the addition of an elemental sulfur to the resulting phosphine derivative afforded (3,5-dihydroxyphenyl)diphenylphosphine sulfide **1** (Scheme 1). The reaction of its dipotassium salt (generated *in situ* upon treatment with Bu^tOK) with $ClC(S)NMe_2$ afforded the target P(S)-functionalized symmetrical pincer ligand **2** in synthetically acceptable yield (see Scheme 1).



Scheme 1 *Reagents and conditions*: i, Mg, THF, then Ph_2PCl; ii, HBr (48% aq.), reflux, 8 h; iii, S_8, PhMe, room temperature, 5 h; iv, Bu^tOK, THF, 5–10 °C, 0.5 h; v, $ClC(S)NMe_2$, 60 °C, 3 h; vi, $(PhCN)_2PdCl_2$, CH_2Cl_2, room temperature, 15 min; vii, $(PhCN)_2PdCl_2$, solvent-free, grinding, 15 min, then 65–70 °C, 15 min.

The cyclopalladation of compound **2** in solution was readily accomplished upon reaction with $(PhCN)_2PdCl_2$ under mild conditions: the yellow discoloration of the dichloromethane reaction mixture was observed in only 15 min (see Scheme 1). The chromatographic purification afforded symmetrical SCS-pincer complex **3** with the intact thiophosphoryl group in high yield. Its structure was confirmed by NMR and IR spectroscopic data as well as X-ray crystallography (Figure 1).† However, the ^{31}P NMR monitoring of the reaction mixture revealed the formation of *ca.* 10% of the P(S)-coordinated product, which we presumed to be unsymmetrical Pd^{II} pincer complex **3′** combining thiocarbamate and thiophosphoryl pendant arms. Although we failed to isolate and characterize this complex in a pure form, a strongly deshielded phosphorus resonance ($\delta_P = 49.8$) unequivocally indicated the coordination of the P=S moiety. Furthermore, the ^{13}C NMR spectrum of the crude product before purification revealed two sets of Me_2N carbon resonances for the minor component, presumably attributed to the coordinated ($\delta_C = 40.0$ and 43.5) and non-coordinated ($\delta_C = 36.5$ and 36.8) thiocarbamate units.

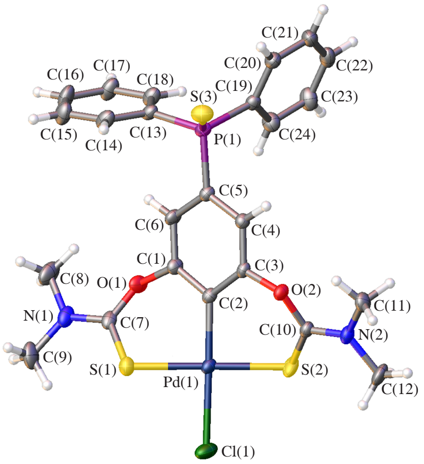
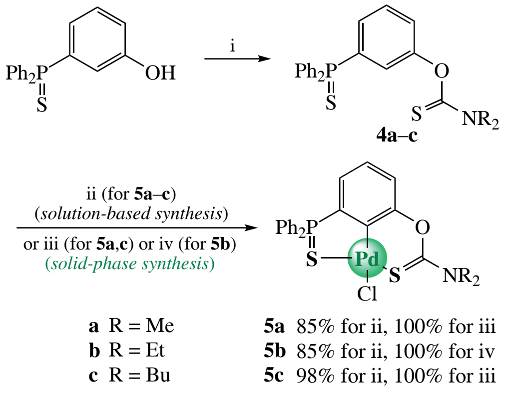


Figure 1 General view of complex **3** in representation of atoms as thermal ellipsoids at 30% probability level. The solvate EtOAc molecule is omitted for clarity.

The reaction of compound **2** with the same Pd^{II} precursor upon grinding in a mortar, unlike the analogous reaction of the non-functionalized bis(thiocarbamate) ligand,[19] resulted in only partial cyclopalladation. Despite this obvious interfering effect of the thiophosphoryl group, the energy intensified processes (grinding the reactants in a vibration ball mill for 30 min or heating the ground sample at 65–70 °C for 15 min) provided a significant improvement in the yield of the target pincer complex. Furthermore, according to the results of the ^{31}P NMR spectroscopic analysis, the solid-phase reactions afforded also some new species, which were not observed during the synthesis in solution, but, unfortunately, they could not be isolated and identified due to the low content in the mixture. Interestingly, isomer **3′** was not formed in this experiment. Anyway, it should be noted that the cyclopalladation of the P(S)-functionalized symmetrical system both in solution and under solvent-free conditions selectively activates a bis(thiocarbamate) pincer pocket.

