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The solid-state hierarchy and iodination potential of [bis(3-acetaminopyridine)iodine(I)]PF_6†

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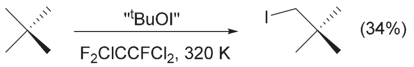
The first iodine(I) complex bearing hydrogen-bond donor and acceptor groups, [bis(3-acetaminopyridine)iodine(I)]PF_6 (3), was synthesised, which exhibited two temperature-dependent solid-state connectivities of the hydrogen bonding. Upon reaction of 3 with ^{t}BuOMe, unprecedented iodination of a ^{t}Bu methyl group proceeded under exceptionally mild conditions in good yield.

Halogen bonding has rapidly matured into one of the most studied intermolecular interactions, and comparisons can be drawn with hydrogen bonding. Hydrogen-bonded networks have a well-established history of practical uses, from body armour to constituting the double helix of our DNA, and whilst not as ubiquitous, the advantages of halogen bonding, like a strictly enforced linear geometry due to its electronic origins as a σ-hole interaction,[1] have been deftly utilised toward constructing supramolecular architectures *via* self-assembling methodologies.[2,3] The subfield of halogen bonding incorporating formally cationic halogen atoms, X^+ (X = Cl, Br, I), termed halogen(I) ions has been known since the 1960s,[4] but was popularised by Barluenga in the 1990s due to the myriad of organic transformations they can perform.[5–7] The closely related family of carbonyl or alkyl hypoiodites (R–OI; R = carbonyl or alkyl), recently demonstrated for the first time to be comparable to halogen-bonded iodine(I) species,[8,9] are often utilised as *in situ* generated reagents.[10,11] Alkyl hypoiodites such as "^{t}BuOI",[12,13] for which the exact reactive species is still under debate,[14] have been reported to perform difficult synthetic conversions such as the synthesis of neopentyl iodide from unactivated neopentane (Scheme 1).[15] However, iodinations are predominantly limited to substrates which possess sacrificial functional groups (*e.g.*, hydroxyl or carboxylic acids),[16–18] require exotic reagents or methodologies,[18–20] and entail multi-step syntheses.[21,22] Given that the formation of C–I functionalities remains non-trivial, this creates a void in the literature that iodine(I) species might be able to fill with further research, especially as C–I compounds are of great utility and can act as feedstocks in a wide range of synthetic procedures such as Pd-cross coupling reactions.[23–25]

The concept of hierarchical materials, that is materials with structural elements which themselves have structure,[26] has found success in a variety of fields including bio-inspired and biomimetic materials,[27,28] as well as toward materials for medical applications.[29,30] To date, examples of iodine(I) complexes in the solid-state incorporate pyridine,[31] or pyridine derivatives with no secondary functional groups capable of meaningful intermolecular interactions,[32,33] with only a handful of examples of a single ligand, 4-aminopyridine (4-NH_2py), capable of enabling strong hydrogen-bonded intermolecular interactions.[34] However, the prior solid-state examples incorporating 4-NH_2py were all limited to demonstrating ion pair interactions with their halide anions, owing to their direct synthesis from I_2 or IX (X = Cl, Br).[34]

The 3-acetaminopyridine (**1**) ligand was synthesised according to a literature procedure from 3-aminopyridine,[35] and straightforwardly incorporated into the iodine(I) complex $[I(\mathbf{1})_2]PF_6$ (**3**) in a one-pot reaction *via* its respective silver(I) complex, $[Ag(\mathbf{1})_2]PF_6$ (**2**; Scheme 2). The ^{1}H NMR spectra in CD_3CN of **1**–**3** were as expected, showing the single alkyl peak for the acetyl group, and five peaks in the aromatic region for the four distinct aromatic groups and the NH group. The series also clearly showed the trend of moving downfield to higher frequency going from **1** to **3** (Fig. 1), with the largest coordination shift (Δ*δ*) of 0.52 ppm observed for the aromatic hydrogen atom at the 2-position (H_a in Fig. 1) of **2** (8.78 ppm)



Scheme 1 The synthesis of neopentyl iodide from unactivated neopentane using the *in situ* generated iodine(I) reagent "^{t}BuOI".

