Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2022, **32**, 205–207

Mendeleev
Communications

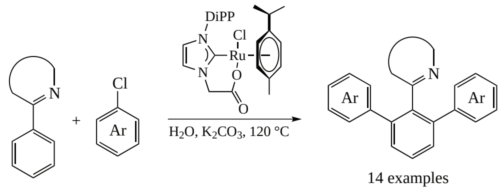
Ruthenium complexes with chelating carboxylate-NHC ligands as efficient catalysts for C–H arylation in water

Konstantin E. Shepelenko,[a] Ksenia A. Nikolaeva,[a] Maxim A. Shevchenko,[a] Yurii N. Tkachenko,[a] Mikhail E. Minyaev[b] and Victor M. Chernyshev*[a]

[a] *Platov South-Russian State Polytechnic University, 346428 Novocherkassk, Russian Federation.*
E-mail: chern13@yandex.ru
[b] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation*

DOI: 10.1016/j.mencom.2022.03.017

Ruthenium(II) complexes with chelating N-heterocyclic carbene (NHC) ligands were studied in the arylation of phenyl group in 2-phenylpyridine and 1-phenylpyrazole with aryl chlorides in water. Complexes with NHC-ligands containing a hemilabile coordinating *N*-carboxylatomethyl group enable fast and selective *ortho*-CH-diarylation in the absence of carboxylate-assisting additives.



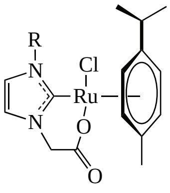
14 examples
85–97% isolated yields

Keywords: ruthenium complexes, CH-activation, arylation, N-heterocyclic carbene ligands, carboxylate assistance.

Transition-metal catalyzed C(sp^2)–H bond arylation becomes an indispensable tool for the synthesis of unsymmetric biaryls, liquid crystals, organic electronic materials, drugs, crop protection agents and many other valuable compounds.[1–3] Ruthenium(II) complexes have been acknowledged as highly efficient catalysts for the site-selective C–H arylation of (hetero)aromatic compounds with N- and O-containing *ortho*-directing groups.[4,5] Ruthenium(II) compounds often provide good tolerance to water, the most green solvent, that is an important benefit over many other transition metals used for catalysis of C–H and C–heteroatom arylation.[6–8] N-Heterocyclic carbenes (NHCs) represent prominent class of ligands used in transition-metal catalyzed C–H activation reactions which often provide higher robustness and lower toxicity of catalytic systems compared to phosphines and many other ligands.[9–13] Complexes of Ru with NHC-ligands (Ru/NHC) were reported as efficient catalysts for site-selective C–H arylation.[14–22] Remarkably, recent study revealed their feasibility for the catalysis of CH-arylation with (hetero)aryl chlorides in water.[22] Ruthenium catalyzed CH-arylation is often conducted in the presence of carboxylic acid salts[19–25] or amides[26] which provide carboxylate(carboxamide)-assistance of C–H bond activation *via* concerted metalation–deprotonation (CMD)[27–29] mechanism peculiar for Ru-catalysis. We proposed that installation of hemilabile carboxylate or carboxamide wingtip groups capable of reversible coordinating with Ru atom on the N-atom of imidazol-2-ylidene ligand can enhance catalytic performance of Ru/NHC systems **1** and **2** owing to participation of the COO$^-$ or CONHR groups in CMD catalysis. In addition, chelated structure of such complexes can enhance their stability against undesired reductive elimination of NHC ligands.[30,31] It should be noted that chelated complexes of general structure **1** were reported previously as catalysts for styrene hydrogenation and revealed significantly higher activity than complexes of close structure without carboxylatomethyl groups.[32] However, to the best of our knowledge, complexes of general types **1** and **2** were never studied before in catalysis of CH-arylation reactions.

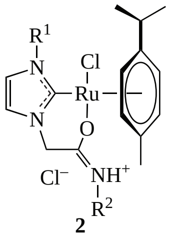
Herein, we report results of our study of chelated complexes **1** and **2** in the arylation of 2-phenylpyridine and 1-phenylpyrazole with aryl chlorides in water and represent a new promising catalyst for directed *ortho*-CH-arylation of aromatic compounds.

