CHAPTER III

SECTION C

In quest of "stereoselective–switch" for on–water hydrothiolation of terminal alkynes using various additives and green synthesis of vicinal dithioethers

III.C.1. Introduction

Organosulfur compounds play a key role in convenient intermediates for chemical synthesis, materials chemistry and important biological intermediates.[1] 1–Alkenyl sulfides are important synthetic intermediates in total synthesis of many naturally occurring and biologically active compounds as well as versatile building blocks for many functionalized molecules.[2] The synthetic utility of alkenyl sulfides has been established by different research groups.[3]

A few examples of the vinyl sulfides as key synthetic intermediate of many potent compounds are shown in the Figure III.C.1 below:

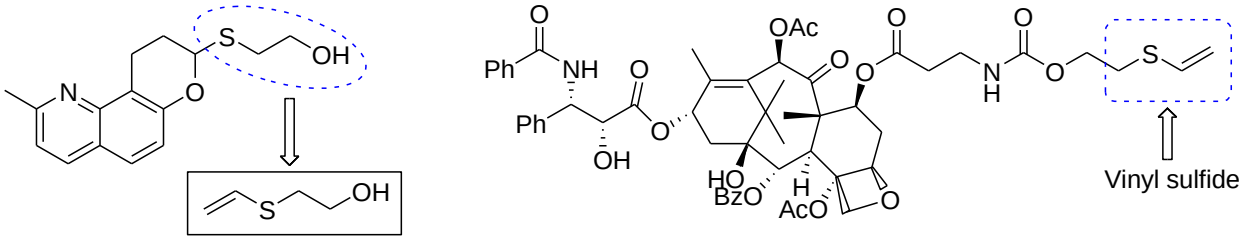


Figure III.C.1. Vinyl sulfides used as synthetic intermediates

Q. Li et al developed a bioorthogonal ligation using *o*–quinolinone quinone methide and vinyl thioether.[4] VT–labeled taxol was prepared by N. Muraoka and his group smoothly.[5] Similarly, some biological molecules containing vinyl sulfide moiety have been synthesized. The vinyl sulfide analogues of Angiotensin II with high affinity and full agonist activity at the AT1 receptor have also been synthesized.[6] The streptogramin antibiotics, Griseoviridin also contained vinyl sulfide with nine–membered macrocycle moiety (Figure III.C.2).[7]

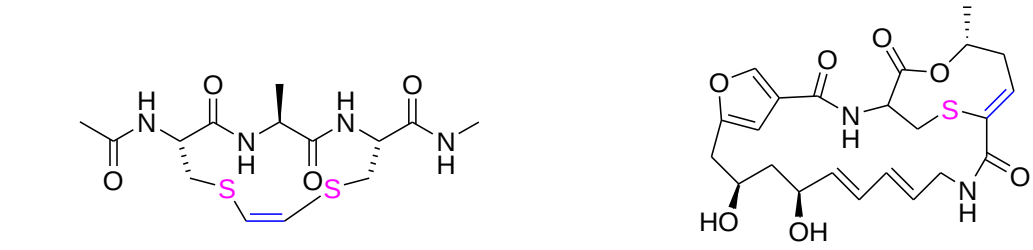
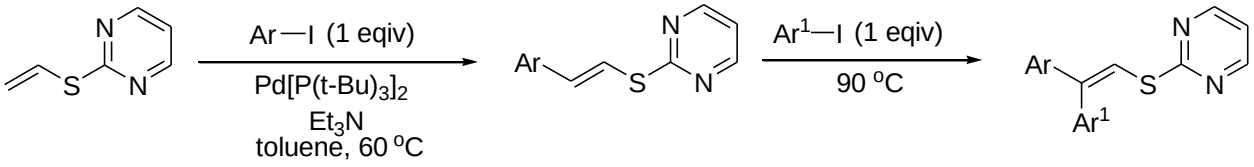


Figure III.C.2. Vinyl sulfides used as biologically active molecules

Multisubstituted olefins, which are important for materials science and pharmaceutical chemistry and these can be synthesized by the Mizoroki–Heck reaction of 2–pyrimidyl vinyl

sulfide.[8]

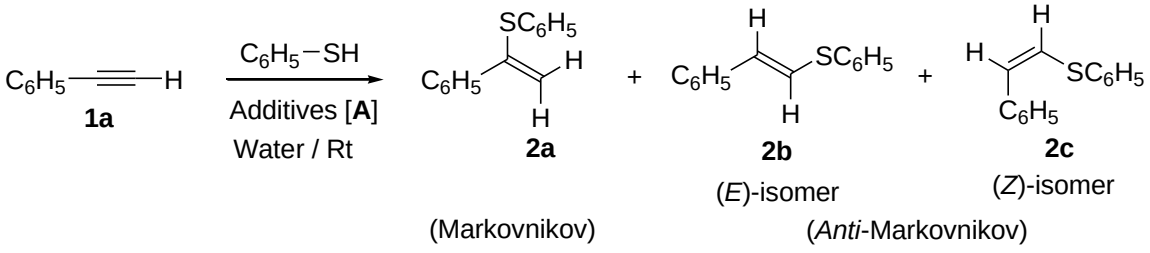


Scheme III.C.1. Substituted 2–pyrimidyl vinyl sulfide used in materials science

III.C.2. Background and Objectives

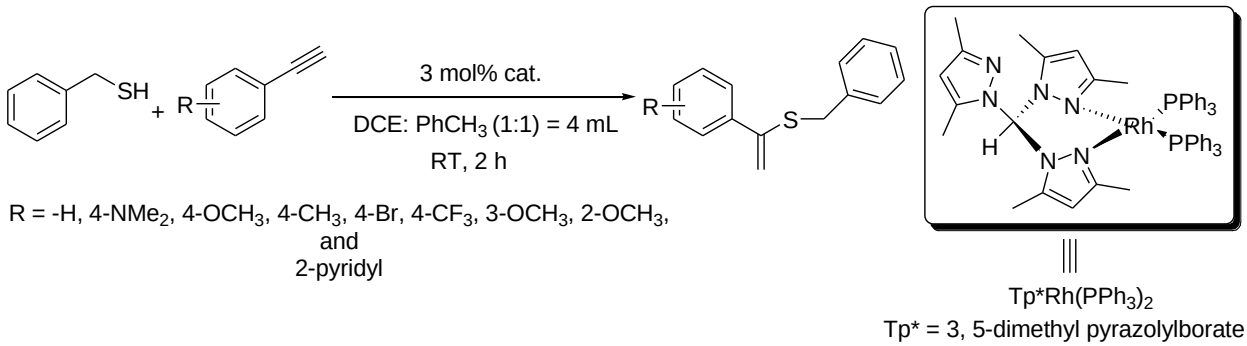
Increasing demand for alkenyl sulfides in material science, organic and bio–organic chemistry has furthered the development of new synthetic methods.[2e,9] The addition of thiols to alkynes is considered as one of the straightforward methods to obtain vinyl sulphides either catalyzed by transition metal complexes,[10–16] or base–promoted[17] and/or through free radicals.[18] This reaction is often judged as a part of "click chemistry" and a process of high atom–economy.[19] Mechanistically, addition of thiols to alkynes is believed to occur (i) via radical pathway producing unselective mixture of (*E/Z*)–*anti*–Markovnikov vinyl sulphides; (ii) base–mediated nucleophilic addition giving all types of adducts or (iii) transition–metal complex catalyzed processes yielding Markovnikov vinyl sulphides and anti–Markovnikov vinyl sulphides (Scheme III.C.2). Varying degrees of stereo– and regioselectivity selectivity and turnover are reported in the literature.