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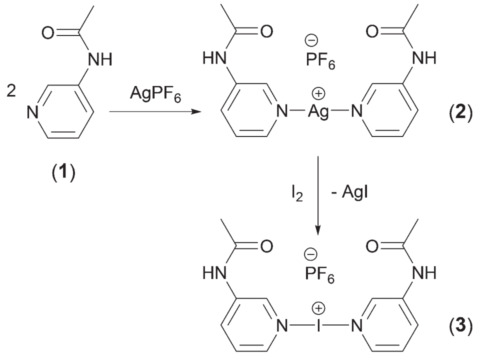
† Electronic supplementary information (ESI) available: Synthesis, NMR and X-ray crystallographic details. CCDC 2193903–2193906. For ESI and crystallographic data in CIF or other electronic format see DOI: **https://doi.org/10.1039/d2ce01225a**



Scheme 2 The synthetic procedure to generate the iodine(I) complex **3** from ligand **1** *via* the silver(I) complex **2**.

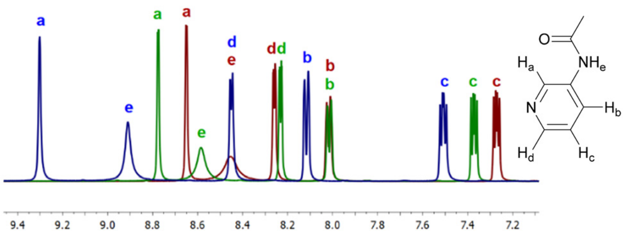


Fig. 1 The superimposed ^1H NMR spectra in CD_3CN (298 K) of **1** (red), **2** (green), and **3** (blue), annotated with the hydrogen atom assignments, showing the downfield-shifted trend of coordination shifts going from **1** to **3**.

and **3** (9.30 ppm). This trend was observed for all ^1H NMR peaks except for the aromatic hydrogen atom at the 4-position (H_b in Fig. 1) of **1** (8.02 ppm) and **2** (8.02 ppm), which was unaffected by coordination to the Ag^+ centre in **2**.

The ^1H–^{15}N HMBC determined ^{15}N NMR chemical resonances also demonstrated the same trend of coordination shifts for the pyridinic peaks of **1** (−63.7 ppm), **2** (−85.8), and **3** (−174.5 ppm), which has been previously observed for similar systems.[8,32] The ^{15}N NMR peak for **2** (−85.8) was lower than other analogous bis(substituted pyridine)silver(I) complexes reported (δ_N ~110–140), but this is due to the NMR solvent being CD_3CN,[36,37] as opposed to the much more commonly used (and non-coordinating) solvent CD_2Cl_2.[32] This was supported by the single crystal X-ray diffraction (SCXRD) structure of **2** (Fig. S1†), where each Ag^+ centre was found to be weakly coordinated to two CH_3CN molecules, with Ag⋯NCMe distances of 2.722(3) and 2.756(3) Å. This did not affect the characteristic Ag–N bond lengths of 2.183(2) and 2.189(2) Å, and a N–Ag–N angle of 174.40(8)°, which agree well with other 2-coordinate silver(I) complexes incorporating pyridine-based ligands.[31]

Interestingly, two solid-state structures of the same composition (polymorphs) were observed for **3**, *viz.* **3_1** and **3_2**, with **3_2** containing two crystallographically independent molecules in the asymmetric unit cell (**3_1** only has one molecule in the asymmetric unit). The important structural features of the two polymorphs both fall within the expected values for iodine(I) complexes, with I–N bond lengths of 2.237(5)/2.296(5) Å for **3_1**, and 2.250(5)/2.251(4) Å and 2.253(4)/2.255(4) Å for the two independent molecules of **3_2**, and N–I–N angles of 175.7(2)° (**3_1**), 177.2(2)° (**3_2**), and 177.8(2)° (**3_2**). Iodine(I) ions, and halogen(I) ions generally, do not typically demonstrate meaningful intermolecular interactions in the solid state, though some examples ($I^+ \cdots I^+$, $I^+ \cdots Ag^+$) have been reported.[32,38–40] Whilst **3_2** exhibited no close contacts, with only $I^+ \cdots F–PF_5$ interactions of 3.779(4) Å or longer (*cf.* van der Waals radii of I + F = 3.45 Å), **3_1** was found to have close $I^+ \cdots F–PF_5$ intermolecular interactions of 3.333(9) and 3.520(6) Å from two disordered positions of the same PF_6 anion. Nevertheless, the main structural difference is the arrangement of the two acetylamino groups, with **3_1** assuming a pseudo-*syn* conformation (40.6° between the planes of the two acetylamino groups) and both independent molecules in **3_2** assuming a pseudo-*anti* conformations (with 137.0° and 137.9° between the planes of the acetylamino groups).

