

SYNTHESIS OF HETEROCYCLIC COMPOUNDS FROM METALLATED UNSATURATED COMPOUNDS AND ISOTHIOCYANATES.* (REVIEW)

L. Brandsma¹, N. A. Nedolya², O. A. Tarasova², and B. A. Trofimov²

Novel syntheses of heterocyclic compounds resulting from reactions of metallated acetylenes, allenes, and conjugated dienes with isothiocyanates and from reactions of the latter with strong bases are reviewed.

Keywords: acetylenes, allenes, conjugated dienes, metallation, isothiocyanates, *in situ* functionalization, base-induced self-condensation, allyl isothiocyanate, cyclization.

1. INTRODUCTION

The reaction between alkyl-, aryl-, and hetaryllithiums or corresponding Grignard compounds and isocyanates or isothiocyanates has been applied to prepare carboxamides and analogous thioamides [1-7]. There are only few data on reactions of these heterocumulenes with unsaturated anionic intermediates [8-10]. In previous investigations the reaction between metallated acetylenes or allenes and carbon disulfide or thiocarbonyl compounds has been applied to syntheses of thiophene derivatives [11-15].

The investigations described in the present review are a continuation of this work. It is shown that the reaction between metallated unsaturated compounds and isothiocyanates gives access to a variety of heterocyclic systems.

2. AVAILABILITY OF ISOTHIOCYANATES AND UNSATURATED COMPOUNDS

A number of isothiocyanates are commercially available. The various synthetic methods for isothiocyanates have been reviewed [16-19]. Perhaps the most general method involves the reaction of primary amines with thiophosgene.

Scheme 1

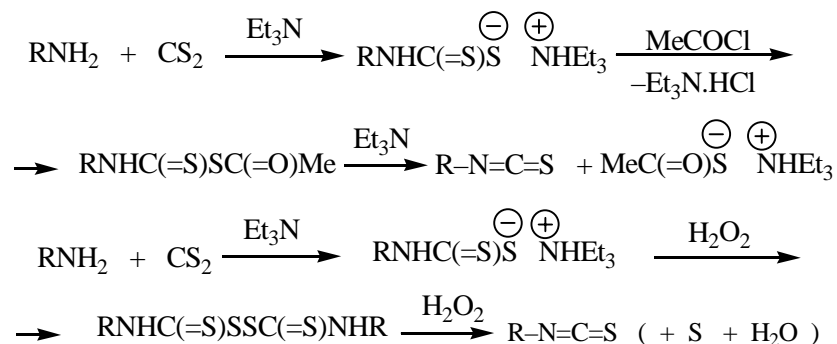


* This account is based on the lectures given during the Conference on Sulfur Chemistry, Kazan, 18-23 October, 1999, on the dissertation of Dr. N. A. Nedolya (Utrecht, May, 1999), and on several unpublished data. Dedicated to Prof. Dr. H. Günther (University of Siegen, Germany) on the occasion of his 65th birthday.

¹ Utrecht University 3584 Utrecht, The Netherlands; e-mail: l.brandsma@chem.uu.nl. ² A. E. Favorsky Institute of Chemistry, Siberian Branch of Russian Academy of Sciences; e-mail: admin@irioch.irk.ru. Published in *Khimiya Geterotsiklicheskikh Soedinenii*, No. 11, pp. 1443-1463, November, 2000. Original article submitted January 25, 2000.

A large number of aliphatic, alicyclic, and aromatic isothiocyanates can be prepared by this method, in most cases in high yields. The procedure involves dropwise addition of the amine, dissolved in dichloromethane, chloroform or water at temperatures in the region of 0°C to a mixture of thiophosgene, dichloromethane, or chloroform, water, and potassium or calcium carbonate; in the case of the more strongly basic aliphatic or alicyclic amines an additional amount of NaOH or KOH should be used to achieve complete conversion of the thiophosgene [20]. Two other promising methods have been published [21, 22].

Scheme 2



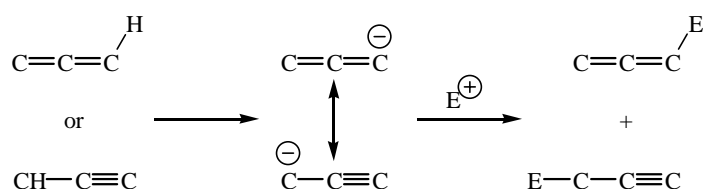
The unsaturated compounds involved in our investigations include 1-alkynes $\text{RC}\equiv\text{CH}$ ($\text{R} = \text{Alk}, \text{CH}_2\text{OR}^1, \text{CH}_2\text{NR}^1_2, \text{OR}^1, \text{NR}^1_2$), 2-alkynes $\text{RC}\equiv\text{CCH}_3$ ($\text{R} = \text{Alk}$ or SAlk), 2-alkynyl ethers and 2-alkynyl amines $\text{RC}\equiv\text{CCH}_2\text{-X}$ ($\text{X} = \text{OR}^1$ or NR^1_2), allenyl ethers and allenyl sulfides $\text{H}_2\text{C}=\text{C}=\text{CHX}$ ($\text{X} = \text{OR}$ or SR), allenic hydrocarbons $\text{RCH}=\text{C}=\text{CH}_2$ and $\text{R}_2\text{C}=\text{C}=\text{CH}_2$, and heterosubstituted dienes, $\text{H}_2\text{C}=\text{CH}-\text{CH}=\text{CHXR}$ ($\text{X} = \text{O}$ or S). Experimental procedures for most of the unsaturated compounds are described in the laboratory manuals [9, 23]; for the heterosubstituted dienes see [24].

3. METALLATION OF UNSATURATED COMPOUNDS AND FUNCTIONALIZATION

Metallation of the unsaturated starting compound is the first step in most of our syntheses of heterocyclic compounds. The methods for generating the polar organometallic intermediates are amply illustrated with representative experimental procedures on a preparative scale in the laboratory manuals [8, 9, 23].

An important aspect of the derivatization of some metallated acetylenes or allenes is the regiochemistry. The anionic species, in principle, can react in mesomeric forms giving rise to the formation of both the acetylenic and the allenic derivative [25].

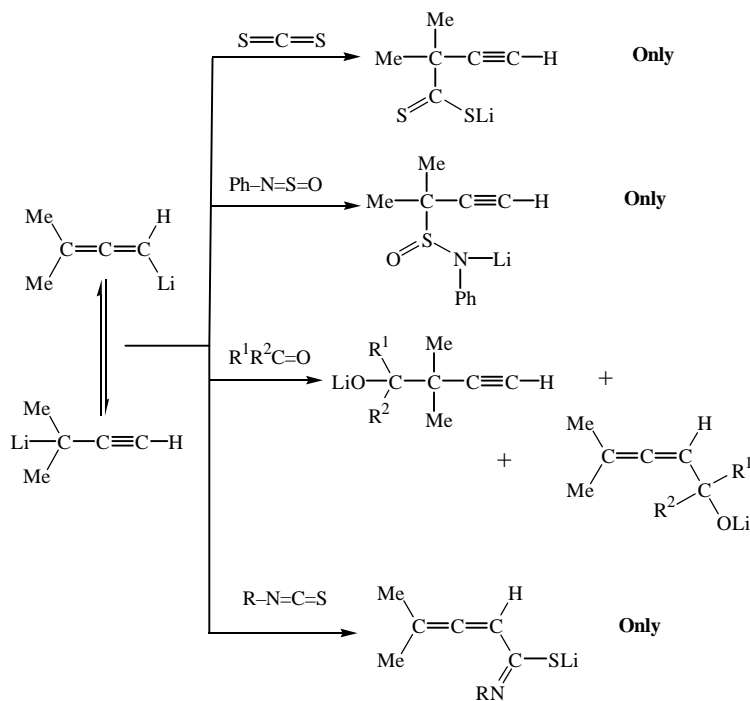
Scheme 3



In some cases it has appeared to be possible to direct the reaction towards one of the products by replacing the metal ion by another one. This may be done by a simple exchange reaction (e.g., addition of MgBr_2 or ZnCl_2 to a solution of the lithium derivative). The regiochemistry may also strongly depend on the nature of the electrophile or on the nature of the substituents in a particular electrophile [25]. The solvent (polarity of the medium) may also strongly influence the regiochemistry, e.g., [26, 27]. The outcome of a derivatization reaction with a mesomeric

acetylenic-allenic anion is in many cases an empirical matter. For example, whereas 1,1-dimethylallenyllithium and carbon disulfide as well as phenylsulfinyl amine [28] give exclusively the acetylenic adduct, mixtures of the acetylenic and allenic carbinolate are formed in reactions with carbonyl compounds [25].

Scheme 4



Remarkably, allenic derivatives were the exclusive or predominant products from the reactions of most acetylenic-allenic anions with *isothiocyanates* [20].