Scheme III.C.2. 1–Alkenyl sulphides from hydrothiolation of terminal alkynes



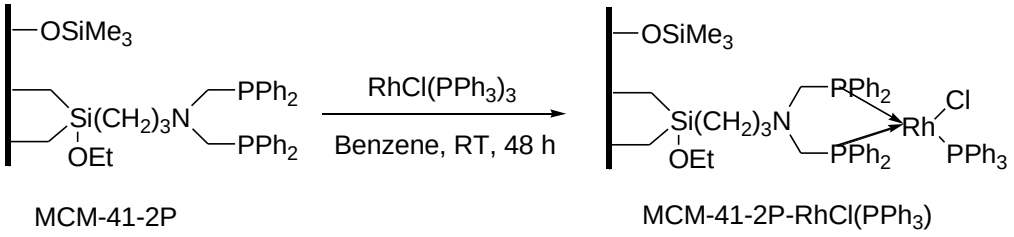
Most reports in the literature described the formation of thermodynamically more stable (*E*)–vinyl sulfide in considerable excess over the (*Z*)–isomer. On the other hand, hydrothiolation, particularly of aryl and benzyl thiols and catalyzed by transition–metal complexes, often produces a mixture of *anti*–Markovnikov (*E*)–alkenyl sulfide (*syn* addition) and Markovnikov adduct and thus suffers from poor regioselectivity. 1,1–Disubstituted alkyl vinyl sulfides were synthesized via rhodium–catalyzed hydrothiolation reaction. The reaction goes through predominantly via Merkovnikov addition by thiols to alkynes. J. A. Love et al

invented such Merkovnikov addition in the presence of 3,5–dimethyl pyrazolylborate–rhodium complex (Scheme III.C.3).[11a]



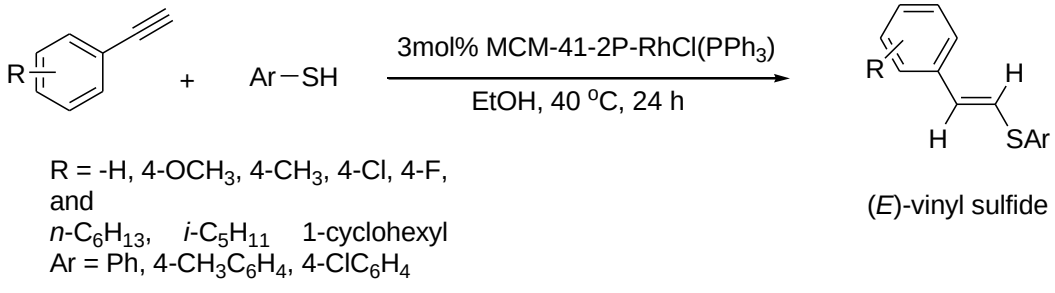
Scheme III.C.3. Synthesis of 1,1–Disubstituted alkyl vinyl sulfides by rhodium catalyst

Similarly diphosphino–functionalized MCM–41 anchored Rh–complex [MCM–41–2P–RhCl(PPh_3)] have exhibited high catalytic activity. This is an example of heterogeneous Rh–catalyzed hydrothiolation of alkynes with thiols.[20]



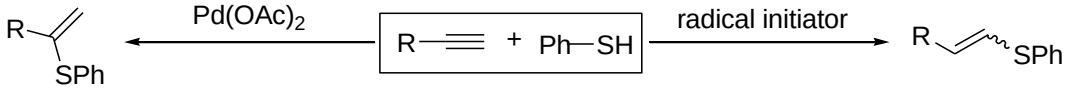
Scheme III.C.4. Preparation of MCM–41–2P–RhCl(PPh_3)

The reaction went through complete *anti*–Merkovnikov fashion and *(E)*–vinyl sulfides formed as major product. The stereochemistry of the addition products were determined by ^{1}H–NMR spectra (Scheme III.C.5).[20]



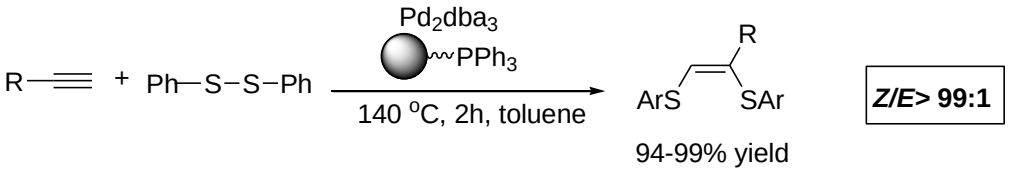
Scheme III.C.5. Hydrothiolation reaction in presence of heterogeneous MCM–41–2P–RhCl(PPh_3) catalyst

Highly stereo– and regio–controlled synthesis of vinyl sulfides via Pd–catalyzed hydrothiolation of alkynes with thiols has been effectively done by A. Ogawa and his group. They had shown the regio–isomer *i.e.* Merkovnikov product was formed exclusively in presence of $Pd(OAc)_2$ whereas the *anti*–Merkovnikov adduct was obtained in presence of radical initiator (Scheme III.C.6).[21]



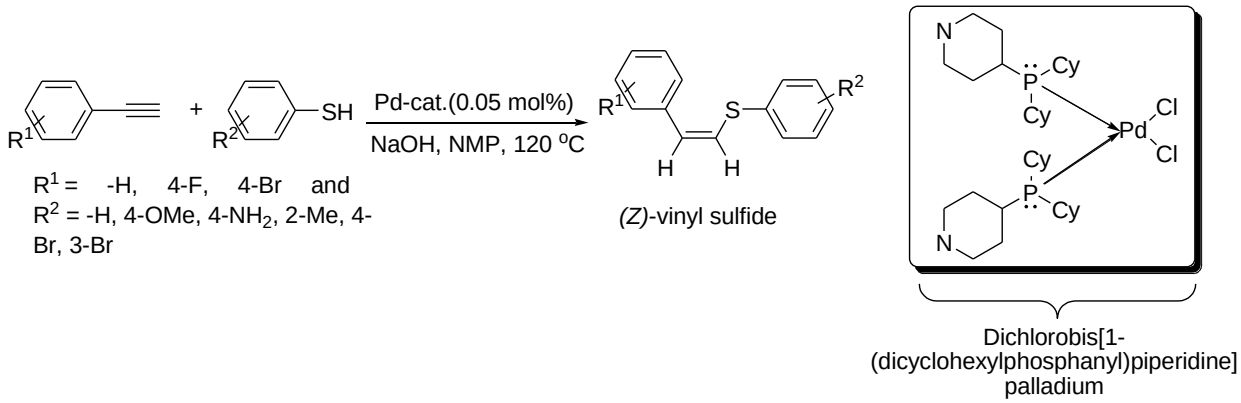
Scheme III.C.6. Stereoslective synthesis of vinyl sulfides by Pd–catalyzed reaction

The first example of polymer–supported palladium catalysts for stereoselective S–S bond addition to terminal alkynes has been established by I. Beletskaya et al. The exclusive *(Z)*–selectivity has been achieved by this methodology. Diselenides did not undergo the reaction under this condition (Scheme III.C.7).[22]



