CHAPTER V

Unprecedented amidation of 'transient' aryl thioaldehydes by *N,N*-dimethylformamide under basic conditions

V.A. Introduction

Usually amides are the least-reactive classes of compounds among carboxylic acid derivatives whereas the replacement of the oxygen atom of amides with a sulfur atom resulting thioamides (Figure V.A.1) are found to be very reactive functionality,[1] which have been vastly used in the field of medicinal and organic chemistry.[2,3] This extraordinary reactivity can be accounted for by the presence of two nucleophilic centres localized on the heteroatoms (sulfur and nitrogen) and an electrophilic centre on thiocarbonyl carbon atom. Due to the presence of those active centres, the reactions of thioamides with dielectrophilic reagents may lead to the formation of different heterocyclic compounds. For example, thiazole derivatives can be synthesized in the reactions of thioamides with 2-chlorooxiranes (Scheme V.A.1).[4]

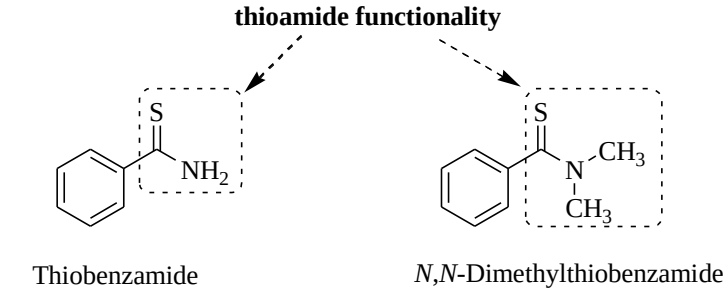
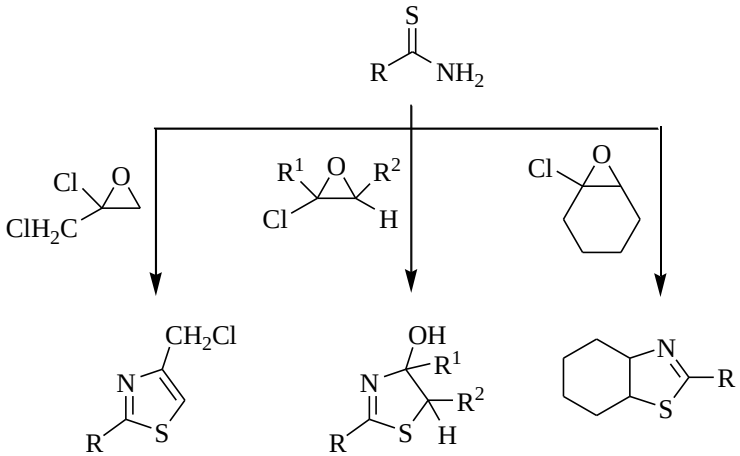


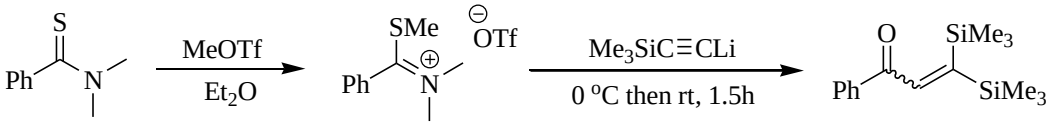
Figure V.A.1. Schematic representation of thioamide group



Scheme V.A.1. Reactions of thioamides with 2-chlorooxiranes towards the synthesis of thiazole derivatives

Biologically active thioamide compounds are used as flotation and vulcanization agents, in plant protection agents or drugs to lubricating oils and greases.[5] It is one of the useful building blocks of various pharmacologically important molecules containing five to six membered nitrogen and sulfur heterocycles.[6] Alkylation of thioamides form thioiminium salts,[7] that used in carboncarbon bond-forming reactions by nucleophilic attack at their

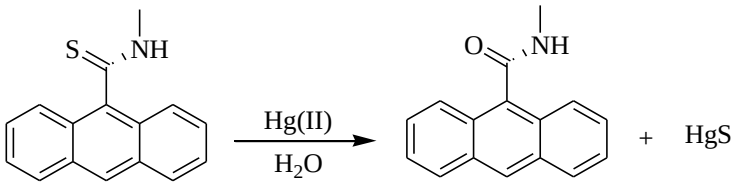
carbon atoms with a range of carbon nucleophiles e.g. Grignard reagents,[8] metal cyanides,[9] and intramolecularly generated enolates.[10] Another utilization of thioiminium salts derived from thiobenzamides by the treatment of MeOTf in diethyl ether followed by the addition of lithium acetylides, are in the synthesis of *α,β*–unsaturated ketones,[11]as shown in scheme V.A.2.



Thioiminium salt

Scheme V.A.2. Utilization of thioiminium salts in the synthesis of α,β–unsaturated ketones

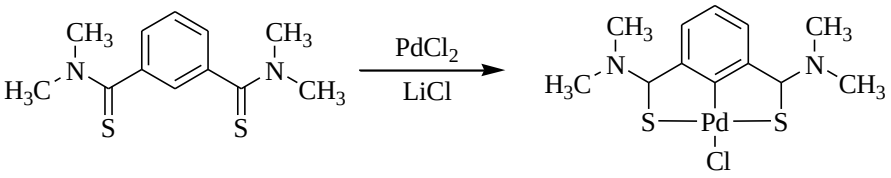
Formation of alkenes from thioiminium salts via extrusion of the sulfur atom has also been achieved in Eschenmoser coupling.[12,13] Recent developments account for its utilisation as fluorescence quencher,[14] and sensor for metal ions.[15] Chemodosimeter contains a thioamide group, used in fluorescent Hg(II) sensor,[16] from aqueous solution by desulfurization and formation of anthrylamide. The irreversible desulfurization reaction is 87% complete after 10 min at room temperature, when one equiv of Hg(II) is employed (Scheme V.A.3).



Scheme V.A.3. Fluorescent Hg(II) sensor in the irreversible desulfurization reaction

Thioamide substitutions can also be used as unique photochemical probes and thioamide bond can act as a quencher of *p*-cyanophenylalanine, tyrosine, and tryptophan fluorescence to monitor protein dynamics.[17,18] Another area of application for thioamides is the study of amyloid protein misfolding in neurological disease, such as in Alzheimer's disease, Parkinson's disease.[17] Thioamides have also used to perturb hydrogenbonding interactions important to misfolding in proteins.

