NJC

ROYAL SOCIETY OF CHEMISTRY

PAPER

View Article Online
View Journal | View Issue

Cite this: *New J. Chem.*, 2026, **50**, 8868

TEMPO-promoted thioacid–amine coupling for peptide synthesis

Surya Pratap Singh,† Upasana Chatterjee,† Daniel T. Glatzhofer and Indrajeet Sharma *

We report a mild and epimerization-free strategy for peptide bond formation based on a TEMPO-promoted oxidative coupling of thiocarboxylic acids with amines. In this protocol, thiocarboxylic acids are selectively oxidized *in situ* to the corresponding diacyl disulfides, which subsequently undergo efficient aminolysis to furnish di- and tripeptides in good yields. The reaction proceeds under operationally simple conditions, tolerates partial aqueous media, and avoids the use of conventional coupling reagents. A broad range of amino acid substrates is compatible, including those bearing sensitive functional groups such as thioethers, secondary amines, and indole moieties. Notably, no detectable epimerization at the α-stereocenter is observed, highlighting the advantage of this redox-driven approach over traditional peptide coupling methods. Mechanistic investigations combining UV-visible spectroscopy, electronic substituent effect analysis, ESI-MS analysis, and density functional theory (DFT) calculations support a TEMPO-promoted oxidation pathway leading to reactive diacyl disulfide intermediates. Overall, this work expands the synthetic utility of TEMPO-based redox chemistry and provides a practical, chemoselective, and stereochemically robust platform for peptide bond assembly under mild conditions.

Received 15th April 2026,
Accepted 1st May 2026

DOI: 10.1039/d6nj01410k

rsc.li/njc

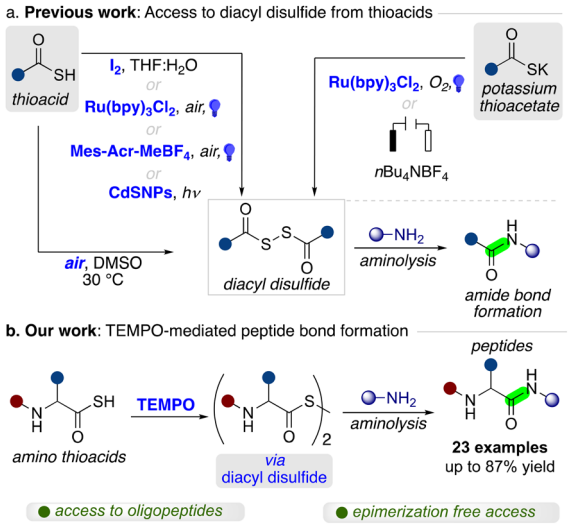
Introduction

Amide bond formation is a cornerstone transformation in organic chemistry, attracting sustained attention due to the pervasive presence of this linkage in pharmaceuticals, biological systems, and natural products.[1] In recent years, considerable efforts have been devoted to developing alternatives to conventional coupling-reagent-based methods, driven by the need to improve atom economy, enhance selectivity, and achieve greater operational robustness while minimizing waste and sensitivity to moisture.[2] In this context, diacyl disulfides have emerged as an efficient class of acyl-transfer reagents, conceptually aligned with the high acyl-transfer potential characteristic of biological thioester systems such as acetyl-CoA.[3–5] The use of diacyl disulfides for amide and peptide bond formation was first introduced by Wieland and co-workers in the early 1950s, who demonstrated that oxidative dimerization of thiocarboxylic acids generates reactive diacyl disulfides capable of undergoing aminolysis under mild conditions.[6–8]

Since these seminal studies, a variety of oxidative strategies have been developed for the *in situ* generation of diacyl disulfides from their parent thioacids. In 2014, Gopi and co-workers reported an iodine-mediated oxidation followed by aminolysis for peptide synthesis.[9] Subsequently, Liu *et al.*[10] and the Ramón group[11] disclosed photoactivated $Ru(bpy)_3Cl_2$-mediated oxidation of potassium thioacetate and thiocarboxylic acids, respectively, to access diacyl disulfide intermediates (Scheme 1a). Complementary photocatalytic approaches CdS nanoparticles (CdSNPs)[12] and Mes-Acr-$MeBF_4$[13] has also been reported for disulfide formation from thioacids. In addition, Guan and co-workers described an electrochemical oxidation of thiocarboxylic acids to diacyl disulfides.[3] More recently, the Kanai group reported aerobic oxidation of amino thioacids to diacyl disulfides, which were further transformed into pyridone-based acyl-transfer intermediates *via N*-hydroxy pyridone activation.[4] Collectively, these elegant strategies have significantly advanced oxidative access to diacyl disulfides as acyl-transfer species; however, their applications have largely remained limited to simple amide bond formation,[3,10–13] with only restricted generality for the synthesis of structurally diverse and sequence-defined peptides.[4,9]

