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Facile synthesis of aliphatic isothiocyanates and thioureas on solid phase using peptide coupling reagents ☆

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Abstract—Peptide coupling reagents can be used as versatile reagents for the formation of aliphatic isothiocyanates and thioureas on solid phase from the corresponding solid-phase anchored aliphatic primary amines. The formation of the thioureas is fast and highly chemoselective, and proceeds via formation of the intermediate isothiocyanate. The isothiocyanate and subsequent thiourea formation take place under standard peptide coupling conditions using carbon disulfide as the 'amino acid'. The thioureas are released from the resin and isolated in moderate to high yields.
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Isothiocyanates and thioureas are valuable functional groups in organic chemistry, and have found wide use in, for example, bioconjugate[1] and heterocyclic chemistry.[2] For this reason, much effort has been devoted to develop efficient routes for the synthesis of these classes of compounds. The traditional synthetic pathway to intermediate isothiocyanates, utilises thiocarbonyl insertion reagents, for example, thiophosgene[3] or dipyridyl thionocarbonate.[4] Other routes utilise electrophilic phosphorous reagents such as triphenylphosphine dibromide and proceed via intermediate iminophosphorane formation, followed by reaction with carbon disulfide.[5] However, these highly reactive reagents suffer from low chemoselectivity and high toxicity. Alternative routes to isothiocyanates proceed via intermediate formation of the dithiocarbamate from the corresponding amine and carbon disulfide. The dithiocarbamate can be desulfurised by a variety of reagents.[6] In these procedures it is of crucial importance to ensure complete formation of the dithiocarbamate to prevent reaction between the electrophilic desulfurising reagent and the amine. Previously, we found that phosphonium- and uronium-based peptide coupling reagents (BOP and TFFH, respectively)[7] together with DIPEA or triethylamine act as mild and chemoselective desulfurising agents for dithiocarbamates in solution.[8,9] The peptide coupling reagents did not react with the precursor amine. The one-pot reaction between the amine, carbon disulfide and the peptide coupling agent gave direct and efficient conversion to the corresponding isothiocyanate, which could then be reacted with, for example, amines for direct formation of thioureas.

Due to the similarity with conventional peptide methodology on solid phase, this method should be easily adapted for solid-phase synthesis (SPS) of isothiocyanates and thioureas. The majority of reports on SPS of thioureas employ the isothiocyanate as the solution reagent reacting with a solid-phase bound amine.[10] However, there are synthetic demands for the formation of the isothiocyanate on solid phase and employment of the amine in solution, especially if the amine is polyfunctional, leading to side reactions upon formation of the corresponding isothiocyanate in solution.

Only very few reports employ SPS of isothiocyanates and derivatives by this 'reversed pathway'. Zaragosa and co-workers synthesised isothiocyanates on solid phase, as precursors for thiophene derivatives, employing tosyl chloride as the desulfurising reagent for the dithiocarbamate.[11] This procedure depends on full conversion of the amine to the dithiocarbamate, before reaction with

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tosyl chloride and base in order to avoid formation of the sulfonamide via a side reaction. Di-(2-pyridyl)thionocarbonate has very recently been applied in the synthesis of isothiocyanates on solid phase in the synthesis of 1,3,4-oxadiazoles[12] and 2-amino-1,3,4-thiadiazines,[13] however, longer reaction times were required. Here, we introduce a rapid method for SPS of isothiocyanates and thioureas using peptide coupling reagents. The formation of the isothiocyanates and thioureas proceeds under traditional peptide coupling conditions, making this new method useful in combinatorial synthesis.

A high loading (1.2–1.9 mmol/g) of 2-chlorotrityl derivatised polystyrene resin was utilised, as the products can be released from the resin under very mild acidic conditions using 20% 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) in dichloromethane.[14] This cleavage method has the advantage that the products can easily be isolated by evaporation of the volatile cleavage mixture.[15]

Initially, the Fmoc-amino acid (tyrosine) was loaded onto the trityl resin and the Fmoc group removed according to literature procedures.[16] The solid-phase bound amine was then reacted with carbon disulfide, DIPEA and the peptide coupling reagents HBTU, HATU, TFFH, DIPCDI, BOP, PyBOP, PyBrOP and BOP-Cl (Fig. 1) under various conditions. Initially, the corresponding isothiocyanate on solid phase was not isolated, but reacted directly with benzylamine to furnish the thiourea.

