A General and Efficient Route to Thionoesters via Thionoacyl Nitrobenzotriazoles

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Introduction

Thionoesters (thiocarboxylic-*O*-esters), a class of sulfur-containing compounds of general structure R−C(S)−OR′, have been a focus of interest due to their altered reactivity relative to their oxygen analogues.[1,2] For example, thionoesters can be readily desulfurized with Raney nickel to form the corresponding ethers.[3] This pathway to convert esters to ethers avoids many of the steric and functional limitations of other methods[4] for ether formation and appears to be general for this conversion. Thionoesters, unlike their oxoester counterparts of lesser electrophilicity of the carbonyl system, react readily with DAST under mild conditions to provide cleanly and in good yield the corresponding α,α-difluoroethers,[5] compounds of current interest. Thionoesters are also considered as suitable starting materials for the synthesis of 1,3,4-oxadiazoles[6] of considerable activity[7,8] as plant cell growth factors, herbicides, and fungicides. Recently, the influence of thionoesters as effective chain transfer agents in the polymerization of styrene, methyl acrylate, and related olefins was reported.[9] This activity was close to the ideal for obtaining narrow molecular-weight distributions in batch polymerizations. Also, of potential utility is the anticipated increased acidity of the α-hydrogens.

Several methods exist for the preparation of thionoesters. One is the sulfo-hydrolysis of imino esters[10] with hydrogen sulfide in pyridine.[11] Thioamides are often a major side product, and the method is limited in scope. Alternatively, sulfo-hydrolysis of dialkoxycarbonium ions[12] has been employed for the synthesis of thionoesters, a procedure involving treatment of the dialkoxycarbonium tetrafluoroborate with anhydrous sodium sulfide or sodium hydrosulfide in acetonitrile. Mixtures of products are often obtained which require extensive purification and ultimately are formed in low yields.[13] Alcoholysis of thioacyl halides[14−16] and addition of alcohols to thioketenes[17,18] are yet other routes for thionoester formation. Thioacyl halides are generally very unstable,[19] and aliphatic thioacyl chlorides decompose rapidly even below −70 °C; only a few thiobenzoyl chlorides continue to find use.[20] Thioketenes are also unstable and can only be isolated at very low temperatures since they tend to dimerize readily. An important development has been the introduction of the phosphetane disulfide reagent[21] as a direct thionating agent for converting the appropriate esters to thionoesters.[22] This procedure, while superior to previous methods, still suffers from the requirements of drastic reaction conditions (refluxing xylene or toluene) and long reaction times that limit its utility with compounds containing sensitive functional groups.[23] This method also provides poor regioselectivity with compounds containing additional ester functionality. Furthermore, esters with conjugated electron-withdrawing groups[3a] failed to give reaction with Lawesson's reagent.[21] Thus, the importance of thionoesters for synthetic applications and the need to overcome the limitations associated with previous methods for their formation has led us to develop a new and general method for thionoester formation that proceeds under mild conditions and in short reaction times.

Results and Discussion

In the course of studies on thiopeptide synthesis, we have demonstrated that α-amino thionoacid derivatives of nitrobenzotriazole are effective thioacylating agents for site-specific incorporation of thioamide linkages into a growing peptide.[24] Stimulated by success with these reagents, we considered applying nitrobenzotriazole as

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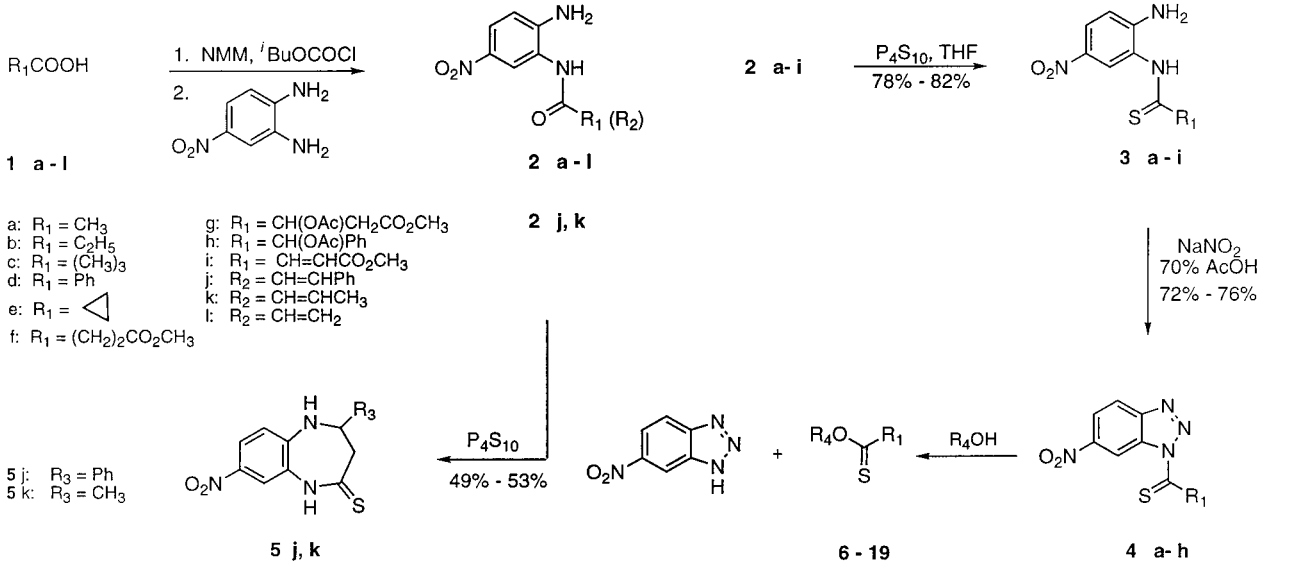
Scheme 1. General Route to Benzotriazole Thioacylating Agents and Thionoesters



a leaving group in thionoester synthesis. The procedure for the preparation of benzotriazole thioacylating agents (**4a**−**h**) is illustrated in Scheme 1. Coupling was effected between 4-nitro-1,2-phenylenediamine and carboxylic acids **1** in THF at 0 °C using mixed carbonic anhydride methodology for amide synthesis. After isolation, this process gave the crystalline anilides **2** in 86−88% yield. Direct thionation of **2** was achieved with a mixture of P_4S_{10} and anhydrous Na_2CO_3 in THF. The reaction proceeded smoothly for a total of 2 h at 0 °C and room temperature to afford thioanilides **3** in good yield (78−82%) with the exception of **2j,k,l**.