In this study, we report a TEMPO-mediated *in situ* oxidation of amino thiocarboxylic acids to diacyl disulfides, which subsequently undergo aminolysis to afford peptides (Scheme 1b). TEMPO is well established as a mild and versatile oxidant for the conversion of primary and secondary alcohols to aldehydes and ketones under both Lewis and Brønsted acidic

Department of Chemistry and Biochemistry, University of Oklahoma, 101 Stephenson Parkway, Norman, Oklahoma 73019-5251, USA.
E-mail: isharma@ou.edu
† These authors contributed equally to this work.



Scheme 1 Synthetic methods to access diacyl disulfide. (a) Previous work: access to diacyl disulfide from thioacids; (b) our work: TEMPO-mediated peptide bond formation.

conditions.[14–33] Recent studies have further demonstrated that TEMPO-derived oxoammonium species can interact with thiols, enabling thiol–disulfide exchange processes.[34,35] Motivated by these precedents, we hypothesized that TEMPO could directly couple thioacids and amines through transient disulfide formation, thereby enabling epimerization-free amide and peptide bond formation under mild, redox-neutral conditions.

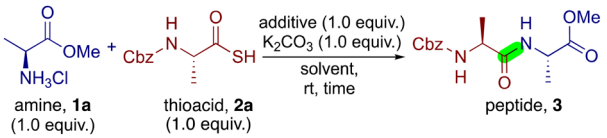
Results and discussion

Optimization of reaction conditions

We initiated our studies using L-alanine methyl ester hydrochloride (**1a**) as a model amine and Z-L-Ala-SH (**2a**) as a model thioacid (Table 1). To neutralize the amine hydrochloride salt, we employed K_2CO_3 as a base and screened TEMPO as an oxidant to oxidize thioacids to diacyl disulfide in acetonitrile.

The reaction proceeded efficiently, delivering the desired peptide (**3**) in good yield within 6 hours (entry 1). Next, we evaluated DDQ as an alternative oxidant, which did lead to product formation, albeit in significantly lower yield (entry 2). Following this, the screening of molecular oxygen (O_2, entry 3) was observed to deliver the desired peptide **3**, inefficiently, confirming TEMPO as the best oxidant. We also tested diisopropylethylamine (DIPEA) as an organic base (Table S1 in SI), which yielded a good result, although K_2CO_3 remained superior in terms of efficiency and reproducibility. Having optimized the oxidant and base, we turned our attention to solvents. In pursuit of greener and industrially viable conditions, we screened methanol (entry 4) and ethanol (entry 5), both of which afforded the product in good yields. However, when we tested tetrahydrofuran (THF), a coordinating and basic solvent (entry 6), and toluene, an aromatic solvent (entry 7), we observed only trace amounts of product, indicating incompatibility. Since biological peptide construction typically occurs in

Table 1 Optimization of reaction conditions[a]



