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Non-innocent behaviour of aromatic isocyanides under visible light: a pathway to thioformimidates and dehydroalanine

We disclose a mild, additive-free, visible-light method for the synthesis of thioformimidates. The study shows that aromatic isocyanides can generate thiyl radicals upon irradiation, enabling radical initiation under simple conditions. Beyond small-molecule synthesis, the approach allows selective activation of cysteine thiols in dipeptides, followed by conversion to dehydroalanine. This creates a practical entry to late-stage peptide modification and expands the toolbox for site-selective transformations in complex biomolecules.

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Non-innocent behaviour of aromatic isocyanides under visible light: a pathway to thioformimidates and dehydroalanine

Minghui Wu, [ID] [a] Jay Hanssens, [ID] [a] Camilla Russo, [ID] [b] Rajat Walia, [ID] [c] Mariateresa Giustiniano, [ID] *[b] Ludovic Troian-Gautier, [ID] [de] Jordy M. Saya, [ID] [a] Romano Orru [ID] *[a] and Prabhat Ranjan [ID] *[ad]

Despite the significant potential of isocyanides to engage in reactions with thiyl radicals to produce nitrogen-containing organic molecules, their widespread use has been limited by the need for high-energy UV light activation. Herein, we disclose the synthesis of thioformimidates under mild reaction conditions employing visible light without additives. This study demonstrates the ability of aromatic isocyanides to generate thiyl radicals under visible light, functioning as radical initiators. Furthermore, the developed methodology reveals its utility in the selective activation of the thiol group in cysteine, which is subsequently converted to dehydroalanine, opening the door to late-stage peptide modification.

Introduction

Isocyanides represent important and versatile building blocks in organic synthetic chemistry due to their unique chameleonic character.[1] Their partial carbenoid nature makes them isoelectronic to carbon monoxide (CO), while their ionic character makes them akin to alkynes. The carbene character of isocyanides has been extensively explored in coordination chemistry, whereas their ionic character enabled the development of well-known multi-component reactions such as the Ugi and Passerini reactions.[2–4] In addition, isocyanides are excellent radical acceptors in one-electron chemistry (known as radical sinks), enabling the efficient generation of diverse heterocyclic and complex molecular scaffolds through cascade reactions.[5] Initially, this chemistry heavily relied on radical initiators like AIBN or peroxides.[6,7] However, recent advances in visible-light photoredox catalysis have revitalized the field, offering a mild and versatile approach to achieve these transformations.[8–10]

In particular, the addition of heteroatom-based radicals to isocyanides holds great potential in organic synthesis to generate heterocyclic scaffolds. Among these, thioformimidate formation following the addition of sulfur-based radicals on isocyanides has been widely investigated.[7] The most common method for the synthesis of thioformimidates involves *S*-alkylation of thioformamides with aryl or alkyl halides (Scheme
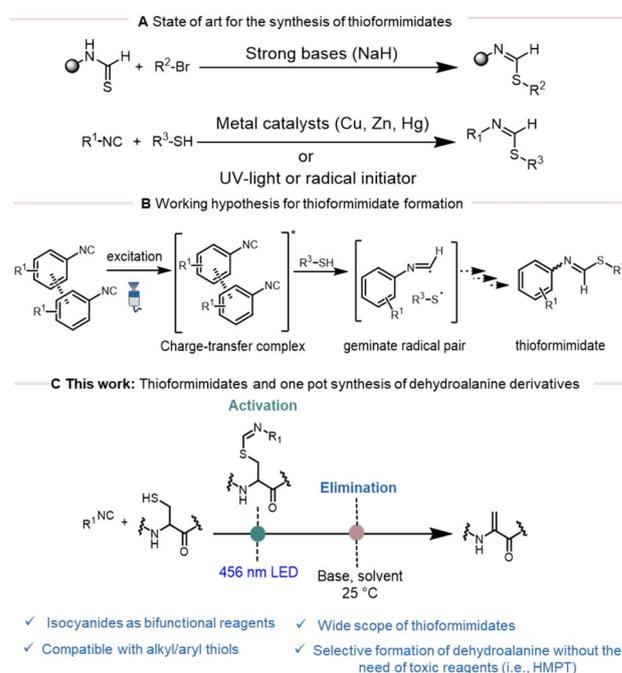
Scheme 1 (A) previous work on the synthesis of thioformimidates; (B) our working hypothesis for the formation of thioformimidates; (C) this work: thioformimidates and one pot synthesis of dehydroalanine derivatives.

