Synthesis of functionalized dithiocarbamates via N-(1-benzotriazolylalkyl)dithiocarbamates

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Abstract
Reactions of 1-(1-hydroxyalkyl)benzotriazoles 19a–d with thiazolidine-2-thione 13, 1,3-thiazinane-2-thione 25, and alkyl N-alkyl dithiocarbamates 29a–c give intermediate N-[1-(benzotriazol-1-yl)alkyl] dithiocarbamates 20a–d, 26a–c, and 30a–e respectively, which gave N-(1-sulfanylalkyl) dithiocarbamates 23a–l, 27a–c and 31a–e or N-[1-(dialkylphosphono)alkyl] dithiocarbamates 24a–e, 28a,b and 32a–d on treatment with thiols or trialkyl phosphates, respectively, in the presence of zinc bromide.

Keywords: Dithiocarbamates, benzotriazole, functionalization

Introduction
Dithiocarbamates of general structure 1 including cyclic derivatives 2–4 show antibacterial,1–4 anthelmintic,5,6 fungicidal,1,2,4,7–10 herbicidal,7,11 antifouling,12 growth depressant,13 and algicidal activity.14 They are also effective catalysts for photopolymerization15 and vulcanization.16,17

Major approaches to the preparation of N,N-dialkyl dithiocarbamates 1 (Scheme 1) utilize reactions of dithiocarbamic acid salts 5 (accessible, or generated in situ from amines with carbon...
disulfide) (i) with alkyl halides,3,13,18–25 (ii) with dialkyl phosphates,26 or (iii) by addition to electron-deficient olefins.27,28 Acylation of amines with less easily available chlorodithioformates 6 (Scheme 1, Route iv) provides another access to dithiocarbamates 1.18 N-Arylsulfonylmethyl dithiocarbamates 1 (R² = R³SO₂CH₂) were prepared by the N-alkylation of dithiocarbamates 7 with sodium p-toluenesulfinate and formaldehyde.29

Scheme 1

Reported preparations of N-alkyl thiazolidine-2-thiones 2 (Scheme 2) employ reactions of carbon disulfide (i) with 2-aminoethanols 8 (X = OH),16,17 2-aminoethyl sulfates 8 (X = OSO₃H),30 and 2-aminoethyl halides 8 (X = Cl, Br);31,32 (ii) with primary amines and 1,2-dibromoethane in the presence of a base;18,19 (iii) with aziridines 9;30,33 (iv) with 2-iminothiazolidines 10.34 The preparation of compounds 2 via cyclization of methyl β-hydroxyalkyldithiocarbamates 11 upon treatment with mesyl chloride in pyridine (Scheme 2, Route v)34 and via cyclization of 2-alkylaminoethanethiols 12 with thiophosgene in the presence of a base (Route vi)33 have also been reported. The alkylation of thiazolidine-2-thiones 13 with alkyl halides in the presence of a base gives 2-alkylthiothiazoles 14 (Scheme 2, Route ix).31,35 2-Methylthiothiazoles 14 (R = Me) are thermally isomerized by catalytic methyl iodide and iodine into the corresponding N-methylthiazolidine-2-thiones 2 (Scheme 2, Route x).30

Scheme 2
The aminoalkylation of thiazolidine-2-thiones 13 (first erroneously reported as giving products of S-alkylation)35,36 succeeded for formaldehyde37,38 (Scheme 2, Route viii) but attempts with higher aldehydes failed.38 N-Alkylated thiazolidine-2-thiones also resulted from Michael-type addition of unsubstituted thiazolidine-2-thiones 13 to electron-deficient olefins (Scheme 2, Route vii).39,40

N-Alkyl-1,3-thiazine-2-thiones 3 have been prepared in similar ways from 3-bromopropylamines 1541 (Scheme 3, Route i) or 2-imino-1,3-thiazines 1642 (Route ii) with carbon disulfide, and from dithiocarbamic acids 17 with 1,3-dibromopropane (Route iii).8

![Scheme 3](image)

However, we have located no reports of the introduction of functionalized N-substituents into either open-chain- or cyclic-dithiocarbamates. Our group has previously functionalized carbamates 18 (Scheme 4) via benzotriazolylalkylation43–45 followed by nucleophilic displacement of benzotriazole with diverse nucleophiles,46–54 such as organozinc reagents,48,51 ester enolates,54 or ammonia.46,47,49 This approach also includes condensation of carbamates 18 and benzotriazole with aliphatic and aromatic aldehydes.47,48,53–56 We have now applied similar methodology to functionalize dithiocarbamates 13, 25 and 29 providing a new route to diverse N-(1-sulfanylalkyl) 23a–l, 27a–c and 31a–e and N-[1-(dialkylphosphono)alkyl] dithiocarbamates 24a–e, 28a,b and 32a–d in good overall yields (Schemes 5, 6 and 7).

![Scheme 4](image)

Results and Discussion

The 1-(1-hydroxyalkyl)benzotriazoles 19a–d were prepared from benzotriazole and the corresponding aldehydes in excellent yields according to the published procedure.57 The reaction
of 1-(1-hydroxyalkyl)benzotriazoles 19a–d with thiazolidine-2-thione 13 in the presence of boron trifluoride in THF at 25 °C gave the 3-(1-benzotriazolyalkyl)thiazolane-2-thiones 20a–d in good isolated yields (Scheme 5). Structures 20a–d were supported by their 1H-NMR and 13C-NMR spectra. The NMR spectra of 20a–d showed sets of signals in the ranges 7.38–7.60 ppm and 7.91–8.07 ppm in the 1H- and about 111, 120, 125, 128, 133 and 146 ppm in the 13C- spectra, characteristic of N-(1-amidoalkyl) benzotriazoles (see Experimental Section).

Nucleophilic substitution of the benzotriazolyl group in the 3-(1-benzotriazolyalkyl)-thiazolane-2-thiones 20b–d with thiols 21a–d in the presence of ZnBr2 in refluxing diethyl ether for 12 h gave thio-derivatives 23a–l of 1,3-thiazolidine-2-thione in excellent isolated yields (Scheme 5, Table 1). Structures 23a–l were confirmed by their 1H-NMR and 13C-NMR spectra. Their NMR spectra no longer showed distinctive signals associated with the benzotriazole ring in the 1H-NMR range 7.38–8.07 ppm or at 111, 120, 125, 133 and 146 ppm in the 13C- spectra. The NMR spectra of 23a–l showed the appearance of a new set of signals corresponding to the introduced alkyl- or aryl-sulfanyl group (R2), as well as upfield shifts in the position of the signals corresponding to the α-CH of the N-alkyl chain from 7.57–7.80 ppm for 20b–d to 6.09–6.54 ppm for 23a–l (1H-NMR) and from 64.5–69.0 ppm to 56.5–66.8 ppm (13C-NMR).

![Scheme 5](image)

**Table 1.** Preparation of functionalized thiazolidine-2-thiones 23a–l and 24a–e

<table>
<thead>
<tr>
<th>Product</th>
<th>R1</th>
<th>R2</th>
<th>Yields, %</th>
<th>Product</th>
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Reaction of the 3-(1-benzotriazolylalkyl)thiazolane-2-thiones 20b–d with trialkyl phosphites 22a,b in the presence of ZnBr₂ in refluxing dichloromethane gave 1-(2-thioxo-1,3-thiazolidin-3-yl)alkylphosphonates 24a–e in good isolated yields (Scheme 5, Table 1). Structures 24a–e were supported by their ¹H- NMR and ¹³C- NMR spectra, which showed the disappearance of signals assigned to the benzotriazolyl group of 20b–d and the appearance of a new set of signals corresponding to dialkyl phosphonate (see Experimental Section). As with 23a–l, the signals for α-CH (between the phosphorus and thiazolidinyl nitrogen) of the dialkyl phosphonates 24a–e appeared in the ranges 5.44–5.67 ppm in the ¹H- and 49.3–55.7 ppm (doublet, J = 152.9–155.7 Hz) in the ¹³C- NMR spectra.