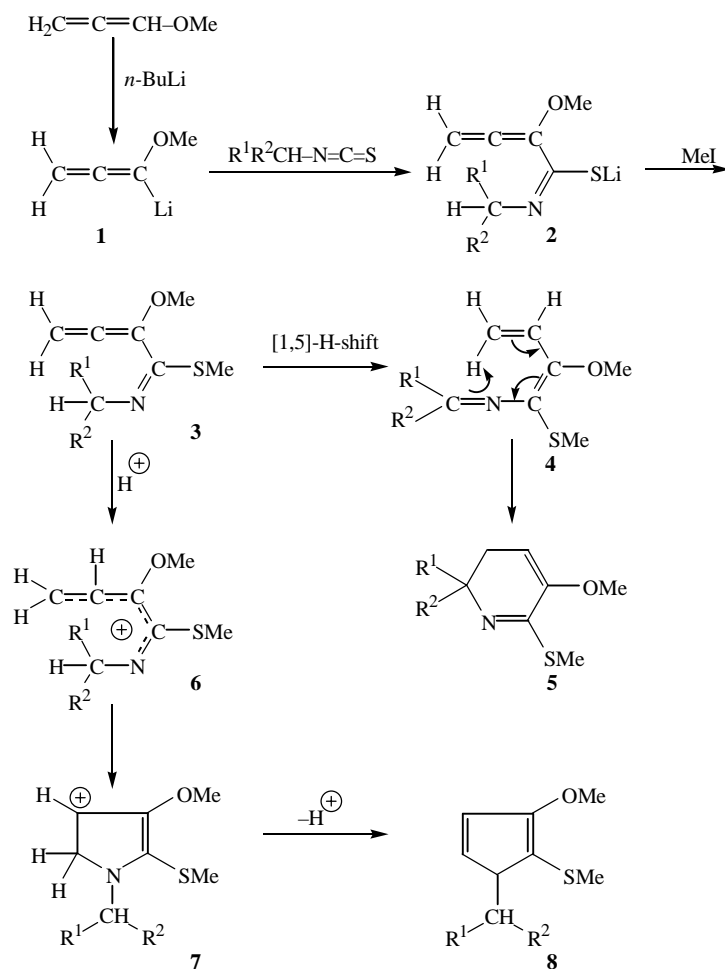
4. SYNTHESIS OF 2,3-DIHYDROPYRIDINES

a. From allenic ethers [20, 29, 30] (Scheme 5).

Addition of alkyl or cycloalkyl isothiocyanates to a strongly cooled solution of lithiated methoxyallene **1** followed by addition of methyl iodide gives the expected azatrienes **3** as mixtures of the *syn*- and *anti*-isomers. These compounds have a low thermal stability, but in a few cases they can be isolated in almost pure state by a careful work-up avoiding bath temperatures higher than 30°C. Heating of the azatriene **3**, obtained from the reaction with methyl isothiocyanate, preferably in the presence of a small amount of a solvent, results in an exothermic reaction affording a ~70 : 30 mixture of the corresponding pyrrole **8** and 2,3-dihydropyridine **5**. Dropwise addition of **3** to hot (~250°C) paraffin oil changes the ratio in favor of **5** (~40 : 60). The combined yields of the heterocycles are excellent. In most other cases **5** was found to be the main product. The formation of **5** may be explained by assuming a [1,5]-sigmatropic H-shift and a subsequent electrocyclization of the fully conjugated azatriene **4** [31].

The assumed intermediate **4** could not be detected when both groups R¹ and R² were H, but moderate heating of the product **3** from the reaction with isopropyl isothiocyanate (R¹ = R² = Me) gave the expected azatriene **4** in a reasonably pure state. Upon stronger heating the dihydropyridine **5** was formed as the predominant product.

Scheme 5



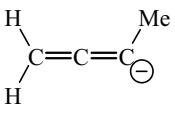
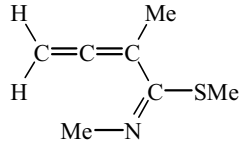
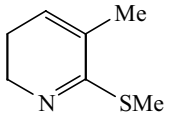
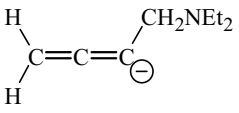
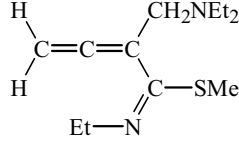
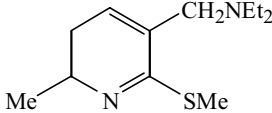
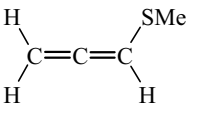
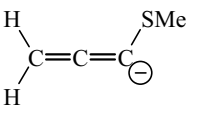
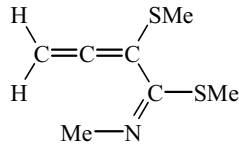
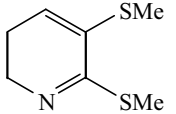
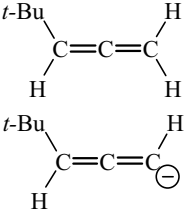
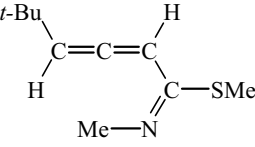
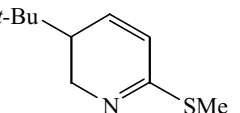
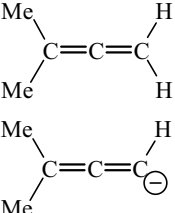
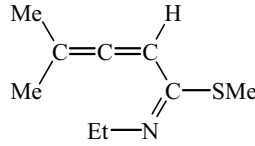
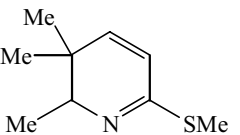
The formation of pyrroles **8** might proceed through the addition of a proton to the allenic system, a subsequent electrocyclization of azacarbenium ion **6** and stabilization of **7** by loss of the proton. Attempts to gain support for this proposal by treating **3** with catalytic amounts of various protonic acids did not give clear results [20].

In all cases compounds **5** and **8** could be quantitatively separated *via* treatment with cold dilute acids, in which only **5** dissolves. This separation procedure gives the possibility to obtain a number of pure 2,3-dihydropyridines **5** or pure pyrroles **8** in fair overall yields.

b. From other allenic or acetylenic compounds [32, 33].

A number of other anionic intermediates generated from acetylenic or allenic compounds by reaction with butyllithium also readily add to alkyl isothiocyanates. The *S*-alkylation products of the adducts undergo thermal rearrangement to fully conjugated azatrienes, which cyclize to give exclusively 2,3-dihydropyridines (cf. Scheme 5). A few examples of syntheses with acetylenes or allenes and methyl or ethyl isothiocyanate are mentioned in Table 1.

TABLE 1.

| Starting compound and anion* | S-Methylated adduct | 2,3-Dihydropyridine |
|--|---|--|
| $\text{Me}-\text{C}\equiv\text{C}-\text{Me}$  |  |  |
| $\text{Me}-\text{C}\equiv\text{C}-\text{CH}_2\text{NEt}_2$  |  |  |
| $\text{Me}-\text{C}\equiv\text{C}-\text{SMe}$ or  <hr style="width: 20%; margin-left: 0;"/>  |  |  |
|  |  |  |
|  |  |  |

* Only the mesomeric structure in which the anion reacts predominantly or exclusively is mentioned.

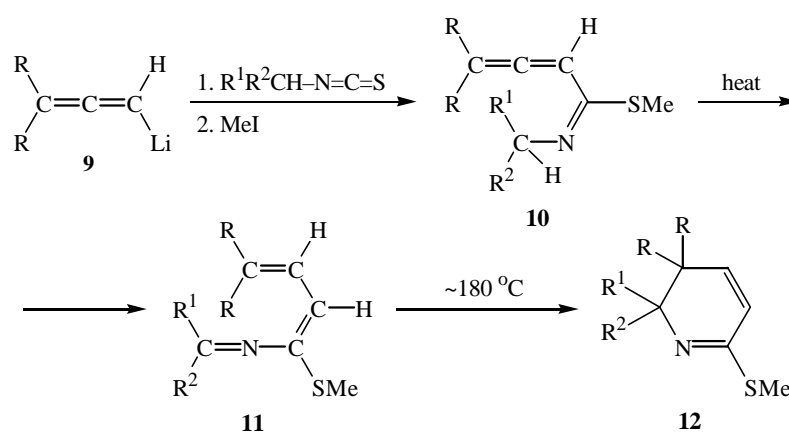
It seems from the results so far obtained that most of the anionic species react exclusively in the allenic form with alkyl isothiocyanates. There are indications, however, that in the reaction of lithiated 2-butyne with *isopropyl* and *cyclohexyl* isothiocyanate small amounts of adducts derived from the acetylenic form are formed [20].

