CHAPTER IV

Cyclic ammonium salts of dithiocarbamic acid: Stable alternative reagents for the synthesis of *S*–alkyl carbodithioates from organyl thiocyanates in water

IV.1. Introduction

S–Alkyl carbodithioate esters are esters of dithiocarbamic acids. These are also known as dithiocarbamate esters (DTCE), are functional organosulfur compounds that were first utilized as fungicides during Second World War.[1] The structures of esters of carbamic acid, thiocarbamic acid and dithiocarbamic acid are given in the Figure IV.1.

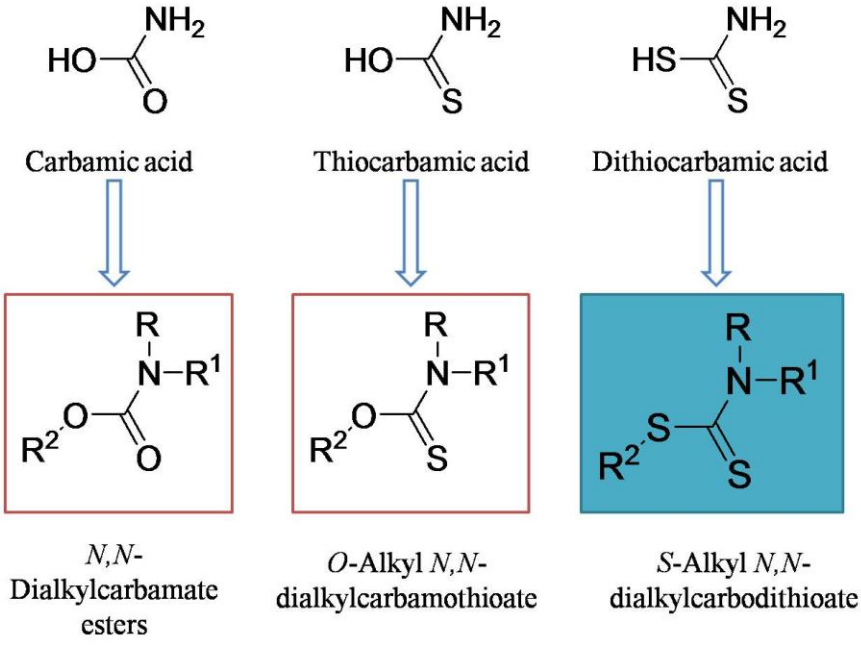
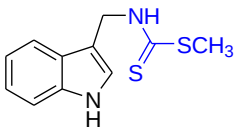
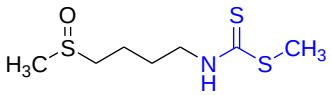


Figure IV.1. Structures of carbamic acid, thiocarbamic acid and dithiocarbamic acid and their esters

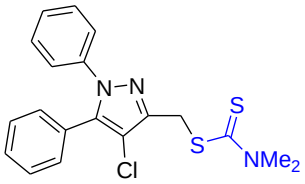
Dithiocarbamates are also mainly used as important fungicides of vegetables, crops and plants.[2–4] *S*–alkyl carbodithioate esters and its derivatives show antibacterial,[5–7] anthelmintic,[8] anticandidal activity and cytotoxicity,[9] antihistaminic,[10] as well as anticancer properties.[8,11–13] They can also be helpful for the treatment of cardiovascular disorders and inflammatory diseases,[14] human myelogenous leukemia K562 cells,[15] and can be used as HIV–I NCp7 inhibitors,[16] or non–vanilloid TRPV1 antagonists.[17] A few structures of *S*–alkyl carbodithioate esters with potential therapeutic value are shown in Figure IV.2. Further utility of carbodithioate ester as linkers in solid–phase organic synthesis is also well documented.[18,19] Carbodithioate esters are widely used as suitable ligands to assemble on metal nanoparticles in surface science and nanomaterial chemistry.[20,21] They are also well–known in rubber industry as sulfur vulcanization acceptors,[22] and radical chain transfer agents in the reversible addition fragmentation chain transfer (RAFT) polymerizations.[23–25] Many useful synthetic intermediates contain the carbodithioate ester moiety.[26,27] As a result, several methods for the synthesis of carbodithioate esters have been developed.[28]



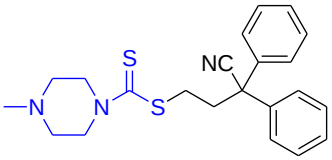
Brassinin,
cancer chemopreventive activity



Sulforamate
cancer chemopreventive agent



RWJ-025856
attenuating effects on tumor necrosis factor a (TNFa)-induced apoptosis in murine fibrosarcoma WEHI 164 cells

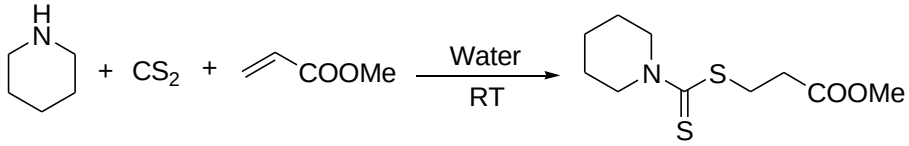


990207
inhibiting the tumor growth of sarcoma 180 (S_{180}), hepatocyte carcinoma 22 (H_{22})

Figure IV.2. Examples of compounds of potential therapeutic value bearing *S*–alkyl carbodithioate esters function

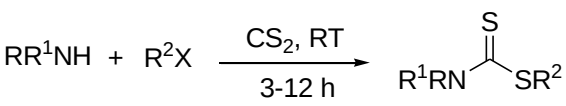
IV.2. Background and objectives

Synthesis of *S*–alkyl/aryl carbodithioate esters is generally achieved by either nucleophilic substitution reactions under basic medium or transition metal–catalyzed cross–coupling reactions. M. R. Saidi reported a highly efficient one–pot amines and carbon disulfide with *α,β*–unsaturated compounds in water. This simple protocol avoids the use of basic and highly toxic organic solvents and catalysts. The catalyst–free, cleaner reaction and simple experimental procedure have been highly acclaimed (Scheme IV.1).[29]



Scheme IV.1. One–pot preparation of dithiocarbamate in water without using any catalyst

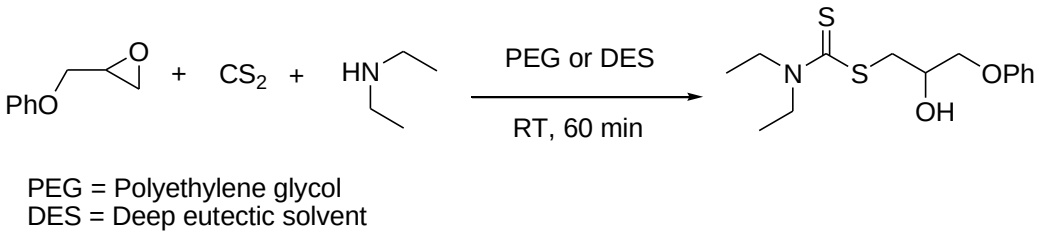
The same group also developed a clean and catalyst–free simple one–pot methodology for the synthesis of *S*–alkyl dithiocarbamate (Scheme IV.2).[30]



Scheme IV.2. One–pot clean method for the synthesis of carbodithioates

A deep eutectic solvent (DES) and polyethylene glycol (PEG) promoted the environmentally friendly and fast synthesis of dithiocarbamate derivatives via a one–pot,

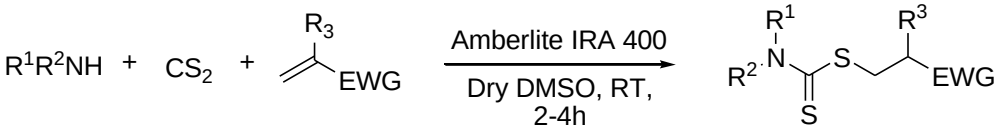
three–component condensation of an amine, carbon disulfide and an epoxide has been developed by N. Azizi et al. The main advantages of the protocol included simple experimental procedures, short reaction times, low cost, efficient yields and use of greener solvent, which made this method as attractive strategy (Scheme IV.3).[31]



PEG = Polyethylene glycol
DES = Deep eutectic solvent

Scheme IV.3. One–pot synthesis of 2–hydroxydithiocarbamates in DES and PEG

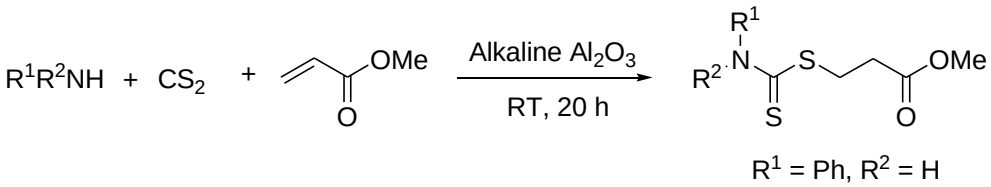
Basic resin (Amberlite IRA 400) supported a highly efficient and one–pot synthesis of dithiocarbamates was done by the Michael addition of dithiocarbamate anion to *α, β*–unsaturated compounds. Dimethyl sulfoxide was used as solvent and the reaction took 2 to 4 hours for completion (Scheme IV.4).[32]