1,3-Thiazinane-2-thione 25 was prepared in 78% yield by the reaction of 3-bromopropylamine hydrobromide with carbon disulfide according to a published procedure. In analogy to the preparation of 20a–d, condensation of compound 25 with 1-(1-hydroxyalkyl)benzotriazoles 19b–d in the presence of boron trifluoride in THF at 25 °C gave 3-(1-benzotriazolylalkyl)thiazine-2-thiones 26a–c in good isolated yields (Scheme 6).

Scheme 6

Nucleophilic substitution of the benzotriazolyl group in the 3-(1-benzotriazolylalkyl)-1,3-thiazinane-2-thiones 26a,b by thiols 21a,c in the presence of ZnBr₂ in refluxing diethyl ether gave 3-[1-(substituted-sulfanyl)alkyl]-1,3-thiazinane-2-thiones 27a–c in 77–79% yields (Scheme 6).

Reaction of 1,3-thiazinane-2-thiones 26a,c with trialkyl phosphite 22a in the presence of ZnBr₂ in refluxing dichloromethane gave 1-(2-thioxo-1,3-thiazinan-3-yl)alkylphosphonates 28a,b in 72–77% yields (Scheme 6). Compounds 26a–c, 27a–c and 28a,b were characterized by elemental analyses and their ¹H- and ¹³C- NMR spectra.

Reaction of alkyl N-alkylidithiocarbamates 29a–c with 1-(1-hydroxyalkyl)benzotriazoles 19a,d in the presence of p-toluenesulfonic acid in toluene under reflux for 24 h gave N-[1-(benzotriazol-1-yl)alkyl]-N-alkylidithiocarbamates 30a–d in good isolated yields (Scheme 7, Table 2). Owing to difficulties with isolation, crude compound 30e was used for the further preparation of 31d,e.
Nucleophilic substitution of the benzotriazolyl group in $30b,d,e$ by thiols $21a,c$ in the presence of ZnBr$_2$ in refluxing diethyl ether gave excellent yields of the alkyl $N$-thioalkyl dithiocarbamates $31a–e$ (Scheme 7, Table 2).

**Scheme 7**

Reaction of intermediates $30b,d$ with trialkyl phosphites $22a,b$ ($R^2 = Et$) in the presence of ZnBr$_2$ in refluxing dichloromethane gave the dialkyl phosphonates $32a–d$ in 83–89% yields (Scheme 7, Table 2). Compounds $30a–d$, $31a–e$ and $32a–d$ were characterized by elemental analyses and by their $^1$H- and $^{13}$C- NMR spectra.

**Table 2. Preparation of dithiocarbamates $30a–e$, $31a–e$ and $32a–d$**

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<thead>
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<th>R$^2$</th>
<th>R$^3$</th>
<th>Yields, %</th>
<th>Product</th>
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<th>R$^1$</th>
<th>R$^2$</th>
<th>R$^3$</th>
<th>Yields, %</th>
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$^a$ Not isolated, used as crude material for the preparation of $31d,e$.

However, attempted nucleophilic substitution of the benzotriazolyl group in $N$-(1-benzotriazolylmethyl)- thiazolane-2-thione $20a$ and $N$-alkyldithiocarbamates $30a,c$ with thiols $21$ and trialkyl phosphites $22$ failed.

In summary, an efficient route has been developed to functionalized $N$-[1-(dialkylphosphono)alkyl]- and $N$-(1 sulfanylalkyl)- dithiocarbamates via substitution of benzotriazole by thiols and trialkyl phosphites in intermediate $N$-[1-
benzotriazolylalkyl)dithiocarbamates. The protocol provides high overall yields of functionalized dithiocarbamates, both in the open-chain series and the cyclic analogs.

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were obtained in CDCl3 with TMS as the internal standard for 1H (300 MHz) or with the solvent as the internal standard for 13C (75 MHz). THF and diethyl ether were dried over sodium / benzophenone, dichloromethane was dried over calcium hydride and used freshly distilled. Column chromatography was conducted on silica gel 200–425 mesh. All of the chemicals were employed as supplied.

General procedure for the preparation of 3-(1-benzotriazolylalkyl)thiazolane-2-thiones 20a–d

Boron trifluoride etherate (3.8 mL, 30 mmol) was added to a solution of thiazolidine-2-thione 13 (1.79 g, 15 mmol) and the 1-(1-hydroxyalkyl)benzotriazole 19a–d (15 mmol) in anhydrous THF (25 mL) at 0 °C. The reaction mixture was stirred for 12 h at room temperature. Ethyl acetate was added, and the organic layer was washed with 10% aqueous sodium carbonate. The organic layer was separated, dried over magnesium sulfate, and then solvent was removed under reduced pressure. The crude product was recrystallized from ethyl acetate to give 20a–d.

3-(Benzotriazol-1-ylmethyl)-1,3-thiazolane-2-thione (20a). White microcrystals from ethyl acetate (93%), mp 176−177 °C; 1H NMR δ 3.24 (t, J = 7.8 Hz, 2H), 4.15 (t, J = 7.8 Hz, 2H), 6.59 (s, 2H), 7.38−7.43 (m, 1H), 7.50−7.55 (m, 1H), 8.02−8.06 (m, 2H); 13C NMR δ 27.2, 54.7, 58.1, 111.1, 119.8, 124.7, 128.4, 132.2, 146.0, 200.2. Anal. Calcd for C10H10N4S2: C, 47.98; H, 4.03; N, 22.38. Found: C, 48.49; H, 3.86; N, 22.14%.

3-[1-(Benzotriazol-1-yl)ethyl]-1,3-thiazolane-2-thione (20b). White microcrystals from ethyl acetate (65%), mp 135−136 °C; 1H NMR δ 2.19 (d, J = 6.9 Hz, 3H), 3.09 (dt, J = 11.0, 8.8 Hz, 1H), 3.24 (dd, J = 11.0, 8.1, 5.8 Hz, 1H), 3.75 (dd, J = 11.3, 8.4, 5.8 Hz, 1H), 4.22 (dt, J = 11.3, 8.4 Hz, 1H), 7.40−7.45 (m, 1H), 7.51−7.56 (m, 1H), 7.80 (q, J = 6.9 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H); 13C NMR δ 16.8, 27.6, 50.7, 64.5, 110.7, 119.7, 124.7, 128.2, 132.5, 145.7, 198.6. Anal. Calcd for C11H12N4S2: C, 49.78; H, 4.03; N, 22.19. Found: C, 50.26; H, 4.65; N, 21.12%.

3-[1-(Benzotriazol-1-yl)propyl]-1,3-thiazolane-2-thione (20c). White microcrystals from ethyl acetate (88%), mp 147−148 °C; 1H NMR δ 1.07 (t, J = 7.4 Hz, 3H), 2.52−2.66 (m, 1H), 2.68−2.83 (m, 1H), 3.12 (dt, J = 11.0, 8.4 Hz, 1H), 3.26 (dd, J = 11.1, 8.2, 6.1 Hz, 1H), 3.91 (dd, J = 11.3, 8.4, 6.1 Hz, 1H), 4.24 (dt, J = 11.3, 8.3 Hz, 1H), 7.39−7.44 (m, 1H), 7.51−7.55 (m, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H); 13C NMR δ 9.7, 24.7, 27.7, 51.1, 69.0, 110.8, 119.7, 124.7, 128.2, 133.0, 145.5, 199.3. Anal. Calcd for C12H14N4S2: C, 51.77; H, 5.07; N, 20.12. Found: C, 51.49; H, 5.18; N, 19.90%.
3-[1-(Benzotriazol-1-yl)butyl]-1,3-thiazolane-2-thione (20d). White microcrystals from ethyl acetate (73%), mp 144–145 °C; ^1H NMR δ 1.04 (t, J = 7.4 Hz, 3H), 1.43 (sextet, J = 7.5 Hz, 2H), 2.46–2.58 (m, 1H), 2.65–2.77 (m, 1H), 3.11 (dt, J = 11.0, 8.4 Hz, 1H), 3.25 (dd, J = 11.1, 8.2, 6.1 Hz, 1H), 3.93 (dd, J = 11.3, 8.4, 6.1 Hz, 1H), 4.24 (dt, J = 11.3, 8.3 Hz, 1H), 7.39–7.44 (m, 1H), 7.51–7.56 (m, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 8.06 (d, J = 8.3 Hz, 1H); ^13C NMR δ 13.5, 18.5, 27.7, 33.1, 51.1, 67.6, 110.8, 119.7, 124.7, 128.2, 133.0, 145.5, 199.1. Anal. Calcd for C_{13}H_{16}N_{4}S_{2}: C, 53.40; H, 5.51; N, 19.16. Found: C, 53.80; H, 5.57; N, 19.10%.

