# Structural Reorganization of Allyl Isothiocyanate into Pyrrole Ring under Superbase: A Straightforward Access to NH-2-(Alkylsulfanyl)-1*H*-pyrroles and *N*-Alkyl-2-(alkylsulfanyl)-1*H*-pyrroles

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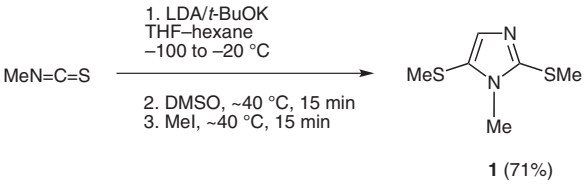
**Abstract:** A novel and facile synthetic route to NH-2-(alkylsulfanyl)-1*H*-pyrroles and *N*-alkyl-2-(alkylsulfanyl)-1*H*-pyrroles is reported. This was achieved by deprotonation of allyl isothiocyanate with the superbasic pair lithium diisopropylamide and potassium *tert*-butoxide (1:1 molar mixture), followed by intramolecular ring closure, deprotonation of cyclic anion with a second equivalent of the superbase, and final sequential N-protolysis/S-alkylation or N,S-dialkylation of the formed N,S-centered pyrrol-2-ylsulfide dianion.

**Key words:** 2-(alkylsulfanyl)-substituted pyrroles, allyl isothiocyanate, superbases, deprotonation, cyclization, alkylation

Pyrroles, in general,[1] and those with an organosulfur group, in particular,[2–8] represent a very important and practically useful class of N-heterocycles. The introduction of sulfur-containing substituents into aromatics, including pyrroles and their derivatives, is of current interest[3] because their reactivity, bioactivity, physical, material, and other properties, as well as synthetic and therapeutic potential can be profoundly altered.[2,4] It was also shown that electron-rich alkylsulfanyl substituents or their oxidized derivatives (alkyl sulfoxides and sulfones) can serve as effective and perspective protecting groups for the 2-position of the pyrrole ring.[2h,5] Therefore, a novel practical method for the synthesis of such compounds is of great interest in synthetic organic chemistry. Among the known methods for the synthesis of multisubstituted 2-(alkylsulfanyl)pyrroles from acyclic precursors,[6,7] the methodology using isothiocyanates both as a structural fragment of pyrrole core and supplier of sulfur atom for sulfa-substituents seems to be the most powerful, simple, and perspective. Thus, the combination of different isothiocyanates (alkyl, cycloalkyl, alkoxyalkyl, aryl) with allenic or acetylenic carbanions, generated in situ from the corresponding allenes or alkynes, affords 1,3-di-, 1,5-di-, or 1,3,5-trisubstituted 2-(alkylsulfanyl)pyrroles in good to excellent yields in one preparative step.[7] However, these approaches[6,7] are unsuitable for the synthesis of 1,3,4,5-unsubstituted 2-(alkylsulfanyl)pyrroles that are applied in the synthesis of porphyrinic macrocycles and related compounds as well as important synthetic intermediates and versatile building blocks.[2d,h,4e,5a,b] Most of the traditional methods for the preparation of these pyrroles are based on utilization of preexisting pyrrole rings. To the 2-position of the latter, alkylsulfanyl groups have been introduced by different but usually multistep ways.[4f,5c,8] Moreover, the yields of the pyrroles are often rather low even at the final step of the synthesis. Recalculation of the yields taking into account those on all stages of the process makes the known methods synthetically even less attractive because of moderate or low overall yields. Also, to the best of our knowledge no publication is known in the literature describing the synthesis of representative numbers of N-substituted and N-unsubstituted 2-(alkylsulfanyl)-1*H*-pyrroles by some general method from a common raw material.

Following our strategy based on the use of isothiocyanate/organometallics systems for the construction of the most of fundamental heterocycles carrying sulfa-substituents,[9] including 2-(alkylsulfanyl)pyrroles,[7] we now report the very simple synthesis of 1,3,4,5- and 3,4,5-unsubstituted 2-(alkylsulfanyl)pyrroles through the superbase-induced structural reorganization of commercially available allyl isothiocyanate into pyrrole ring.

Earlier we have shown that treatment of methyl isothiocyanate with the system LDA/*t*-BuOK (potassium diisopropylamide) leads to 1-methyl-2,5-bis(methylsulfanyl)-1*H*-imidazole (**1**) in good yield (Scheme 1).[10]




**1** (71%)

**Scheme 1** Synthesis of imidazole **1** via deprotonation and dimerization of methyl isothiocyanate

In an attempt to prepare the imidazole derivative **2** from allyl isothiocyanate under conditions similar to those leading to the formation of imidazole **1** from methyl isothiocyanate, the former was reacted with the system LDA/*t*-BuOK in the presence of DMSO (as a co-solvent). However, we were surprised to find that instead of the ex-