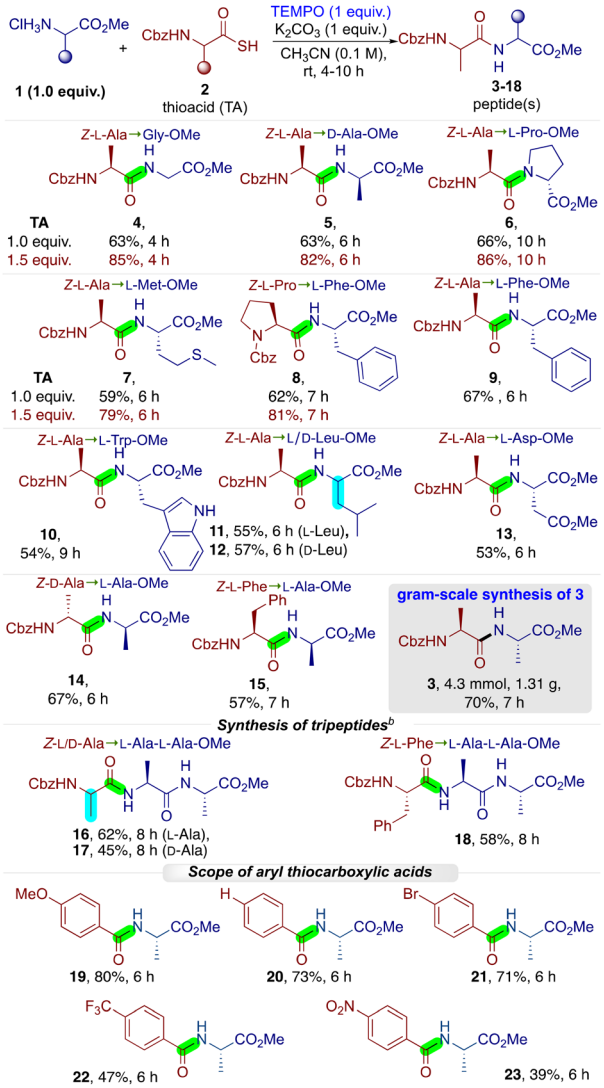
Entry	Additive	Solvent	Time	3, yield %[b]
1	TEMPO	CH_3CN	6 h	65(60)[c]
2	DDQ	CH_3CN	6 h	50
3	O_2 (15 psi)	CH_3CN	24 h	19
4	TEMPO	MeOH	24 h	55
5	TEMPO	EtOH	24 h	50
6	TEMPO	THF	24 h	<10
7	TEMPO	Toluene	24 h	<10
8	TEMPO	$CH_3CN:H_2O$ (9 : 1)	8 h	50
9	TEMPO	$CH_3CN:H_2O$ (8 : 2)	9 h	43
10[d]	TEMPO	CH_3CN	6 h	80
11	—	CH_3CN	24 h	19
12[e]	—	CH_3CN	24 h	<5

[a] All reactions until specified were conducted with amine 1 (0.1 mmol, 1.0 equiv.), thioacid 2 (1.0 equiv.), additive (1.0 equiv.), and solvent (1.0 mL, 0.1 M). [b] Yields were calculated by analyzing 1H-NMR of crude sample with 1,3,5-trimethoxybenzene as an internal standard. [c] Isolated yield. [d] 1.5 equiv. thioacid was added. [e] Reaction mixture was degassed by using the freeze–pump–thaw method.Note: The mentioned reaction time was noted upon complete consumption of thiocarboxylic acid **2a**.

aqueous media, we also explored aqueous solvent systems (entries 8 and 9). Acetonitrile containing up to 30% water supported product formation in reasonable yields, but increasing the water content to 40% and 50% drastically reduced the yield to trace levels (Table S1 in SI). To further improve productivity, we increased the loading of thioacid to 1.5 equivalents (entry 10), and a significant yield improvement was observed. In the end, we performed the coupling without oxidant, which results in the poor efficiency (entry 11), further probing the essential role of TEMPO. Notably, this reaction outcome could be explained by the formation of diacyl disulfide by the oxidation of thioacid *via* oxygen present in the reaction solvent, as described by Kanai.[4] Furthermore, we performed the reaction under degassed conditions (entry 12), and we did not observe any significant peptide coupling. In summary, the optimized conditions involve using TEMPO as the oxidant, K_2CO_3 as the base, CH_3CN as the solvent, and 1.0–1.5 equivalents of the thioacid; keeping thioacid accessibility, equimolar amounts were preferred for scope exploration.

Substrate scope studies

With the optimized conditions in hand, the scope of the reaction was evaluated using a variety of amino thiocarboxylic acids and amino acid methyl esters (Scheme 2). Coupling of thioacid **2a** with glycine and D-alanine methyl esters proceeded smoothly, affording the corresponding dipeptides **4** and **5** in high yields. Secondary amino acids were also compatible, as demonstrated by the efficient coupling of **2a** with L-proline to furnish dipeptide **6**. Reaction with L-methionine methyl ester likewise proceeded efficiently, highlighting the functional-group tolerance of the protocol (7). Variation of the thioacid



Scheme 2 Substrate scope[a]. [a] All reactions were conducted with amine **1** (0.1 mmol, 1.0 equiv.), thioacid **2** (1.0–1.5 equiv.), TEMPO (1.0 equiv.), K_2CO_3 (1.0 equiv.) and CH_3CN (1.0 mL, 0.1 M). [b] Reactions were performed without base (K_2CO_3).