EWG = $-COCH_3$, $-COOCH_3$, $-CONH_2$, -CN

Scheme IV.4. Basic resin (Amberlite IRA 400) supported one–pot synthesis of dithiocarbamate

Alkaline Al_2O_3 mediated Michael addition of electron deficient alkenes with aryl amines and carbondisulfide has been reported by X. Wang et al. A wide range of amines were used and the reaction was clean and reused without complex workup (Scheme IV.5).[33]

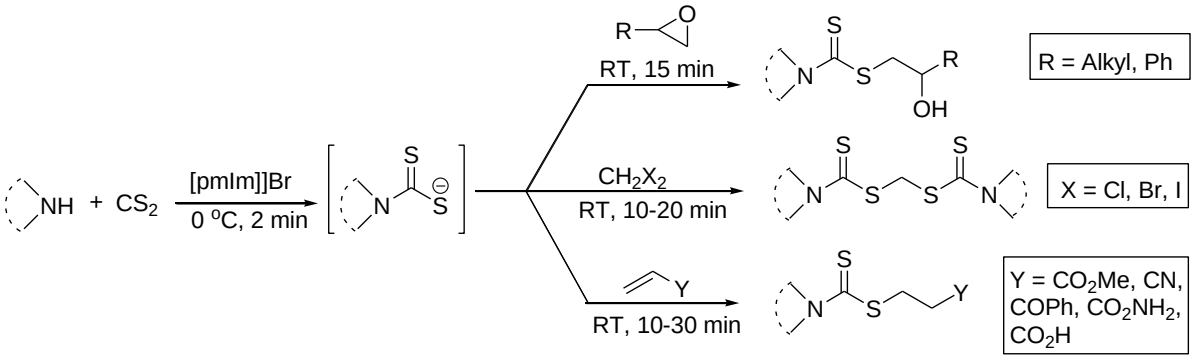


R^1 = Ph, R^2 = H

Scheme IV.5. Michael addition of aryl amines towards electron deficient alkenes

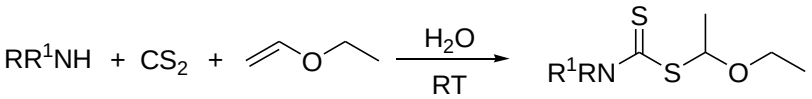
Ranu et al developed a new methodology for the synthesis of dithiocarbamate by one–pot three component condensation of an amine, carbon disulfide and an activated

alkene/dichloromethane/epoxide using a room–temperature ionic liquid (RTIL). The reactions were found to be very fast and symmetrical dithiocarbamates have been synthesized by this methodology (Scheme IV.6).[34]



Scheme IV.6. Synthesis of dithiocarbamates using [pmIm]Br ionic liquid

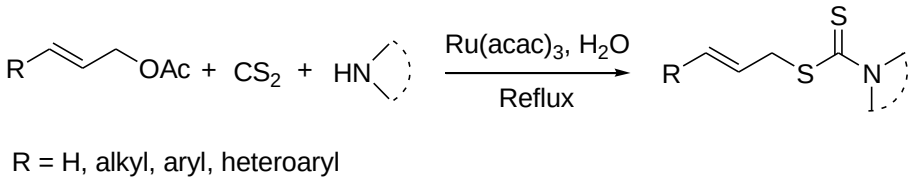
A very common methodology of one–pot three component reactions has been established by A. Z. Halimehjani et al. In this protocol the ethyl vinyl ether was used as an electrophile. This reaction was complete regioselective towards Markovnikov addition (Scheme IV.7).[35]



RR^1NH = Piperidine, pyrrolidine, morpholine, diisopropyl amine, *n*-butyl amine, allyl amine, diallyl amine, benzyl amine

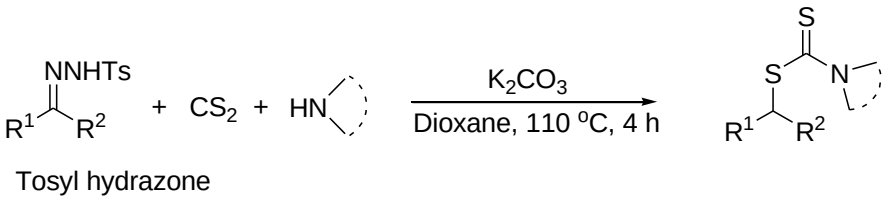
Scheme IV.7. Markovnikov addition reaction of dithiocarbamate to ethyl vinyl ether

Allyl and cinnamyl acetates are rarely used as electrophiles in dithiocarbamates preparation. A convenient and efficient one–pot three component condensation of nonactivated allyl/cinnamyl acetate, carbon disulfide and an amine in presence of $Ru(acac)_3$ in water has been demonstrated by B. C. Ranu et al. The reaction underwent via a catalytic Ru(II) species, generated in situ during the reaction. The methodology was found to be attractive due its operational simplicity, use of low catalyst loading, excellent stereoselectivity in the reactions of trans–cinnamyl acetate and use of water as solvent (Scheme IV.8).[36]



Scheme IV.8. $Ru(acac)_3$ catalyzed synthesis of allyl/cinnamyl dithiocarbamates

Like allyl or cinnamyl acetates tosyl hydrazones were rarely used for the formation of carbodithioates. A new, convenient and efficient transition metal–free synthesis of *S*–alkyl dithiocarbamates through one–pot reaction of *N*–tosylhydrazones, carbon disulfide and amines was reported by Y.–Y. Wei et al. The reaction required a base, high temperature and an organic solvent, dioxane (Scheme IV.9).[37]



Scheme IV.9. Metal free three–component reaction of *N*–tosylhydrazones, carbon disulfide and amines

Anilines can also be used for the preparation of carbodithioate ester bearing *sec*. NH group in the presence of DMSO and strong base like NaOH.[38] Most of the procedures involve harsh reaction conditions, long reaction time, hazardous organic solvents, metal catalysts and bases. Organyl thiocyanates, often considered as psuedohalides and are easily available, were not used as the starting materials, presumably because of the fact that the thiocyanate may undergo disulfide (–S–S–) bond formation under basic medium.[39,40] We found that the reaction of a *sec*. amine with CS_2 produces a stable salt, which can be isolated easily in almost quantitative yield and stored for several weeks in the air. The salt can efficiently react with alkyl/aroyl methyl/cinnamyl thiocyanates in water medium at room temperature to afford corresponding carbodithioate esters in good to excellent yields without formation of any other by–products such as organyl disulfide. Here we describe an efficient, base– and metal–free protocol for the synthesis of various *S*–substituted carbodithioate esters by using variety of cyclic *sec*. amine–based dithiocarbamate salts from diverse organyl thiocyanates. To the best of our knowledge organyl thiocyantes have not been used previously as the precursor for preparation of carbodithioate esters. The other main advantages of this protocol

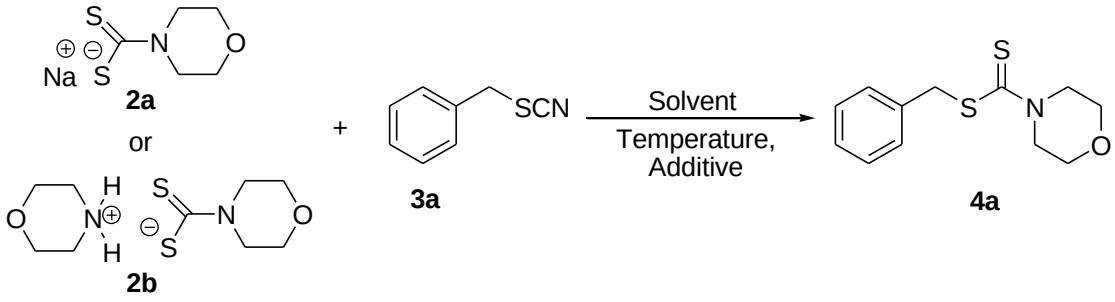
are metal– and alkali–free, which possibly leads to avoid the disulfide bond formation, clean reaction affording excellent yields and can be carried out in water medium at ambient condition.