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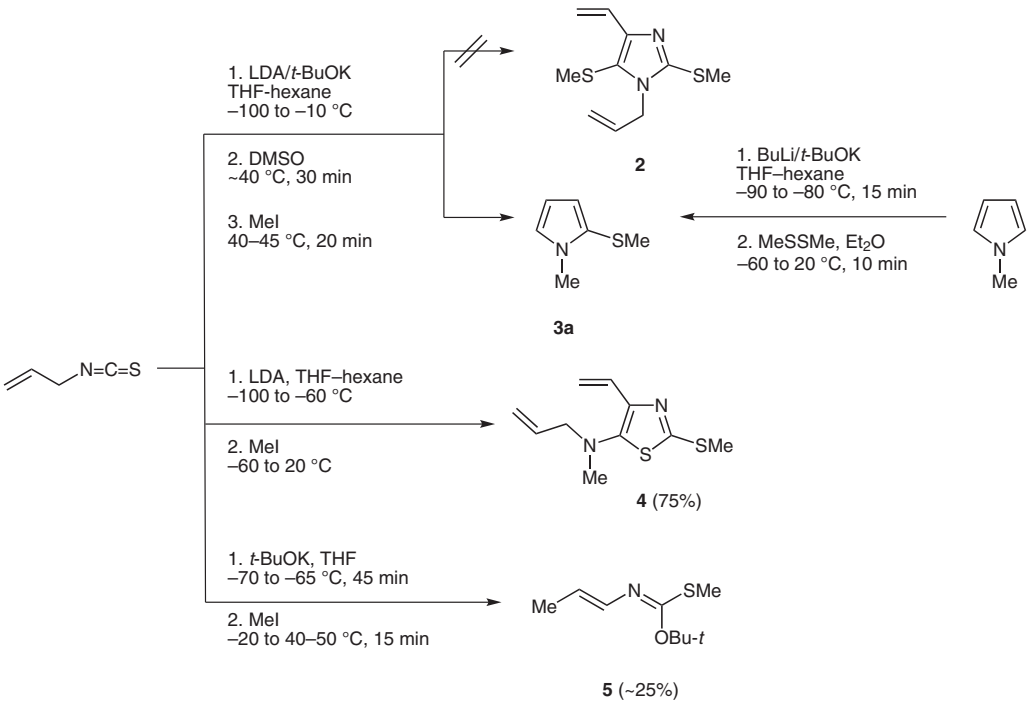
pected imidazole **2**, *N*-methyl-2-(methylsulfanyl)-1*H*-pyrrole (**3a**) was formed in ~30% yield, along with a number of volatile and nonvolatile products (Scheme 2).[11] The product **3a** was identical with the sample, prepared by the known reaction of α-metalated *N*-methyl-1*H*-pyrrole with dimethyl disulfide[12] (Scheme 2).

Further investigation of the reaction of allyl isothiocyanate with superbases have shown that treatment of allyl isothiocyanate with LDA (without *t*-BuOK) led to thiazole **4** in 75% yield (via deprotonation, addition of formed carbanion to a second molecule of isothiocyanate, cyclization, deprotonation of thiazolyl anion by a second molecule of superbase, and final N,S-dialkylation) (Scheme 2).[13] In attempts to deprotonate allyl isothiocyanate with potassium *tert*-butoxide (without LDA) the azadienic compound **5** was obtained in moderate yield (Scheme 2). The main reaction in this case was the addition of *t*-BuOK to N=C=S function, followed by S-methylation of the initial adduct and base-catalyzed migration of the double bond in allylimine fragment. When *t*-BuOK was added after the interaction between allyl isothiocyanate and LDA, only nonvolatile products were found. Hence the combination of two superbases – lithium organylamide and alkali metal alkoxide (for instance, LDA and *t*-BuOK, as was found originally) – is strongly required to direct the reaction in the direction of pyrrole ring formation. We have also shown that the use of DMSO in the pyrrole synthesis does not give significant advantages over reactions, carried out in its absence.

These studies have resulted in the development of a novel synthetically valuable method of the one-pot synthesis of *N*-alkyl-2-(alkylsulfanyl)-1*H*-pyrroles **3a**–**d** and NH-2-(alkylsulfanyl)-1*H*-pyrroles **6a**–**f**, including earlier unknown representatives, through transformations of allyl isothiocyanate under action of two equivalents of LDA/*t*-BuOK system (1:1 molar mixture) in THF–hexane followed by N,S- or S-alkylation with alkyl halides or dialkyl sulfates (Table 1).

Based on the experimental facts mentioned, the formation of the pyrrole core can be explained by assuming an electrocyclization of the primarily generated anion **7**, followed by a fast deprotonation of cyclic anion **8** with a second equivalent of basic reagent resulting in the N,S-centered pyrrolyl dianion **9**. Final alkylation of dianionic species **9** with excess or, at least, with two equivalents of alkyl iodide or dialkyl sulfate leads to *N*-alkyl-2-(alkylsulfanyl)-1*H*-pyrroles **3** (Scheme in Table 1).