Thioamides are widely used in transition-metal coordination chemistry and material chemistry.[18] Thioamide-based tridentate ligands, 1,3-benzenedicarbothioamides, were used to afford luminescent pincer palladium(II) complexes,[19] and found application in the light-emitting diodes (Scheme V.A.4).



Scheme V.A.4. Luminescent pincer palladium(II) complexes based on1,3-benzenedicarbothioamides

Another example of thioamide-based pincer platinum complexes having luminescent property are shown in figure V.A.2.[18c] These two phosphorescent pincer Pt(II) complexes with different k^3S,C,S and k^3N,C,N coordination systems were photoluminescent in a glassy frozen state and in the solid and the second complex was found to emit light even in solutions at room temperature. The electrochemical, UV-vis, and photoluminescence data supported the fact that the emission from the first one originates from the ^{3}MLCT excited state. On the other hand, the emission from the second complex is considered to originate from $^3(\pi^*–\pi)$ emission.

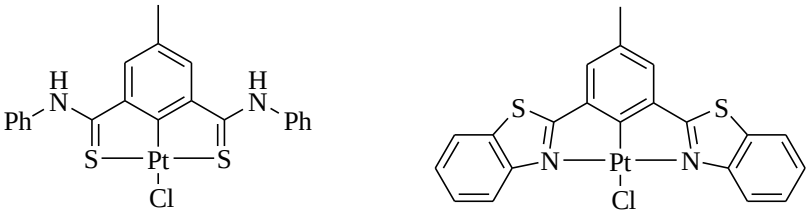
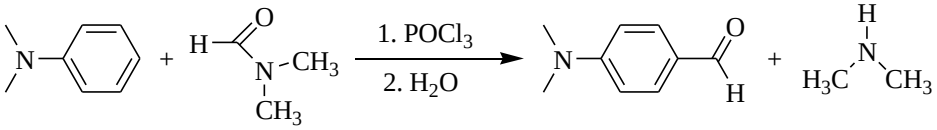


Figure V.A.2. Thioamide-based phosphorescent pincer Pt(II) complexes

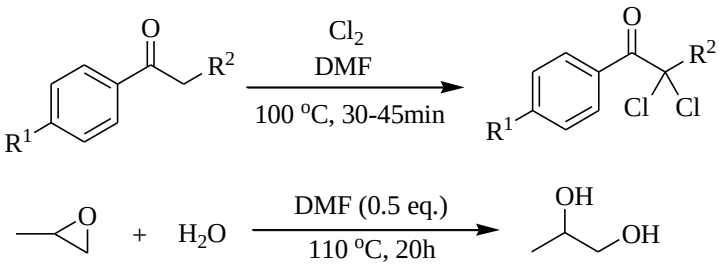
On the other hand *N*,*N*-Dimethylformamide (DMF) is commonly used as a polar organic solvent with high boiling point and low evaporation rate. The structure of DMF is believed to be a combination of two resonating forms, as evidenced from its IR and NMR spectra. DMF structurally contains two functionalities: the amide and the aldehyde functions.[20] DMF is not only used as a solvent but as a reagent also.[21] It can be used as a source to introduce different functionalities such as formyl, carbonyl, dimethylamino unit, Me_2NCO unit, ether, formate unit, Me_2NCH, radical, CHOH unit and besides these used as a dehydrating agent, addendum and also participates in cycloaddition reactions. Some of them are discussed here. In reagent chemistry, DMF is used as a reagent in Vilsmeier-Haack reaction,[22] to introduce formyl group (–CHO) in electron-rich arenes in the presence of $POCl_3$.



Scheme V.A.5. Vilsmeier-Haack reaction where DMF is usedas a reagent to introduce formyl (–CHO) group

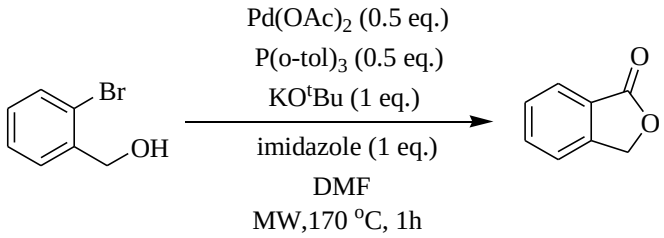
It is believed that the combination of DMF and $POCl_3$ produces an electrophilic iminium cation, which undergoes electrophilic aromatic substitution reaction followed by hydrolysis of the arene-iminium ion intermediate to form the aryl aldehyde.[22]

The bis-*α*-chlorination of aromatic ketones is due to catalysis by DMF.[23] It also catalyzes the hydrolysis of epoxides,[24] via the formation of N,N-dimethylformamide ethylene acetal derivatives (Scheme V.A.6).



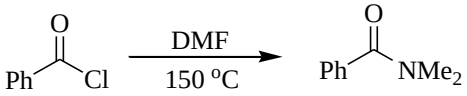
Scheme V.A.6. DMF-catalyzed bis-α-chlorination of aromatic ketones and hydrolysis of epoxides

Alterman et al. have used DMF as the carbon monoxide source for the synthesis of phthalide from 2-bromobenzyl alcohol under microwave irradiation.[25]



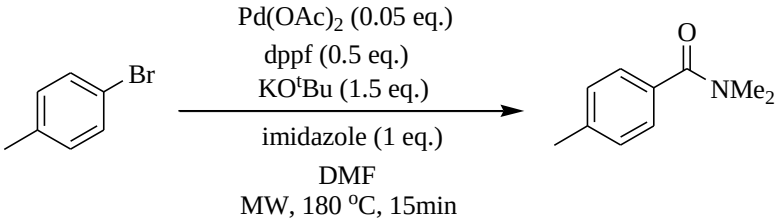
Scheme V.A.7. DMF act as the carbon monoxide source for the synthesis of phthalide from 2-bromobenzyl alcohol

Acid chlorides to the corresponding amides have been synthesized by using DMF as the source of $-NMe_2$ unit.[26]



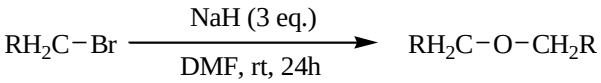
Scheme V.A.8. DMF as the source of $-NMe_2$ unit towards the synthesis of amides from acid chlorides

Pd-catalyzed,[27] aminocarbonylation of aryl bromides to the corresponding dimethylamide was achieved where DMF acted as a source of the Me_2NCO unit.