The packing of these two polymorphs is where the differences truly emerge, with **3_1** demonstrating a 1D polymeric chain of the $[I(\mathbf{1})_2]^+$ cations coordinating along the axis of their N–I–N halogen bond, connected *via* C═O⋯H–N hydrogen bonding of the carbonyl oxygen atom and the NH group of adjacent cations (Fig. 2). The other pair of NH and C═O groups per cation were found to terminate through coordination to a PF_6 anion (N–H⋯F) or with no identifiable intermolecular interactions, respectively. Conversely, the packing of **3_2** was found to be constructed of 1D polymeric sheets of $[I(\mathbf{1})_2]^+$ cations coordinating perpendicular to the axis of their N–I–N halogen bond, and connected *via* pairs of C═O⋯H–N hydrogen bonds to each of their adjacent cations (Fig. 3).

These two polymorphs were reproducibly isolated from the same crystallisation solvents (7 : 1 CH_2Cl_2 : MeCN vapour diffused with pentane),‡ though at different temperatures, with crystals of **3_2** being prepared at ambient temperature, and crystals of **3_1** at 253 K. The data for the two polymorphs even had to be collected at different experimental temperatures: 200 K for **3_1**, and 120 K for **3_2**, which was due to the crystals of **3_1** catastrophically shattering below 200 K, even when introduced at higher temperatures and slowly cooled with ramp rates of 1 K min^{-1}, and highlights the untapped potential of such hydrogen-bonded iodine(I) complexes to create different molecular assemblies through functional group modification and *via* temperature control.

Upon attempted crystallisation of a CH_2Cl_2 : MeCN (7 : 1) solution of **3** with ^{t}BuOMe over 48 hours, the unexpected reaction product $[(\mathbf{1})CMe_2(CH_2I)]PF_6$ (**4**) was isolated in 65% yield (based on I^+ content of **3**) as a crystalline solid, with the identity of **4** definitely confirmed by SCXRD (Fig. 4). The two important features highlighted by the SCXRD analysis was the incorporation of a ^{t}Bu group from the ^{t}BuOMe anti-solvent, and more interestingly, the installation of an iodine atom on a methyl group of that ^{t}Bu group. As best as can be determined, no similar reactivity of iodine(I) complexes reacting with routinely used etheric solvents (commonly used

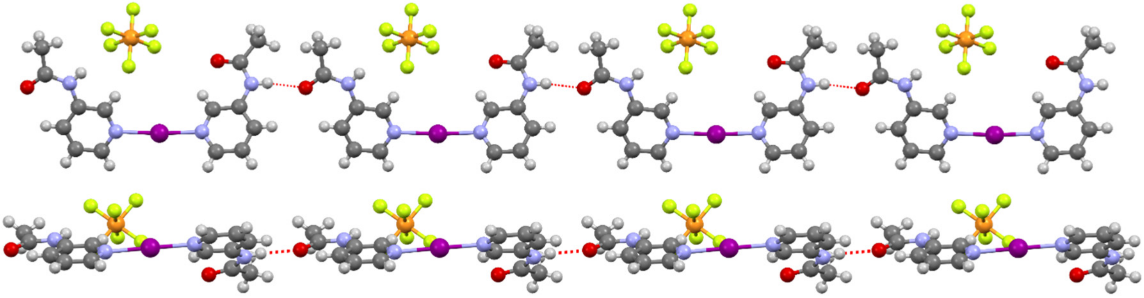


Fig. 2 The solid-state packing of four molecules of **3_1** (top; viewed down the *a*-axis) showing the 1D chain of hydrogen-bonded iodine(I) cations (hydrogen bonds represented by red dashed lines), and sideview (bottom).

as anti-solvents in the halogen(I) field) have been reported, and especially not as a major product. Similarly, precedent for the introduction of an iodine atom to an non-functionalised alkyl group is difficult to find, though the closely related field of alkyl hypoiodites reported the conversion of neopentane to neopentyl iodide in a modest yield of 34%.[15] However, this reaction used *in situ* generated "^{t}BuOI", for which the structure of the actual reactive species performing the reaction is still under debate.[14,15]

Whilst there is precedent for the installation of N–C bonds to aromatic amines and the activation of benzylic positions,[41,42] a ^{t}Bu group installed at the nitrogen position of a pyridine would still present the same synthetic challenge of introducing an iodine atom at one of the ^{t}Bu methyl positions, therefore mechanistically it can be surmised that the iodine atom is introduced prior to, or concomitantly with, the introduction of the ^{t}Bu substituent to a molecule of **1**. As this phenomenon is unique to an iodine(I) complex incorporating ligand **1**, it is also reasonable to propose that the acetylamino substituent facilitates the process in some manner.