General procedure for the preparation of 3-[1-(sulfanyl)alkyl]-1,3-thiazolidine-2-thione 23a–l
To a solution of 3-(1-benzotriazolylalkyl) thiazolane-2-thiones 20b–d (2 mmol) and thiols 21a–d (8 mmol) in anhydrous diethyl ether (25 mL) under nitrogen was added anhydrous zinc bromide (2 mmol). The mixture was heated under reflux for 12h, and then cooled to room temperature. A precipitate was filtered off and washed with diethyl ether. The filtrate (plus washings) was washed with 5 % aqueous sodium hydroxide (2 x 25 mL) and water (2 x 25 mL). The ethereal solution was dried over magnesium sulfate and solvent was evaporated in vacuum. The product was purified by column chromatography on silica gel (hexanes / ethyl acetate 9:1).

3-[1-(Ethylsulfanyl)ethyl]-1,3-thiazolane-2-thione (23a). Colorless oil (96%); ^1H NMR δ 1.29 (t, J = 7.3 Hz, 3H), 1.46 (d, J = 7.0 Hz, 3H), 2.43–2.55 (m, 1H), 2.57–2.69 (m, 1H), 3.22–3.37 (m, 2H), 3.90–3.99 (m, 1H), 4.38–4.47 (m, 1H), 6.39 (q, J = 7.0 Hz, 1H); ^13C NMR δ 15.1, 18.8, 25.3, 27.7, 50.4, 57.5, 196.6. Anal. Calcd for C_{7}H_{13}NS_{3}: C, 40.54; H, 6.32; N, 6.75. Found: C, 41.19; H, 6.37; N, 7.21%.

3-[1-(Ethylsulfanyl)propyl]-1,3-thiazolane-2-thione (23b). Colorless oil (95%); ^1H NMR δ 1.00 (t, J = 7.4 Hz, 3H), 1.29 (t, J = 7.3 Hz, 3H), 1.63–1.90 (m, 2H), 2.44–2.55 (m, 1H), 2.58–2.70 (m, 1H), 3.24–3.39 (m, 2H), 3.84–3.93 (m, 1H), 4.37–4.45 (m, 1H), 6.20 (dd, J = 8.8, 6.6 Hz, 1H); ^13C NMR δ 11.0, 15.2, 25.0, 26.6, 27.8, 50.6, 63.2, 197.2. Anal. Calcd for C_{8}H_{15}NS_{3}: C, 43.40; H, 6.83; N, 6.33. Found: C, 43.68; H, 6.87; N, 6.67%.

3-[1-(Ethylsulfanyl)butyl]-1,3-thiazolane-2-thione (23c). Colorless oil (93%); ^1H NMR δ 0.96 (t, J = 7.3 Hz, 3H), 1.29 (t, J = 7.4 Hz, 3H), 1.34–1.55 (m, 2H), 1.61–1.80 (m, 2H), 2.43–2.55 (m, 1H), 2.58–2.70 (m, 1H), 3.23–3.38 (m, 2H), 3.84–3.93 (m, 1H), 4.36–4.45 (m, 1H), 6.28 (dd, J = 8.6, 6.8 Hz, 1H); ^13C NMR δ 13.6, 15.2, 19.6, 25.0, 27.8, 35.2, 50.6, 61.5, 197.0. Anal. Calcd for C_{9}H_{17}NS_{3}: C, 45.91; H, 6.83; N, 5.95. Found: C, 46.18; H, 7.40; N, 6.01%.

3-[1-(tert-Butylsulfanyl)ethyl]-1,3-thiazolane-2-thione (23d). Colorless oil (89%); ^1H NMR δ 1.37 (s, 9H), 1.44 (d, J = 7.1 Hz, 3H), 3.18–3.34 (m, 2H), 3.89–3.99 (m, 1H), 4.53–4.61 (m, 1H), 6.31 (q, J = 7.1 Hz, 1H); ^13C NMR δ 19.7, 27.4, 31.2, 44.8, 51.1, 56.5, 194.6. Anal. Calcd for C_{9}H_{17}NS_{3}: C, 45.91; H, 7.28; N, 5.95. Found: C, 46.40; H, 7.47; N, 5.89%.

3-[1-(tert-Butylsulfanyl)propyl]-1,3-thiazolane-2-thione (23e). Colorless oil (94%); ^1H NMR δ 1.00 (t, J = 7.4 Hz, 3H), 1.38 (s, 9H), 1.63–1.85 (m, 2H), 3.19–3.34 (m, 2H), 3.82–3.91 (m, 1H), 4.50–4.58 (m, 1H), 6.09 (t, J = 7.8 Hz, 1H); ^13C NMR δ 11.0, 27.5, 27.6, 31.4, 44.6, 51.5, 62.2,
195.2. Anal. Calcd for C_{10}H_{19}NS_{3}: C, 48.15; H, 7.68; N, 5.61. Found: C, 48.60; H, 7.94; N, 5.91%.

3-[1-(tert-Butylsulfanyl)butyl]-1,3-thiazolane-2-thione (23f). Colorless oil (91%); \(^1\)H NMR \(\delta\) 0.95 (t, J = 7.3 Hz, 3H), 1.37 (s, 9H), 1.43–1.77 (m, 4H), 3.18–3.33 (m, 2H), 3.82–3.92 (m, 1H), 4.50–4.58 (m, 1H), 6.17 (t, J = 7.4 Hz, 1H); \(^{13}\)C NMR \(\delta\) 13.5, 19.6, 27.6, 31.4, 36.2, 44.6, 51.5, 60.7, 194.9. Anal. Calcd for C_{11}H_{21}NS_{3}: C, 50.14; H, 8.03; N, 5.32. Found: C, 50.24; H, 8.22; N, 5.58%.

3-[1-(Phenylsulfanyl)propyl]-1,3-thiazolane-2-thione (23h). Colorless oil (95%); \(^1\)H NMR \(\delta\) 1.06 (t, J = 7.4 Hz, 3H), 1.76–2.04 (m, 2H), 3.00–3.19 (m, 2H), 3.84–3.93 (m, 1H), 4.35–4.43 (m, 1H), 6.46 (dd, J = 8.5, 6.7 Hz, 1H), 7.22–7.32 (m, 3H), 7.41–7.45 (m, 2H); \(^{13}\)C NMR \(\delta\) 11.1, 26.6, 27.8, 51.0, 65.6, 127.7, 129.0, 131.8, 131.9, 197.3. Anal. Calcd for C_{12}H_{15}NS_{3}: C, 53.49; H, 5.61; N, 5.20. Found: C, 53.57; H, 5.57; N, 5.42%.