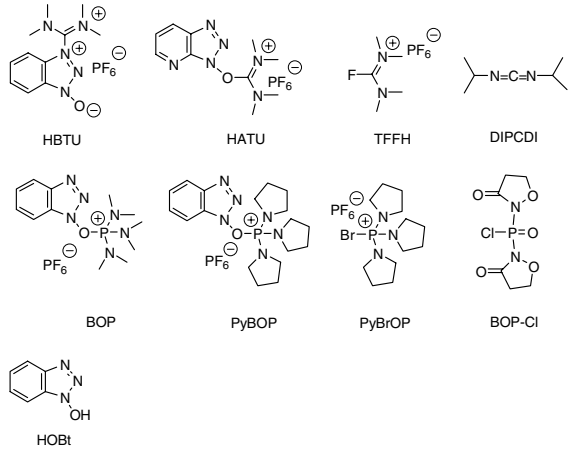
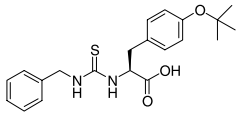
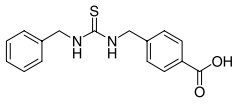
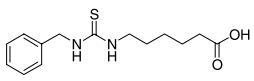
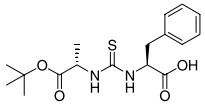
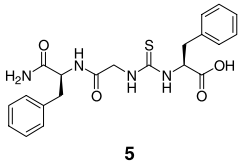
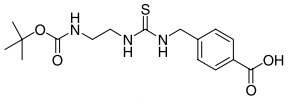
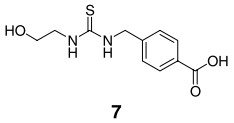
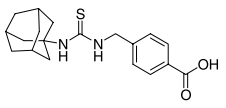
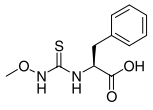


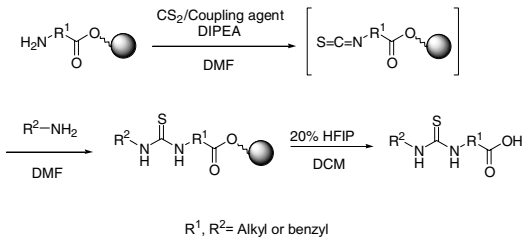
Figure 1.

HPLC-MS analysis showed that these peptide coupling reagents were capable of fast and complete formation of thiourea **1** (Table 1) on solid phase. The phosphorus-based PyBrOP and BOP-Cl gave slightly slower (2 h reaction time) conversion to the intermediate isothiocyanate in comparison with the 30 min reaction time for the remaining coupling reagents. With all coupling reagents it was found that a large excess (50–100 fold) of carbon disulfide was needed for fast and efficient formation of the isothiocyanate. The reaction can be carried out in apolar solvents like dichloromethane or in polar solvents like DMF or NMP. As the reaction does not depend on the full formation of the dithiocarbamate the reactants can be mixed together in a one-pot reaction to furnish the aliphatic isothiocyanate within 30 min, for subsequent reaction with an amine or other nucleophile (Scheme 1).[17]

Solid-phase infrared analysis (KBr) of the intermediate isothiocyanate showed two bands at approximately 2100 cm^{-1} after reaction between the solid-phase bound amine, carbon disulfide, DIPEA and coupling agent

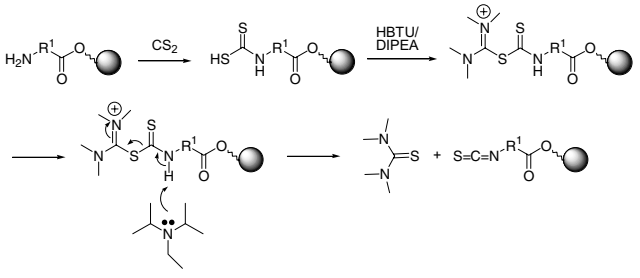
Table 1

Compound[18]	Yield[19] (%) HBTU/PyBOP
 **1**	60/70
 **2**	quant/98
 **3**	58/71
 **4**	quant/76
 **5**	quant/quant
 **6**	95/quant
 **7**	47/81
 **8**	60/73
 **9**	quant/quant



Scheme 1.