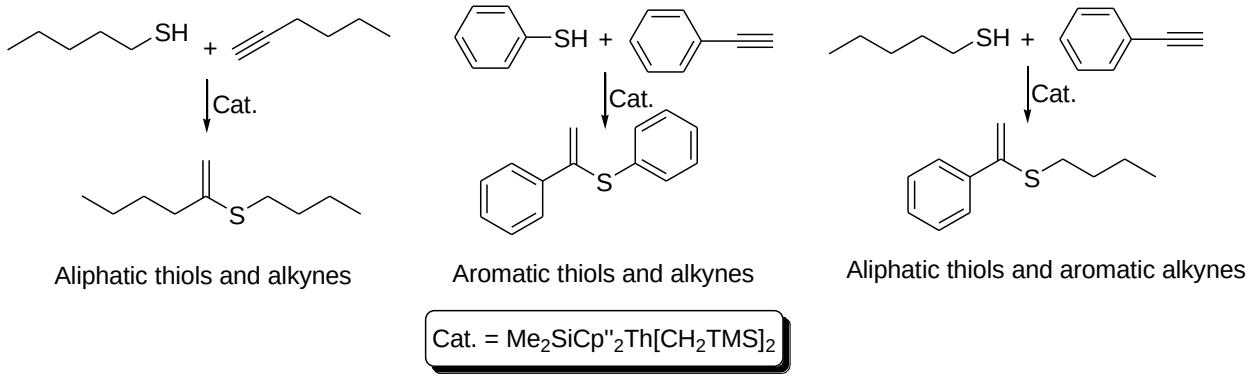
Scheme III.C.7. Polymer–supported palladium catalyst for stereoselective S–S bond addition to terminal alkynes

The Stereoselective (*Z)*–vinyl sulfides can be effectively synthesized by C. M. Frech and his group in presence of dichloro(amine phosphine) complex of palladium. Selective formation of *cis*–configured vinyl thioethers have been achieved by this methodology. The addition followed *anti*–Merkovnikov fashion. A large number of alkynes and thiols were participated in this reaction (Scheme III.C.8).[12a]



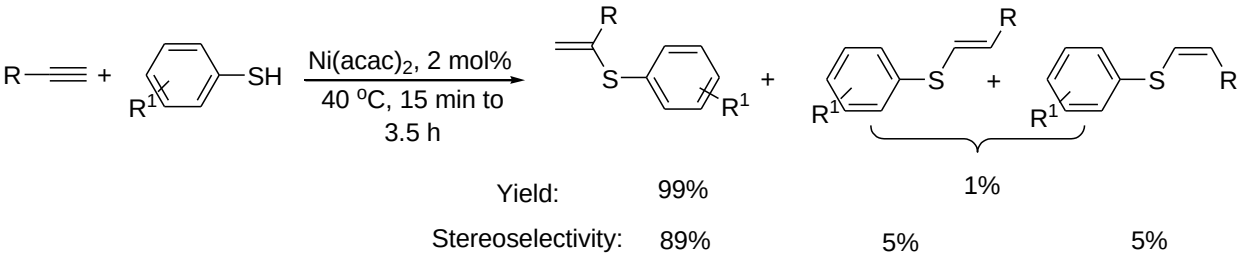
Scheme III.C.8. Palladium–catalyzed synthesis of *cis*–configured vinyl thioethers

Organoactinide complexes can also use as hydrothiolation of alkynes with various thiols. A large number of aliphatic, aromatic and benzylic thiols were participated in this methodology. This was the first report of the use of f–element catalysts to affect the efficient hydrothiolation with high degree of Markovnikov selectivity (Scheme III.C.9).[23]



Scheme III.C.9. Organoactinide–mediated hydroyhiolation of terminal alkynes with aliphatic, aromatic and benzylic thiols

Efficient and convenient synthesis of *β*–vinyl sulfides by Ni–catalyzed regioselective addition of thiols to alkynes has been achieved. I. P. Beletskaya and his group developed this methodology using $Ni(acac)_2$ as the catalyst. 2 mol% of the catalyst was sufficient for this conversion. Only 15 min to 3.5 h was required for complete conversion of products (Scheme III.C.10).[24]



R = -C_5H_{11}, -CH_2CH_2OH, -$C(Me_2)OH$, -$C(Me_2)OMe$, -$C(Me_2)OCOMe$, Ph
R^1 = -H, 4-CH_3, 4-Cl

Scheme III.C.10. Ni(acac)$_2$–catalyzed regioselective synthesis of *β*–vinyl sulfides by hydrothiolation reaction

NHC–based Nickel catalysts have been found for the selective transfer of a single arylthio group in the catalytic hydrothiolation reaction. Some structures of NHC are depicted in the Figure III.C.3 below:

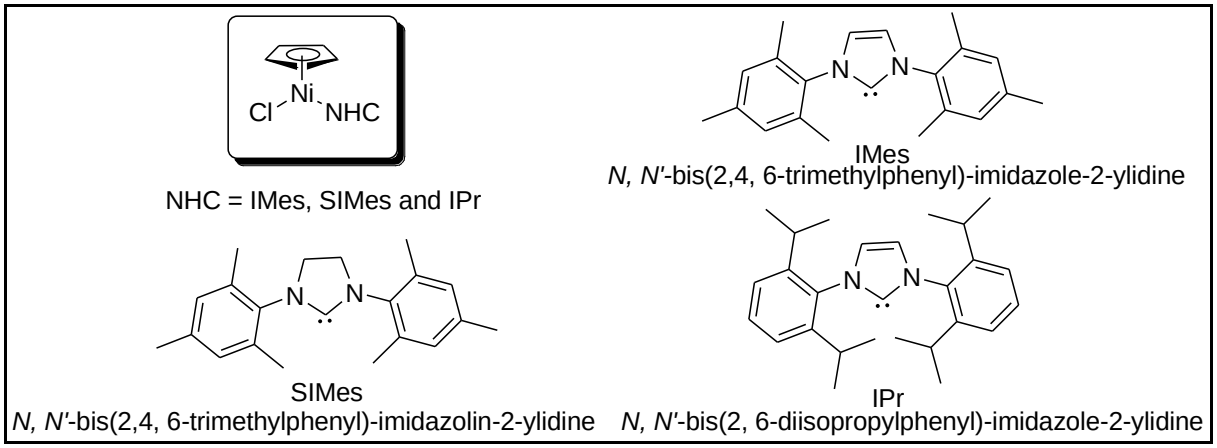
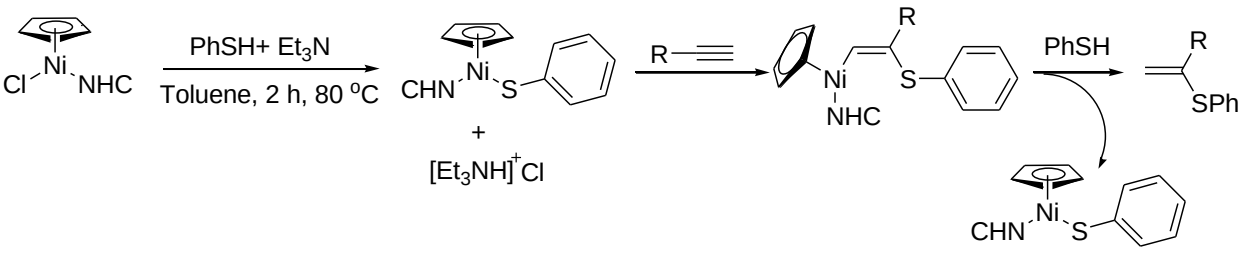