Scheme V.A.9. Pd-catalyzed aminocarbonylation of aryl bromides to the corresponding dimethylamide

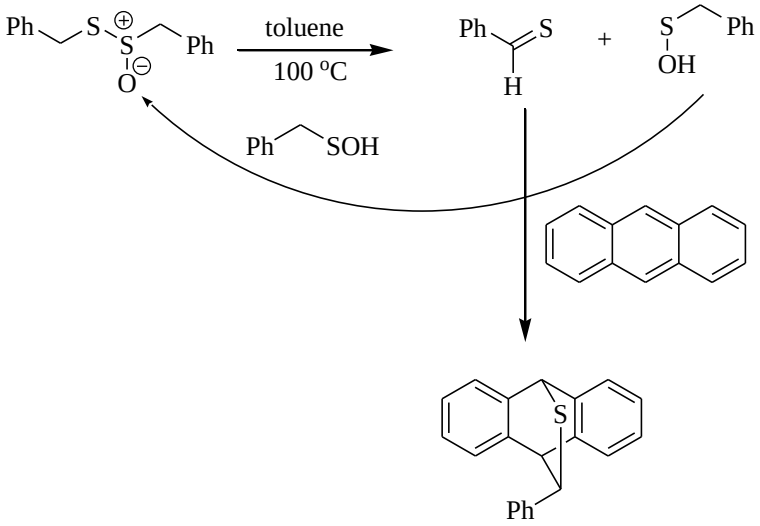
The treatment of allylic and benzylic bromides by sodium hydride in DMF affords the corresponding symmetrical ethers,[28] in high yields, where DMF acts as the source of oxygen atom.



Scheme V.A.10. DMF acts as the source of oxygen atom to afford symmetrical ethers from allylic and benzylic bromides

V.B. Background and objectives

Generally thioamide synthesis proceeds via thiobenzaldehyde formation which is very unstable, except some highly substituted aryl thioaldehydes.[29] Various synthetic routes have been developed towards the synthesis of thioamides, most of which require harsh reaction conditions. Although several methods are known to produce aryl thioaldehydes,



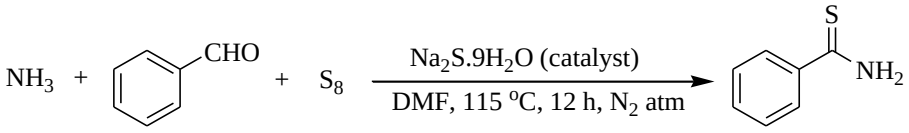
Scheme V.A.11. Unstable thiobenzaldehydes are prepared from S-alkyl thiosulphinate and being trapped by the adduct with anthracene

they are considered as reactive intermediates and being trapped by suitable reagents to afford a stable product e.g. cycloaddition with diene,[30] condensation with hydrazine,[31] or

addition of suitable amines.[32] For example, unstable thiobenzaldehydes are prepared from S-alkyl thiosulphinate,[33] by heating at 100 °C in toluene and being trapped by the adduct with anthracene as shown in scheme V.A.11.

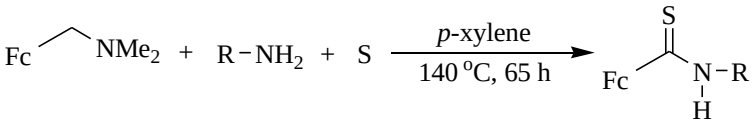
Several authors have reported generation of 'transient' thioaldehydes in reactions such as: (i) 'Bunte salts' (*S*-alkyl/aryl thiosulfates) in the presence of NEt_3,[30] (ii) photolytic Norrish type-II cleavage of phenacyl sulfides,[34a-c] (iii) from dibenzyl disulfides in the presence of Na_2CO_3 in DMF,[31] (iv) reaction of phosphonium ylides with elemental sulphur,[34d] or (v) fluoride-induced elimination of α-silyldisulfides,[34e] besides the classical Willgerodt-Kindler (WK) reaction under harsh conditions,[34f,g] or use of *S*-transfer Lawesson's reagent,[34h] and others.[34i,j]

Following WK reaction, Kanbara et al.,[34g] prepared primary thiobenzamide from aqueous ammonia, benzaldehyde in the presence of catalytic amount of $Na_2S.9H_2O$. Generally as is in the case also WK reactions are associated with harsh reaction condition like high temperature or microwave irradiation.



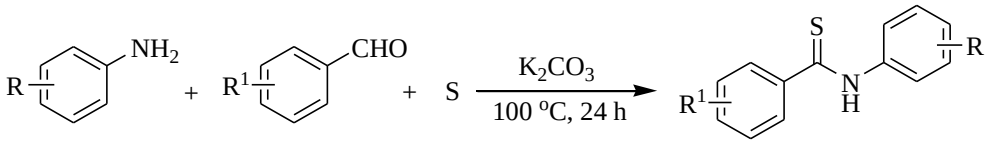
Scheme V.B.12. Primary thiobenzamide synthesis using catalytic amount of $Na_2S.9H_2O$

Ferrocenyl and ruthenocenyl thioamide derivatives have been successfully synthesized by Patra and Gasser et al. using a single step three component condensation reactions between ferrocene derivatives and organic amine in the presence of elemental sulfur.[35] Requirement of huge reaction time (65h) and high temperature are major drawbacks of this reaction.



Scheme V.B.13. Three-component reactions for ferrocenyl and ruthenocenyl thioamide derivatives

Another three component reaction between amines, aldehydes and elemental sulfur powder has been developed by Deng and Zhou et al.,[36] to synthesize thioamides in good to excellent yield through a simple one-pot procedure in water without any catalyst. Substrates containing electron withdrawing groups suffer from lower yields.