Surprisingly, thionation of the cinnamoyl derivative **2j** with P_4S_{10} did not afford the corresponding thioamide but rather a single cyclization product. Four possible structures were considered, resulting from addition to the double bond by (a) the sulfur of the thioamide to give a four-membered ring, (b) the acylated nitrogen to give a β-lactam, (c) the ortho amino group to the α-position to give a six-membered ring, or (d) the ortho amino group to the β-position to give a 1,5-benzodiazepine. Since analysis of the NMR spectra was not definitive, an X-ray crystal structure determination was made, and from it the structure was established as 8-nitro-5-phenyl-2-thiono-1,5-benzodiazepine (**5j**), shown in Figure 1. The propensity for this Michael addition with the weakly nucleophilic amine *para* to the nitro group was surprising and warranted further investigation. Therefore, three allylic derivatives were prepared to determine whether the phenyl group on the cinnamoyl derivative **2j** was influencing the cyclization. The first derivative was the methyl-substituted acryloyl derivative **2k** which readily underwent cyclization in a manner similar to give the benzodiazepine **5k** in 49% yield. The second was the nonsubstituted acryloyl derivative **2l** which upon thionation with P_4S_{10} did not yield the thioamide but rather polymerization products which were not further characterized. While cyclization occurred when the β-substituent was methyl or phenyl, none was observed with the fumaroyl derivative **2i** containing a β-carboxy methyl ester substituent; the normal thioamide was formed.

Intramolecular cyclization of thioamides **3** using nitrous acid generated in situ with $NaNO_2$ in AcOH gave benzotriazoles **4** in 72−76% yield, with the exception of **3i** which failed to yield the corresponding benzotriazole derivative. These compounds are orange-red solids, stable to storage, and can be used without further purification.

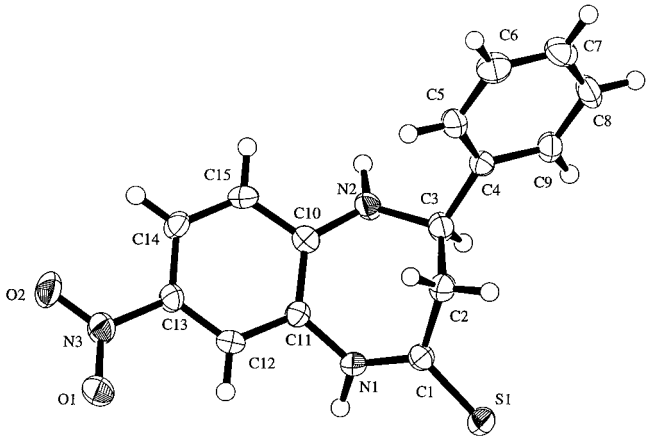


Figure 1. Structure of 8-nitro-5-phenyl-2-thiono-1,5-benzodiazepine (**5j**) as determined by X-ray crystallography.

Our initial attempts at thionoester formation were made by coupling thioacylating agent **4d** with benzyl alcohol in THF at ambient and elevated temperatures as well as by catalysis of the reaction with the addition of base such as Bu_3P, Et_3N, or DMAP. These attempts resulted in either no reaction or disappointingly low yields (24−29%) which required tedious purification by chromatography. After much experimentation, including thionoimidazolide formation and methylation to the imidazolium species[25] and use of the alkoxide,[26] general and mild procedures giving high yields were developed. These involved use of imidazole, pyridine (neat), and DBU in either CH_2Cl_2, THF, or DMF. Times varied from 1 to 48 h, and temperatures were generally ambient, as summarized in Table 1. These relatively mild conditions should be compatible with numerous functional groups. Exemplary alcohols, considered reasonably representative, included primary (benzyl) and secondary (cyclohexyl,

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Table 1. Reaction Parameters for Formation of Thionoesters 6−19 from Alcohols R_4OH and Thionoacylbenztriazoles 4

entry	thionoacyl benztriazole **4**, R_1	alcohol R_4OH	thionoester $R_4O(C{=}S)R_1$	solvent	time (h)/temp (°C)	yield (%)
1	CH_3	Bn	**6**	CH_2Cl_2/Im	48/25	81
2	CH_3CH_2	Bn	**7**	CH_2Cl_2/Im	48/25	83
3	$C(CH_3)_3$	Bn	**8**	pyridine	2/50	79
4	C_6H_5	Bn	**9**	THF/DBU	1/0−25	89
5	C_6H_5	cyclohexyl	**10**	THF/DBU	2/0−25	74
6	C_6H_5	menthyl	**11**	THF/DBU	3/0−25	69
7	C_6H_5	*N*-BOC serinyl methyl ester	**12**	DMF/DBU	2/0−25	74
8	C_6H_5	*N*-BOC threoninyl methyl ester	**13**	DMF/DBU	2/0−25	66
9	C_6H_5	6-*β*-methhl glucosidyl	**14**	pyridine	24/25	79
10	C_6H_5	3-pyridyl	**15**	THF/DBU	1/0−25	67
11	cyclopropyl	Bn	**16**	THF/DBU	1/0−25	83
12	succinoyl *β*-methyl ester	Bn	**17**	THF/Im	48/25	63
13	*O*-acetylmaloyl *β*-methylester	Bn	**18**	THF/Im	48/25	53
14	*O*-acetylmandeloyl	Bn	**19**	THF/DBU	2/0	64

menthyl) alcohols and a number containing other functionalities.

A number of entries in Table 1, as they potentially extrapolate to ether formation, warrant further comment. Thus, entry 11 demonstrates the ready formation of a cyclopropylcarboxylic acid thionester. Coupled with the known conversion of thionoesters to ethers,[3] this offers an attractive method for preparing cyclopropylmethyl ethers.[27,28] Benzylation of hydroxy amino acids, namely serine and threonine (entries 7 and 8), is another potential use of thionoester methodology. Direct benzylation procedures using Williamson ether synthesis lead to racemization, and the alternative present preparation of these compounds is quite complex.[29] Formation of the thionoesters **12** and **13** proceeds with no epimerization, as would also be anticipated for the further conversion to ethers.[3] Two other examples of interest for further ether formation are the thionoester of 3-pyridol (entry 10) and that of *β*-methyl glucoside, avoiding any protection protocol.[30]

A further demonstration of the versatility of the present method is its application to mono-thionation of methyl succinate (entry 12) and the resulting regiospecificity which is not achievable by literature methodology. It was interesting to observe that thionation of the amide derived from methyl succinate **2f** smoothly afforded the corresponding thioamide **3f** in 62% yield, while the analogous amide derived from aspartic acid methyl ester gave an acylthioimidate derivative as the major product.[24] To clarify the influence of the NHBOC substituent on cyclization, other substituted succinates were examined. Thus the acetoxysuccinic acid *β*-methyl esters were prepared.[31] Unlike the aspartic acid analogue, α-acetoxysuccinic acid *β*-methyl ester derivative **2g** did not undergo cyclization upon treatment with P_4S_{10}, thus providing an example of regiospecific monothionation of a triester (entry 13). Interestingly, the *β*-acetoxy derivative did not give the corresponding amide upon reaction with 4-nitro-1,2-phenylenediamine but rather underwent elimination to afford the α,*β*-unsaturated methyl ester derivative **2i** whose structure was verified by comparison with an authentic sample prepared from maleic anhydride.[32]

Of major concern was the question of the enantiomeric integrity of the thionoester components. This was investigated with the acetyl mandelic acid derivartive **4h**, considered potentially highly susceptible to epimerization. The enantiomeric composition of the thionoester **19** was determined by chiral HPLC using racemic **19** as control, and the enantomeric ratio (er) was found to be 92/8.