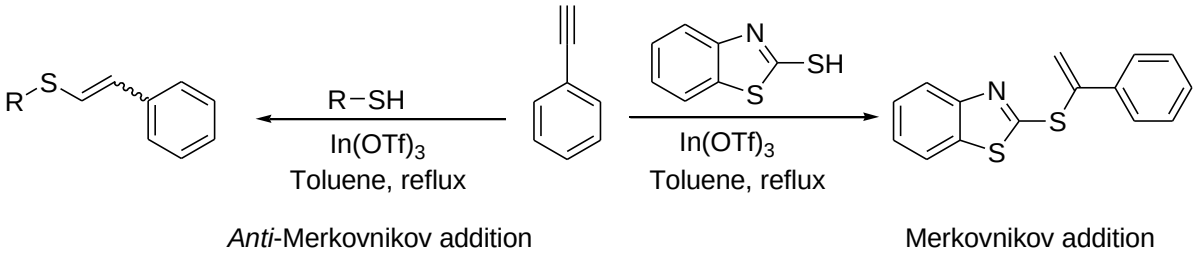
Figure III.C.3. Structures of Ni–NHC complex and some NHCs

The reaction was performed at 80 °C with triethyl amine as base and toluene as solvent. Reaction required 5 hours for desired conversion of the products. The exact mechanism was described by the authors and this is presented below (Scheme III.C.11).[10]



Scheme III.C.11. Mechanism of Ni–NHC–catalyzed hydrothiolation reaction

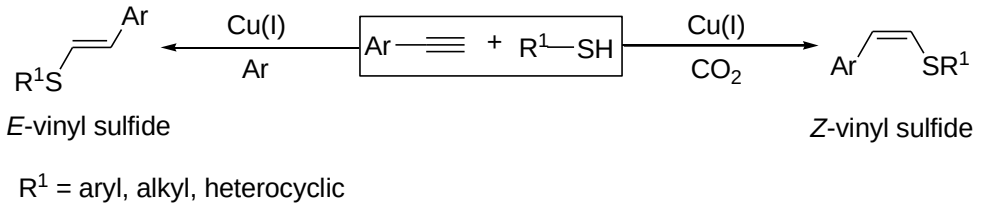
Recently it has been shown that $In(OTf)_3$ selectively catalyzes both Markovnikov and *anti*–Markovnikov hydrothiolation of terminal alkynes. When 2–mercapto benzothiazole, 2–mercapto benzoxazole or 2–mercapto oxazole reacted with terminal alkynes Merkovnikov adduct has been found to form. In the case of aliphatic or aromatic thiols, *anti*–Merkovnikov adduct was formed (Scheme III.C.12).[16]



R = Cyclohexyl, cyclopentyl, *n*-propyl, *iso*-propyl, *p*-tolyl

Scheme III.C.12. In(III)–catalyzed substrate selective hydrothiolation of terminal alkynes

The (*E*)– and (*Z*)– selectivity of the vinyl sulfide can be achieved by tuning the reaction environment under Cu(I)–catalyzed hydrothiolation reaction. Under argon and CO_2 atmospheres *E*–isomer and Z–isomer was formed respectively with major amounts (Scheme III.C.13).[25]



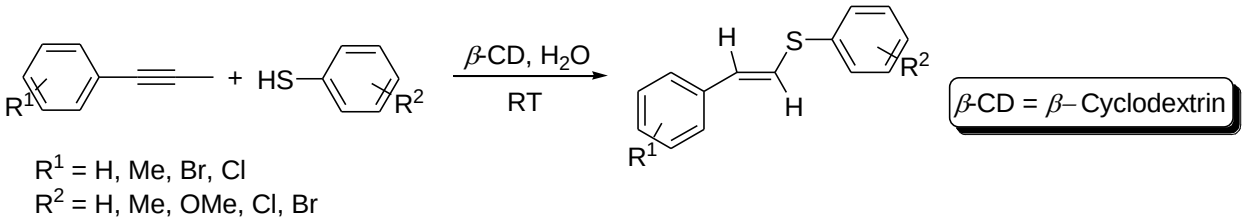
R^1 = aryl, alkyl, heterocyclic

Scheme III.C.13. Cu(I)–catalyzed hydrothiolation under CO_2 and argon atmosphere

However, transition metal complexes are generally expensive, their uses are not eco–friendly and the course of the reaction might suffer deactivation due to the formation of strong metal–sulphur bonds.[26]

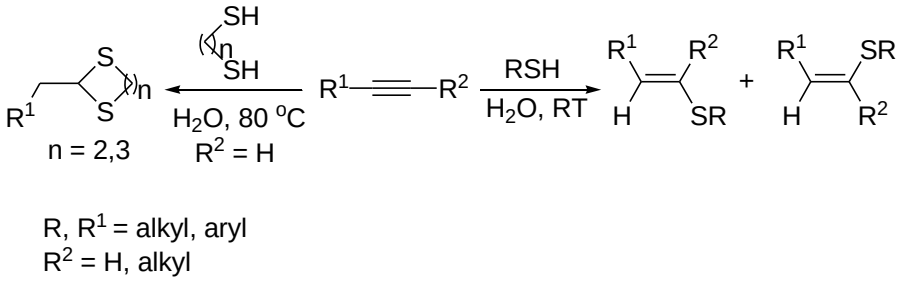
Moreover regioselective (*anti*–Markovnikov) on–water hydrothiolation processes have been reported in the absence or presence of some additives.[18] Although the development of new methodologies using metal catalysts attract much interest in hydrothiolation reaction, the

use of greener solvent media seek importance to the aspect of Green Chemistry. *β*–Cyclodextrine promoted stereoselective hydrothiolation reaction was performed by K. R. Rao and his group. They have shown that the complete formation (*E*)–vinyl sulfides can be achieved in water medium. In this protocol only aromatic terminal alkynes and aromatic thiols were participated. The addition pattern in this case was totally *anti*–Merkovnikov fashion and the product was absolutely (*E*)–vinyl sulfide (Scheme III.C.14).[27]



Scheme III.C.14. Hydrothiolation of alkynes with thiophenols in presence of *β*–Cyclodextrin in Water

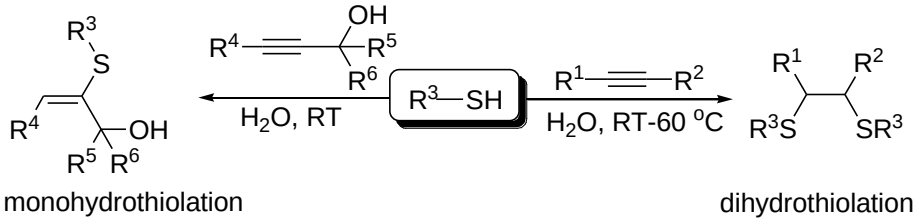
Water–promoted regioselective hydrothiolation of alkynes was performed by B. C. Ranu et al. They have shown that an internal alkyne adds thiols to give both (*E*)– and (*Z*)– products at room temperature. When dithio compounds were used and reacted with terminal alkynes, a cylic dithio compound was formed. It is to be noted that no uniformity of the *E:Z* ratio of the products have been achieved in this methodology. The reaction was found to be retarded down in absence of water (Scheme III.C.15).[28]



Scheme III.C.15. Water–promoted regioselective hydrothiolation reaction

Similarly water mediated hydrothiolation of aromatic and aliphatic alkynes have been performed by G. B. Hammond and his group. This methodology did not require any metal catalysts and hazardous solvent. Vicinal dithioethers were formed by the reaction of one equivalent of aliphatic alkynes and two equivalents of aromatic or aliphatic thiols. Aryl thiols were more reactive than aliphatic thiols. In this case the radical initiator could be the dioxygen in the air. The specific role of the solvent was not clear at this case but it seemed

water has some ability to stabilize the radical intermediate and therefore facilitate the radical mediated reaction. When aromatic thiols reacted with the aliphatic alkynes, dihydrothiolated products have been achieved. But in the case of propergyl alcohols, monohydrothiolation product has been achieved (Scheme III.C.16).[18]