Complexes Ru/NHC **1a**–**c**, **2a**–**d** and **3a**,**b** studied in this work were obtained from the corresponding NHC-proligands by transmetalation of *in situ* generated Ag/NHC complexes with [RuCl$_2$(cymene)]$_2$ (for details and characteristics of compounds **1c**, **2a**–**c**, see Online Supplementary Materials). Compound **3c** was synthesized by previously reported method.[33] Complexes **1** and **2** represent air-stable orange microcrystalline compounds. Their structures were confirmed by elemental analyses, NMR and ESI-MS spectra as well as single crystal X-ray studies of compounds **1c** and **2a**–**c** (Figure 1).† Spectral data for previously



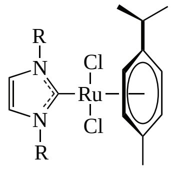
1

a R = Me
b R = Mes
c R = DiPP



2

a R^1 = Me, R^2 = DiPP
b R^1 = Mes, R^2 = Bu^t
c R^1 = R^2 = Mes
d R^1 = DiPP, R^2 = Bu^t

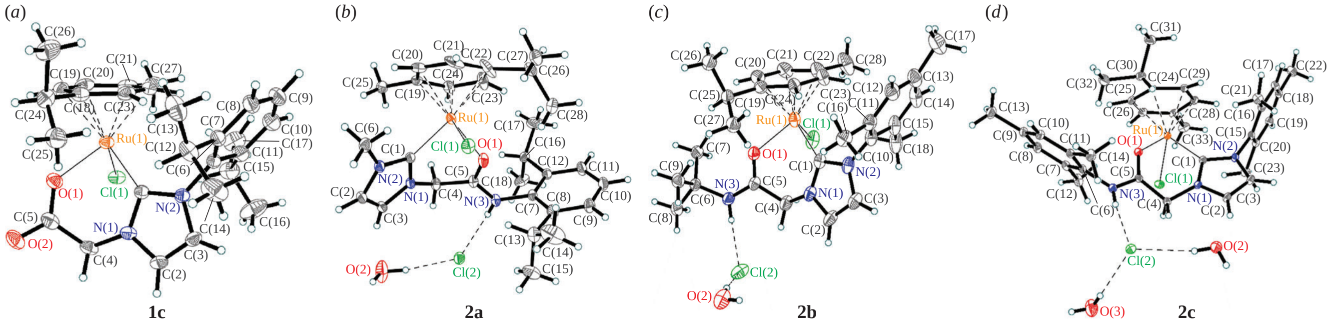


3

a R = Me
b R = Bu
c R = Mes

---

† *Crystal data for* **1c**·Et$_2$O. C$_{31}$H$_{45}$ClN$_2$O$_3$Ru (M = 630.21), triclinic, space group $P\bar{1}$ at 100(2) K, a = 10.4819(2), b = 10.8202(2) and c = 14.2449(3) Å, β = 96.5280(10)°, V = 1493.16(5) Å^3, Z = 2, d_{calc} = 1.402 g cm^{-3}, μ(MoKα) = 0.648 mm^{-1}, F(000) = 660. Total of 72541 reflections were collected (10812 independent reflections, R_{int} = 0.0782) and used in the refinement, which converged to $wR(F^2)$ = 0.0868, GOOF



1c **2a** **2b** **2c**

Figure 1 General view of (*a*) complex **1c**, (*b*) complex **2a**, (*c*) complex **2b** and (*d*) complex **2c** in the representation of atoms *via* thermal ellipsoids at the 50% probability level. Disorder is omitted.

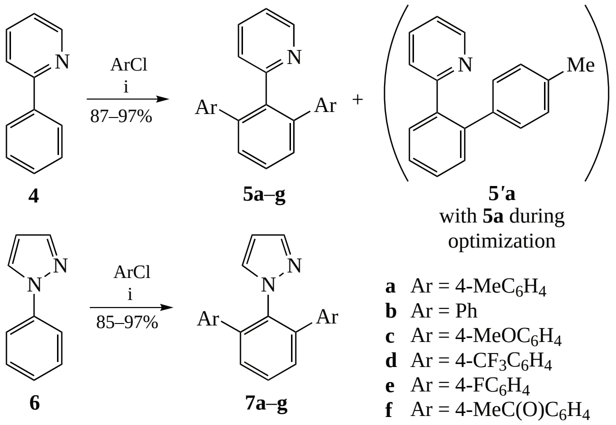
described complexes **1a**,**b**, **3a**–**c** correspond to those reported in literature.[32] X-ray structures of compounds **1c** and **2a**–**c** are analogous to those of described Ru/NHC complexes containing similar chelating NHC-ligands and *p*-cymene co-ligand.[32,34,35]