As for the unsymmetrical thiophosphoryl–thiocarbamate pincer systems, earlier we have demonstrated that the C–H bond activation of Me_2N-substituted ligand **4a** under the action of Pd^{II} ions readily proceeded both in solution and in the absence of a solvent, although required thermal activation in the latter case (Scheme 2).[10] To explore the influence of the thiocarbamate donor group, in this work we obtained the analogs of ligand **4a** featuring ethyl and *n*-butyl substituents, using 3-diphenylthiophosphorylphenol as a key predecessor.[10]

As well as in the case of Me_2N-substituted prototype **4a**, the cyclopalladation of compounds **4b**,**c** in solution smoothly proceeded under mild conditions to yield the target 5,6-membered hybrid palladacycles in high yields (compound **5b**,**c**, see Scheme 2), whose structures were supported by both spectral techniques and XRD (Figure 2).† However, the solid-state reactivity of these hybrid derivatives strongly differed. Thus, Et_2N-substituted ligand **4b** readily afforded the target Pd^{II} pincer



Scheme 2 *Reagents and conditions*: i, NaH, THF, room temperature, 2 h, then ClC(S)NR$_2$, 50 °C, 5 h; ii, $(PhCN)_2PdCl_2$, CH_2Cl_2, room temperature, 24 h (for **5a**), 3 h (for **5b**), 12 h (for **5c**); iii, $(PhCN)_2PdCl_2$, solvent-free, 75–80 °C, 5 min (for **5a**), 85–90 °C, 5 min (for **5c**); iv, $(PhCN)_2PdCl_2$, solvent-free, room temperature, 15 min grinding.

---

† *Crystal data for* **3**·0.5EtOAc. $C_{26}H_{28}ClN_2O_3PPdS_3$ ($M = 685.50$), monoclinic, space group $P2_1/c$, $a = 18.6960(18)$, $b = 7.9857(8)$ and $c = 20.343(2)$ Å, $\alpha = 90°$, $\beta = 105.1570(10)°$, $\gamma = 90°$, $V = 2931.6(5)$ Å^3, $Z = 4$, $T = 220$ K, μ(Mo-Kα) = 10.23 cm^{-1}, $d_{calc} = 1.553$ g cm^{-1}. Total of 32940 reflections were measured, and 7065 independent reflections ($R_{int} = 0.0893$) were used in the further refinement. The refinement converged to $wR_2 = 0.0965$ and GOF = 1.019 for all independent reflections [$R_1 = 0.0436$ was calculated against F for 5305 observed reflections with $I > 2\sigma(I)$].

Crystal data for **5b**. $C_{23}H_{23}ClNOPPdS_2$ ($M = 566.36$), monoclinic, space group $P2_1/c$, $a = 17.117(17)$, $b = 8.993(9)$ and $c = 16.176(16)$ Å, $\alpha = 90°$, $\beta = 110.580(13)°$, $\gamma = 90°$, $V = 2331(4)$ Å^3, $Z = 4$, $T = 220$ K, μ(Mo-Kα) = 11.74 cm^{-1}, $d_{calc} = 1.614$ g cm^{-1}. Total of 15325 reflections were measured, and 4073 independent reflections ($R_{int} = 0.2165$) were used in the further refinement. The refinement converged to $wR_2 = 0.1534$ and GOF = 0.872 for all independent reflections [$R_1 = 0.0670$ was calculated against F for 2054 observed reflections with $I > 2\sigma(I)$].

Crystal data for **5c**. $C_{27}H_{31}ClNOPPdS_2$ ($M = 622.47$), monoclinic, space group $P2_1/c$, $a = 13.3562(5)$, $b = 12.9986(5)$ and $c = 15.7305(5)$ Å, $\alpha = 90°$, $\beta = 103.001(2)°$, $\gamma = 90°$, $V = 2661.00(17)$ Å^3, $Z = 4$, $T = 100$ K, μ(Mo-Kα) = 10.36 cm^{-1}, $d_{calc} = 1.554$ g cm^{-1}. Total of 25835 reflections were measured, and 7079 independent reflections ($R_{int} = 0.0520$) were used in the further refinement. The refinement converged to $wR_2 = 0.1117$ and GOF = 1.018 for all independent reflections [$R_1 = 0.0411$ was calculated against F for 5118 observed reflections with $I > 2\sigma(I)$].