Scheme III.C.16. Green synthesis of vicinal dithioethers and alkenyl thioethers

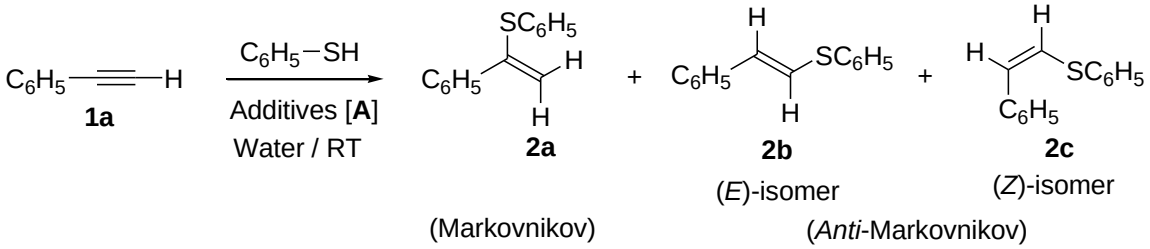
So it is clearly envisaged from the above schemes that a large variety of reagents/catalysts that are used in the hydrothiolation of terminal alkynes with varying degrees of success in controlling stereo– and regioselectivity. However, many reports include expensive metal catalysts, non–aqueous solvents and high temperature and moreover lacks from (*E/Z*)–stereoselectivity. In practice, there is no general guideline by which one can proceed to prepare a specific stereoisomer of a vinylic sulfide using this straightforward and atom–economic reaction under mild and environment–friendly conditions. Moreover, there are conditions that give rise to selective formation of the thermodynamically favoured (*E*)–alkenyl sulfide, it remains a challenge to develop such optimum conditions that selectively produce (*Z*)–alkenyl sulfides under complete metal–free, base–free and on–water conditions. Here, we examined a systematic investigation on the stereo– and regioselective addition of aliphatic and aromatic thiols to terminal alkynes in the presence of different additives in catalytic or stoichiometric quantities under on–water conditions.

III.C.3. Present work: Results and Discussion

Preliminary studies on the influence of catalyst and/or promoter in hydrothiolation were studied with a model reaction of phenyl acetylene (**1a**) and benzenethiol in the presence of various metal salts, homogeneous and heterogeneous additives/promoters under on–water conditions at room temperature. The reaction was optimized using various additives/promoters included inorganic salts, water–soluble organic molecules, amino acids, surfactants or heterogeneous ion–exchange resins, and the results are summarized in Table III.C.1. Since the hydrothiolated adducts were formed in varying ratios (*E/Z* ratios), the results in the Table III.C.1 have been arranged showing gradual change in the formation of (*E*)–vinyl sulfide (**2b**) to the (*Z*)–isomer (**2c**). The neat condition and the reaction with water

yielded the (*E/Z*) ratio as 83:17 and 80:20 respectively (Table III.C.1, entry 1 and 2). The screening shows that the *E/Z* ratio in favor of (*E*)–vinyl sulfide (87:13) is formed in the presence of NaCl (Table III.C.1., entry 3). The gradual diminish in *E* stereoselectivity has been observed from sucrose to starch in Table III.C.1. (entries 4 to 10). Bronstead acid (trifluoro acetic acid) and Lewis acid (BF_3–Et_2O) also increase the *Z* stereoselectivity (entries of 5 and 6). Similarly, amino acids enhanced the *Z* stereoselectivity (entries 8 and 9). But, the stereochemical outcome favouring the (*E*)–isomer was also seen when the reaction was carried out at higher temperature (65 ^oC) and continued for longer reaction time (10 h) (entry 11; *E/Z* ratio 88:12). On the other side the *Z* stereoselectivity has been found to gradually increase from entry 13 to entry 23 in Table III.C.1. The major (*Z*)–vinyl sulfide was obtained in the presence of a combination of Amberlite resins (Cl) and $FeCl_3.6H_2O$ (entry 23; *E/Z* ratio 22:78). However, a specific observation has to be noted from this study that the on–water additions did not give rise to the formation of any Markovnikov adduct, i.e. other regioisomer (**2a**) was not obtained. The NMR spectral data of the crude products indicated only a mixture of **2b** and **2c** and indeed there was no existance of **2a**.

Table III.C.1. Role of additives in the addition of PhSH to phenylacetylene under on–water and at room temperature conditions.[a]



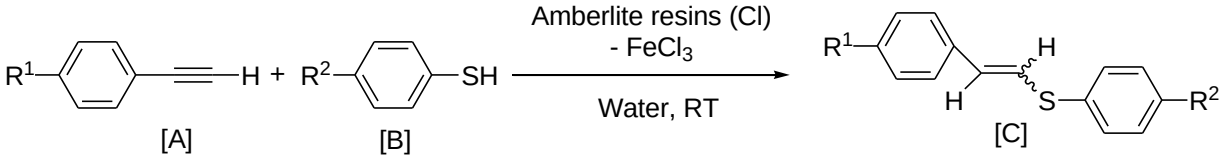
Entry	Additive [A][b]	(*E/Z*) ratio[c,d]	Entry	Additive [A][b]	(*E/Z*) ratio[c,d]
1	Nil (Neat)	83:17	13	CuI–Catechol Violet	60:40
2	Nil (Water)	80:20	14	Amberlite Resins (Cl)	58:42
3	NaCl	87:13	15	n–Bu_4Br	57:43
4	Sucrose	85:15	16	D–Glucose	56:44
5	CF_3COOH	78:22	17	CuI	52:48
6	$BF_3{\cdot}Et_2O$	76:24	18	Cholesterol	51:49
7	Catechol Violet	75:25	19	CTAB	49:51
8	L–Proline	70:30	20	$FeCl_3{\cdot}6H_2O$	44:56
9	Glycin	69:31	21	Amberlite Resins (OH)	40:60
10	Starch	64:36	22	D–Glucose & $FeCl_3{\cdot}6H_2O$	35:65
11[e]	Water (65 ^oC)	88:12	**23**	**Amberlite Resins (Cl) &**	**22:78**

12	Water (65 ^{o}C)	64:36	**$FeCl_3 \cdot 6H_2O$**

[a]Reaction conditions: Phenyl acetylene (0.5 mmol), PhSH (0.55 mmol), water (1 mL), 2 h.
[b]Additive [**A**] (2 mol %).
[c]*E/Z* ratio was determined by ^{1}H NMR of the crude mixture.
[d]Yield of the mixture of stereoisomers after chromatographic purification varies in the range 80–90%.
[e]The reaction was continued for 10 h; all other reactions were carried at room temperature unless mentioned.

At this point, effect of functional groups in the aromatic moiety in either of the addition partners could be worth investigating. Since a combination of ion–exchange resins and ferric chloride showed a better selectivity towards the formation of (*Z*)–vinyl sulfide, this study was performed under similar conditions. The results are presented in Table III.C.2. It is seen that both electron–donating and electron–withdrawing functional groups present on the aryl ring can give rise to the *anti*–Markovnikov hydrothiolation products in excellent yields (85–94%). Highest (*Z*)–selectivity was found in the reaction between phenyl acetylene and *p*–methoxybenzenethiol (Table III.C.2, entry 4; *E/Z* 12:88), possibly due to easy emulsification of the alkyne in water upon stirring, which might be supportive in addition to the presence of the additive. On the other hand, presence of electron–withdrawing group (fluorine) on the thiol part did not show any appreciable influence towards stereoselective addition yielding the (*E*)– isomer in major (entries 6–7). It seems that there is not much electronic influence of the functional groups in the aryl ring of either of the addition partners; rather their stability in water in the presence of the additive might have some control towards *anti*–Markovnikov stereoselectivity.