HBTU or PyBOP.[20] These bands were absent in the amino functionalised resin, and can be assigned to the asymmetrical vibration of the corresponding isothiocyanate.[21] In order to elucidate the reaction pathway further, the filtrate from the reaction between carbon disulfide, the solid-phase bound amine, coupling reagent and DIPEA was analysed by HPLC-MS. Analysis of the HBTU mediated isothiocyanate formation showed that the coupling agent acted as a desulfurising agent creating the corresponding tetramethyl thiourea as well as HOBt as byproducts (Scheme 2). However, in the analysis of the PyBOP mediated formation of the isothiocyanate, only the phosphine oxide was found in the mixture, with no traces of phosphine sulfide. In addition almost no HOBt was present in the filtrate. ^{31}P NMR analysis of the BOP mediated formation of isothiocyanates in solution, similarly showed no formation of the P=S compound during the reaction. Also here, the phosphine oxide (HMPA) was the only byproduct, suggesting that the formation of isothiocyanates by phosphonium based coupling reagents may proceed via another reaction pathway.



Scheme 2.

Amino acids were easily converted to the corresponding isothiocyanates and thioureas, and in some cases the isothiocyanate could be released from the resin and isolated.[22] However, attempts to convert longer peptides on solid phase to the corresponding thioureas or isothiocyanates resulted in complex mixtures. It has been reported that thiohydantoin formation is a major side reaction in the formation of peptide isothiocyanates in solution.[23,24]

In summary, a new facile route for the formation of thioureas and isothiocyanates on solid phase has been developed. The method employs standard peptide coupling conditions, and may thus be of interest to chemists working in the area of solid-phase organic chemistry and combinatorial chemistry. The thioureas were isolated in good yields and high crude purity. The intermediate solid-phase bound isothiocyanates can furthermore serve as useful intermediates in the formation of heterocycles[3,12,13] or thioamides[11] offering a wide scope for this new method in solid-phase organic chemistry.

Acknowledgements

The authors would like to thank Theis Brock-Nannestad for assistance in performing the IR measurements, and the Danish Agricultural and Veterinary Research Council for financial support.

References and Notes

1. For a general review on isothiocyanates and thioureas, see: *The Chemistry of Cyanates and their Thioderivatives*; Patai, S., Ed.; Wiley: Chichester, 1977; Applications of isothiocyanates as useful intermediates in bioconjugate chemistry, see for example, Fernández, J. M. G.; Mellet, C. O.; Blanco, J. L. J.; Mota, J. F.; Gadelle, A.; Coste-Sarguet, A.; Defaye, J. *Carbohydr. Res.* **1995**, *268*, 57–71.
2. For a review in the use of isothiocyanates in the synthesis of heterocycles, see: Mukerjee, A. K.; Ashare, R. *Chem. Rev.* **1991**, *91*, 1–24.
3. Rathke, A. *Chem. Ber.* **1872**, *5*, 799; Dyson, G. M.; George, H. J. *J. Chem. Soc.* **1924**, *125*, 1702–1708.
4. Kim, S.; Yi, K. Y. *Tetrahedron Lett.* **1985**, *26*, 1661–1664.
5. Molina, P.; Alajarin, M.; Tamiaki, H. *Synthesis* **1982**, 596–597.
6. See, for example, Jochims, J. C.; Seeliger, A. *Angew. Chem.* **1967**, *79*, 151.
7. Abbreviations used, BOP: (Benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate; BOP-Cl: Bis(2-oxo-3-oxazolidinyl) phosphinic chloride; DIPCDI: *N*,*N*′-Diisopropylcarbodiimide; Fmoc: Fluorenyloxycarbonyl; HATU: *O*-(7-Azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate; HBTU: *N*-[(1*H*-benzotriazol-1-yl)(dimethylamino)methylene]-*N*-methyl-methanaminium hexafluorophosphate *N*-oxide; HOBt: 1-hydroxybenzotriazole; PyBOP: (Benzotriazol-1-yloxy)tris(pyrrolidino)phosphonium hexafluorophosphate; PyBrOP: Bromo-tris(pyrrolidino)phosphonium hexafluorophosphate; TFFH: Fluoro-*N*,*N*,*N*′,*N*′-tetramethylformamidinium hexafluorophosphate.
8. Boas, U.; Jakobsen, M. H. *J. Chem. Soc., Chem. Commun.* **1995**, 1995–1996.
9. Boas, U.; Pedersen, B.; Christensen, J. B. *Synth. Commun.* **1998**, *28*, 1223–1231.
10. See, for example, Makino, S.; Suzuki, N.; Nakanishi, E.; Tsuji, T. *Tetrahedron Lett.* **2000**, *41*, 8333–8337; Li, M.; Wilson, L. J.; Portlock, D. E. *Tetrahedron Lett.* **2001**, *42*, 2273–2275; Kesarwani, A. P.; Srivastava, G. K.; Rastogi, S. K.; Kundu, B. *Tetrahedron Lett.* **2002**, *43*, 5579–5581.
11. Stephensen, H.; Zaragosa, F. *J. Org. Chem.* **1997**, *62*, 6096–6097.
12. Kilburn, J. P.; Lau, J.; Jones, R. C. F. *Tetrahedron Lett.* **2001**, *42*, 2583–2586.
13. Kilburn, J. P.; Lau, J.; Jones, R. C. F. *Tetrahedron Lett.* **2002**, *43*, 3309–3311.
14. Bollhagen, R.; Schmiedberger, M.; Barlos, K.; Grell, E. *J. Chem. Soc., Chem. Commun.* **1994**, 2559–2560.
15. Bp (HFIP): 58 °C Purcell, K. F.; Stikeleather, J. A.; Brunk, S. D. *J. Am. Chem. Soc.* **1969**, *91*, 4019–4027.