component was well tolerated: L-proline-derived thioacid coupled readily with L-alanine methyl ester to afford dipeptide **8**. Optimal yields were obtained using 1.5 equiv. of the thioacid, consistent with enhanced formation of the reactive diacyl disulfide intermediate; however, subsequent scope studies were conducted with equimolar amounts to improve atom economy. To assess the influence of stereochemistry and side-chain steric and electronic effects, L-phenylalanine, L-tryptophan, L-leucine, and D-leucine methyl esters were examined, all delivering dipeptides **9–12** in consistently high yields. L-Aspartic acid was also compatible under the reaction conditions, affording dipeptide **13** efficiently. In addition, thioacids derived from D-alanine and L-phenylalanine were synthesized and coupled with a representative amine partner to give dipeptides **14** and **15** in excellent yields. The practicality of the method was further demonstrated by a gram-scale synthesis of dipeptide **3**, which proceeded without erosion in yield. The utility of this protocol was further extended to tripeptide synthesis. Using commercially available H-L-Ala-L-Ala-OMe as the dipeptide amine, coupling with L-alanine (**2a**), D-alanine (**2b**), and L-phenylalanine (**2c**) thioacids furnished tripeptides **16–18** in good yields. Furthermore, we turned our attention to aryl thiocarboxylic acids bearing different functional groups at the para position. The electron-donating group (–OMe) was observed to produce the coupled product **19** in high yields. The coupling outcome with an electronically neutral (–H) substituent works equally efficiently and produces **20** in high yields. In case of electron-withdrawing substituents (–Br, $-CF_3$, and $-NO_2$), the efficiency was observed to decrease as the electron-withdrawing capability increases. More specifically, bromo produced **21** in high yield, while trifluoromethyl and nitro produced reduced yields of the desired coupling products **22** and **23**. Overall, this method provides an efficient and general approach to di- and tripeptide synthesis, displaying broad compatibility with diverse side chains, stereochemical configurations, both primary and secondary amines, and electronically distinct substituents.

Epimerization analyses

Traditional peptide coupling strategies often suffer from epimerization,[36] leading to loss of stereochemical integrity in the desired oligopeptides.[37,38] To establish the robustness of our methodology as an alternative solution, we conducted detailed NMR analyses on the crude reaction mixture (Fig. 1). Notably, we observed well-resolved methyl ester peaks corresponding to tripeptides **16** and **17**, along with clearly distinguishable splitting patterns of the benzylic protons, supporting the formation of stereochemically pure products.

Mechanistic studies

Following the substrate scope evaluation, we examined the mechanistic pathway. Control experiments revealed the dual role of the amine, functioning first as a base and subsequently as a nucleophile in peptide bond formation. Coupling of thioacid **2a** with benzylamine in the absence of K_2CO_3 afforded the product in excellent yield of **24**, confirming the amine's intrinsic basicity (Scheme 3a). In the absence of a nucleophile, oxidation of the thioacid by TEMPO furnished the corresponding transient diacyl disulfide along with TEMPOH.

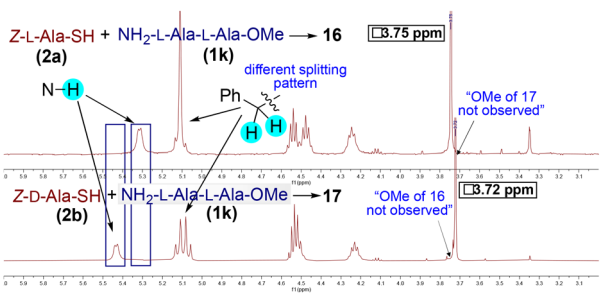
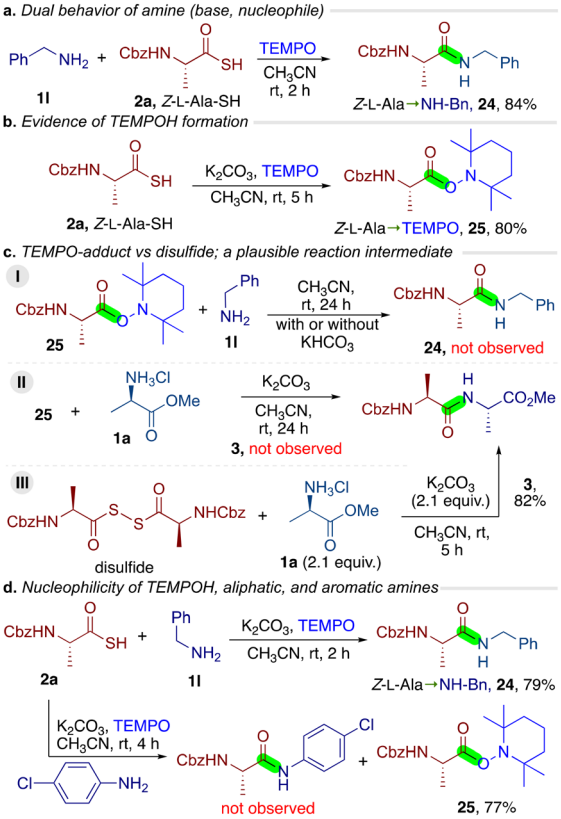