In summary, we provide a general and efficient method for thionoester synthesis. The simplicity of reagent preparation and product isolation, high yields, mild conditions, and enhanced reactivity of the thioacylating agents should make it widely applicable.

Experimental Section

General. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded in DMSO unless otherwise stated at 400 and 100.6 MHz, and chemical shifts are reported relative to either a tetramethylsilane internal standard or the solvent signals. Chemical shifts (*δ*) are reported in ppm, and coupling constants are in hertz. TLC was carried out using precoated sheets (Merck silica gel 60-F_{250}, layer thickness 0.2 mm) which, after development, were visualized by UV light (254 nm) and/or by spraying with 0.3% solution of ninhydrin in *tert*-BuOH/AcOH (93/3, v/v) or silver nitrate/ammonium hydroxide−sodium chloride solutions and heating. Merck silica gel 60 (70−230 mesh) was used for column chromatography. Epimerization studies were conducted by analytical HPLC on an 0.46 × 25 cm CHIRALCEL OD column, eluting with hexane/2-propanol (99/1) and utilizing detection at 254 nm. All reactions were conducted under a nitrogen or argon atmosphere. Solvents were distilled prior to use (THF over Na/benzophenone; *N*-methylmorpholine and triethylamine over CaH_2) and dried over 4 Å molecular sieves. Organic extracts were dried over anhydrous $MgSO_4$, filtered, and evaporated under reduced pressure at 30−40 °C unless otherwise indicated. Microanalysis were performed by College of Chemistry Micro Analytical Laboratory, University of California at Berkeley.

General Procedure for the Preparation of Acyl *2*-Amino-5-nitroanilines 2a−l. Coupling of Carboxylic Acids (1a−l) with 4-Nitro-1,2-phenylenediamine. *N*-Methylmorpholine (2.2 mL, 20 mmol) was added to a solution of carboxylic acid (**1a**−**l**) in THF (100 mL) at −15 °C, followed by dropwise addition of isobutyl chloroformate (1.3 mL, 10 mmol). The mixture was stirred for 10 min, and then 4-nitro-1,2-phenylenediamine (1.53 g, 10 mmol) was added and the resulting slurry stirred at −15 °C for 2 h and at room temperature overnight. The mixture was filtered and the filtrate evaporated to dryness. The residue, dissolved in EtOAc (250 mL), was washed successively with 1 M NaH_2PO_4, brine, 5% $NaHCO_3$, and brine and then dried and

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evaporated to dryness. Crystallization of the residue from EtOAc/hexane afforded pure **2a**−**l** as yellow solids in 86−88% yield.

***N*-Acetyl-2-amino-5-nitroaniline (2a):**[33] mp 202 °C; ^{1}H NMR δ 9.16 (s, 1H), 8.2 (d, 1H, J = 2.56), 7.8 (dd, 1H, J = 2.6, 9), 6.7 (d, 1H, J = 9), 6.4 (s, 2H), 2.03 (s, 3H); ^{13}C NMR δ 169.4, 149.4, 135.9, 123.1, 122.1, 121.7, 114, 23.9. Anal. Calcd for $C_8H_9N_3O_3$: C, 49.2; H, 4.7; N, 21.5. Found: C, 49.1; H, 4.6; N, 21.4.

***N*-Propionyl-2-amino-5-nitroaniline (2b):**[34] mp 190−191 °C; 1H NMR δ 9.0 (s, 1H), 8.2 (s, 1H), 7.7 (d, 1H, J = 8.95), 6.7 (d, 1H, J = 8.95), 6.4(s, 2H), 2.3 (m, 2H), 1.1 (m, 3H); ^{13}C NMR δ 177.8, 154.1, 140.7, 127.8, 126.9, 126.4, 118.8, 34.2, 14.7. Anal. Calcd for $C_9H_{11}N_3O_3$: C, 51.7; H, 5.3; N, 20.1. Found: C, 51.7; H, 5.6; N, 19.8.

***N*-Pivaloyl-2-amino-5-nitroaniline (2c):** mp 177 °C; ^{1}H NMR δ 8.8 (s, 1H), 7.9 (d, 1H, J = 2.35), 7.8 (dd, 1H, J = 2.3, 8.9), 6.7 (d, 1H, J = 9.0), 6.2 (s, 2H), 1.21 (s, 9H); ^{13}C NMR δ 182.6, 155.8, 140.7, 128.9, 128.5, 127.0, 119.1, 32.5. Anal. Calcd for $C_{11}H_{15}N_3O_3$: C, 55.7; H, 6.4; N, 17.7. Found: C, 55.7; H, 6.4; N, 17.6.

***N*-Benzoyl-2-amino-5-nitroaniline (2d):** mp 214 °C; ^{1}H NMR δ 9.74 (s, 1H), 8.1 (dd, 2H, J = 7.2, 2.27), 7.9 (dd, 2H, J = 9.0, 2.5), 7.5 (m, 3H), 6.8 (d, 1H, J = 9.0), 6.5 (s, 2H); ^{13}C NMR δ 171.3, 155.9, 140.6, 139.5, 136.9, 133.5, 133.2, 128.8, 126.5, 119.1. Anal. Calcd for $C_{13}H_{11}N_3O_3$: C, 60.7; H, 4.3; N, 16.3. Found: C, 60.7; H, 4.3; N, 16.3.

***N*-(Cyclopropylcarbonyl)-2-amino-5-nitroaniline (2e):** mp 183 °C; ^{1}H NMR (DMSO) δ 9.41 (s, 1H), 8.32 (s, 1H), 7.79 (dd, 1H, J = 2.37, 6.58), 6.72 (d, 1H, J = 9), 1.82 (s, 2H), 1.94 (S, 1H), 0.8 (m, 4H); ^{13}C NMR δ 177.5, 153.4, 140.8, 127.5, 127.1, 125.7, 118.9, 25.9, 12.6. Anal. Calcd for $C_{10}H_{11}N_3O_3$: C, 54.3; H, 5.0; N, 19.0. Found: C, 54.2; H, 5.1 N, 19.3.

***N*-(β-(Methoxycarbonyl)propionyl)-2-amino-5-nitroaniline (2f):** mp 168 °C; ^{1}H NMR δ 9.25 (s, 1H), 8.17 (d, 1H, J = 2.53), 7.8 (dd, 1H, J = 9, 2.5), 6.7 (d, 1H, J = 9), 6.4 (s, 2H), 3.5 (s, 3H), 2.6 (m, 4H); ^{13}C NMR δ 178.2, 175.8, 154.2, 140.7, 128, 126.7, 126.5, 118.7, 35.6, 33.8. Anal. Calcd for $C_{11}H_{13}N_3O_5$: C, 49.4; H, 4.9; N, 15.7. Found: C, 49.9; H, 4.8; N, 16.1.