IV.3. Present work: Results and Discussion

As a part of preliminary study, as presented in Table IV.1, we had conducted the reaction of a neat mixture of benzyl thiocyanate, CS_2 and morpholine in one–pot manner, which led to the pure desired benzyl morpholine–4–carbodithioate ester **4a** in only 72% isolated yield (Table IV.1, entry 1). Moreover, the reaction showed partial formation of dibenzyl disulfide on tlc monitoring of the experiment, although it was not isolated in considerable quantity after column chromatography. Considering that the intermediate salt derived from the amine and CS_2 could be the actual nucleophile, the sodium salt of morpholinodithioformate **2a** was used to react with benzyl thiocyanate **3a** (Table IV.1, entry 2). However, we obtained the desired carbodithioate ester **4a** again with the formation of dibenzyl disulfide, presumably attributable to the basic reaction medium that facilitates the disulfide from benzyl thiocyanate **3a**.[39,40] In order to avoid the basic reaction medium, we considered that the dithiocarbamate salt consisting of both organyl cationic and anionic part might be suitable and accordingly, we prepared the salt **2b** from a mixture of morpholine and CS_2 in diethyl ether following the reported procedure.[41] The salt **2b** now contains morpholino–based cationic and anionic part and stirring a mixture of benzyl thiocyanate **3a** with the salt **2b** (in equimolar quantity) in water at room temperature gave rise to clean reaction without any trace of disulfide formation, producing **4a** in 76% isolated yield (Table IV.1, entry 3). Heating the reaction mixture of **2b** and **3a** in water or ethanol at 60 ^oC resulted in rather better yield of **4a** (78–82%; Table IV.1, entries 4 and 5). On the other hand, use of water–ethanol (1:1) as the solvent and conducting the reaction at room temperature gave **4a** in 80% yield (Table IV.1, entry 6). It is likely that organyl thiocyanates are poorly soluble in water, and we employed two different phase transfer agents, *n*–tetrabutyl ammonium bromide (TBAB) and sodium dodecyl sulfate (SDS). While the use of TBAB was found to improve marginal increase in the yield of **4a** (Table IV.1, entry 7), the presence of SDS (either in stoichiometric or in 10 mol%) afforded **4a** in excellent yield (96%) (Table IV.1, entries 8 and 9). Thus, excellent conversion of benzyl thiocyanate to benzyl morpholine–4–carbodithioate ester **4a** is practically possible if we use separately–prepared amine–based salt and perform the reaction under conditions as in entry 9 of Table IV.1. In aqueous medium reactions, anionic phase

transfer agents as additive are usually more effective than cationic agents.[42] Here, we used both TBAB (cationic) and SDS (anionic) additives and the results are in conformity with previous reports. The better functioning of the anionic phase transfer agents like SDS might be explained in the light of considering the whole system as a microreactor, where organyl thiocyanate having resided in the hydrophobic dodecyl core may come in contact with the reactant (here the dithocarbamate salt) being present in water through the formation of hydrogen bond with anionic sulfate ion.

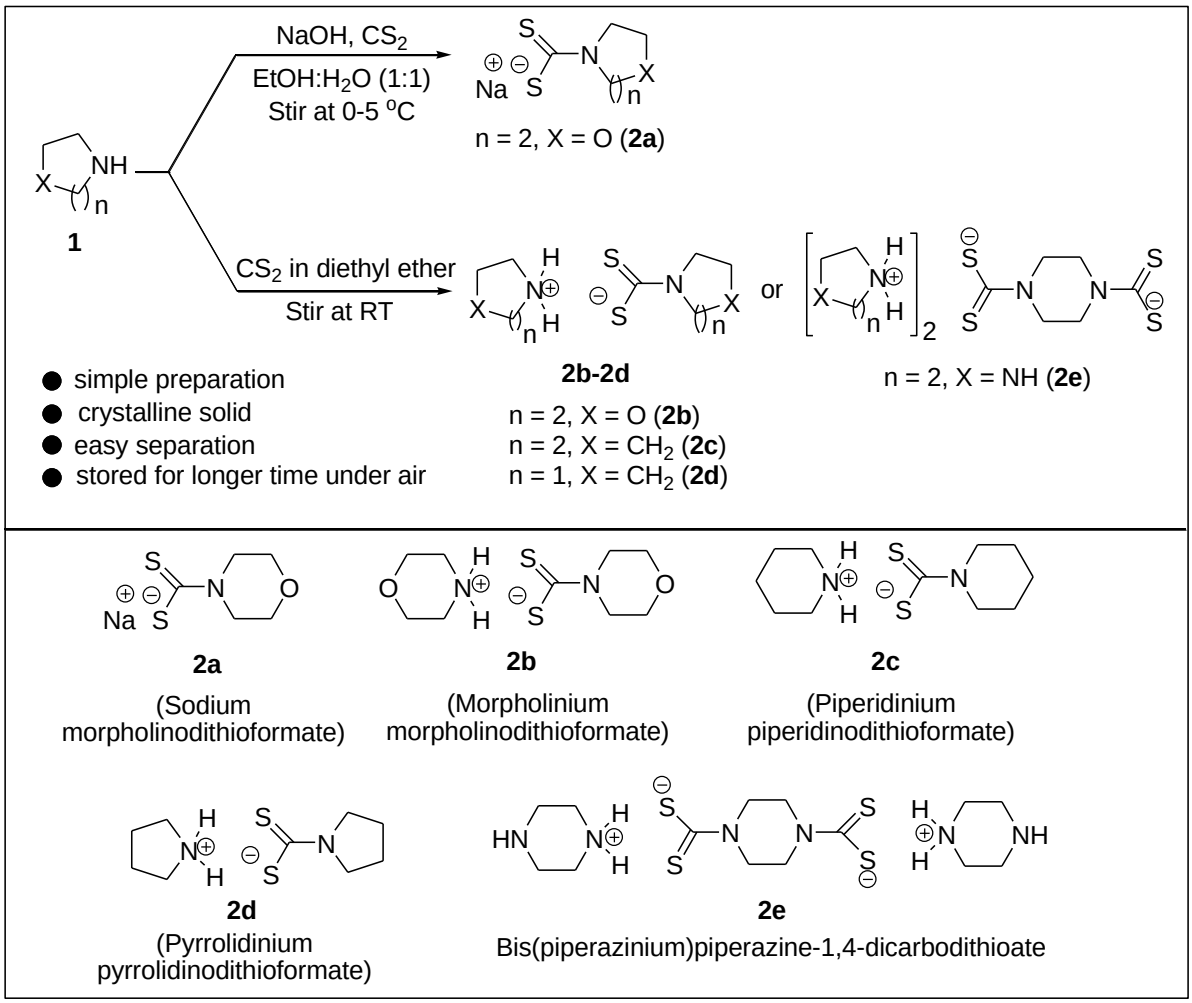
Table IV.1. Optimization of the reaction conditions for the conversion of benzyl thiocyanate to *S*–alkyl cabodithioates.



Entry	Solvent (2 mL)	T (°C)	Additive	Time(h)	Yield[a] (%)
1[b]	Neat	RT	No	1	72
2[c]	Water	RT	No	1	60[d]
3[e]	Water	RT	No	1	76
4	Water	60	No	1	78
5	EtOH	60	No	1	82
6	Water: EtOH	RT	No	1	80
7[f]	Water	RT	TBAB	1	84
8[g]	Water	RT	SDS	1	96
9[h]	**Water**	**RT**	**SDS**	**1**	**96**

[a]Yield represents pure isolated product after purification by column chromatography.
[b]Mixture of benzyl thiocyanate (1 mmol), morpholine (2 mmol) and CS_2 (1 mmol) was stirred at room temperature.
[c]Salt 2a was used.
[d]20% dibenzyl disulphide was isolated.
[e]Salt 2b was used.
[f]Tetrabutyl ammonium bromide (TBAB; stoichiometric) was used.
[g]Sodium dodecyl sulfate (SDS; stoichiometric) was used.
[h]10 mol% SDS was used.

Being encouraged by this observation, we wanted to develop a general and practical procedure for the conversion of organyl thiocyanate into carbodithioate ester. We prepared other dithiocarbamate salts (**2c–2e**) from three different cyclic *sec.* amines such as piperidine, pyrrolidine and piperazine (Scheme IV.10).

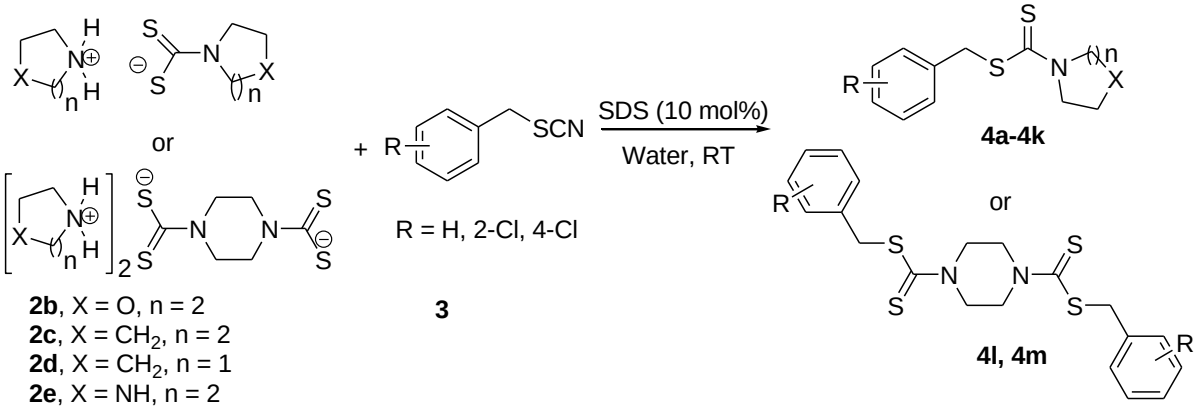


Scheme IV.10. Synthesis of *sec*. cyclic aliphatic amine–based dithiocarbamate salts