[a]Biobased Organic Chemistry, Aachen-Maastricht Institute for Biobased Materials (AMIBM), Maastricht University, Urmonderbaan 22, 6167RD Geleen, The Netherlands

[b]Department of Pharmacy, University of Naples Federico II, Via D. Montesano 49, 80131 Napoli, Italy

[c]Institute of Functional Nano and Soft Materials (FUNSOM), Joint International Research Laboratory of Carbon-Based Functional Materials and Devices, Soochow University, Suzhou, People's Republic of China

[d]UCLouvain, Institut de la Matière Condensée et des Nanosciences (IMCN), Molecular Chemistry, Materials and Catalysis (MOST), Place Louis Pasteur 1/L4.01.02, B-1348 Louvain-la-Neuve, Belgium. E-mail: prabhat.ranjan@uclouvain.be; pranjan057@gmail.com

[e]Wel Research Institute, Avenue Pasteur 6, 1300 Wavre, Belgium

1A).[11,12] However, these processes often suffer from several limitations and purification problems due to the instability of thioformimidates and consequently suffer from limited substrate scope. Conversely, thioformimidates can also be synthesized through the reaction of isocyanides and thiols using metal catalysts, UV-light or in the presence of radical initiators such as AIBN (Scheme 1A).[13,14] Generally, the reaction proceeds with the formation of a thiyl radical followed by thiyl radical addition to the isocyanide to generate an α-thioimidoyl radical.[13] This radical can then undergo H-atom abstraction from thiols to form the final thioformimidates product. Despite the convenience of this method, less attention has been directed to this pathway due to the following reasons: (a) the requirement of UV-light; (b) poor reaction efficiency and (c) the formation of unwanted side products such as 1,1-bisthiolation adducts.

Recently, our research group reported the ability of tryptamine isocyanide to undergo aggregation-based charge transfer. Building on this concept and previous literature,[15,16] we hypothesized that this phenomenon could also be applied to other aromatic isocyanides to trigger the generation of thiyl radicals under visible light followed by the formation of thioformimidates (Scheme 1B). In light of their chemical properties and to broaden the synthetic utility of thioformimidates, we envisioned their use as an activating group for thiol derivatives. In the context of peptide chemistry, we further explored whether this strategy could enable the chemo- and regioselective activation of cysteine residues as a precursor of dehydroalanine (Scheme 1C).

Adhering to this hypothesis and given both the significance of thioformimidates as synthetic intermediates and the limitations of current methods, we sought to develop an innovative, exogeneous photocatalyst-free, visible-light-driven approach for their synthesis. During this study, we also investigated a previously camouflaged role of isocyanides in the generation of thiyl radicals using steady-state and time-resolved fluorescence spectroscopy. Moreover, we discovered the involvement of thioformimidates in the chain initiation and propagation step, a role that had been overlooked until now. Beyond reaction development, we report an application of this strategy to the selective activation of cysteine residues, to be able to further convert them into dehydroalanine derivatives, thereby introducing a sustainable and selective alternative to traditional methods of synthesizing dehydroalanine from cysteine residues in peptides.

Results and discussion

Optimization studies

Our optimization studies began with isocyanide **1a** and thiophenol **1b** in 1,2-dichloroethane (DCE) under visible light irradiation ($\lambda = 456$ nm). To our delight, the desired product **2** was obtained in 91% yield after 12 h (Table 1, entry 1). Being aware of the role of the solvent in charge transfer complexes, we evaluated a variety of polar and non-polar solvents (for more details see SI).[17] We observed good to moderate yields in polar as well as moderately polar solvents (Table 1, entries 2 and 3).

Table 1 Optimization and control experiments for the synthesis of thioformimidate **2** [a]
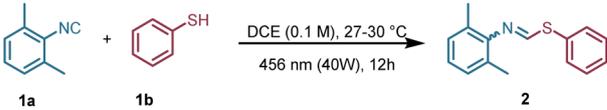
Entry	Deviations from the optimized conditions	Yield[b] (%)
1	None	91
2	MeCN	81
3	2-MeTHF	60
4	Water	87
5	Cs$_2$CO$_3$	8
6	DIPEA	10
7	0.5 M instead of 0.1 M	83
8	0.05 M instead of 0.1 M	67
9	No light, 80 °C	0
10	Air instead of N$_2$	<10

[a] All reactions were performed using **1a** (0.24 mmol, 1.2 equiv.) and **1b** (0.2 mmol, 1 equiv., 0.1 M). [b] Yields were determined by ^{1}H NMR using CH$_2$Br$_2$ as an internal standard.

Interestingly, water also proved to be an effective solvent, providing 87% of the desired product (Table 1, entry 4). However, the addition of an additive like meglumine, which can increase the solubility of isocyanide **1a** and thiol **1b** in water, had an inverse effect on the product yield (11%, see SI).[18] This result could be rationalized by the better chance of forming aggregates of **1a** in pure water due to the hydrophobic effect. Following the solvent screening, the effect of a base was evaluated, as in a basic medium, thiol **1b** ($pK_a = 10.2$ in DMSO)[19] is deprotonated.