16. Barlos, K.; Gatos, D.; Kallitis, J.; Papaphotiu, G.; Sotiriu, P.; Yao, W. Q.; Schafer, W. *Tetrahedron Lett.* **1989**, 3943–3946.
17. *SPS of thioureas*, *general procedure*: Deprotected amino acid derivatised 2-chlorotrityl resin (0.10 g, 0.19 mmol, theoretical loading: 1.9 mmol/g) was suspended in DMF (0.50 mL). Carbon disulfide (1.00 mL) was added followed by HBTU (0.29 g, 0.76 mmol) or PyBOP (0.40 g, 0.76 mmol) and DIPEA (0.39 mL, 2.28 mmol). The suspension was shaken for 30 min at rt. The solvent was removed by suction, and the resin was washed with DCM (10 times), DMF (5 times), and air was flushed through for 10 min to remove residual carbon disulfide. The derivatised resin was swelled in DMF (1.5 mL) and amine (5 equiv, 0.95 mmol) was added. If the amine was a hydrochloride, DIPEA (0.33 mL, 1.9 mmol) was added and the mixture was shaken for 2 h at rt. The solvent was removed by suction and the resin was washed with DMF (5 times) and DCM (5 times). The thiourea compound was released from the resin using 20% HFIP (2.5 mL) for 30 min, the product was collected by suction and the cleavage mixture was removed in vacuo.
18. Analytical data for compounds **1**–**9**: (**1**): ^{1}H NMR (250 MHz, d_6-DMSO): δ 1.27 (s, 9H), 2.93 (m, 2H), 4.64 (d, $J = 4.9$ Hz, 2H), 5.15 (br q, 1H), 6.85 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.4$ Hz, 2H), 7.23 (m, 5H), 7.58 (d, $J = 7.7$ Hz, 1H), 8.12 (t, $J = 5.5$ Hz, 1H); ^{13}C (63 MHz, d_6-DMSO): δ 28.6, 36.6, 47.1, 57.8, 77.8, 123.4, 123.6, 126.9, 127.0, 127.3, 128.2, 128.3, 129.8, 130.3, 131.7, 139.1, 153.7, 173.2, 182.9. HPLC (220 nm): $t_R = 22.549$ min; 97% crude purity. HR-MS (TOF-ES$^+$) calcd for $C_{21}H_{27}N_2O_3S$ (MH$^+$) 387.1739 (mono-isotopic); found. 387.1739 (**2**): ^{1}H NMR (250 MHz, d_6-DMSO): δ 4.62 (br s, 2H), 4.75 (br s, 2H), 7.25–7.40 (m, 7H), 7.90 (d, $J = 7.3$ Hz, 2H), 8.05 (br s, 2H), 12.71 (br s, 1H). ^{13}C (63 MHz, d_6-DMSO): δ 46.6, 47.0, 126.9, 127.1, 127.3, 128.3, 129.4, 144.7, 167.3; HPLC (220 nm): $t_R = 18.468$ min; 98% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{16}H_{17}N_2O_2S$ (MH$^+$) 301.1037 (mono-isotopic); found. 301.1073 (**3**): ^{1}H NMR (250 MHz, d_6-DMSO): δ 1.27 (qn, $J = 6.6$ Hz, 2H), 1.50 (m, 4H), 2.20 (t, $J = 7.3$ Hz, 2H), 4.64 (br s, 2H), 7.15–7.40 (m, 5H), 7.50 (br s, 1H), 7.80 (br s, 1H); ^{13}C (63 MHz, d_6-DMSO): δ 24.3, 26.0, 28.6, 33.8, 43.5, 46.9, 126.8, 127.3, 128.3, 139.9, 174.6; HPLC (220 nm): $t_R = 18.633$ min; 98% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{14}H_{21}N_2O_2S$ (MH$^+$) 281.1324 (mono-isotopic); found. 