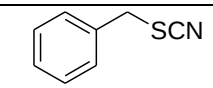
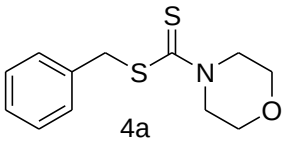
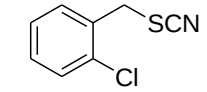
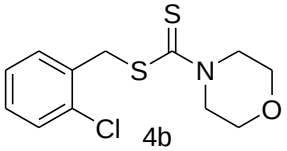
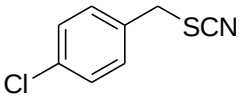
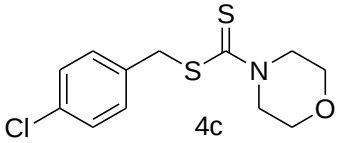
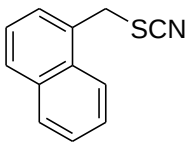
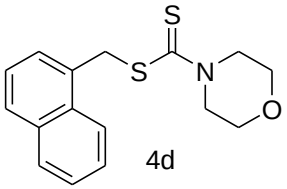
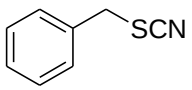
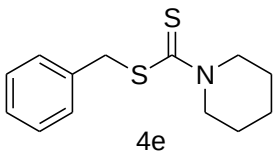
Being encouraged by this observation, we wanted to develop a general and practical procedure for the conversion of organyl thiocyanate into carbodithioate ester. We prepared other dithiocarbamate salts (**2c–2e**) from three different cyclic *sec.* amines such as piperidine, pyrrolidine and piperazine (Scheme IV.10), and employed our optimized conditions (as in entry 9) for reaction with various functionalized organyl thiocyanates. The results are presented in Table IV.2. It is clearly evident that different substituted benzyl thiocyanates and naphthyl methyl thiocyanate underwent smooth conversion to the corresponding dithiocarboate esters with all types of dithiocarbamate salts. While 2– and 4–chloro benzyl

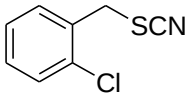
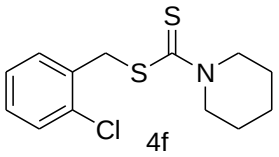
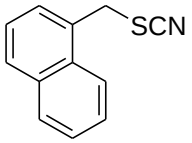
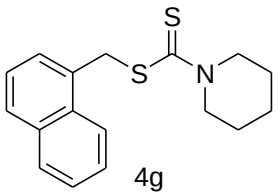
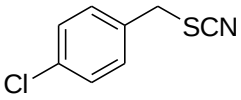
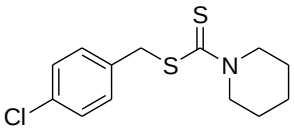
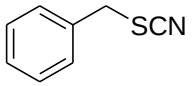
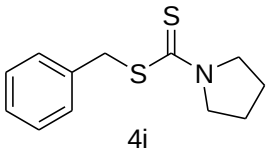
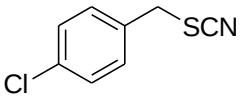
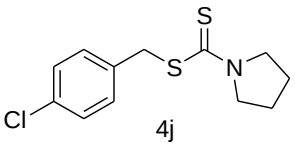
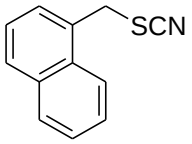
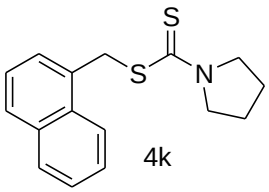
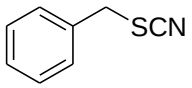
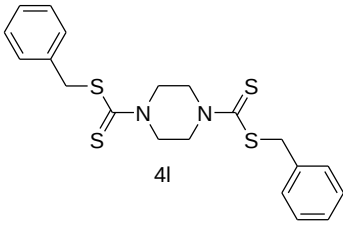
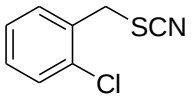
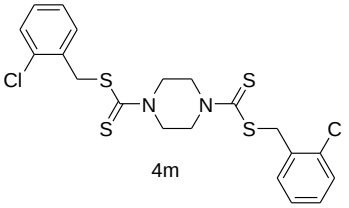
thiocyanates worked equally efficiently without any steric encumbrance, the piperazine–based dithiocarbamate salt **2e** reacted with benzyl or 2–chlorobenzyl thiocyanates to produce bis–carbodithioate esters in 82–83% yields within 3h (**4l** and **4m**).

Table IV.2. Synthesis of diverse *S*–alkyl carbodithioates by varying organyl thiocyanates and dithiocarbamate salts.[a,b]



2b, X = O, n = 2
2c, X = CH_2, n = 2
2d, X = CH_2, n = 1
2e, X = NH, n = 2

Entry	R^1–SCN **(3)**	Salt **(2)**	Time (h)	T (^oC)	Product **(4)**	Yield (%)
1		**2b**	1.0	RT	 4a	96
2		**2b**	1.0	RT	 4b	98
3		**2b**	1.0	RT	 4c	97
4		**2b**	1.5	RT	 4d	87
5		**2c**	1.0	RT	 4e	95

6		**2c**	1.0	RT	 4f	98
7		**2c**	1.5	RT	 4g	89
8		**2c**	1.0	RT	 4h	97
9		**2d**	2.0	RT	 4i	94
10		**2d**	2.5	RT	 4j	96
11		**2d**	2.5	RT	 4k	86
12		**2e**	3.0	RT	 4l	82
13		**2e**	3.0	RT	 4m	83

[a]A mixture of 2 (1.0 mmol), 3 (1.0 mmol), SDS (10 mol%) in water (2 mL) was stirred at RT in open air. For 4l and 4m, 2 mmol of 3 was used.

[b]Yield represents pure product isolated by column chromatography.

The carbodithioate esters are identified by melting point and compared with literature report (for solid compounds) and hence characterized by ^{1}H–NMR, ^{13}C–NMR spectroscopy. High resolution mass spectrometry was performed in some cases to identify the carbodithioate esters. The HRMS spectra of compound **4b** are given in Figure IV.3 below:

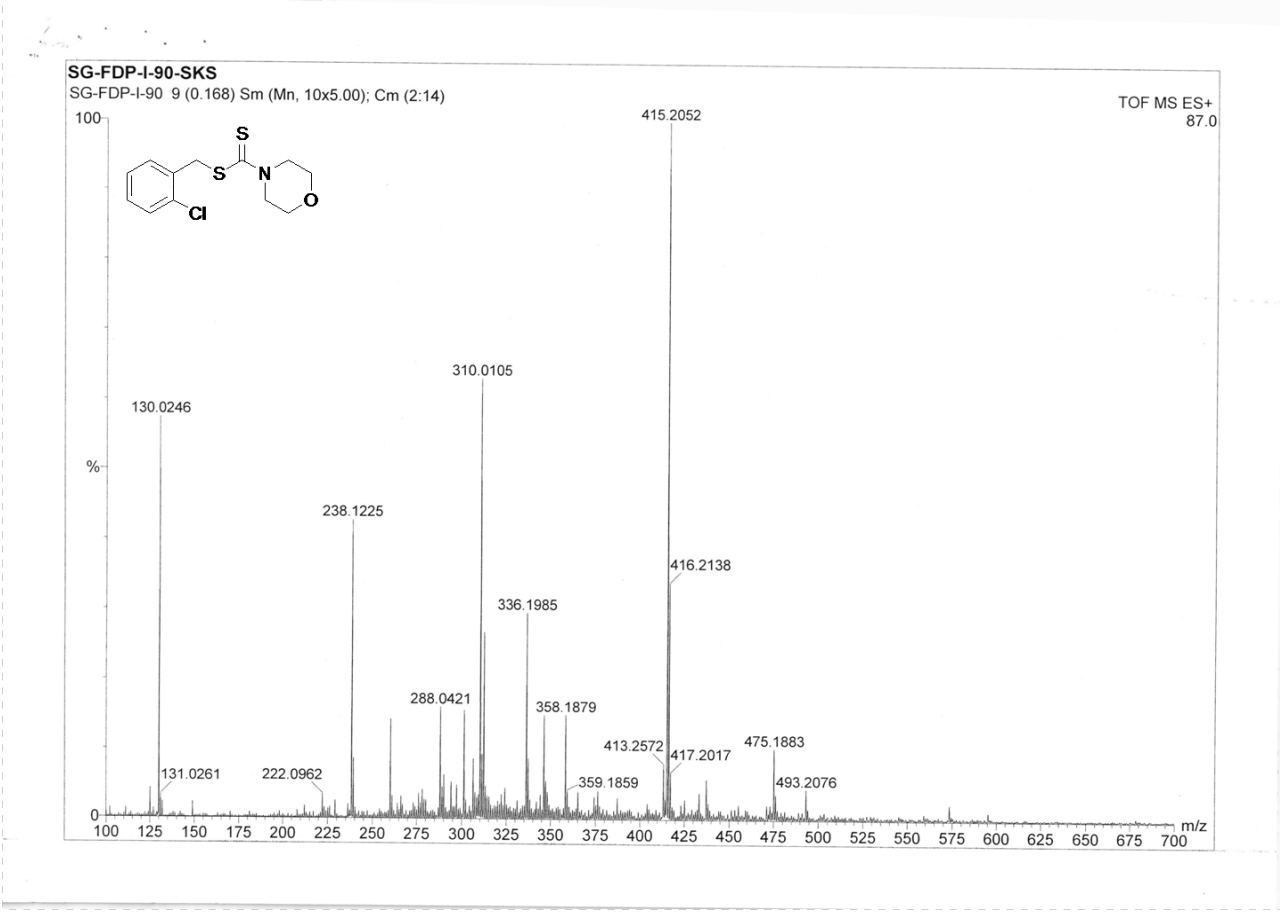
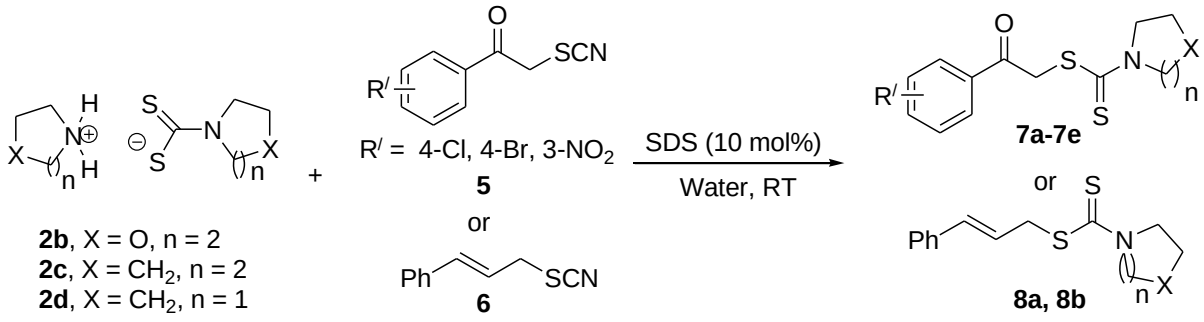