***N*-(α-Acetoxy-β-(methoxycarbonyl)propionyl)-2-amino-5-nitroaniline (2g)** was prepared from methyl 3-acetoxysuccinate according to the general procedure described above: mp 166 °C; ^{1}H NMR δ 9.55 (s, 1H), 8.18 (d, 1H, J = 2.6), 7.8 (dd, 1H, J = 9, 2.6), 6.7 (d, 1H, J = 9), 6.4 (s, 2H), 5.3 (m, 1H), 3.6 (s, 3H), 2.8 (m, 2H), 2.07 (s, 3H); ^{13}C NMR δ 175.3, 175.2, 173.0, 155.2, 140.6, 128.9, 127.9, 125.5, 118.9, 75.2, 57.0, 41.1, 25.8. Anal. Calcd for $C_{13}H_{15}N_3O_7$: C, 48.0; H, 4.7; N, 12.9. Found: C, 47.9; H, 4.6; N, 13.2.

***N*-(*O*-Acetyl-D-mandeloyl)-2-amino-5-nitroaniline (2h):** mp 160 °C; ^{1}H NMR δ 9.7 (s, 1H), 8.1 (d, 1H, J = 2.4), 7.8 (dd, 1H, J = 6.55, 2.49), 7.5 (m, 2H), 7.3 (m, 3H), 6.7 (d, 1H, J = 9.0), 6.4 (s, 2H), 6.0 (s, 1H), 2.14 (s, 3H); ^{13}C NMR δ 175.5, 172.9, 154.4, 140.9, 140.4, 134.1, 133.9, 132.7, 128.6, 126.8, 125.7, 119.1, 118.8, 80.5, 25.9. Anal. Calcd for $C_{16}H_{15}N_3O_5$: C, 58.4; H, 4.6; N, 12.8. Found: C, 58.1; H, 4.3; N, 12.4.

***N*-(β-(Methoxycarbonyl)acryloyl)-2-amino-5-nitroaniline (2i):** mp 201 °C; ^{1}H NMR δ 9.75 (s, 1H), 8.36 (d, 1H, J = 2.5), 7.8 (dd, 1H, J = 8.9, 2.5), 7.24 (d, 1H, J = 15.4), 6.75 (s, 2H), 6.75 (d, 1H, J = 2.3), 6.7 (d, 1H, J = 9), 3.7 (s, 3H); ^{13}C NMR δ 170.7, 167.2, 154.0, 142.8, 140.7, 134.2, 128.4, 126.3, 125.9, 119.0, 57.3. Anal. Calcd for $C_{11}H_{11}N_3O_5$: C, 49.8; H, 4.2; N, 15.8. Found: C, 49.7; H, 3.9; N, 15.5.

***N*-Cinnamoyl-2-amino-5-nitroaniline (2j):** mp 223 °C; ^{1}H NMR δ 9.43 (s, 1H), 8.4 (s, 1H), 7.8 (d, 1H, J = 6.58), 7.6 (s, 1H), 7.5 (m, 2H), 7.4 (m, 3H), 6.55 (s, 2H), 6.74 (d, 1H, J = 9), 6.87 (d, 1H, J = 15.7); ^{13}C NMR δ 169.3, 153.8, 145.6, 140.8, 139.9, 135.0, 134.2, 133.0, 127.9, 127.1, 126.8, 125.9, 119.0. Anal. Calcd for $C_{15}H_{13}N_3O_3$: C, 63.6; H, 4.6; N, 14.8. Found: C, 63.6; H, 4.5; N, 14.6.

***N*-Crotonoyl-2-amino-5-nitroaniline (2k):** mp 178 °C; ^{1}H NMR δ 9.1 (s, 1H), 8.36 (s, 1H), 7.79 (dd, 1H, J = 9, 2.6), 6.7 (d, 1H, J = 8.3), 6.8 (m, 1H), 6.4 (s, 2H), 6.2 (d, 1H, J = 15.27) 1.8 (d, 3H, J = 1.4); ^{13}C NMR δ 175.5, 169.2, 153.7, 145.4, 140.8, 130.8, 127.7, 126.9, 125.9, 118.9. Anal. Calcd for $C_{10}H_{11}N_3O_3$: C, 54.3; H, 5.0; N, 19.0. Found: C, 54.2; H, 4.5; N, 19.0.

***N*-Acryloyl-2-amino-5-nitroaniline (2l):** mp 183 °C; ^{1}H NMR δ 9.3 (s, 1H), 8.3 (d, 1H, J = 2.4), 7.8 (dd, 1H, J = 9.8, 2.8), 6.75 (d, 1H, J = 9), 6.5 (s, 2H), 6.4 (m, 1H), 6.2 (dd, 1H, J = 17, 2), 5.7 (dd, 1H, J = 9.8, 1.8); ^{13}C NMR δ 169.0, 153.9, 140.8, 136.7, 132.3, 128.0, 126.5, 126.2, 119.0. Anal. Calcd for $C_9H_9N_3O_3$: C, 52.2; H, 4.4; N, 20.3. Found: C, 52.0; H, 4.5; N, 20.4.

General Procedure for the Preparation of Thioanilides (3a−i). Under a flow of argon, purified P_4S_{10} (1.1 g, 2.47 mmol) was mixed with Na_2CO_3 (0.27 g, 2.5 mmol) in THF (100 mL). The mixture was stirred for 1 h at 25 °C and then cooled to 0 °C. To this clear solution was added anilides **2a**−**i** (5 mmol, 200 mol %), and the reaction was stirred at this temperature for 30 min and then at room temperature for 2.5 h. The solution was filtered through Celite, and the filtrate was evaporated to dryness. The residue was dissolved in EtOAc/heptane (2/1, v/v, 75 mL) and washed with 5% $NaHCO_3$ (2 × 30 mL), and the aqueous layers were back extracted with EtOAc/heptane (75 mL). The combined organic layer was washed with brine, dried, and evaporated. The resulting yellow solid was crystallized from ethyl acetate/hexane in yields of 78−82%.

***N*-Thioacetyl-2-amino-5-nitroaniline (3a):** mp 184 °C; 1H NMR δ 9.56 (s, 1H), 7.9 (m, 2H), 6.7 (d, 1H, J = 9.0), 6.56 (s, 2H), 2.59 (s, 3H); ^{13}C NMR δ 216.3, 151.5, 151.3, 135.6, 123.2, 114.8, 114.5, 34.1. Anal. Calcd for $C_8H_9N_3O_2S$: C, 45.5; H, 4.3; N, 19.9. Found: C, 45.6; H, 4.3; N, 19.8.

***N*-Thiopropionyl-2-amino-5-nitroaniline (3b):** mp 168 °C; 1H NMR δ 10.59 (s, 1H), 7.9 (s, 1H), 7.7 (d, 1H, J = 6.5), 6.8 (d, 1H, J = 9.1), 6.59 (s, 2H), 2.7 (m, 2H), 1.4 (m, 3H); ^{13}C NMR δ 213.9, 156.0, 140.3, 130.3, 129.9, 127.9, 119.2, 18.9. Anal. Calcd for $C_9H_{11}N_3O_2S$: C, 48.0; H, 4.9; N, 18.7. Found: C, 47.8; H, 4.6; N, 18.4.