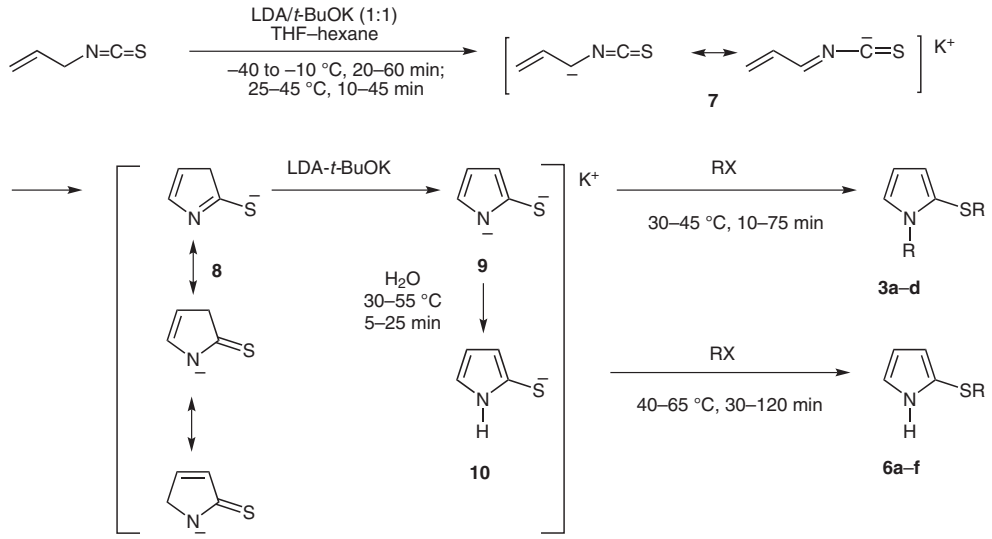
Several experiments on the effect of varying the temperature as well as the nature and amount of superbase were carried out. Reasonable isolated yields (between 54 and 71%) of pyrroles **3** (R = alkyl) were obtained when a solution of allyl isothiocyanate in THF was added dropwise (over 30–60 min) to a solution of two equivalents of the 1:1 molar mixture of LDA and *t*-BuOK in THF–hexane at temperatures in the range of –40 to –20 °C. When allyl isothiocyanate was added to the base at ca. –70 °C or lower temperatures, mainly the thiazole **4** was detected in the crude product. Similar results were also obtained, when the reaction was carried out at ca. –70 °C in the presence of HMPT. In all the cases, the content of pyrrole **3a** in the crude product was ~15–20% (GC).



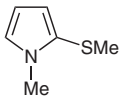
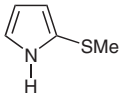
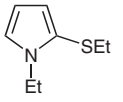
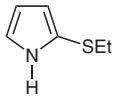
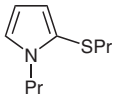
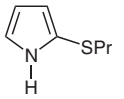
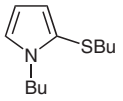
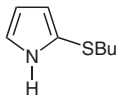
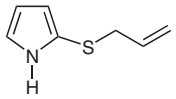
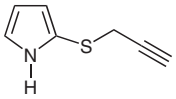

**Scheme 2** Synthesis of compounds **3a**, **4**, and **5** via reactions of allyl isothiocyanate with superbases

**Table 1** Synthesis of *N*-Alkyl-2-(alkylsulfanyl)-1*H*-pyrroles **3a–d** and NH-2-(alkylsulfanyl)-1*H*-pyrroles **6a–f** via Structural Reorganization of Allyl Isothiocyanate under Superbase




R = Me (**a**), Et (**b**), *n*-Pr (**c**), *n*-Bu (**d**), $CH_2$=$CHCH_2$ (**e**), HC≡$CCH_2$ (**f**); X = Br, I, $RSO_4$

| Pyrroles **3** | | Yield (%)[a] | Pyrroles **6** | | Yield (%)[a,b] |
|---|---|---|---|---|---|
| **3a** |  | 61 | **6a** |  | 66 |
| **3b** |  | 54 | **6b** |  | 58 |
| **3c** |  | 58 | **6c** |  | 54<br>68[c] |
| **3d** |  | 71 | **6d** |  | 68<br>46[c] |
| | | | **6e** |  | 60 |
| | | | **6f** |  | 47 |

[a] After distillation.
[b] Intermediate **9** was at first quenched with water and then with an alkylating agent (method A).
[c] Water was not used; alkyl iodide (1 equiv) was added dropwise (method B) (Scheme 3).

Use of three equivalents of LDA/*t*-BuOK did not demonstrate any notable influence on the reaction course or the pyrrole yields. Under similar conditions (with 2 equiv of the base) the yields of pyrrole **3a** were comparable. Realization of the reaction with one equivalent of the same base also gave pyrrole **3a** but the yield was in the range of 30–40%. This result is consistent with the mechanism (scheme in Table 1) requiring two equivalents of the superbase for the formation of pyrrole ring from allyl isothiocyanate.

Experiments carried out with LDA/*t*-BuONa gave a somewhat lower yield than with LDA/*t*-BuOK, but nevertheless with significantly high yield (~52%) of pyrrole **3a**. The reaction of allyl isothiocyanate with 1:1 molar combination of LDA/*t*-AmOCs followed by alkylation furnished 2-(alkylsulfanyl)-1*H*-pyrroles in yields that were a

little (by 5 to 10%) higher than those obtained with LDA/*t*-BuOK. But *t*-AmOCs is not a cheap and easily accessible base and for this reason could not be more preferable than the commercial *t*-BuOK as a component of superbasic system for the reaction.

The more interesting and important pyrrole derivatives **6** could be obtained in yields varying from ~47 (R = $CH_2C{\equiv}CH$) to ~58–68% (R = alkyl, allyl) by adding a certain amount of water prior to performing the alkylation of intermediate **9** (method A, Table 1). The yields of the pyrrole derivatives **6** are not very high, but it should be pointed out that our direct method is preferred over the multistep route for NH-2-substituted pyrroles, which involves N-protection of the pyrrole, treatment of the N-protected compound with two equivalents of *n*-BuLi, reaction with an electrophilic reagent at the 2-position, and deprotection.[14]

At least pyrroles **6c** and **6d** can also be obtained in moderate to good yields without the use of water before alkylation. For this, one equivalent of the corresponding alkyl iodide was added dropwise to the reaction mixture (method B) (Scheme 3).