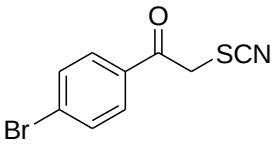
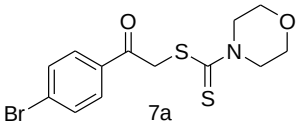
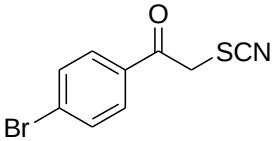
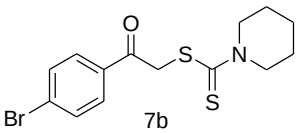
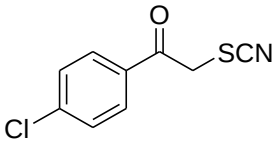
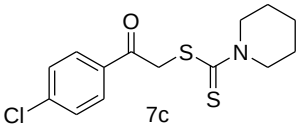
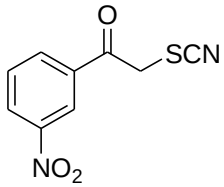
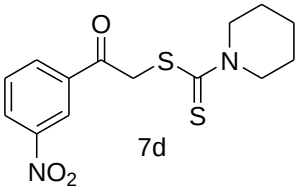
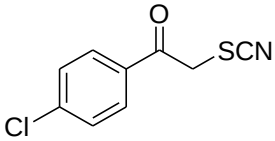
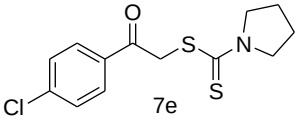
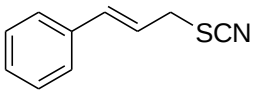
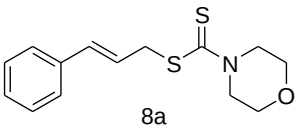
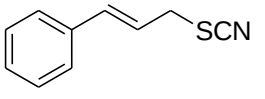
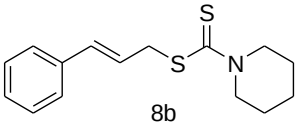
Figure IV.3. HRMS of compound **4b**

To broaden the scope of the reaction further, alkyl thiocyanates bearing *β*–carbonyl function, **5** (e.g. aroyl methyl thiocyanates) or *β*–alkenyl function, **6** (e.g. styrenyl methyl thiocyanates) were subjected to similar reaction. Corresponding organic carbodithioate esters containing carbonyl or styrenyl methyl group could be easily synthesized in aqueous medium at ambient temperature. Three different dithiocarbamate salts of *sec*. amine (**2b–2d**) were used and the results are presented in Table IV.3 (**7a–7e**, **8a** and **8b**). In all cases, corresponding benzoyl methyl carbodithioates bearing Cl, Br or NO_2 groups attached with the aromatic ring were prepared in excellent isolated yields (**7a–7e**). All the compounds were characterized by spectral data and compared with melting points wherever known and reported. Facile preparation of these functionalized carbodithioate esters via easy

nucleophilic substitution reaction from alkyl thiocyanates in aqueous medium at ambient temperature is notable and not reported previously via one–pot three–component reaction.

Table IV.3. Further functionalizations in the synthesis of *S*–alkyl carbodithioates.[a,b]

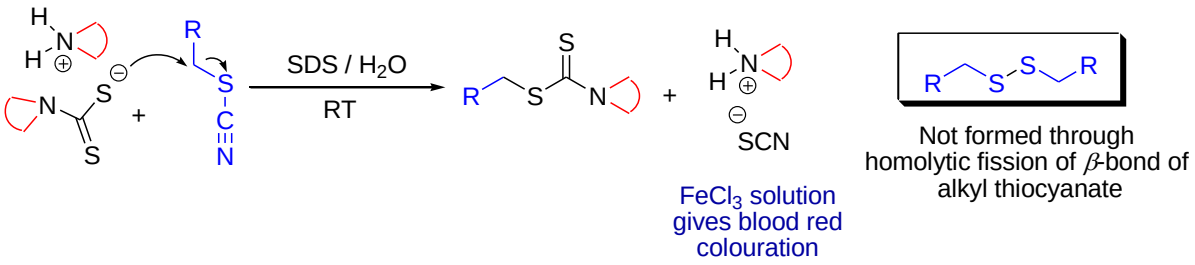


Entry	R^2–SCN (**5** and **6**)	Salt (**2**)	Time(h)	T(°C)	Product (**7** and **8**)	Yield (%)
1		**2b**	3.0	RT	 7a	95
2		**2c**	3.0	RT	 7b	94
3		**2c**	4.0	RT	 7c	95
4		**2c**	3.5	RT	 7d	86
5		**2d**	3.0	RT	 7e	96
6		**2b**	1.5	RT	 8a	92
7		**2c**	1.5	RT	 8b	93

[a] A mixture of 2 (1.0 mmol), 5 or 6 (1.0 mmol), SDS (10 mol%) in water (2 mL) was stirred at RT in open air.
[b] Yield represents pure product isolated by column chromatography.

IV.4. Mechanism

The reaction presumably occurs via simple nucleophilic substitution reaction. Organyl thiocyanates are considered as psuedohalides that might not produce the corresponding carbocation easily and hence the reaction is expected to proceed via S_N2 pathway (Scheme IV.11). The dithiocarbamate salt consisting of both organyl cationic and anionic system seems to be more active than using in situ mixture of *sec*. amine and CS_2. Use of additives like SDS might help organic reactants to become rather homogeneous affording excellent conversions. The possibility of formation of thiyl radical via *β*–bond cleavage of the alkyl thiocyanate can be excluded as reaction conditions neither support radical formation nor the corresponding disulfide is formed in the reaction.[43,44] On the other hand, aqueous ferric chloride solution produces blood–red coloration suggesting the formation of thiocyanate anion.



Scheme IV.11. Proposed reaction mechanism

IV.5. Conclusion

In conclusion, we have shown that easily accessible and air–stable cyclic *sec.* amine–based dithiocarbamate salts could serve as an efficient reagent for the preparation of a large variety of *S*–substituted carbodithioate esters from rarely used organyl thiocyanates as a common strategy. The use of this type salt not only shows superior activity to the existing one–pot three–component procedure but also establishes as alternative reagent, obtained easily in quantitative conversion, for the preparation of carbodithioate esters. The simple procedure can be carried out at room temperature, in water medium and afforded with excellent yields.

IV.6. Experimental section

IV.6.1. General information

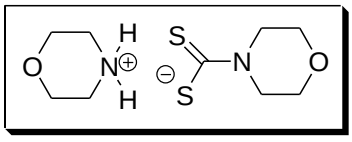
Morpholine, piperidine and pyrrolidine were purchased from Lancaster and used after distillation. Piperazine was purchased from Loba Chemie. Carbon disulfide (CS_2) and sodium dodecyl sulfate (SDS) were purchased from SDFCL and used directly. Benzyl, naphthyl methyl, cinnamyl and aroyl methyl thiocyanates were prepared from reported procedure and purified by column chromatography before use. Melting point of the solid compounds was determined in concentrated H_2SO_4 bath. FT–IR spectra were recorded with a FT–IR–8300 SHIMADZU spectrophotometer using a KBr pellet method for solid compounds and in neat for liquid compounds. NMR spectra were taken in $CDCl_3$ using a Bruker AV–300 spectrometer operating for ^1H at 300 MHz and for ^{13}C at 75 MHz. The spectral data were measured using TMS as the internal standard. HRMS was performed by Micromass Q–TOF Spectrometer under ESI (positive mode).