***N*-Thiopivaloyl-2-amino-5-nitroaniline (3c):** mp 203 °C; ^{1}H NMR δ 10.36 (s, 1H), 7.9 (d, 1H, J = 9.0), 7.74 (s, 1H), 6.7 (d, 1H, J = 9.1), 6.2 (s, 2H), 1.3 (s, 9H); ^{13}C NMR δ 220.6, 156.2, 140.6, 130.7, 129.9, 129.1, 119.4, 35.2. Anal. Calcd for $C_{11}H_{15}N_3O_2S$: C, 52.2; H, 6.0; N, 16.6. Found: C, 52.4; H, 6.1; N, 16.7.

***N*-Thiobenzoyl-2-amino-5-nitroaniline (3d):** mp 210 °C; ^{1}H NMR δ 10.25 (s, 1H), 8.0 (d, 1H, J = 2.5), 7.9 (m, 3H), 7.53 (s, 1H,), 7.50 (d, 1H, J = 9.0), 7.44 (d, 1H, J = 7.7), 6.8 (d, 1H, J = 9.12), 6.6 (s, 2H); ^{13}C NMR δ 204.0, 156.2, 146.2, 140.5, 136.3, 133.2, 133.0, 130.7, 130.0, 128.5, 119.5. Anal. Calcd for $C_{13}H_{11}N_3O_2S$: C, 57.1; H, 4.1; N, 15.4. Found: C, 57.0; H, 4.1; N, 15.1.

***N*-(Cyclopropylthiocarbonyl)-2-amino-5-nitroaniline (3e):** mp 184 °C; ^{1}H NMR δ 10.37 (s, 1H), 7.9 (s, 1H), 7.8 (dd, 1H, J = 9, 2.7), 6.7 (d, 1H, J = 9), 6.55 (s, 2H), 2.29 (m, 1H), 1.15 (m, 2H), 0.9 (m, 2H);); ^{13}C NMR δ 213.8, 155.9, 140.4, 130.4, 129.7, 127.9, 119.4, 28.7, 17.5. Anal. Calcd for $C_{10}H_{11}N_3O_2S$: C, 50.6; H, 4.7; N, 17.7. Found: C, 50.4; H, 4.6; N, 17.5.

***N*-Thio(β-(methoxycarbonyl)propionyl)-2-amino-5-nitroaniline (3f):** mp 174 °C; ^{1}H NMR δ 10.38 (s, 1H), 7.9 (d, 1H, 8.9), 7.8 (s, 1H), 6.8 (d, 1H, J = 9), 6.5 (s, 2H), 3.5 (s, 3H), 2.8 (m, 4H), ^{13}C NMR δ 210.7, 178.1, 156, 140.4, 130.2, 130.1, 127.7, 119.2, 56.7, 37.8. Anal. Calcd for $C_{11}H_{13}N_3O_4S$: C, 46.6; H, 4.6; N, 14.8. Found: C, 46.7; H, 4.4; N, 14.9.

***N*-Thio(α-acetoxy-β-(methoxycarbonyl)propionyl)-2-amino-5-nitroaniline (3g):** mp 144 °C; ^{1}H NMR δ 10.23 (s, 1H), 7.96 (d, 1H, J = 9), 7.8 (s, 1H), 6.79 (d, 1H, J = 9.1), 6.3 (s, 2H), 5.6 (m, 1H), 3.6 (s, 3H), 3.12 (m, 2H), 2.09 (s, 3H); ^{13}C NMR δ 206.2, 175.4, 175.3, 155.9, 140.6, 130.4, 130.2, 127.0, 119.3, 80.8, 57.1, 26.1. Anal. Calcd for $C_{13}H_{15}N_3O_6S$: C, 45.7; H, 4.4; N, 12.3. Found: C, 46.0; H, 4.6; N, 12.3.

***N*-Thio(*O*-acetyl)-D-mandeloyl-2-amino-5-nitroaniline (3h):** mp 137 °C; ^{1}H NMR δ 9.9 (s, 1H), 7.9 (dd, 1H, J = 6.54, 2.58), 7.7 (d, 1H, J = 2.49), 7.6 (m, 2H), 7.4 (m, 3H), 6.8 (d, 1H, J = 9.1), 6.5 (s, 1H), 6.2 (s, 2H), 2.15 (s, 3H); ^{13}C NMR δ 206.3, 175.6, 155.7, 141.9, 140.8, 134.0, 133.7, 132.6, 130.4, 129.9, 126.9, 119.5, 85.8, 26.3. Anal. Calcd for $C_{16}H_{15}N_3O_4S$: C, 55.6.; H, 4.4; N, 12.2. Found: C, 55.8; H, 4.3; N, 12.5.

***N*-Thio(β-(methoxycarbonyl)acryloyl)-2-amino-5-nitroaniline(3i)** was prepared from methyl hydrogen fumarate

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according to the general procedure described above. It was purified by column chromatography, eluting with hexane/ethyl acetate (1/1): yield 41%; mp 158 °C (dec); ^{1}H NMR δ 10.0 (s, 1H), 8.05 (s, 1H), 7.9 (d, 1H, J = 7.37), 7.5 (d, 1H, J = 15.24), 6.8 (d, 1H, J = 15.2), 6.75 (d, 1H, J = 9.15), 6.7 (s, 2H), 3.6 (s, 3H); ^{13}C NMR δ 197.8, 170.8, 155.8, 147.5, 140.2, 133.3, 130.2, 130.0, 126.9, 119.4, 57.3. Anal. Calcd for $C_{11}H_{11}N_3O_4S$: C, 47.0; H, 3.9; N, 15.0. Found: C, 47.2; H, 3.9; N, 14.7.

4-Phenyl-2-thiono-1,5-benzodiazepine (5j) was prepared by treating **2j** with P_4S_{10} according to the general procedure described above. It was purified by column chromatography, eluting with hexane/ethyl acetate (1/1) and then crystallized from THF/hexane: yield 53%; mp 227 °C; ^{1}H NMR δ 9.5 (s, 1H), 8.02 (d, 1H, J = 2.5), 7.8 (dd, 1H, J = 17.1, 2.5), 7.75 (s, 1H), 7.3 (m, 5H), 7.0 (s, 1H), 4.9 (d, 1H, J = 8.05), 3.4 (m, 1H), 3.2 (m, 1H); ^{13}C NMR δ 205.9, 151.3, 141.6, 141.8, 133.7, 132.9, 131.7, 128.5, 127.2, 124.9, 123.7, 65.3, 60.1. Anal. Calcd for $C_{15}H_{13}N_3O_2S$: C, 60.2; H, 4.4; N, 14.0. Found: C, 60.1; H, 4.4; N, 14.2.