Comparison of these procedures for the synthesis of above mentioned pyrroles **6** did not reveal the advantages of one technique over another. For instance, in the case of pyrrole **6c** (R = *n*-Pr) its yield was higher, 68% against 54%, when alkylating agent (propyl iodide) was added dropwise to the reaction mixture (without preliminary quenching with water). But in the case of pyrrole **6d** (R = *n*-Bu), on the contrary, the yield was higher, 68% against 46%, when the reaction mixture was treated with some amount of water before alkylation with butyl iodide. Similar to alkyl iodides, alkyl bromides can be used as alkylating agents.

The structures of the products have been assigned using IR, $^1$H, $^{13}$C, and heteronuclear 2D ($^1$H-$^{13}$C HMBC) NMR spectroscopy, and mass spectrometry.

The synthetic usefulness of the present approach to NH-2-(alkylsulfanyl)-1*H*-pyrroles received recently experimental confirmation. Namely, our procedure for 2-(methylsulfanyl)-1*H*-pyrrole synthesis, described earlier in a short communication,[11a] was used in a multistep synthesis of regiospecifically α-$^{13}$C-labeled porphyrins for studies of ground-state hole transfer in multiporphyrin arrays.[5a]

In conclusion, a new efficient strategy of the pyrrole ring construction via an unprecedented reorganization of commercially available allyl isothiocyanate under the action of LDA/potassium *tert*-butoxide system in THF–hexane opens a novel and very simple approach to synthetically and pharmacologically promising N-substituted and N-unsubstituted 2-(alkylsulfanyl)-1*H*-pyrroles. Advantages of this methodology providing a new short one-pot synthesis of 2-(alkylsulfanyl)-substituted pyrroles compared with those described in the literature (mostly via multistep sulfanylation of preexisting pyrrole core)[8] are evident.

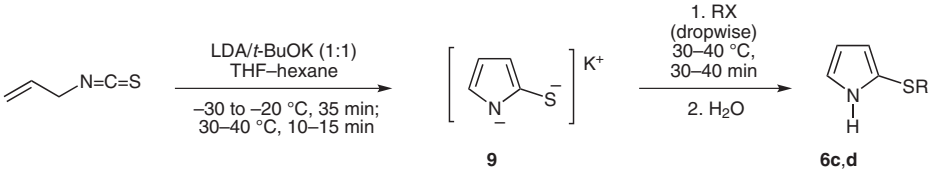
Synthetic potential of this approach for the construction of pyrrole ring bearing alkylsulfanyl substituent at 2-position from easily accessible allyl isothiocyanate is not certainly limited to the described examples. Successful introduction of other electrophiles in this reaction also seems possible and will be reported elsewhere.

Allyl isothiocyanate, *n*-BuLi (1.6 M solution in hexane), *t*-BuOK, *i*-$Pr_2NH$, alkylating agents, and solvents are commercially available. All solvents were purified and dried according to standard procedures. All reactions were performed under anhydrous conditions and in a $N_2$ atmosphere. For all reactions at low temperatures a cooling bath with liquid $N_2$ was used. All reactions were monitored by GC and $^1$H NMR analyses.

IR spectra were measured neat on a Specord IR-75 spectrophotometer. The NMR spectra were recorded on Bruker DPX-400, Bruker AV-400 [400.13 ($^1$H), 100.62 MHz ($^{13}$C)], and Varian EM-390 [90 MHz ($^1$H)] spectrometers in $CDCl_3$ and $CCl_4$ solutions, respectively, at r.t., referenced to HMDS and TMS as internal standards. Assignments of spectra were carried out using 2D experiments. The mass spectra (EI, 60 eV) were recorded on a LKB-2091 instrument. GC analyses were carried out on a Varian 3400 gas chromatograph (15 m capillary column coated with a 1.5 μ DB-5, internal diameter 0.53 mm). The microanalyses were performed on a Flash EA 1112 Series elemental analyzer.

### *N*-Methyl-2-(methylsulfanyl)-1*H*-pyrrole (3a); Typical Procedure

To a stirred solution of *i*-$Pr_2NH$ (13 g, 0.13 mol) and *t*-BuOK (22 g, 0.20 mol) in THF (60 mL) under $N_2$, at ca. –50 °C was added a solution of *n*-BuLi (0.12 mol) in hexane (72 mL). A solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (55 mL) was added dropwise over 30 min while keeping the temperature of the solution between –40 and –20 °C. After the addition, the reaction mixture was stirred for 15 min at 25 °C and then cooled to –40 °C. Then, dimethyl sulfate (25 g, 0.20 mol) was added in one portion, and the reaction mixture was heated for 10 min at 30–35 °C. Ice-water (80 mL) was then added and the product was extracted with pentane (2 × 30 mL) and $Et_2O$ (2 × 30 mL). The combined organic extracts were washed with $H_2O$ (3 × 40 mL), dried ($K_2CO_3$), and concentrated under re-




**6c**: R = *n*-Pr, 68%; **6d**: R = *n*-Bu, 46%

**Scheme 3** Synthesis of NH-pyrroles **6c**,**d** via dropwise addition of one equivalent of alkylating agent to intermediate **9**

duced pressure. Distillation of the remaining liquid through a 20 cm Vigreux column gave the pyrrole **3a** as a light-yellow liquid; yield: 3.9 g (61%); bp 111–115 °C/3 Torr; $n_D^{20}$ 1.5480 (Lit.[12] bp 70 °C/15 mmHg, $n_D^{21}$ 1.5496).