IV.6.2. General Procedure for the synthesis of cyclic ammonium salts of dithiocarbamic acid (2b–2e)[41]

A solution of CS_2 (5 mmol) in diethyl ether (5 mL) was slowly added to a solution of morpholine (10 mmol) or piperidine (10 mmol) or pyrrolidine (10 mmol) in diethyl ether (5 mL). The reaction mixtures were stirred for 30 min at room temperature. Solid salts were precipitated during this time and were filtered off through Buchner funnel, washed with diethyl ether and dried under vacuum to obtain the desired salts **2b**–**2d**. In the case of **2e**, a solution of CS_2 (6 mmol) in diethyl ether (5 mL) was slowly added to a solution of piperazine (9 mmol) in diethyl ether (6 mL). The reaction mixture was stirred for 45 min at room temperature. The grey solids were filtered off, washed with diethyl ether and dried under vacuum to get the desired salt **2e**.

IV.6.2.1. Physical properties and spectral data of cyclic ammonium salts of dithiocarbamic acid (2b–2e)

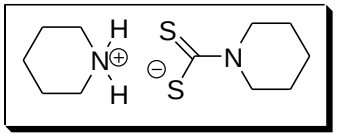
Morpholinium morpholinodithioformate (Salt 2b)[41]



White solid; yield: 1.23 g (98%); mp 197–200 ^oC (Lit.[41] Mp 195–197 ^oC)

IR (KBr): ν_{max} = 2854, 2711, 2475, 1583, 1420, 1255, 1215, 1112, 978, 876 cm^{-1}.

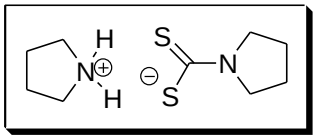
Piperidinium piperidinodithioformate (Salt 2c)



White solid; yield: 1.20 g (98%); mp 164–166 ^{o}C (Lit.[41] Mp 160 ^{o}C)

IR (KBr): ν_{max} = 2936, 2843, 2731, 2497, 1583, 1409, 1215, 1122, 958 cm^{-1}.

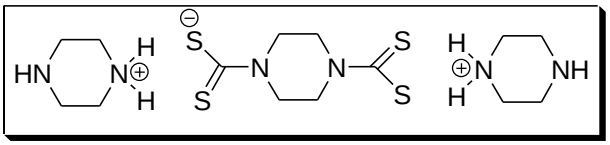
Pyrrolidinium pyrrolidinodithioformate (Salt 2d)



Off–white solid; yield: 1.05 g (96%); mp 149–151 ^{o}C

IR (KBr): ν_{max} = 2946, 2864, 2516, 2393, 1390, 1318, 1164, 999, 938 cm^{-1}.

Bis(piperazinium)piperazine–1,4–dicarbodithioate (Salt 2e)



Grey solid; yield: 1.19 g (97%); mp 238–242 ^{o}C

IR (KBr): ν_{max} = 3162, 2915, 2434, 2331, 1634, 1390, 1225, 1123, 958, 855 cm^{-1}.

IV.6.3. General procedure for the synthesis of *S*–alkyl carbodithioate esters

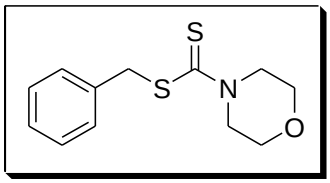
A mixture of organyl thiocyanate (1 mmol), dithiocarbamate salt (1 mmol) and sodium dodecyl sulfate (SDS, 0.1 mmol) in water (2 mL) was stirred vigorously with a magnetic bar at room temperature. The progress of the reaction was monitored by tlc. After the reaction was continued for specified time, as mentioned in Table IV.2 & IV.3, the reaction mixture was extracted with ethyl acetate (3×5 mL) and the combined organic extracts were collected over anhydrous Na_2SO_4. Evaporation of the volatiles afforded the crude product, which was further purified by column chromatography over silica gel. Elution with a mixture of EtOAc−PE furnished the desired product. Yields of the products are shown in Table IV.2 & IV.3.

All products were identified and characterized by spectral data (FT–IR, ^{1}H– &, ^{13}C–NMR), by melting point for solid compounds (compared wherever known). Unknown carbodithioate esters were further analyzed either by HRMS or by elemental analysis.

IV.6.3.1. Physical properties and spectral data of carbodithioate esters

Table IV.2, 4a

Benzyl morpholine–4–carbodithioate[37]



Light yellow solid, mp 64–65 ^{o}C (Lit.[32] 59–60 ^{o}C)

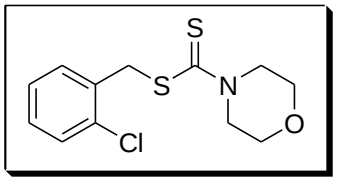
IR (KBr): ν_{max} = 3038, 2976, 2869, 1920, 1635, 1617, 1559, 1489, 1456, 1304, 1271, 1235, 924, 825, 725, 543 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.73 (s, 4H, 2 × OCH_2), 4.01–4.33 (m, 4H, 2 × NCH_2), 4.57 (s, 2H, SCH_2), 7.22–7.39 (m, 5H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 42.0 (SCH_2), 50.8 (NCH_2), 66.3 (OCH_2), 127.6, 128.7, 129.4, 135.8, 197.1 (C=S).

Table IV.2, 4b

2–Chlorobenzyl morpholine–4–carbodithioate



White crystalline solid, mp 94–96 ^{o}C

IR (KBr): ν_{max} = 3053, 2992, 2931, 2855, 1918, 1654, 1635, 1617, 1542, 1444, 1347, 1310, 1271, 1053, 1028, 868, 731, 582 cm^{-1}.

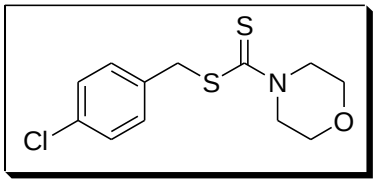
^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.77 (s, 4H, 2 × OCH_2), 4.17 (s, br, 4H, 2 × NCH_2), 4.76 (s, 2H, SCH_2), 7.21–7.64 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 39.5 (SCH_2), 50.9 (NCH_2), 66.2 (OCH_2), 126.9, 129.1, 129.6, 131.6, 134.1, 134.6, 196.9 (C=S).

HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{12}H_{14}ClNONaS_2$: 310.0103; found 310.0105.

Table IV.2, 4c

4–Chlorobenzyl morpholine–4–carbodithioate



White crystalline solid, mp 79–81 ^{o}C

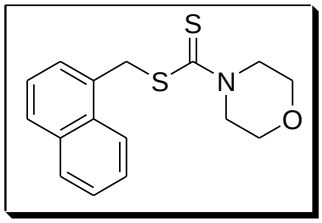
IR (KBr): ν_{max} = 3007, 2977, 2916, 2870, 1833, 1656, 1620, 1542, 1423, 1268, 1217, 1034, 998, 837, 643 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.66 (s, 4H, 2 × OCH_2), 3.90 (s, 2H, NCH_2), 4.17 (s, 2H, NCH_2), 4.47 (s, 2H, SCH_2), 7.17–7.25 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 40.83 (SCH_2), 50.83 (NCH_2), 66.10 (OCH_2), 128.60, 130.57, 133.26, 134.59, 196.50 (C=S).

Table IV.2, 4d

(Naphthalen–1–yl) methyl morpholine–4–carbodithioate



Light brown solid, mp 115–117 ^{o}C

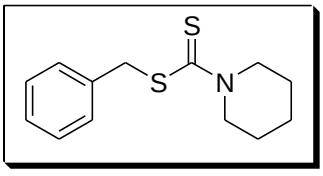
IR (KBr): ν_{max} = 3053, 2976, 2900, 2869, 1699, 1578, 1538, 1420, 1356, 1301, 1271, 1189, 998, 786, 630 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.66 (s, 4H, 2 × OCH_2), 3.91–4.06 (m, 4H, 2 × NCH_2), 4.95 (s, 2H, SCH_2), 7.31–7.52 (m, 4H), 7.71–7.98 (m, 2H), 8.00–8.01 (m, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 40.3 (SCH_2), 50.5 (NCH_2), 66.2 (OCH_2), 123.9, 125.4, 126.0, 126.5, 128.3, 128.8, 128.8, 131.0, 131.8, 133.9, 197.2 (C=S).