The thiolate formed under basic conditions could either potentially form an intermolecular electron donor–acceptor (EDA) complex with isocyanide **1a** or be excited under visible light to induce a single electron transfer (SET).[20,21] However, the addition of a base had a detrimental effect on the product yield, possibly due to the inhibition of the hydrogen atom transfer (HAT) step to the intermediate imidoyl radical (Table 1, entries 5 and 6).[13] Finally, we performed some control experiments to substantiate the need for light and to provide evidence of the radical nature of this transformation (Table 1, entries 9 and 10). Quantum yield measurements further indicated a radical chain mechanism, in accordance with the reported literature (see SI).[22]

Reaction scope

Having established the optimal conditions, the scope and limitations of thioformimidate formation were investigated. Aromatic thiols bearing electron-withdrawing or donating substituents delivered the desired products in good to moderate yields (47–91%, Scheme 2). However, *ortho*-Me and *ortho*-CO$_2$Me substituted aromatic thiols delivered the corresponding products in lower yields (Scheme 2, **4** and **9**). Pleasingly, an aromatic thiol having a carboxylic acid group at the benzylic position (Scheme 2, **10**) was also compatible under these
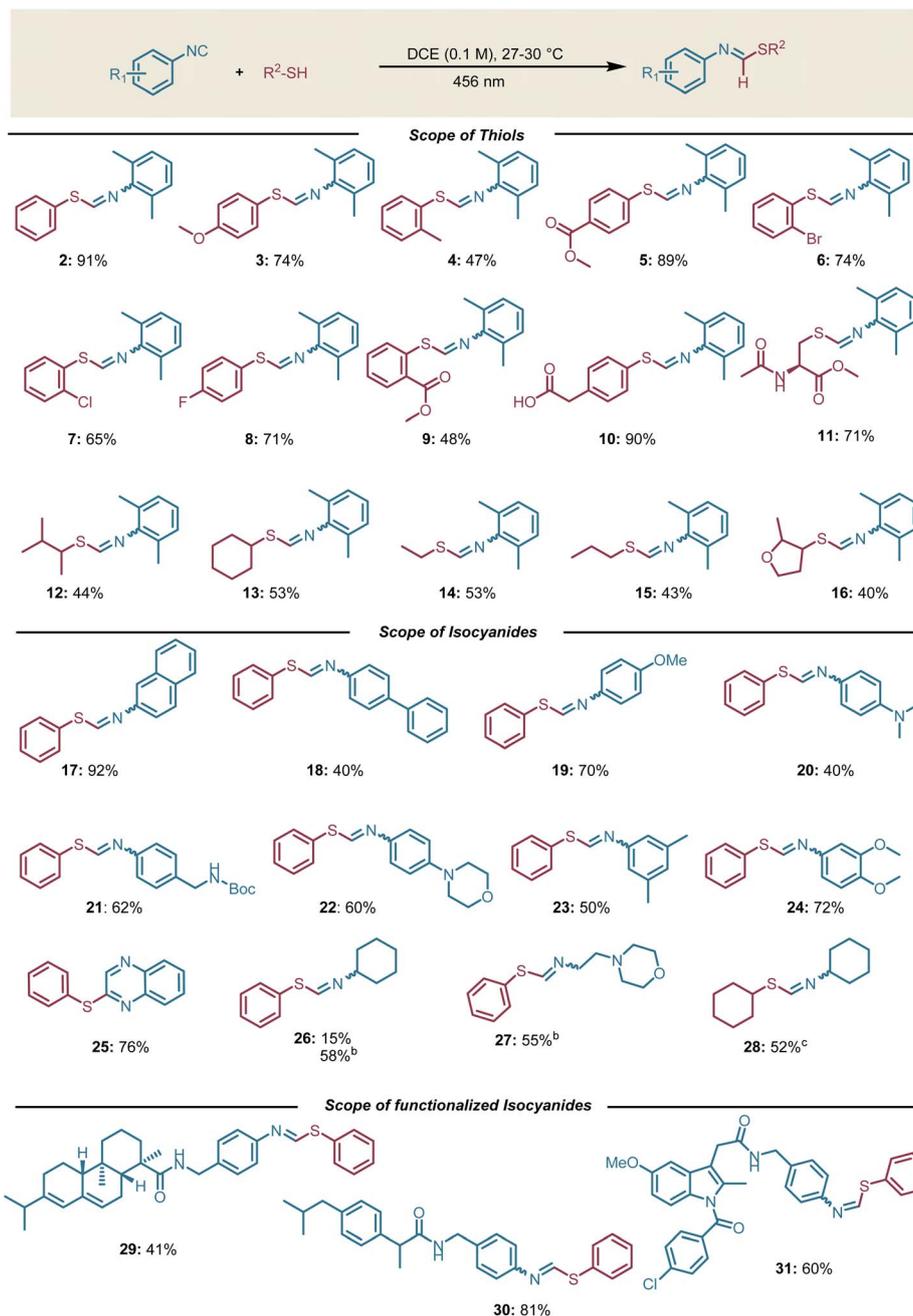
Scheme 2 Scope of thioformimidates: [a]conditions unless otherwise noted: all reactions were performed using isocyanide (0.24 mmol, 1.2 equiv.), thiol (0.2 mmol, 1 equiv.), dry DCE (0.1 M), 12 h, irradiating with a Kessil lamp 456 nm (40 W). [b]Concentration (1 M). [c]PhSSPh (10–20 mol%) used as an additive, concentration (1 M).

conditions. This transformation is typically challenging to be achieved in the presence of photocatalysts due to the tendency of the benzylic carboxylic group to undergo decarboxylation.[23] Based on our initial hypothesis, we anticipated that the generation of a thiyl radical should also be feasible from aliphatic thiols employing aromatic isocyanides. This expectation materialized as aliphatic thiols like N-acetyl-L-cysteine methyl ester and cyclohexyl thiol delivered the desired products in good yields (Scheme 2, **11–16**). In particular, thioformimidate formation from N-acetyl-L-cysteine methyl ester paves the way to harness isocyanides as thiol-activating groups in peptides and

proteins. It is worth emphasizing that the reaction described herein is compatible with aqueous conditions and other additives (Table S3).