2,3-Dihydropyridines are a scarcely known class of compounds [34-36]. Our approach gives access to a variety of representatives all having an S-alkyl group at the 6-position.

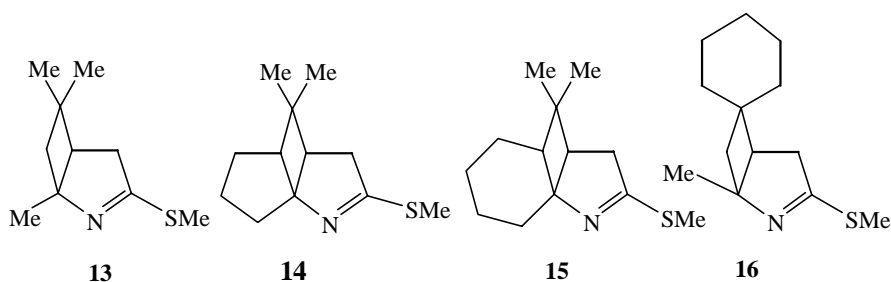
5. FORMATION OF CYCLOBUTANOPYRROLINES

Investigation of the scope of the reaction between 1,1-dimethyl-allenyllithium ($R = \text{Me}$) (**9**) and alkyl or cycloalkyl isothiocyanates led to the discovery of a new, peculiar reaction (Scheme 6). In all cases the expected azatriene **10** was obtained as a crude product after S-alkylation. Upon moderate heating or during distillation in a vacuum, **10** isomerized to the fully conjugated azatriene **11**, presumably by a [1,5]-sigmatropic H-shift. If one of the groups R^1 and R^2 was hydrogen, the final electrocyclic cyclization to dihydropyridine **12** could be achieved by strong heating. Thus, the dihydropyridines **12** having $R^1 = R^2 = \text{H}$ and $R^1 = \text{H}$, $R^2 = \text{Me}$ were synthesized with at least 80% overall yields [20].

Scheme 6



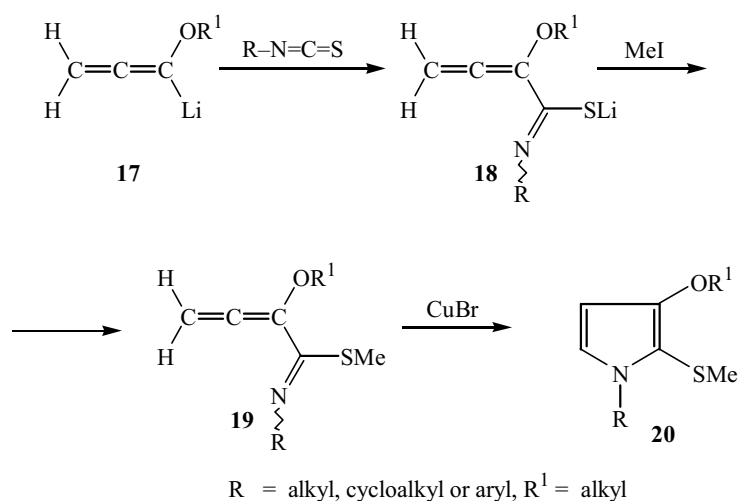
During heating of the azatrienes **11**, having $R_2\text{C} = \text{Me}_2\text{C}$ or $(\text{CH}_2)_5\text{C}$ and $R^1R^2\text{C} = \text{Me}_2\text{C}$, $(\text{CH}_2)_4\text{C}$ or $(\text{CH}_2)_5\text{C}$, however, cyclobutanopyrrolone derivatives **13**, **14**, **15** and **16**, respectively, were obtained in good to excellent yields [37]. Only speculative proposals for the mechanism can be given as yet, e.g., in [38].



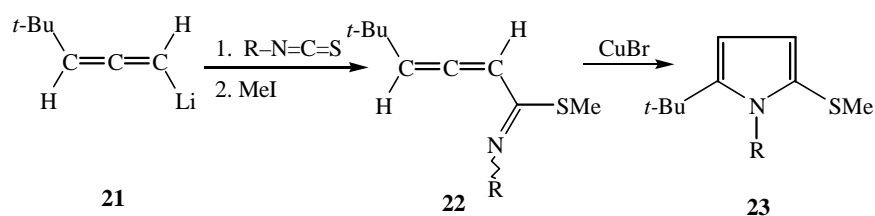
6. COPPER HALIDE-CATALYZED SYNTHESIS OF PYRROLE DERIVATIVES

In order to direct the cyclization of azatrienes **19** towards pyrroles **20** several transition metal catalysts were tried, only copper(I) halides being successful. A number of N-(cyclo)alkyl and N-arylpyrroles **20** and **23** were synthesized in fair to good overall yields starting from lithiated allenic ethers **17** [39] (Scheme 7) or from lithiated *t*-butyllallene **21** [20] (Scheme 8).

Scheme 7

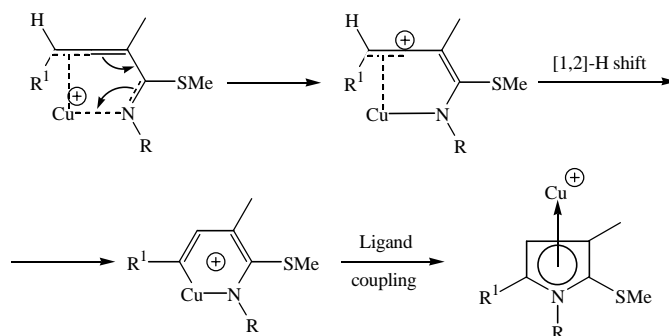


Scheme 8



A mechanistic proposal for the copper-catalyzed formation of pyrroles is given in Scheme 9 [20, 40].

Scheme 9

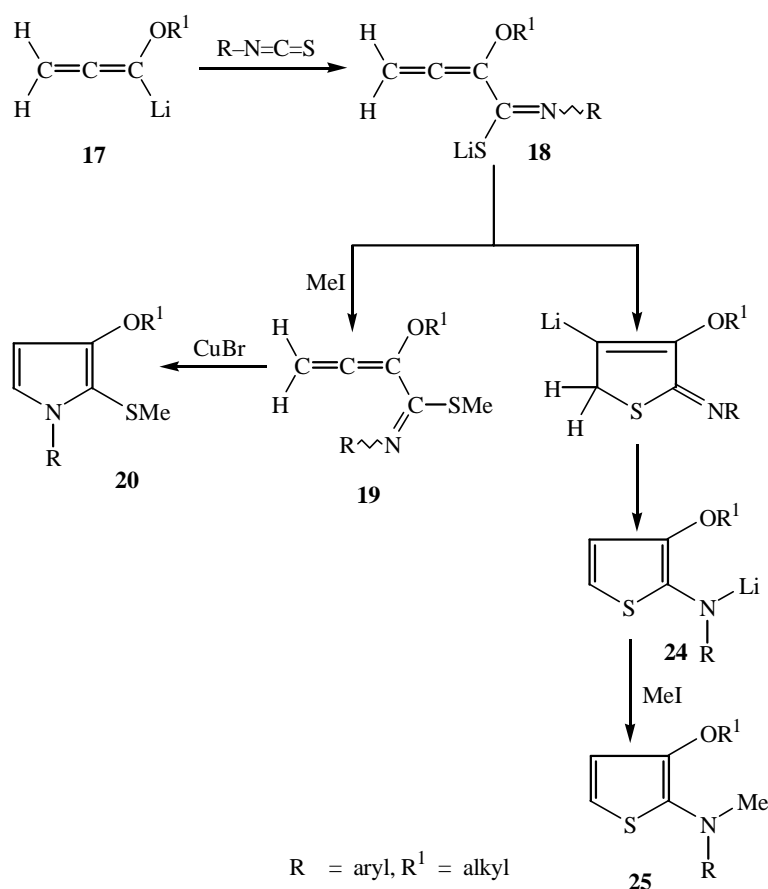


The syntheses with lithiated allenic ethers **17** can be conveniently carried out in one pot [39]. Azatrienes **22** obtained from *t*-butylallene undergo cyclization less easily: in these cases the reaction times can be shortened considerably by removing part of the solvent after addition of copper halide [20].

The synthesis of 1-arylpyrroles **20** (R = aryl) from lithioalkoxyallene **17** and aryl isothiocyanates needs special comments. Especially the adducts from isothiocyanates that have a halogen atom at the *ortho*, *meta*, or *para* position of the phenyl ring can undergo spontaneous cyclization at temperatures far below 0°C. This cyclization takes place in the absence of any proton donor and ultimately leads to the formation of the amide **24**. In some cases appreciable amounts of 2-aminothiophenes **25** may be formed in addition to the pyrroles **20** [20].