281.1319 (**4**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.30 (d, $J_2 = 7.1$ Hz, 3H), 1.40 (s, 9H), 2.95 (dd, $J_1 = 13.7$ Hz, $J_2 = 6.4$ Hz, 2H), 4.60 (qn, $J = 7.1$ Hz, 1H), 4.95 (br q, 1H), 7.20–7.30 (m, 5H), 7.65 (br d, $J = 7.1$ Hz, 1H), 8.00 (br d, $J = 6.2$ Hz, 1H), 10.20 (br s, 1H); ^{13}C (101 MHz, d_6-DMSO): δ 27.7, 31.4, 37.2, 52.7, 57.7, 80.5, 126.4, 128.1, 129.4, 137.2, 171.9, 172.8, 182.1; HPLC (220 nm): $t_R = 22.632$ min; 99% crude purity HR-MS (TOF-ES$^+$) calcd for $C_{17}H_{25}N_2O_4S$ (MH$^+$) 353.1535 (mono-isotopic); found. 353.1547 (**5**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 2.80–3.05 (m, 4H), 4.11 (d, $J = 10.1$ Hz, 2H), 4.40 (m, 2H), 4.92 (br s, 2H), 7.15–7.30 (m, 10H), 7.80 (br s, 1H), 7.92 (br s, 1H), 8.17 (br d, 1H), 10.42 (br s, 1H); ^{13}C (101 MHz, d_6-DMSO): δ 42.3, 47.0, 58.3, 59.8, 67.3, 126.3, 126.9, 127.8, 128.3, 129.2, 129.3, 129.5, 130.2, 135.2, 137.5, 137.8, 138.1, 165.3, 168.4, 172.6, 182.3; HPLC (220 nm): $t_R = 20.824$ min; 90% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{21}H_{25}N_4O_4S$ (MH$^+$) 429.1596 (mono-isotopic); found. 429.1606 (**6**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.38 (s, 9H), 3.08 (q, $J = 5.9$ Hz, 2H), 3.48 (br s, 2H), 4.73 (br s, 2H), 6.85 (br s, 1H), 7.38 (d, $J = 8.4$ Hz, 2H), 7.60 (br t, 1H), 7.88 (d, $J = 8.4$ Hz, 2H), 8.05 (br s, 1H), 12.60 (br s, 1H); ^{13}C (101 MHz, d_6-DMSO): δ 28.3, 39.0, 40.2, 77.8, 127.1, 129.3, 129.5, 155.7, 167.2; HPLC (220 nm): $t_R = 18.061$ min; 99% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{16}H_{24}N_3O_4S$ (MH$^+$) 354.1487 (mono-isotopic); found. 354.1492 (**7**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 2.45 (t, poorly resolved, 2H), 3.49 (br t, 2H), 4.75 (br s, 2H), 7.38 (d, $J = 8.4$ Hz, 2H), 7.59 (br s, 1H), 7.88 (d, $J = 6.6$ Hz, 2H), 8.05 (br s, 1H). ^{13}C (101 MHz, d_6-DMSO): δ 38.9, 40.2, 59.6, 127.2, 129.3, 132.9, 142.1, 167.3, 170.1; HPLC (220 nm): $t_R = 15.201$ min; 99% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{11}H_{15}N_2O_3S$ (MH$^+$) 255.0803 (mono-isotopic); found. 255.0825 (**8**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 1.50–1.70 (m, 10H), 1.75 (m, 3H), 4.68 (br d, $J = 5.3$ Hz, 2H), 7.17 (br s, 1H), 7.30 (d, $J = 8.2$ Hz, 2H), 7.75 (br t, $J = 5.4$ Hz, 1H), 7.82 (d, $J = 8.2$ Hz, 2H); ^{13}C (101 MHz, d_6-DMSO): δ 28.4, 29.0, 35.2, 36.0, 38.6, 40.6, 41.2, 42.0, 46.2, 49.2, 50.8, 52.9, 126.9, 127.0, 129.3, 143.7, 167.8, 181.5; HPLC (220 nm): $t_R = 19.457$ min; 93% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{19}H_{25}N_2O_2S$ (MH$^+$) 345.1637 (mono-isotopic); found. 