IR (neat): 3100, 2960, 2910, 2850, 1510, 1460, 1430, 1410, 1310, 1300, 1200, 1090, 1050, 1000, 970, 790, 720, 680, 600 $cm^{-1}$.

$^1H$ NMR (90 MHz, $CCl_4$): δ = 2.18 (s, 3 H, $SCH_3$), 3.64 (s, 3 H, $NCH_3$), 5.95 (m, 1 H, H-4), 6.18 (m, 1 H, H-3), 6.58 (m, 1 H, H-5).

MS (EI, 60 eV): *m*/*z* (%) = 127 (100, $[M]^+$) (Lit.[15]).

Anal. Calcd for $C_6H_9NS$: C, 56.65; H, 7.13; N, 11.01; S, 25.20. Found: C, 56.71; H, 7.08; N, 11.15; S, 25.10.

### *N*-Ethyl-2-(ethylsulfanyl)-1*H*-pyrrole (3b)

To a solution of *i*-$Pr_2NH$ (16.1 g, 0.16 mol), *t*-BuOK (16.2 g, 0.14 mol), and *n*-BuLi (0.15 mol) in THF (60 mL) and hexane (92 mL) was added dropwise a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (70 mL) during 60 min at –40 to –30 °C. After stirring for 10 min at 35 °C, EtI (26.2 g, 0.17 mol) was added in one portion at –10 °C, and the reaction mixture was stirred for 30 min at ~45 °C. Workup as described above afforded **3b** as a light-yellow liquid; yield: 4.2 g (54%); bp ~40 °C/0.7 Torr; $n_D^{20}$ 1.5148.

IR (neat): 3100, 2965, 2920, 2860, 1510, 1450, 1435, 1370, 1350, 1280, 1260, 1200, 1120, 1100, 1080, 1060, 1040, 1030, 1000, 965, 950, 880, 790, 760, 720, 660, 610 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 1.15 (t, *J* = 7.4 Hz, 3 H, $CH_3$), 1.32 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 2.54 (q, *J* = 7.4 Hz, 2 H, $SCH_2$), 4.02 (q, *J* = 7.2 Hz, 2 H, $NCH_2$), 6.10 (m, 1 H, H-4), 6.31 (m, 1 H, H-3), 6.76 (m, 1 H, H-5).

$^{13}C$ NMR ($CDCl_3$): δ = 14.73 ($CH_3$), 17.02 ($CH_3$), 31.66 ($SCH_2$), 41.41 ($NCH_2$), 108.14 (C-4), 117.58 (C-3), 120.21 (C-2), 122.66 (C-5).

The $^1H$-$^{13}C$ HMBC 2D experiment provided additional support for the proposed structure.

MS (EI, 60 eV): *m*/*z* (%) = 155 (67, $[M]^+$) (Lit.[15]).

Anal. Calcd for $C_8H_{13}NS$: C, 61.89; H, 8.44; N, 9.02; S, 20.65. Found: C, 61.73; H, 8.55; N, 8.92; S, 20.87.

### *N*-Propyl-2-(propylsulfanyl)-1*H*-pyrrole (3c)

To a solution of *i*-$Pr_2NH$ (13.9 g, 0.14 mol), *t*-BuOK (13.3 g, 0.12 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (72 mL) was added dropwise a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (35 mL) during 30 min at –30 to –25 °C. After stirring for 10 min at 35–38 °C, *n*-PrI (25.9 g, 0.15 mol) was added in one portion at 8 °C, and the reaction mixture was stirred for 75 min at ~40 °C. Workup as described above afforded **3c** as a light-yellow liquid; yield: 5.3 g (58%); bp ~70 °C/0.5 Torr; $n_D^{20}$ 1.5208.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.3 Hz, 3 H, $CH_3$), 0.95 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 1.52 (m, 2 H, $CH_2$), 1.74 (m, 2 H, $CH_2$), 2.51 (t, *J* = 7.3 Hz, 2 H, $SCH_2$), 3.94 (t, *J* = 7.2 Hz, 2 H, $NCH_2$), 6.09 (m, 1 H, H-4), 6.30 (m, 1 H, H-3), 6.74 (m, 1 H, H-5).

$^{13}C$ NMR ($CDCl_3$): δ = 11.04 ($CH_3$), 12.96 ($CH_3$), 22.54 ($CH_2$), 24.81 ($CH_2$), 39.65 ($SCH_2$), 48.16 ($NCH_2$), 107.70 (C-4), 116.95 (C-3), 119.95 (C-2), 122.99 (C-5).

MS (EI, 60 eV): *m*/*z* (%) = 183 (59, $[M]^+$) (Lit.[15]).

Anal. Calcd for $C_{10}H_{17}NS$: C, 65.52; H, 9.35; N, 7.64; S, 17.49. Found: C, 65.67; H, 9.29; N, 7.57; S, 17.52.