This undesired cyclization of adduct **18** could be considerably suppressed by keeping the temperature during the addition of the aryl isothiocyanate to the lithiated allenic ether as low as possible and subsequently performing the methylation with a very large excess of methyl iodide, likewise at very low temperatures. We found

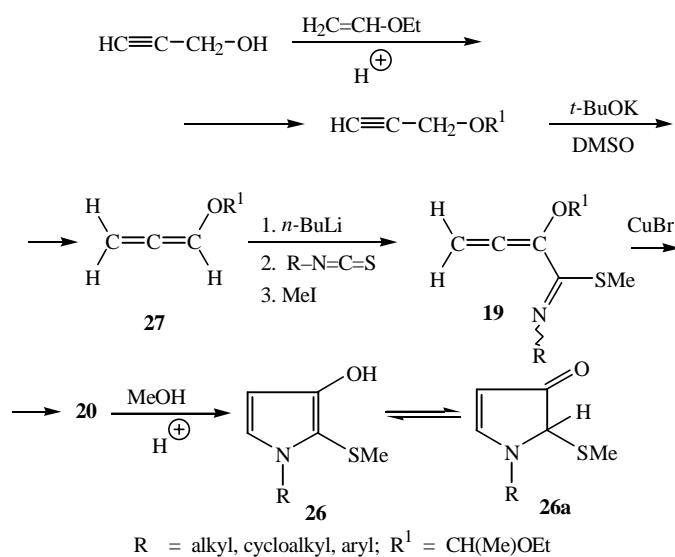
Scheme 10



an efficient method to separate the aminothiophene and the pyrrole, consisting of extraction of the aminothiophene with a 30% aqueous solution of hydrochloric acid. Surprisingly the pyrrole completely survives these conditions [20].

Our copper-catalyzed cyclization to pyrrole derivatives could be usefully applied in a synthesis of 3-hydroxypyrroles **26**. The starting compound **27** can be prepared in large amounts by a simple one-pot procedure in overall yields of at least 90% [20] (Scheme 11).

Scheme 11

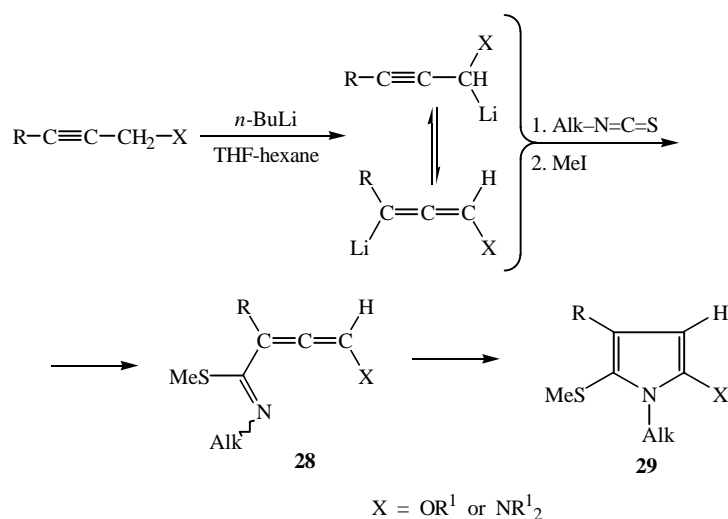


In the last step the protecting group R^1 is removed by treatment of pyrrole **20** with a trace of hydrochloric acid in methanol [20]. A few 1-alkyl-3-hydroxypyrroles have been prepared by us in reasonable overall yields. The hydroxy-tautomer **26** predominates in chloroform or carbon tetrachloride solutions (only ~10% **26a**). In most known 3-hydroxypyrroles the keto-enol equilibrium lies strongly on the side of the keto-tautomer [41].

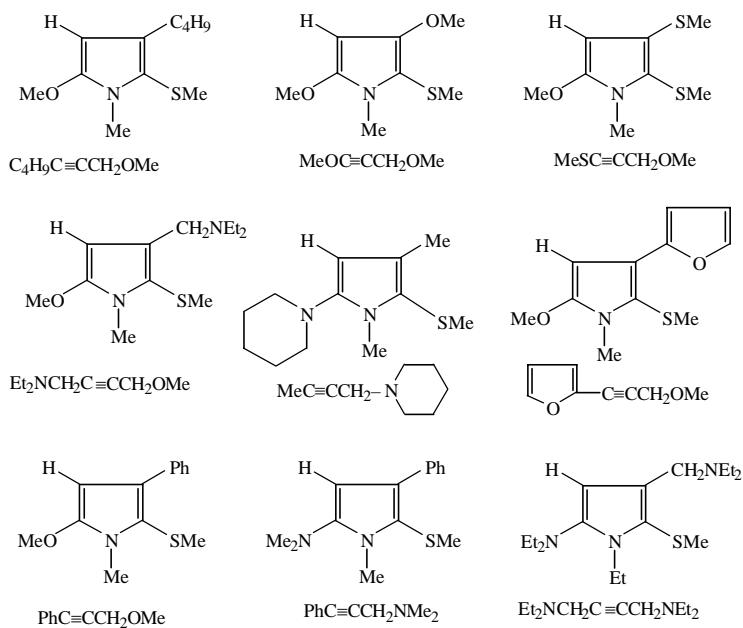
7. SYNTHESIS OF 1,2,3,5-TETRASUBSTITUTED PYRROLES

Our one-pot synthesis of 1,2,3,5-tetrasubstituted pyrroles [42] (Scheme 12) is based on the finding that, with a few exceptions only, lithiated 2-alkynyl amines and corresponding ethers give exclusively γ -adducts in their reaction with alkyl isothiocyanates [43-46]). In several cases the pyrroles were obtained in good overall yields.

Scheme 12



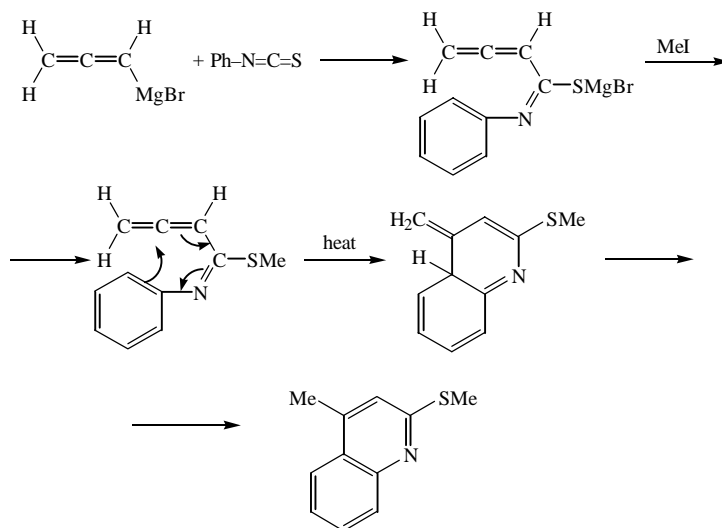
The final cyclization of the azatrienes **28** could be considerably facilitated by adding small amounts of copper halide. The scope of this method may be illustrated with the following structures of pyrrole derivatives **29** all prepared in good yields, the starting acetylenes being shown below each pyrrole.



8. SYNTHESIS OF QUINOLINE DERIVATIVES

The formation of quinoline derivatives by cyclization of the system $\text{H}_2\text{C}=\text{C}=\text{CHC}(\text{NR}_2)=\text{N}-\text{Ar}$ is described by Ried and Weidemann [46]. This cyclization seems to proceed under mild conditions. Thuiller et al. [10] more recently reported that heating of the product obtained from allenylmagnesium bromide and phenyl isothiocyanate and subsequent *S*-methylation gave an analogous quinoline derivative (Scheme 13). A synthesis starting with 1,1-dimethylallenylithium proceeded similarly.