Catalytic properties of the obtained Ru/NHC complexes **1**–**3** as well as $[RuCl_2(cymene)]_2$ (for comparison) were evaluated in CH-arylation of 2-phenylpyridine **4** with 4-chlorotoluene in water (Table 1, Scheme 1) under conditions typical for the Ru-catalyzed arylations.[22,36,37] Moderate conversions of starting compound **4** were observed at 80–100 °C (see Table 1, entries

Table 1 Comparison of Ru/NHC complexes in the arylation of compound **4**.[a]

Entry	Catalyst	Solvent	Base	*T*/°C	Conversion (%)[b]	Yield (%)[c]	
						5a	**5′a**
1	**1a**	H_2O	K_2CO_3	120	99	82	17
2	**1b**	H_2O	K_2CO_3	120	99	79	20
3	**1c**	H_2O	K_2CO_3	80	60	9	51
4	**1c**	H_2O	K_2CO_3	100	90	85	5
5	**1c**	H_2O	K_2CO_3	120	100	99 (97),[d] 99,[e] 64[f]	1, 1,[e] 32[f]
6	**1c**	H_2O	K_2CO_3	120	95	85[g]	10
7	**1c**	H_2O	Na_2CO_3	120	95	82	13
8	**1c**	H_2O	Cs_2CO_3	100	86	73	13
9	**1c**	H_2O	Cs_2CO_3	120	91	76	15
10	**1c**	H_2O	KOH	120	92	86	6
11	**1c**	H_2O	K_3PO_4	120	98	72	26
12	**1c**	NMP	K_2CO_3	120	83	36	47
13	**1c**	Toluene	K_2CO_3	120	40	2	38
14	**2a**	H_2O	K_2CO_3	120	100	65	35
15	**2b**	H_2O	K_2CO_3	120	74	26	48
16	**2c**	H_2O	K_2CO_3	120	100	80	20
17	**2d**	H_2O	K_2CO_3	120	98	71	27
18	**3a**	H_2O	K_2CO_3	120	85	52	33
19	**3b**	H_2O	K_2CO_3	120	76	31	45
20	**3c**	H_2O	K_2CO_3	120	89	17	72
21	$[RuCl_2(cymene)]_2$	H_2O	K_2CO_3	120	92	47	45
22	none	H_2O	K_2CO_3	120	0	0	0

[a] *Reagents and conditions*: 2-phenylpyridine **4** (0.1 mmol), $4\text{-}MeC_6H_4Cl$ (0.25 mmol), [Ru] (0.0025 mmol, 2.5 mol%), K_2CO_3 (0.25 mmol), H_2O (1 ml), 12 h. [b] Conversion of 2-phenylpyridine. [c] GC-MS yield. [d] Isolated yield. [e] With 5 mol% **1c**. [f] With 1 mol% **1c**. [g] 8 h.



4 **5a–g** **5′a** with **5a** during optimization

6 **7a–g**

a Ar = $4\text{-}MeC_6H_4$
b Ar = Ph
c Ar = $4\text{-}MeOC_6H_4$
d Ar = $4\text{-}CF_3C_6H_4$
e Ar = $4\text{-}FC_6H_4$
f Ar = $4\text{-}MeC(O)C_6H_4$
g Ar = $3\text{-}MeC_6H_4$

Scheme 1 *Reagents and conditions*: i, **4** or **6** (0.1 mmol), ArCl (0.25 mmol), K_2CO_3 (0.25 mmol), catalyst **1c** (2.5 mol%), H_2O (1 ml), 120 °C, 12 h.

1.020 for all independent reflections [R_1 = 0.0446 was calculated for 8156 reflections with $I > 2\sigma(I)$].