Fig. 1 Comparison of ^{1}H-NMR of crude samples for the synthesis of **16** and **17**.



Scheme 3 Mechanistic studies[a]. (a) Dual behaviour of amine; (b) evidence of TEMPOH formation; (c) TEMPO-adduct *vs.* disulfide: a plausible reaction intermediate; (d) nucleophilicity of TEMPOH, aliphatic and aromatic amines. [a] All reactions were conducted under standard conditions.

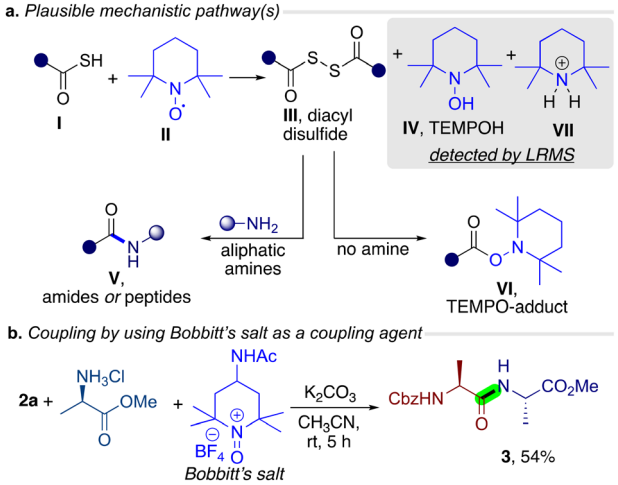


Fig. 2 (a) Plausible mechanistic pathways; (b) replacing TEMPO with Bobbitt's salt to couple thioacid and amines.

Notably, TEMPOH reacted further with the diacyl disulfide to yield a stable TEMPO adduct (**25**) in high yield (Scheme 3b). Subjecting this adduct **25** to benzylamine or L-alanine methyl ester hydrochloride (**1a**) under standard conditions produced no coupling, indicating that the TEMPO adduct is a stable species under these reaction conditions, not part of the productive pathway. In contrast, diacyl disulfide efficiently afforded the dipeptide under standard conditions, establishing it as the plausible intermediate (Scheme 3c). To further investigate this, we conducted couplings of **2a** with aliphatic (benzylamine, good nucleophile) and aromatic (4-chloroaniline, weak nucleophile) amines. In the case of benzylamine, we observed efficient coupling with the thioacid; however, for 4-chloroaniline, we observed the formation of TEMPO adduct **25**. This outcome further indicated the formation of a transient diacyl disulfide intermediate (Scheme 3d).

Spectroscopic and physical observations further supported the mechanistic studies. The reaction mixture exhibited the distinct colour change from bright orange to off-white is consistent with the consumption of TEMPO (bright orange) and formation of TEMPOH and a 2,2,6,6-tetramethyl piperidinium salt (both are colourless and were detected by low-resolution ESI-MS technique) (Fig. S3, SI). UV-vis analysis revealed the disappearance of the TEMPO's absorption band, indicative of TEMPO consumption and essential role in the coupling (Fig. S4, SI). Cyclic voltammetry studies ruled out direct Single-Electron transfer (SET) between TEMPO and the potassium thioacetate (Fig. S5, SI). The oxidation potential of the potassium thioacetate (E_{ox} = 0.25 V) and the reduction potential of TEMPO (E_{red} = −1.37 V) correspond to a calculated ΔG of +37.4 kcal mol^{-1} for the SET process, rendering it thermodynamically unfavourable. Collectively, these results substantiate the consumption of TEMPO and *in situ* generation of TEMPOH along with diacyl disulfide in the transformation.