Table III.C.2. Hydrothiolation of aryl acetylene [A] with aromatic thiols [B] in (1:1.1) molar ratios in water at room temperature.



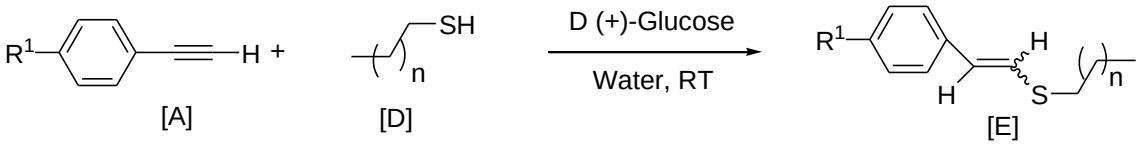
Entry	[A]	[B]	Time (h)	Yield[a] (%) [C]	*E* / *Z* [C][b]
1	R^1 = H	R^2 = H	2.0	85	22 : 78
2	R^1 = CH_3	R^2 = H	3.5	91	40 : 60
3	R^1 = CH_3	R^1 = CH_3	2.5	88	29 : 71
4	R^1 = H	R^1 = OCH_3	3.0	93	12 : 88
5	R^1 = CH_3	R^1 = OCH_3	2.0	90	22 : 78

6	R^1 = H	R^2 = F	2.0	88	80: 20
7	R^1 = CH_3	R^2 = F	2.0	94	39: 61

[a]Yield represents the product [C] after purification by column chromatography.
[b]*E/Z* ratio was determined by ^{1}H NMR of the crude mixture.

In cases of aryl acetylenes and aliphatic thiols combination, D(+)–glucose plays a vital role for achieving (*Z*)–stereoselectivity. Hydrothiolation of aryl acetylenes (terminal) with aliphatic thiols in the presence of one equivalent of D(+)–glucose showed a general trend in favour of the formation of (*Z*)–vinyl sulphides. For example, phenyl acetylene undergoes hydrothiolation in the presence of *n*–alkyl thiols afforded the corresponding 1–alkenyl sulphides with (*E/Z*) ratios (14:86). The results are listed below in Table III.C.3.

Table III.C.3. Hydrothiolation aromatic terminal alkynes with aliphatic thiols.



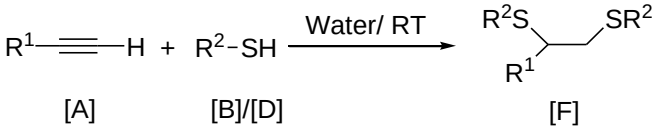
[A] [D] [E]

Entry	[A]	[D]	Time (h)	Yield[a] (%) [E]	*E / Z* [C][b]
1	R^1 = H	n = 3	3.0	75	20 : 80
2	R^1 = H	n = 5	3.0	64	14 : 86
3	R^1 = CH_3	n = 3	4.5	79	14 : 86
4	R^1 = CH_3	n = 5	5.0	51	21 : 79

[a]Yield represents the product [E] after purification by column chromatography.
[b]*E/Z* ratio was determined by ^{1}H NMR of the crude product mixture.

Since there is significant reactivity difference between aliphatic and aromatic thiols,[29] we ought to investigate the stereochemical outcome in two other cases: hydrothiolation of (i) aliphatic terminal alkynes and aliphatic thiols and (ii) aliphatic terminal alkynes and aromatic thiols. It has been seen from previous reports that aliphatic alkynes undergo dihydrothiolation yielding *vicinal* disulfides only irrespective of nature of the thiol.[18a,28] Thus, aliphatic terminal alkynes were subjected to hydrothiolation with aromatic and aliphatic thiols under on–water conditions. Apparently, there was influence of additives in this double–addition reaction. The results are presented in Table III.C.4, which show that aliphatic terminal alkynes undergo double– additions yielding finally 1, 2–disulfides only in the presence or absence of D (+)–Glucose.

Table III.C.4. Dihydrothiolation of aliphatic alkyne with thiols in water at room temperature.



Entry	[A]	[B]/[D][a]	Time (h)	Yield[b] (%) [F]
1[c]	$R^1 = CH_3–CH_2–CH_2$	R^2 = Ph	5	88
2	$R^1 = CH_3–CH_2–CH_2$	R^2 = Ph	5	76
3	$R^1 = CH_2OAc$	R^2 = Ph	6	79
4	$R^1 = CH_3–CH_2–CH_2$	$R^2 = CH_3(CH_2)_6SH$	9	58

[a][A]:[B] is 1:2.2 molar ratios.
[b]Yield represents the product [F] after purification by column chromatography.
[c]D (+) Glucose (1 equiv) was added.

As regards to the mechanism of hydrothiolation of terminal alkynes in water, the literature reports are of different views. For example, Ranu et al,[28] found that the water–promoted regioselective hydrothiolation excluded the radical pathway because the reaction proceeds in the presence of dissolved oxygen whereas Hammond et al,[7a] hinted that the reaction probably proceeds through a radical mechanism under similar conditions. The latter group further observed that the reaction did not occur in the presence of galvinoxyl free radical. But this was not only the proof for radical mechanism.[30] Our studies demonstrated a role of additives in governing the stereoselectivity but the specific function of the additive, particularly in aqueous medium and the mechanistic routes are not cleared. Furthermore, carrying out the reaction in the presence of radical initiator (AIBN) or light did not make the process faster appreciably. Several transition metal complexes are known to catalyze the process of hydrothiolation via radical intermediates leading to major *anti*–Markovnikov 1–alkenyl sulfides. In the absence of such metal complexes, the stabilization of the reactive species has been achieved by water as well as by the additive might alter the course of the reaction pathway.

III.C.4. Conclusions

In search of finding ‘stereoselective–switch’ for the hydrothiolation of terminal alkynes under on–water conditions, we have found two types of additives that could lead to the stereoselective formation of the (*Z*)–1–alkenyl sulfides in substantial quantities depending on

the nature of both reacting partners. Here we are able to give a direction for the formation of (Z)–isomer by mild and green reaction conditions.

III.C.5. Experimental section

III.C.5.1. General information

All the reactions were carried out in closed vessel under ambient conditions. Amberlyst® IRA–900, Cl form was purchased from ACROS Organics, India. $FeCl_3.6H_2O$ and D(+)–glucose were purchased from Sd–fine Chem. Ltd. and Glaxo Laboratories (India) Ltd. respectively. For column chromatography: silica (60–120 mesh) (SRL, India), and for tlc, Merck plates coated with silica gel 60, F_{254} were used. All compounds were identified by ^{1}H– and ^{13}C–NMR spectra, recorded on a Bruker AV300 spectrometer operating at 300 and 75 MHz respectively and supported by FT–IR spectra. All NMR spectra were measured in $CDCl_3$. Chemical shifts are given in δ (ppm) downfield from TMS. Characterization of sulfanes (Table III.C.2, Table III.C.3 and Table III.C.4) has been made from melting point and ^{1}H– and ^{13}C–NMR spectral data.