After screening thiol compatibility, we evaluated various aromatic isocyanides under the optimized conditions. We obtained good yields in all cases (Scheme 2, **17–24**). Furthermore, 1,2-diisocyanobenzene selectively afforded 2-(phenylthio)quinoxaline without any detectable formation of 2,3-bis(phenylthio)quinoxaline (Scheme 2, **25**).[7] Based on our initial hypothesis, we assumed that aliphatic isocyanides would not be suitable substrates under our optimal conditions. Nevertheless, we

obtained 15% yield of the desired thioformimidate when cyclohexyl isocyanide was employed (Scheme 2, **26**). Surprised by this result, we performed additional control experiments and we found that the diphenyl disulfide is responsible for the desired product formation.[13]

The *in situ* formation of diphenyl disulfide can be explained by the tendency of thiols to self-oxidize in the presence of residual oxygen in the solvent (see SI, Section 4.8). As the only absorbing species in the reaction mixture would have been the diphenyl disulfide, we increased its concentration in an attempt to prove our assumption and promote the reactivity. As expected, we obtained a higher yield at 1 M reaction concentration compared to the reaction with 0.1 M concentration. Similarly, with cyclohexyl isocyanide and cyclohexyl thiol, we employed a catalytic amount of diphenyl disulfide to start the radical chain reaction to deliver the desired product (Scheme 2, **28**). It is important to note that we did not observe any 1,1-bisthiolation side product in any case. To further probe the functional group compatibility, we employed isocyanides functionalized with complex molecular scaffolds such as the benzoamide derivatives of the drugs abietic acid, ibuprofen, and indomethacine that gave the desired products in moderate to good yields (**29**, **30**, and **31**, respectively, Scheme 2).
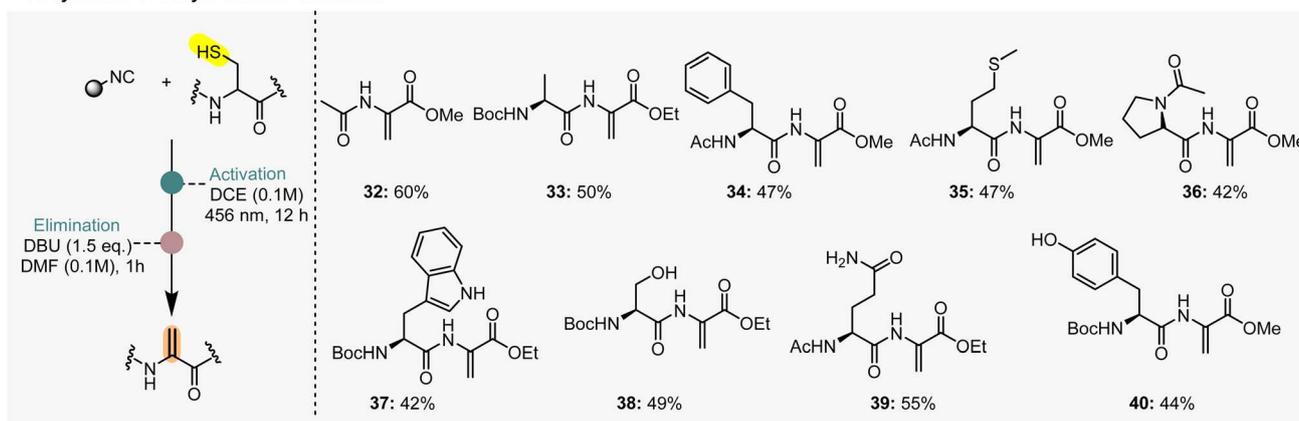
Application of thioformimidates

After establishing the scope of the thioformimidate formation, we focused our attention on the synthesis of dehydroalanine (DHA) derivatives, an amino acid residue important in both biological and synthetic chemistry.[24,25] There is substantial research focused on the site-selective incorporation of dehydroalanine into peptides and proteins. Among these, the conversion of cysteine residues to dehydroalanine holds great potential for protein modification because of the strong nucleophilicity of sulfur and the ease of incorporating cysteine into proteins using standard biochemical techniques. Over the past decade, many methods have been documented, but none of them enables a general, chemo-and site-selective incorporation of dehydroalanine.[26] For instance, the synthesis of dehydroalanine from cysteine using the *O*-mesitylenesulfonylhydroxylamine (MSH) is incompatible with peptides containing serine, asparagine, tyrosine, or tryptophane derivatives.[26]

We were therefore pleased to achieve the formation of DHA using *N*-acetyl cysteine methyl ester and eight different dipeptides (**32–40**, Scheme 3A). We first carried out the photochemical transformation on the cysteine residues for the formation of the thioformimidate intermediates. After confirming the formation of the latter through LC-MS, we redissolved the crude reaction products in *N,N*-dimethylformamide (DMF), in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base, to yield the desired dehydroalanine derivatives. Dipeptides containing amino acids such as alanine, phenylalanine, methionine, and proline delivered the desired products in good yields within 1 h (Scheme 3A, **33–36**). Next, we employed proteinogenic amino acids such as serine, asparagine, tyrosine and tryptophan (Scheme 3A, **37–40**) that also led to the selective formation of dehydroalanine, showcasing good functional group tolerance.