Crystal data for **2a**·H_2O. $C_{28}H_{41}Cl_2N_3O_2Ru$ (M = 623.61), triclinic, space group $P\bar{1}$ at 100(2) K, a = 10.1277(2), b = 10.3823(2) and c = 15.5175(3) Å, β = 92.7864°, V = 1454.35(5) Å^3, Z = 2, d_{calc} = 1.424 g cm^{-3}, μ(MoKα) = 0.752 mm^{-1}, $F(000)$ = 648. Total of 143979 reflections were collected (14087 independent reflections, R_{int} = 0.0307) and used in the refinement, which converged to $wR(F^2)$ = 0.0600, GOOF 1.052 for all independent reflections [R_1 = 0.0262 was calculated for 12943 reflections with $I > 2\sigma(I)$].

Crystal data for **2b**·H_2O. $C_{28}H_{41}Cl_2N_3O_2Ru$ (M = 623.61), triclinic, space group $P\bar{1}$ at 100(2) K, a = 9.8425(5), b = 9.8425(5) and c = 15.3995(8) Å, β = 76.7820(10)°, V = 1628.14(15) Å^3, Z = 2, d_{calc} = 1.272 g cm^{-3}, μ(MoKα) = 0.672 mm^{-1}, $F(000)$ = 648. Total of 79315 reflections were collected (11766 independent reflections, R_{int} = 0.0545) and used in the refinement, which converged to $wR(F^2)$ = 0.1335, GOOF 1.029 for all independent reflections [R_1 = 0.0566 was calculated for 9354 reflections with $I > 2\sigma(I)$].

Crystal data for **2c**·1.82 H_2O. $C_{33}H_{44.63}Cl_2N_3O_{2.82}Ru$ (M = 700.40), monoclinic, space group $P2_1/n$ at 100(2) K, a = 9.76421(13), b = 21.3530(3) and c = 15.6948(2) (3) Å, β = 97.3468(13)°, V = 3245.43(8) Å^3, Z = 4, d_{calc} = 1.433 g cm^{-3}, μ(MoKα) = 0.684 mm^{-1}, $F(000)$ = 1456.7. Total of 58895 reflections were collected (13264 independent reflections, R_{int} = 0.0301) and used in the refinement, which converged to $wR(F^2)$ = 0.0613, GOOF 1.040 for all independent reflections [R_1 = 0.0247 was calculated for 11678 reflections with $I > 2\sigma(I)$].

X-ray diffraction data were collected at 100 K on a Bruker Quest D8 diffractometer equipped with a Photon-III area-detector (crystals **1c** and **2a**,**b**) and on a Rigaku Synergy-S diffractometer equipped with a HyPix600HE area-detector (**2c**), using graphite-monochromatized MoKα-radiation and shutterless ω-scan technique. The intensity data were integrated by the SAINT program[38] and were corrected for absorption and decay using SADABS[39] (**1c** and **2a**,**b**) or were integrated and corrected by CrysAlisPro[40] (**2c**). The structures were solved by direct methods using SHELXT[41] and refined on F^2 using SHELXL-2018.[42] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters; a rotating group model was applied for methyl groups. Unidentified disordered non-coordinating solvent molecules in crystal channels of **2b** were removed by the SQUEEZE method.[43]

CCDC 2109279–2109282 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

3, 4). However, conversion of **4** and yield of the diarylated product **5a** were improved significantly when the reaction was performed at 120 °C (entry 5). Among various Ru complexes, compound **1c** containing chelating *N*-carboxylatomethyl group and bulky *N′*-DiPP substituent in the NHC-ligand (DiPP is 2,6-diisopropylphenyl) demonstrated the best catalytic performance (entries 3–13). Complexes **1a**,**b** containing the same *N*-carboxylatomethyl group but less bulky N′-substituents also provided complete conversion of the starting compound **4**, although gave slightly lower yields of the diarylated product **5a**. Complexes **2a**–**d** with chelating *N*-carboxamidomethyl groups in the NHC-ligands also demonstrated good activities, however resulted in slightly lower yields of product **5a** (entries 14–17) than complex **1c**. Complexes **2a,c** containing aromatic *N*-aryl group in the carboxamide moiety revealed higher conversions of **4** and higher yields of **5a** (entries 14, 16) compared to complexes **2b**,**d** with *N*-Bu^t group in the carboxamide moiety (entries 15, 17). Nonchelated complexes **3a**–**c** containing simple *N*,*N*-dialkyl(aryl) ligands were less efficient catalysts (entries 18–20), their catalytic performance was even lower than the performance of $[\mathrm{RuCl_2(cymene)}]_2$ used for comparison (see Table 1 and Figure S1 of Online Supplementary Materials). After optimization of the reaction conditions by varying Ru loadings, reaction times and bases (see Table 1), conditions of entry 5 were accepted as the optimal. Remarkably, experiments with other solvents often used for Ru-catalyzed C–H arylations (entries 12, 13) revealed that water was a more efficient solvent.