Plausible reaction pathways

Based on our mechanistic findings and literature precedents,[20,34,35] we propose the pathway depicted in Fig. 2a. Where thioacid **I** in the presence of TEMPO **II** under standard reaction conditions undergoes oxidation to diacyl disulfide **III** and provides TEMPOH **IV**. Then this disulfide intermediate **III** engages with the amine and undergoes aminolysis to produce peptides **V**. However, in the absence of amine, TEMPOH reacts with disulfide and produces TEMPO-adduct **VI**, which remains inert under reaction conditions. The detailed mechanistic pathways for the formation of diacyl disulfide by TEMPO have been provided in the SI (Fig. S6). Density functional theory (DFT) studies supported the proposed mechanistic pathways (Fig. S7–S9). To further validate the formation of diacyl disulfide as an intermediate, we replaced TEMPO with Bobbitt's salt, which is known to oxidize thiols into disulfides.[35] The outcome, as expected, provided the desired dipeptide **3** (Fig. 2b) in moderate yields, further supporting our mechanistic hypothesis.

Conclusions

In summary, we disclose a TEMPO-promoted thioacid-amine coupling that enables mild and epimerization-free peptide bond formation. Selective oxidation of thiocarboxylic acids generates reactive diacyl disulfide intermediates, which undergo efficient aminolysis to afford di- and tripeptides across

diverse amino acid substrates. Mechanistic studies combining UV-visible spectroscopy, substituent effect analysis, and DFT calculations support a diacyl disulfide-mediated pathway, establishing a redox-driven and stereochemically robust alternative to conventional peptide coupling methods.

Author contributions

I. S. and S. P. S. conceived and directed the project. S. P. S. and U. C. performed reaction optimization, mechanistic studies, and UV-visible experiments. U. C. and S. P. S. carried out the substrate scope. U. C. performed DFT calculations. We thank DG for the helpful discussion for mechanistic insights. The manuscript was written by S. P. S., U. C., and I. S., with all authors approving the final version.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this study are available in the article and its supplementary information (SI). Supplementary information: experimental procedures and spectroscopic data. See DOI: https://doi.org/10.1039/d6nj01410k.

Acknowledgements

This work was supported by the University of Oklahoma. We gratefully acknowledge Dr. Novruz G. Akhmedov (Research Support Services, University of Oklahoma) for assistance with NMR analyses. We thank Sohom Chandra, Amila Wanasinghe, and Dr Yitong Dong (University of Oklahoma) for their support with UV–Vis studies, and Kanika Parashar (University of Oklahoma) for assistance with data processing using Origin. We also thank Hafsa Abdul Ghuffar and Dr. Hyunho Noh (University of Oklahoma) for help with cyclic voltammetry experiments. Finally, we acknowledge Deacon Herndon (University of Oklahoma) for valuable discussions related to DFT calculations and mechanistic analysis.