Table IV.2, 4e

Benzyl piperidine–1–carbodithioate[45]



Pale yellow viscous liquid

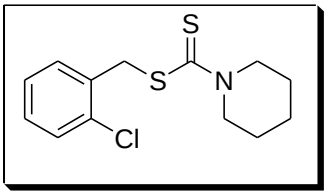
IR (neat): ν_{max} = 3040, 2974, 2864, 1945, 1620, 1590, 1545, 1495, 1358, 1340, 1291, 1279, 1222, 1016, 980, 840, 742 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.62 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.80 (s, br, 2H, NCH_2), 4.21 (s, br, 2H, NCH_2), 4.49 (s, 2H, SCH_2), 7.15–7.33 (m, 5H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2CH_2\underline{CH_2}$), 25.8 ($NCH_2\underline{CH_2}$), 42.2 ($SCH_2$), 52.7 ($NCH_2$), 127.4, 128.6, 129.4, 136.1, 195.3 (C=S).

Table IV.2, 4f

2–Chlorobenzyl piperidine–1–carbodithioate



Yellow viscous liquid

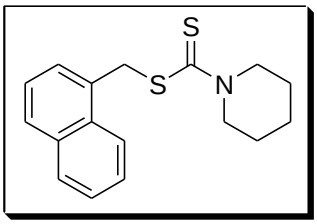
IR (neat): ν_{max} = 3010, 2970, 2860, 1996, 1580, 1546, 1493, 1357, 1340, 1280, 1224, 1074, 946, 840, 746, 650 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.69 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.87 (s, br, 2H, NCH_2), 4.29 (s, br, 2H, NCH_2), 4.72 (s, 2H, SCH_2), 7.18–7.23 (m, 2H), 7.34–7.38 (m, 1H), 7.54–7.58 (m, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2CH_2\underline{CH_2}$), 25.6 ($NCH_2\underline{CH_2}$), 39.7 ($SCH_2$), 51.4 ($NCH_2$), 53.1 ($NCH_2$), 126.9, 128.9, 129.5, 131.6, 134.4, 134.5, 194.9 (C=S).

Table IV.2, 4g

(Naphthalen–1–yl) methyl piperidine–1–carbodithioate



White solid, mp 93–95 ^oC

IR (KBr): ν_{max} = 3038, 2947, 2870, 1620, 1596, 1563, 1542, 1474, 1435, 1399, 1365, 1281, 1235, 1210, 1113, 980, 870, 776, 670, 588 cm^{-1}.

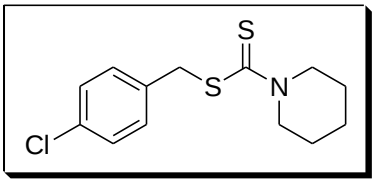
^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.63 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.75 (s, br, 2H, NCH_2), 4.27 (s, br, 2H, NCH_2), 4.93 (s, 2H, SCH_2), 7.31–7.58 (m, 4H), 7.71–7.85 (m, 2H), 8.0–8.01 (m, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2CH_2\underline{CH_2}$), 25.9 ($NCH_2\underline{CH_2}$), 40.6 ($SCH_2$), 52.8 ($NCH_2$), 124.1, 125.5, 125.9, 126.4, 128.3, 128.6, 128.8, 131.4, 131.9, 133.9, 195.3 (C=S).

HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{17}H_{19}NNaS_2$: 324.0857; found 324.0855.

Table IV.2, 4h

4–Chlorobenzyl piperidine–1–carbodithioate



White solid, mp 83–85 ^oC

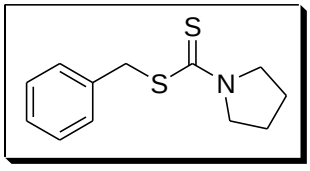
IR (KBr): ν_{max} = 3007, 1961, 2855, 1632, 1617, 1577, 1542, 1508, 1481, 1429, 1378, 1281, 1225, 1110, 1080, 974, 843, 746, 652 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.62 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.79 (s, br, 2H, NCH_2), 4.22 (s, br, 2H, NCH_2), 4.44 (s, 2H, SCH_2), 7.15–7.27 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2CH_2\underline{CH_2}$), 25.5 ($NCH_2\underline{CH_2}$), 41.2 ($SCH_2$), 53.1 ($NCH_2$), 128.7, 130.7, 133.2, 135.0, 194.7 (C=S).

Table IV.2, 4i

Benzyl pyrrolidine–1–carbodithioate[45]



Yellow liquid

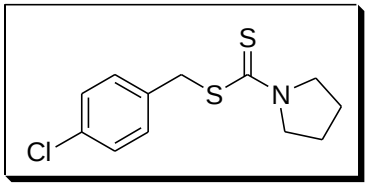
IR (neat): ν_{max} = 3048, 2970, 2865, 1903, 1590, 1440, 1365, 1308, 1216, 1070, 1012, 944, 826, 780, 503 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.92–2.10 (m, 4H, $NCH_2(\underline{CH_2})_2$) 3.62 (t, *J* = 6.3 Hz, 2H, NCH_2), 3.93 (t, *J* = 6.9 Hz, 2H, NCH_2), 4.58 (s, 2H, SCH_2), 7.22–7.33 (m, 3H), 7.38–7.41 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2\underline{CH_2}$), 26.1 ($NCH_2\underline{CH_2}$), 41.3 (SCH_2), 50.5 (NCH_2), 55.0 (NCH_2), 127.4, 128.6, 129.3, 136.5, 192.4 (C=S).

Table IV.2, 4j

4–Chlorobenzyl pyrrolidine–1–carbodithioate



Pale yellow solid, mp 60–62 ^{o}C

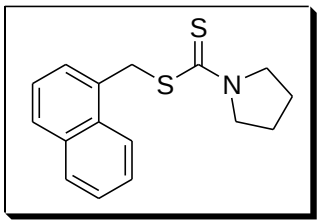
IR (KBr): ν_{max} = 2966, 2864, 1903, 1595, 1441, 1328, 1092, 1009, 948, 825, 744, 507 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.92–2.10 (m, 4H, $NCH_2(\underline{CH_2})_2$) 3.62 (t, *J* = 6.3 Hz, 2H, NCH_2), 3.93 (t, *J* = 6.9 Hz, 2H, NCH_2), 7.24–7.27 (m, 2H), 7.32–7.35 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.2 ($NCH_2\underline{CH_2}$), 26.0 ($NCH_2\underline{CH_2}$), 40.2 (SCH_2), 50.6 (NCH_2), 55.1 (NCH_2), 128.6, 130.6, 133.1, 135.4, 191.8 (C=S).

Table IV.2, 4k

(Naphthalen–1–yl) methyl pyrrolidine–1–carbodithioate



White solid, mp 116–118 ^{o}C

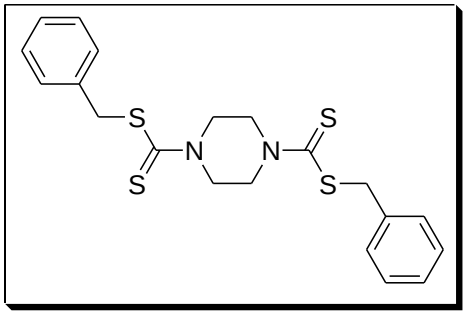
IR (KBr): ν_{max} = 3040, 2950, 2880, 1542, 1450, 1400, 1364, 1342, 1280, 1210, 1134, 1072, 980, 808, 770, 672, 540 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.87–1.97 (m, 4H, $NCH_2(\underline{CH_2})_2$), 3.51 (t, *J* = 6.9 Hz, 2H, NCH_2), 3.94 (t, *J* = 6.6 Hz, 2H, NCH_2), 5.01 (s, 2H, SCH_2), 7.34–7.40 (m, 1H), 7.43–7.54 (m, 2H), 7.58 (d, *J* = 6.9 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.81–7.84 (m, 1H), 8.08 (d, *J* = 8.1 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2\underline{CH_2}$), 26.1 ($NCH_2\underline{CH_2}$), 39.6 (SCH_2), 50.5 (NCH_2), 55.0 (NCH_2), 124.1, 125.5, 125.9, 126.4, 128.2, 128.6, 128.8, 131.8, 131.8, 133.9, 192.3 (C=S).

Table IV.2, 4l

Dibenzyl piperazine–1,4–dicarbodithioate[46]



White solid, mp 124–126 ^{o}C (Lit.[46] 122–123 ^{o}C)

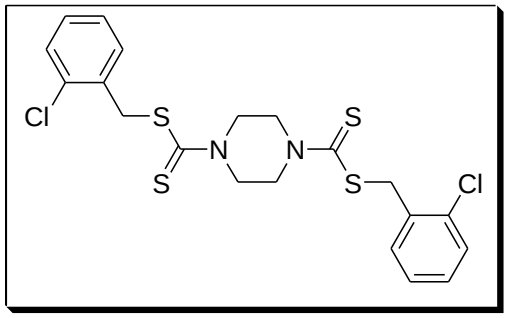
IR (KBr): ν_{max} = 3068, 3038, 2931, 1538, 1505, 1474, 1435, 1413, 1277, 1210, 1159, 1043, 924, 849, 694 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 4.18 (s, br, 8H, 4 × NCH_2), 4.51 (s, 4H, 2 × SCH_2) 7.19–7.32 (m, 10H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 42.2 (SCH_2), 48.7 (NCH_2), 127.7, 128.7, 129.4, 135.5, 197.5 (C=S).