A straightforward mechanistic explanation for **4** would be the reaction of ^{t}BuOMe with complex **3** as a source of "I^+", generating the reactive hypoiodite species IOMe and ^{t}Bu$^+$ (Fig. S7†). The ^{t}Bu$^+$ would then go on to lose a proton to become 2-methylpropene (isobutene). The alkene group of the 2-methylpropene would in turn react with a source of "I^+" (either from complex **3** or the *in situ* generated IOMe) and a molecule of **1** (liberated from **3** to generate the initial reactive source of "I^+", $[I(\mathbf{1})]^+$)[43,44] would act as a nucleophile to form the new pyridinic N–C bond with the newly formed $[CMe_2(CH_2I)]^+$ fragment. Whilst grounded in the literature, this proposed mechanism does not explain why this reactivity is only observed for **3** and has not been reported for other iodine(I) complexes, given that ^{t}BuOMe is a commonly used crystallisation anti-solvent, *e.g.*, $[I(\text{quinuclidine})_2]ClO_4$,[36] or whilst ^{t}BuOMe was used as the solvent during the iodination of other substrates.[45]

In conclusion, the first example of a hydrogen-bonded halogen(I) complex, $[\text{bis(3-acetaminopyridine)iodine(I)}]PF_6$ (**3**), was synthesised from the 3-acetaminopyridine (**1**) ligand *via* the analogous silver(I) complex **2**. Complex **3** was found to possess all the expected spectroscopic and structural features of an iodine(I) complex, and two temperature-dependent crystallographic polymorphs were observed (**3_1** and **3_2**) that demonstrated different hydrogen-bonded connectivities

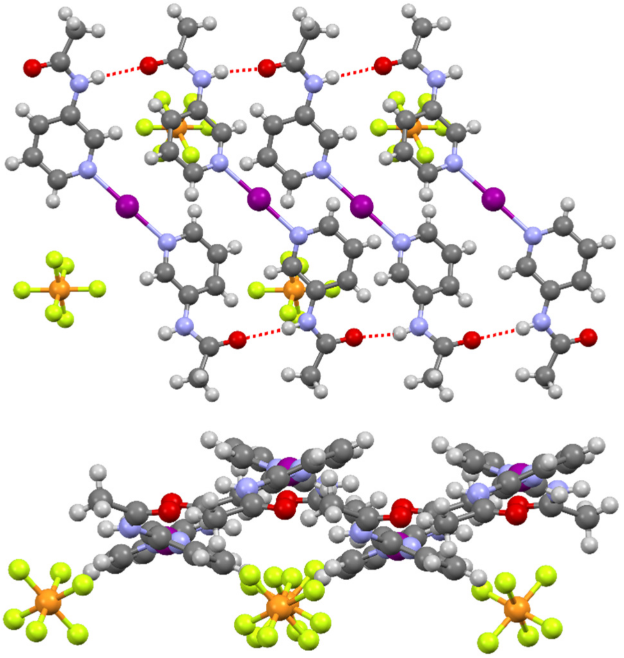


Fig. 3 The solid-state packing of four molecules of **3_2** (top; viewed down the *b*-axis) showing the 1D sheets of hydrogen-bonded iodine(I) cations (hydrogen bonds represented by red dashed lines), and sideview (bottom).

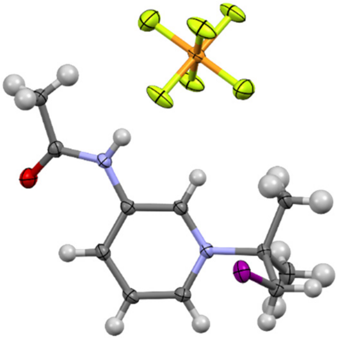


Fig. 4 The solid-state structure of complex **4** (thermal ellipsoids at 50% probability).

between the $[I(\mathbf{1})_2]^+$ cations of **3**. In solution, complex **3** was found to demonstrate never before observed reactivity for an iodine(I) complex, whereupon it reacted with ^{t}BuOMe to give the complex **4** in good yield, which incorporated an iodinated ^{t}Bu substituent. The observation of **4** is highly novel and more extensive studies are currently underway to explore its future utilisation of **3** in organic transformations.