References

1 A. El-Faham and F. Albericio, Peptide Coupling Reagents, More than a Letter Soup, *Chem. Rev.*, 2011, **111**, 6557–6602.
2 M. T. Sabatini, L. T. Boulton, H. F. Sneddon and T. D. Sheppard, A green chemistry perspective on catalytic amide bond formation, *Nat. Catal.*, 2019, **2**, 10–17.
3 L. Tang, J. H. Matuska, Y.-H. Huang, Y.-H. He and Z. Guan, Amide Synthesis from Thiocarboxylic Acids and Amines by Spontaneous Reaction and Electrosynthesis, *ChemSusChem*, 2019, **12**, 2570–2575.
4 T. Tatsumi, K. Sasamoto, T. Matsumoto, R. Hirano, K. Oikawa, M. Nakano, M. Yoshida, K. Oisaki and M. Kanai, Practical N-to-C peptide synthesis with minimal protecting groups, *Commun. Chem.*, 2023, **6**, 231.
5 K. Burton, The free energy change associated with the hydrolysis of the thiol ester bond of acetyl coenzyme A, *Biochem. J.*, 1955, **59**, 44–46.
6 S. L. Scinto, D. A. Bilodeau, R. Hincapie, W. Lee, S. S. Nguyen, M. Xu, C. W. Am Ende, M. G. Finn, K. Lang, Q. Lin, J. P. Pezacki, J. A. Prescher, M. S. Robillard and J. M. Fox, Bioorthogonal chemistry, *Nat. Rev. Methods Primers*, 2021, **1**, 30.
7 H. Jiang, G. D. D'Agostino, P. A. Cole and D. R. Dempsey, in *Methods Enzymol*, ed. D. M. Chenoweth, Academic Press, 2020, vol. 639, pp. 333–353.
8 K. Ghosh and W. D. Lubell, N- to C-Peptide Synthesis, Arguably the Future for Sustainable Production, *J. Pept. Sci.*, 2025, **31**, e70019.
9 S. M. Mali and H. N. Gopi, Thioacetic Acid/NaSH-Mediated Synthesis of N-Protected Amino Thioacids and Their Utility in Peptide Synthesis, *J. Org. Chem.*, 2014, **79**, 2377–2383.
10 H. Liu, L. Zhao, Y. Yuan, Z. Xu, K. Chen, S. Qiu and H. Tan, Potassium Thioacids Mediated Selective Amide and Peptide Constructions Enabled by Visible Light Photoredox Catalysis, *ACS Catal.*, 2016, **6**, 1732–1736.
11 D. Procopio, X. Marset, G. Guillena, M. L. Di Gioia and D. J. Ramón, Visible-Light-Mediated Amide Synthesis in Deep Eutectic Solvents, *Adv. Synth. Catal.*, 2024, **366**, 870–876.
12 S. Das, S. Ray, A. B. Ghosh, P. K. Samanta, S. Samanta, B. Adhikary and P. Biswas, Visible light driven amide synthesis in water at room temperature from Thioacid and amine using CdS nanoparticles as heterogeneous Photocatalyst, *Appl. Organometal. Chem.*, 2018, **32**, e4199.
13 W. Song, K. Dong and M. Li, Visible Light-Induced Amide Bond Formation, *Org. Lett.*, 2020, **22**, 371–375.
14 Y. Ma, C. Loyns, P. Price and V. Chechik, Thermal decay of TEMPO in acidic media via an *N*-oxoammonium salt intermediate, *Org. Biomol. Chem.*, 2011, **9**, 5573–5578.
15 X. Zhao, J.-D. Yang and J.-P. Cheng, Revisiting the Electrochemistry of TEMPOH Analogues in Acetonitrile, *J. Org. Chem.*, 2023, **88**, 540–547.
16 R. Amorati, G. F. Pedulli, D. A. Pratt and L. Valgimigli, TEMPO reacts with oxygen-centered radicals under acidic conditions, *Chem. Commun.*, 2010, **46**, 5139–5141.
17 Y. Tian, Y. Li, Y. Li, Z. Zhao, G.-G. Ying, K. Shih and Y. Feng, New insights into the singlet oxygen-independent formation of TEMPO signals in electron paramagnetic resonance analysis, *Sep. Purif. Technol.*, 2025, **355**, 129564.
18 M. Rafiee, K. C. Miles and S. S. Stahl, Electrocatalytic Alcohol Oxidation with TEMPO and Bicyclic Nitroxyl Derivatives: Driving Force Trumps Steric Effects, *J. Am. Chem. Soc.*, 2015, **137**, 14751–14757.
19 S. Jiang, Y. Xie, Y. Xie, L.-J. Yu, X. Yan, F.-G. Zhao, C. J. Mudugamuwa, M. L. Coote, Z. Jia and K. Zhang, Lewis Acid-Induced Reversible Disproportionation of TEMPO Enables Aqueous Aluminum Radical Batteries, *J. Am. Chem. Soc.*, 2023, **145**, 14519–14528.