345.1680 (**9**): ^{1}H NMR (400 MHz, d_6-DMSO): δ 3.15 (d, $J = 5.3$ Hz, 2H), 3.50 (s, 3H), 5.12 (q, $J = 5.9$ Hz, 1H), 7.11–7.35 (m, 6H), 8.03 (d, $J = 8.6$ Hz, 1H), 12.72 (br s, 1H); ^{13}C (101 MHz, d_6-DMSO): δ 53.7, 57.1, 63.1, 128.2, 129.2, 137.6, 172.7, 179.5; HPLC (220 nm): $t_R = 16.572$ min; 95% crude purity; HR-MS (TOF-ES$^+$) calcd for $C_{11}H_{15}N_2O_3S$ (MH$^+$) 255.0803 (mono-isotopic); found. 255.0797.
19. The yields are based on the amount of amino acid coupled to the resin. The actual loading of amino acid was determined by Fmoc quantification: 5 mg resin (ca. 10 μmol theoretical loading) was swelled in 20% piperidine/DMF (25 mL), the mixture was shaken for 30 min and the absorption (290 nm) was measured. A 20% piperidine/DMF solution was used as reference.
20. IR-spectral data can be found in the supporting information.
21. Dolphin, D.; Wick, A. *Tabulation of Infrared Spectral Data*; Wiley & Sons, 1977; p 412.
22. 4-Isothiocyanatomethylbenzoic acid: Deprotected amino acid derivatised 2-chlorotrityl resin (0.10 g, 0.19 mmol) was suspended in DMF (0.50 mL). Carbon disulfide (1.00 mL) was added followed by HBTU (0.29 g, 0.76 mmol) or PyBOP (0.40 g, 0.76 mmol) and DIPEA (0.39 mL, 2.28 mmol). The suspension was shaken for 30 min at rt. The solvent was removed by suction, and the resin was washed with DCM (10 times), DMF (5 times), and air was flushed through for 10 min to remove residual carbon disulfide. The isothiocyanate was released from the resin by 20% HFIP (2.5 mL) for 30 min, the product was collected by suction and the cleavage mixture was removed in vacuo, the product was obtained as an off-white powder. Yield (HBTU): 13.6 mg (76%); Yield (PyBOP): 13.8 mg (77%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.77 (s, 2H), 7.38 (d, $J = 8.1$ Hz, 2H), 8.07 (d, $J = 8.2$ Hz, 2H); ^{13}C (101 MHz, $CDCl_3$): δ 47.4, 125.7, 128.4, 129.8, 130.0 (low intensity); 139.0, 152.4; HPLC (220 nm): $t_R = 21.066$ min; 97% crude purity; MS (FAB$^+$) calcd for $C_9H_7NO_2S$ (m/z) 193.23; found. 216.96 (M+Na$^+$).
23. Nowick, J.; Holmes, D. L.; Noronba, G.; Smith, E. M.; Nguyen, T. M.; Huang, S.-L. *J. Org. Chem.* **1996**, *61*, 3929–3934.
24. A way to circumvent the formation of thiohydantoins could be to introduce 2-hydroxy-4-methoxybenzyl (Hmb) protection of the last backbone amide at the N-terminal. The Hmb group has found wide use for preventing peptide aggregation during Fmoc solid-phase peptide synthesis, see for example, Johnson, T.; Quibell, M. *Tetrahedron Lett.* **1994**, *35*, 463–466.