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Conflicts of interest

There are no conflicts to declare.

Notes and references

‡ The data for **3_2** reported herein was actually collected on crystals grown by MeCN evaporation for reasons of crystal quality, however, the unit cell and packing motif of **3_2** was also identified from crystals grown from CH_2Cl_2 : MeCN (7 : 1)/pentane.

1 J. Pancholi and P. D. Beer, *Coord. Chem. Rev.*, 2020, **416**, 213281.

2 L. Turunen, U. Warzok, R. Puttreddy, N. K. Beyeh, C. A. Schalley and K. Rissanen, *Angew. Chem., Int. Ed.*, 2016, **55**, 14033–14036.

3 A. Vanderkooy, A. K. Gupta, T. Földes, S. Lindblad, A. Orthaber, I. Pápai and M. Erdélyi, *Angew. Chem., Int. Ed.*, 2019, **58**, 9012–9016.

4 J. A. Creighton, I. Haque and J. L. Wood, *Chem. Commun.*, 1966, 229.

5 G. Cavallo, P. Metrangolo, R. Milani, T. Pilati, A. Priimagi, G. Resnati and G. Terraneo, *Chem. Rev.*, 2016, **116**, 2478–2601.

6 J. Barluenga, J. M. González, M. A. Garcia-Martin, P. J. Campos and G. Asensio, *J. Chem. Soc., Chem. Commun.*, 1992, 1016–1017.

7 J. Ezquerra, C. Pedregal, C. Lamas, J. Barluenga, M. Pérez, M. A. García-Martín and J. M. González, *J. Org. Chem.*, 1996, **61**, 5804–5812.

8 S. Yu, J. S. Ward, K.-N. Truong and K. Rissanen, *Angew. Chem., Int. Ed.*, 2021, **60**, 20739–20743.

9 E. Kramer, S. Yu, J. S. Ward and K. Rissanen, *Dalton Trans.*, 2021, **50**, 14990–14993.

10 J. L. Courtneidge, J. Lusztyk and D. Pagé, *Tetrahedron Lett.*, 1994, **35**, 1003–1006.

11 A. Yoshimura and V. V. Zhdankin, *Chem. Rev.*, 2016, **116**, 3328–3435.

12 J. Barluenga, F. González-Bobes and J. M. González, *Angew. Chem., Int. Ed.*, 2002, **41**, 2556–2558.

13 R. Kawasumi, S. Narita, K. Miyamoto, K. Tominaga, R. Takita and M. Uchiyama, *Sci. Rep.*, 2017, **7**, 17967.

14 R. Montoro and T. Wirth, *Org. Lett.*, 2003, **5**, 4729–4731.

15 D. D. Tanner, G. C. Gidley, N. Das, J. E. Rowe and A. Potter, *J. Am. Chem. Soc.*, 1984, **106**, 5261–5267.

16 M. R. Whalon, C. H. Bushweller and W. G. Anderson, *J. Org. Chem.*, 1984, **49**, 1185–1190.

17 F. Munyemana, I. George, A. Devos, A. Colens, E. Badarau, A.-M. Frisque-Hesbain, A. Loudet, E. Differding, J.-M. Damien, J. Rémion, J. Van Uytbergen and L. Ghosez, *Tetrahedron*, 2016, **72**, 420–430.

18 J. Li, C.-Y. Huang and C.-J. Li, *Angew. Chem., Int. Ed.*, 2022, **61**, e202112770.

19 N. A. Hirscher, N. Ohri, Q. Yang, J. Zhou, J. M. Anna, E. J. Schelter and K. I. Goldberg, *J. Am. Chem. Soc.*, 2021, **143**, 19262–19267.