4-Methyl-2-thiono-1,4-benzodiazepine (5k) was prepared by treating **2k** with P_4S_{10} according to the general procedure described above. It was purified by column chromatography, eluting with hexane/ethyl acetate (2/1): yield 49%; mp 222 °C; ^{1}H NMR δ 9.65 (s, 1H), 7.9 (s, 1H), 7.7 (d, 1H, J = 8.5), 7.5 (s, 1H), 6.8 (d, 1H, J = 9), 3.8 (s, 1s), 3.0 (m, 2H), 1.25 (d, 3H, J = 6.3); ^{13}C NMR δ 206.8, 151.1, 141.2, 127.8, 127.1, 125.0, 123.2, 57.2, 57.0, 28.2. Anal. Calcd for $C_{10}H_{11}N_3O_2S$: C, 50.6; H, 4.7; N, 17.7. Found: C, 50.6; H, 4.7; N, 17.6.

General Procedure for the Preparation of Benzotriazole Thioacylating Reagents (4a−h). To a solution of thioanilides **3a**−**h** (2 mmol) dissolved by gentle warming at 40 °C and then cooling to 0−5 °C in 70% acetic acid (15 mL) was added $NaNO_2$ (0.21 g, 3 mmol, 150 mol %) in small portions with stirring. After 30 min, ice−water (100 mL) was added, and the precipitate was filtered off, washed with water, and dried in vacuo to afford benzotriazoles **4a**−**h** as orange solids of sufficient purity for further use without additional purification. For elemental analyses the benzotriazoles were crystallized from CH_2Cl_2 in yields of 72−76%.

1-Thioacetyl-6-nitrobenzotriazole (4a): mp 108 °C; ^{1}H NMR ($CDCl_3$) δ 9.6 (d, 1H, J = 2.1), 8.4 (dd, 1H, J = 2.0, 8.9), 8.2 (d, 1H, J = 8.9), 3.4 (s, 3H); ^{13}C NMR δ 205.4, 149.5, 149.2, 131.6, 121.9, 121.3, 113.0, 36.5. Anal. Calcd for $C_8H_6N_4O_2S$: C, 43.2; H, 2.7; N, 25.2. Found: C, 43.3; H, 2.7; N, 25.1.

1-Thiopropionyl-6-nitrobenzotriazole (4b): mp 94−95 °C; ^{1}H NMR ($CDCl_3$) δ 9.58 (d, 1H, J = 1.7), 8.3 (dd, 1H, J = 8.9, 1.8), 8.2 (d, 1H, J = 9), 3.7 (m, 2H), 1.47 (m, 3H); ^{13}C NMR δ 211.6, 149.4, 149.0, 131.7, 121.7, 113.0, 40.5, 13.3. Anal. Calcd for $C_9H_6N_4O_2S$: C, 45.7; H, 3.4; N, 23.7. Found: C, 45.2; H, 3.3; N, 23.4.

1-Thiopivaloyl-6-nitrobenzotriazole (4c): mp 79 °C; ^{1}H NMR ($CDCl_3$) δ 9.47 (s, 1H), 8.37 (dd, 1H, J = 2, 9.1), 8.2 (dd, 1H, J = 0.6, 8.9), 1.6 (s, 9H); ^{13}C NMR δ 219.2, 149.2, 147.9, 133.0, 121.5, 120.9, 113.4, 51.1, 31.2. Anal. Calcd for $C_{11}H_{12}N_4O_2S$: C, 50.0; H, 4.6; N, 21.2. Found: C, 50.1; H, 4.7; N, 21.2.

1-Thiobenzoyl-6-nitrobenzotriazole (4d): mp 158 °C; ^{1}H NMR ($CDCl_3$) δ 9.4 (s, 1H), 8.4 (d, 1H, J = 8.9), 8.3 (d, 1H, J = 8.9), 7.7 (d, 2H, J = 8.2), 7.6 (t, 1, J = 7.0), 7.4 (t, 2H, J = 7.5); ^{13}C NMR δ 201.2, 149.0, 142.0, 133.4, 133.0, 130.8, 128.3, 121.8, 121.3, 112.2. Anal. Calcd for $C_{13}H_8N_4O_2S$: C, 54.9; H, 2.8; N, 19.7. Found: C, 55.0; H, 2.9; N, 19.6.

1-(Cyclopropylthiocarbonyl)-6-nitrobenzotriazole (4e): mp 137 °C; ^{1}H NMR ($CDCl_3$) δ 9.69 (d, 1H, J = 1.67), 8.37 (dd, 1H, J = 8.9, 2.05), 8.2 (d, 1H, J = 8.9), 4.1 (m, 1H), 1.8 (m, 2H), 1.46 (m, 2H); ^{13}C NMR δ 211, 149.2, 149.1, 131.8, 121.6, 121.6, 121.1, 113.2, 26.9, 19.5. Anal. Calcd for $C_{10}H_8N_4O_2S$: C, 48.4; H, 3.3; N, 22.6. Found: C, 48.5; H, 3.4; N, 22.7.

1-Thio-(β-(methoxycarbonyl)propionyl)-6-nitrobenzotriazole (4f): mp 92 °C; ^{1}H NMR ($CDCl_3$) δ 9.6 (s, 1H), 8.4 (dd, 1H, J = 8.9, 1.8), 8.2 (d, 1H, J = 9), 4.0 (m, 2H), 3.78 (s, 3H), 3.1 (m, 2H); ^{13}C NMR δ 207.2, 172.2, 149.5, 149.1, 131.8, 121.9, 121.4, 112.9, 52.1, 40.8, 31.9. Anal. Calcd for $C_{11}H_{10}N_4O_4S$: C, 44.9; H, 3.4; N, 19.0. Found: C, 44.9; H, 3.4; N, 19.2.

1-Thio-(α-acetoxy-β-(methoxycarbonyl)propionyl)-6-nitrobenzotriazole (4g): mp 98 °C; ^{1}H NMR ($CDCl_3$) δ 9.03 (d, 1H, J = 1.9), 8.8 (d, 1H, J = 9.2), 8.5 (dd, 1H, J = 9.1, 1.9), 7.0 (m, 1H), 3.7 (s, 3H), 3.1 (m, 2H), 2.1 (s, 3H); ^{13}C NMR δ 202.4, 169.7, 168.9, 146.5, 146.4, 135, 126.4, 116.5, 112.6, 74.7, 52.3, 38.9, 20.8. Anal. Calcd for $C_{13}H_{12}N_4O_6S$: C, 44.3; H, 3.4; N, 15.9. Found: C, 44.2; H, 3.3; N, 15.6.

1-Thio-(*O*-acetyl)-D-mandeloyl-6-nitrobenzotriazole (4h): mp 136 °C; ^{1}H NMR ($CDCl_3$) δ 9.5 (d, 1H, J = 1.95), 8.4 (dd, 1H, J = 8.9, 1.93), 8.2 (d, 1H, J = 8.9), 7.8 (s, 1H), 7.7 (m, 2H), 7.3 (m, 3H), 2.25 (s, 3H); ^{13}C NMR δ 202.2, 170.2, 149.6, 148.8, 134.4, 131.9, 129.6, 128.9, 128.5, 122.3, 121.5, 112.7, 79.8, 21.1. Anal. Calcd for $C_{16}H_{12}N_4O_4S$: C, 53.9; H, 3.3; N, 15.7. Found: C, 54.1; H, 3.0; N, 15.9.