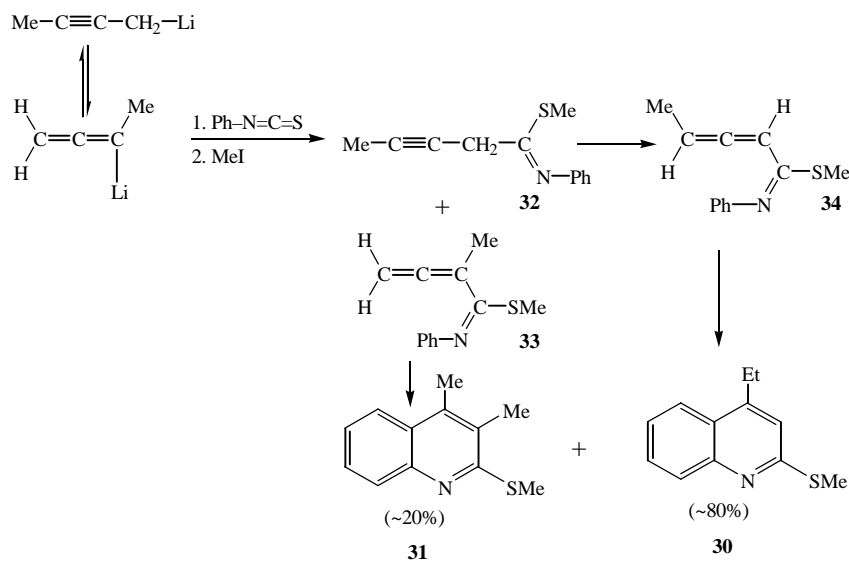
Scheme 13



We isolated a number of quinoline derivatives in high yields from reactions involving lithiated *t*-BuCH=C=CH₂, Me₂C=C=CH₂, vinylidenecyclohexane (CH₂)₅C=C=CH₂ or MeSCH=C=CH₂, and phenyl or other aryl isothiocyanates [47-50].

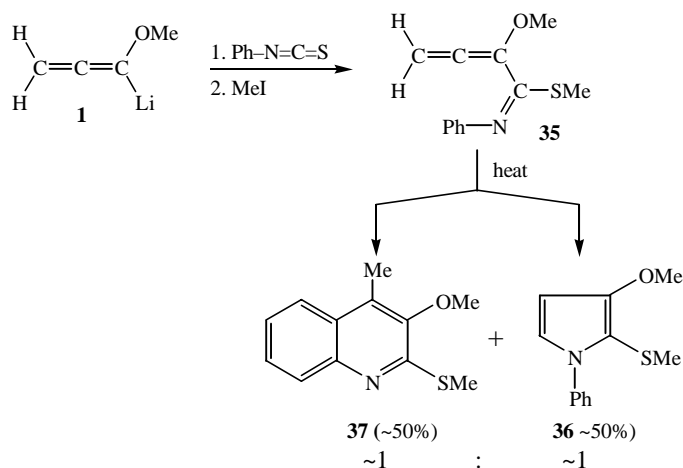
The procedure with lithiated 2-butyne and PhN=C=S led to a 4 : 1 mixture of quinolines **30** and **31** [51]. This result may be explained by assuming that lithiated 2-butyne reacts in both tautomeric forms giving rise, after methylation, to compounds **32** and **33**, the latter cyclizing to **31**. Intermediate **34**, which gives quinoline **30**, is assumed to be formed under the weakly basic conditions of the alkylation as well as during the very exothermic cyclization, possibly catalyzed by traces of the drying agent K₂CO₃ (Scheme 14).

Scheme 14



Reaction of methoxyallenylithium **1** with PhN=C=S and subsequent methylation gives exclusively the allenic derivative **35**. This can be converted into pyrrole **36** by treatment with copper halide (Section 6). Heating of **35** in the absence of this salt gives a ~1 : 1 mixture of **36** and the quinoline **37**, which can be separated in the components *via* extraction with dilute aqueous hydrochloric acid [50] (Scheme 15).

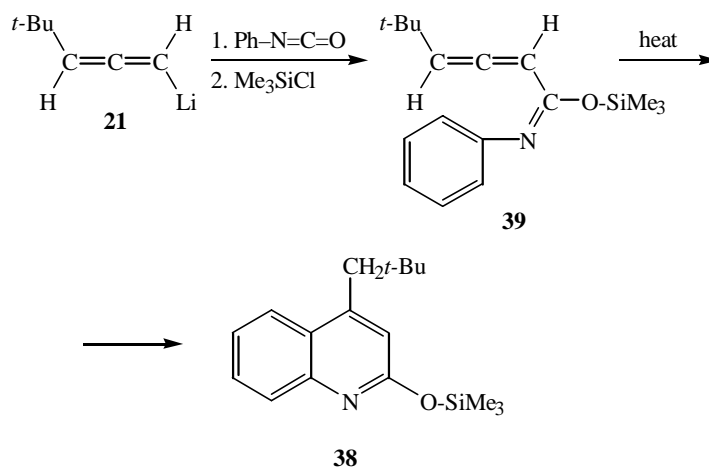
Scheme 15



The accompanying formation of pyrroles in the absence of copper halide has never been observed in the syntheses starting with other allenic derivatives and aryl isothiocyanates.

In a preliminary paper we reported the formation of a quinoline derivative **38** by strong heating of the O-silylated adduct **39** from phenyl isocyanate and *t*-butylallenylithium **21** [52] (Scheme 16).

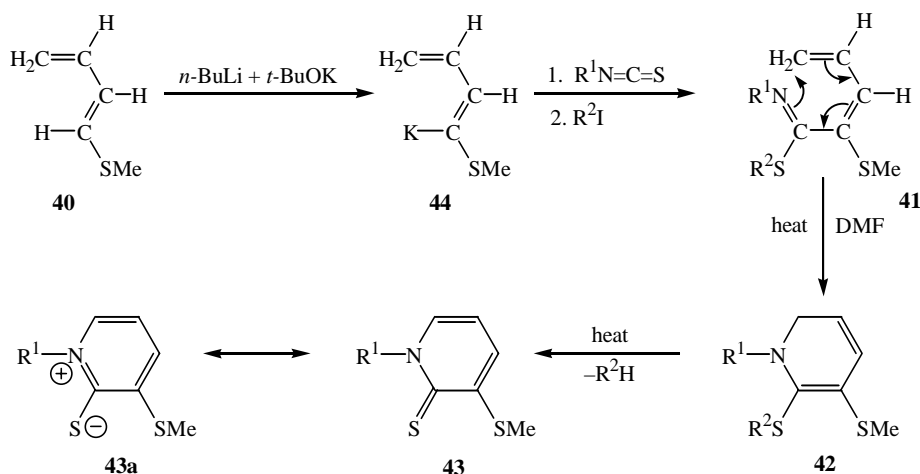
Scheme 16



9. SYNTHESIS OF DERIVATIVES OF 2H-THIOPYRAN AND 1,2-DIHYDROPYRIDINE

The regiospecific metallation [53] of the readily available [24] (*trans* : *cis* ~95 : 5) methylthiobutadiene **40** by treatment with a 1 : 1 molar mixture of *n*-BuLi and *t*-BuOK has enabled us to develop routes to some derivatives of 1,2-dihydropyridine and 2H-thiopyran. The S-alkylated adducts **41** obtained from *E*-**40** and isothiocyanates have a structure favorable for electrocyclization to 1,2-dihydropyridines **42** (Scheme 17).

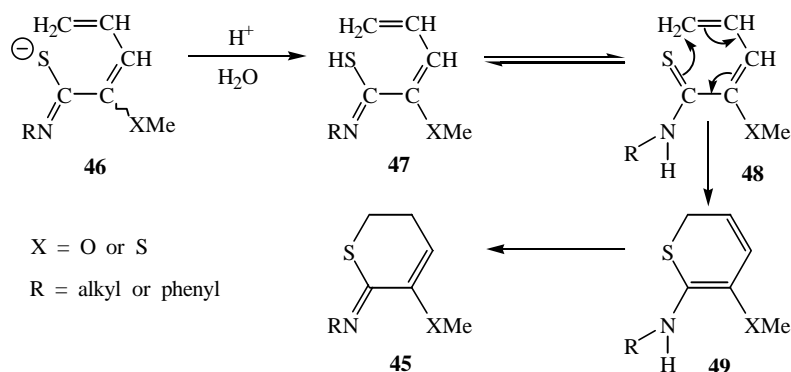
Scheme 17



The cyclization could be achieved in good yields by heating mixtures of **41** ($\text{R}^1 = \text{alkyl}$) and dimethylformamide for a few minutes under reflux [54]. If 1,2-dihydropyridines **42** are heated in the absence of a solvent, cyclic thioamides **43** are formed. Remarkably, the same compound is formed from the *S*-methyl and *S*-ethyl derivative, which means that methane and ethane, respectively, must have been eliminated. The driving force for this reaction may be the high resonance stabilization (high contribution of the aromatic structure **43a**) of the thioamide.

Iminothiopyrans **45** ($\text{X} = \text{S}$) are formed in good yields if the adducts **46** from the reaction between potassium derivative **44** and isothiocyanates are treated with the calculated amount of dilute acid [55] (Scheme 18). It is assumed that imidothiol **47** is in equilibrium with the thioamide **48**. The latter can undergo electrocyclic cyclization to 2H-thiopyran derivative **49**, which tautomerizes to iminothiopyran **45**. In some cases the thioamide **48** was present in the crude product. Iminothiopyran **45** ($\text{X} = \text{O}$, $\text{R} = \text{Ph}$) was obtained in a good yield from $\text{PhN}=\text{C}=\text{S}$ and a mixture of comparable amounts of *cis*- and *trans*- $\text{H}_2\text{C}=\text{CH}-\text{CH}=\text{CH}-\text{OMe}$ [55].