We also explored the possibility to involve thioformimidates in [3 + 2]-cycloaddition reactions with 1,3-dipoles such as chlorooxime **41** (Scheme 3B) to get amidine derivatives such as
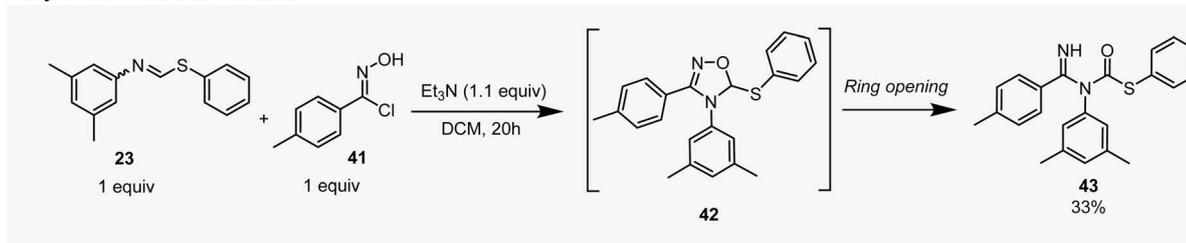
Scheme 3 Application of thioformimidates to the synthesis of dehydroalanine and amidine derivatives. [a]Yields refer to a two-step process.

43, likely formed upon a based catalyzed ring-opening of intermediate **42** (Scheme 3B). A similar product was previously reported by Yamamoto and co-workers in 1971, using benzyl cyanide and *n*-butyl di-*n*-butylthioboronite.[27] Our approach offers direct access to generate this complex molecular scaffold in a two-step one-pot reaction.

Mechanistic investigations

Based on both the initial hypothesis and the previous findings, we anticipated that aromatic isocyanides could undergo aggregation-based charge transfer. Yu, Ma, and co-workers previously reported a similar behaviour in 1,2-di-isocyanoarenes.[16] To investigate if a similar mechanism operates in the presence of compound **1a**, we first recorded its UV-Vis absorption spectra in DCE at varying concentrations (Fig. 1a). A pronounced bathochromic shift was observed at higher concentrations, indicating potential aggregation effects. It is important to note that the purity of **1a** was crucial for this observation as samples exhibiting a yellow colour showed an absorption peak around 390 nm at higher concentrations, likely due to impurities or gradual decomposition/polymerization over time. Unlike the well-defined absorption peak in the visible region reported by Yu, Ma and coworkers, we observed a broader absorption band.[16] This difference may derive from the distinct packing structure of **1a** in solution. Indeed, the reported crystal structure of **1a** shows intermolecular distances ranging from 3.47 Å to 4.65 Å, which could influence the observed absorption features.[28] We then recorded the steady-state fluorescence spectra of **1a** at different excitation wavelengths. Excitation at 355 nm led to a vibronically-resolved

photoluminescence centered around 400 nm. Interestingly, exciting at 420 nm, *i.e.* within the novel absorption features apparent at high concentrations, a steady-state photo-luminescence spectra with a maximum at 500 nm was observed. This observation suggests relaxation from different electronic states, a common characteristic of aggregates (Fig. 1b).

Following the confirmation of aggregate formation in **1a**, we next recorded the UV-Vis spectra of mixtures of **1a** and **1c** (*N*-acetyl-L-cysteine methyl ester) to check the possibility of a ground-state donor–acceptor (EDA) complex formation. We selected **1c** because it is a solid, non-volatile compound devoided of the strong pungent odor typical of more volatile thiols. However, the study in DCE was inconclusive due to the poor solubility of **1c**, which led to significant scattering. Therefore, we recorded the UV-vis spectrum in a mixture of DCE and MeCN, where the solubility of both **1a** and **1c** was better. We did not observe any appreciable bathochromic shift above 420 nm (Fig. 1c and Fig. S6–S8). However, the absorption spectrum of **1a** and **1c** exhibited a hyperchromic shift compared to the sum of the individual absorption spectra below 420 nm (dashed and solid lines in Fig. 1c). Although not conclusive, this hyper-chromic shift could point towards a ground-state association between **1a** and **1c**. To further probe a ground-state interaction, we measured the UV-vis spectrum of a mixture of **1a**, **1b** and cyclohexyl thiol, which revealed again no significant bath-ochromic shift (Fig. S9 and S12). In addition, the formation of an excimer between **1a** and **1c** was also ruled out as we did not observe any appreciable shift in the steady-state photo-luminescence spectrum of **1a** and in the mixture of **1a** and **1c**.