20 A. Paik, S. Paul, S. Bhowmik, R. Das, T. Naveen and S. Rana, *Asian J. Org. Chem.*, 2022, **11**, e202200060.

21 J. F. King, S. M. Loosmore, J. D. Lock and M. Aslam, *J. Am. Chem. Soc.*, 1978, **100**, 1637–1639.

22 J. F. King, S. M. Loosmore, M. Aslam, J. D. Lock and M. J. McGarrity, *J. Am. Chem. Soc.*, 1982, **104**, 7108–7122.

23 K. Sonogashira, *J. Organomet. Chem.*, 2002, **653**, 46–49.

24 E. Negishi, Z. Huang, G. Wang, S. Mohan, C. Wang and H. Hattori, *Acc. Chem. Res.*, 2008, **41**, 1474–1485.

25 N. V. Tzouras, I. K. Stamatopoulos, A. T. Papastavrou, A. A. Liori and G. C. Vougioukalakis, *Coord. Chem. Rev.*, 2017, **343**, 25–138.

26 R. Lakes, *Nature*, 1993, **361**, 511–515.

27 K. S. Katti, D. R. Katti, S. M. Pradhan and A. Bhosle, *J. Mater. Res.*, 2005, **20**, 1097–1100.

28 S. M. Zhang, F. Z. Cui, S. S. Liao, Y. Zhu and L. Han, *J. Mater. Sci.: Mater. Med.*, 2003, **14**, 641–645.

29 C. Du, F. Z. Cui, X. D. Zhu and K. de Groot, *J. Biomed. Mater. Res.*, 1999, **44**, 407–415.

30 K. Furuichi, Y. Oaki, H. Ichimiya, J. Komotori and H. Imai, *Sci. Technol. Adv. Mater.*, 2006, **7**, 219–225.

31 C. R. Groom, I. J. Bruno, M. P. Lightfoot and S. C. Ward, *Acta Crystallogr., Sect. B: Struct. Sci., Cryst. Eng. Mater.*, 2016, **72**, 171–179.

32 J. S. Ward, G. Fiorini, A. Frontera and K. Rissanen, *Chem. Commun.*, 2020, **56**, 8428–8431.

33 C. Di Nicola, Effendy, F. Marchetti, C. Nervi, C. Pettinari, W. T. Robinson, A. N. Sobolev and A. H. White, *Dalton Trans.*, 2010, **39**, 908–922.

34 E. Kukkonen, H. Malinen, M. Haukka and J. Konu, *Cryst. Growth Des.*, 2019, **19**, 2434–2445.

35 C. B. Aakeröy, I. Hussain, S. Forbes and J. Desper, *CrystEngComm*, 2007, **9**, 46–54.

36 J. S. Ward, A. Frontera and K. Rissanen, *Dalton Trans.*, 2021, **50**, 8297–8301.

37 E. Taipale, M. Siepmann, K.-N. Truong and K. Rissanen, *Chem. – Eur. J.*, 2021, **27**, 17412–17419.

38 S. Yu, P. Kumar, J. S. Ward, A. Frontera and K. Rissanen, *Chem*, 2021, **7**, 948–958.

39 J. S. Ward, A. Frontera and K. Rissanen, *Inorg. Chem.*, 2021, **60**, 5383–5390.

40 J. S. Ward, K.-N. Truong, M. Erdélyi and K. Rissanen, in *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering*, Elsevier, 2022, DOI: **10.1016/B978-0-12-823144-9.00043-1**.

41 W.-K. Luo, X. Shi, W. Zhou and L. Yang, *Org. Lett.*, 2016, **18**, 2036–2039.

42 J. Zhuge, Z. Jiang, W. Jiang, G. Histand and D. Lin, *Org. Biomol. Chem.*, 2021, **19**, 5121–5126.

43 S. Lindblad, K. Mehmeti, A. X. Veiga, B. Nekoueishahraki, J. Gräfenstein and M. Erdélyi, *J. Am. Chem. Soc.*, 2018, **140**, 13503–13513.

44 D. von der Heiden, F. B. Németh, M. Andreasson, D. Sethio, I. Pápai and M. Erdélyi, *Org. Biomol. Chem.*, 2021, **19**, 8307–8323.

45 P. Bovonsombat, W. Lorpaiboon, S. Laoboonchai, P. Sriprachaya-anunt, W. Yimkosol, N. Siriphatcharachaikul, P. Siricharoensang, T. Kangwannarakul, J. Maeda, S. Losuwanakul and M. Mahesh Abhyankar, *Tetrahedron Lett.*, 2020, **61**, 152461.