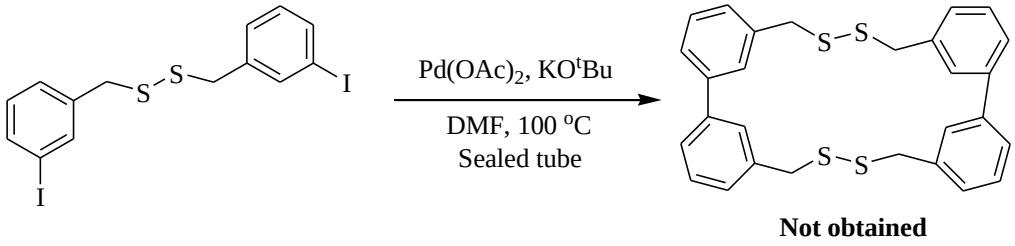


Scheme V.B.14. One-pot thioamides synthesis using elemental sulfur powder

N,*N*-dialkyl thioaryl amides are important building blocks for the synthesis of diverse heterocyclic compounds of biological relevance,[2g,6a-c,11,37] or in the synthesis of *α*,*β*–unsaturated ketones,[11] and also find applications as in coordination chemistry and materials science.[18c,14a,c,15b,c] In this context, we have established that DMF plays a unique role of delivering the dimethylamino group (−NMe_2) to the reactive and *in situ* formed thiobenzaldehydes to finally produce the corresponding *N*,*N*-dimethyl thioaryl amides.

V.C. Results and discussion

Firstly we attempted a homocoupling reaction on 1,2-bis(3-iodobenzyl)disulfane using potassium *tert*-butoxide (KO^tBu) as base and palladium acetate $Pd(OAc)_2$ as catalyst in DMF solvent at 100 °C. But we did not get our desired product (Scheme V.C.15). Rather we obtained a new product more polar than the starting ones.

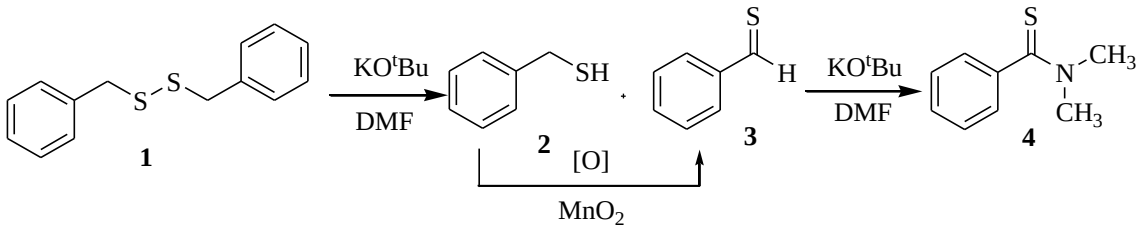


Not obtained

Scheme V.C.15. Homocoupling reaction on 1,2-bis(3-iodobenzyl)disulfane

We tried the same reaction on 1,2-bis(benzyl)disulfane and 1,2-bis(4-chlorobenzyl)disulfane again producing new products. Since there were no halo substitution on 1,2-bis(benzyl)disulfane we can conclude that no homocoupling reaction occurred at all, instead a new reaction happened there. Then we characterized the new products obtained from 1,2-bis(benzyl)disulfane and 1,2-bis(4-chlorobenzyl)disulfane by ^1H and ^{13}C NMR spectroscopy which supports the formation of *N*,*N*-dimethylbenzothioamide (Table V.C.2. **4a**) and 4-chloro-*N*,*N*-dimethylbenzothioamide (Table V.C.2. **4d**) respectively. Melting point and FT-IR also accounted for the same products. To confirm we further carried out HRMS and single-crystal X-ray structures for thiobenzamides (experimental section).

We found that the reaction of dibenzyl disulfide in the presence of potassium *tert*-butoxide (KO^tBu) in DMF at heating to 100 °C afforded *N*,*N*-(dimethyl)thiobenzamide in 43% yield. Based on literature reports,[31] it was presumed that dibenzyl disulfide under the basic conditions suffered 1,2-elimination with the formation of benzylthiol and thiobenzaldehyde, and the latter could react with DMF to form *N*,*N*-dimethylthiobenzamide, as outlined in Scheme V.C.16.



Scheme V.C.16. Amidation of thiobenzaldehyde, derived from dibenzyl disulfide, in the presence of DMF under basic conditions

Since one part of the dibenzyl disulfide produces phenylmethyl thiol, the reaction was also carried out in the presence of an oxidizing agent (MnO_2). It is interesting that the ultimate product, *N*,*N*-dimethylthiobenzamide, was then isolated in 91% yield. Further changes of the base and varying temperature, however, did not provide practically any better observation. Optimization of the reaction conditions is presented in Table V.C.1. Moreover, use of K_2CO_3 as the base did not result in the formation of thiobenzamide (Table V.C.1, entry 4), though it is reported that treatment of Na_2CO_3 with dibenzyl disulfide could form 'transient' thioaryl aldehyde.[34]

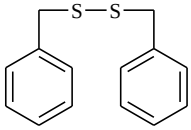
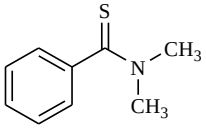
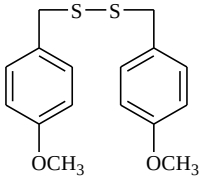
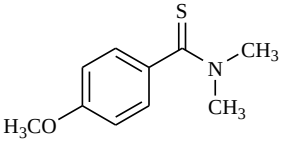
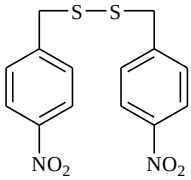
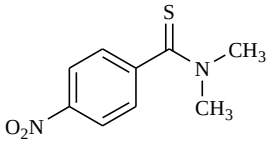
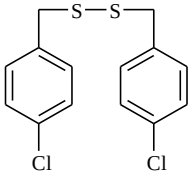
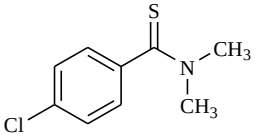
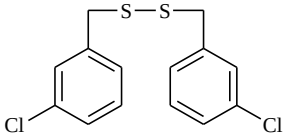
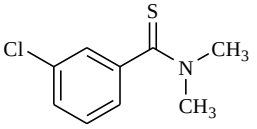
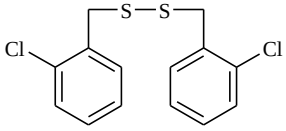
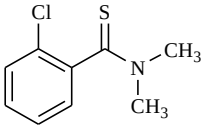
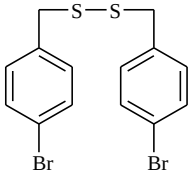
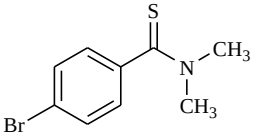
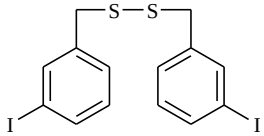
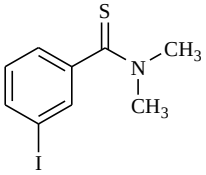
Table V.C.1. Optimization of the one-pot thiobenzamide synthesis reaction[a]