After having identified the main photo-absorbing species under our reaction conditions, we turned our attention to delineate the mechanism of radical generation from thiol. To do that, we performed Stern–Volmer fluorescence quenching experiments using either **1a** or 4-isocyanoanisole (Fig. S21–S25). In case of **1a**, a very low Stern–Volmer constant (K_{sv}: 8 M^{-1}) was obtained. In the case of 4-isocyanoanisole, the Stern–Volmer constant rose to 56 M^{-1}. Based on this result, we envision two possible pathways for the generation of thiyl radical from **1c**. The first involves the electron transfer from **1c** to the excited isocyanide, followed by protonation, while the second possibility involves a proton coupled electron transfer (PCET) process.

To further discriminate between these two pathways, we performed Stern–Volmer quenching experiments with phenol and 1,3,5-trimethoxybenzene. Whereas **1c** efficiently quenched the excited state of 4-isocyanoanisole isocyanide ($K_{sv} = 56$ M^{-1}), only moderate quenching was observed using phenol ($K_{sv} = 11$ M^{-1}) and trimethoxybenzene showed no measurable quenching (Fig. 1d, S24 and S25). This indicates the possibility of proton coupled electron transfer, since the oxidation potential of phenol and 1,3,5-trimethoxybenzene are comparable. Note however that the corresponding Stern–Volmer plot for the quenching of 4-isocyanoanisole by **1c** exhibits some deviation from linearity, especially at low concentration of **1c** (Fig. 1d). We believe that this deviation occurs from the degradation of 4-isocyanoanisole that has been observed in solution, leading to an additional emission peak around 650 nm that would in fine
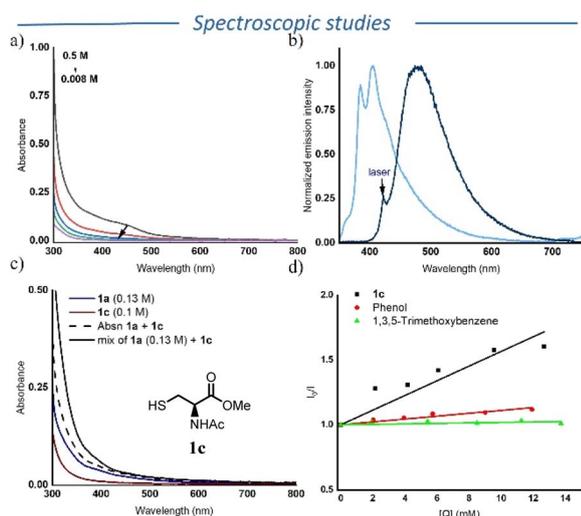

Fig. 1 (a) absorption spectra of **1a** in DCE at different concentrations; (b) emission spectra of **1a** (0.1 M) in DCE, sky blue excitation at 355 nm and navy blue excitation at 420 nm; (c) absorption spectra of individual components and reaction mixture, recorded in 40% MeCN in DCE: [**1c**] = 0.13 M; [**1a**] = 0.1 M; [**1a** + **1c**] = solution of 0.13 M of **1c** and 0.1 M of **1a**, dotted black line represent the sum of absorption of **1a** and **1c**; (d) Stern–Volmer quenching of 4-isocyanoanisole with **1c**, phenol and 1,3,5-trimethoxybenzene.

influence the corresponding Stern–Volmer plot. Furthermore, TD-DFT calculations reveal that the first excited state (S_1) possesses a 16.6% charge-transfer (CT) character from the phenyl ring to the isocyanide (–NC) unit, with the remaining contribution arising from locally excited (LE) transitions within the phenyl framework (Fig. S30). This partial CT character indicates a redistribution of electron density over the phenyl ring accompanied by electron migration toward the NC bond. This shift of electron density can enhance hydrogen bonding in the excited state, which can lead to higher quenching, as observed in the case of **1c** and phenol in comparison with 1,3,5-trimethoxybenzene, supporting the PCET mechanism.

To complete the mechanistic investigation, we further analysed the role of the reaction product. We wondered whether there could be the possibility of an autocatalytic reaction, where product **11** acts as a radical initiator, or participates in the radical propagation step. We therefore carried out reactions using **11** (that absorbs in the visible region) in varying amounts, in the presence of an aliphatic thiol and an aliphatic isocyanide (Fig. 2b), that do not absorb in the visible region. To our surprise, we observed the formation of the desired product, though in low yields, even when higher loadings of product **11** were added (for details see SI). Based on these results, the

product can act as a radical initiator (though not efficiently). Nevertheless, we cannot generalize this behaviour because not all the products acted as initiators.