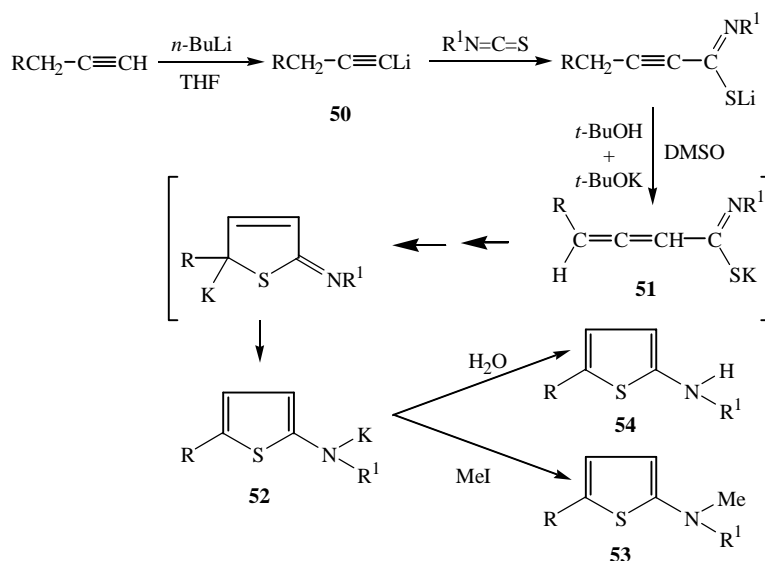
Scheme 18



10. SYNTHESIS OF 5-SUBSTITUTED 2-AMINOTHIOPHENES AND 2-IMINO-2,5-DIHYDROTHIOPHENES

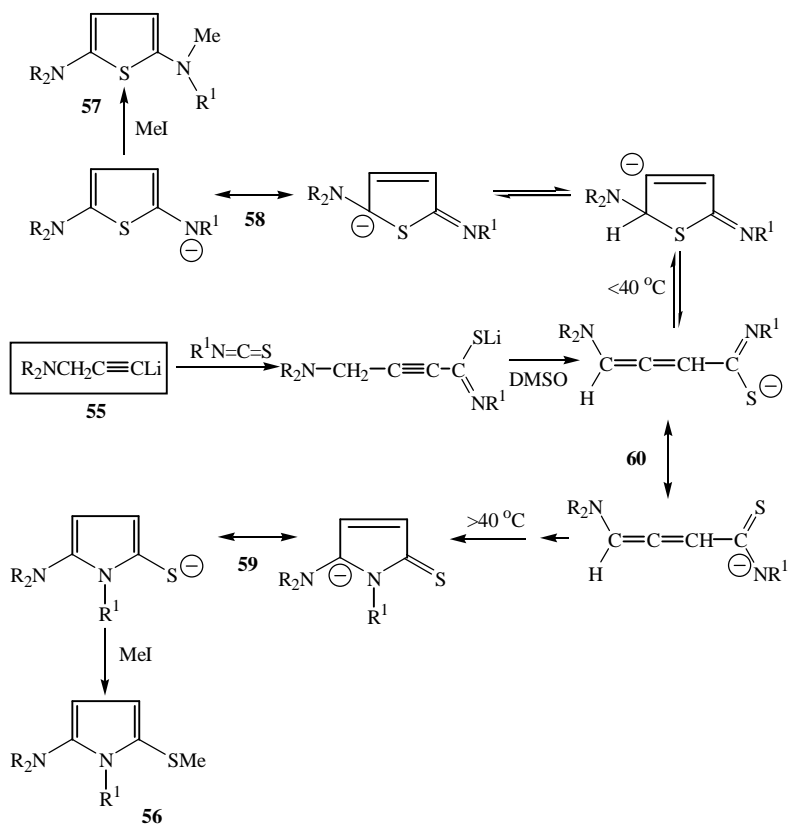
Terminally lithiated acetylenes **50** add to isothiocyanates at temperatures in the range 5 to 35°C. This addition is the first step in a novel one-pot synthesis of 5-substituted 2-aminothiophenes [56] (Scheme 19). In the second step the adduct is treated with the strongly basic combination of *t*-BuOK and DMSO. The allenic isomer **51**, which is assumed to be formed under these conditions, can undergo ring closure, ultimately leading to the amide **52**. The latter can be either methylated or hydrolyzed affording **53** and **54**, respectively, in fair to good yields. It should be mentioned that only a few satisfactory methods for the synthesis of 2-aminothiophenes have been published so far [57].

Scheme 19

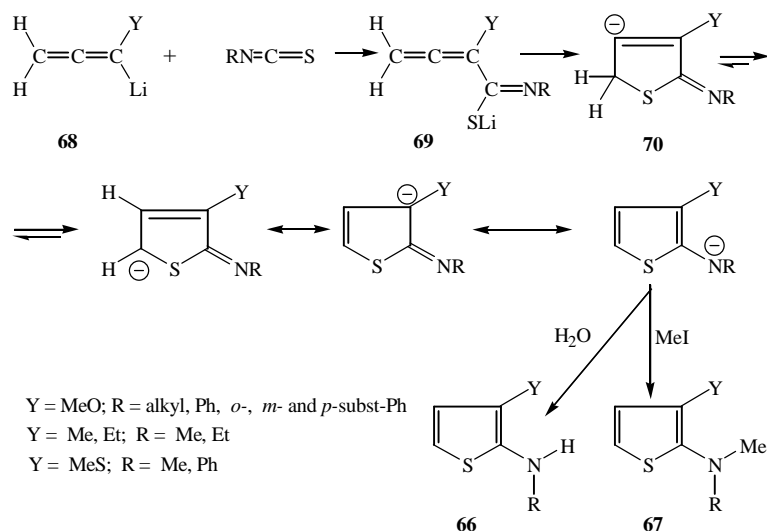


In reactions with some metallated propargylic amines **55** pyrrole derivatives **56** were isolated in fair to good yields instead of the expected thiophenes **57** when prior to carrying out the final methylation the temperature was increased to 40°C or higher [20, 58]. This surprising result may be explained by assuming an equilibrium between anions **58** and **59**: these intermediates may result from two modes of ring closure in resonance hybrid **60** (Scheme 20).

Scheme 20

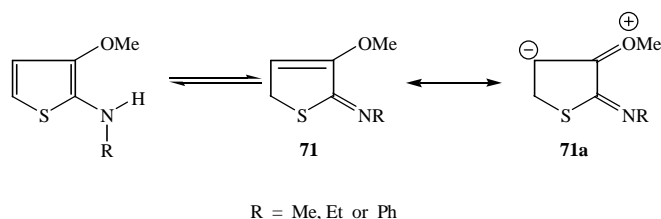


Scheme 23



N-Monosubstituted 2-aminothiophenes having a methoxy group at the 3-position show amino-imino tautomerism [59] (Scheme 24).

Scheme 24

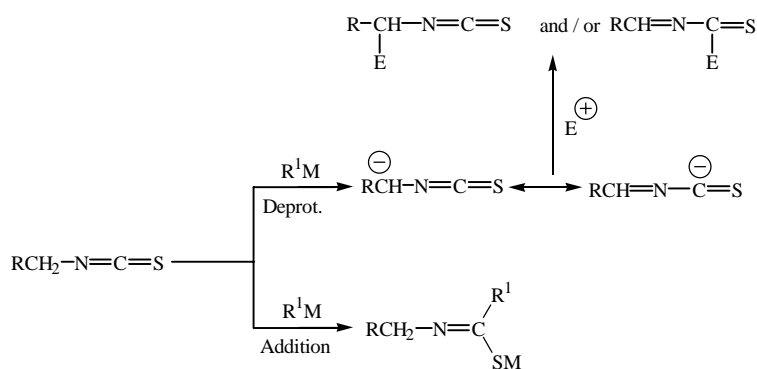


Compounds having an SMe group at this position exist only in the amino form. The stability of the imino tautomer may be explained by assuming a relatively high contribution of resonance structure **71a**.

12. METALLATION AND FUNCTIONALIZATION OF ISOTHIOCYANATES

The first step in the syntheses of the heterocyclic compounds described in the preceding sections is the *addition* of a metallated unsaturated compound to the heterocumulene system of an isothiocyanate. Using suitable conditions it should also be possible to *deprotonate* alkyl isothiocyanates and subsequently obtain derivatives by adding electrophiles (Scheme 25).