### *N*-Butyl-2-(butylsulfanyl)-1*H*-pyrrole (3d)

To a solution of *i*-$Pr_2NH$ (15.3 g, 0.15 mol), *t*-BuOK (15.6 g, 0.14 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (75 mL) was added dropwise a solution of allyl isothiocyanate (6.3 g, 0.06 mol) in THF (40 mL) during 35 min at –30 to –20 °C. After stirring for 15 min at 42–45 °C, *n*-BuI (33.2 g, 0.18 mol) was added in one portion at 30 °C, and the reaction mixture was stirred for 40 min at 35–45 °C. Then, DMSO (50 mL) was added at 25 °C, and stirring was continued for an additional 15 min. After carrying out the typical workup as described above, the combined organic extracts were washed with $H_2O$ (5 × 30 mL) (to free from DMSO), dried ($K_2CO_3$), and concentrated under reduced pressure; light-yellow liquid; yield: 9 g (71%); bp 145–155 °C/0.5 Torr; $n_D^{20}$ 1.5074.

IR (neat): 3100, 2950, 2920, 2860, 1500, 1450, 1420, 1370, 1360, 1280, 1210, 1200, 1180, 1100, 1065, 1000, 900, 860, 780, 745, 700, 600 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.3 Hz, 3 H, $CH_3$), 0.91 (t, *J* = 7.2 Hz, 3 H, $CH_3$), 1.30 (m, 2 H, $CH_2$), 1.36 (m, 2 H, $CH_2$), 1.49 (m, 2 H, $CH_2$), 1.69 (m, 2 H, $CH_2$), 2.54 (t, *J* = 7.3 Hz, 2 H, $SCH_2$), 3.98 (t, *J* = 7.2 Hz, 2 H, $NCH_2$), 6.08 (m, 1 H, H-4), 6.29 (m, 1 H, H-3), 6.73 (m, 1 H, H-5).

$^{13}C$ NMR ($CDCl_3$): δ = 13.46 ($CH_3$), 13.55 ($CH_3$), 19.77 ($CH_2$), 21.50 ($CH_2$), 31.36 ($CH_2$), 33.70 ($CH_2$), 37.39 ($SCH_2$), 40.25 ($NCH_2$), 107.73 (C-4), 116.89 (C-3), 120.82 (C-2), 122.86 (C-5).

MS (EI, 60 eV): *m*/*z* (%) = 211 (90, $[M]^+$) (Lit.[15]).

Anal. Calcd for $C_{12}H_{21}NS$: C, 68.19; H, 10.01; N, 6.63; S, 15.17. Found: C, 68.23; H, 10.15; N, 6.55; S, 15.14.

### 2-(Methylsulfanyl)-1*H*-pyrrole (6a); Typical Procedure

*Method A*: A solution of *n*-BuLi (0.10 mol) in hexane (65 mL) was added to a stirred solution of *i*-$Pr_2NH$ (13.5 g, 0.13 mol) and *t*-BuOK (15.3 g, 0.14 mol) in THF (60 mL) under $N_2$ at ca. –50 °C, which was followed by dropwise addition of a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (40 mL) over 30 min at –20 to –15 °C. The resulting mixture was stirred at 45 °C for 30 min, after which $H_2O$ (8 g, 0.44 mol) was added with intensive stirring. After stirring for 20 min at ~30 °C, MeI (14 g, 0.10 mol) was added in one portion and stirring was continued for 40 min at 50 °C. The reaction mixture was quenched with ice-water (100 mL) and the aqueous layer was extracted with pentane (2 × 30 mL) and $Et_2O$ (2 × 30 mL). The combined organic extracts were washed with $H_2O$ (3 × 40 mL), dried ($K_2CO_3$), concentrated under reduced pressure, and the residue distilled through a short Vigreux column; light liquid; yield: 3.7 g (66%); bp 30–40 °C/0.5 Torr; $n_D^{20}$ 1.5445 (Lit. bp 87–90 °C/15 mmHg;[8a] bp 60–65 °C/3 mmHg[8g]).

IR (neat): 3370, 3100, 3050, 2960, 2900, 2860, 1520, 1420, 1410, 1400, 1375, 1300, 1100, 1070, 1020, 960, 920, 870, 800, 720, 640, 550 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, $SCH_3$), 6.16 (m, 1 H, H-4), 6.32 (m, 1 H, H-3), 6.72 (m, 1 H, H-5), 8.30 (br s, 1 H, NH).

$^{13}C$ NMR ($CDCl_3$): δ = 20.94 ($SCH_3$), 109.62 (C-4), 114.61 (C-3), 119.94 (C-5), 121.03 (C-2).

MS (EI, 60 eV): *m*/*z* (%) = 113 (100, $[M]^+$) (Lit.[15]).

Anal. Calcd for $C_5H_7NS$: C, 53.06; H, 6.23; N, 12.38; S, 28.33. Found: C, 53.23; H, 6.46; N, 12.45; S, 27.94.

### 2-(Ethylsulfanyl)-1*H*-pyrrole (6b)

*Method A*: To a solution of *i*-$Pr_2NH$ (14.2 g, 0.14 mol), *t*-BuOK (14.9 g, 0.13 mol), and *n*-BuLi (0.12 mol) in THF (50 mL) and hexane (75 mL) was added dropwise a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (40 mL) during 35 min at –18 to –15 °C. After stirring for 30 min at 35–40 °C, $H_2O$ (8.7 g, 0.48 mol) was added at 35 °C, and the mixture stirred for 25 min at 40–50 °C. Then, EtI (11.8 g, 0.08 mol) was added in one portion, and stirring was continued for 2 h at 40–45 °C. Workup as described above afforded **6b** as a light liquid; yield: 3.7 g (58%); bp 50–60 °C/0.5 Torr; $n_D^{20}$ 1.5348.