Table IV.2, 4m

Bis–(2–chlorobenzyl) piperazine–1,4–dicarbodithioate



Grey solid, mp 148–150 ^{o}C

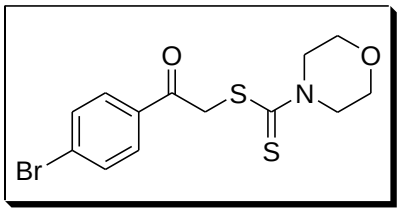
IR (KBr): ν_{max} = 2916, 1640, 1420, 1276, 1041, 990, 928, 846, 744 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 4.28 (s, br, 8H, 4 × NCH_2), 4.72 (s, 4H, 2 × SCH_2) 7.18–7.26 (m, 4H), 7.35–7.39 (m, 2H), 7.53–7.56 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 39.6 (SCH_2), 48.9 (NCH_2), 126.9, 129.2, 129.6, 131.5, 133.8, 134.6, 197.2 (C=S).

Table IV.3, 7a

4–Bromo phenacyl morpholine–4–carbodithioate



White solid, mp 164–166 ^{o}C

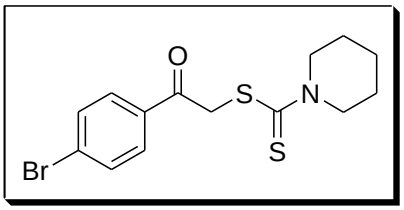
IR (KBr): ν_{max} = 2967, 2906, 2855, 1686, 1583, 1430, 1276, 1125, 1112, 990, 816, 539 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.71 (t, *J* = 4.8 Hz, 4H, 2 × OCH_2), 3.97 (s, br, 2H, NCH_2), 4.2 (s, br, 2H, NCH_2), 4.77 (s, 2H, SCH_2), 7.54–7.59 (m, 2H), 7.84–7.88 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 44.3 (SCH_2), 51.5 (NCH_2), 66.2 (OCH_2), 128.8, 130.1, 132.1, 134.9, 192.3 (C=O), 195.65 (C=S).

Table IV.3, 7b

4–Bromo phenacyl piperidine–1–carbodithioate



White solid, mp 116–118 ^{o}C

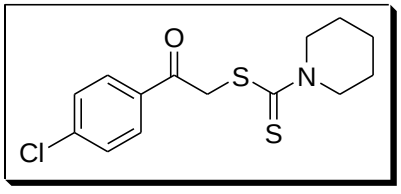
IR (KBr): ν_{max} = 3007, 2947, 2869, 1687, 1584, 1438, 1362, 1286, 1253, 973, 858, 666 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.65 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.89 (s, br, 2H, NCH_2), 4.18 (s, br, 2H, NCH_2), 4.77 (s, 2H, SCH_2), 7.54–7.57 (m, 2H), 7.86–7.89 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.2 ($NCH_2CH_2\underline{CH_2}$), 25.9 ($NCH_2\underline{CH_2}$), 44.5 ($SCH_2$), 51.7 ($NCH_2$), 53.6 ($NCH_2$), 128.6, 130.1, 131.9, 135.0, 192.7 (C=O), 193.7 (C=S).

Table IV.3, 7c

4–Chloro phenacyl piperidine–1–carbodithioate



Yellowish white solid, mp 110–112 ^{o}C

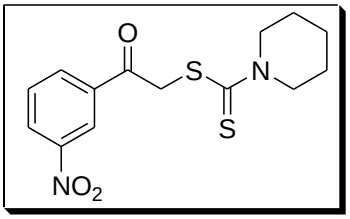
IR (KBr): ν_{max} = 3007, 2961, 2855, 1690, 1587, 1438, 1347, 1244, 1113, 971, 858, 682, 548 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.65 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.89 (s, br, 2H, NCH_2), 4.19 (s, br, 2H, NCH_2), 4.77 (s, 2H, SCH_2), 7.54–7.58 (m, 2H), 7.85–7.90 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.2 ($NCH_2CH_2\underline{CH_2}$), 25.4 ($NCH_2\underline{CH_2}$), 26.1 ($NCH_2\underline{CH_2}$), 44.5 ($SCH_2$), 51.8 ($NCH_2$), 53.7 ($NCH_2$), 128.7, 130.1, 132.0, 135.0, 192.7 (C=O), 193.6 (C=S).

Table IV.3, 7d

3–Nitro phenacyl piperidine–1–carbodithioate



Pale yellow solid, mp 109–111 ^{o}C

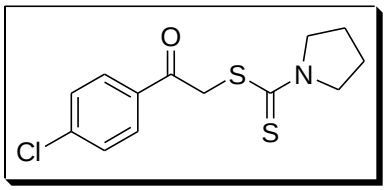
IR (KBr): ν_{max} = 2926, 2854, 1697, 1613, 1532, 1430, 1337, 1204, 1112, 1072, 979, 804, 733, 672 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.73 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.97 (s, br, 2H, NCH_2), 4.25 (s, br, 2H, NCH_2), 4.86 (s, 2H, SCH_2), 7.69–7.74 (m, 1H), 8.40–8.46 (m, 2H), 8.90–8.91 (m, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.16 ($NCH_2CH_2\underline{CH_2}$), 26.02 ($NCH_2\underline{CH_2}$), 44.09 ($SCH_2$), 52.09 ($NCH_2$), 53.79 ($NCH_2$), 123.45, 127.49, 129.95, 134.13, 137.87, 148.58, 191.84 (C=O), 193.39 (C=S).

Table IV.3, 7e

4–Chloro phenacyl pyrrolidine–1–carbodithioate



Pale yellow solid, mp 102–104 ^{o}C

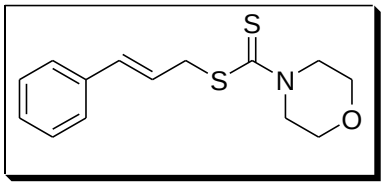
IR (KBr): ν_{max} = 2957, 2876, 1676, 1583, 1430, 1286, 1184, 1080, 990, 958, 825, 528 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.94–2.03 (m, 2H, $NCH_2\underline{CH_2}$), 2.06–2.14 (m, 2H, $NCH_2\underline{CH_2}$), 3.74 (t, *J* = 6.9 Hz, 2H, NCH_2), 3.9 (t, *J* = 6.9 Hz, 2H, NCH_2), 4.85 (s, 2H, SCH_2), 7.44–7.47 (m, 2H), 8.01–8.04 (m, 2H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2\underline{CH_2}$), 26.1 ($NCH_2\underline{CH_2}$), 44.0 (SCH_2), 50.8 ($N\underline{CH_2}$), 55.5 ($N\underline{CH_2}$), 128.9, 130.0, 134.4, 139.8, 190.7 (C=O), 192.4 (C=S).

Table IV.3, 8a

(*E*)–Cinnamyl morpholine–4–carbodithioate[36]



White crystalline solid, mp 80–82 ^{o}C (Lit.[36] reported as yellowish viscous liquid)

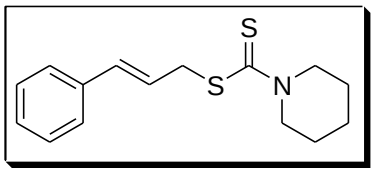
IR (KBr): ν_{max} = 3038, 2961, 2869, 1720, 1620, 1577, 1469, 1304, 1268, 1220, 1113, 992, 755 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.78 (t, *J* = 4.5 Hz, 4H, 2 × OCH_2), 4.17–4.24 (m, 6H, 2 × NCH_2, SCH_2), 6.28–6.38 (m, 1H, PhCH=C$\underline{H}CH_2$), 6.67 (d, *J* = 15.6 Hz, 1H, PhCH), 7.23–7.41 (m, 5H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 39.97 (SCH_2), 50.90 (NCH_2), 66.26 (OCH_2), 123.68, 126.45, 127.76, 128.56, 133.95, 136.60, 197.03 (C=S).

Table 3, 8b

(*E*)–Cinnamyl piperidine–1–carbodithioate[36]



White crystalline solid, mp 73–75 ^{o}C (Lit.[36] reported as yellowish viscous liquid)

IR (KBr): ν_{max} = 3048, 2947, 2869, 1617, 1566, 1472, 1435, 1265, 1235, 1135, 1116, 1110, 973, 743 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 1.63 (s, 6H, $NCH_2(\underline{CH_2})_3$), 3.82 (s, br, 2H, NCH_2), 4.01–4.13 (m, 2H, SCH_2), 4.23 (s, br, 2H, NCH_2), 6.20–6.31 (m, 1H, PhCH=C$\underline{H}CH_2$), 6.56 (d, *J* = 15.9 Hz, 1H, PhCH), 7.12–7.31 (m, 5H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 24.3 ($NCH_2CH_2\underline{CH_2}$), 26.0 ($NCH_2\underline{CH_2}$), 40.2 ($SCH_2$), 51.4 ($NCH_2$), 124.2, 126.4, 127.7, 128.5, 133.6, 136.7, 195.0 (C=S).

IV.7. References

References are given in BIBLIOGRAPHY under Chapter IV (pp. 150–153).