3-[1-(Phenylsulfanyl)butyl]-1,3-thiazolane-2-thione (23i). Colorless oil (98%); \(^1\)H NMR \(\delta\) 0.98 (t, J = 7.3 Hz, 3H), 1.33–1.62 (m, 2H), 1.73–1.92 (m, 2H), 2.99–3.18 (m, 2H), 3.84–3.93 (m, 1H), 4.34–4.43 (m, 1H), 6.54 (dd, J = 8.1, 6.9 Hz, 1H), 7.22–7.31 (m, 3H), 7.42–7.45 (m, 2H); \(^{13}\)C NMR \(\delta\) 13.6, 19.7, 27.8, 35.1, 50.9, 64.1, 127.8, 129.0, 131.8, 131.9, 197.1. Anal. Calcd for C_{13}H_{17}NS_{3}: C, 55.08; H, 6.04; N, 4.94. Found: C, 55.43; H, 6.12; N, 5.37%.

3-[1-(4-Methoxyphenylsulfanyl)ethyl]thiazolidine-2-thione (23j). Colorless oil (99%); \(^1\)H NMR \(\delta\) 1.52 (d, J = 6.9 Hz, 3H), 3.05–3.20 (m, 2H), 3.77 (s, 3H), 3.88–3.98 (m, 1H), 4.36–4.44 (m, 1H), 6.48 (q, J = 6.9 Hz, 1H), 6.82 (d, J = 8.8 Hz, 2H), 7.37 (d, J = 8.8 Hz, 2H); \(^{13}\)C NMR \(\delta\) 18.4, 27.8, 50.8, 55.4, 61.0, 114.7, 122.1, 135.0, 160.1, 196.6. HRMS Calcd. for C_{12}H_{15}NOS_{3}: [M\(^+\)]: 285.0316, Found: 285.0323.

3-[1-(4-Methoxyphenylsulfanyl)propyl]thiazolidine-2-thione (23k). White microcrystals (99%); \(^1\)H NMR \(\delta\) 1.03 (t, J = 7.3 Hz, 3H), 1.73–1.92 (m, 2H), 2.99–3.18 (m, 2H), 3.84–3.93 (m, 1H), 4.34–4.43 (m, 1H), 6.46 (dd, J = 8.5, 6.7 Hz, 1H), 7.22–7.32 (m, 3H), 7.41–7.45 (m, 2H); \(^{13}\)C NMR \(\delta\) 13.6, 19.7, 27.8, 50.8, 55.4, 61.0, 114.7, 122.1, 135.0, 160.1, 197.3. HRMS Calcd. for C_{12}H_{15}NOS_{3}: [M\(^+\)]: 299.0472, Found: 299.0469.

3-[1-(4-Methoxyphenylsulfanyl)butyl]thiazolidine-2-thione (23l). Colorless oil (91%); \(^1\)H NMR \(\delta\) 0.96 (t, J = 7.3 Hz, 3H), 1.34–1.51 (m, 2H), 1.70–1.86 (m, 2H), 3.05–3.21 (m, 2H), 3.78 (s, 3H), 3.82–3.92 (m, 1H), 4.37–4.45 (m, 1H), 6.33 (dd, J = 8.6, 6.4 Hz, 1H), 6.81 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H); \(^{13}\)C NMR \(\delta\) 13.6, 19.7, 27.8, 28.0, 51.0, 55.4, 66.8, 114.7, 122.1, 135.2, 160.1, 197.3. HRMS Calcd. for C_{14}H_{19}NOS_{3}: [M\(^+\)]: 313.0629, Found: 313.0628.

General procedure for the preparation of 1-(2-thioxo-1,3-thiazolidin-3-yl)alkylphosphonates 24a–e

To a solution of 3-(1-benzotriazolylalkyl)thiazolane-2-thione 20b–d (2 mmol) in anhydrous dichloromethane (20 mL) at 20–25 °C was added anhydrous zinc bromide (4 mmol) followed by the appropriate trialkyl phosphite 22a,b (4 mmol). The reaction mixture was heated under reflux for 16 h. The reaction mixture was cooled to 20–25 °C, quenched with a 10% aqueous solution...
of sodium carbonate and extracted with dichloromethane. The combined organic layers were washed with brine and dried over magnesium sulfate. The solvent was removed in vacuum and the product was purified by column chromatography on silica gel (hexanes / ethyl acetate 2:1).

**Diethyl 1-(2-thioxo-1,3-thiazolan-3-yl)ethylphosphonate (24a).** Colorless oil (78%); \(^1\)H NMR \(\delta 1.34 (t, \nu = 7.1 Hz, 3H), 1.35 (t, \nu = 7.0 Hz, 3H), 1.49 (dd, \nu = 16.3, 7.3 Hz, 3H), 3.99–4.08 (m, 4H), 4.41–4.49 (m, 1H), 5.61 (dq, \nu = 17.7, 7.3 Hz, 1H); \(^13\)C NMR \(\delta 12.3, 16.3 (d, \nu = 5.2 Hz, 1C), 16.4 (d, \nu = 5.1 Hz, 1C), 27.7, 49.3 (d, \nu = 155.7 Hz, 1C), 52.7, 62.7 (d, \nu = 10.9 Hz, 1C), 62.8 (d, \nu = 10.9 Hz, 1C), 197.6. Anal. Calcd for C\(_9\)H\(_{18}\)NO\(_3\)PS\(_2\): C, 38.15; H, 6.40; N, 4.94. Found: C, 38.18; H, 6.67; N, 5.13%.

**Diethyl 1-(2-thioxo-1,3-thiazolan-3-yl)propylphosphonate (24b).** Colorless oil (81%); \(^1\)H NMR \(\delta 0.97 (t, \nu = 7.4 Hz, 3H), 1.33 (dt, \nu = 7.0, 4.1 Hz, 6H), 1.80–2.12 (m, 2H), 3.22–3.39 (m, 2H), 3.96 (dt, \nu = 11.4, 8.2 Hz, 1H), 4.08–4.24 (m, 4H), 4.42 (ddd, \nu = 11.4, 8.0, 6.3 Hz, 1H), 5.49 (ddd, \nu = 18.0, 11.5, 4.4 Hz, 1H); \(^13\)C NMR \(\delta 10.8 (d, \nu = 14.9 Hz, 1H), 20.7, 27.8, 52.6, 55.2 (d, \nu = 152.9 Hz, 1C), 62.7 (d, \nu = 5.1 Hz, 1C), 62.8 (d, \nu = 5.1 Hz, 1C), 198.3 (d, \nu = 7.4 Hz, 1C). Anal. Calcd for C\(_{10}\)H\(_{20}\)NO\(_3\)PS\(_2\): C, 40.39; H, 6.78; N, 4.71. Found: C, 40.10; H, 6.87; N, 5.03%.

**Diisopropyl 1-(2-thioxo-1,3-thiazolan-3-yl)propylphosphonate (24c).** Colorless oil (78%); \(^1\)H NMR \(\delta 0.96 (t, \nu = 7.3 Hz, 3H), 1.32–1.37 (m, 12 H), 1.77–2.11 (m, 2H), 3.21–3.37 (m, 2H), 3.95 (dt, \nu = 11.4, 8.4 Hz, 1H), 4.42 (ddd, \nu = 11.4, 8.0, 6.3 Hz, 1H), 5.49 (ddd, \nu = 18.0, 11.5, 4.4 Hz, 1H); \(^13\)C NMR \(\delta 10.8 (d, \nu = 14.9 Hz, 1H), 20.7, 27.8, 52.6, 55.7 (d, \nu = 154.6 Hz, 1C), 71.6 (d, \nu = 6.9 Hz, 2C), 198.2 (d, \nu = 7.4 Hz, 1C). Anal. Calcd for C\(_{12}\)H\(_{24}\)NO\(_3\)PS\(_2\): C, 44.29; H, 7.43; N, 4.30. Found: C, 43.90; H, 7.48; N, 4.40%.