Scheme 25

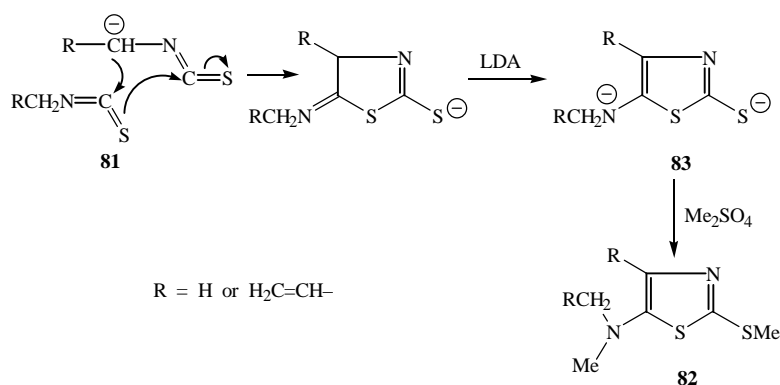


13. SYNTHESIS OF THIAZOLE AND IMIDAZOLE DERIVATIVES

Attempts to generate anions from alkyl isothiocyanates and functionalize them in a separate subsequent operation appear to be unsuccessful because the intermediates immediately add to a neutral molecule or (as in the case of allyl isothiocyanate) undergo electrocyclicization (see Section 12). This condensation reaction was applied to synthesize certain thiazole and imidazole derivatives [69-76].

Addition of methyl isothiocyanate **81** ($R = H$) to a strongly cooled solution of two molar equivalents of LDA in THF followed by treatment with dimethyl sulfate at somewhat higher temperatures gave the *N,N*-disubstituted aminothiazole **82** ($R = H$) in ~80% yield. Analogous products were obtained from allyl and benzyl isothiocyanate [20]. The formation of the thiazoles is visualized in Scheme 28.

Scheme 28

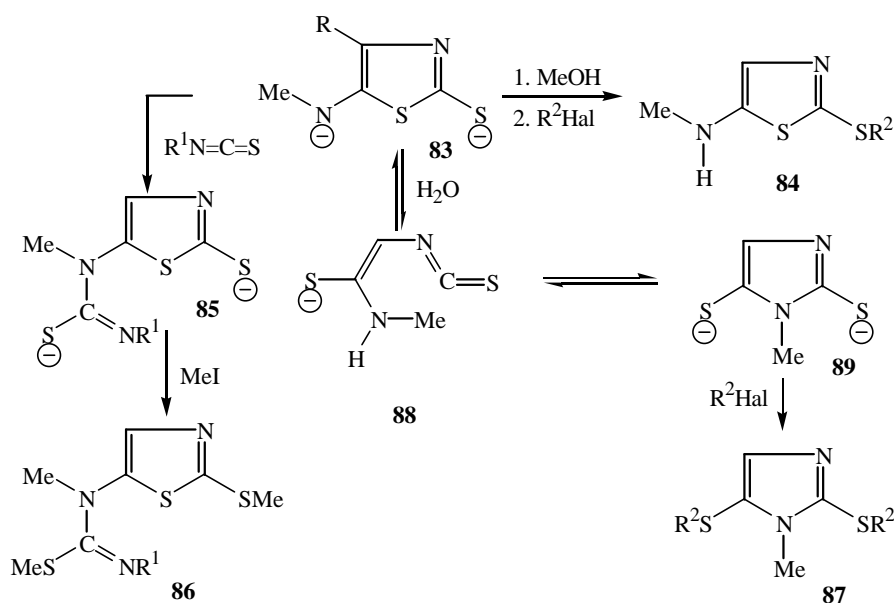


Starting from the condensation product **83** ($R = H$) other heterocyclic compounds could be synthesized (Scheme 29).

A. By addition at -20°C of a slight excess of methanol, the most strongly basic N^- center is protonated. Subsequent alkylation takes place exclusively on sulfur with formation of *N*-monosubstituted 2-aminothiazoles **84**.

B. Addition of a further amount of methyl isothiocyanate gave thiolate anion **85**, which by subsequent methylation afforded the “trimeric” condensation product **86** ($R^1 = \text{Me}$). A similar result was obtained with phenyl isothiocyanate. Apparently, also isothiocyanates prefer to react with the N^- center.

Scheme 29



C. Interaction between dianion **83** and (excess of) water at room temperature followed by alkylation surprisingly led to formation of the imidazole derivatives **87**. We assume that **83** equilibrates with the ring-opened intermediate **88**, which can undergo re-closure to **89**.

Condensation reactions with the less acidic *ethyl* isothiocyanate using LDA as a reagent were unsuccessful, the main product being the adduct EtN=C(SMe)N(*i*-Pr)₂ (after methylation). Preliminary experiments with the kinetically more efficient 1 : 1 molar combination of LDA and *t*-BuOK gave promising results [20].

REFERENCES

1. B. J. Wakefield, *Organolithium Methods*, Academic Press, London, 1988, 96, 102.
2. K. A. Petrov and L. N. Andreev, *Usp. Khim.*, **38**, 41 (1969).
3. M. S. Kharash and O. Reinmuth, Chapter 19 in: *Grignard Reactions of Nonmetallic Substances*, Prentice-Hall, New York, 1954, 1199.
4. N. A. LeBel, R. M. Cherluck, and E. A. Custin, *Synthesis*, 678 (1973).
5. D. A. Shirley and M. D. Cameron, *J. Am. Chem. Soc.*, **72**, 664 (1972).
6. J. J. Fitt and H. W. Gschwend, *J. Org. Chem.*, **44**, 303 (1979).
7. P. Gosselin, S. Masson, and A. Thuiller, *Tetrahedron Lett.*, 2715 (1978).
8. L. Brandsma and H. D. Verkrujisse, *Preparative Polar Organometallic Chemistry*, Springer-Verlag, Heidelberg, 1987, Vol. **1**; 1991, Vol. **2**.
9. L. Brandsma, *Preparative Acetylenic Chemistry*, 2nd ed., Elsevier, Amsterdam, 1988.
10. G. Darnault, M. Saquet, and A. Thuiller, *Chem. Ind. (London)*, N 10, 391 (1983).
11. R. L. P. de Jong, H. D. Verkrujisse, and L. Brandsma, in *Perspectives in the Organic Chemistry of Sulfur*, B. Zwanenburg and A. J. H. Klunder (eds.), Elsevier, Amsterdam, 1987, 105.
12. R. L. P. de Jong and L. Brandsma, *J. Organomet. Chem.*, **238**, C-17 (1982).
13. R. L. P. de Jong and L. Brandsma, *J. Chem. Soc., Chem. Commun.*, 1056 (1983).
14. R. L. P. de Jong and L. Brandsma, *J. Organomet. Chem.*, **316**, C-21 (1986).
15. R. L. P. de Jong and L. Brandsma, *Synth. Commun.*, **20**, 3427 (1990).
16. M. Bögemann, S. Petersen, O.-E. Schulz, and H. Söll, in: *Methoden der Organischen Chemie*, Houben-Weyl, 1955, **9**, 867.
17. Hartmann, in: *Methoden der Organischen Chemie*, Houben-Weyl, 1983, **E-4**, 834.
18. L. Drobnica, P. Kristian, and J. Augustin, in: *The Chemistry of the N=C=S Group*, S. Patai (ed.), John Wiley, Chichester, 1977, 1003.
19. N. A. Nedolya, B. A. Trofimov, A. Senning, *Sulfur Rep.*, **17**, 183 (1996).
20. N. A. Nedolya, Dissertation, Utrecht, May, 1999; N. A. Nedolya and L. Brandsma, unpublished observations.
21. B. A. Trofimov, N. A. Nedolya, V. V. Gerasimova, and M. G. Voronkov, *Sulfur Lett.*, **81**, 73 (1988).
22. G. Li, H. Tajima, and T. Ohtani, *J. Org. Chem.*, **62**, 4539 (1997).
23. L. Brandsma and H. D. Verkrujisse, *Synthesis of Acetylenes, Allenes, and Cumulenes*, Elsevier, Amsterdam, 1988.
24. R. H. Everhardus, A. Peterse, P. Vermeer, L. Brandsma, and J. F. Arens, *Recl. Trav. Chim., Pays-Bas*, **93**, 90 (1974).
25. R. Epsztein, in: *Comprehensive Carbanion Chemistry*, Part B, E. Buncl and T. Durst (eds.), Elsevier, Amsterdam, 1984, 107.
26. L. Brandsma, C. Jonker, and M. H. Berg, *Recl. Trav. Chim. Pays-Bas*, **84**, 560 (1965).
27. A. Schaap, L. Brandsma, and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **86**, 393 (1967).
28. H. Westmijze, K. Ruitenber, J. Meijer, and P. Vermeer, *Synthesis*, 551 (1981).
29. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 917 (1996); *Zh. Obshch. Khim.*, **66**, 2042 (1996).