IR (neat): 3370, 3100, 3050, 2950, 2910, 2860, 1520, 1440, 1420, 1400, 1370, 1360, 1250, 1100, 1070, 1040, 1020, 960, 920, 870, 800, 750, 720, 640, 550 $cm^{-1}$.

$^1$H NMR (90 MHz, $CCl_4$): δ = 1.18 (t, *J* = 7.4 Hz, 3 H, $CH_3$), 2.54 (q, *J* = 7.4 Hz, 2 H, $SCH_2$), 6.10 (m, 1 H, H-4), 6.28 (m, 1 H, H-3), 6.68 (m, 1 H, H-5), 8.40 (br s, 1 H, NH).

MS (EI, 60 eV): *m*/*z* (%) = 127 (88, $[M]^+$) (Lit.[16]).

Anal. Calcd for $C_6H_9NS$: C, 56.65; H, 7.13; N, 11.01; S, 25.20. Found: C, 56.77; H, 7.21; N, 10.90; S, 25.18.

**2-(Propylsulfanyl)-1*H*-pyrrole (6c)**

*Method A*: To a solution of *i*-$Pr_2NH$ (10.2 g, 0.10 mol), *t*-BuOK (11.5 g, 0.10 mol), and *n*-BuLi (0.10 mol) in THF (60 mL) and hexane (65 mL) was added dropwise a solution of allyl isothiocyanate (5.3 g, 0.05 mol) in THF (40 mL) during 40 min at –28 to –25 °C. After stirring for 20 min at 40–43 °C, $H_2O$ (6 g, 0.33 mol) was added at 40 °C and the mixture stirred for 15 min at ~30 °C. Then, *n*-PrI (14.6 g, 0.08 mol) was added in one portion, and stirring was continued for 30 min at 45–55 °C. Workup as described above afforded **6c** as a light liquid; yield: 3.8 g (54%); bp ~70 °C/0.8 Torr; $n_D^{20}$ 1.5338.

*Method B*: To a solution of *i*-$Pr_2NH$ (13.4 g, 0.13 mol), *t*-BuOK (15.6 g, 0.14 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (72 mL) was added dropwise a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (35 mL) for 35 min at –30 to –20 °C. After stirring for 10 min at ~40 °C, *n*-PrI (11 g, 0.06 mol) was added dropwise during 15 min at ~30 °C and stirred for an additional 10 min. Then the reaction mixture was heated to 45 °C and stirred for 30 min. The workup was carried out as described in method A; yield: 4.8 g (68%).

IR (neat): 3370, 3100, 2950, 2930, 2860, 2810, 1530, 1450, 1435, 1410, 1400, 1380, 1370, 1335, 1290, 1240, 1170, 1110, 1065, 1035, 930, 900, 870, 830, 800, 775, 720, 650, 550 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.3 Hz, 3 H, $CH_3$), 1.53 (m, 2 H, $CH_2$), 2.56 (t, *J* = 7.3 Hz, 2 H, $SCH_2$), 6.16 (m, 1 H, H-4), 6.32 (m, 1 H, H-3), 6.74 (m, 1 H, H-5), 8.40 (br s, 1 H, NH).

$^{13}$C NMR ($CDCl_3$): δ = 12.91 ($CH_3$), 23.01 ($CH_2$), 39.69 ($SCH_2$), 109.62 (C-4), 116.13 (C-3), 119.24 (C-2), 120.13 (C-5).

MS (EI, 60 eV): *m*/*z* (%) = 141 (50, $[M]^+$) (Lit.[16]).

Anal. Calcd for $C_7H_{11}NS$: C, 59.53; H, 7.85; N, 9.92; S, 22.70. Found: C, 59.66; H, 7.79; N, 9.83; S, 22.78.

**2-(Butylsulfanyl)-1*H*-pyrrole (6d)**

*Method A*: To a solution of *i*-$Pr_2NH$ (15.9 g, 0.16 mol), *t*-BuOK (15.0 g, 0.13 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (75 mL) was added dropwise a solution of allyl isothiocyanate (5.3 g, 0.05 mol) in THF (40 mL) for 25 min at –18 to –15 °C. After stirring for 35 min at 40–43 °C, $H_2O$ (5.3 g, 0.29 mol) was added at 30 °C (the temperature rose to 50 °C). In 5 min, *n*-BuI (16.2 g, 0.09 mol) was added in one portion, and stirring was continued for 30 min at 50–65 °C. Workup as described above afforded **6d** as a light liquid; yield: 5.3 g (68%); bp 70–80 °C/0.8 Torr; $n_D^{20}$ 1.5235.

*Method B*: To a solution of *i*-$Pr_2NH$ (17.9 g, 0.18 mol), *t*-BuOK (16.3 g, 0.14 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (75 mL) was added dropwise a solution of allyl isothiocyanate (5.4 g, 0.05 mol) in THF (35 mL) during 35 min at ca. –20 °C. After stirring for 10 min at –20 to 0 °C, then for an additional 15 min at 30–38 °C, *n*-BuI (11.2 g, 0.06 mol) was added dropwise for 20 min at 35–42 °C, and stirred for an additional 40 min. Workup was carried out as described in method A; yield: 3.6 g (46%).