Benzyl Thionoacetate (6). A mixture of benzotriazole **4a** (0.44 g, 2 mmol, 100% mol), benzyl alcohol (0.32 g, 3 mmol, 150% mol), and imidazole (0.16, 2.4 mmol, 120% mol) in anhydrous CH_2Cl_2 (20 mL) was stirred at room temperature for 48 h. The solvent was removed in vacuo, and the residue was digested with hexane (2 × 40 mL). The insoluble material was removed by filtration and after solvent evaporation, the residue was chromatographed on a short column of silica gel, eluting with hexane, to afford pure **6** in 81% yield: ^{1}H NMR ($CDCl_3$) δ 7.4 (s, 5H), 5.48 (s, 2H), 2.65 (s, 3H); ^{13}C NMR δ 219.6, 135.1, 128.7, 128.6, 74.2, 34.5. Anal. Calcd for $C_9H_{10}OS$: C, 65.0; H, 6.1. Found: C, 65.3; H, 6.2.

Benzyl thionopropionate (7) was prepared from **4b** according to the procedure described for the preparation of **6**: yield 83%; ^{1}H NMR ($CDCl_3$) δ 7.3 (s, 5H), 5.49 (s, 2H), 2.8 (m, 2H), 1.28 (m, 3H); ^{13}C NMR δ 225.1,135.1, 128.6, 128.4, 73.9, 40.1, 12.9. Anal. Calcd for $C_{10}H_{12}OS$: C, 66.6; H, 6.7. Found: C, 66.3; H, 6.9.

Benzyl Thionopivalate (8). A mixture of benzotriazole **4c** (0.53 g, 2 mmol, 100% mol) and benzyl alcohol (0.32 g, 3 mmol, 150% mol) in anhydrous pyridine (10 mL) was heated with stirring at 50 °C for 1.5 h. The solution was cooled to room temperature, diluted with H_2O (40 mL), and extracted with ether (2 × 40). The combined ether layer was washed with H_2O, dried, and evaporated. The residue was purified by column chromatography, eluting with hexane: yield 79%; ^{1}H NMR ($CDCl_3$) δ 7.4 (s, 5H), 5.5 (s, 2H), 1.36 (s, 9H); ^{13}C NMR δ 231, 135.6, 128.6, 128.3, 127.9, 127.9, 73.9, 47.4, 30.0. Anal. Calcd for $C_{12}H_{16}OS$: C, 69.2; H, 7.8. Found: C, 68.9; H, 7.9.

Benzyl Thionobenzoate (9). To a cooled solution (0 °C) of benzotriazole **4d** (0.57 g, 2 mmol, 100% mol) and benzyl alcohol (0.32 g, 3 mmol, 150%) in THF (20 mL) was added DBU (0.3 g, 2 mmol, 100% mol) in THF (10 mL) in small intervals over a period of 20 min. The progress of the reaction was followed by TLC, and after complete disappearance of the starting material, the solvent was evaporated and the residue digested with hexane and filtered. The filtrate was concentrated and chromatographed, eluting with hexane, to give thionoester **9** in 89% yield. Similar results were obtained when the reaction was carried out in pyridine at room temperature for 8 h: ^{1}H NMR ($CDCl_3$) δ 8.3 (d, 2H, J = 7.36), 7.6−7.4 (m, 8H), 5.7 (s, 2H); ^{13}C NMR δ 211.0, 138.4, 135.5, 133.0, 129.1, 128.8, 128.7, 128.6, 128.5, 128.3, 74.2. Anal. Calcd for $C_{14}H_{12}OS$: C, 73.6; H, 5.3. Found: C, 73.3; H, 5.5.

Cyclohexyl thionobenzoate (10) was prepared from **4d** according to the procedure described for the preparation of **9**: yield 74%;^{1}H NMR ($CDCl_3$) δ 8.2 (dd, 2H, J = 1.05, 7.22), 7.5 (dd, 1H, J = 7.3, 13.53), 7.38 (dd, 2H, J = 7.9, 13.8), 5.7 (m, 1H), 2.05 (dd, 2H, J = 3.8, 9.89), 1.8−1.7 (m, 4H), 1.6−1.3 (m, 4H); ^{13}C NMR δ 210.6, 139.1, 132.5, 128.8, 128.0, 80.1, 30.8, 25.5, 23.6. Anal. Calcd for $C_{13}H_{16}OS$: C, 70.9; H, 7.3. Found: C, 71.0; H, 7.5.

Menthyl thionobenzoate (11) was prepared from **4d** according to the procedure described for the preparation of **9**: yield 69%; ^{1}H NMR ($CDCl_3$) δ 8.18 (d, 2H, J = 7.25), 7.5 (t, 3H, J = 7.3), 7.3 (t, 2H, J = 7.84), 5.66−5.62 (m, 1H), 2.3 (d, 1H, J = 11.5), 1.95 (dd, 1H, J = 4.56, 6.87), 1.7 (m, 2H), 1.59 (m, 1H), 1.24−1.07 (m, 3H), 1.04−0.92 (m, 5H), 0.81−0.79 (d, 2H, J = 6.93); ^{13}C NMR δ 210.7, 138.9, 132.5, 128.9, 128.0, 82.2, 47.5, 39.4, 34.4. Anal. Calcd for $C_{17}H_{24}OS$: C, 73.9; H, 8.8. Found: C, 73.9; H, 8.9.

***N*-BOC-(*O*-thionobenzoyl)-L-serine Methyl Ester (12).** To a cooled solution (0 °C) of *N*-(*tert*-butoxycarbonyl)-L-serine methyl ester (0.45 g, 2 mmol, 100 mol %) and benzotriazole **4d** (0.57 g, 2 mmol, 100 mol %) in dry DMF (10 mL) was added DBU (0.3 g, 2 mmol, 100% mol) in small intervals over a period of 20 min. The solution was stirred at 0 °C and room temperature for 2 h

when TLC indicated the disappearance of starting material; it was then diluted with H_2O (40 mL) and extracted with ether (2 × 40), and the combined ether layer was washed with H_2O and dried. Evaporation of the solvent left a brown oil that was purified by chromatography (hexane/ethyl acetate, 3/1) to afford **12** as a yellow oil in 74% yield: ^{1}H NMR ($CDCl_3$) δ 8.1(d, 2H, J = 7.3), 7.5(t, 1H, J = 7.4, 7.3), 7.37 (t, 2H, J = 8.1, 7.4), 5.4 (d, 1H, J = 7.4), 4.8 (m, 3H), 3.7 (S, 3H), 1.4 (S, 9H); ^{13}C NMR ($CDCl_3$) δ 210.5, 170.3, 155.1, 137.7, 133.1, 128.8, 128.2, 80.5, 72.1, 52.9, 52.8, 28.3. Anal. Calcd for $C_{16}H_{21}NO_5S$: C, 56.6; H, 6.2; N, 4.1. Found: C, 56.7; H, 6.2; N, 4.2.