30. N. A. Nedolya, R.-J. de Lang, L. Brandsma, and B. A. Trofimov, *Zh. Org. Khim.*, **33**, 87 (1997).
31. R. Fuks, R. Merenyi, and H. G. Viehe, *Bull. Soc. Chim. Belg.*, **83**, 147 (1976).
32. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Izv. Akad. Nauk, Ser. Khim.*, 2813 (1996); *Russ. Chem. Bull.*, **45**, 2670 (1996).
33. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Dokl. Akad. Nauk*, **350**, 68 (1996).
34. I. Meyers and J. J. Ritter, *J. Org. Chem.*, **23**, 1918 (1958).
35. I. Meyers, J. Schneller, and N. K. Ralhan, *J. Org. Chem.*, **28**, 2944 (1963).
36. I. Meyers, B. J. Betrus, N. K. Ralhan, and K. B. Rao, *J. Heterocycl. Chem.*, **1**, 13 (1964).
37. L. Brandsma, N. A. Nedolya, W. Heerma, A. C. T. H. M. van der Kerk, E. T. H. G. Lutz, R.-J. de Lang, A. V. Afonin, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 572 (1997); *Izv. Akad. Nauk, Ser. Khim.*, 865 (1997); *Zh. Org. Khim.*, **33**, 1435 (1997); L. Brandsma, N. A. Nedolya, H. D. Verkruisje, N. L. Owen, Du Li, and B. A. Trofimov, *Tetrahedron Lett.*, **38**, 6905 (1997).
38. B. A. Trofimov, N. A. Nedolya, L. Brandsma, Yu. L. Frolov, E. Yu. Larionova, D. S. D. Toryashinova, V. B. Kubyshev, and N. M. Vitskovskaya, *Sulfur Lett.*, **22**, 249 (1999).
39. N. A. Nedolya, L. Brandsma, O. A. Tarasova, H. D. Verkruisje, and B. A. Trofimov, *Tetrahedron Lett.*, **39**, 2409 (1998).
40. B. A. Trofimov, *J. Heterocycl. Chem.*, **36**, 1469 (1999).
41. H. McNab and L. C. Monahan, in: *The Synthesis, Reactivity and Physical Properties of Substituted Pyrroles*, Part 2, in the series *The Chemistry of Heterocyclic Compounds*. A Series of Monographs, E. C. Taylor (ed.), John Wiley, New York, 1992, 525.
42. L. Brandsma, N. A. Nedolya, and B. A. Trofimov, *Eur. J. Org. Chem.*, 2663 (1999).
43. E. J. Corey and S. Terashima, *Tetrahedron Lett.*, 690 (1972).
44. F. Mercier, R. Epsztein, and S. Holland, *Bull. Soc. Chim. France*, 690 (1972).
45. R. Epsztein and F. Mercier, *Synthesis*, 183 (1977).
46. W. Ried and P. Weidemann, *Chem. Ber.*, **104**, 3329 (1971).
47. L. Brandsma, N. A. Nedolya, R.-J. de Lang, and B. A. Trofimov, *Izv. Akad. Nauk, Ser. Khim.*, 3024 (1996); *Russ. Chem. Bull.*, **45**, 2873 (1996).
48. L. Brandsma, N. A. Nedolya, R.-J. de Lang, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 571 (1997).
49. N. A. Nedolya, L. Brandsma, R.-J. de Lang, and B. A. Trofimov, *Zh. Org. Khim.*, **33**, 1437 (1997).
50. L. Brandsma, N. A. Nedolya, O. A. Tarasova, L. V. Klyba, L. M. Sinegovskaya, and B. A. Trofimov, *Zh. Org. Khim.*, **35**, 953 (1999).
51. F. Taherirastgar, N. A. Nedolya, L. Brandsma, R.-J. de Lang, and B. A. Trofimov, *Dokl. Akad. Nauk*, **353**, 64 (1997).
52. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Mendeleev Commun.*, 92 (1997).
53. R. H. Everhardus, R. Gräfin, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, **97**, 69 (1978).
54. N. A. Nedolya, L. Brandsma, A. C. T. H. M. van der Kerk, V. Yu Vvedensky, and B. A. Trofimov, *Tetrahedron Lett.*, **39**, 1995 (1998); N. A. Nedolya, L. Brandsma, H. D. Verkruisje, A. C. T. H. M. van der Kerk, and B. A. Trofimov, *Dokl. Akad. Nauk*, **360**, 356 (1998).
55. N. A. Nedolya, L. Brandsma, H. D. Verkruisje, A. C. T. H. M. van der Kerk, and B. A. Trofimov, *Tetrahedron Lett.*, **39**, 2631 (1998); N. A. Nedolya, L. Brandsma, H. D. Verkruisje, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 626 (1998).
56. O. A. Tarasova, L. V. Klyba, V. Yu Vvedensky, N. A. Nedolya, B. A. Trofimov, H. D. Verkruisje, and L. Brandsma, *Eur. J. Org. Chem.*, 253 (1998).
57. H. Hartmann and S. Scheithauer, *J. Prakt. Chem.*, **311**, 827 (1969); D. Priem and G. Kirsch, *Tetrahedron*, **55**, 6511 (1999) and Refs. cited therein.
58. O. A. Tarasova, N. A. Nedolya, V. Yu Vvedensky, L. Brandsma, and B. A. Trofimov, *Tetrahedron Lett.*, **38**, 7241 (1997).
59. L. Brandsma, N. A. Nedolya, O. A. Tarasova, L. V. Klyba, L. M. Sinegovskaya, and B. A. Trofimov, *Dokl. Akad. Nauk*, **357**, 350 (1997); L. Brandsma, V. Yu Vvedensky, N. A. Nedolya, O. A. Tarasova, and B. A. Trofimov, *Tetrahedron Lett.*, **39**, 2433 (1998).

60. L. Brandsma, O. A. Tarasova, V. Yu. Vedensky, R. L. P. de Jong, H. D. Verkruisje, L. V. Klyba, N. A. Nedolya, and B. A. Trofimov, *Zh. Org. Khim.*, **35**, 1255 (1999).
61. D. Hoppe and R. Follmann, *Chem. Ber.*, **109**, 3047 (1976).
62. I. Hoppe, D. Hoppe, and U. Schöllkopf, *Tetrahedron Lett.*, 609 (1976).
63. D. Hoppe and M. Kloft, *Lieb. Ann. Chem.*, 1850 (1976).
64. L. Brandsma, N. A. Nedolya, H. D. Verkruisje and B. A. Trofimov, *Synthesis*, 423 (1997).
65. T. Hirao, A. Yamada, Y. Oshiro and T. Agawa, *Angew. Chem.*, **93**, 95 (1981); *Angew. Chem., Int. Ed. (Engl.)*, **20**, 126 (1981).
66. L. Brandsma, N. A. Nedolya and B. A. Trofimov, *Mendeleev Commun.*, 232 (1997).
67. N. A. Nedolya, L. Brandsma and B. A. Trofimov, *Zh. Org. Khim.*, **34**, 950 (1998); L. Brandsma, N. A. Nedolya and B. A. Trofimov, *Dokl. Akad. Nauk*, **358**, 196 (1998).
68. N. A. Nedolya, L. Brandsma, H. D. Verkruisje, and B. A. Trofimov, *Tetrah Lett.*, **38**, 7247 (1997).
69. N. A. Nedolya, L. Brandsma, A.C.T.H.M. van der Kerk, A. V. Afonin, R.-J. de Lang, and B. A. Trofimov, *Zh. Obshch. Khim.*, **67**, 701 (1997).
70. L. Brandsma, N. A. Nedolya, H. D. Verkruisje, and B. Trofimov, *Khim. Geterotsikl. Soedin.*, 1275 (1997).
71. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Tetrahedron Lett.*, **38**, 6279 (1997).
72. L. Brandsma, N. A. Nedolya, and B. A. Trofimov, *Izv. Akad. Nauk, Ser. Khim.*, 186 (1998); *Russ. Chem. Bull.*, 187 (1998).
73. N. A. Nedolya, L. Brandsma, and B. A. Trofimov, *Dokl. Akad. Nauk*, **358**, 72 (1998).
74. L. Brandsma, N. A. Nedolya, and B. A. Trofimov, *Izv. Akad. Nauk, Ser. Khim.*, 541 (1998); *Russ. Chem. Bull.*, 523 (1998).
75. N. A. Nedolya, L. Brandsma, A. C. T. H. M. van der Kerk, A. V. Afonin, R.-J. de Lang, and B. A. Trofimov, *Zh. Org. Khim.*, **34**, 722 (1998).
76. N. A. Nedolya, L. Brandsma, A. C. H. T. M. van der Kerk, H. D. Verkruisje, G. I. Sarapulova, A. V. Afonin, and B. A. Trofimov, *Zh. Org. Khim.*, **35**, 946 (1999).