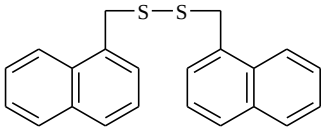
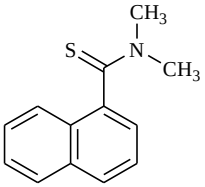
entry	base	oxidant	temp. (^{o}C)	time (h)	Yield (%)[b]
1	KO^{t}Bu	nil	100	4	43
2	**KO^{t}Bu**	**MnO_2**	**100**	**4**	**91**
3	NaH	nil	100	4	39
4	K_2CO_3	nil	100	15	nil
5	KO^{t}Bu	MnO_2	rt	24	nil
6	KO^{t}Bu	MnO_2	50	24	nil
7	KO^{t}Bu	MnO_2	80	10	54

[a]Reactions were performed with dibenzyl disulfide (1 mmol), base (3.0 mmol), MnO_2 (1.5 mmol, for entries 2, 5-7) and DMF (2 mL) in a sealed tube. [b]Isolated yields after passing though a short-path silica gel column.

The optimized reaction condition, as in entry 2 (Table V.C.1), was employed to a variety of diaryl disulfides. Table V.C.2 shows that different substituents attached to the aromatic ring can survive the reaction conditions resulting in the formation of thiobenzamides.

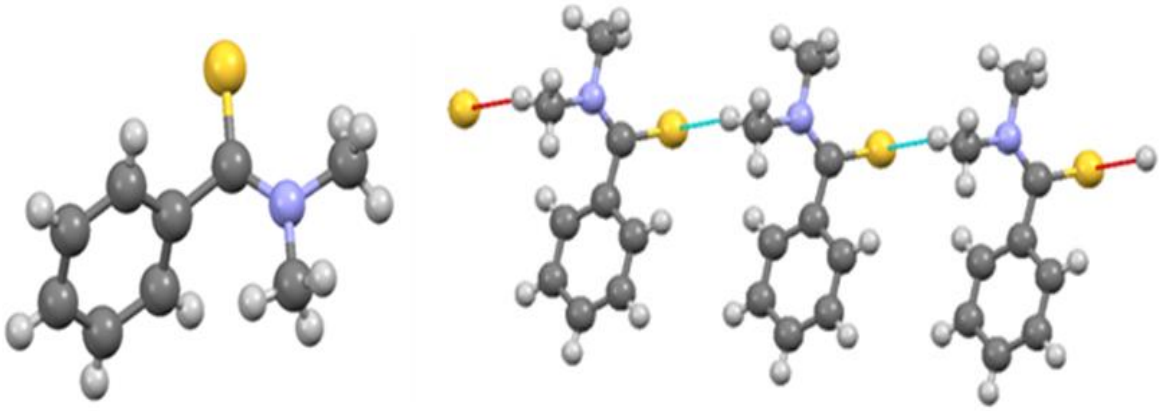
Table V.C.2. Reactions of different diaryl disulfides with DMF[a]

entry	disulfide **1**	time (h)	product 4	Yield (%)[b]
1		4		91
2		4		85
3		4		83
4		4		89
5		5		83
6		6		86
7		4		87
8		5		79

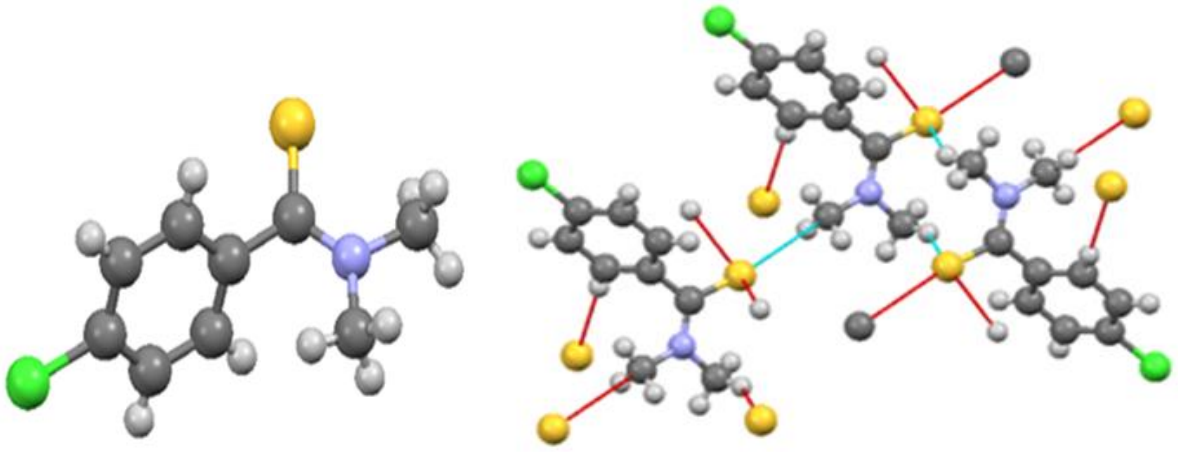
9			4		87

[a] Reaction conditions: disulfide (1 mmol), KO^{t}Bu (3.0 mmol), MnO_2 (1.5 eq.) in DMF (2 mL) in a sealed tube and gentle magnetic stirring at 100 ^{o}C for the time as mentioned. [b] Isolated yields after passing through short column silica gel.

For example, electron-donating (–OMe), strong electron-withdrawing (–NO_2) or different halides attached at *ortho*, *meta* or *para* positions underwent clean reactions affording corresponding *N*,*N*-dimethyl aryl thioamides in good to excellent yields (table V.C.2, entries 2-8). It clearly reveals the endurance of various substituents to the reaction condition and



4a



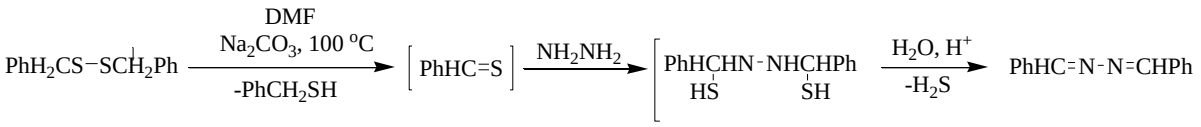
4d

Figure V.C.3. Single-crystal X-ray structures for thiobenzamides **4a** and **4d**. Possible contacts or bonding for compounds **4a** and **4d** Ellipsoids set at 50% probability; all H-atoms are shown.

establishes the generality of the reaction procedure. Similar reaction was performed with dinaphthyl disulfide to afford *N*,*N*-dimethyl 1-naphthyl thioamide in 87% isolated yield (entry 9).