***N*-BOC-(*O*-thionobenzoyl)-L-threonine methyl ester (13)** was prepared according to the procedures described for the preparation of **12**: yield 66%; mp 93 °C; ^{1}H NMR (CDCl3) δ 8.04 (d, 2H, J = 7.2), 7.55 (m, 1H), 7.35 (m, 2H), 6.2 (m, 1H), 4.68 (m, 1H), 3.6 (S, 3H), 1.46 (S, 9H), 1.48 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 210, 170.5, 155.8, 138.5, 133.2, 132.9, 129.7, 128.4, 80.5, 57.4, 52.7, 28.3, 17.0. Anal. Calcd for $C_{17}H_{23}NO_5S$: C, 57.8; H, 6.6; N, 4.0. Found: C, 58.2; H, 6.5; N, 4.1.

Methyl 2,3,4-Tri-*O*-acetyl-6-*O*-thionobenzoyl-α-D-glucopyranoside (14). To a cooled (0 °C) solution of methyl α-D-glucopyranoside (0.426 g, 2 mmol, 110 mol %) in dry pyridine was added benzotriazole **4d** (0.57 g, 2 mmol, 100 mol %). The reaction mixture was kept at this temperature overnight, and after addition of AcOH (0.5 mL), the solvent was evaporated at 40 °C. The residue was partitioned between phosphate buffer (pH 7, 30 mL) and EtOAc/*n*-butanol (4/1, v/v, 30 mL). The aqueous phase was extracted twice with the same mixed solvent (2 × 20 mL), and the combined organic layer was washed with H_2O and dried. The solvent was evaporated and the residue was chromatographed on silica gel, eluting with ethyl acetate/hexane, 4/1, to give the corresponding thionoester as an amorphous yellow solid. It was characterized as its triacetyl derivative (from pyridine/acetic anhydride at 0 °C following the usual literature procedures) which was crystallized from ethanol in 79% overall yield: mp 95 °C; ^{1}H NMR ($CDCl_3$) δ 8.11 (d, 2H, J = 7.2), 7.5 (t, 1H, J = 7.3, 7.4), 7.3 (m, 2H), 5.8 (m, 1H), 5.5 (t, 1H, J = 9.8, 9.5), 5.2 (m, 2H), 4.8 (m, 1H), 4.2 (m, 1H), 3.37 (s, 3H), 2.1 (S, 3H), 2.04 (S, 3H), 1.91 (S, 3H); ^{13}C NMR ($CDCl_3$) δ 211, 170.7, 170.2, 169.6, 138.1, 137.7, 133.3, 128.3, 96.8, 95.9, 70.2, 69.9, 68.5, 66.9, 20.8. Anal. Calcd for $C_{20}H_{24}O_9S$: C, 54.5; H, 5.5. Found: C, 54.5; H,5.6.

3-Pyridyl thionobenzoate (15) was prepared according to the procedure described for the preparation of **9:** yield 67%; ^{1}H NMR ($CDCl_3$) δ 8.5 (dd, 1H, J = 4.6, 1.3), 8.44 (d, 1H, J = 2.4), 8.34 (d, 1H, J = 1.3), 8.32 (d, 1H, J = 1.3), 7.6 (m, 1H), 7.4 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 210.5, 151.4, 147.4, 144.1, 138, 134.1, 133.8, 130.3, 129.5, 128.4, 127.6. Anal. Calcd for $C_{12}H_9NOS$: C, 67.0; H, 4.2; N, 6.5. Found: C, 66.9; H,4.3; N, 6.8.

Benzyl thionocyclopropylate (16) was prepared according to the procedure described for the preparation of **9:** yield 83%; ^{1}H NMR ($CDCl_3$) δ 7.4 (s, 5H), 5.53 (s, 2H), 2.37 (m, 1H), 1.5 (m, 2H), 1.0 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 224.7, 135.3, 128.7, 128.6, 128.5, 128.4, 73.6, 30.4, 26.4, 14.4. Anal. Calcd for $C_{11}H_{12}$-OS: C, 68.7; H, 6.3. Found: C, 68.8; H, 6.4.

Benzyl 1-thio-β-(methoxycarbonyl)propionate (17) was prepared according to the procedure described for the preparation of **6:** yield 63%; ^{1}H NMR ($CDCl_3$) δ 7.37 (s, 5H), 5.4 (s, 2H), 3.64 (s, 3H), 3.03 (t, 2H, J = 14.0, 6.9), 2.8 (t, 2H, J = 14.0, 6.9); ^{13}C NMR ($CDCl_3$) δ 221, 172.6, 134.9, 128.9, 128.6, 128.6, 128.5, 74.0, 51.8, 40.7, 32.1. Anal. Calcd for $C_{12}H_{14}O_3S$: C, 60.5; H, 5.9. Found: C, 60.4; H, 5.9.

Benzyl 1-thio-α-(acetoxy-β-(methoxycarbonyl)propionate (18) was prepared according to the procedure described for the preparation of **6:** yield 53%; ^{1}H NMR ($CDCl_3$) δ 7.34 (s, 5H), 5.48 (m, 1H), 5.15 (s, 2H), 3.94 (s, 3H), 2.9 (m, 2H), 2.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 221, 215.6, 170.9, 159.0, 136.0, 128.7, 128.6, 128.4, 128.2, 66.3, 54.0, 52.1, 38.5, 21.8. Anal. Calcd for $C_{14}H_{16}O_5S$: C, 56.7; H, 5.5. Found: C, 56.3; H, 5.7.

Benzyl 1-thio-(*O*-acetyl)-D-mandelate (19) was prepared according to the procedure described for the preparation of **6:** yield 64%; ^{1}H NMR ($CDCl_3$) δ 7.5 (m, 2H), 7.37 (m, 6H), 7.25 (m, 2H), 6.4 (s, 1H), 5.4 (m, 2H), 2.2 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 215.5, 170.1, 135.6, 135.0, 134.6, 130.1, 129.1, 128.7, 128.5, 128, 127.6, 81.3, 74.0, 21.1. Anal. Calcd for $C_{17}H_{16}O_3S$: C, 68.0; H, 5.4. Found: C, 68.2; H, 5.5. To determine the enantiomeric integrity of the product, a crude sample of **19** was analyzed by chiral HPLC, and the results were compared with those obtained from a sample prepared by coupling racemic benzotriazole **4h** with benzyl alcohol: mobile phase, hexane/IPA, 99.1, flow rate 0.5 mL/min, t_R 18.2 min for benzyl 1-thio-(*O*-acetyl)-D-mandelate; t_R 19.7 min for benzyl 1-thio-(*O*-acetyl)-L-mandelate; er for **19**, 92/8.

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