III.C.5.2. General procedure for mono–hydrothiolation of alkynes

To a mixture of alkyne (1 mmol), thiol (1.1 mmol) in water (0.5 mL) was added the additive (1 mmol) and stirred at room temperature (25–30 ^{o}C) for 2–5 h (tlc). The reaction mixture was extracted with diethyl ether (3×10 mL), and the combined organic layer was washed with brine and then dried over Na_2SO_4. Evaporation of solvent under *vacuo* afforded an oily residue, which was passed through a short bed of silica gel and NMR spectrum was recorded to evaluate the percent of (*E/Z*) isomers. NMR spectral data and scanned copies of selected NMR spectra are given in the supporting information and found to be in good agreement with those reported.

III.C.5.3. General procedure for di–hydrothiolation of alkynes

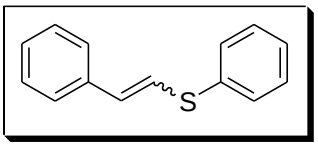
A mixture of alkyne (1 mmol), thiol (2.2 mmol) in water (0.5 mL) was stirred for 5–9 h at room temperature (tlc). The reaction mixture was then extracted with diethyl ether (3×10 mL), and the combined organic layer was washed with brine and then dried over Na_2SO_4. Evaporation of solvent under *vacuo* afforded an oily residue, which was passed through a short bed of silica gel to afford 1, 2–disufides in good to excellent yields. The products were identified on the basis of ^{1}H–, ^{13}C–NMR spectral data, and/or by comparison with the data

reported in the literature. NMR spectral data and scanned copies of selected NMR spectra (^{1}H– & ^{13}C–) are given in the supporting information.

III.C.5.4. Physical properties and spectral data of compounds

Table III.C.2, Entry 1

Mixture of (*E/Z*)–phenyl(styryl)sulfane[31]



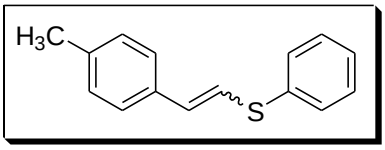
Pale yellow oil, *E/Z* ratio = 28:72 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 6.49 (d, *J* = 10.8 Hz), 6.58 (d, *J* = 10.8 Hz), 6.72 (d, *J* = 15.6 Hz), 6.88 (d, *J* = 15.6 Hz), 7.19–7.52 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 123.3, 126.0, 126.9, 127.1, 127.2, 127.2, 127.6, 128.3, 128.7, 128.7, 129.1, 129.8, 130.0, 131.8, 135.2, 136.2, 136.4, 136.5.

Table III.C.2, Entry 2

Mixture of (*E/Z*)–phenyl(4–methylstyryl)sulfane



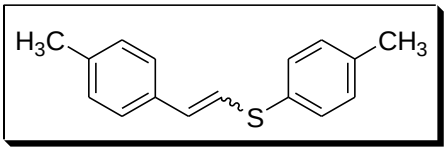
Pale yellow crystalline solid, mp 39–40 ^{o}C; *E/Z* ratio = 40:60 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 2.32, 2.34 (s, $–CH_3$), 6.42 (d, *J* = 10.5 Hz), 6.56 (d, *J* = 10.8 Hz), 6.72 (d, *J* = 15.3 Hz), 6.81 (d, *J* = 15.6 Hz), 7.09–7.45 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 21.2, 21.3 (CH_3), 121.7, 124.7, 125.9, 126.7, 127.0, 127.3, 128.9, 129.0, 129.3, 129.4, 129.7, 129.9, 132.3, 133.6, 133.7, 134.1, 135.5, 136.3, 136.9, 137.5.

Table III.C.2, Entry 3

Mixture of (*E/Z*)–(4–methylphenyl)(4–methylstyryl)sulfane



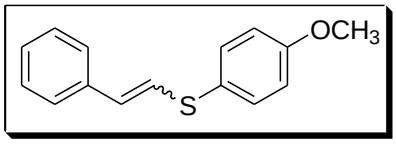
White crystalline solid, mp 48–49 ^{o}C; *E/Z* ratio = 29:71 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 2.31, 2.32 (s, –CH_3), 6.38 (d, *J* = 10.8 Hz), 6.50 (d, *J* = 10.8 Hz), 6.64 (d, *J* = 15.3 Hz), 6.79 (d, *J* = 15.3 Hz), 7.07–7.43 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 21.0, 21.1, 21.2 (CH_3), 122.9, 125.8, 125.9, 126.6, 128.7, 128.9, 129.3, 129.7, 129.9, 130.3, 130.4, 131.0, 137.0, 137.2, 137.3.

Table III.C.2, Entry 4

Mixture of (*E/Z*)–(4–methoxyphenyl)(styryl)sulfane[32]



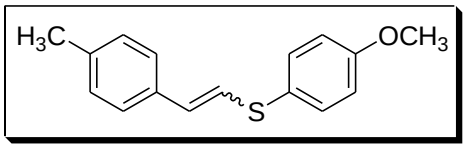
White crystalline solid, mp 61 ^{o}C (Lit. mp 58–60 ^{o}C); *E/Z* ratio = 12:88 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 3.74, 3.76 (s, –OCH_3), 6.38 (d, *J* = 11.1 Hz), 6.46 (d, *J* = 10.8 Hz), 6.49 (d, *J* = 15.6 Hz), 6.81 (d, *J* = 15.6 Hz), 6.84–7.52 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 55.0, 55.3, 55.5, 55.8 (OCH_3), 114.8, 114.9, 125.7, 126.8, 127.1, 127.9, 128.2, 128.3, 128.4, 128.6, 128.8, 128.9, 128.9, 129.1, 132.5, 132.8, 132.9, 133.1, 133.4, 136.6, 136.7, 159.5.

Table III.C.2, Entry 5

Mixture of (*E/Z*)–(4–methoxyphenyl)(4–methylstyryl)sulfane



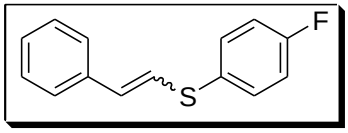
White crystalline solid, mp 68 ^{o}C; *E/Z* ratio = 22:78 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 2.30, 2.34 (s, –CH_3), 3.77 (s, –OCH_3), 6.32 (d, *J* = 10.8 Hz), 6.45 (d, *J* = 10.8 Hz), 6.75 (d, *J* = 15.3 Hz), 6.84–7.41 (m, Ar–H and olefinic H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 21.3, 21.4 (CH_3), 55.0, 55.3, 55.5, 55.8 (OCH_3), 113.9, 114.7, 114.8, 124.2, 124.8, 125.3, 125.8, 126.7, 127.0, 127.2, 127.7, 127.8, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 129.0, 129.0, 129.1, 129.3, 129.4, 129.5, 130.0, 131.9, 132.4, 132.7, 132.8, 133.0, 133.1, 133.3, 133.9, 134.0, 136.8, 137.1.

Table III.C.2, Entry 6

Mixture of (*E/Z*)–(4–fluorophenyl)(styryl)sulfane



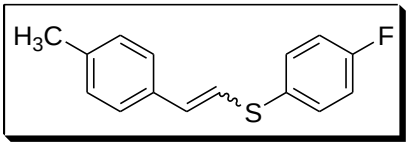
Pale yellow oil, *E/Z* ratio = 80:20 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 6.41 (d, *J* = 10.5 Hz), 6.58 (d, *J* = 10.5 Hz), 6.65 (d, *J* = 15.3 Hz), 6.83 (d, *J* = 15.6 Hz), 7.01–7.43 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 116.2, 116.53, 123.8, 123.9, 125.9, 126.0, 126.1, 126.5, 127.0, 127.7, 128.6, 128.8, 129.8, 129.9, 131.1, 132.5, 132.6, 132.7, 136.4, 160.6, 163.9.