With the optimal conditions in hands, we studied arylation of compound **4** and 1-phenylpyrazole **6** with various aryl chlorides (see Scheme 1). It has been found that the developed catalytic system provides efficient *ortho*-diarylation of both substrates with aryl chlorides containing electron-withdrawing as well as electron-donating substituents in the absence of additional carboxylate ligands.

In conclusion, Ru complexes with NHC ligands containing chelating *N*-carboxylatomethyl or *N*-carboxamidomethyl groups were studied as catalysts in the *ortho*-arylation of benzene ring directed by pyridine or pyrazole groups. A new Ru/NHC complex containing *N*-carboxylatomethyl-*N′*-DiPP-imidazol-2-ylidene ligand was found to be an efficient catalyst for the *ortho*-diarylation in water with aryl chlorides. The use of water as the green solvent, cheap base (K_2CO_3) and the absence of necessity in carboxylate ligand additives represent important advantages of the developed catalytic system.

This work was supported by the Russian Science Foundation (grant no. 19-73-20085). The authors are grateful to Academician of the Russian Academy of Sciences, Professor V. P. Ananikov for a fruitful discussion of the results of this work and valuable comments. The authors also thank the Shared Research Center ‘Nanotechnologies’ of the Platov South-Russian State Polytechnic University for NMR and GC-MS services, and the Shared Research Center of Zelinsky Institute of Organic Chemistry for mass-spectrometry and X-ray analyses.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.03.017.