Single crystals of the compounds explored were obtained by slow crystallization from a CH_2Cl_2–EtOAc (**3**), CH_2Cl_2–Et_2O (**5b**), or $CHCl_3$–hexane (**5c**) mixture. The data were collected with a Bruker APEXII Quazar CCD diffractometer using graphite monochromated Mo-Kα radiation ($\lambda = 0.71073$ Å, ω-scans). Using Olex2,[23] the structures were solved with the ShelXT[24] structure solution program using Intrinsic Phasing and refined with the XL[25] refinement package using Least-Squares minimization against F^2 in anisotropic approximation for non-hydrogen atoms. Positions of hydrogen atoms were calculated, and they were refined in the isotropic approximation in the riding model. Severely disordered molecules of lattice ethyl acetate in **3**·0.5EtOAc (its content was tentatively assigned to 0.5) were treated as a diffuse contribution to the overall scattering by using the Solvent Mask option of Olex.[23]

CCDC 2408382 (**3**·0.5EtOAc), 2408383 (**5b**), and 2408384 (**5c**) contain the supplementary crystallographic information for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk.

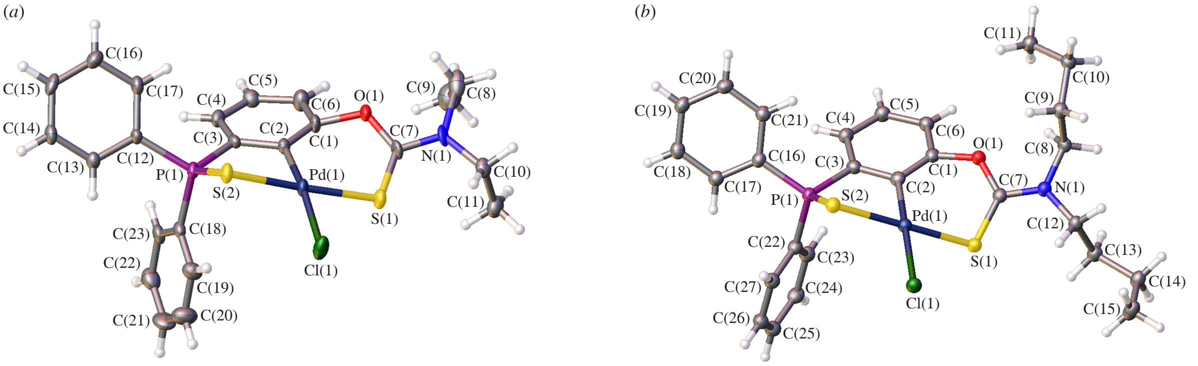


Figure 2 General view of complexes (*a*) **5b** and (*b*) **5c** in representation of atoms as thermal ellipsoids at 30% probability level; the minor component of the disordered NEt_2 group for compound **5b** is omitted for clarity.

complex already upon grinding the reactants in a mortar, although an analytically pure sample was obtained after subsequent short-term heating at 65–70 °C. At the same time, the analogous reaction of butyl-substituted derivative **4c** upon mechanical agitation afforded a mixture of the target Pd^{II} pincer complex, unreacted starting compounds, and an additional product which was not observed in the solution-based synthesis. Based on the results of IR spectroscopic and elemental analyses, we assume that this product is a molecular complex of $[L \cdot PdCl_2]$ composition featuring S,S-bidentate coordination of the non-metalated ligand. Further heating of this solid residue led to the quantitative formation of pincer complex **5c**. Differences in the samples before and after heating were also evident from the results of SEM/EDS analysis (Figure 3). The sample before thermal treatment represented a fine powder with a relatively monodisperse character of crystals, whereas the sample obtained after heating contained larger particles, presumably resulting from the crystallization of an amorphous mass, whose formation was visually detected during heating. Furthermore, the elemental maps of the sample before thermal treatment revealed some regions with non-uniform distribution of the composing elements (for example, Pd and P, see Figure 3), while the EDS images of the sample after heating demonstrated the homogeneity of their distribution (see Online Supplementary Materials, Figures S38 and S39).