Table III.C.2, Entry 7

Mixture of (*E/Z*)–(4–fluorophenyl)(4–methylstyryl)sulfane



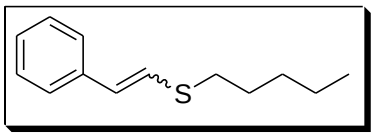
White crystalline solid, mp 60–61 ^{o}C; *E/Z* ratio = 39:61(from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 2.35 (s, $–CH_3$), 6.32 (d, *J* = 10.5 Hz), 6.53 (d, *J* = 10.5 Hz), 6.64 (d, *J* = 15.6 Hz), 6.74 (d, *J* = 15.0 Hz), 7.00–7.37 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 21.2, 21.3, 21.4 ($–CH_3$), 116.1, 116.4, 122.3, 125.3, 125.9, 126.0, 126.8, 127.2, 127.6, 128.2, 128.5, 128.8, 129.0, 129.0, 129.1, 129.4, 130.2, 130.2, 131.5, 131.6, 131.8, 132.1, 132.3, 132.4, 132.5, 132.6, 133.5, 133.6, 137.1, 137.6, 160.6, 163.8, 163.9.

Table III.C.3, Entry 1

Mixture of (*E/Z*)–pentyl(styryl)sulfane



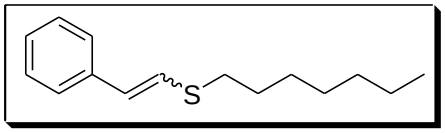
Pale yellow oil, *E/Z* ratio = 20:80 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.90 (t), 1.20–1.58 (m), 1.63–1.73 (m), 2.76 (t), 6.23 (d, *J* = 11.1 Hz), 6.42 (d, *J* =10.8 Hz), 6.45 (d, *J* = 15.3 Hz), 6.72 (d, *J* = 15.6 Hz), 7.16–7.49 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 14.0, 22.3, 29.1, 29.9, 30.7, 31.0, 35.9, 125.2, 126.5, 127.7, 127.8, 128.1, 128.4, 128.7, 129.0, 137.0.

Table III.C.3, Entry 2

Mixture of (*E/Z*)–heptyl(styryl)sulfane



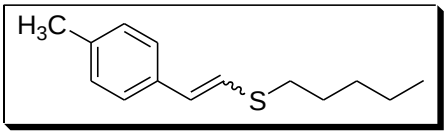
Pale yellow oil, *E/Z* ratio = 14:86 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.88 (t), 1.28–1.78 (m), 2.78 (t), 6.24 (d, *J* = 10.8 Hz), 6.43 (d, *J* = 11.1 Hz), 6.45 (d, *J* = 15.3 Hz), 6.72 (d, *J* = 15.6 Hz), 7.20–7.49 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 14.0, 22.6, 28.6, 30.3, 31.7, 35.9, 125.2, 126.5, 127.7, 128.2, 128.6, 137.0.

Table III.C.3, Entry 3

Mixture of (*E/Z*)–pentyl(4–methylstyryl)sulfane



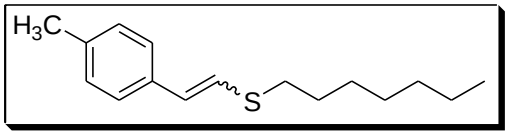
Colourless oil, *E/Z* ratio = 14:86 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.90 (t), 1.29–1.43 (m), 1.68 (m), 2.33 (s), 2.77 (t), 6.17 (d, *J* = 10.8 Hz), 6.40 (d, *J* = 10.8 Hz), 6.65 (d, *J* = 15.3 Hz), 7.08–7.39 (m, Ar–H and olefinic H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 13.9, 21.2, 22.3, 29.1, 29.9, 30.7, 30.9, 32.6, 35.8, 125.2, 125.3, 126.5, 128.5, 129.3, 134.2, 134.3, 136.3.

Table III.C.3, Entry 4

Mixture of (*E/Z*)–heptyl(4–methylstyryl)sulfane



Yellow oil

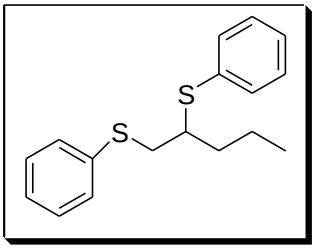
E/Z ratio = 21:79 (from ^{1}H–NMR spectral data)

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.90 (t), 1.20–1.39 (m), 1.52–1.72 (m), 2.31 (s), 2.65–2.79 (t), 6.16 (d, *J* = 10.8 Hz), 6.39 (d, *J* = 10.8 Hz), 6.65(d, *J* = 16.8 Hz), 7.07–7.93 (m, Ar–H and olefinic H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 14.1, 21.2, 21.3, 22.6, 28.6, 28.9, 30.2, 31.7, 35.8, 122.2, 126.5, 128.1, 128.4, 128.6, 128.9, 129.3, 134.2, 136.3.

Table III.C.4, Entry 1

1–(1–(Phenylthio)pentan–2–ylthio)benzene



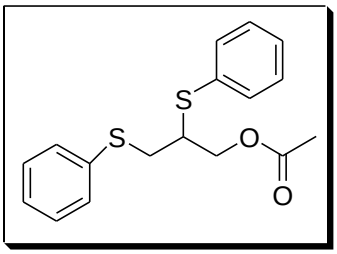
Colourless oil

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.93 (t, *J* = 3.6 Hz, 3H), 1.49–1.60 (m, 4H), 2.84–2.92 (m, 1H), 3.10–3.27 (m, 2H), 7.16–7.33 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 13.8, 20.0, 34.8, 39.5, 48.1, 126.2, 127.2, 128.9, 128.9, 128.9, 129.8, 132.5, 134.4, 135.9.

Table III.C.4, Entry 2

2,3–Bis(Phenylthio)propyl acetate



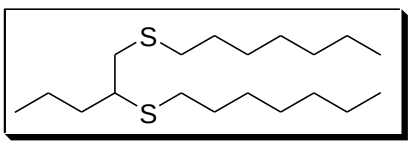
Pale yellow oil

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 2.10 (s, 3H), 3.13–3.24 (m, 2H), 3.34–3.37 (m, 1H), 4.29–4.42 (m, 2H), 7.21–7.39 (m, Ar–H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 20.7, 35.8, 47.1, 64.5, 126.6, 127.8, 129.0, 129.2, 129.9, 132.9, 135.2, 170.7.

Table III.C.4, Entry 3

1–(1–(Heptylthio)pentan–2–ylthio)heptane



Colourless oil

^{1}H NMR ($CDCl_3$, 300 MHz): δ/ppm 0.86–0.95 (m, 9H), 1.28–1.80 (m, 24H), 2.50–2.75 (m, 6H), 2.82–2.87 (dd, *J* = 4.2 and 12 Hz, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz): δ/ppm 13.2, 13.9, 14.0, 14.8, 19.9, 22.6, 28.4, 28.8, 28.9, 29.4, 29.8, 29.9, 30.3, 30.8, 31.7, 33.1, 35.7, 38.4, 45.5.

III.C.6. References

References are given in BIBLIOGRAPHY under Chapter III, Section C (pp. 149–150).