Single-crystal X-ray diffraction analyses for thiobenzamides **4a** and **4d** not only confirmed their structures unambiguously but also revealed possible contacts between sulfur and methyl hydrogen. In the case of **4a**, possible contacts exist between the *S* and *N*-methyl Hs, whereas for the compound **4d**, there are Ar-Hs that show contacts with the *S* atom of the amide (Figure V.C.3).

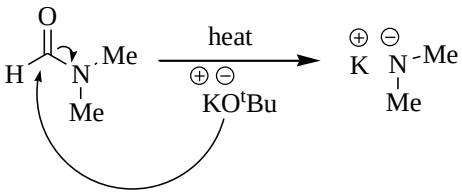
Towards plausible mechanism of this unique conversion, the literature reports revealed that DMF can act as a source of $-NMe_2$ group in reactions with acid chloride, ester or anhydride involving the attack of the acyl group by the nitrogen atom of DMF.[26,38] Further substitution by the $-NMe_2$ group is reported in active halides like benzyl chloride,[26] or electron-deficient aryl chlorides, usually at high temperature.[39] On the other hand, Okuma and co-workers reported that thioaldehydes, prepared *in situ*, can undergo reaction with amine to produce corresponding thioamides via formation of aminal and subsequent reaction with H_2S, though secondary amines like diisopropylamine or morpholine do not give rise to the formation of thiobenzamides bearing *N*-diisopropyl or *N*-morpholino groups.[32] In our study, we believe that the dibenzyldisulfide produces 'transient' thiobenzaldehyde, as evidenced by trapping it with $PhNHNH_2$ and isolating the addition product benzalazine (Scheme V.C.17).[31]



Scheme V.C.17. Trapping of'transient' thiobenzaldehyde formation by benzalazine formation

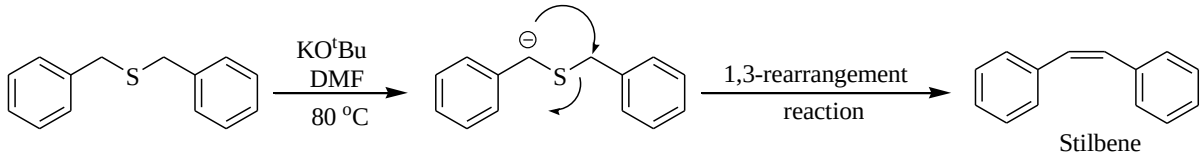
Nasipuri suggested that a mixture of DMF and NaH can produce *N*,*N*-dimethylsodamide.[40a] In a recent finding on metal-catalyzed hetero cross coupling reaction of aryl halides, DMF has been shown to act as one of the coupling partners and the *N*,*N*-dimethyl aryl amines are believed to be formed via transmetalation with $KNMe_2$ that is generated during the reaction condition.[40b]

With this background, our observations, and considering that the reaction was carried out under strong basic medium, we tend to postulate the mechanism, as outlined in scheme V.C.6. The reaction starts with the formation of a benzyl carbanion **5** from dibenzyl disulfide **1**, which undergoes cleavage of the disulfide linkage affording benzylthiol **2** and the



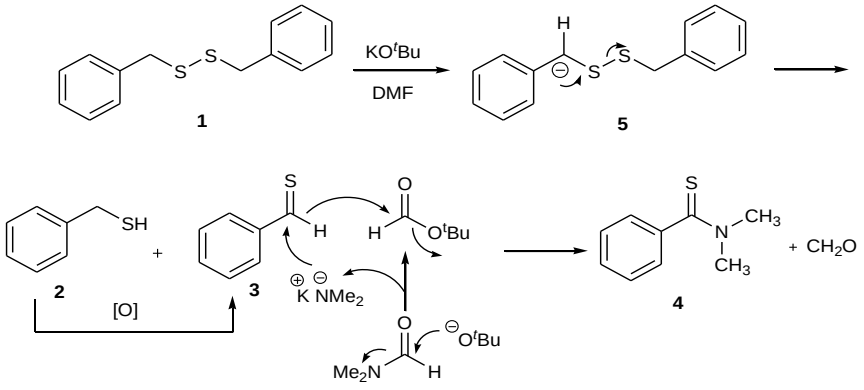
Scheme V.C.18. Reaction of DMF with KO^{t}Bu forms $KNMe_2$

'transient' thiobenzaldehyde **3**. It may be mentioned that dibenzylsulfide decomposes in the presence of KO^{t}Bu in DMF producing stilbene through the formation of benzyl carbanion and subsequent elimination of sulfide ion (Scheme V.C.19).[41]



Scheme V.C.19. Decomposition of dibenzylsulfide in the presence of KO^{t}Bu in DMF producing stilbene

On the other hand, DMF reacts with the base (–O^{t}Bu) to produce the amide ($KNMe_2$) that attacks at the thiocarbonyl carbon and eliminates the hydride to form eventually *N*,*N*-dimethylthiobenzamide **4** and formaldehyde. A reaction was carried out in the presence of hydrazine hydrochloride (3 eq.). After the reaction, TLC of the reaction mixture showed two spots corresponding to thiobenzamide (R_f = 0.43) and benzalazine (R_f = 0.21) in ethyl acetate–light petroleum (1:4). Both compounds were easily isolated by column chromatography over silica gel and comparison with melting point data (m.p. 90-92 ^{o}C; lit.,[31] 91-93 ^{o}C). Formation of thiobenzaldehyde **3** was confirmed by the isolation of benzalazine in 62% yield along with the thiobenzamide **4a** (18%), and the reaction carried out in the presence of MnO_2 affording higher yield of thiobenzamide (43% to 91%) confirmed the mechanistic sequence (scheme V.C.20). The role of a strong base is essential to produce the



Scheme V.C.20. Plausible mechanism involving attack of the dimethylamide anion to thiobenzaldehyde

amide (–NMe_2) from DMF and the use of K_2CO_3 did not result in the formation of thiobenzamide (table V.C.1, entry 4), although generation of thiobenzaldehyde from dibenzyl disulfide was reported by using Na_2CO_3 in DMF.[20]

V.D. Conclusion

Thus a complete new process of amidation of 'transient' thiobenzaldehyde using *N*,*N*-dimethylformamide, which bears both amide and aldehyde functionalities, has been established under metal-catalyst free conditions. The reaction possibly proceeds with the formation *N*,*N*-dimethylpotassiumamide ($KNMe_2$) and subsequent attack at the thiocarbonyl carbon, which is reported for the first time. Since aryl thioamides are important class of compounds, the present study involving inexpensive DMF could not only replace the common Willgerodt-Kindler (WK) reaction, but also spur diverse reactions with the aid of DMF beyond its uses as a solvent.