To summarize, the thiophosphoryl-functionalized thiocarbamate pincer ligands readily undergo direct cyclopalladation both in solution and under solvent-free conditions to form palladacycles with either free or coordinated P=S units. Therewith, even small changes in a pincer ligand structure can alter the cyclopalladation features under solvent-free conditions, resulting in more diverse reactivity patterns, especially in mechanochemically activated processes.

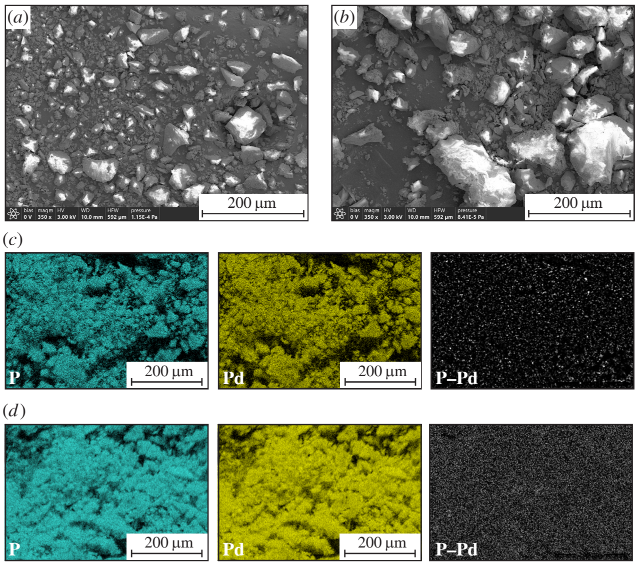


Figure 3 SEM images and elemental maps of the samples obtained by grinding ligand **4c** with $(PhCN)_2PdCl_2$ in a mortar (*a*), (*c*) before and (*b*), (*d*) after heating (magnification 350×).

This work was supported by the Russian Science Foundation (grant no. 22-13-00267). NMR spectroscopic studies were performed using the equipment of the Center for Molecular Composition Studies of INEOS RAS with financial support from the Ministry of Science and Higher Education of the Russian Federation (agreement no. 075-00276-25-00). SEM/EDS measurements were performed in the Federal Research Center for Chemical Physics shared research facilities no. 506694.

Online Supplementary Materials

Supplementary data associated with this article (the experimental section, the NMR and IR spectra of the compounds explored, the IR and NMR spectra of the residues obtained after solid-phase reactions under different conditions, and the EDS elemental maps of the samples obtained from the solid-phase syntheses) can be found in the online version at doi: 10.71267/mencom.7705.

References

1 D. V. Aleksanyan and V. A. Kozlov, *Mendeleev Commun.*, 2023, **33**, 287; https://doi.org/10.1016/j.mencom.2023.04.001.

2 F. Leon and F. Garcia, in *Comprehensive Coordination Chemistry*, 3rd edn., Elsevier, Amsterdam, 2021, vol. 9, ch. 9.19, pp. 620–679; https://doi.org/10.1016/B978-0-08-102688-5.00031-3.

3 A. Beillard, X. Bantreil, T.-X. Métro, J. Martinez and F. Lamaty, *Chem. Rev.*, 2019, **119**, 7529; https://doi.org/acs.chemrev.8b00479.

4 N. R. Rightmire and T. P. Hanusa, *Dalton Trans.*, 2016, **45**, 2352; https://doi.org/10.1039/c5dt03866a.

5 N. J. Coville and L. Cheng, *J. Organomet. Chem.*, 1998, **571**, 149; https://doi.org/10.1016/S0022-328X(98)00914-0.

6 V. A. Kozlov, D. V. Aleksanyan, S. G. Churusova, A. A. Spiridonov, E. Yu. Rybalkina, E. I. Gutsul, S. A. Aksenova, A. A. Korlyukov, A. S. Peregudov and Z. S. Klemenkova, *Int. J. Mol. Sci.*, 2023, **24**, 17331; https://doi.org/10.3390/ijms242417331.