Taking into account all these observations, we propose the following mechanism for the formation of thioformimidates (Fig. 2a). Upon excitation of **1a**, a PCET transfer between **1a*** and thiol happens, forming radical pair **II**. At this stage, the radical pair can undergo in-cage radical coupling to generate the desired product (termination step). Alternatively, the thiyl radical escapes the solvent cage, initiating a radical chain by reacting with another isocyanide molecule. The formation of a TEMPO adduct with the thiyl derivative supports the formation of thiyl radical species (Fig. 2c). We would also like to emphasize that, in case of aromatic thiols, other mechanistic scenarios, such as the involvement of diphenyl disulfide or EDA-complex formation, could play a relevant role in the radical initiation step. Compared to previously reported UV-light-induced reactions between thiols and isocyanides, we hypothesize that the high selectivity for the thioformamide formation in our reaction is due to the unique ability of aromatic isocyanides to be involved in the generation of a thiyl radical and the subsequent fast HAT step (see Scheme S3).
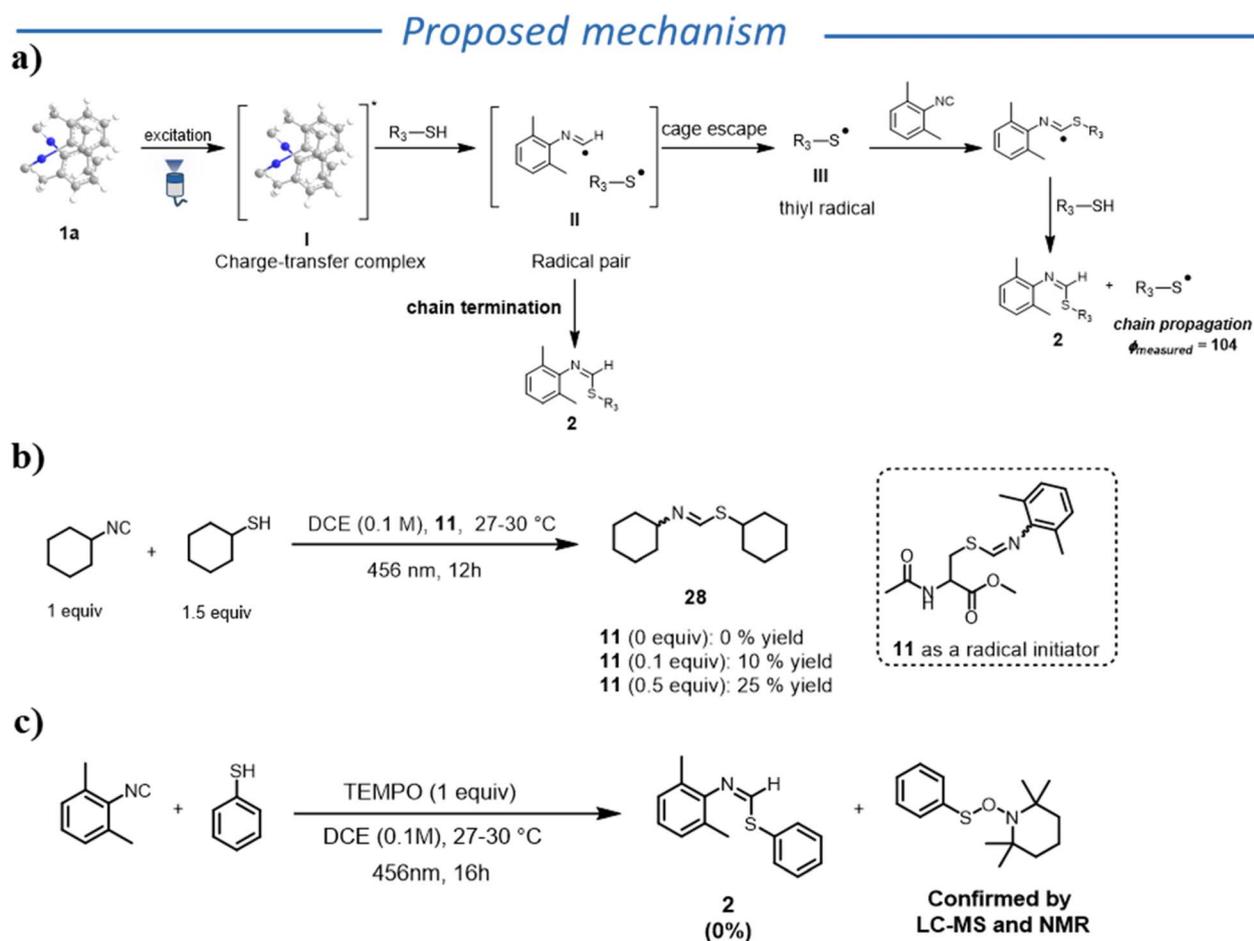

Fig. 2 (a) proposed mechanism; (b and c) control experiments.

Conclusions

In conclusion, we demonstrated the potential of aromatic isocyanides to serve as radical initiators in the formation of thioformimidates. Beyond the thioformimidate formation, we developed a one-pot method for synthesizing dehydroalanine in dipeptides with good yields and excellent chemo-selectivity. We also explored [3 + 2] cycloaddition reactions with 1,3-dipoles, such as Z-chlorooximes, to generate amidine derivatives. Overall, this new methodology paves the way for sustainable and cost-effective routes to thioformimidates and catalyst free generation of thiyl radicals.