References

1 J. C. K. Chu and T. Rovis, *Angew. Chem., Int. Ed.*, 2018, **57**, 62.
2 P. Gandeepan and L. Ackermann, *Chem.*, 2018, **4**, 199.
3 P. Gandeepan, T. Müller, D. Zell, G. Cera, S. Warratz and L. Ackermann, *Chem. Rev.*, 2019, **119**, 2192.
4 M. Seki, *Org. Process Res. Dev.*, 2016, **20**, 867.
5 T. Cernak, K. D. Dykstra, S. Tyagarajan, P. Vachal and S. W. Krska, *Chem. Soc. Rev.*, 2016, **45**, 546.
6 S. Shome and S. P. Singh, *Chem. Rec.*, 2019, **19**, 1935.
7 G.-F. Zha, H.-L. Qin and E. A. B. Kantchev, *RSC Adv.*, 2016, **6**, 30875.
8 P. Nareddy, F. Jordan and M. Szostak, *ACS Catal.*, 2017, **7**, 5721.
9 Q. Zhao, G. Meng, S. P. Nolan and M. Szostak, *Chem. Rev.*, 2020, **120**, 1981.
10 E. Rufino-Felipe, R. Nayely Osorio-Yáñez, M. Vera, H. Valdés, L. González-Sebastián, A. Reyes-Sanchez and D. Morales-Morales, *Polyhedron*, 2021, **204**, 115220.
11 K. E. Shepelenko, S. B. Soliev, A. S. Galushko, V. M. Chernyshev and V. P. Ananikov, *Inorg. Chem. Front.*, 2021, **8**, 1511.
12 O. V. Khazipov, K. E. Shepelenko, D. V. Pasyukov, V. V. Chesnokov, S. B. Soliev, V. M. Chernyshev and V. P. Ananikov, *Org. Chem. Front.*, 2021, **8**, 2515.
13 J. Cabanes, M. Odnoroh, C. Duhayon, C. Bijani, A. Sournia-Saquet, R. Poli and A. Labande, *Mendeleev Commun.*, 2021, **31**, 620.
14 I. Özdemir, S. Demir, B. Çetinkaya, C. Gourlaouen, F. Maseras, C. Bruneau and P. H. Dixneuf, *J. Am. Chem. Soc.*, 2008, **130**, 1156.
15 S. Yaşar, Ö. Doğan, I. Özdemir and B. Çetinkaya, *Appl. Organomet. Chem.*, 2008, **22**, 314.
16 S. Demir, I. Özdemir and B. Çetinkaya, *J. Organomet. Chem.*, 2009, **694**, 4025.
17 İ. Özdemir, S. Demir, N. Gürbüz, B. Çetinkaya, L. Toupet, C. Bruneau and P. H. Dixneuf, *Eur. J. Inorg. Chem.*, 2009, 1942.
18 S. Demir, I. Özdemir, O. Şahin, B. Çetinkaya and O. Büyükgüngör, *Synlett*, 2010, 496.
19 A. Prades, M. Poyatos and E. Peris, *Adv. Synth. Catal.*, 2010, **352**, 1155.
20 S. Sabater, J. A. Mata and E. Peris, *Organometallics*, 2012, **31**, 6450.
21 S. Gonell and E. Peris, *ACS Catal.*, 2014, **4**, 2811.
22 N. Kaloğlu, İ. Özdemir, N. Gürbüz, H. Arslan and P. H. Dixneuf, *Molecules*, 2018, **23**, 647.
23 L. Ackermann, R. Vicente, H. K. Potukuchi and V. Pirovano, *Org. Lett.*, 2010, **12**, 5032.
24 E. Diers, N. Y. Phani Kumar, T. Mejuch, I. Marek and L. Ackermann, *Tetrahedron*, 2013, **69**, 4445.
25 J. Hubrich, T. Himmler, L. Rodefeld and L. Ackermann, *ACS Catal.*, 2015, **5**, 4089.
26 J. Zhang, Q. Yang, Z. Zhu, M. L. Yuan, H. Y. Fu, X. L. Zheng, H. Chen and R. X. Li, *Eur. J. Org. Chem.*, 2012, 6702.
27 L. Ackermann, *Chem. Rev.*, 2011, **111**, 1315.
28 I. Fabre, N. von Wolff, G. Le Duc, E. Ferrer Flegeau, C. Bruneau, P. H. Dixneuf and A. Jutand, *Chem. – Eur. J.*, 2013, **19**, 7595.
29 C. Shan, L. Zhu, L.-B. Qu, R. Bai and Y. Lan, *Chem. Soc. Rev.*, 2018, **47**, 7552.
30 V. M. Chernyshev, E. A. Denisova, D. B. Eremin and V. P. Ananikov, *Chem. Sci.*, 2020, **11**, 6957.
31 V. M. Chernyshev, O. V. Khazipov, D. B. Eremin, E. A. Denisova and V. P. Ananikov, *Coord. Chem. Rev.*, 2021, **437**, 213860.
32 C. Gandolfi, M. Heckenroth, A. Neels, G. Laurenczy and M. Albrecht, *Organometallics*, 2009, **28**, 5112.
33 N. Ledoux, B. Allaert and F. Verpoort, *Eur. J. Inorg. Chem.*, 2007, 5578.
34 J. DePasquale, N. J. White, E. J. Ennis, M. Zeller, J. P. Foley and E. T. Papish, *Polyhedron*, 2013, **58**, 162.
35 A. Mangalum, C. D. McMillen and A. G. Tennyson, *Inorg. Chim. Acta*, 2015, **426**, 29.
36 P. B. Arockiam, C. Fischmeister, C. Bruneau and P. H. Dixneuf, *Green Chem.*, 2013, **15**, 67.
37 C. Binnani, R. K. Rai, D. Tyagi, S. M. Mobin and S. K. Singh, *Eur. J. Inorg. Chem.*, 2018, 1435.
38 *Bruker APEX-III*, Bruker AXS Inc., Madison, WI, 2019.
39 L. Krause, R. Herbst-Irmer, G. M. Sheldrick and D. Stalke, *J. Appl. Crystallogr.*, 2015, **48**, 3.
40 *CrysAlisPro, Version 1.171.41.106a*, Rigaku Oxford Diffraction, 2021.
41 G. M. Sheldrick, *Acta Crystallogr.*, 2015, **A71**, 3.
42 G. M. Sheldrick, *Acta Crystallogr.*, 2015, **C71**, 3.
43 A. L. Spek, *Acta Crystallogr.*, 2015, **C71**, 9.

Received: 16th September 2021; Com. 21/6694