7 D. V. Aleksanyan, S. G. Churusova, E. V. Dubasova, I. V. Ananyev, O. I. Artyushin, A. S. Peregudov, Z. S. Klemenkova, G. L. Denisov and V. A. Kozlov, *Polyhedron*, 2023, **233**, 116303; https://doi.org/10.1016/j.poly.2023.116303.

8 K. J. Ardila-Fierro, M. Rubčić and J. G. Hernández, *Chem. – Eur. J.*, 2022, **28**, e202200737; https://doi.org/10.1002/chem.202200737.

9 T. E. Shaw, L. Mathivathanan and T. Jurca, *Organometallics*, 2019, **38**, 4066; https://doi.org/10.1021/acs.organomet.9b00575.

10 D. V. Aleksanyan, S. G. Churusova, Z. S. Klemenkova, R. R. Aysin, E. Yu. Rybalkina, Yu. V. Nelyubina, O. I. Artyushin, A. S. Peregudov and V. A. Kozlov, *Organometallics*, 2019, **38**, 1062; https://doi.org/10.1021/acs.organomet.8b00867.

11 A. Bjelopetrović, S. Lukin, I. Halasz, K. Užarević, I. Đilović, D. Barišić, A. Budimir, M. Juribašić Kulcsár and M. Ćurić, *Chem. – Eur. J.*, 2018, **24**, 10672; https://doi.org/10.1002/chem.201802403.

12 T. E. Shaw, L. R. Shultz, L. R. Garayeva, R. G. Blair, B. C. Noll and T. Jurca, *Dalton Trans.*, 2018, **47**, 16876; https://doi.org/10.1039/c8dt03608j.

13 J. G. Hernández and C. Bolm, *Chem. Commun.*, 2015, **51**, 12582; https://doi.org/10.1039/c5cc04423e.

14 H. Font, M. Font-Bardia, K. Gómez, G. González, J. Granell, I. Macho and M. Martínez, *Dalton Trans.*, 2014, **43**, 13525; https://doi.org/10.1039/c4dt01463d.

15 M. Juribašić, K. Užarević, D. Gracin and M. Ćurić, *Chem. Commun.*, 2014, **50**, 10287; https://doi.org/10.1039/c4cc04423a.

16 A. N. Chernyshev, N. A. Bokach, P. V. Gushchin, M. Haukka and V. Yu. Kukushkin, *Dalton Trans.*, 2012, **41**, 12857; https://doi.org/10.1039/c2dt30986f.

17 Yu. Yu. Scaffidi-Domianello, A. A. Nazarov, M. Haukka, M. Galanski, B. K. Keppler, J. Schneider, P. Du, R. Eisenberg and V. Yu. Kukushkin, *Inorg. Chem.*, 2007, **46**, 4469; https://doi.org/10.1021/ic062414k.

18 D. V. Aleksanyan, Z. S. Klemenkova, A. A. Vasil'ev, A. Ya. Gorenberg, Yu. V. Nelyubina and V. A. Kozlov, *Dalton Trans.*, 2015, **44**, 3216; https://doi.org/10.1039/C4DT03477E.

19 D. V. Aleksanyan, S. G. Churusova, R. R. Aysin, Z. S. Klemenkova, Yu. V. Nelyubina and V. A. Kozlov, *Inorg. Chem. Commun.*, 2017, **76**, 33; https://doi.org/10.1016/j.inoche.2016.12.006.

20 R. Zhiani, S. M. Sadeghzadeh, S. Emrani and M. Abasian, *J. Organomet. Chem.*, 2018, **855**, 1; https://doi.org/10.1016/j.jorganchem.2017.11.027.

21 Z. Kiani, R. Zhiani, S. Khosroyar, A. Motavalizadehkakhky and M. Hosseiny, *Inorg. Chem. Commun.*, 2021, **124**, 108382; https://doi.org/10.1016/j.inoche.2020.108382.

22 S. Lorraine, K. Abdur-Rashid, W. Jia, K. Abdur-Rashid, P. Maragh and T. Dasgupta, *Inorg. Chim. Acta*, 2020, **511**, 119850; https://doi.org/10.1016/j.ica.2020.119850.

23 O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339; https://doi.org/10.1107/S0021889808042726.

24 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Adv.*, 2015, **71**, 3; https://doi.org/10.1107/S2053273314026370.

25 G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, **64**, 112; https://doi.org/10.1107/S0108767307043930.

Received: 9th December 2024; Com. 24/7705