**Diethyl 1-(2-thioxo-1,3-thiazolan-3-yl)butylphosphonate (24d).** Colorless oil (76%); \(^1\)H NMR \(\delta 0.97 (t, \nu = 7.3 Hz, 3H), 1.31–1.42 (m, 8H), 1.85–1.96 (m, 2H), 3.21–3.38 (m, 2H), 3.96 (dt, \nu = 11.5, 8.1 Hz, 1H), 4.08–4.24 (m, 4H), 4.40 (ddd, \nu = 14.6, 8.0, 6.6 Hz, 1H), 5.50–5.67 (m, 1H); \(^13\)C NMR \(\delta 13.4, 19.4 (d, \nu = 14.3 Hz, 1C), 28.0, 29.3 (d, \nu = 154.3 Hz, 1C), 71.7 (d, \nu = 7.5 Hz, 1C), 71.8 (d, \nu = 6.9 Hz, 1C), 198.1 (d, \nu = 7.5 Hz, 1C). Anal. Calcd for C\(_{11}\)H\(_{22}\)NO\(_3\)PS\(_2\): C, 42.38; H, 7.12; N, 4.50. Found: C, 42.38; H, 7.29; N, 4.78%.

**Diisopropyl 1-(2-thioxo-1,3-thiazolan-3-yl)butylphosphonate (24e).** Colorless oil (88%); \(^1\)H NMR \(\delta 0.97 (t, \nu = 7.3 Hz, 3H), 1.25–1.41 (m, 8H), 1.85–1.96 (m, 2H), 3.21–3.38 (m, 2H), 3.96 (dt, \nu = 11.5, 8.1 Hz, 1H), 4.08–4.24 (m, 4H), 4.40 (ddd, \nu = 14.6, 8.0, 6.6 Hz, 1H), 5.50–5.67 (m, 1H); \(^13\)C NMR \(\delta 12.8, 19.4 (d, \nu = 14.3 Hz, 1C), 24.0–24.4 (m, 4C), 28.0, 29.3 (d, \nu = 154.3 Hz, 1C), 71.7 (d, \nu = 7.5 Hz, 1C), 71.8 (d, \nu = 6.9 Hz, 1C), 198.1 (d, \nu = 7.5 Hz, 1C). Anal. Calcd for C\(_{13}\)H\(_{26}\)NO\(_3\)PS\(_2\): C, 46.00; H, 7.72; N, 4.13. Found: C, 45.88; H, 8.08; N, 3.99%.

**General procedure for the preparation of 3-(1-benzotriazolylalkyl)thiazine-2-thiones 26a–c**

Boron trifluoride etherate (3.8 mL, 30 mmol) was added to a solution of 1,3-thiazinane-2-thione 25 (2 g, 15 mmol) and the 1-(1-hydroxyalkyl)benzotriazole 19b–d (15 mmol) in anhydrous THF (25 mL) at 0 °C. The reaction mixture was stirred for 12 h at room temperature. Ethyl acetate
was added, and the organic layer was washed with 10% aqueous sodium carbonate (2 x 25 mL). The organic layer was separated, dried over magnesium sulfate, and solvent removed under reduced pressure. The crude product was recrystallized from an appropriate solvent.

3-[1-(Benzotriazol-1-yl)ethyl]-1,3-thiazinane-2-thione (26a). White microcrystals from ethyl acetate (69%), mp 156–157 °C; 1H NMR δ 1.73–1.86 (m, 1H), 2.08–2.17 (m, 1H), 2.17 (d, J = 6.9 Hz, 3H), 2.78–2.85 (m, 1H), 2.92–3.00 (m, 1H), 3.10 (ddd, J = 13.6, 7.6, 2.2 Hz, 1H), 3.57 (dd, J = 13.6, 8.5, 2.3 Hz, 1H), 7.40–7.46 (m, 1H), 7.52–7.57 (m, 1H), 7.92 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.74 (q, J = 6.9 Hz, 1H); 13C NMR δ 15.8, 22.8, 31.9, 42.9, 66.9, 110.7, 119.8, 124.8, 128.4, 132.5, 145.8, 194.2. Anal. Calcd for C12H14N4S2: C, 51.77; H, 5.07; N, 20.12. Found: C, 52.09; H, 5.03; N, 19.69%.

3-[1-(Benzotriazol-1-yl)propyl]-1,3-thiazinane-2-thione (26b). White microcrystals from ethyl acetate (65%), mp 166–167 °C; 1H NMR δ 1.13 (t, J = 7.3 Hz, 3H), 1.73–1.86 (m, 1H), 2.11–2.23 (m, 1H), 2.52–2.67 (m, 1H), 2.70–2.85 (m, 2H), 2.92–3.00 (m, 1H), 3.30 (ddd, J = 13.7, 8.8, 2.5 Hz, 1H), 7.40–7.45 (m, 1H), 7.51–7.57 (m, 1H), 8.04 (dd, J = 15.0, 8.2 Hz, 2H), 8.59 (t, J = 7.6 Hz, 1H); 13C NMR δ 9.7, 22.8, 23.9, 31.9, 43.5, 71.2, 111.0, 119.7, 124.7, 128.3, 133.0, 145.6, 195.1. Anal. Calcd for C13H16N4S2: C, 53.40; H, 5.51; N, 19.16. Found: C, 53.70; H, 5.57; N, 18.95%.

3-[1-(Benzotriazol-1-yl)butyl]-1,3-thiazinane-2-thione (26c). White microcrystals from ethyl acetate (70%), mp 93–94 °C; 1H NMR δ 1.05 (t, J = 7.4 Hz, 3H), 1.40–1.62 (m, 2H), 1.74–1.86 (m, 1H), 2.11–2.23 (m, 1H), 2.43–2.56 (m, 1H), 2.68–2.84 (m, 2H), 2.92–3.00 (m, 1H), 3.32 (dd, J = 13.6, 7.3, 2.3 Hz, 1H), 3.62 (dd, J = 13.7, 8.7, 2.3 Hz, 1H), 7.39–7.44 (m, 1H), 7.51–7.56 (m, 1H), 8.01–8.07 (m, 2H), 8.65 (t, J = 7.4 Hz, 1H); 13C NMR δ 13.9, 18.6, 23.0, 32.1, 32.5, 43.8, 70.0, 111.1, 119.8, 124.9, 128.5, 133.2, 145.8, 195.0. Anal. Calcd for C14H18N4S2: C, 54.87; H, 5.92; N, 18.28. Found: C, 55.13; H, 5.89; N, 18.28%.

General procedure for the preparation of 3-[1-(substituted- sulfanyl)alkyl]-1,3-thiazinane-2-thiones 27a–c
To a solution of the 3-(1-benzotriazoylalkyl)-1,3-thiazinane-2-thione 26a–c (2 mmol) and thiol 21a,c (8 mmol) in anhydrous diethyl ether (25 mL) under nitrogen was added anhydrous zinc bromide (2 mmol). The mixture was heated under reflux for 12h, and then cooled to room temperature. A precipitate was filtered off and washed with diethyl ether. The filtrate (plus washings) was washed with 5 % aqueous sodium hydroxide (2 x 25 mL) and water (2 x 25 mL). The ethereal solution was dried over magnesium sulfate and solvent was removed in vacuum. The product was purified by column chromatography on silica gel (hexanes / ethyl acetate 9:1).