V.E. Experimental section:

V.E.I. General information

General informations of experimental section are given in Chapter II under II.E.1. General information (Page–47).

V.E.2. General procedure for the synthesis of 4a–4i

To a solution of diaryl disulfide **1** (1 mmol) in freshly distilled DMF (2 mL) were added KO^{t}Bu (3 mmol) and MnO_2 (1.5 eq.) and the reaction mixture taken in a screw-capped sealed tube was heated at 100 ^oC with magnetic stirring for 4-6 h. The mixture was then cooled, diluted with water (5 mL) and extracted with diethyl ether (3x10 mL). The combined ethereal extracts were dried (anhy. Na_2SO_4) and concentrated to afford the product in almost pure form. However, for spectroscopic characterization (FT-IR, ^1H- and ^{13}C-NMR), the product was passed through a short-path of silica gel column. All products (**4a-i**) gave satisfactory spectral analytical data, melting points wherever solid compounds and also compared with those reported in the literature.

V.E.3. X-ray analysis data and ortep diagram for compounds 4a & 4d

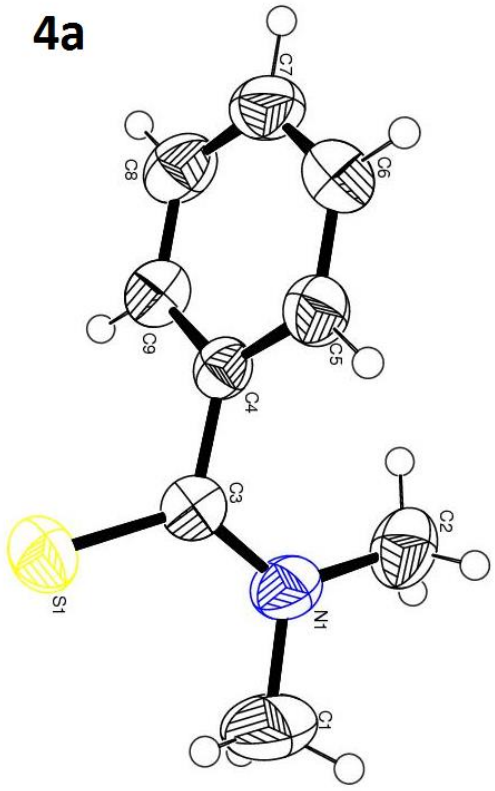
The crystal data of compound **4a** and **4d** has already been deposited at Cambridge Crystallographic Data Centre. The CCDC reference numbers are 994136 and 994137 respectively. Software used for data collection is Mercury 3.3.

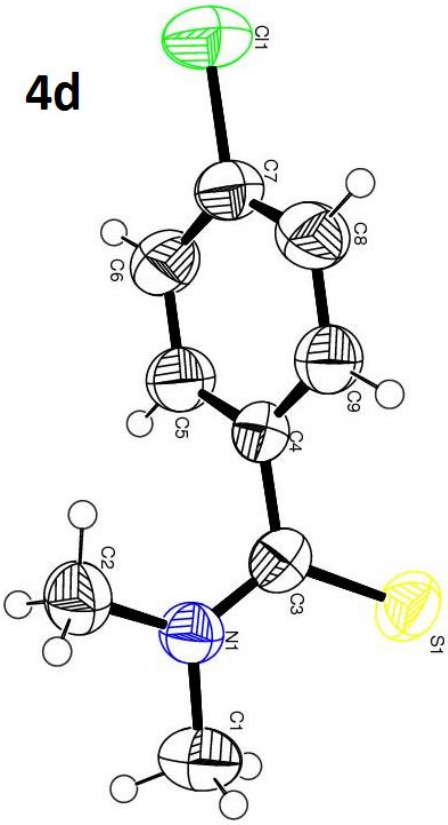
V.E.3.a. X-ray analysis data for compounds 4a and 4d

Identification code	4a (smk-164)	4d (smk-170)
Empirical formula	$C_9H_{11}NS$	$C_9H_{10}ClNS$
Formula weight	165.25	199.69
Temperature	296 K	296 K
Wave length	0.71073	0.71073
Bond precision(C-C)	0.0027 Å	0.0030 Å
Space group	P2 (1) /n	P2 (1)/c
Hall group	-P 2yn	-P 2ybc
Unit cell dimensions	a = 5.9271 (15) Å	a = 10.1194 (3) Å
	b = 12.790 (3) Å	b = 14.4115 (4) Å
	c = 12.361 (3) Å	c = 7.3247 (2) Å
	$\alpha = 90^o$	$\alpha = 90^o$
	$\beta = 100.163\ (13)^o$	$\beta = 106.198\ (2)^o$
	$\gamma = 90^o$	$\gamma = 90^o$
Volume (calculated)	922.4 (4) $Å^3$	1026.18 (5) $Å^3$
Density (calculated)	1.190 g/cm^3	1.293 g/cm^3
Z	4	4
Absorption coefficient (Mu)	0.287 mm^{-1}	0.522 mm^{-1}
F(000)	352.0	416.0
Index ranges (h, k, l max)	7, 15, 14	12, 17, 8
Nref (calculated)	1610	1808

Data completeness	98.9%	99.9%
Theta (max)	24.99º	25.00º
R(reflections)/wR2 (reflections)	0.0342 (1290)/0.0958 (1593)	0.0439 (1355)/0.1340 (1807)
S	1.005	1.049
Npar = Npar	103	112

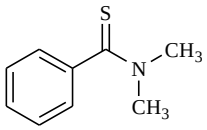
V.E.3.b. Ortep diagrams for compounds 4a and 4d





V.E.4. Spectral data

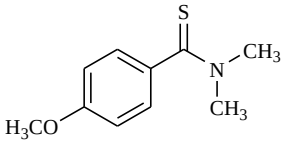
Table 2; entry 1



4a

***N,N*-Dimethylbenzothioamide (4a)**, Yellow solid, mp 69-71 ^{o}C.,[42] IR (KBr, *v* cm^{-1}): 1525.6, 1386.7, 1272.9, 1134.1, 989.4, 759.9. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.12 (s, 3H, NCH_3), 3.56 (s, 3H, NCH_3), 7.28-7.31 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 42.8, 43.8, 125,3, 127.9, 128.1, 143.0, 200.6. HRMS (ESI) calcd for $C_9H_{11}NKS_2$ 165.2553; found 166.0552.