Author contributions

The authors confirm their contribution to the paper as follows: study conception: P. R.; design and methodology: P. R., M. W., M. G. and J. M. S.; experimentation: P. R., M. W., C. R. and J. H.; spectroscopy: P. R. and L. T. G.; theoretical studies: R. W.; writing, review and editing: P. R. with input from M. W., M. G., L. T. G., J. M. S., and R. V. A. O.; acquiring funding: P. R. and R. V. A. O.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: optimization details, NMR spectra, spectroscopic data and DFT data. See DOI: https://doi.org/10.1039/d5sc07984e.

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Notes and references

1 G. dos P. Gomes, Y. Loginova, S. Z. Vatsadze and I. V. Alabugin, *J. Am. Chem. Soc.*, 2018, **140**, 14272–14288.

2 M. Knorn, E. Lutsker and O. Reiser, *Chem. Soc. Rev.*, 2020, **49**, 7730–7752.

3 L. Banfi, A. Basso, C. Lambruschini, L. Moni and R. Riva, *Chem. Sci.*, 2021, **12**, 15445–15472.

4 E. Ruijter, R. Scheffelaar and R. V. A. Orru, *Angew. Chem., Int. Ed.*, 2011, **50**, 6234–6246.

5 B. Zhang and A. Studer, *Chem. Soc. Rev.*, 2015, **44**, 3505–3521.

6 L. Benati, R. Leardini, M. Minozzi, D. Nanni, R. Scialpi, P. Spagnolo, S. Strazzari and G. Zanardi, *Angew. Chem., Int. Ed.*, 2004, **43**, 3598–3601.

7 A. Ogawa and Y. Yamamoto, *Beil. J. Org. Chem.*, 2024, **20**, 2114–2128.

8 G. A. Coppola, S. Pillitteri, E. V. Van der Eycken, S.-L. You and U. K. Sharma, *Chem. Soc. Rev.*, 2022, **51**, 2313–2382.

9 M. Martín, R. M. Romero, C. Portolani and M. Tortosa, *ACS Catal.*, 2024, **14**, 17286–17292.

10 I. Quirós, M. Martín, M. Gomez-Mendoza, M. J. Cabrera-Afonso, M. Liras, I. Fernández, L. Nóvoa and M. Tortosa, *Angew. Chem., Int. Ed.*, 2024, **63**, e202317683.

11 K. de la Vega-Hernández, R. Senatore, M. Miele, E. Urban, W. Holzer and V. Pace, *Org. Biomol. Chem.*, 2019, **17**, 1970–1978.

12 T. S. Jagodziński, *Chem. Rev.*, 2003, **103**, 197–228.

13 F. Dénès, M. Pichowicz, G. Povie and P. Renaud, *Chem. Rev.*, 2014, **114**, 2587–2693.

14 T. Saegusa, S. Kobayashi, K. Hirota, Y. Okumura and Y. Ito, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 1638–1642.

15 M. Wu, J. M. Saya, P. Han, R. Walia, B. Pradhan, M. Honing, P. Ranjan and R. V. A. Orru, *Chem. Sci.*, 2024, **15**, 6867–6873.

16 W. Wang, X. Sun, J. Qu, X. Xie, Z.-H. Qi, D. Hong, S. Jing, D. Zheng, Y. Tian, H. Ma, S. Yu and J. Ma, Phy, *Phys. Chem. Chem. Phys.*, 2017, **19**, 31443–31451.

17 C. G. S. Lima, T. de M. Lima, M. Duarte, I. D. Jurberg and M. W. Paixão, *ACS Catal.*, 2016, **6**, 1389–1407.

18 Y. Tian, E. Hofmann, W. Silva, X. Pu, D. Touraud, R. M. Gschwind, W. Kunz and B. König, *Angew. Chem., Int. Ed.*, 2023, **62**, e202218775.

19 F. G. Bordwell and D. L. Hughes, *J. Org. Chem.*, 1982, **47**, 3224–3232.

20 B. Liu, C.-H. Lim and G. M. Miyake, *J. Am. Chem. Soc.*, 2017, **139**, 13616–13619.

21 S. Wang, H. Wang and B. König, *Chem*, 2021, **7**, 1653–1665.

22 T. Saegusa, S. Kobayashi and Y. Ito, *J. Org. Chem.*, 1970, **35**, 2118–2121.

23 J. Xuan, Z. Zhang and W. Xiao, *Angew. Chem., Int. Ed.*, 2015, **54**, 15632–15641.

24 D. E. Palmer, C. Pattaroni, K. Nunami, R. K. Chadha, M. Goodman, T. Wakamiya, K. Fukase, S. Horimoto and M. Kitazawa, *J. Am. Chem. Soc.*, 1992, **114**, 5634–5642.

25 G. Jung, *Angew. Chem., Int. Ed.*, 1991, **30**, 1051–1068.

26 J. M. Chalker, S. B. Gunnoo, O. Boutureira, S. C. Gerstberger, M. Fernández-González, G. J. L. Bernardes, L. Griffin, H. Hailu, C. J. Schofield and B. G. Davis, *Chem. Sci.*, 2011, **2**, 1666.

27 T. Mukaiyama, S. Yamamoto and K. Inomata, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 2807–2810.

28 W. W. Brennessel, B. E. Kucera, V. G. Young and J. E. Ellis, *Acta Crystallogr.*, 2019, **75**, 1118–1127.