20 V. Golubev, E. Rozantsev and M. Neiman, Some reactions of free iminoxyl radicals with the participation of the unpaired electron, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1965, **14**, 1898–1904.
21 S. Wertz and A. Studer, Nitroxide-catalyzed transition-metal-free aerobic oxidation processes, *Green Chem.*, 2013, **15**, 3116–3134.
22 X. He, Z. Shen, W. Mo, N. Sun, B. Hu and X. Hu, TEMPO-*tert*-Butyl Nitrite: An Efficient Catalytic System for Aerobic Oxidation of Alcohols, *Adv. Synth. Catal.*, 2009, **351**, 89–92.
23 L. Tebben and A. Studer, Nitroxides: Applications in Synthesis and in Polymer Chemistry, *Angew. Chem., Int. Ed.*, 2011, **50**, 5034–5068.
24 J. M. Bobbitt, C. BrüCkner and N. Merbouh, *Org. React.*, 2010, 103–424.
25 A. De Mico, R. Margarita, L. Parlanti, A. Vescovi and G. Piancatelli, A Versatile and Highly Selective Hypervalent Iodine (III)/2,2,6,6-Tetramethyl-1-piperidinyloxyl-Mediated Oxidation of Alcohols to Carbonyl Compounds, *J. Org. Chem.*, 1997, **62**, 6974–6977.
26 J. M. Bobbitt, Oxoammonium salt oxidations of alcohols, *ChemInform*, 2011, **42**(21).
27 P. Lucio Anelli, C. Biffi, F. Montanari and S. Quici, Fast and selective oxidation of primary alcohols to aldehydes or to carboxylic acids and of secondary alcohols to ketones mediated by oxoammonium salts under two-phase conditions, *J. Org. Chem.*, 1987, **52**, 2559–2562.
28 R. A. Sheldon and I. W. C. E. Arends, Organocatalytic Oxidations Mediated by Nitroxyl Radicals, *Adv. Synth. Catal.*, 2004, **346**, 1051–1071.
29 J. M. Hoover, B. L. Ryland and S. S. Stahl, Mechanism of Copper(I)/TEMPO-Catalyzed Aerobic Alcohol Oxidation, *J. Am. Chem. Soc.*, 2013, **135**, 2357–2367.
30 J. E. Nutting, K. Mao and S. S. Stahl, Iron(III) Nitrate/TEMPO-Catalyzed Aerobic Alcohol Oxidation: Distinguishing between Serial versus Integrated Redox Cooperativity, *J. Am. Chem. Soc.*, 2021, **143**, 10565–10570.
31 I. Sajenko, V. Pilepić, C. Jakobušić Brala and S. Uršić, Solvent Dependence of the Kinetic Isotope Effect in the Reaction of Ascorbate with the 2,2,6,6-Tetramethylpiperidine-1-oxyl Radical: Tunnelling in a Small Molecule Reaction, *J. Phys. Chem. A*, 2010, **114**, 3423–3430.
32 Z.-W. Mei, T. Omote, M. Mansour, H. Kawafuchi, Y. Takaguchi, A. Jutand, S. Tsuboi and T. Inokuchi, A high performance oxidation method for secondary alcohols by inductive activation of TEMPO in combination with pyridine–bromine complexes, *Tetrahedron*, 2008, **64**, 10761–10766.
33 A. E. J. d Nooy, A. C. Besemer and H. v Bekkum, On the Use of Stable Organic Nitroxyl Radicals for the Oxidation of Primary and Secondary Alcohols, *Synthesis*, 1996, 1153–1176.
34 H. Maeda, H.-Y. Wu, Y. Yamauchi and H. Ohmori, Important Role of the 3-Mercaptopropionamide Moiety in Glutathione: Promoting Effect on Decomposition of the Adduct of Glutathione with the Oxoammonium Ion of TEMPO, *J. Org. Chem.*, 2005, **70**, 8338–8343.
35 S. M. Weierbach, R. P. Reynolds, S. M. Stephens, K. V. Vlasakakis, R. T. Ritter, O. M. White, N. H. Patel, E. C. Hayes, S. Dunmire and K. M. Lambert, Chemoselective Oxidation of Thiols with Oxoammonium Cations, *J. Org. Chem.*, 2023, **88**, 11392–11410.
36 S. Duengo, M. I. Muhajir, A. T. Hidayat, W. J. A. Musa and R. Maharani, Epimerisation in Peptide Synthesis, *Molecules*, 2023, **28**, 8017.
37 G. Windridge and E. C. Jorgensen, 1-Hydroxybenzotriazole as a racemization-suppressing reagent for the incorporation of im-benzyl-L-histidine into peptides, *J. Am. Chem. Soc.*, 1971, **93**, 6318–6319.
38 Y. Zhou, H. Li, Y. Huang, J. Li, G. Deng, G. Chen, Z. Xi and C. Zhou, Suppression of alpha-carbon racemization in peptide synthesis based on a thiol-labile amino protecting group, *Nat. Commun.*, 2023, **14**, 5324.