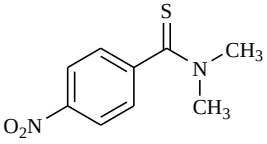
Table 2; entry 2



4b

4-Methoxy-*N*,*N*-dimethylbenzothioamide (4b), Pale yellow liquid. IR (Nujol, *v* cm^{-1}): 1525.3, 1394.4, 1277.6, 1141.8, 1086.8, 989.4, 823.3. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.22 (s, 3H, NCH_3), 3.58 (s, 3H, NCH_3), 3.92 (s, 3H, OCH_3), 6.86-6.88 (m, 2H, ArH), 7.27-7.32 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.5, 44.2, 56.4, 111.2, 126.8, 131.1, 156.2, 199.4.

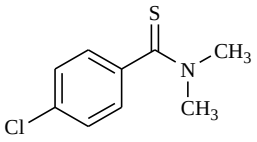
Table 2; entry 3



4c

***N,N*-Dimethyl-4-nitrobenzothioamide (4c)**, Yellow solid, mp 142-144 ^{o}C.,[43] IR (KBr, *v* cm^{-1}): 1525.6, 1382.7, 1273.9, 1134.5, 989.4, 752.9. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.18 (s, 3H, NCH_3), 3.61 (s, 3H, NCH_3), 7.46 (d, *J* = 8.7 Hz, 2H, ArH), 8.22 (d, *J* = 9.0 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 42.9, 43.9, 123.8, 126.5, 147.2, 148.8, 197.8.

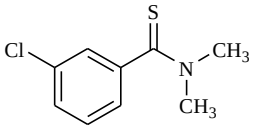
Table 2; entry 4



4d

4-Chloro-*N*,*N*-dimethylbenzothioamide (4d), Yellow solid, mp 80-82 ºC.,[44] IR (KBr, *v* cm^{-1}): 1525.6, 1394.4, 1280.6, 1141.8, 1087.8, 989.4, 829.3. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.15 (s, 3H, NCH_3), 3.57 (s, 3H, NCH_3), 7.22-7.32 (m, 4H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.3, 44.1, 127.3, 128.6, 134.6, 141.7, 200.0.

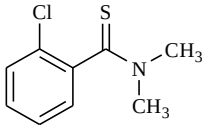
Table 2; entry 5



4e

3-Chloro-*N*,*N*-dimethylbenzothioamide (4e), Pale yellow liquid. IR (Nujol, *v* cm^{-1}): 1525.6, 1394.4, 1280.6, 1141.8, 1087.8, 989.4, 829.3. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.17 (s, 3H, NCH_3), 3.59 (s, 3H, NCH_3), 7.15-7.19 (m, 1H, ArH), 7.27-7.30 (m, 3H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.1, 44.1, 123.7, 125.8, 128.5, 129.7, 134.2, 144.7, 199.1.

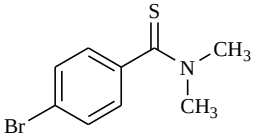
Table 2; entry 6



4f

2-Chloro-*N*,*N*-dimethylbenzothioamide (4f), Pale yellow liquid. IR (Nujol, *v* cm^{-1}): 1525.6, 1394.4, 1280.6, 1141.8, 1087.8, 989.4, 829.3. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.11 (s, 3H, NCH_3), 3.61 (s, 3H, NCH_3), 7.26-7.35 (m, 4H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 42.3, 42.8, 127.3, 127.7, 128.1, 129.3, 129.6, 142.0, 196.8.

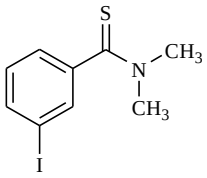
Table 2; entry 7



4g

4-Bromo-*N*,*N*-dimethylbenzothioamide (4g), Yellow solid, mp 120-122 ^{o}C.,[44] IR (KBr, *v* cm^{-1}): 1525.6, 1394.4, 1280.6, 1141.8, 1087.8, 989.4, 829.3. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.18 (s, 3H, NCH_3), 3.59 (s, 3H, NCH_3), 7.17-7.21 (m, 2H, ArH), 7.47-7.53 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.2, 44.1, 122.7, 127.4, 131.5, 142.0, 199.8.

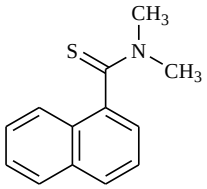
Table 2; entry 8



4h

3-Iodo-*N*,*N*-dimethylbenzothioamide (4h), Pale yellow liquid. IR (Nujol, *v* cm^{-1}): 1521.7, 1394.4, 1294.1, 1137.9, 997.1, 759.9, 698.2. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 3.15 (s, 3H, NCH_3), 3.56 (s, 3H, NCH_3), 7.06-7.11 (m, 1H, ArH), 7.23-7.27 (m, 2H, ArH), 7.64-7.66 (m, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 43.1, 44.1, 94.0, 124.8, 130.0, 134.3, 137.5, 145.0, 198.9.

Table 2; entry 9



4i

***N*,*N*-Dimethylnaphthalene-1-carbothioamide (4i)**, Pale yellow liquid. IR (Nujol, *v* cm^{-1}): 1525.6, 1384.2, 1274.0, 1144.1, 983.2, 759.7. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 2.94 (s, 3H, NCH_3), 3.69 (s, 3H, NCH_3), 7.34-7.37 (m, 1H, ArH), 7.42-7.51 (m, 3H, ArH), 7.69-7.72 (m, 1H, ArH), 7.77-7.84 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 42.4, 43.3, 122.8, 124.3, 125.2, 126.1, 126.9, 127.7, 128.1, 128.2, 133.3, 140.8, 199.5.

V.F. References

References for chapter V are given in Bibliography section (Page 145–148).