3-[1-(Phenylsulfanyl)ethyl]-1,3-thiazinane-2-thione (27a). Colorless oil (78%); 1H NMR δ 1.52 (d, J = 6.9 Hz, 3H), 1.78–1.91 (m, 1H), 2.14–2.25 (m, 1H), 2.70–2.77 (m, 1H), 2.92 (ddd, J = 11.8, 9.5, 4.8 Hz, 1H), 3.31 (ddd, J = 13.5, 9.5, 2.8 Hz, 1H), 3.96 (ddd, J = 13.5, 6.9, 2.8 Hz, 1H), 7.20–7.32 (m, 3H), 7.40–7.43 (m, 2H), 7.64 (q, J = 6.9 Hz, 1H); 13C NMR δ 17.9, 23.3, 32.3, 43.4, 62.7, 127.5, 129.2, 130.7, 132.6, 193.3. Anal. Calcd for C12H15NS3: C, 53.49; H, 5.61; N, 5.20. Found: C, 53.34; H, 5.63; N, 5.17%.
3-[1-(Ethylsulfanyl)propyl]-1,3-thiazinane-2-thione (27b). Colorless oil (77%); \(^1\)H NMR  \(\delta 1.01\) (t,  \(J = 7.4\) Hz, 3H), 1.31 (t,  \(J = 7.4\) Hz, 3H), 1.65–1.81 (m, 2H), 2.08–2.22 (m, 1H), 2.33–2.44 (m, 1H), 2.52 (dq,  \(J = 20.3, 7.4\) Hz, 1H), 2.70 (dq,  \(J = 20.5, 7.4\) Hz, 1H), 2.90–2.97 (m, 1H), 3.07 (dd,  \(J = 11.7, 10.0, 4.7\) Hz, 1H), 3.21 (dd,  \(J = 12.4, 9.8, 2.3\) Hz, 1H), 3.92–3.99 (m, 1H), 7.20–7.25 (m, 1H); \(^{13}\)C NMR  \(\delta 10.9, 15.4, 23.1, 24.9, 26.1, 32.2, 43.1, 66.4, 193.1\). Anal. Calcd for C\(_9\)H\(_{17}\)NS\(_3\): C, 45.91; H, 7.28; N, 5.95. Found: C, 46.07; H, 7.66; N, 5.85%.

3-[1-(Phenylsulfanyl)propyl]-1,3-thiazinane-2-thione (27c). Colorless oil (79%); \(^1\)H NMR  \(\delta 1.09\) (t,  \(J = 7.4\) Hz, 3H), 1.79–1.92 (m, 3H), 2.18–2.29 (m, 1H), 2.72–2.79 (m, 1H), 2.94 (dd,  \(J = 11.8, 9.7, 2.5\) Hz, 1H), 3.25 (dd,  \(J = 12.0, 9.5, 2.5\) Hz, 1H), 3.94–4.01 (m, 1H), 7.21–7.32 (m, 3H), 7.44–7.48 (m, 2H), 7.52 (t,  \(J = 7.6\) Hz, 1H); \(^{13}\)C NMR  \(\delta 11.0, 23.1, 26.3, 32.1, 43.6, 68.2, 127.4, 129.0, 131.0, 132.3, 193.7\). Anal. Calcd for C\(_{13}\)H\(_{17}\)NS\(_3\): C, 55.08; H, 6.04; N, 4.94. Found: C, 55.25; H, 6.06; N, 4.83%.

**General procedure for the preparation of 1-(2-thioxo-1,3-thiazinan-3-yl)alklyphosphonates (28a,b)**

To a solution of 3-(1-benzotriazolylalkyl)-1,3-thiazinane-2-thione 26a,c (2 mmol) in anhydrous dichloromethane (20 mL) at 20–25 °C was added anhydrous zinc bromide (4 mmol) followed by triethyl phosphite 22a (4 mmol). The reaction mixture was heated under reflux for 14 h, then cooled to 20–25 °C, quenched with a 10% aq. sodium carbonate (20 mL) and extracted with dichloromethane (2 x 25 mL). The combined organic layers were washed with brine and dried over magnesium sulfate. The solvent was evaporated and the residue purified by column chromatography on silica gel (hexanes / ethyl acetate 2:1).

**Diethyl 1-(2-thioxo-1,3-thiazinan-3-yl)ethylphosphonate (28a).** Colorless oil (72%); \(^1\)H NMR  \(\delta 1.28\) (td,  \(J = 7.1, 1.4\) Hz, 6H), 1.42 (dd,  \(J = 16.3, 7.4\) Hz, 3H), 2.17–2.24 (m, 2H), 2.86–3.01 (m, 2H), 3.41–3.49 (m, 1H), 3.86 (dt,  \(J = 13.7, 4.9\) Hz, 1H), 4.00–4.18 (m, 4H), 6.54 (dd,  \(J = 19.1, 14.7, 7.3\) Hz, 1H); \(^{13}\)C NMR  \(\delta 12.0, 16.2\) (d,  \(J = 5.7\) Hz, 1C), 16.3 (d,  \(J = 4.0\) Hz, 1C), 23.0, 32.2, 46.0, 51.76 (d,  \(J = 152.9\) Hz, 1C), 62.5 (d,  \(J = 6.9\) Hz, 1C), 62.67 (d,  \(J = 6.9\) Hz, 1C), 193.2 (d,  \(J = 8.0\) Hz, 1C). Anal. Calcd for C\(_{10}\)H\(_{20}\)NO\(_3\)PS\(_2\): C, 40.39; H, 6.78; N, 4.71. Found: C, 40.35; H, 7.03; N, 4.61%.

**Diethyl 1-(2-thioxo-1,3-thiazinan-3-yl)butylphosphonate (28b).** Colorless oil (77%); \(^1\)H NMR  \(\delta 0.98\) (t,  \(J = 7.3\) Hz, 3H), 1.32–1.48 (m, 8H), 1.83–2.01 (m, 2H), 2.24–2.32 (m, 2H), 2.93–3.08 (m, 2H), 3.40–3.48 (m, 1H), 3.90 (dt,  \(J = 13.6, 4.8\) Hz, 1H), 4.10–4.26 (m, 4H), 6.61 (dd,  \(J = 19.1, 10.3, 5.1\) Hz, 1H); \(^{13}\)C NMR  \(\delta 13.7, 16.2\) (d,  \(J = 5.2\) Hz, 1C), 16.3 (d,  \(J = 5.7\) Hz, 1C), 19.2 (d,  \(J = 13.8\) Hz, 1C), 23.0, 28.9, 32.2, 46.0, 56.1 (d,  \(J = 150.0\) Hz, 1C), 62.5 (d,  \(J = 1.7\) Hz, 1C), 62.6 (d,  \(J = 1.7\) Hz, 1C), 193.9 (d,  \(J = 7.4\) Hz, 1C). Anal. Calcd for C\(_{12}\)H\(_{24}\)NO\(_3\)PS\(_2\): C, 44.29; H, 7.43; N, 4.30. Found: C, 44.35; H, 7.77; N, 4.54%.
General procedure for the preparation of alkyl $N$-[1-(benzotriazol-1-yl)alkyl]-$N$-ethyl dithiocarbamates 30a–e
The methyl $N$-ethyl dithiocarbamate 29a–c (10 mmol), 1-(1-hydroxy-alkyl)benzotriazole 19a,d (10 mmol) and $p$-toluenesulfonic acid (0.1 g, as catalyst) in toluene (50 mL) were heated under reflux in a Dean-Stark apparatus for 24 h. The reaction mixture was concentrated in vacuum to give the crude products 30a–e. The products 30a–d were purified by column chromatography on silica gel; 30e was used in the crude state.

Ethyl $N$-[1-(benzotriazol-1-ylmethyl)]-$N$-methyl carbamodithioate (30a). Colorless oil (56%); $^1$H NMR $\delta$ 1.38 (t, $J = 7.4$ Hz, 3H), 3.32 (q, $J = 7.4$ Hz, 2H), 3.54 (br s, 3H), 6.89 (br s, 2H), 7.39–7.42 (m, 2H), 7.87–7.92 (m, 2H); $^{13}$C NMR $\delta$ 13.2, 29.7, 32.3, 70.6, 118.5, 127.0, 144.6, 202.4. Anal. Calcd for C$_{11}$H$_{14}$N$_4$S$_2$: C, 49.60; H, 5.30; N, 21.03. Found: C, 50.22; H, 5.43; N, 20.85%.