IR (neat): 3380, 3100, 2950, 2920, 2860, 2850, 1530, 1460, 1430, 1400, 1370, 1270, 1210, 1110, 1070, 1035, 930, 910, 880, 800, 720, 650, 550 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 0.86 (t, *J* = 7.3 Hz, 3 H, $CH_3$), 1.35 (m, 2 H, $CH_2$), 1.49 (m, 2 H, $CH_2$), 2.60 (t, *J* = 7.3 Hz, 2 H, $SCH_2$), 6.17 (m, 1 H, H-4), 6.33 (m, 1 H, H-3), 6.75 (m, 1 H, H-5), 8.30 (br s, 1 H, NH).

$^{13}$C NMR ($CDCl_3$): δ = 13.70 ($CH_3$), 21.65 ($CH_2$), 32.07 ($CH_2$), 37.65 ($SCH_2$), 109.91 (C-4), 116.36 (C-3), 119.58 (C-2), 120.26 (C-5).

MS (EI, 60 eV): *m*/*z* (%) = 155 (33, $[M]^+$) (Lit.[16]).

Anal. Calcd for $C_8H_{13}NS$: C, 61.89; H, 8.44; N, 9.02; S, 20.65. Found: C, 61.95; H, 8.32; N, 9.11; S, 20.58.

**2-(Allylsulfanyl)-1*H*-pyrrole (6e)**

*Method A*: To a solution of *i*-$Pr_2NH$ (13.7 g, 0.14 mol), *t*-BuOK (14.3 g, 0.13 mol), and *n*-BuLi (0.12 mol) in THF (60 mL) and hexane (75 mL) was added dropwise a solution of allyl isothiocyanate (5.3 g, 0.05 mol) in THF (40 mL) for 22 min at –20 to –18 °C. After stirring for 45 min at 40–45 °C, $H_2O$ (7.4 g, 0.41 mol) was added at 30 °C, and the mixture stirred for 20 min at 35–45 °C. Then, allyl bromide (15.2 g, 0.12 mol) was added in one portion at 30 °C, and stirring was continued for 30 min at ~45 °C. Workup as described above afforded **6e** as a light liquid; yield: 4.15 g (60%); bp 50–60 °C/0.5 Torr; $n_D^{20}$ 1.5607 (Lit.[8e] bp 60 °C/0.3 Torr).

IR (neat): 3380, 3100, 3070, 2970, 2950, 2910, 1630, 1525, 1425, 1400, 1220, 1110, 1080, 1020, 990, 925, 915, 880, 870, 800, 720, 650, 575, 550 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 3.22 (d, *J* = 7.3 Hz, 2 H, $SCH_2$), 4.92 (dd, $J_{cis}$ = 9.9 Hz, $J_{gem}$ = 1.1 Hz, 1 H, $CH_2$=), 4.98 (dd, $J_{trans}$ = 17.1 Hz, 1 H, $CH_2$=), 5.84 (m, 1 H, CH=), 6.16 (m, 1 H, H-4), 6.34 (m, 1 H, H-3), 6.76 (m, 1 H, H-5), 8.30 (br s, 1 H, NH).

$^{13}$C NMR ($CDCl_3$): δ = 41.20 ($SCH_2$), 109.84 (C-4), 116.71 (C-3), 117.37 ($CH_2$=), 118.77 (C-2), 120.63 (C-5), 134.66 (CH=).

MS (EI, 60 eV): *m*/*z* (%) = 139 (77, $[M]^+$) (Lit.[16]).

Anal. Calcd for $C_7H_9NS$: C, 60.39; H, 6.52; N, 10.06; S, 23.03. Found: C, 60.17; H, 6.70; N, 10.29; S, 22.94.

**2-(2-Propynylsulfanyl)-1*H*-pyrrole (6f)**

*Method A*: To a solution of *i*-$Pr_2NH$ (13.5 g, 0.13 mol), *t*-BuOK (14.3 g, 0.13 mol), and *n*-BuLi (0.11 mol) in THF (50 mL) and hexane (70 mL) was added dropwise a solution of allyl isothiocyanate (5.3 g, 0.05 mol) in THF (35 mL) for 20 min at –15 to –10 °C. After stirring for 25 min at 40–45 °C, $H_2O$ (8.3 g, 0.46 mol) was added at 40 °C, and the mixture stirred for 10 min at 45–53 °C. Then, propargyl iodide (12.5 g, 0.08 mol) was added in one portion at 35 °C, and stirring was continued for 30 min at ~45 °C. Workup as described above afforded **6f** as a light liquid; yield: 3.2 g (47%); bp ~60 °C/0.5 Torr; $n_D^{20}$ 1.5847.

IR (neat): 3400, 3280, 3100, 2950, 2910, 1525, 1425, 1400, 1220, 1110, 1070, 1020, 925, 880, 870, 800, 720, 680, 635, 540 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 2.24 (t, *J* = 2.4 Hz, 1 H, ≡CH), 3.27 (d, *J* = 2.4 Hz, 2 H, $SCH_2$), 6.18 (m, 1 H, H-4), 6.44 (m, 1 H, H-3), 6.79 (m, 1 H, H-5), 8.48 (br s, 1 H, NH).

$^{13}$C NMR ($CDCl_3$): δ = 26.24 ($SCH_2$), 72.36 (≡CH), 80.98 (C≡), 110.01 (C-4), 117.24 (C-3), 117.85 (C-2), 121.48 (C-5).

MS (EI, 60 eV): *m*/*z* (%) = 137 (66, $[M]^+$) (Lit.[16]).

Anal. Calcd for $C_7H_7NS$: C, 61.28; H, 5.14; N, 10.21; S, 23.37. Found: C, 61.24; H, 5.09; N, 10.08; S, 23.63.

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