Ethyl $N$-[1-(benzotriazol-1-ylbutyl)]-$N$-methyl carbamodithioate (30b). White microcrystals from ethyl acetate (61%), mp 49–50 °C; $^1$H NMR $\delta$ 1.04 (t, $J = 7.3$ Hz, 3H), 1.37 (t, $J = 7.3$ Hz, 3H), 1.39–1.57 (m, 2H), 2.45–2.58 (m, 1H), 2.66–2.78 (m, 1H), 3.17 (s, 3H), 3.26–3.38 (m, 2H), 7.37–7.42 (m, 1H), 7.48–7.53 (m, 1H), 7.96 (d, $J = 8.2$ Hz, 1H), 8.06 (d, $J = 8.4$ Hz, 1H), 8.58 (t, $J = 7.4$ Hz, 1H); $^{13}$C NMR $\delta$ 13.2, 13.7, 18.4, 31.6, 32.9, 33.0, 71.5, 110.9, 119.7, 124.5, 128.0, 133.1, 145.6, 201.2. Anal. Calcd for C$_{14}$H$_{20}$N$_4$S$_2$: C, 54.51; H, 6.54; N, 18.16. Found: C, 54.79; H, 6.62; N, 18.10%.

Methyl $N$-(benzotriazol-1-ylmethyl)-$N$-ethyl carbamodithioate (30c). White microcrystals from ethyl acetate (61%), mp 104–105 °C; $^1$H NMR $\delta$ 1.17 (t, $J = 7.1$ Hz, 3H), 2.70 (s, 3H), 3.91 (q, $J = 7.1$ Hz, 2H), 6.98 (s, 2H), 7.39 (t, $J = 7.3$ Hz, 1H), 7.51 (t, $J = 8.1$ Hz, 1H), 8.04–8.10 (m, 2H); $^{13}$C NMR $\delta$ 11.8, 20.3, 45.2, 62.0, 111.4, 119.7, 124.5, 128.0, 132.4, 146.0, 202.3. Anal. Calcd for C$_{11}$H$_{14}$N$_4$S$_2$: C, 49.60; H, 5.30; N, 21.03. Found: C, 49.94; H, 5.41; N, 21.03%.

Methyl $N$-[1-(benzotriazol-1-yl)butyl]-$N$-ethyl carbamodithioate (30d). White microcrystals from ethyl acetate (63%), mp 91–92 °C; $^1$H NMR $\delta$ 0.70 (t, $J = 7.0$ Hz, 3H), 1.03 (t, $J = 7.3$ Hz, 3H), 1.36–1.55 (m, 2H), 2.40–2.52 (m, 1H), 2.71 (s, 3H), 2.76–2.88 (m, 1H), 3.78–3.84 (m, 2H), 4.0 (t, $J = 7.4$ Hz, 1H), 7.51 (t, $J = 7.9$ Hz, 1H), 7.89 (d, $J = 7.9$ Hz, 1H), 8.06 (d, $J = 8.2$ Hz, 1H), 8.63 (br s, 1H); $^{13}$C NMR $\delta$ 13.1, 13.6, 18.4, 20.1, 32.9, 41.6, 72.0, 110.7, 119.7, 124.6, 128.1, 133.3, 145.5, 201.2. Anal. Calcd for C$_{14}$H$_{20}$N$_4$S$_2$: C, 54.51; H, 6.54; N, 18.16. Found: C, 54.94; H, 6.60; N, 18.21%.

General procedure for the preparation of alkyl $N$-thioalkyl dithiocarbamates 31a–e
To a solution of either 30b,d, or e (2 mmol) and a thiol 21a or c (8 mmol) in anhydrous diethyl ether (25 mL) under nitrogen was added anhydrous zinc bromide (0.45 g, 2 mmol). The mixture was heated under reflux for 12 h, and then cooled to room temperature. The precipitate was filtered off and washed with diethyl ether. The filtrate (plus washings) was washed with 5% aqueous sodium hydroxide (2 x 25 mL) and water (2 x 25 mL). The ethereal solution was dried over magnesium sulfate, the solvent was evaporated in vacuum, and the residue purified by column chromatography on silica gel (hexanes / ethyl acetate 9:1).
Ethyl N-methyl-N-[1-(phenylsulfanyl)butyl]carbamodithioate (31a). Colorless oil (97%); \(^1\)H NMR \(\delta\) 0.96 (t, \(J = 7.3\) Hz, 3H), 1.25 (1.10) (t, \(J = 7.3\) Hz, 3H), 1.33–1.54 (m, 2H), 1.76–1.89 (m, 2H), 3.00–3.24 (m, 2H), 3.27 (3.48) (s, 3H), 7.22–7.28 (m, 3H), 7.41–7.44 (m, 2H), 7.46 (6.14) (t, \(J = 7.4\) Hz, 1H); \(^13\)C NMR \(\delta\) 13.5, 13.7, 13.7, 13.8, 19.6 (19.7), 29.7, 31.2, 33.4, 35.2, 35.7, 36.9, 68.7, 70.1, 127.4, 128.6, 128.8, 128.9, 132.1, 132.5, 134.5, 199.7. Anal. Calcd for \(\text{C}_{14}\text{H}_{21}\text{NS}_3\): C, 56.14; H, 7.07; N, 4.68. Found: C, 55.50; H, 6.99; N, 4.76%.

Methyl N-ethyl-N-[1-(phenylsulfanyl)butyl]carbamodithioate (31b). Colorless oil (98%); \(^1\)H NMR \(\delta\) 0.97 (t, \(J = 7.3\) Hz, 3H), 1.25–1.38 (m, 3H), 1.40–1.64 (m, 2H), 1.79–1.89 (m, 2H), 2.59 (2.45) (s, 3H), 3.99–4.26 (3.72–3.84) (m, 2H), 7.19–7.26 (m, 3H), 7.37–7.40 (m, 2H), 7.48 (6.15) (t, \(J = 7.4\) Hz, 1H); \(^13\)C NMR \(\delta\) 13.1, 13.5, 13.7, 14.2, 19.7, 19.8, 35.8, 36.1, 42.1, 44.6, 69.4, 70.6, 126.8, 127.5, 128.2, 128.7, 130.6, 132.0, 132.5, 133.3, 133.6, 198.6, 199.9. Anal. Calcd for \(\text{C}_{14}\text{H}_{21}\text{NS}_3\): C, 56.14; H, 7.07; N, 4.68. Found: C, 56.61; H, 7.16; N, 4.87%.

Methyl N-ethyl-N-[1-(ethylsulfanyl)butyl]carbamodithioate (31c). Colorless oil (95%); \(^1\)H NMR \(\delta\) 0.94 (t, \(J = 7.3\) Hz, 3H), 1.26 (t, \(J = 7.3\) Hz, 3H), 1.32–1.43 (m, 4H), 1.46–1.58 (m, 1H), 1.66–1.80 (m, 2H), 2.36–2.48 (m, 1H), 2.55–2.61 (m, 1H), 2.66 (s, 3H), 3.95–4.12 (3.69–3.81) (m, 2H), 7.29 (5.95) (t, \(J = 7.4\) Hz, 1H); \(^13\)C NMR \(\delta\) 13.3, 13.7, 13.9, 14.5, 15.0, 15.4, 19.8, 20.0, 24.8, 36.0, 36.2, 41.6, 44.3, 66.9, 67.4, 198.0, 200.2. Anal. Calcd for \(\text{C}_{10}\text{H}_{21}\text{NS}_3\): C, 47.76; H, 8.42; N, 5.57. Found: C, 48.52; H, 8.61; N, 5.91%.

Ethyl N-butyl-N-[1-(phenylsulfanyl)butyl]carbamodithioate (31d). Colorless oil (98%); \(^1\)H NMR \(\delta\) 0.92–1.02 (m, 6H), 1.26 (1.10) (t, \(J = 7.3\) Hz, 3H), 1.34–1.66 (m, 5H), 1.72–1.89 (2.02–2.15) (m, 2H), 3.12–3.31 (2.99–3.08) (m, 2H), 3.87–4.14 (3.57–3.67) (m, 2H), 7.16–7.25 (m, 3H), 7.38 (d, \(J = 7.8\) Hz, 2H), 7.49 (6.18) (t, \(J = 7.4\) Hz, 1H); \(^13\)C NMR \(\delta\) 13.5, 13.6, 13.7, 13.8, 19.6, 19.9, 20.4, 29.4, 30.7, 31.2, 35.9, 36.2, 47.5, 49.6, 69.2, 70.6, 127.0, 128.3, 128.8, 131.0, 132.1, 133.3, 133.8, 197.9, 199.3. Anal. Calcd for \(\text{C}_{17}\text{H}_{27}\text{NS}_3\): C, 59.77; H, 7.97; N, 4.10. Found: C, 60.09; H, 8.21; N, 4.51%.

Ethyl N-butyl-N-[1-(ethylsulfanyl)butyl]carbamodithioate (31e). Colorless oil (95%); \(^1\)H NMR \(\delta\) 0.92–1.00 (m, 6H), 1.26 (1.12) (t, \(J = 7.3\) Hz, 3H), 1.34–1.66 (m, 5H), 1.72–1.89 (2.02–2.15) (m, 3H), 3.12–3.31 (2.99–3.08) (m, 2H), 3.87–4.14 (3.57–3.67) (m, 2H), 7.16–7.25 (m, 3H), 7.38 (d, \(J = 7.8\) Hz, 2H), 7.49 (6.18) (t, \(J = 7.4\) Hz, 1H); \(^13\)C NMR \(\delta\) 13.3, 13.6, 13.7, 19.8, 19.9, 20.4, 29.4, 30.7, 31.2, 35.9, 36.2, 47.5, 49.6, 69.2, 70.6, 127.0, 128.3, 128.8, 131.0, 132.1, 133.3, 133.8, 197.9, 199.3. Anal. Calcd for \(\text{C}_{17}\text{H}_{27}\text{NS}_3\): C, 59.77; H, 7.97; N, 4.10. Found: C, 60.09; H, 8.21; N, 4.51%.

General procedure for the preparation of dialky 1-[ethyl(methylsulfanylthiocarbonyl) amino]butylphosphonates (32a–d)

To a solution of \(30\)b, or \(d\) (2 mmol) in anhydrous dichloromethane (20 mL) at 20–25 °C was added anhydrous zinc bromide (0.9 g, 4 mmol) followed by a trialkyl phosphite \(22\)a, or \(b\) (4 mmol). The mixture was heated under reflux for 16 h and cooled to 20–25 °C. It was then quenched with a 10% aqueous solution of sodium carbonate (20 mL) and the product was extracted with dichloromethane (2 x 25 mL). The combined organic layers were washed with
brine and dried over magnesium sulfate. The solvent was evaporated and the residue purified by column chromatography on silica gel (hexanes / ethyl acetate 2:1).

**Diethyl 1-[(ethylsulfanyl)carbothioyl](methyl)amino]butylphosphonate (32a).** Colorless oil (86%); $^1$H NMR δ 0.93–0.99 (m, 3H), 1.27–1.41 (m, 11H), 1.82–2.00 (m, 2H), 3.25 (3.48) (s, 3H), 4.06–4.23 (m, 4H), 6.55 (5.04) (ddd, $J = 20.2, 10.7 & 4.1$ Hz, 1H); $^{13}$C NMR δ 13.3, 13.6, 13.8, 16.3 (d, $J = 5.2$ Hz, 1C), 16.4 (d, $J = 5.8$ Hz, 1C), 19.2 (d, $J = 13.7$ Hz, 1C), 29.9 (29.6), 32.0, 35.3 (38.8), 57.9 (58.8) (d, $J = 150.6$ Hz, 1C), 62.4 (d, $J = 6.9$ Hz, 1C), 62.5 (d, $J = 7.0$ Hz, 1C), 200.7 (d, $J = 7.4$ Hz, 1C). Anal. Calcd for $C_{12}H_{26}NO_3PS_2$: C, 44.02; H, 8.00; N, 4.28. Found: C, 44.01; H, 8.25; N, 4.82%.

**Diisopropyl 1-[(ethylsulfanyl)carbothioyl](methyl)amino]butylphosphonate (32b).** Colorless oil (83%); $^1$H NMR δ 0.85–0.91 (m, 3H), 1.19–1.32 (m, 17H), 1.72–1.96 (m, 2H), 3.07–3.26 (m, 2H), 3.27 (3.40) (s, 3H), 4.58–4.73 (m, 2H), 6.43 (4.91) (ddd, $J = 19.6, 10.2 & 5.1$, 1H); $^{13}$C NMR δ 13.1, 13.4, 13.5, 13.6, 13.8, 19.2 (d, $J = 13.7$ Hz, 1C), 23.7, 23.8, 23.9, 24.0, 24.1, 24.2, 24.3, 29.7, 29.8, 31.8, 31.9, 35.2, 38.8, 58.4 (59.2) (d, $J = 152.3$ Hz, 1C), 71.1, 71.2, 71.3, 71.4, 71.9, 72.0, 200.4 (d, $J = 7.4$ Hz, 1C). Anal. Calcd for $C_{14}H_{30}NO_3PS_2$: C, 47.30; H, 8.51; N, 3.94. Found: C, 47.88; H, 8.95; N, 4.15%.

**Diethyl 1-[(ethyl(methylsulfanylcarbothioyl)amino]butylphosphonate (32c).** Colorless oil (89%); $^1$H NMR δ 0.93–1.00 (m, 3H), 1.27–1.46 (m, 11H), 1.93 (p, $J = 7.1$ Hz, 2H), 2.68 (2.65) (s, 3H), 3.85–4.05 (m, 2H), 4.07–4.22 (m, 4H), 6.58–6.72 (m, 1H); $^{13}$C NMR δ 12.5, 13.6 (d, $J = 8.6$ Hz, 1C), 16.1 (d, $J = 1.7$ Hz, 1C), 16.2 (d, $J = 1.7$ Hz, 1C), 19.1 (d, $J = 13.7$ Hz, 1C), 20.3, 29.8 (d, $J = 1.7$ Hz, 1C), 43.6, 58.7 (d, $J = 150.6$ Hz, 1C), 62.2 (d, $J = 7.4$ Hz, 1C), 62.3 (d, $J = 7.4$ Hz, 1C). Anal. Calcd for $C_{12}H_{26}NO_3PS_2$: C, 44.02; H, 8.00; N, 4.28. Found: C, 44.46; H, 8.27; N, 4.44%.

**Diisopropyl 1-{ethyl[(methylsulfanyl)carbothioyl]amino}butylphosphonate (32d).** Colorless oil (80%); $^1$H NMR δ 0.93–1.00 (m, 3H), 1.26–1.46 (m, 17H), 1.85–1.95 (m, 2H), 2.67 (2.64) (s, 3H), 3.84–4.07 (4.24–4.36) (m, 2H), 4.66–4.78 (m, 2H), 4.89–5.00 (ddd, $J = 20.6, 10.2 & 3.8$ Hz, 0.28H), 6.59 (dt, $J = 20.3 & 7.4$ Hz, 0.72H); $^{13}$C NMR δ 12.6, 13.7, 13.8, 13.9, 19.2, 19.4, 19.6, 20.3, 20.5, 23.5, 23.6, 23.7, 23.8, 23.9, 24.0, 24.1, 24.1, 24.2, 24.3, 30.1, 30.1, 43.7, 46.5, 59.6 (59.9) (d, $J = 154.6$ Hz, 1C), 71.1 (71.2) (d, $J = 3.4$ Hz, 1C), 71.3 (71.8) (d, $J = 7.4$ Hz, 1C), 201.2 (199.3) (d, $J = 6.9$ Hz, 1C). Anal. Calcd for $C_{14}H_{30}NO_3PS_2$: C, 47.30; H, 8.51; N, 3.94. Found: C, 47.14; H, 8.75; N, 4.10%.

**References**